Nanobiotechnology for Plant Protection

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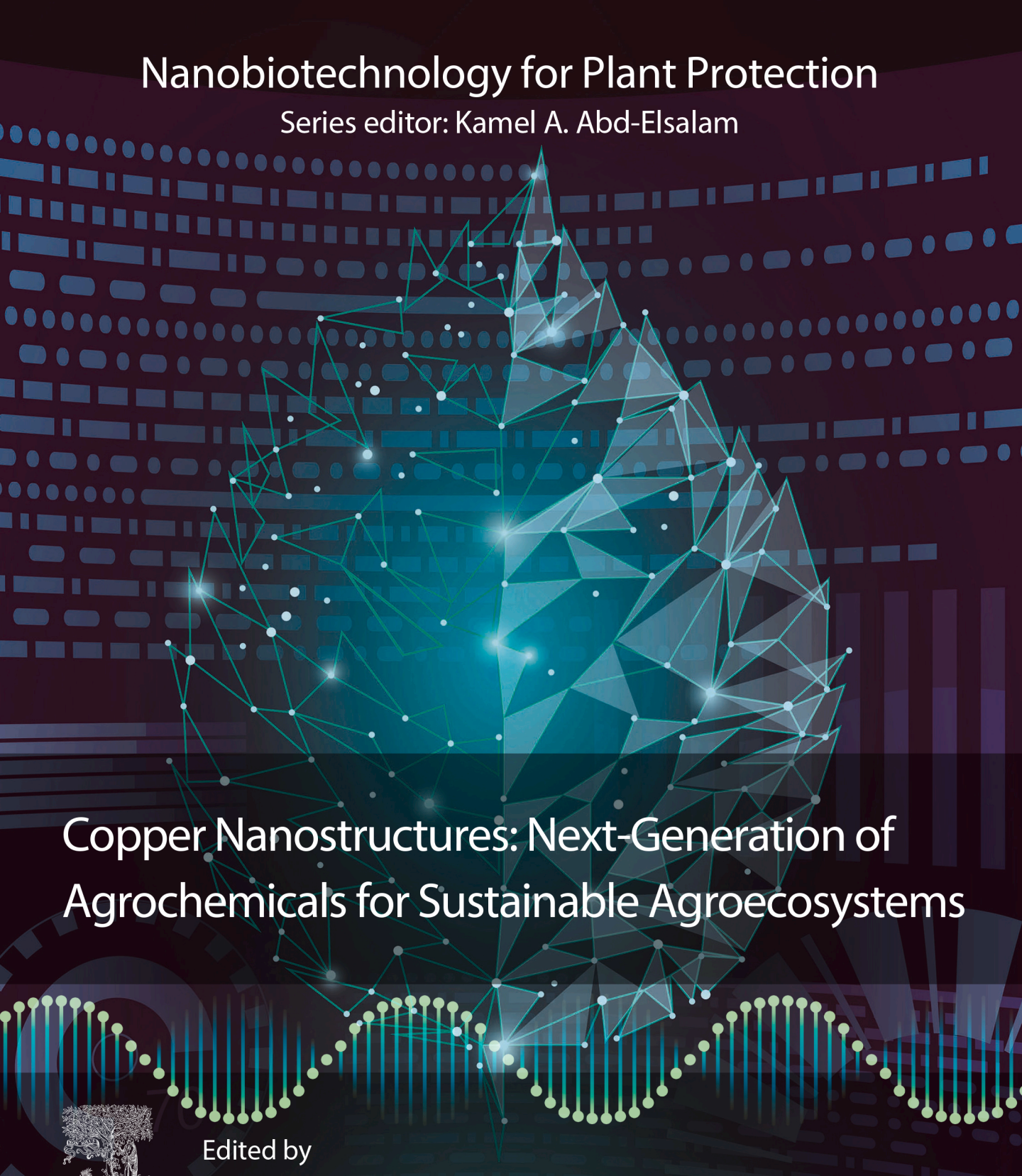

Copper Nanostructures: Next-Generation of Agrochemicals for Sustainable Agroecosystems

Edited by

Kamel A. Abd-Elsalam

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Series Editor

Kamel A. Abd-Elsalam

Edited by

Kamel A. Abd-Elsalam
Research Professor, Plant Pathology Research Institute, Giza,
Agricultural Research Center, Giza, Egypt

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Contributors

Kamel A. Abd-Elsalam
Plant Pathology Research Institute, Agricultural Research Center (ARC), Giza, Egypt

Shagufta Afreen
CAS Key Laboratory of Bio-Based Materials, Qingdao Institute of Bioenergy and Bioprocess Technology, Chinese Academy of Sciences, Qingdao, PR China

Iffat Zareen Ahmad
Department of Bioengineering, Integral University, Lucknow, Uttar Pradesh, India

Mariam A. Akanbi-Gada
Environmental Biology unit, Department of Plant Biology, Faculty of Life Sciences, University of Ilorin, Ilorin; Department of Biological Sciences, Kwara State University, Malete, Nigeria

Cristiano José de Andrade
Department of Chemical Engineering and Food Engineering (EQA), Federal University of Santa Catarina (UFSC), Florianópolis, Brazil

Lidiane Maria de Andrade
Department of Chemical Engineering. University of São Paulo (USP), São Paulo, Brazil

Mohammad Ashfaq
Advanced Ceramics and Nanotechnology Laboratory, Department of Materials Engineering, Faculty of Engineering, University of Concepción, Concepción, Chile; School of Life Science, BS Abdur Rahman Institute of Science and Technology, Chennai, India

P.K. Bajpai
Advanced Material Research Laboratory, Department of Pure and Applied Physics, Guru Ghasidas Vishwavidyalaya, Bilaspur, India

Mansi Bakshi
Department of Civil Engineering, Indian Institute of Technology Delhi, New Delhi, India

Vo-Van Quoc Bao
College of Agriculture and Forestry, Hue University, Hue City, Vietnam

Jorge G.S. Batista
Institute for Energy and Nuclear Research, National Nuclear Energy Commission-IPEN/CNEN-SP, São Paulo, Brazil

V. Bhuvaneshwari
Department of Biotechnology, Sri Shakthi Institute of Engineering and Technology, Coimbatore, Tamil Nadu, India

R. Britto Hurtado
Department of Physics Research, University of Sonora; State University of Sonora, Hermosillo, Sonora, Mexico

Drexel H. Camacho
Chemistry Department, De La Salle University, Manila, Philippines

Rafael G. Campos-Montiel
ICAP—Instituto de Ciencias Agropecuarias, Universidad Autónoma del Estado de Hidalgo, Tulancingo, Hidalgo, México

Rachid Chaibi
Department of Biology; Laboratory of Biological and Agronomic Sciences, Faculty of Science, University of Amar Tlidji, Laghouat, Algeria

Divya Chauhan
Department of Chemical and Biomedical Engineering, University of South Florida, Tampa, FL, United States

R.C. Chikte
Nanobioscience Group, Agharkar Research Institute, Pune, India

Nguyen Huu Chuc
Hue Industrial College, Hue City, Vietnam,

M. Cortez-Valadez
CONACYT—Department of Physics Research, University of Sonora, Hermosillo, Sonora, Mexico

Y. Delgado-Beleño
Department of Physics Research, University of Sonora, Hermosillo, Sonora, Mexico; Optical and Laser Spectroscopy Group, Popular University of Cesar, Valledupar, Colombia

Khemchand Dewangan
Department of Chemistry, Indira Gandhi National Tribal University, Amarkantak, Madhya Pradesh, India

Ahmed M.A. El-Hamaky
Animal Health Research Institute (AHRI), Agriculture Research Center (ARC), Giza, Egypt

Fabián Fernández-Luqueño
Sustainability of Natural Resources and Energy Programs, Cinvestav-Saltillo, Ramos Arizpe, Coahuila, Mexico

Aryel H. Ferreira
Institute for Energy and Nuclear Research, National Nuclear Energy Commission-IPEN/CNEN-SP, São Paulo, Brazil

M. Flores-Acosta
Department of Physics Research, University of Sonora, Hermosillo, Sonora, Mexico

Lucas F. Freitas
Institute for Energy and Nuclear Research, National Nuclear Energy Commission-IPEN/CNEN-SP, São Paulo, Brazil

Mohamed Amine Gacem
Department of Biology, Faculty of Science, University of Amar Tlidji, Laghouat, Algeria

Selvia García-Mayagoitia
Sustainability of Natural Resources and Energy Programs, Cinvestav-Saltillo, Ramos Arizpe, Coahuila, Mexico

Narasimha Golla
Department of Virology, Sri Venkateswara University, Tirupati, Andhra Pradesh, India

Atef A. Hassan
Animal Health Research Institute (AHRI), Agriculture Research Center (ARC), Giza, Egypt

Dachamir Hotza
Department of Chemical Engineering and Food Engineering (EQA), Federal University of Santa Catarina (UFSC), Florianópolis, Brazil

Josef Jampílek
Department of Analytical Chemistry, Faculty of Natural Sciences, Comenius University, Bratislava, Slovakia; Department of Chemical Biology, Faculty of Science, Palacký University, Olomouc, Czech Republic

S. Kalaivani
Department of Biotechnology, Kongunadu Arts and Science College, Coimbatore, Tamil Nadu, India

Tushar Kant
School of Studies in Chemistry, Pt. Ravishankar Shukla University, Raipur, Chhattisgarh, India

Sharba Kausar
Department of Microbiology, Jawaharlal Nehru Medical College, Aligarh Muslim University, Aligarh, Uttar Pradesh, India

Keshu
Dr B R Ambedkar National Institute of Technology, Jalandhar, Punjab, India

Aruna Jyothi Kora
National Centre for Compositional Characterisation of Materials (NCCCM), Bhabha Atomic Research Centre (BARC), ECIL PO, Hyderabad; Homi Bhabha National Institute (HBNI), Mumbai, India

Katarína Král'ová
Institute of Chemistry, Faculty of Natural Sciences, Comenius University, Bratislava, Slovakia

Suresh Babu Naidu Krishna
Research Post Graduate Support, Durban University of Technology, Durban, South Africa,

Arun Kumar
Department of Civil Engineering, Indian Institute of Technology Delhi, New Delhi, India

D. Karthik Kumar
Viyen Biotech LLP, Coimbatore, Tamil Nadu, India

S. Idhaya Kumar
Department of Biotechnology, Kongunadu Arts and Science College, Coimbatore, Tamil Nadu, India

Le Van Luan
Hue Industrial College, Hue City, Vietnam,

Caroline S.A. de Lima
Institute for Energy and Nuclear Research, National Nuclear Energy Commission-IPEN/CNEN-SP, São Paulo, Brazil

Michaela Olisha S. Lobregas
Chemistry Department, De La Salle University, Manila, Philippines

Ademar B. Lugão
Institute for Energy and Nuclear Research, National Nuclear Energy Commission-IPEN/CNEN-SP, São Paulo, Brazil

Danielle Maass
Institute of Science and Technology (ICT), Federal University of São Paulo (UNIFESP), São José dos Campos, Brazil

R.V. Mangalaraja
Advanced Ceramics and Nanotechnology Laboratory, Department of Materials Engineering, Faculty of Engineering, University of Concepción, Concepción, Chile

K. Girija Mangatayaru
Department of Chemistry, Palamuru University, Mahabub Nagar, Telangana, India,

Mogda K. Mansour
Animal Health Research Institute (AHRI), Agriculture Research Center (ARC), Giza, Egypt

C.E. Martinez-Nuñez
Department of Physics Research, University of Sonora, Hermosillo, Sonora, Mexico; Optical and Laser Spectroscopy Group, Popular University of Cesar, Valledupar, Colombia

Felipe Mondaca
Cinvestav-Saltillo, Ramos Arizpe, Coahuila, Mexico

Manal Mostafa
Organic Egypt, Heliopolis University for Sustainable Development, Cairo, Egypt

Arturo I. Mtz-Enriquez
Cinvestav-Saltillo, Ramos Arizpe, Coahuila, Mexico

Kamila M. Nogueira
Institute for Energy and Nuclear Research, National Nuclear Energy Commission-IPEN/CNEN-SP, São Paulo, Brazil

Clement O. Ogunkunle
Environmental Biology unit, Department of Plant Biology, Faculty of Life Sciences, University of Ilorin, Ilorin; Department of Plant Biology, Osun State University, Osogbo, Nigeria

Débora de Oliveira
Department of Chemical Engineering and Food Engineering (EQA), Federal University of Santa Catarina (UFSC), Florianópolis, Brazil

Rishabh Anand Omar
Center for Environmental Science and Engineering, Indian Institute of Technology Kanpur, Kanpur, India

Noha H. Oraby
Animal Health Research Institute (AHRI), Agriculture Research Center (ARC), Giza, Egypt

Semih Otles
Engineering Faculty, Food Engineering Department, Ege University, Izmir, Turkey

Stephen Oyedeji
Environmental Biology unit, Department of Plant Biology, Faculty of Life Sciences, University of Ilorin, Ilorin, Nigeria

K.M. Paknikar
Nanobioscience Group, Agharkar Research Institute, Pune, India

Nicolaza Pariona
Department of Advanced Molecular Studies, The Institute of Ecology A.C. (INECOL), Xalapa, Veracruz, Mexico

Hermes Pérez-Hernández
El Colegio de la Frontera Sur (CONACYT), Agroecología, Unidad Campeche, Campeche, Mexico

Dao Anh Quang
Hue Industrial College, Hue City, Vietnam,

Periakaruppan Rajiv
Department of Biotechnology, Karpagam Academy of Higher Education, Coimbatore, India

Chandrasekaran Rajkuberan
Department of Biotechnology, Karpagam Academy of Higher Education, Coimbatore, India

J.M. Rajwade
Nanobioscience Group, Agharkar Research Institute, Pune, India

Nirmal Kumar Ramasamy
Department of Biotechnology, PSGR Krishnammal College for Women, Coimbatore, Tamil Nadu, India

Samridhi Rana
Department of Civil Engineering, Indian Institute of Technology Delhi, New Delhi, India

Manviri Rani
Malaviya National Institute of Technology, Jaipur, Rajasthan, India

D. Madhusudan Reddy
Department of Microbiology, Palamuru University, Mahabub Nagar, Telangana, India,

G. Bhagavanth Reddy
Department of Chemistry, Palamuru University, Mahabub Nagar, Telangana, India,

Buket Yalcin Sahyar
Işık Tarım Ürünleri San.ve Tic. A.S., R&D Center, Izmir, Turkey

Rasha M.H. Sayed-ElAhl
Animal Health Research Institute (AHRI), Agriculture Research Center (ARC), Giza, Egypt

Shraddha Shahane
Department of Civil Engineering, Indian Institute of Technology Delhi, New Delhi, India

Uma Shanker
Dr B R Ambedkar National Institute of Technology, Jalandhar, Punjab, India

Kamlesh Shrivas
School of Studies in Chemistry, Pt. Ravishankar Shukla University, Raipur, Chhattisgarh, India

N. Singh
Nanobioscience Group, Agharkar Research Institute, Pune, India

Alviya Sultana
School of Sciences, Monash University, Subang Jaya, Malaysia

Neetu Talreja
Advanced Ceramics and Nanotechnology Laboratory, Department of Materials Engineering, Faculty of Engineering, University of Concepción, Concepción, Chile

Velaphi C. Thipe
Institute for Energy and Nuclear Research, National Nuclear Energy Commission-IPEN/CNEN-SP, São Paulo, Brazil; Department of Radiology, School of Medicine, University of Missouri-Columbia, Missouri, United States

Patricio Andrés Torres-Gómez
Sustainability of Natural Resources and Energy Programs, Cinvestav-Saltillo, Ramos Arizpe, Coahuila, Mexico

Kubra Ulucan-Altuntas
Department of Environmental Engineering, Yildiz Technical University, Davutpasa, Istanbul, Turkey

D. Vaidehi
Department of Biotechnology, Kongunadu Arts and Science College, Coimbatore, Tamil Nadu, India

Alexsandra Valério
Department of Chemical Engineering and Food Engineering (EQA), Federal University of Santa Catarina (UFSC), Florianópolis, Brazil

Mayank Varun
Department of Botany, Hislop College, Nagpur, Maharashtra, India

Le Dai Vuong
School of Engineering and Technology—Hue University, Hue City, Vietnam

Sandhya Yadav
Advanced Material Research Laboratory, Department of Pure and Applied Physics, Guru Ghasidas Vishwavidyalaya, Bilaspur, India

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Series preface

The field application of engineered nanomaterials (ENMs) has not been well investigated in plant promotion and protection in agro-environment yet, and lots of components have been taken into consideration theoretically or with prototypes, which make it hard to evaluate the utility of ENMs for plant promotion and protection. Nanotechnology applications in the food industry involve: encapsulation and delivery of materials to targeted sites, developing flavor, introducing nano-antimicrobials agents into food, improvement of shelf life, sensing contamination, improved food preservative, monitoring, tracing, and logo protection. The list of environmental problems that the world faces may be huge, but a few strategies for fixing them are small. Scientists throughout the globe are developing nanomaterials that could use selected nanomaterials to capture poisonous pollutants from water and degrade solid waste into useful products. The market intake of nanomaterials is rushing, and the Freedonia Group predicts that nanostructures will grow to $100 billion through 2025. Nanotechnology research and development has been growing on a sharp slope across all scientific disciplines and industries. Based on this background, the scientific series titled "Nanobiotechnology for Plant Protection" was inspired by the desire of the Editor, Kamel A. Abd-Elsalam, to put together detailed, up-to-date, and applicable studies on the field of nanobiotechnology applications in agro-ecosystems, to foster awareness and extend our view of future perspectives.

The main appeal of the present book series is its specific focus on plant protection in agri-food and environment, which is one of the most topical nexus areas in the many challenges faced by humanity today. The discovery and highlights of new book inputs, based on nanobiotechnology, that can be used at lower application rates will be critical to eco-agriculture sustainability. The research carried out in the concerned fields is scattered and not in a single place. The book series covers the applications in agri-food and environment sectors, which is the new topic of research in the field of nanobiotechnology. This book series is a comprehensive account of the literature on specific nanomaterials and their applications in agriculture, food, and environment. The audience will be able to gather information from a single book series. Students, teachers, researchers from colleges, universities, research institutes, as well as industry will benefit from this book series. Four specific features make the current book series one of a kind. *First*, the book series has a very specific editorial focus, and researchers can locate nanotechnology information precisely without looking into various full-text. *Second*, and more importantly, the series offers a crucial evaluation of the content material along with nanomaterials, technologies, applications, methods and equipment, and safety and regulatory aspects in agri-food and environmental sciences. *Third*, the series offers the reader a concise precision of the content material; it offers nano-scientists with clarity and deep information. *Finally*, it presents researchers with insights on new discoveries. The current series gives the researchers a sense of what to do, what they would need to do, and how

to do it properly—by searching for others who have done it. The sixth book titled, **Copper Nanostructures: Next-Generation of Agrochemicals for Sustainable Agroecosystems**, describes the gathered know-how, observations, and effective applications of zinc-based nanomaterials in environmental and agri-food systems. The expected readership for the current book series would be researchers in the field of food, agriculture, and environmental sciences. Some readers may be chemists, material scientists, agro and food industry players, and academicians and also come from green chemistry industry and government regulatory agencies. A few industrial personnel would also be interested in it. This book series is useful to a wide audience of food, agriculture, and environmental sciences, researchers, undergraduate and graduate students, postgraduates, etc. In addition, agricultural producers could benefit from the applied knowledge that will be highlighted in the book, which otherwise would be buried in different journals. Both primary and secondary audiences are seeking the up-to-date knowledge of the nanotechnology application in food, agriculture, and environmental sciences. It is a trending area, and lots of new studies are published every week. The readers need some good summaries to help them learn the latest key findings, which could be review articles and/or books. This book series will help to put these pockets of knowledge together, and make it more easily accessible globally.

Kamel A. Abd-Elsalam
Agricultural Research Center, Giza, Egypt

Preface

The present book represents the sixth volume of a series titled "**Nanobiotechnology for Plant Protection**," the original book series approved by Elsevier. The present volume contains 30 chapters prepared by outstanding authors from Algeria, Brazil, Chile, Iran, India, Egypt, KSA, Philippines, Republic of Korea, Japan, Mexico, Romania, Tunisia, Turkey, Vietnam, and United States. The book titled "**Copper Nanostructures: Next-Generation of Agrochemicals for Sustainable Agroecosystems**" in 30 chapters has collected the knowledge, discoveries, and the fruitful findings of green synthesis of copper nanoparticles via plants, agricultural wastes, and various microorganisms and their applications in agroecosystems.

This volume is divided into six main parts. **Part 1** (four chapters) *highlights* green synthesis of copper nanoparticles: production mechanisms, eco-safety, and future perspectives. The increasing importance of copper nanomaterials in plant protection applications is reflected in the seven chapters of **Part 2**. **Part 3** includes four chapters that describe the use of copper nanostructures in plant science applications such as multifunctional copper-based nanocomposites and their agroecosystem applications, impact of copper-based nanoparticles on economically important plants, copper nanoparticles in soil: uptake, mechanism of toxicity, and biotransformation in plants, and copper/carbon-based nanostructured materials as a growth stimulator of the plants, in addition to understanding the interaction of copper-based nanoparticles with soil during agricultural applications. **Part 4** of this volume is devoted to one of the most innovative topics of nanobiotechnology which concerns antimicrobial applications. This part (three chapters) summarizes current approaches to use copper nanomaterials as antimicrobials and antibacterial agents. **Part 5** (two chapters) describes applications of copper nanostructures as antimicrobial agents against animal pathogens, as well as safety considerations of copper nanoparticles as food and feed additives. **Finally**, applications of copper nanoparticles against plant and animal parasitic nematodes are described. The final part (Part 6) is divided into nine chapters, which summarizes current applications of copper nanomaterials in agroecosystem like copper nanoparticles as nanosensors, their negative ecological effects, estimation of risks of exposure to copper-based agrochemicals, understanding their interaction with blue-green algae, and wastewater treatment. This book contains current research on the development and administration of ecologically safe formulations to protect crops against insects and illnesses that cause pathogen, as well as plant science, antimicrobial, agroecosystem and veterinary medicine applications.

The book is of an interdisciplinary nature and will be very useful for students, teachers, and researchers, agri-food environmental scientists and agrochemical companies working in nanotechnology, materials science, biology, chemistry, physics, plant science, chemical technology, microbiology, plant physiology, biotechnology, and further groups of interests such as industry working. Additionally, this will be

a useful tool for industrial scientists investigating technology to update their nanotoxicology and nanosafety understanding. Copper nanoparticles have been used in a variety of applications, including antibacterial agents, plant disease management, mycotoxin reduction, pesticide detection and degradation, wastewater treatment, and veterinary uses. We seriously hope to have offered a balanced, interesting, and innovative perspective in the area not only for advanced readers but also for industrial decision-makers and for those approaching the field with limited knowledge. The expected audience for the current book include researchers, graduate students, and postgraduate students from various fields of science and technology.

Our aim is to give experienced readers as well as technical decision-makers, and people with limited knowledge of the field, a reliable, insightful, and innovative perspective in this regard. The authors are very grateful to us for presenting this high-quality collection of manuscripts. We thank all the authors who have made suggestions based on their experiences in the chapters of the book and in this edited book. Without their participation and commitment, writing this book would not have been possible. Elsevier Publisher is also very highly praised, since the project has put forth a very high degree of experience, reliability, and tolerance.

We express our sincere gratitude for the support they have provided and the efforts to achieve this number of Elsevier personnel, notably Simon Holt, Rafael Trombaco, Editorial Project Manager for Intern, Nirmala Arumogam, and Narmathe Mohan. We thank all the reviewers who expanded on each chapter giving their precious time. We also thank the family members for their continued care and encouragement.

Kamel A. Abd-Elsalam
Agricultural Research Center, Giza, Egypt

CHAPTER

Copper-based nanomaterials: Next-generation agrochemicals: A note from the editor

1

Kamel A. Abd-Elsalam

Plant Pathology Research Institute, Agricultural Research Center (ARC), Giza, Egypt

1 Introduction

Today there are three primary difficulties for the crop protection sector. First, the persistent issue of fungal and bacterial resistance and transmission (Jeger et al., 2021). Second, the decrease in residual impact and environmental dangers of registered pesticides (Damalas and Eleftherohorinos, 2011.). Third, customers are becoming aware of their preferences for more eco-friendly food products (Fortunati et al., 2019). As a result, other plant protection methods are unavoidable. Agrochemicals are often used in crop management to improve agricultural production and output, reduce crop losses, combat plant-related illnesses, and improve food quality (Popp et al., 2013). Nano-enabled agrochemicals, also known as agro-nanochemicals, may hold the key to the development of integrated pest and disease management since they provide controlled release of active ingredients and site-specific delivery, boosting their efficacy and efficiency (Ghormade et al., 2011; De et al., 2014). Furthermore, the global use of agrochemicals has been estimated to increase by 3.5 million tons by 2020 (Zhang, 2018). The global use of agrochemicals (pesticides, fertilizers, growth hormones, and so on) is expected to reach $266 billion by 2021, with a 4.5% annual growth rate (Grillo et al., 2020). Despite the benefits and necessity for the agri-food sector, the extensive use of agrochemicals results in the release of massive amounts of dangerous contaminants into the environment (Nuruzzaman et al., 2016).

Agricultural nanotechnology can enhance crops in a variety of ways, including nanofertilizer and agrichemical formulation, novel agrichemical delivery systems, nanosensors for disease detection, nanodevices for genetic alteration, and postharvest crop management. A critical review of plant nanotechnology has been described in detail in a study by Giraldo et al. (2019,). Nano-agrochemicals are expected to dominate this field soon, as they reduce the amount of chemicals released into the environment and, therefore, have a slight ecological footprint when compared to conventional pesticides and fertilizers, as well as several inorganic nanomaterials such as copper (Gabal et al., 2018), aluminum (Shenashen et al., 2017), and silver (Gupta et al., 2018).

Copper Nanostructures: Next-Generation of Agrochemicals for Sustainable Agroecosystems.
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Copper has been used as a fungicide since 1882 in the Bordeaux region of France when researchers discovered that a combination of copper sulfate and calcium reduced the proportion of grapevines infected with *Plasmopara viticola* fungus dramatically. This mixture, known as the Bordeaux mixture, is still used to prevent fungi-related crop damage in a variety of crops (Mukerjee and Srivastava, 1957). However, since before the discovery of Bordeaux, the antifungal effects of copper sulfate were recognized for the treatment of wheat seeds against smut spores and wood preservation (Johnson 1935). Copper is naturally present in the environment, is an omnipresent element with a concentration of around 60 g/ton in the Earth's crust (Ojha et al., 2017), and a major plant growth nutrient in certain quantities. In mitochondrial respiration, hormonal signals, metabolism of a cell wall, iron mobility, and transportation of electron are also predicted to play a vital role (Yruela, 2009). Copper nanoparticles are one of the most significant nanomaterials due to their various characteristics, uses, and manufacturing economics. Copper-based nanoparticles provide fertilizers and insecticides with a broader specific surface area. Nanomaterials also make it easier to provide nutrients with greater crop protection in a site-oriented and regulated way than distinct agrochemicals suppliers (Gabal et al., 2018). There is not a specific book available on "copper nanomaterials applications in the agri-food sector," therefore the current volume is a unique contribution in the field with almost no competition. Almost all of the contents of the chapters in Part 1 deals with the sustainable production of copper-based nanostructures, Part 2 focuses on plant protection applications. Part 3 reviews appropriate technological developments in plant science applications, Part 4 comprising seven chapters provides antimicrobial applications of copper nanomaterials in agri-food sector. Part 5 is oriented to present specific examples of nanobiotechnological applications in veterinary. The last part of the book (Part 6) presents the application of copper nanoparticles in agroecosystems, there are no books available on the application of copper-based nanomaterials in the mentioned sectors.

2 Nanoparticle-based agrochemicals

The potential of nanotechnology to improve the agriculture sector has been demonstrated recently by the efficiency of agricultural inputs and solutions to agricultural problems for improving food productivity and safety. The worldwide consumption of agrochemicals has increased by almost 2 million tons over the last decade and the global utilization of agrochemicals has been predicted to increase by 3.5 million tons by 2020 (Zhang, 2018). The application of Cu-nanoscale agrochemicals in agriculture, such as nanofertilizers, nanopesticides, nanosensors, and nanoformulation, has revolutionized traditional agro-practice and made it more sustainable and efficient (Fig. 1). In reality, however, application of these nano-products raises concerns regarding nanomaterial safety, exposure, and their toxicological effects on environment and human health (Singh et al., 2021).

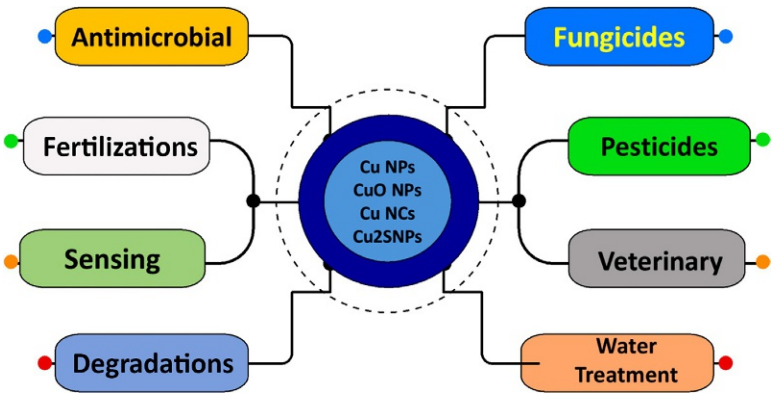

FIG. 1

Application of copper-based nanomaterials in the agri-food sector.

Today, these nano-agrochemicals have acquired appeal since they are more efficient than conventional agrochemicals, making them economically viable and environmentally sustainable. Nanoagrochemicals also assisted the farmers in economic ways by enhancing both qualitative and quantitative yields by replacing plant fertilizers and pesticides to optimize output and maintain the input leading to economic success due to their great benefit in agriculture (Qazi and Dar, 2020). Copper nanoencapsulated agrochemicals are prepared to avoid the negative effects of agrochemicals used in polluted water and in soil due to the leaching of chemical products, as well as their degradation due to the repeated use of these chemical agents for an effective concentration. Their chemical content usually is lower than the minimum concentration (Gabal et al., 2018).

3 Applications in the agriculture and food sector

3.1 Smart fertilizers

Copper is the major micronutrient for plant growth, activating many enzymes, and participating in a diversity of physiological activities, such as photosynthesis, respiration, carbohydrates, nitrogen metabolism, and protection against oxidative stress (Abd El-Aziz et al., 2019). Copper is used for foliar application, which promoted the yield of corn when compared with the control assay. Additionally, it improves the production and physiological role of the corn plant (Syuhada et al., 2014). The implementation of Cu NPs can generate bio-stimulation in particular the antioxidant capacity of plants (Hernández-Hernández et al., 2019; Pérez-Labrada et al., 2019). Moreover, the foliar spraying of Cu nanoparticles (NPs) can enhance the contents of bioactive ingredients in tomato fruits, e.g., all treatments did significantly increase vitamin C content in tomato fruits. Cu NPs also enhanced the firmness of tomato

fruits, thereby potentially increasing the shelf life of tomato fruits. Thus, tomato fruit quality can be preserved for a longer time (López-Vargas et al., 2018). However, Se in combination with Cu NPs at the optimal concentrations would be a good option for improving tomato crop production, particularly to produce higher quality crops. In addition, a combination of Se and Cu NPs can enhance the ingredients of non-enzymatic antioxidant, firmness, total soluble solids, and titratable acidity, which improves the quality of nutraceutical and commercial traits (Hernández-Hernández et al., 2019). Furthermore, foliar spray of copper nanoparticles can stimulate plant antioxidant systems; it is a viable technique for regulating and/or alleviating salt stress damage in tomatoes (Pérez-Labrada et al., 2019). Recently, Cu-based nanomaterials such as nanofertilizers, nanofungicides, nematicides, or nanopesticides have been used for nutrient management, genetic improvement, plant protection, and plant growth promotion at various phases of plant development (Fig. 2).

3.2 Antimicrobials

The use of copper as a microbiological agent goes back to 2000 BC (Grass et al., 2011). Biogenic CuNPs have become a novel type of antimicrobial products with the potential to combat a range of pathogens (Chowdhury et al., 2014). The specific CuNPs operating mechanism is not yet fully known. *Clavibacter michiganensis* was effectively combined with Cu NPs and potassium silicate in tomato plants with all the dosages examined found to reduce disease severity. The loss of yield from

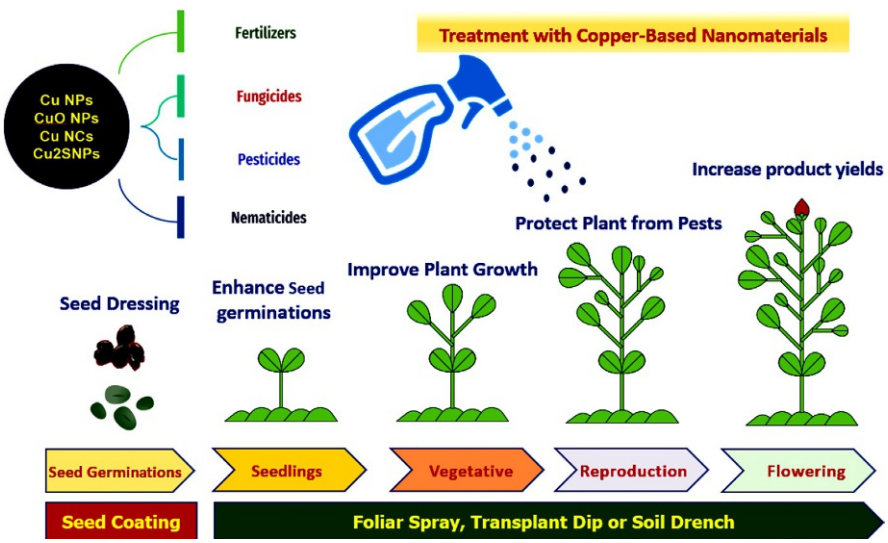

FIG. 2

Application of Cu-based nanomaterials at different phases and stages of plant growth for plant promotion and protection.

phytobacteria was further decreased, in particular the treatments with a low Cu NPs dosage (Cumplido-Nájera et al., 2019). CuNP1 and CuNP2 in two concentrations were produced in two distinct CuNP products (1500 or 300 ppm). The antibacterial effectiveness of Cu NPs against some pathogens, such as *Pseudomonas savastanoi* pv. *savastanoi* or *Xanthomonas campestris* pv. *campestris*, was investigated in vitro. The evaluation was based on the comparisons between Kocide (copper hydroxide) and Nordox bactericides (copper oxide). CuNP1 reduced the growth of five species, restricted growth in *Xanthomonas campestris* pv. *campestris,* and had no impact on *Pseudomonas corrugata*. However, CuNP2 reduced *Erwinia amylovora* development and restricted *Pseudomonas savastanoi* pv. *savastanoi* (Varympopi et al., 2020).

3.3 Pesticides

Different research teams across the world have shown that CuNPs are superior defenders of plants. CuNPs were shown to be more efficient in the management of several common fungal and bacterial illnesses compared to bulk copper. The CuNPs degrade the cell wall and change the cell organelle function, resulting in the death of pathogens. This makes nanoscale copper better suited to the fight against plant diseases. In addition, the packaging may be used to improve the shelf life of food and food items (Rai et al., 2018). Bio-CuNPs can be utilized as a biocontrol agent for the control of pests such as *Tribolium castaneum* in stored grain. Produced biogenic CuNPs using different type of bioresources is ecofriendly and affordable method (El-Saadony et al., 2020). Biogenic CuONPs were synthesized using metabolites present in the biomass filtrate of *Aspergillus niger*. The effectiveness of green-based CuONPs as insecticides against *Sitophilus granarius* and *Rhyzopertha dominica* wheat grain insects has been assessed. Low mycogenic CuONP concentration led to considerable improvement in the features of wheat growth, photosynthetic pigments, and the activity of antioxidant wheat herb enzymes. Carbohydrate or protein content was not significantly altered (Badawy et al., 2021).

3.4 Fungicides

The widespread use of CuNPs has received a lot of attention from all around the world. In situations of soil copper deficiency, copper nanoparticles can also be employed both as a source of micronutrient and as a fungicide (Lopez-Lima et al., 2021). Copper is an essential ingredient in several inorganic fungicides that were used to manage many diseases of plants caused by *Fusarium oxysporum, Curvularia lunata, Phoma destructiva,* and *Alternaria alternata* (Borkow and Gabbay, 2009; Kanhed et al., 2014). Biogenic copper fungicide produced by *Streptomyces griseus* might be a viable alternative to control Poria hypolateritia-causing tea-root disease (Elango et al., 2015). The results of Zabrieski et al. (2015) revealed that CuO's nanoparticles at 500 mg/L conc. decreased fungal radial growth up to 50% compared to the untreated control and that there were variables in response to pathogenic *Pythium ultimum* and *Pythium aphanidermatum.* The impregnation by chitosan with

the organosols Cu-acetone and Cu-toluene was used to produce two C@Chit nanocomposites produced by metal-vapor synthesis. The manufacture of Cu@Chit NCs and testing of these materials with two pathogenic plant fungi *Rhizoctonia solani* AG-4 and *Sclerotium rolfsii* was examined (Rubina et al., 2017). Chickpea seeds coated with nanoparticles of chitosan-thiamine had a greater germination rate of 90% compared with chitosan-thiamine combination and control. The cell deaths of *F. oxysporum*-infected roots also decreased considerably compared to control (Muthukrishnan et al., 2019). CuO-CFNPs fabricated with a green approach showed potential antifungal activities in tomato against Fusarium wilt. CuO-CFNP exposure enhanced the buildup of bioactive chemicals and the number and size of tomato fruit increased (Ashraf et al., 2021).

3.5 Sensing

Copper-oxide nanoparticles were employed for the detection of the most prevalent dangerous gases and environmental contaminants, and have been widely used for high-performance gas-sensing equipment (Steinhauer, 2021). Research on comparable sensors and sensing systems for the detection of by-products of pathogens and for monitoring of physiological changes in plants caused by infections must be expanded. The nanoparticles and nanolayers of copper oxides and spray pyrolysis were produced using sol-gel and spraying methods. The detection of *Aspergillus niger* was carried out using both CuO and nanostructural layer biosensors (Etefagh et al., 2013). Wang et al. (2016) employed CuNPs modified by gold electrode for indirect stimulation to produce a sensible electrochemical sensor to monitor salicylic acid levels in oilseeds for the detection of the pathogen of *Sclerotinia sclerotiorum*. They measured salicylic acid using this sensor successfully and precisely. Monodisperse copper selenide NPs have a strong potential not only in different areas of mercury ion pollution but also in the discovery of novel nanomaterials to address other heavy metal ions (Zhang and Xia, 2016; Yang et al., 2020).

3.6 Degradation of pesticides

Large-scale remediation of agrochemical products in soil, water, and farm products is achieved using nanoparticles, such as fixed-bed thin-film reactors and nanophytoremediation systems (Sebastian et al., 2020). Various forms of nanomaterials have been utilized for the detection, degradation, and removal of pesticides, such as metal nanoparticles, bimetal hybrid nanomaterials such as nanocomposites (Rawtani et al., 2018). The preparation and use of nano-biocomposites combining two nanofillers with biopolymer were evaluated to remediate dichlorvos pollution. Higher removal of CuO-Montmorillonite-chitosan dichlorvos and CuO-Montmorillonite gum ghatti nano-biocomposites biopolymers can play an important role in pesticide adsorption. The application of nano-biocomposites in pesticide removal is rarely reported (Sahithya et al., 2015). New composite materials produced from montmorillonite (MK10) or quartz sand coated with were CuNPs were used for atrazine degradation.

Enhanced MK10 and sand are extremely effective materials for advanced processes of oxidation and may increase process performance to different pesticides (Kalidhasan et al., 2017). In the presence of water-soluble methyl parathion in the water sample under solar light irradiation circumstances and ultrasonic cavitation conditions, nanocomposites produced using sonocoprecipitation were utilized as a photocatalyst for synthesizing the linked metal oxides of the ZnO and CuO. ZnO/CuO linked metal oxide has been effectively utilized for parathion photocatalytic degradation (Aghaei et al., 2020). For the first time, CuONPs were employed in the hydrolytic decomposition of methyl parathion, the most hazardous organophosphate insecticide currently in use. Cu_2O NPs have high surface basicity, which allows them to degrade methyl parathion without the use of additional chemicals or photocatalysts that create free radicals (Rizo et al., 2020).

4 Toxicity

Although, there are numerous positive effects of CuNPs, it may also have a harmful environmental effect. In general, the toxicity of NPs relies on size, surface charge, and pH of the environment (Chang et al., 2012). In many studies, researchers have shown that CuNPs are unsafe for plants when it utilized beyond a certain concentration. CuNPs applied at high doses affect plant metabolism, thereby impacting the yield quantity and quality. Thus, for a safer use of CuNPs in agriculture, there is a pressing need to have a clear understanding of nanoparticle-plant interactions. For instance, the implementation of CuONPs notably decreased the growth of cucumber plants that were cultivated on soil microcosm systems (Kim et al., 2013).

Phytotoxicity of CuNPs on the physiological, phenotypical, biochemical, and genomic levels of *Cucumis sativus* plant was assessed. Experimented CuNPs at the size of 10–30 nm were toxic for *Cucumis sativus* plant. The total biomass of *Cucumis sativus* plant decreased when treated with CuNPs (Mosa et al., 2018). In another study, the oxidative stress was caused by the uptake and accumulation of CuNP, which restricted the growth and development phases of the plants that were more noticeable in roots than in shoots, because of the direct contact between the membrane root and CuNPs (AlQuraidi et al., 2019).

The potential effect of the different particle size and concentrations of CuONPs on the architecture of the root system, soil-root interaction, and CuONPs accumulation was observed. Soil amended with CuONPs, particularly with the small sized CuONPs (25 nm) notably improved the nutritional Cu value in soybean seeds, also discovered to be a good source of nutritional Cu when compared with many other food items that provide nutritional Cu, viz., avocado, asparagus, ground turkey, pasta, etc. (Fig. 3).

Nevertheless, before CuONP-fortified soybean seeds are recommended for daily human consumption in order to address global Cu deficiency and associated illnesses in humans, it is critical to understand the potential toxicity and risk associated with the consumption of soybean seeds containing Cu-based NPs (Yusefi-Tanha et al., 2020). Phytotoxicity effect of green and chemically synthesized nanoparticles was carried

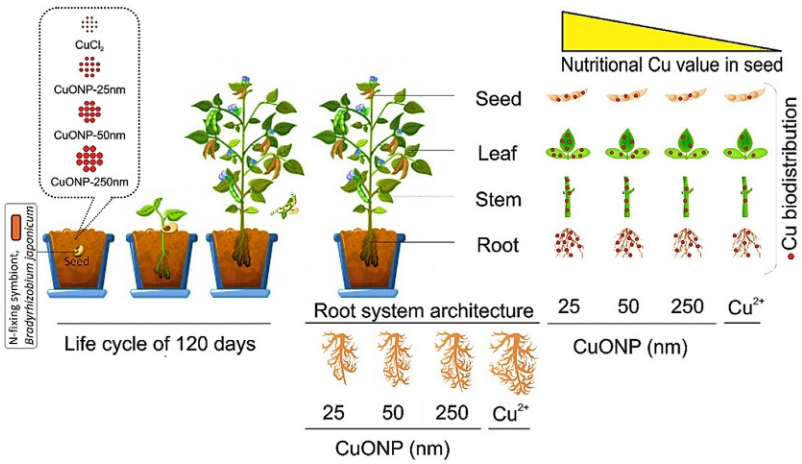

FIG. 3

The potential influence of various particle size and concentration of CuONPs on root system architecture, soil-root interaction, and CuONPs accumulation in *Glycine max* grown in soil amended with CuONPs.

Data from Yusefi-Tanha, E., Fallah, S., Rostamnejadi, A., Pokhrel, L.R., 2020. Root system architecture, copper uptake and tissue distribution in soybean (Glycine max (L.) Merr.) grown in copper oxide nanoparticle (CuONP)-amended soil and implications for human nutrition. Plants 9(10), 1326, with permission from MDPI under a Creative Commons Attribution 4.0 International License.

out using both seed germination and seedling growth of two species of lettuce and tomato plants. Chemically manufactured CuONPs have a vigorous inhibitory effects on germination, hence green CuONPs with the effects of toxicity less than chemically synthesized CuONPs can be identified as eco-friendly NPs (Khaldari et al., 2021).

Although previous studies have indicated the phytotoxic impacts of CuNPs on the plants, the underlying physiological, cellular, and molecular mechanisms require more experimentation. More studies should be focused on evolution of environmental risk for evaluating accurately analysis of Cu risks via the organisms in soil and water, also the productivity of sustainable agriculture, because the standard tests for determining the toxicity of Cu in soil and water biota like those found in other fields of ecotoxicology are unavailable yet (Lamichhane et al., 2018). Additionally, there is a requirement for knowing information about plant genome sequence that promotes our understanding of NP phytotoxicity via deep molecular and gene expression, and also omics analysis studies.

5 Advantages

Nano-agrochemicals have gained appeal because they are more effective than conventional agrochemicals, making them both economically and environmentally feasible.

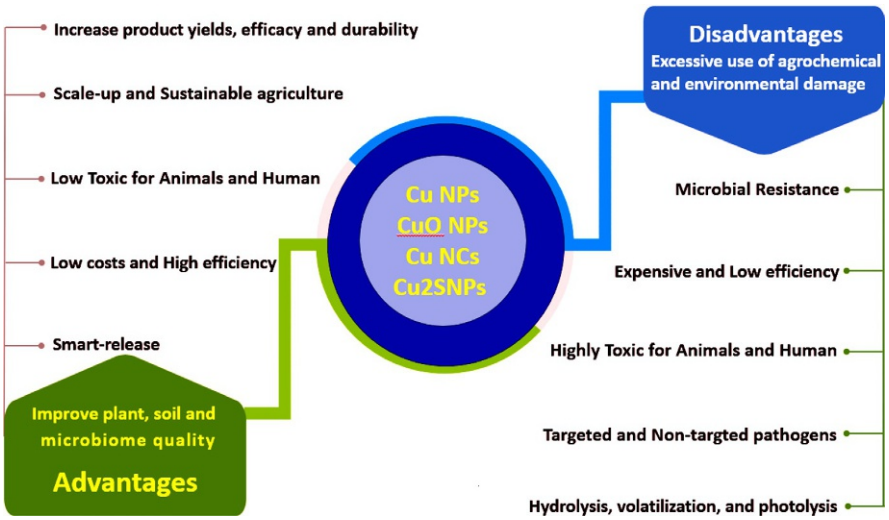

FIG. 4

Advantages and disadvantages of Cu-nanobased agrochemicals, compared to conventional Cu-agrochemicals, and future trends for sustainable agriculture.

Nanofertilizers have an advantage over traditional fertilizers in that they improve soil fertility, yield, and quality characteristics of the crop while also being nontoxic and environmentally benign, lowering input costs, and increasing profit. Copper is one of the most critical minerals for plant growth and development. In agriculture, CuNP-based fertilizer and herbicide can be employed for plant promotion and protection. For example, CuONPs treatment considerably improved plant height, number of leaves, fresh and dry weight, yield, and bulb quality when compared to Cu sulfate and chelates. Although Cu sulfate is the least expensive type of Cu supplementation, the current study suggests that CuONPs were not only safe to employ, but also resulted in the highest onion yield and quality (Mottaleb et al., 2021). Cu is less expensive and more widely available than metals such as silver and gold. As a result, using copper nanoparticles in many agricultural applications is a cost-effective option (Fig. 4). CuNPs demonstrated no phytotoxicity effect on plants when sprayed at concentrations equal to or more than the permissible levels. The nano copper compounds investigated in this study can be manufactured in large quantities and at a cost comparable to standard copper insecticides.

6 Futuristic strategies

It is important to assess the performance of copper agro-nanochemicals in tackling the genuine difficulties facing the agricultural industry compared to traditional agrochemicals. Alternatively, agrochemical active components can be loaded or

encapsulated into nanoparticles for the formation of a powerful biocidal agent and a protective wall which results in nontoxic and biocompatible chitosan nanoparticles to safeguard the plants from the adverse effects loaded into them (Maluin and Hussein, 2020). Chitosan-based agronanochemical products are also designed to improve the efficient provision of active agents at the target site, sustaining them for a long time, thereby improving the efficacy of agrochemicals. In addition, the designed systems can improve consumption and minimize leaching and runoff of agrochemicals that could affect health and the environment (Maluin and Hussein, 2020). Advancements in nano-enabled agrochemicals must be aligned with specific yield limitations and requirements of the low productivity and improved regions. Furthermore, additional data are necessary to identify the actual mechanism of movement of the copper-based nanomaterials in a plant based on particle size, morphology, surface load, solubility, bioavailability, type of plant, and efficient exposure levels to the uptake, the translocation, and the transport of nano-copper.

7 Conclusion

Agro-nanotechnological advances such as nano-agrochemicals are a short-term solution for the difficulties facing the current industry. In addition, agro-nanochemical products, such as nano-copper, can reduce agrochemical toxicity, improve agrochemical consumption, increase solubility and stability, and limit volatilization, lixiviation, and exhaustion of agrochemicals that may cause environmental and health concerns. The rising use of Cu-based NPs shows their harmful effects on ecosystems. The toxicity and behavior of Cu-based NPs in water, living organisms, soil and sediments, and their toxicity in combination with other substances are therefore important to research. Copper nanoparticles can also be utilized in cases of deficiency in copper and as fungicides for the supply of micronutrients. The bipolar role of copper nanoparticles has been established, which will have a good impact on crops and the environment in terms of sustainability. The existing depleted arsenal of antifungal, nematicides, bactericidal, and pesticides will strengthen the commercial manufacture of these stable and pure chemicals. The implementation of a smart delivery system based on nanoparticles and nanosensors promises a controlled release of agrochemicals and a targeted on-site supply of diverse macromolecules necessary for better plant resistance, efficient use of nutrients, and increased plant defense. In the following chapters, we highlighted green synthesis of copper nanoparticles: production mechanisms, eco-safety, and future perspectives. The increasing importance of copper nanomaterials in plant protection applications. Also, we described the use of copper nanostructures in plant science applications such as multifunctional copper-based nanocomposites and their agroecosystem applications, the impact of copper-based nanoparticles on economically important plants, copper nanoparticles in soil: uptake, mechanism of toxicity, and biotransformation in plants, copper-/carbon-based nanostructured materials as a growth stimulator of the plants. In addition to understanding the interaction of copper-based nanoparticles with soil during agricultural applications. Antifungals,

antibacterial, and nematicide applications were investigated in detail. In addition, copper nanostructures applications in animal health, safety considerations of copper nanoparticles as food and feed additives were evaluated. Finally, applications of copper nanoparticles against plant and animal parasitic nematodes are described. The final part (Part 6) is divided into nine chapters that summarizes current applications of copper nanomaterials in agroecosystem like copper nanoparticles as nanosensors, their negative ecological effects, estimation of risks of exposure to copper-based agrochemicals, understanding their interaction with blue-green algae, and wastewater treatment.

References

Abd El-Aziz, M.E., Morsi, S.M.M., Salama, D.M., Abdel-Aziz, M.S., Abd Elwahed, M.S., Shaaban, E.A., Youssef, A.M., 2019. Preparation and characterization of chitosan/polyacrylic acid/copper nanocomposites and their impact on onion production. Int. J. Biol. Macromol. 123, 856–865.

Aghaei, M., Sajjadi, S., Keihan, A.H., 2020. Sono-coprecipitation synthesis of ZnO/CuO nanophotocatalyst for removal of parathion from wastewater. Environ. Sci. Pollut. Res. 27 (11). 115541-11553.

AlQuraidi, A.O., Mosa, K.A., Ramamoorthy, K., 2019. Phytotoxic and genotoxic effects of copper nanoparticles in coriander (*Coriandrum sativum*-Apiaceae). Plants 8 (1), 19.

Ashraf, H., Anjum, T., Riaz, S., Ahmad, I., Irudayaraj, J., Javed, S., Qaiser, U., Naseem, S., 2021. Inhibition mechanism of green-synthesized copper-oxide nanoparticles from Cassia fistula towards *Fusarium oxysporum* by boosting growth and defense responses in Tomatoes. Environ. Sci.: Nano 8, 1729–1748.

Badawy, A.A., Abdelfattah, N.A., Salem, S.S., Awad, M.F., Fouda, A., 2021. efficacy assessment of biosynthesized copper oxide nanoparticles (CuO-NPs) on stored grain insects and their impacts on morphological and physiological traits of wheat (*Triticum aestivum* L.) plant. Biology 10 (3), 233.

Borkow, G., Gabbay, J., 2009. Copper, an ancient remedy returning to fight microbial, fungal and viral infections. Curr. Chem. Biol. 3 (3), 272–278.

Chang, Y.-N., Zhang, M., Xia, L., Zhang, J., Xing, G., 2012. The toxic effects and mechanisms of CuO and ZnO nanoparticles. Materials 5, 2850–2871.

Chowdhury, S., Basu, A., Kundu, S., 2014. Green synthesis of protein capped silver nanoparticles from phytopathogenic fungus *Macrophomina phaseolina* (Tassi) Goid with antimicrobial properties against multidrug-resistant bacteria. Nanoscale Res. Lett. 9, 1–11.

Cumplido-Nájera, C.F., González-Morales, S., Ortega-Ortíz, H., Cadenas-Pliego, G., Benavides-Mendoza, A., Juárez-Maldonado, A., 2019. The application of copper nanoparticles and potassium silicate stimulate the tolerance to *Clavibacter michiganensis* in tomato plants. Sci. Hortic. 245, 82–89.

Damalas, C.A., Eleftherohorinos, I.G., 2011. Pesticide exposure, safety issues, and risk assessment indicators. Int. J. Environ. Res. Public Health 8 (5), 1402–1419.

De, A., Bose, R., Kumar, A., Mozumdar, S., 2014. Targeted Delivery of Pesticides Using Biodegradable Polymeric Nanoparticles. Springer, New Delhi, India.

Elango, V., Manjukarunambika, K., Ponmurugan, P., Marimuthu, S., 2015. Evaluation of Streptomyces spp. for effective management of *Poria hypolateritia* causing red root-rot disease in tea plants. Biol. Control 89, 75–83.

El-Saadony, M.T., El-Hack, A., Mohamed, E., Taha, A.E., Fouda, M.M., Ajarem, J.S., Maodaa, S.N., Allam, A.A., Elshaer, N., 2020. Ecofriendly synthesis and insecticidal application of copper nanoparticles against the storage pest *Tribolium castaneum*. Nanomaterials 10 (3), 587.

Etefagh, R., Azhir, E., Shahtahmasebi, N., 2013. Synthesis of CuO nanoparticles and fabrication of nanostructural layer biosensors for detecting *Aspergillus niger* fungi. Sci. Iran 20 (3), 1055–1058.

Fortunati, E., Mazzaglia, A., Balestra, G.M., 2019. Sustainable control strategies for plant protection and food packaging sectors by natural substances and novel nanotechnological approaches. J. Sci. Food Agric. 99, 986–1000.

Gabal, E., Ramadan, M.M., Alghuthaymi, M.A., Abd-Elsalam, K.A., 2018. Copper nanostructures applications in plant protection. In: Nanobiotechnology Applications in Plant Protection. Springer, Cham, pp. 63–86.

Ghormade, V., Deshpande, M.V., Paknikar, K.M., 2011. Perspectives for nano-biotechnology enabled protection and nutrition of plants. Biotechnol. Adv. 29, 792–803.

Giraldo, J.P., Wu, H., Newkirk, G.M., Kruss, S., 2019. Nanobiotechnology approaches for engineering smart plant sensors. Nat. Nanotechnol. 14 (6), 541–553.

Grass, G., Rensing, C., Solioz, M., 2011. Metallic copper as an antimicrobial surface. Appl. Environ. Microbiol. 77 (5), 1541–1547.

Grillo, R., Fraceto, L.F., Amorim, M.J., Scott-Fordsmand, J.J., Schoonjans, R., Chaudhry, Q., 2020. Ecotoxicological and regulatory aspects of environmental sustainability of nanopesticides. J. Hazard. Mater. 404. 124148.

Gupta, N., Upadhyaya, C.P., Singh, A., Abd-Elsalam, K.A., Prasad, R., 2018. Applications of silver nanoparticles in plant protection. In: Nanobiotechnology Applications in Plant Protection. Springer, Cham, pp. 247–265.

Hernández-Hernández, H., Quiterio-Gutiérrez, T., Cadenas-Pliego, G., Ortega-Ortiz, H., Hernández-Fuentes, A.D., Cabrera de la Fuente, M., Valdés-Reyna, J., Juárez-Maldonado, A., 2019. Impact of selenium and copper nanoparticles on yield, antioxidant system, and fruit quality of tomato plants. Plants 8 (10), 355.

Jeger, M., Beresford, R., Bock, C., Brown, N., Fox, A., Newton, A., Vicent, A., Xu, X., Yuen, J., 2021. Global challenges facing plant pathology: multidisciplinary approaches to meet the food security and environmental challenges in the mid-twenty-first century. CABI Agric. Biosci. 2 (1), 1–18.

Johnson, G.F., 1935. The early history of copper fungicides. Agric. Hist. 9, 67–79.

Kalidhasan, S., Dror, I., Berkowitz, B., 2017. Atrazine degradation through PEI-copper nanoparticles deposited onto montmorillonite and sand. Sci. Rep. 7 (1), 1–13.

Kanhed, P., Birla, S., Gaikwad, S., Gade, A., Seabra, A.B., Rubilar, O., Duran, N., Rai, M., 2014. In vitro antifungal efficacy of copper nanoparticles against selected crop pathogenic fungi. Mater. Lett. 115, 13–17.

Khaldari, I., Naghavi, M.R., Motamedi, E., 2021. Synthesis of green and pure copper oxide nanoparticles using two plant resources via solid-state route and their phytotoxicity assessment. RSC Adv. 11 (6), 3346–3353.

Kim, S., Sin, H., Lee, S., Lee, I., 2013. Influence of metal oxide particles on soil enzyme activity and bioaccumulation of two plants. J. Microbiol. Biotechnol. 23, 1279–1286.

Lamichhane, J.R., Osdaghi, E., Behlau, F., Köhl, J., Jones, J.B., Aubertot, J.N., 2018. Thirteen decades of antimicrobial copper compounds applied in agriculture. A review. Agron. Sustain. Dev. 38 (3), 1–18.

Lopez-Lima, D., Mtz-Enriquez, A.I., Carrión, G., Basurto-Cereceda, S., Pariona, N., 2021. The bifunctional role of copper nanoparticles in tomato: effective treatment for Fusarium wilt and plant growth promoter. Sci. Hortic. 277, 109810.

López-Vargas, E.R., Ortega-Ortíz, H., Cadenas-Pliego, G., de Alba Romenus, K., Cabrera de La Fuente, M., Benavides-Mendoza, A., Juárez-Maldonado, A., 2018. Foliar application of copper nanoparticles increases the fruit quality and the content of bioactive compounds in tomatoes. Appl. Sci. 8 (7), 1020.

Maluin, F.N., Hussein, M.Z., 2020. Chitosan-based agronanochemicals as a sustainable alternative in crop protection. Molecules 25 (7), 1611.

Mosa, K.A., El-Naggar, M., Ramamoorthy, K., Alawadhi, H., Elnaggar, A., Wartanian, S., Ibrahim, E., Hani, H., 2018. Copper nanoparticles induced genotoxicty, oxidative stress, and changes in superoxide DISMUTASE (SOD) gene expression in cucumber (*Cucumis sativus*) plants. Front. Plant Sci. 9, 872.

Mottaleb, S.A., Hassan, A.Z., El-Bahbohy, R., Mahmoud, A.W.M., 2021. Are copper nanoparticles toxic to all plants? A case study on onion (*Allium cepa* L.). Agronomy 11 (5), 1006.

Mukerjee, L.N., Srivastava, S.N., 1957. Bordeaux mixture and related compounds as emulsifiers. Colloid Polym. Science 150 (2), 148–151.

Muthukrishnan, S., Murugan, I., Selvaraj, M., 2019. Chitosan nanoparticles loaded with thiamine stimulate growth and enhances protection against wilt disease in Chickpea. Carbohydr. Polym. 212, 169–177.

Nuruzzaman, M.D., Rahman, M.M., Liu, Y., Naidu, R., 2016. Nanoencapsulation, nano-guard for pesticides: a new window for safe application. J. Agric. Food Chem. 64 (7), 1447–1483.

Ojha, N.K., Zyryanov, G.V., Majee, A., Charushin, V.N., Chupakhin, O.N., Santra, S., 2017. Copper nanoparticles as inexpensive and efficient catalyst: a valuable contribution in organic synthesis. Corros. Rev. 353, 1–57.

Pérez-Labrada, F., López-Vargas, E.R., Ortega-Ortiz, H., Cadenas-Pliego, G., Benavides-Mendoza, A., Juárez-Maldonado, A., 2019. Responses of tomato plants under saline stress to foliar application of copper nanoparticles. Plants 8 (6), 151.

Popp, J., Pető, K., Nagy, J., 2013. Pesticide productivity and food security. A review. Agron. Sustain. Dev 33, 243–255.

Qazi, G., Dar, F.A., 2020. Nano-agrochemicals: economic potential and future trends. In: Nanobiotechnology in Agriculture. Springer, Cham, pp. 185–193.

Rai, M., Ingle, A.P., Pandit, R., Paralikar, P., Shende, S., Gupta, I., Biswas, J.K., da Silva, S.S., 2018. Copper and copper nanoparticles: role in management of insect-pests and pathogenic microbes. Nanotechnol. Rev. 7 (4), 303–315.

Rawtani, D., Khatri, N., Tyagi, S., Pandey, G., 2018. Nanotechnology-based recent approaches for sensing and remediation of pesticides. J. Environ. Manag. 206, 749–762.

Rizo, J., Díaz, D., Reyes-Trejo, B., Arellano-Jiménez, M.J., 2020. Cu_2O nanoparticles for the degradation of methyl parathion. Beilstein J. Nanotechnol. 11 (1), 1546–1555.

Rubina, M.S., Vasil'kov, A.Y., Naumkin, A.V., Shtykova, E.V., Abramchuk, S.S., Alghuthaymi, M.A., Abd-Elsalam, K.A., 2017. Synthesis and characterization of chitosan–copper nanocomposites and their fungicidal activity against two sclerotia-forming plant pathogenic fungi. Journal of Nanostructure in Chemistry 7 (3), 249–258.

Sahithya, K., Das, D., Das, N., 2015. Effective removal of dichlorvos from aqueous solution using biopolymer modified MMT-CuO composites: equilibrium, kinetic and thermodynamic studies. J. Mol. Liq. 211, 821–830.

Sebastian, A., Nangia, A., Prasad, M.N.V., 2020. Advances in agrochemical remediation using nanoparticles. In: Agrochemicals Detection, Treatment and Remediation. Butterworth-Heinemann, pp. 465–485.

Shenashen, M., Derbalah, A., Hamza, A., Mohamed, A., El Safty, S., 2017. Antifungal activity of fabricated mesoporous alumina nanoparticles against root rot disease of tomato caused by *Fusarium oxysporum*. Pest Manag. Sci. 73 (6), 1121–1126.

Singh, H., Sharma, A., Bhardwaj, S.K., Arya, S.K., Bhardwaj, N., Khatri, M., 2021. Recent advances in the applications of nano-agrochemicals for sustainable agricultural development. Environ. Sci.: Process. Impacts 23 (2), 213–239.

Steinhauer, S., 2021. Gas sensors based on copper oxide nanomaterials: a review. Chemosensors 9 (3), 51.

Syuhada, N., Jahan, M.S., Khandaker, M.M., Nashriyah, M., Khairi, M., Nozulaidi, M., Razali, M.B., 2014. Application of copper increased corn yield through enhancing physiological functions. Aust. J. Basic Appl. Sci. 8 (16), 282–286.

Varympopi, A., Dimopoulou, A., Theologidis, I., Karamanidou, T., Kaldeli Kerou, A., Vlachou, A., Karfaridis, D., Papafotis, D., Hatzinikolaou, D.G., Tsouknidas, A., Skandalis, N., 2020. Bactericides based on copper nanoparticles restrain growth of important plant pathogens. Pathogens 9 (12), 1024.

Wang, L., Liu, Y., Liu, J., Zhang, Y., Zhang, X., Pan, H., 2016. The *Sclerotinia sclerotiorum* FoxE2 gene is required for apothecial development. Phytopathology 106 (5), 484–490.

Yang, J., Zhang, Y., Guo, J., Fang, Y., Pang, Z., He, J., 2020. Nearly monodisperse copper selenide nanoparticles for recognition, enrichment, and sensing of mercury ions. ACS Appl. Mater. Interfaces 12 (35), 39118–39126.

Yruela, I., 2009. Copper in plants: acquisition, transport and interactions. Funct. Plant Biol. 36, 409–430.

Yusefi-Tanha, E., Fallah, S., Rostamnejadi, A., Pokhrel, L.R., 2020. Root system architecture, copper uptake and tissue distribution in soybean (*Glycine max* (L.) Merr.) grown in copper oxide nanoparticle (CuONP)-amended soil and implications for human nutrition. Plants 9 (10), 1326.

Zabrieski, Z., Morrell, E., Hortin, J., Dimkpa, C., McLean, J., Britt, D., Anderson, A., 2015. Pesticidal activity of metal oxide nanoparticles on plant pathogenic isolates of Pythium. Ecotoxicology 24, 1305–1314.

Zhang, W., 2018. Global pesticide use: profile, trend, cost/benefit and more. Proc. Int. Acad. Ecol. Environ. Sci. 8, 1.

Zhang, H., Xia, Y., 2016. Ratiometry, wavelength, and intensity: triple signal readout for colorimetric sensing of mercury ions by plasmonic Cu2-xSe nanoparticles. ACS Sensors 1 (4), 384–391.

PART

1 Green synthesis

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CHAPTER

Green synthesis of copper-based nanoparticles using microbes

2

Michaela Olisha S. Lobregas and Drexel H. Camacho
Chemistry Department, De La Salle University, Manila, Philippines

1 Introduction

Technologies involving nano-sized (i.e., 10^{-9} m) materials have evolved elegantly from simple curiosity to various applications. The driving force behind this rapidly advancing field is the unique phenomena exhibited by the nanomaterials that enable the explorations for novel applications in industry, electronics, health, food, and agriculture (Hussain et al., 2016). Owing to the enhanced surface area-to-volume ratio, high surface energy, and quantum confinement, nanoparticles (NPs) exhibit unique optical, electronic, chemical, mechanical, and magnetic properties compared to their bulk material counterpart (Thakkar et al., 2010). Metallic NPs (MNPs) are particularly interesting as these have shown versatile applications in the food industry (Sanguansri and Augustin, 2006), medical diagnostics (Doria et al., 2012), antimicrobials (Bantang et al., 2021), health therapeutics (Zhang and Webster, 2009), antioxidants (Sytu and Camacho, 2018), wastewater treatment (Li et al., 2008), heavy-metal sensing (Lobregas et al., 2019), environmental remediation (Shan et al., 2009), agricultural production (Nair et al., 2010), and crop protection (Khot et al., 2012; Bergeson, 2010). Among the transition metals, interest is being shown to copper-based nanoparticles mainly because they are generally cheaper than the widely studied silver, gold, palladium, and platinum NPs making them readily scalable. Moreover, copper-based nanoparticles offer better physical and chemical stability over silver and can be mixed with polymers easily (Mallik et al., 2001). Copper-based nanoparticles offer unique properties that have been exploited for applications in electronics (Kruis et al., 1998), optical devices (Liu et al., 2002), nanocomposite coatings (Anyaogu et al., 2008), thermal transfer nanofluids (Eastman et al., 2001), catalysis (Gawande et al., 2016), lubrication (Tarasov et al., 2002), feed additive (Scott et al., 2018), and pollutant degradation (Rosbero and Camacho, 2017), among others.

The synthesis of copper-based NPs can be achieved by a physical process using laser ablation where colloidal and spherical copper nanoparticles (CuNPs) were produced from a copper plate in various solvents (Goncharova et al., 2019; Moniri et al., 2017; Muniz-Miranda et al., 2013; Tilaki et al., 2007). Magnetron-sputtering

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in cold buffer gas was also used as a liquid-free technique for the synthesis of CuNPs and copper oxide nanoparticles (CuONPs) (Kousal et al., 2018; Verma et al., 2015). Similarly, nanosphere lithography and alkaline etching were also applied to prepare CuNPs (Chan et al., 2007; Liu et al., 2006). These physical techniques, however, require the use of expensive instruments and consume excessive energy making it highly restrictive (Thakkar et al., 2010). The chemical process of synthesizing copper-based NPs employs organic solvents and harsh reducing agents such as sodium borohydride (Jin et al., 2008), hydrazine (Feng et al., 2015), sodium hydroxide (Galletti et al., 2013), and acotinic acid (Zhao et al., 2020) to reduce the Cu^{2+} from aqueous copper solutions to Cu^{0} that collectively forms into nanoparticles. Moreover, the chemical process requires stabilizing agents such as poly(vinylpyrrolidone), polyethylene glycol, and pluronic surfactants to obtain copper-based nanoparticles with controlled sizes (Dang et al., 2011; Lee et al., 2008; Park et al., 2007). Despite the unique properties and wide range of applications, the chemical approach to nanometal synthesis has received ethical criticisms since large-scale production poses toxicity problems, health hazards, and environmental issues. There is an emerging need to develop a sustainable and ecological approach to nanoparticle synthesis without the need for high energy and toxic chemicals.

Plant extract-assisted synthesis of nanoparticles is an eco-friendly, clean, and viable alternative to chemical and physical methods (Pal et al., 2019). This green process involves the use of marine and terrestrial plant extracts in the reduction of metal ions into zero-valent atoms, which form clusters of few atoms to form 1–100 nm-sized particles (Hussain et al., 2016). Various metabolites present in the extracts, such as flavonoids, alkaloids, phenolic acids, polyphenols, proteins, sugars, etc. facilitate the metal reduction process (Ahmad et al., 2010). These metabolites can also serve as a capping agent to the resulting MNPs allowing for the reduction and stabilization processes to be done in one-pot (Bantang et al., 2021). However, for aqueous systems, obtaining the metabolites from plants requires heat to extract the phytochemicals efficiently. Unfortunately, the heating process destroys the integrity of the chemical structure of compounds, which makes it difficult to determine whether the metal-reducing agent is natural or a by-product of the heating process. Since the metabolites present in the extracts vary, control in the uniformity of the particle size is difficult to achieve. The reduction process is also generally triggered by high temperatures to activate the metal-reducing agent (Rosbero and Camacho, 2017). The development of mild and reliable methods for the synthesis of nanomaterials with high control on the MNP size is highly desired.

The biosynthetic approach employing microorganisms has emerged as a mild, reliable, and scalable alternative to plant extracts (Pathak et al., 2019). Microbes (bacteria, fungi, actinomycetes) are good agents in the synthesis of MNPs and fit well with the global demand for green and sustainable chemistry (Alghuthaymi et al., 2015). Microbes are well known to evolve mechanisms to survive when placed in a harsh toxic metal environment by transforming the toxic metal ions into their corresponding nontoxic forms like metal sulfide/oxides (Neis, 1999). Moreover, some microorganisms, particularly target-specific metal ions, can be exploited for

the MNP synthesis. Bacteria are easy to culture under mild experimental conditions (pH, temperature) and have easy downstream processing to afford MNPs at a short generation time (Parikh et al., 2008). Fungi as biomanufacturing units for MNPs are promising because most fungal species are nonpathogenic. Reviews on microbially synthesized metal nanoparticles (Singh and Singh, 2019), biologically synthesized CuNPs, (Santhoshkumar et al., 2019), and green synthesis of CuONPs (Waris et al., 2021) are available elsewhere. This chapter discusses the recent developments in microbially synthesized copper-based NPs, their applications, and future directions.

2 Methods and mechanism of microbe-assisted synthesis of copper-based nanoparticles

The first step in synthesizing copper-based NPs using microbes is the choice of the microorganism. The microbes must be copper-resistant so that they can grow in the presence of copper ions and produce metabolites that can cause the reduction of Cu^{2+} into Cu^{0}. The copper-resistant microbe is determined by growing colonies in a medium, and a sterilized Cu solution is added, then incubated at a certain temperature and time. The presence of bacterial growth is observed and colonies that grow are considered copper-resistant (El-Saadony et al., 2020). Isolates are then recultured and properly identified by standard microbial techniques.

The microbe-assisted synthesis of MNPs generally involves three schemes: (1) culturing of microorganisms in media containing metal ions, (2) reduction of such metal ions into its elemental form through the action of biological compounds, and (3) capping of nanoparticles with the same biological components from the microorganisms. Thus, the conversion of metal ions into elemental form and the MNP stabilization are the primary roles of a microorganism in the biosynthesis of nanoparticles. The microbe, however, has to be isolated from a source and then grown in a culturing media to promote population growth. They are cultured in growth media such as Luria Bertani broth, MRS broth, citrate minimal medium, yeast peptone dextrose, and tryptone yeast extract broth done at neutral pH, either ambient temperature at neutral pH and either at ambient temperature (28–30°C) or at slightly warm temperature of 37°C. The culture media is then centrifugated to separate the cell-free extract and the cell biomass and both can be both used in MNP biosynthesis depending on two approaches: extracellular or intracellular. Fig. 1 shows the schematic diagram of the two approaches for microorganism-mediated synthesis of nanoparticles.

In extracellular synthesis, the cell-free extract is collected and added to the metal salt solution. The secreted biomolecules such as enzymes, proteins, amino acids, and polysaccharides in the extract act as both the reducing agent and the capping agent of the resulting MNPs. *Pseudomonas fluorescens* MAL2 was isolated from metal-contaminated soil samples and the cell-free culture was added to sterilized $CuSO_4$ solution to produce CuNPs (El-Saadony et al., 2020). Culture of endophytic actinomycetes *Streptomyces capillispiralis* Ca-1 isolated from the leaves of medicinal plant *Convolvulus arvensis* was mixed with $CuSO_4$ solution to obtain CuNPs (Hassan et al., 2018). Likewise, marine

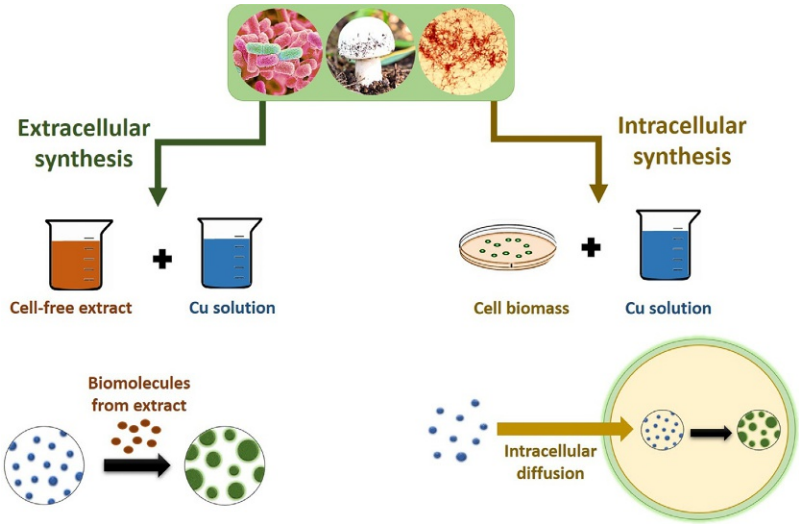

FIG. 1

Overview of the two methods of approach for the microbe-mediated synthesis of copper nanoparticles.

endophytic actinomycetes from seaweeds were isolated and cultured, and the culture supernatant was used for the synthesis of CuNPs (Rasool and Hemalatha, 2017). Isolates of actinobacteria *Streptomyces* sp. MHM38 from marine sediments were inoculated and the collected supernatant liquid was added to $CuSO_4$ solution to produce CuONPs nanoparticles (Hamed et al., 2020). Mycelium-free extracts of fungus *Stereum hirsutum* was mixed with different copper salt solutions such as $CuCl_2$, $Cu(NO_3)_2$, and $CuSO_4$ for the preparation of CuNPs and CuONPs (Cuevas et al., 2015). Supernatant bacteria culture of *Salmonella typhimurium* was obtained and reacted with $Cu(NO_3)_2$ to yield CuNPs (Ghorbani et al., 2015b). Generally, extracellular synthesis of nanoparticles has an easier purification process due to the direct utilization of the biomass-free filtrate extract resulting in a more convenient and cost-effective method (Singh and Singh, 2019).

In intracellular synthesis, the cellular mass is collected and resuspended in a metal salt solution. The metal ions are transported and diffused into the cell wall in which they are trapped inside the cellular system and are reduced through metabolic actions such as respiration and photosynthesis. In the preparation of CuNPs using dead biomass of the yeast *Rhodotorula mucilaginosa*, the copper ions from the Cu salt solution that diffused through the cell wall are reduced by the proteins and enzymes present on the cytoplasmic membrane and within the cytoplasm (Salvadori et al., 2014a). Also, dead biomass of fungi *Hypocrea lixii* and *Trichoderma koningiopsis* isolated from the copper-contaminated mine wastewater was used in powdered form and combined with Cu^{2+} stock solution to obtain CuNPs (Correa et al., 2014). Moreover, a bacterial colony of *Shewanella loihica* PV-4 was cultured in a medium containing Cu^{2+} ions for the synthesis of CuNPs (Lv et al., 2018). The facultative

anaerobic *S. loihica* used Cu^{2+} as an electron acceptor for its aerobic respiration and consequently produced CuNPs. When using *Shewanella oneidensis* MR-1, CuNPs were observed to be produced in the periplasm and cytoplasm (Kimber et al., 2018). Several mechanisms were proposed for such observation: (1) Cu^{2+} ions enter the periplasm and cytoplasm and a reductase reduces and precipitates the CuNPs; (2) the produced CuNPs are transported across the cytoplasmic membrane and facilitates membrane damage caused by Cu toxicity; and (3) Cu^{2+} is reduced to Cu^{+}, which are exported and subsequently disproportionated to form Cu^{0} and Cu^{2+} (Kimber et al., 2018). Moreover, particles nucleating inside the cellular membrane are limited and thus its size is smaller compared to particles produced within the cell walls as was observed in the extracellular approach (Narayanan and Sakthivel, 2010).

Both extracellular and intracellular processes are widely used in the preparation of copper-based nanoparticles affording a colloidal solution, which are subsequently subjected to purification and characterization. Despite the differences in the synthesis techniques, it is important to determine the elemental identity of nanoparticles and their morphological characteristics that will be the basis for the particles' application in various fields.

3 Microbe-assisted synthesis of copper-based nanoparticles

3.1 Bacteria

Bacteria are single-celled organisms that are very abundant in the environment and are capable of living in different harsh environmental conditions such as in high toxic metal concentrations. They are used widely in metallic nanoparticle synthesis because of their ability to reduce metal ions into their corresponding elemental form either intracellularly or extracellularly. Bacteria used in nanoparticle synthesis are mostly isolated from soil and wastewater because they are easy to culture and can be used in synthesis under mild conditions such as ambient temperature and neutral pH. It is advantageous in large-scale nanoparticle synthesis because it is biorenewable, widely available, low cost, and eco-friendly. They have been used to synthesize a wide variety of MNPs such as silver, gold, zinc oxide, titanium dioxide, cadmium selenide, and iron oxide (Fatemi et al., 2018; Jayaseelan et al., 2012; Khaleghi et al., 2019; Khan and Fulekar, 2016; Rostami et al., 2018; Siva Kumar et al., 2014; Ulloa et al., 2016; Khan et al., 2021; Naseer et al., 2022). Bacterial species used in the synthesis of such metal nanoparticles have also been used in the preparation of copper-based nanoparticles as summarized in Table 1.

Alcaligenes is a genus of Gram-negative, aerobic, rod-shaped, and bioflocculant-producing bacteria. The strain *Alcaligenis faecalis* HCB2 was used in the preparation of CuNPs, which was confirmed through UV-Vis, EDX, and XRD (Dlamini et al., 2019). Other elements and functional groups like amine and hydroxyl groups were also identified to be from the bioflocculants used in the synthesis.

Table 1 Different bacteria used in the synthesis of copper-based nanoparticles.

Particle	Name of organism	Gram classification	Particle size (nm)	References
CuNP	*Alcaligenis faecalis* HCB2	–	53	Dlamini et al. (2019)
CuNP	*Bacillus cereus*	+	11–33	Tiwari et al. (2016)
CuONP	*Bacillus* sp. FU4	+	2–41	Taran et al. (2017)
CuNP	*Enterococcus faecalis*	+	20–90	Chavan et al. (2014)
CuONP	*Escherichia coli*	–	10–40	Singh et al. (2010)
CuONP	*Escherichia coli*	–	5	Ghorbani et al. (2015a)
CuNP	*Escherichia* sp. SINT7	–	28.55	Noman et al. (2020b)
CuNP	*Halomonas elongata* IBRC-M 10214	–	56–73	Taran et al. (2016)
CuONP	*Halomonas elongata* IBRC-M 10214	–	57–79	Rad et al. (2018)
CuNP	*Klebsiella pneumoniae* SN35	–	19.0–47.47	Noman et al. (2020a)
CuONP	*Lactobacillus casei* subsp. *casei*	+	30–75	Kouhkan et al. (2020)
CuONP	*Morganella morganii*	–	13	Ghasemi et al. (2017)
CuNP	*Morganella morganii*	–	15–20	Shobha et al. (2014)
CuNP	*Morganella morganii* RP42 *Morganella psychrotolerans*	–	3–10	Ramanathan et al. (2011)
CuNP	*Morganella psychrotolerans*	–	4–60	Pantidos et al. (2018)
CuNP	*Morganella psychrotolerans*	–	15–20	Shobha et al. (2014)
CuONP	*Proteus mirabilis* 10B	–		Eltarahony et al. (2018)
CuNP	*Pseudomonas fluorescens*	–	5–25	Natesan et al. (2020)
CuNP	*Pseudomonas fluorescens*	–	49	Shantkriti and Rani (2014)
CuNP	*Pseudomonas fluorescens* MAL2	–	10–70	El-Saadony et al. (2020)

Table 1 Different bacteria used in the synthesis of copper-based nanoparticles—cont'd

Particle	Name of organism	Gram classification	Particle size (nm)	References
CuNP	*Pseudomonas stutzeri*	–	8–15	Varshney et al. (2010)
CuNP	*Pseudomonas stutzeri*	–	8–15	Shobha et al. (2014)
CuNP	*Salmonella typhimurium*	–	49	Ghorbani et al. (2015b)
CuONP	*Serratia* sp.	–	10–30	Hasan et al. (2008)
CuONP	*Shewanella indica*	–	400	Zarasvand and Rai (2016)
CuNP	*Shewanella loihica* PV-4	–	10–16	Lv et al. (2018)
CuNP	*Shewanella oneidensis*	–	20–40	Kimber et al. (2018)
CuSNP	*Shewanella oneidensis* MR-1	–	5	Zhou et al. (2016)
CuNP	*Shigella flexneri* SNT22	–	17.24–38.03	Noman et al. (2020c)

The *Bacillus* genus, a Gram-positive, aerobic, endospore-forming, rod-shaped bacteria, are abundant in nature and are highly present in the soil, water, and plant-based food products. In the work of Tiwari et al. (2016), *Bacillus cereus* isolated from copper mine was used to synthesize CuNPs that have a good antimicrobial property and has low toxicity against normal cell lines. CuONPs with sizes between 2 and 41 nm were synthesized from *Bacillus* sp. FU4 by the group of Taran et al. (2017) using an optimized method having $CuSO_4$ concentration, incubation time, and culturing time as the controllable factors. The Gram-positive bacterium *Enterococcus faecalis* can be found in the human gut and the gastrointestinal tract of other mammals and birds. It can also be found in soil and in water, which denotes their contamination with fecal matter. It shows a unique potential in the environment-friendly production of CuNPs as shown in the study of Chavan et al. (2014).

Escherichia, a genus of Gram-negative, anaerobic, rod-shaped bacteria, are commonly found in the gastrointestinal tract of mammals. Its common species, the *E. coli*, was used in the bioproduction of CuONPs with sizes ranging from 5 to 40 nm (Ghorbani et al., 2015a; Singh et al., 2010). Also, its native copper-resistant strain, the *Escherichia* sp. SINT, was used for the preparation of CuNPs that has high efficiency in the degradation of azo dyes of up to 100 mg L^{-1} concentration and has excellent potential in recycling textile effluents. *Halomonas elongate*, another rod-shaped, Gram-negative bacterium that is salt-tolerating naturally found in saline environments was also able to biosynthesize copper-based NPs. The strain *H. elongata* IBRC-M 10214 was used to synthesize spherical CuNPs and rectangular CuONPs

that have both antimicrobial properties against *E. coli* and *S. aureus* (Rad et al., 2018; Taran et al., 2016). Moreover, the Gram-negative *Klebsiella pneumoniae*, which is an anaerobic, lactose-fermenting, rod-shaped bacteria facilitated the synthesis of CuNPs. The strain *Klebsiella pneumoniae* SN35 was used to produce CuNPs that were employed to assess the physiological response of wheat in CuNP-treated, Cr-rich soil (Noman et al., 2020a).

The *Lactobacillus casei*, which is a Gram-positive, anaerobic, nonspore-forming, mesophilic bacteria that is found in the human gut, fermented dairy products, and fermented plant products have been used to synthesize copper-based NPs. CuONPs from *L. casei* were determined to have antimicrobial property against *P. aeruginosa* and *S. aureus*, and anticancer property against HT-29 and AGS cell lines (Kouhkan et al., 2020).

Morganella is a genus of Gram-negative, facultative, anaerobic, rod-shaped bacteria. It is a known silver-resistant bacteria that was used to produce AgNPs and was also found out to be effective in synthesizing CuNPs using *Morganella morganii* (Shobha et al., 2014), strains of *M. morganii* RP42, and *M. psychrotolerans* (Pantidos et al., 2018; Ramanathan et al., 2011; Shobha et al., 2014). CuONPs were also shown to be produced from *M. morganii* (Ghasemi et al., 2017). *Proteus mirabilis*, which is a Gram-negative, facultatively anaerobic, rod-shaped bacterium, was shown to produce CuONPs (Eltarahony et al., 2018). *Pseudomonas* is a genus of Gram-negative, nonspore-forming, thin, rod-shaped bacteria. *P. fluorescens* and *P. stutzeri* isolated from soils were used in synthesizing spherical CuNPs with sizes ranging from 5 to 70 nm (Natesan et al., 2020; El-Saadony et al., 2020; Varshney et al., 2010; Shobha et al., 2014). *Salmonella typhimurium* is a Gram-negative pathogenic, rod-shaped bacterium that can cause infections in humans and animals. Its supernatant culture was used for the preparation of CuNPs that was confirmed using UV-vis spectroscopy and characterized in terms of its size using DLS and SEM (Ghorbani et al., 2015b).

Serratia, a genus of Gram-negative, facultative, anaerobic, pathogenic, rod-shaped bacteria were shown to synthesize copper-based NPs. In the work of Hasan et al. (2008), *Serratia* sp. isolated from the midgut of a Cerambicid beetle called *Stibara* was used for the biosynthesis of CuONPs. Another genus of motile, rod-shaped, Gram-negative bacteria that is capable of copper-based NPs synthesis is *Shewanella,* which is mainly found in marine environments and harsh aquatic habitats with very low temperature and extremely high pressure. *Shewanella indica* isolated from the biofilm formed on the ship hull was used to synthesize CuONPs that inhibits the growth of sulfate-reducing bacterium *Desulfovibrio marinisediminis* (Zarasvand and Rai, 2016). The strain *Shewanella loihica* PV-4 was used to produce CuNPs with antimicrobial property against *E. coli* and showed potential as a disinfecting agent for drinking water. *Shewanella oneidensis* was also utilized for the preparation of CuNPs (Kimber et al., 2018) while the MR-1 strain was able to biosynthesize small copper sulfide nanoparticles with a uniform size of 5 nm (Zhou et al., 2016). *Shigella flexneri*, a diarrhea-causing Gram-negative bacteria in the genus Shigella, is a copper-resistant bacteria used to prepare biogenic CuNPs for the prevention of translocation of cadmium from soil to wheat plants (Noman et al., 2020c).

3.2 Fungi

The fungus is a kingdom of eukaryotic, nonmotile, heterotrophic, spore-forming organisms. Microorganisms such as yeasts, molds, mushrooms, and truffles are classified under kingdom fungi that usually inhabit a moist and warm environment. They are important in recycling the nutrients from dead and decayed matter, and they are also used in food such as in beer-brewing and bread-making. Fungi have also been used in the green synthesis of different MNPs such as silver, gold, titanium oxide, selenium oxide, silicon oxide, germanium oxide, gold oxide, and silver oxide (Fayaz et al., 2010; Loshchinina et al., 2018; Mishra et al., 2014; Mosallam et al., 2018; Rajakumar et al., 2012; Singh et al., 2013; Soliman et al., 2018; Osorio-Echavarría et al., 2021). Its potential as a green reagent for nanoparticle biosynthesis has also been applied in preparations of copper-based nanoparticles as listed in Table 2.

Agaricus bisporus, known as the white button mushroom, has hydroxyl and amide groups that can reduce copper ions to its nanoparticle form. Its aqueous extract was treated with copper nitrate solution to produce biogenic CuNPs that has antimicrobial property, antioxidant capacity, and cytotoxic effects (Sriramulu et al., 2020). The *Aspergillus* genus, a common pathogenic mold that exists in an asexual state but can reproduce and spread into different environments through spore formation, was able to biosynthesize copper-based NPs. The strain *Aspergillus fumigatus* Fresenius AUMC 13024 isolated from soil sample was used to prepare spherical CuONPs that are highly stable for at least 6 months under cold storage (Ghareib et al., 2019). The filamentous fungi, *Aspergillus versicolor* that gradually grows in food products and damp indoor environments, was used to synthesize small, stable, round to polygonal-shaped CuNPs with antifungal activity against rotting plant pathogens (Ammar et al., 2019). *Aspergillus flavus*, a known pathogen in cereal grains and legumes, has also been used in CuNP preparation (Saitawadekar and Kakde, 2020). On the other hand, CuONPs were produced from *Aspergillus terreus* (Mousa et al., 2020). *Botrytis cinerea*, a necrotrophic fungus that affects many plant species, notably wine grapes, afforded CuONPs (Kovačec et al., 2017)

In the work of Eftekhari et al. (2018), various copper-resistant fungi such as *Fusarium solani* and *Rhizopus oryzae* isolated from coppersmiths soil and copper plating wastewater, respectively, were used to produce hexahedron-shaped CuNPs with sizes varying from 17 to 29 nm. Novel endophytic fungi, *Hypocrea lixii* isolated from copper waste from mine, was utilized in the green synthesis of CuNPs, which afforded particle sizes of 15–35 nm (Correa et al., 2014; Salvadori et al., 2013).

Ureolytic fungi such as *Neurospora crassa*, *Pestalotiopsis* sp., *Myrothecium gramineum* were used for green synthesis of spherical copper carbonate nanoparticles with a minimum particle size of 10 nm and contains two different surfaces: a smooth surface with short mineral columns and a rough surface consisting of rod-shaped minerals (Li and Gadd, 2017).

Penicillium, a genus of blue or green molds has shown the capability to produce copper-based NPs. Cultures of three species of *Penicillium* sp. treated with $CuSO_4$ afforded CuNPs with varying sizes (Honary et al., 2012). The commonality of *Penicillium*, which is found almost everywhere—from the soil to decaying and

Table 2 Different fungal species used in the synthesis of copper-based nanoparticles.

Particle	Name of species	Particle size (nm)	Particle shape	References
CuNP	*Agaricus bisporus*	2–10	Spherical	Sriramulu et al. (2020)
CuNP	*Aspergillus flavus*	2–60	Spherical	Saitawadekar and Kakde (2020)
CuONP	*Aspergillus fumigatus*	6	Spherical	Ghareib et al. (2019)
CuONP	*Aspergillus terreus*	15.75	Spherical	Mousa et al. (2020)
CuNP	*Aspergillus versicolor*	23–82	Round to polygonal	Ammar et al. (2019)
CuONP	*Botrytis cinerea*	60–80	Irregular spherical	Kovačec et al. (2017)
CuNP	*Fusarium solani* CBS490.63 *Paecilomyces variotii* BAB-1547 *Rhizopus oryzae* JBM-56 *Aspergillus niger* sp.	17–29	Hexahedron	Eftekhari et al. (2018)
CuNP	*Hypocrea lixii* *Trichoderma koningiopsis*	15–35 70–95	Spherical	Correa et al. (2014)
CuNP	*Hypocrea lixii*	24.5	Spherical	Salvadori et al. (2013)
Cu carbonate NP	*Neurospora crassa* *Pestalotiopsis* sp. *Myrothecium gramineum*	At least 10 nm	Spherical	Li and Gadd (2017)
CuNP	*Penicillium aurantiogriseum* *Penicillium citrinum* *Penicillium waksmanii*	85–295	Spherical	Honary et al. (2012)
CuONP	*Penicillium chrysogenum*	9.70	Spherical	El-Batal et al. (2020)
CuNP	*Pleurotus ostreatus*	25–36	Irregular spherical	El-Batal et al. (2018)
CuNP	*Rhodotorula mucilaginosa*	10.5	Spherical	Salvadori et al. (2014b)
CuNP	*Stereum hirsutum*	5–20	Spherical	Cuevas et al. (2015)
CuONP	*Trichoderma asperellum*	10–190	Spherical	Saravanakumar et al. (2019)
CuNP	*Trichoderma atroviride*	5–25	Irregular spherical	Natesan et al. (2020)
CuNP	*Trichoderma koningiopsis*	87.5	Spherical	Salvadori et al. (2014a)

rotting plants and fruits, and even indoors like on the carpet, fabrics, etc., makes it easily accessible. Moreover, its role in the production of the modern antibiotic penicillin, makes it a well-studied fungus and mature technology ready for safe large-scale production. Recently, El-Batal et al. (2020) utilized *Penicillium chrysogenum* for the synthesis of CuONP with the aid of gamma rays to afford CuONPs where increasing gamma-ray doses has a direct proportion with CuONPs production up to 50.0 kGy while elevated doses decrease its production. Similarly, CuNPs were synthesized under the action of *Pleurotus ostreatus* (as a reducing and preserving means), through the influence of gamma irradiation (El-Batal et al., 2018).

The *Rhodotorula mucilaginosa* a saprophytic yeast that inhabits soil, water, and the air is known as a common airborne contaminant of skin, lungs, urine, and feces. In the work of Salvadori et al. (2014a), it was isolated from the water collected from a copper waste pond and was used for the intracellular biosynthesis of CuNPs. A common species of genus *Stereum*, *S. hirsutum* is known for its hard, thick, crusty appearance forming on dead wood. Aqueous culture extracts of *S. hirsutum* were utilized to produce spherical CuNPs with sizes ranging from 5 to 20 nm (Cuevas et al., 2015). The genus *Trichoderma*, a green, nonpathogenic fungus that inhabits the soil and decaying wood, was also able to synthesize copper-based NPs. *Trichoderma asperellum* and *Trichoderma atroviride*, known to be biocontrol agents of plant pathogens, were used to synthesize spherical CuONPs and CuNPs, respectively (Saravanakumar et al., 2019; Natesan et al., 2020).

3.3 Actinomycetes

An actinomycete is a group of Gram-positive, unicellular, anaerobic bacteria belonging to the order Actinomycetales. They are spore-forming, filament-shaped bacteria that are found primarily in soil and decomposing organic matter in soil. It has a branched growth pattern and has a slow growth rate compared to other bacteria and fungi. They are important in various soil processes like ammonium fixation, cellular tissue decomposition, and nitrogen fixation. They can be found mostly in terrestrial environments but can also be found in aquatic environments such as marine and freshwater locations. They are stable and polydisperse, making them an effective candidate for intracellular and extracellular metal nanoparticle synthesis. Terrestrial and marine actinomycetes used in green synthesis of copper-based nanoparticles are shown in Table 3.

Streptomyces, a genus of Actinobacteria that exists largely in soil and decaying vegetation notable for its earthy odor, are the commonly used actinomycetes species in nanoparticulate biosynthesis (Bukhari et al., 2021). They have been shown to synthesize CuNPs (Omran, 2020). The species *Streptomyces cyaneus* was able to promote the formation of CuONP (El-Batal et al., 2017). The strain *Streptomyces* sp. MHM38, which was isolated from marine sediment was used for the biosynthesis of CuONPs with antimicrobial, antioxidant, and hepatoprotective properties (Hamed et al., 2020; Bukhari et al., 2021).

Streptomyces capillispiralis Ca-1 isolated from medicinal plant *Convolvulus arvensis* were used to prepare spherical-mono-dispersed shaped CuNPs (Hassan et al., 2018). *Streptomyces zaomyceticus* Oc-5 and *Streptomyces pseudogriseolus* Acv-11

Table 3 Different actinomycete species used in the synthesis of copper-based nanoparticles.

Particle	Name of species	Particle size (nm)	Particle shape	References
CuNP	Marine actinomycetes from seaweeds	Furry clusters	Irregular clusters	Rasool and Hemalatha (2017)
CuNP	*Streptomyces*	91	Spherical	Omran (2020)
CuONP	*Streptomyces cyaneus*	29.8	Spherical	El-Batal et al. (2017)
CuONP	*Streptomyces* sp. MHM38	1.06 to 6.5	Spherical	Hamed et al. (2020)
CuONP	*Streptomyces* sp. MHM38	1.72–13.49	Spherical	Bukhari et al. (2021)
CuNP	*Streptomyces capillispiralis* Ca-1 isolated from healthy medicinal plant (*Convolvulus arvensis*)	3.6–59	Spherical	Hassan et al. (2018)
CuNP	*Streptomyces griseus*	5–25	Irregular spherical	Natesan et al. (2020)
CuONP	*Streptomyces zaomyceticus* Oc-5 *Streptomyces pseudogriseolus* Acv-11	78 and 80	Spherical	Hassan et al. (2019)
CuONP	VITBN4 isolate	61.7	Agglomerated clusters	Nabila and Kannabiran (2018)

from *Oxalis corniculata* L were utilized in the biosynthesis of CuONPs with an average size of 78 and 80 nm, respectively (Hassan et al., 2019). *Streptomyces griseus* isolated from Indian tea soils were also effective for the preparation of CuNPs with potential application in disease management of tea plantations (Natesan et al., 2020).

Marine actinomycetes isolated from seaweeds were used to synthesize a furry cluster of CuNPs with antimicrobial properties against human pathogens (Rasool and Hemalatha, 2017). Also, freshwater actinomycetes VITBN4 isolated from soil of lake bed were used to prepare clusters of CuONPs with an average particle size of 61.7 nm (Nabila and Kannabiran, 2018).

4 Characterization techniques

In CuNP studies, several characterization techniques are used to confirm the identity of copper and describe its morphological characteristics. Since the synthesis of CuNPs involves the reduction of Cu^{2+} ions to elemental Cu^{0}, it is important to detect the presence of the zero-valent metal in the final product. The formation

of nanoparticles can easily be confirmed using UV-Vis spectroscopy. As the metal nanoparticles are irradiated under the electromagnetic wave, the electric field causes the highly mobile electrons to consistently oscillate and form clusters of oscillations known as plasmons. The strong interaction between the plasmons and the visible light results in a phenomenon called surface plasmon resonance (SPR), which can be identified by a sharp peak in the absorption spectra. Generally, CuNPs shows an SPR band in the wavelength range of 540–650 nm (El-Saadony et al., 2020; Ghorbani et al., 2015b; Hassan et al., 2018; LewisOscar et al., 2015; Varshney et al., 2010), while CuONPs have broader SPR band range of 285–650 nm (Abboud et al., 2014; Ghareib et al., 2019; Hassan et al., 2019; Saravanakumar et al., 2019). In the same range also appears the SPR peak of cuprous oxide nanoparticles, which is usually formed in a mixture with CuONPs during synthesis (Abboud et al., 2014; Cuevas et al., 2015). SPR bands have a wide absorption range and can vary depending on different factors such as size, shape, monodispersity, capping agents, metal-dielectric functions, and medium environment including the composition, surface-absorbed species, and ligand-nanoparticle interactions (Honary et al., 2012; Varshney et al., 2010). Consequently, the broad absorption range of SPR peak results also in a variety of observed color of the solutions, which can vary from blue (Cuevas et al., 2015), green (El-Saadony et al., 2020; Ghareib et al., 2019), yellow (Varshney et al., 2010), orange (Ghorbani et al., 2015b), and up to brown (Hassan et al., 2018; Honary et al., 2012).

Whereas elemental analysis using energy dispersive X-ray (EDX) determines the presence of elements such as copper in the surface of NPs, it is the X-ray photoelectron spectroscopy (XPS) that confirms the presence of zero-valent copper (Cu^0) in the nanoparticles. XPS determines the binding energies of Cu $2p_{3/2}$ and Cu $2p_{1/2}$ at around 934 and 955 eV, respectively, which is uniquely attributed to the Cu 2p of Cu^0 (Lv et al., 2018). This technique can also be used for stability studies of CuNPs where copper is determined if it remained in elemental nature or oxidized to copper ions over a long storage period after production (Pantidos et al., 2018). X-ray diffraction (XRD) is used to verify the presence of naturally crystalline face-centered cubic structure of metallic copper having [111], [200], and [220] planes that are represented generally at around $2\theta = 43$, 51, and 74, respectively (Cuevas et al., 2015; Lv et al., 2018; Varshney et al., 2010). Similarly, the presence of other forms of copper nanoparticles such as cupric oxide (CuO) and cuprous oxide (Cu_2O) can also be detected through their characteristic diffraction peaks signifying their unique indices. The identity of the monoclinic CuO and cubic Cu_2O is confirmed through comparison of the diffraction peaks with the reported values in the Joint Committee on Powder Diffraction Standards (JCPDS) file numbers 45-0937 and 05-0667, respectively (Abboud et al., 2014; Cuevas et al., 2015). Sharp diffraction peaks denote the high crystalline structure of the copper nanoparticles (Ghareib et al., 2019) while the peak intensity ratios signify the proportion of the mixed phases (Abboud et al., 2014). Moreover, particle size can be calculated using the Debye-Scherrer equation:

$$D = \frac{K\lambda}{B\cos\theta}$$

where D is the particle size, K is the Scherrer's constant also referred to as the crystallite-shape factor, λ is the wavelength of the X-ray radiation source, B is the width of the XRD peak at half height expressed in radians, and θ is the Bragg angle (Holzwarth and Gibson, 2011).

In addition, determining the morphological characteristics such as the size and shape of nanoparticles is another fundamental part of nanoparticle study as it is related to stability that can affect the performance of the nanoparticles in a solution. Imaging techniques like scanning electron microscopy (SEM) and transmission electron microscopy (TEM) are used to determine the size and the shape as well as evaluate the agglomeration and size distribution of the nanoparticles. Copper-based nanoparticles are commonly observed as spherical but vary in size depending on different factors and conditions in synthesis. Moreover, imaging analysis is combined with elemental analysis for the simultaneous determination of the elements present in a focused point of the nanoparticle. For example, SEM-EDX is used to determine the amount of elemental copper present in an image of a copper nanoparticle (Dlamini et al., 2019; Nabila and Kannabiran, 2018). Similarly, imaging combined with crystallography like the TEM with Selected Area Electron Diffraction (SAED) is used to show the Scherrer ring patterns associated with the FCC lattice of copper from a high-resolution TEM image of copper nanoparticles (Lv et al., 2018; Nabila and Kannabiran, 2018). Atomic force microscopy is also an imaging technique that can be used to determine the topographic structure and provide additional supporting data to the spherical shape and smooth surface of copper-based nanoparticles shown in its SEM images (Honary et al., 2012).

Dynamic light scattering (DLS) is another technique to determine the particle size distribution, polydispersity index (PDI), and zeta potential. The particle size is measured as a hydrodynamic diameter and assumes a spherical form since the nanoparticle interacts with the solvent. A uniform size distribution has a PDI value between 0.01 and 0.7, while a value greater than 0.7 means a very broad size distribution (Honary et al., 2012). The zeta potential is another characterization to assess the stability of nanoparticles as determined from its surface charge. Zeta potential values greater than + 30 mV or less than − 30 mV are considered stable and have less agglomeration tendency resulting in the long-term stability of copper nanoparticles (El-Saadony et al., 2020; Składanowski et al., 2017).

Determination of functional groups on the nanoparticle surface using FTIR is also an essential technique to verify the presence of hydroxyl, carbonyl, and amino groups from the biological source used in the biosynthesis. In the study of Abboud et al. (2014), they compared the FTIR spectra of *B. bifurcata* extract with that of the CuO nanoparticle prepared from biosynthesis using the same plant extract. It was confirmed that the diterpenoids in the plant extract were able to act both as a reducing and stabilizing agent as evident in the decrease in the intensity of the aliphatic C−H peak and the disappearance of the C=O stretching vibration peak associated with α, β-unsaturated ketone. Additionally, peaks denoting the metal-oxygen vibration are identified in FTIR spectra and can also be used to support the presence of CuO nanoparticles (Ghareib et al., 2019; Nabila and Kannabiran, 2018).

Different biological agents and preparation methods used in the biological synthesis of copper-based nanoparticles produce their nanoparticles with unique characteristics and properties. Thus, the use of various characterization techniques is vital to differentiate the resulting copper-based nanoparticles and identify their best attributes suitable for potential applications.

5 Factors affecting the microbe-assisted synthesis of copper-based nanoparticles

The size and stability of nanoparticles are greatly influenced by different factors in syntheses such as salt concentration, pH, temperature, and reaction time. Determining the optimized parameters is important to obtain controlled and uniform particle size, which has a huge impact on the stability of the nanoparticles and their potential applications in different fields.

5.1 Concentration of metal ions

$CuSO_4$ is a common copper salt used in the synthesis of copper-based nanoparticles. Salt concentration determines the amount of Cu^{2+} ions available for reduction to Cu^0. $CuSO_4$ concentration was identified as the most contributing factor in controlling the formation of CuONPs as determined using the Taguchi method (Rad et al., 2018). In the study of Hasan et al. (2008), different concentrations of $CuSO_4$ ranging from 1.0 to 10 mM were used to synthesize CuNPs and CuONPs from cultures of *Serratia* spp. bacteria and it was determined that the production of nanoparticles was maximum at 5.0 mM $CuSO_4$ as evaluated through the absorption spectra of the resulting nanoparticle solution. At a higher concentration, a broad absorption peak was observed due to the overlapping spectra of copper oxide and the presence of residual $CuSO_4$ (Hasan et al., 2008). Also, in a *K. pneumonia* SN35 bacteria-mediated CuNP synthesis, a larger $CuSO_4$ concentration range from 0.5 to 15 mM was utilized. It was identified similarly that 5.0 mM was the suitable concentration to produce the highest amount of CuNPs (Noman et al., 2020a). In studies using 5.0 mM $CuSO_4$, bacteria-mediated synthesis produced spherical nanoparticles with a wider size range of 4.0–70 nm (El-Saadony et al., 2020; Pantidos et al., 2018) while fungi-mediated synthesis resulted in hexahedron nanoparticles with a smaller size range of 17–29 nm (Eftekhari et al., 2018).

5.2 pH

The pH of the reaction mixture is another important factor in nanoparticle synthesis as it affects the size and dispersity as well as the duration of particle formation. In the synthesis of copper-based nanoparticles from a mixture containing mycelium-free extract of *S. hirsutum* and $CuCl_2$ solution, it was determined that the absorbance peak of the formed nanoparticles shifted from 670 nm at pH 5.0 to 620 nm at pH 7.0 and

9.0 (Cuevas et al., 2015). It was also determined that at higher pH, the formation of CuNPs was faster, and thus, pH 9.0 was used as the optimized pH for the synthesis of monodispersed and spherical CuNPs with a size range from 5.0 to 20 nm. Regrowth of nanoparticles through resuspension in buffers with different pH has also a significant effect on particle size. Ultracentrifugation followed by resuspension of nanoparticles in different buffers is a purification technique employed by Pantidos et al. (2018) in which copper nanoparticles produced from *M. psychotolerans* were resuspended in buffers of pH 6.5 and 7.5 and resulted in the formation of uniform, highly dispersed particles with approximate diameters of 200 and 100 nm, respectively, which were both larger than the original nanoparticles that ranged in size from 4.0 to 60 nm (Pantidos et al., 2018). Likewise, the copper absorption of dead biomass of *R. mucilaginosa* was observed at different pH from 2.0 to 6.0 and its maximum copper absorption was determined at pH 5.0 in which more negatively charged ligands were exposed and thus more attraction sites were available for Cu^{2+} ions and consequently, more nanoparticles were formed (Salvadori et al., 2014a).

5.3 Reaction temperature

Green synthesis of nanoparticles has the advantage of being a low-energy and low-cost preparation technique due to its efficiency to be utilized at ambient temperature. Basically, it involves either ambient temperature or a slightly warm temperature that is required for culturing microorganisms, but the general reaction condition only involves a minimum room temperature to produce spherical, stable, and monodispersed nanoparticles. A high temperature is not suitable in microorganism-mediated synthesis due to the degradation of biological materials in the reaction mixture, which resulted in a decrease in bioreduction activity (El-Saadony et al., 2020). In the study of Varshney et al. (2010), *P. stutzeri* were cultured at 37°C prior to its reaction with $CuSO_4$ solution at room temperature to produce uniformed-sized CuNPs with a size range of 8.0–15 nm. In other cases, the same ambient temperature could be used for both the incubation of microorganisms and the reaction with a copper salt. In the preparation of CuONPs from *E. coli*, 28°C was applied as incubation temperature for bacterial cell growth and in its reaction with $CuSO_4$ to form quasispherical nanoparticles ranging from 10 to 40 nm in size (Singh et al., 2010). Similarly, in the synthesis of CuONPs from *D. marinisediminis* bacteria, the same temperature of 27°C was used in both bacterial incubation and reaction with copper salt that resulted in larger particles with an average diameter of 400 nm (Zarasvand and Rai, 2016).

5.4 Reaction time

Reaction time is also a contributing factor in nanoparticle synthesis that should be considered for the optimization of reaction parameters. Generally, a shorter reaction time results in the formation of a smaller number of nanoparticles while a longer reaction time resulted in particle aggregation. In the synthesis of CuNPs from *P. fluorescens* at different reaction times (30, 60, 90, 120, 150, and 180 min),

the formation of nanoparticles was determined through its absorption peak at 610 nm at which a gradual increase in the absorbance was observed at particles produced from 30 to 90 min and a sudden decline in the absorbance was observed for the particles produced at 120 min onwards (El-Saadony et al., 2020). A similar observation was also noted in the preparation of CuNPs from *M. psychotolerans*, which was observed every day for 5 days and eventually determined that 3 days was already enough to produce a suitable amount of CuNPs (Pantidos et al., 2018).

6 Applications of microbe-synthesized Cu-based nanoparticles

Metal-based nanoparticles have been demonstrated to have an expansive range of applications such as in biomedical, catalysis, and electronics fields (Javani et al., 2015; Khaleghi et al., 2019; Mishra et al., 2014; Mosallam et al., 2018; Soliman et al., 2018; Taran et al., 2018; Ulloa et al., 2016). Similarly, copper-based nanoparticles produced from microorganisms have also shown numerous functions that make them as useful as the nanoparticles synthesized from other preparation techniques. Fig. 2 illustrates the different fields of application of microbe-synthesized copper nanoparticles.

6.1 Antimicrobial agent

Antibacterial properties of metal-based nanoparticles are well known. This is because metal nanoparticles have an elevated surface-volume ratio, tiny size, and elevated dispersion characteristics that enable them to interact with microbial surfaces. Similarly, CuNPs and CuONPs have shown antibacterial efficacies against Gram-positive and Gram-negative bacteria (Abboud et al., 2014; Chavan et al., 2014; Nabila and Kannabiran, 2018; Rad et al., 2018). The inhibitory action of CuONPs is associated

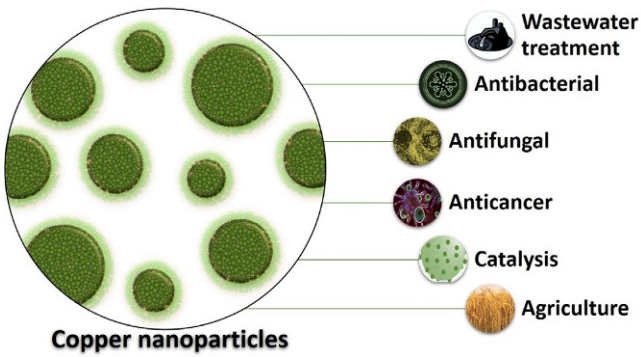

FIG. 2

Summary of the applications of copper nanoparticles.

with an inactivated surface protein responsible for transporting material across cytoplasmic membranes and destroying selective permeability (Espirito Santo et al., 2008). CuNPs were determined to be a stable and robust antibacterial agent that can be safely used in drinking water purification (Lv et al., 2018). Moreover, it can also be used as a textile coating to obtain an antibacterial fabric (Taran et al., 2016). Copper nanoparticles can also be used as an antifungal agent against plant rotting pathogens like *F. oxysporum* and *P. parasitica*. Its inhibitory effect was enhanced by coating it with gelatin, which served as protection against nanoparticle oxidation resulting in a well-dispersed particle that was stable for up to 6 months. Maintaining the small-sized nanoparticles is important for the particles to diffuse into the cell walls of pathogens and disrupt their DNA amplification, and interrupt the sporulation of fungal pathogens that eventually result in their growth inhibition (Ammar et al., 2019).

6.2 Wastewater treatment

The reaction between microorganisms and copper solutions during the production of copper-based nanoparticles have already shown potential for a green and low-cost process in treating copper-contaminated wastewater (Salvadori et al., 2014b). Moreover, it is also capable of dye degradation and can be used for industrial wastewater treatment. CuNPs produced from *K. pneumoniae* has effectively decolorized 100 mg L^{-1} of azo dyes such as Congo red, malachite green, direct blue-1, and reactive black-5 with degradation percentages of 83.90%, 31.08%, 62.32%, and 76.84%, respectively, after 5 h of sunlight exposure (Noman et al., 2020a). Similarly, CuONPs from *A. fumigatus* degrades methylene blue dye with a degradation percentage of 97% after 200 min of sunlight exposure (Ghareib et al., 2019). Aside from dyes, copper-based nanoparticles can also be used as heavy metal adsorbents like Cr^{6+}, which was effectively adsorbed by copper sulfide nanocrystals from *S. oneidensis* (Xiao et al., 2017).

6.3 Catalysis

Nanoparticles have excellent catalytic properties due to their nanometer size that gives a high surface-to-volume ratio and chemical capability. CuNPs reduced by *S. oneidensis* was determined to have good catalytic activity for azide-alkyne cycloaddition reaction for the synthesis of 1,2,3-triazole derivatives (Kimber et al., 2018). Likewise, the dye-degradation ability of copper-based nanoparticles was due to the solar-activated catalytic property of copper nanoparticles in which electron-hole pairs are produced as the valence electrons are excited to the conduction band (Ghareib et al., 2019).

6.4 Agriculture

The utilization of green-synthesized nanoparticles is a promising and eco-friendly approach in addressing problems and managing productivity in agriculture. The characteristic of *K. pneumoniae*-synthesized CuNPs as an effective chromium-caused stress

reliever of wheat plants was associated with the reduced reactive oxygen species generation, improved cell oxidative damage repair, and enhanced antioxidative defense mechanism of the copper nanoparticle-treated wheat plant (Noman et al., 2020a). Similarly, *S. flexneri*-synthesized CuNPs reduced the translocation of cadmium from soil to wheat plants by immobilizing Cd onto its surface resulting in alleviated Cd-caused stress in plants (Noman et al., 2020c). Moreover, CuNPs from *P. fluorescens* was also used as a green and low-cost biocontrol agent against stored-grain pests like the red flour beetle *Tribolium castaneum* (El-Saadony et al., 2020).

7 Conclusion and future outlook

Copper-based nanoparticles are gaining research interest due to their low cost, better physical and chemical stability, and good polymer compatibility. Its green preparation using microorganisms such as bacteria, fungi, and actinomycetes is a promising approach for eco-friendly and sustainable research and development. Optimization of different synthesis factors such as pH, reaction time, temperature, and salt concentration is necessary as it has shown a great impact on the size, shape, and stability of nanoparticles. Its antibacterial, antifungal, and anticancer characteristics make it highly potential for utilization in fields like biomedical, wastewater treatment, and agriculture.

In the large-scale preparation of Cu-based NPs from microbes, a critical aspect involves thorough risk analysis since a huge amount of pathogenic bacterial and fungal strains might impose hazards during nanoparticle production. Although numerous studies have already demonstrated the laboratory protocols and conditions needed for the safe synthesis, it would be considered advantageous to engage additional larger scope of microbe-synthesized copper-based nanoparticles to provide more safe assurance to the community. The possible contamination and toxicity risks in humans and in the environment should be thoroughly studied.

Many aspects of microbe-assisted CuNP preparation are still needed for further explorations. It is essential to establish the complex mechanisms involved in the bioreduction of copper ions to metallic copper through the action of several compounds from the microbes. Systematic investigations on the exact metabolite responsible for the facile reduction of the copper ions at mild conditions is worth pursuing as it would open a new venture into its synthesis toward a microbe-free method in preparing CuNPs at mild conditions. Understanding the exact mechanism of synthesis could open novel preparation techniques that could usher in developing methods for large-scale preparation.

The investigation on coreduction of two or more metals using a single microbe is worth pursuing as the multimetal nanoparticle can offer new morphologies, novel chemistries, and fresh applications. Varying the concentrations of the metal ions and the reaction conditions can give insights on the preference of the microbe to reduce specific ions in the presence of two or more metal cations. Moreover, performing

advanced techniques like TEM-EDX elemental mapping can distinguish the distribution map of the multimetal distribution in the nanoparticle.

A design of metal incubation techniques can be implemented to carry out a core-shell type bi-metal nanoparticle using two kinds of microbes. One microbe can synthesize specific metal such as copper, then followed by incubation of the CuNP in another microbe that can biosynthesize silver or gold NPs. This way, the cheaper Cu serves as the inner core while the expensive Ag or Au can serve as a thin layer of the outer shell. The unique chemistries of these bi-metallic NPs should offer interesting activities widening the application scopes.

The systematic investigation on the interaction of the NPs with the capping and stabilizing agents from the microbe is highly recommended. It would be worth investigating the metabolite profile from the microbe responsible for the stability of the NPs. The identification of the specific interactions will provide insights into the understanding of the long-term stability of the NPs. Moreover, the characterization of the NP-metabolite interaction can also lead to the NP-assisted separation of the metabolite from the crude microbe soup, which can be removed from the NP, characterized, and tested for new applications. The separation of metabolites from the crude extract is a tedious process. This technique can provide a fast and easy way to isolate metabolites produced from microbes.

Investigations into the long-term stability of the CuNPs by embedding them in a matrix for future use are worth pursuing. NPs are beset with coagulation problems when dried or stored in an aqueous solution. It would be interesting to keep the NPs in a matrix that can be stored for a long time then released by dissolving in water for point-of-use applications such as sensing or remediation applications. It would also lead to slow-release applications particularly for agricultural applications where the CuNPs combat plant pathogens by designing the matrix to degrade slowly upon the action of water or sunlight. While there is a vast advancement in the understanding of the nanoparticles and their applications, further studies and improvements are still needed to address the practical utilization of microbe-assisted copper-based nanoparticles.

References

Abboud, Y., Saffaj, T., Chagraoui, A., El Bouari, A., Brouzi, K., Tanane, O., Ihssane, B., 2014. Biosynthesis, characterization and antimicrobial activity of copper oxide nanoparticles (CONPs) produced using brown alga extract (*Bifurcaria bifurcata*). Appl. Nanosci. 4, 571–576.

Ahmad, N., Sharma, S., Alam, M.K., Singh, V.N., Shamsi, S.F., Mehta, B.R., Fatma, A., 2010. Rapid synthesis of silver nanoparticles using dried medicinal plant of basil. Colloids Surf. B 81, 81–86.

Alghuthaymi, M.A., Almoammar, H., Rai, M., Said-Galiev, E., Abd-Elsalam, K.A., 2015. Myconanoparticles: synthesis and their role in phytopathogens management. Biotechnol. Biotechnol. Equip. 29, 221–236.

Ammar, H.A., Rabie, G.H., Mohamed, E., 2019. Novel fabrication of gelatin-encapsulated copper nanoparticles using *Aspergillus versicolor* and their application in controlling of rotting plant pathogens. Bioprocess Biosyst. Eng. 42, 1947–1961.

Anyaogu, K.C., Fedorov, A.V., Neckers, D.C., 2008. Synthesis, characterization, and antifouling potential of functionalized copper nanoparticles. Langmuir 24, 4340–4346.

Bantang, J.P.O., Bigol, U.P., Camacho, D.H., 2021. Gel and film composites of silver nanoparticles in κ-, ι-, and λ-carrageenans: one-pot synthesis, characterization, and bioactivities. BioNanoScience 11, 53–66.

Bergeson, L.L., 2010. Nanosilver pesticide products: what does the future hold? Environ. Qual. Manag. 19, 73–82.

Bukhari, S.I., Hamed, M.M., Al-Agamy, M.H., Gazwi, H.S.S., Radwan, H.H., Youssif, A.M., 2021. Biosynthesis of copper oxide nanoparticles using *Streptomyces* MHM38 and its biological applications. J. Nanomater. 2021, 6693302.

Chan, G.H., Zhao, J., Hicks, E.M., Schatz, G.C., Van Duyne, R.P., 2007. Plasmonic properties of copper nanoparticles fabricated by nanosphere lithography. Nano Lett. 7, 1947–1952.

Chavan, D., Jahanara, K., Kelmani, C.R., 2014. Biosynthesis and characterization of copper nanoparticles from *Enterococcus faecalis*. Int. J. Pharma Bio Sci. 5, 204–211.

Correa, B., Nascimento, C.A.O., Salvadori, M.R., 2014. Process for obtaining copper nanoparticles from a fungus selected between *Hypocrea lixii* and *Trichoderma koningiopsis* and use of fungi selected between *Hypocrea lixii* and *Trichoderma koningiopsis* in bioremediation of wastewater and production of copper nanoparticles. United States patent US20140363871A1.

Cuevas, R., Durán, N., Diez, M.C., Tortella, G.R., Rubilar, O., 2015. Extracellular biosynthesis of copper and copper oxide nanoparticles by *Stereum hirsutum*, a native white-rot fungus from Chilean forests. J. Nanomater. 2015, 789089.

Dang, T.M.D., Le, T.T.T., Fribourg-Blanc, E., Dang, M.C., 2011. Synthesis and optical properties of copper nanoparticles prepared by a chemical reduction method. Adv. Nat. Sci. Nanosci. Nanotechnol. 2, 015009.

Dlamini, N.G., Basson, A.K., Pullabhotla, V.S.R.R., 2019. Biosynthesis and characterization of copper nanoparticles using a bioflocculant extracted from *Alcaligenis faecalis* HCB2. Adv. Sci. Eng. Med. 11, 1064–1070.

Doria, G., Conde, J., Veigas, B., Giestas, L., Almeida, C., Assuncao, M., Rosa, J., Baptista, P.V., 2012. Noble metal nanoparticles for biosensing applications. Sensors 12, 1657–1687.

Eastman, J.A., Choi, S.U.S., Li, S., Yu, W., Thompson, L.J., 2001. Anomalously increased effective thermal conductivities of ethylene glycol-based nanofluids containing copper nanoparticles. Appl. Phys. Lett. 78, 718–720.

Eftekhari, R., Doudi, M., Amiri, G., 2018. Biosynthesis and characterization of copper nanoparticles constructed by fungi isolated from several industrial centers in Isfahan. Int. J. Mol. Clin. Microbiol. 8, 1006–1015.

El-Batal, A.I., El-Sayyad, G.S., El-Ghamery, A., Gobara, M., 2017. Response surface methodology optimization of melanin production by *Streptomyces cyaneus* and synthesis of copper oxide nanoparticles using gamma radiation. J. Clust. Sci. 28 (3), 1083–1112.

El-Batal, A.I., Al-Hazmi, N.E., Mosallam, F.M., El-Sayyad, G.S., 2018. Biogenic synthesis of copper nanoparticles by natural polysaccharides and *Pleurotus ostreatus* fermented fenugreek using gamma rays with antioxidant and antimicrobial potential towards some wound pathogens. Microb. Pathog. 1 (118), 159–169.

El-Batal, A.I., El-Sayyad, G.S., Mosallam, F.M., Fathy, R.M., 2020. *Penicillium chrysogenum*-mediated mycogenic synthesis of copper oxide nanoparticles using gamma rays for in vitro antimicrobial activity against some plant pathogens. J. Clust. Sci. 31 (1), 79–90.

El-Saadony, M.T., Abd El-Hack, M.E., Taha, A.E., Fouda, M.M.G., Ajarem, J.S., Maodaa, S.N., Allam, A.A., Elshaer, N., 2020. Ecofriendly synthesis and insecticidal application of copper nanoparticles against the storage pest *Tribolium castaneum*. Nanomaterials 10, 587.

Eltarahony, M., Zaki, S., Abd-El-Haleem, D., 2018. Concurrent synthesis of zero- and one-dimensional, spherical, rod-, needle-, and wire-shaped CuO nanoparticles by *Proteus mirabilis* 10B. J. Nanomater. 1, 2018.

Espirito Santo, C., Taudte, N., Nies, D.H., Grass, G., 2008. Contribution of copper ion resistance to survival of *Escherichia coli* on metallic copper surfaces. Appl. Environ. Microbiol. 74 (4), 977–986.

Fatemi, M., Mollania, N., Momeni-Moghaddam, M., Sadeghifar, F., 2018. Extracellular biosynthesis of magnetic iron oxide nanoparticles by *Bacillus cereus* strain HMH1: characterization and in vitro cytotoxicity analysis on MCF-7 and 3T3 cell lines. J. Biotechnol. 270, 1–11.

Fayaz, A.M., Balaji, K., Girilal, M., Yadav, R., Kalaichelvan, P.T., Venketesan, R., 2010. Biogenic synthesis of silver nanoparticles and their synergistic effect with antibiotics: a study against Gram-positive and Gram-negative bacteria. Nanomed. Nanotechnol. Biol. Med. 6, 103–109.

Feng, Y., Wang, A., Yin, H., Yan, X., Shen, L., 2015. Reduction of 3-nitro-4-methoxy-acetylaniline to 3-amino-4-methoxy-acetylaniline catalyzed by metallic Cu nanoparticles at low reaction temperature. Chem. Eng. J. 262, 427–435.

Galletti, A.M.R., Antonetti, C., Marracci, M., Piccinelli, F., Tellini, B., 2013. Novel microwave synthesis of Cu nanoparticles in the absence of any stabilizing agent and their antibacterial and antistatic applications. Appl. Surf. Sci. 280, 610–618.

Gawande, M.B., Goswami, A., Felpin, F.X., Asefa, T., Huang, X., Silva, R., Zou, X., Zboril, R., Varma, R.S., 2016. Cu and Cu-based nanoparticles: synthesis and applications in catalysis. Chem. Rev. 116, 3722–3811.

Ghareib, M., Abdallah, W.E., Abu-Tahon, M., Tallima, A., 2019. Biosynthesis of copper oxide nanoparticles using the preformed biomass of *Aspergillus fumigatus* and their antibacterial and photocatalytic activities. Digest J. Nanomater. Biostruct. 14, 291–303.

Ghasemi, N., Jamali-Sheini, F., Zekavati, R., 2017. CuO and Ag/CuO nanoparticles: biosynthesis and antibacterial properties. Mater. Lett. 1 (196), 78–82.

Ghorbani, H.R., Fazeli, I., Fallahi, A.A., 2015a. Biosynthesis of copper oxide nanoparticles using extract of *E. coli*. Orient. J. Chem. 31, 515–517.

Ghorbani, H.R., Mehr, F.P., Poor, A.K., 2015b. Extracellular synthesis of copper nanoparticles using culture supernatants of *Salmonella typhimurium*. Orient. J. Chem. 31, 527–529.

Goncharova, D.A., Kharlamova, T.S., Lapin, I.N., Svetlichnyi, V.A., 2019. Chemical and morphological evolution of copper nanoparticles obtained by pulsed laser ablation in liquid. J. Phys. Chem. C 123, 21731–21742.

Hamed, M., Gazwi, H.S.S., Youssif, A.M., 2020. Biosynthesis of copper oxide nanoparticles by marine Streptomyces MHM38 and their preventive efficacy against paracetamol-inducing hepatic damage of albino rats. Res. Sq. https://doi.org/10.21203/rs.3.rs-37392/v1.

Hasan, S.S., Singh, S., Parikh, R.Y., Dharne, M.S., Patole, M.S., Prasad, B.L.V., Shouche, Y.S., 2008. Bacterial synthesis of copper/copper oxide nanoparticles. J. Nanosci. Nanotechnol. 8, 3191–3196.

Hassan, S.E.D., Salem, S.S., Fouda, A., Awad, M.A., El-Gamal, M.S., Abdo, A.M., 2018. New approach for antimicrobial activity and bio-control of various pathogens by biosynthesized copper nanoparticles using endophytic actinomycetes. J. Radiat. Res. Appl. Sci. 11, 262–270.

Hassan, S.E.D., Fouda, A., Radwan, A.A., Salem, S.S., Barghoth, M.G., Awad, M.A., Abdo, A.M., El-Gamal, M.S., 2019. Endophytic actinomycetes *Streptomyces* spp mediated biosynthesis of copper oxide nanoparticles as a promising tool for biotechnological applications. J. Biol. Inorg. Chem. 24, 377–393.

Holzwarth, U., Gibson, N., 2011. The Scherrer equation versus the 'Debye-Scherrer equation'. Nat. Nanotechnol. 6, 534.

Honary, S., Barabadi, H., Gharaei-Fathabad, E., Naghibi, F., 2012. Green synthesis of copper oxide nanoparticles using *Penicillium aurantiogriseum*, *Penicillium citrinum* and *Penicillium waksmanii*. Digest J. Nanomater. Biostruct. 7, 999–1005.

Hussain, I., Singh, N.B., Singh, A., Singh, H., Singh, S.C., 2016. Green synthesis of nanoparticles and its potential application. Biotechnol. Lett. 38, 545–560.

Javani, S., Marín, I., Amils, R., Abad, J.P., 2015. Four psychrophilic bacteria from Antarctica extracellularly biosynthesize at low temperature highly stable silver nanoparticles with outstanding antimicrobial activity. Colloids Surf. A Physicochem. Eng. Asp. 483, 60–69.

Jayaseelan, C., Rahuman, A.A., Kirthi, A.V., Marimuthu, S., Santhoshkumar, T., Bagavan, A., Gaurav, K., Karthik, L., Rao, K.V.B., 2012. Novel microbial route to synthesize ZnO nanoparticles using *Aeromonas hydrophila* and their activity against pathogenic bacteria and fungi. Spectrochim. Acta A 90, 78–84.

Jin, L., Yang, S.P., Tian, Q.W., Wu, H.X., Cai, Y.J., 2008. Preparation and characterization of copper metal nanoparticles using dendrimers as protectively colloids. Mater. Chem. Phys. 112, 977–983.

Khaleghi, M., Khorrami, S., Ravan, H., 2019. Identification of *Bacillus thuringiensis* bacterial strain isolated from the mine soil as a robust agent in the biosynthesis of silver nanoparticles with strong antibacterial and anti-biofilm activities. Biocatal. Agric. Biotechnol. 18, 101047.

Khan, R., Fulekar, M.H., 2016. Biosynthesis of titanium dioxide nanoparticles using *Bacillus amyloliquefaciens* culture and enhancement of its photocatalytic activity for the degradation of a sulfonated textile dye reactive red 31. J. Colloid Interface Sci. 475, 184–191.

Khan, S., Akhtar, N., Rehman, S.U., Shujah, S., Rha, E.S., Jamil, M., 2021. Biosynthesized iron oxide nanoparticles (Fe_3O_4 NPs) mitigate arsenic toxicity in rice seedlings. Toxics 9 (1), 1–11.

Khot, L.R., Sankaran, S., Maja, J.M., Ehsani, R., Schuster, E.W., 2012. Applications of nanomaterials in agricultural production and crop protection: a review. Crop Prot. 35, 64–70.

Kimber, R.L., Lewis, E.A., Parmeggiani, F., Smith, K., Bagshaw, H., Straborg, T., Joshi, N., Figueroa, A.I., van der Laan, G., Cibin, G., et al., 2018. Biosynthesis and characterization of copper nanoparticles using *Shewanella oneidensis*: application for click chemistry. Small 14, 1703145.

Kouhkan, M., Ahangar, P., Babaganjeh, L.A., Allahyari-Devin, M., 2020. Biosynthesis of copper oxide nanoparticles using *Lactobacillus casei* Subsp. *Casei* and its anticancer and antibacterial activities. Curr. Nanosci. 16 (1), 101–111.

Kousal, J., Shelemin, A., Schwartzkopf, M., Polonskyi, O., Hanus, J., Solar, P., Vaidulych, M., Nikitin, D., Pleskunov, P., Krtous, Z., et al., 2018. Magnetron-sputtered copper nanoparticles: lost in gas aggregation and found by in situ x-ray scattering. Nanoscale 10, 18275–18281.

Kovačec, E., Regvar, M., van Elteren, J.T., Arčon, I., Papp, T., Makovec, D., Vogel-Mikuš, K., 2017. Biotransformation of copper oxide nanoparticles by the pathogenic fungus *Botrytis cinerea*. Chemosphere 1 (180), 178–185.

Kruis, F.E., Fissan, H., Peled, A., 1998. Synthesis of nanoparticle in the gas phase for electronic, optical and magnetic applications - a review. J. Aerosol Sci. 29, 511–535.

Lee, Y., Choi, J., Lee, K.J., Stott, N.E., Kim, D., 2008. Large-scale synthesis of copper nanoparticles by chemically controlled reduction for applications of inkjet-printed electronics. Nanotechnology 19, 415604.

LewisOscar, F., MubarakAli, D., Nithya, C., Priyanka, R., Gopinath, V., Alharbi, N.S., Thajuddin, N., 2015. One pot synthesis and anti-biofilm potential of copper nanoparticles (CuNPs) against clinical strains of *Pseudomonas aeruginosa*. Biofouling 31, 379–391.

Li, Q., Gadd, G.M., 2017. Biosynthesis of copper carbonate nanoparticles by ureolytic fungi. Appl. Microbiol. Biotechnol. 101, 7397–7407.

Li, Q., Mahendra, S., Lyon, D.Y., Brunet, L., Liga, M.V., Li, D., Alvarez, P.J.J., 2008. Antimicrobial nanomaterials for water disinfection and microbial control: potential applications and implications. Water Res. 42, 4591–4602.

Liu, X., Cai, W.P., Bi, H.J., 2002. Optical absorption of copper nanoparticles dispersed within pores of monolithic mesoporous silica. J. Mater. Res. 17, 1125–1128.

Liu, Y., Arenas, M.A., Skeldon, P., Thompson, G.E., Habazak, H., Shimizu, K., Bailey, P., Noakes, T.C.Q., 2006. Generation of copper nanoparticles during alkaline etching of an Al-30 at.%Cu alloy. Corros. Sci. 48, 1874–1884.

Lobregas, M.O.S., Bantang, J.P.O., Camacho, D.H., 2019. Carrageenan-stabilized silver nanoparticle gel probe kit for colorimetric sensing of mercury (II) using digital image analysis. Sens. Biosens. Res. 26, 10030.

Loshchinina, E.A., Vetchinkina, E.P., Kupryashina, M.A., Fursky, V.F., Nikitina, V.E., 2018. Nanoparticles synthesis by Agaricus soil basidiomycetes. J. Biosci. Bioeng. 126, 44–52.

Lv, Q., Zhang, B., Xing, X., Zhao, Y., Cai, R., Wang, W., Gu, Q., 2018. Biosynthesis of copper nanoparticles using *Shewanella loihica* PV-4 with antibacterial activity: novel approach and mechanisms investigation. J. Hazard. Mater. 347, 141–149.

Mallik, K., Mandal, M., Pradhan, N., Pal, T., 2001. Seed mediated formation of bimetallic nanoparticles by UV irradiation: a photochemical approach for the preparation of "core-shell" type structures. Nano Lett. 1, 319–322.

Mishra, A., Kumari, M., Pandey, S., Chaudhry, V., Gupta, K.C., Nautiyal, C.S., 2014. Biocatalytic and antimicrobial activities of gold nanoparticles synthesized by *Trichoderma* sp. Bioresour. Technol. 166, 235–242.

Moniri, S., Ghoranneviss, M., Hantehzadeh, M.R., Asadabad, M.A., 2017. Synthesis and optical characterization of copper nanoparticles prepared by laser ablation. Bull. Mater. Sci. 40, 37–43.

Mosallam, F.M., El-Sayyad, G.S., Fathy, R.M., El-Batal, A.I., 2018. Biomolecules-mediated synthesis of selenium nanoparticles using *Aspergillus oryzae* fermented lupin extract and gamma radiation for hindering the growth of some multidrug-resistant bacteria and pathogenic fungi. Microb. Pathog. 122, 108–116.

Mousa, A.M., Aziz, O.A., Al-Hagar, O.E., Gizawy, M.A., Allan, K.F., Attallah, M.F., 2020. Biosynthetic new composite material containing CuO nanoparticles produced by *Aspergillus terreus* for 47Sc separation of cancer theranostics application from irradiated Ca target. Appl. Radiat. Isot. 20, 109389.

Muniz-Miranda, M., Gellini, C., Simonelli, A., Tiberi, M., Giammanco, F., Giorgetti, E., 2013. Characterization of copper nanoparticles obtained by laser ablation in liquids. Appl. Phys. A Mater. Sci. Process. 110, 829–833.

Nabila, M.I., Kannabiran, K., 2018. Biosynthesis, characterization and antibacterial activity of copper oxide nanoparticles (CuO NPs) from actinomycetes. Biocatal. Agric. Biotechnol. 15, 56–62.

Nair, R., Varghese, S.H., Nair, B.G., Maekawa, T., Yoshida, Y., Kumar, D.S., 2010. Nanoparticulate material delivery to plants. Plant Sci. 179, 154–163.

Narayanan, K.B., Sakthivel, N., 2010. Biological synthesis of metal nanoparticles by microbes. Adv. Colloid Interf. Sci. 156, 1–13.

Naseer, Q.A., Xue, X., Wang, X., Dang, S., Din, S.U., Kalsoom, Jamil, J., 2022. Synthesis of silver nanoparticles using *Lactobacillus bulgaricus* and assessment of their antibacterial potential. Braz. J. Biol. 82, e232434.

Natesan, K., Ponmurugan, P., Gnanamangai, B.M., Manigandan, V., Joy, S.P.J., Jayakumar, C., Amsaveni, G., 2020. Biosynthesis of silica and copper nanoparticles from *Trichoderma, Streptomyces* and *Pseudomonas* Spp. evaluated against collar canker and red root-rot disease of tea plants. Arch. Phytopathol. Plant Protect., 1–30. https://doi.org/10.1080/03235408.2020.1817258.

Neis, D.H., 1999. Heavy-metal resistance. Appl. Microbiol. Biotechnol. 51, 730–750.

Noman, M., Shahid, M., Ahmed, T., Tahir, M., Naqqash, T., Muhammad, S., Song, F., Arslan Abid, H.M., Aslam, Z., 2020a. Green copper nanoparticles from a native *Klebsiella pneumoniae* strain alleviated oxidative stress impairment of wheat plants by reducing the chromium bioavailability and increasing the growth. Ecotoxicol. Environ. Saf. 192, 110303.

Noman, M., Shahid, M., Ahmed, T., Niazi, M.B.K., Hussain, S., Song, F., Manzoor, I., 2020b. Use of biogenic copper nanoparticles synthesized from a native *Escherichia* sp. as photocatalysts for azo dye degradation and treatment of textile effluents. Environ. Pollut. 257, 113514.

Noman, M., Ahmed, T., Hussain, S., Niazi, M.B.K., Shahid, M., Song, F., 2020c. Biogenic copper nanoparticles synthesized by using a copper-resistant strain *Shigella flexneri* SNT22 reduced the translocation of cadmium from soil to wheat plants. J. Hazard. Mater. 398, 123175.

Omran, B.A., 2020. Prokaryotic microbial synthesis of nanomaterials (the world of unseen). In: Nanobiotechnology: A Multidisciplinary Field of Science. Nanotechnology in the Life Sciences. Springer, Cham, pp. 37–79.

Osorio-Echavarría, J., Osorio-Echavarría, J., Ossa-Orozco, C.P., Gómez-Vanegas, N.A., 2021. Synthesis of silver nanoparticles using white-rot fungus anamorphous *Bjerkandera* Sp. R1: influence of silver nitrate concentration and fungus growth time. Sci. Rep. 11 (1), 3842.

Pal, G., Rai, P., Pandey, A., 2019. Green synthesis of nanoparticles: a greener approach for a cleaner future. In: Shukla, A.K., Iravani, S. (Eds.), Green Synthesis Characterization and Applications of Nanoparticles. Elsevier, Amsterdam, pp. 1–26 (Chapter 1).

Pantidos, N., Edmundson, M.C., Horsfall, L., 2018. Room temperature bioproduction, isolation and anti-microbial properties of stable elemental copper nanoparticles. New Biotechnol. 40, 275–281.

Parikh, R.Y., Singh, S., Prasad, B.L.V., Patole, M.S., Sastry, M., Shouche, Y.S., 2008. Extracellular synthesis of crystalline silver nanoparticles and molecular evidence of silver resistance from *Morganella* sp.: towards understanding biochemical synthesis mechanism. ChemBioChem 9 (9), 1415–1422.

Park, B.K., Jeong, S., Kim, D., Moon, J., Lim, S., Kim, J.S., 2007. Synthesis and size control of monodisperse copper nanoparticles by polyol method. J. Colloid Interface Sci. 311, 417–424.

Pathak, J., Rajneesh Ahmed, H., Singh, D.K., Pandey, A., Singh, S.P., Sinha, R.P., 2019. Recent developments in green synthesis of metal nanoparticles utilizing cyanobacterial cell factories. In: Tripathi, D.K., Ahmad, P., Chauhan, D.K., Dubey, N.K. (Eds.), Nanomaterials in Plants, Algae and Microorganisms: Concepts and Controversies, vol. 2. Academic Press, London, pp. 237–265 (Chapter 12).

Rad, M., Taran, M., Alavi, M., 2018. Effect of incubation time, $CuSO_4$ and glucose concentrations on biosynthesis of copper oxide (CuO) nanoparticles with rectangular shape and antibacterial activity: Taguchi method approach. Nano Biomed. Eng. 10, 25–33.

Rajakumar, G., Abdul Rahuman, A., Mohana Roopan, S., Gopiesh Khanna, V., Elango, G., Kamaraj, C., Abduz Zahir, A., Velayutham, K., 2012. Fungus-mediated biosynthesis and characterization of TiO_2 nanoparticles and their activity against pathogenic bacteria. Spectrochim. Acta A Mol. Biomol. Spectrosc. 91, 23–29.

Ramanathan, R., Bhargava, S.K., Bansal, V., 2011. Biological synthesis of copper/copper oxide nanoparticles. In: Conference Proceedings Chemeca 2011: Engineering a Better World, Sydney, Australia.

Rasool, U., Hemalatha, S., 2017. Marine endophytic actinomycetes assisted synthesis of copper nanoparticles (CuNPs): characterization and antibacterial efficacy against human pathogens. Mater. Lett. 194, 176–180.

Rosbero, T.M.S., Camacho, D.H.C., 2017. Green preparation and characterization of tentacle-like silver/copper nanoparticles for catalytic degradation of toxic chlorpyrifos in wáter. J. Environ. Chem. Eng. 5, 2524–2532.

Rostami, H., Khosravi, F., Mohseni, M., Rostami, A.A., 2018. Biosynthesis of Ag nanoparticles using isolated bacteria from contaminated sites and its application as an efficient catalyst for hydrazine electrooxidation. Int. J. Biol. Macromol. 107, 343–348.

Saitawadekar, A., Kakde, U.B., 2020. Green synthesis of copper nanoparticles using *Aspergillus flavus*. J. Crit. Rev. 7 (16), 1083–1090.

Salvadori, M.R., Lepre, L.F., Ando, R.A., Oller do Nascimento, C.A., Corrêa, B., 2013. Biosynthesis and uptake of copper nanoparticles by dead biomass of *Hypocrea lixii* isolated from the metal mine in the Brazilian Amazon region. PLoS One 8, e80519.

Salvadori, M.R., Ando, R.A., Oller do Nascimento, C.A., Corrêa, B., 2014a. Intracellular biosynthesis and removal of copper nanoparticles by dead biomass of yeast isolated from the wastewater of a mine in the Brazilian Amazonia. PLoS One 9, e87968.

Salvadori, M.R., Ando, R.A., Oller do Nascimento, C.A., Corrêa, B., 2014b. Bioremediation from wastewater and extracellular synthesis of copper nanoparticles by the fungus *Trichoderma koningiopsis*. J. Environ. Sci. Health A 49, 1286–1295.

Sanguansri, P., Augustin, M.A., 2006. Nanoscale materials development-a food industry perspective. Trends Food Sci. Technol. 17, 547–556.

Santhoshkumar, J., Agarwal, H., Menon, S., Rajeshkumar, S., Kumar, S.V., 2019. A biological synthesis of copper nanoparticles and its potential applications. In: Shukla, A.K., Iravani, S. (Eds.), Green Synthesis Characterization and Applications of Nanoparticles. Elsevier, Amsterdam, pp. 199–221 (Chapter 9).

Saravanakumar, K., Shanmugam, S., Varukattu, N.B., MubarakAli, D., Kathiresan, K., Wang, M.H., 2019. Biosynthesis and characterization of copper oxide nanoparticles from indigenous fungi and its effect of photothermolysis on human lung carcinoma. J. Photochem. Photobiol. B Biol. 190, 103–109.

Scott, A., Vadalasetty, K.P., Chwalibog, A., Sawosz, E., 2018. Copper nanoparticles as an alternative feed additive in poultry diet: a review. Nanotechonol. Rev. 7, 69–93.

Shan, G., Surampalli, R.Y., Tyagi, R.D., Zhang, T.C., 2009. Nanomaterials for environmental burden reduction, waste treatment, and nonpoint source pollution control: a review. Front. Environ. Sci. Eng. China 3, 249–264.

Shantkriti, S., Rani, P., 2014. Biological synthesis of copper nanoparticles using *Pseudomonas fluorescens*. Int. J. Curr. Microbiol. Appl. Sci. 3, 374–383.

Shobha, G., Moses, V., Ananda, S., 2014. Biological synthesis of copper nanoparticles and its impact. Int. J. Pharm. Sci. Invent. 3 (8), 6–28.

Singh, V.K., Singh, A.K., 2019. Role of microbially synthesized nanoparticles in sustainable agriculture and environmental management. In: Kumar, A., Singh, A.K., Choudhary, K.K. (Eds.), Role of Plant Growth Promoting Microorganisms in Sustainable Agriculture and Nanotechnology. Woodhead Publishing, Duxford, UK, pp. 55–73 (Chapter 4).

Singh, A.V., Patil, R., Anand, A., Milani, P., Gade, W.N., 2010. Biological synthesis of copper oxide nano particles using *Escherichia coli*. Curr. Nanosci. 6, 365–369.

Singh, D., Rathod, V., Ninganagouda, S., Herimath, J., Kulkarni, P., 2013. Biosynthesis of silver nanoparticle by endophytic fungi *Pencillium* sp. isolated from *Curcuma longa* (turmeric) and its antibacterial activity against pathogenic Gram negative bacteria. J. Pharm. Res. 7, 448–453.

Siva Kumar, K., Kumar, G., Prokhorov, E., Luna-Barcenas, G., Buitron, G., Khanna, V.G., Sanchez, I.C., 2014. Exploitation of anaerobic enriched mixed bacteria (AEMB) for the silver and gold nanoparticles synthesis. Colloids Surf. A Physicochem. Eng. Asp. 462, 264–270.

Składanowski, M., Wypij, M., Laskowski, D., Golinska, P., Dahm, H., Rai, M., 2017. Silver and gold nanoparticles synthesized from *Streptomyces* sp. isolated from acid forest soil with special reference to its antibacterial activity against pathogens. J. Clust. Sci. 28, 59–79.

Soliman, H., Elsayed, A., Dyaa, A., 2018. Antimicrobial activity of silver nanoparticles biosynthesised by *Rhodotorula* sp. strain ATL72. Egypt. J. Basic Appl. Sci. 5, 228–233.

Sriramulu, M., Shanmugam, S., Ponnusamy, V.K., 2020. *Agaricus bisporus* mediated biosynthesis of copper nanoparticles and its biological effects: an in-vitro study. Colloids Interface Sci. Commun. 35, 100254.

Sytu, M.R., Camacho, D.H., 2018. Green synthesis of silver nanoparticles (AgNPs) from *Lenzites betulina* and the potential synergistic effect of AgNP and capping biomolecules in enhancing antioxidant activity. BioNanoScience 8, 835–844.

Taran, M., Rad, M., Alavi, M., 2016. Biological synthesis of copper nanoparticles by using *Halomonas elongata* IBRC-M 10214. Ind. Textilă 67, 351–356.

Taran, M., Rad, M., Alavi, M., 2017. Antibacterial activity of copper oxide (CuO) nanoparticles biosynthesized by *Bacillus* sp. FU4: optimization of experiment design. Pharm. Sci. 23, 198–206.

Taran, M., Rad, M., Alavi, M., 2018. Biosynthesis of TiO_2 and ZnO nanoparticles by *Halomonas elongata* IBRC-M 10214 in different conditions of medium. BioImpacts 8, 81–89.

Tarasov, S., Kolubaev, A., Belyaev, S., Lerner, M., Tepper, F., 2002. Study of friction reduction by nanocopper additives to motor oil. Wear 252, 63–69.

Thakkar, K.N., Mhatre, S.S., Parikh, R.Y., 2010. Biological synthesis of metallic nanoparticles. Nanomed. Nanotechnol. Biol. Med. 6, 257–262.

Tilaki, R.M., Iraji Zad, A., Mahdavi, S.M., 2007. Size, composition and optical properties of copper nanoparticles prepared by laser ablation in liquids. Appl. Phys. A Mater. Sci. Process. 88, 415–419.

Tiwari, M., Jain, P., Hariharapura, R.C., Narayanan, K., Bhat, U., Udupa, N., Rao, J.V., 2016. Biosynthesis of copper nanoparticles using copper-resistant *Bacillus cereus*, a soil isolate. Process Biochem. 51, 1348–1356.

Ulloa, G., Collao, B., Araneda, M., Escobar, B., Alvarez, S., Bravo, D., Perez-Donoso, J.M., 2016. Use of acidophilic bacteria of the genus *Acidithiobacillus* to biosynthesize CdS fluorescent nanoparticles (quantum dots) with high tolerance to acidic pH. Enzym. Microb. Technol. 95, 217–224.

Varshney, R., Bhadauria, S., Gaur, M.S., Pasricha, R., 2010. Characterization of copper nanoparticles synthesized by a novel microbiological method. JOM 62, 102–104.

Verma, M., Gupta, V.K., Dave, V., Chandra, R., Prasad, G.K., 2015. Synthesis of sputter deposited CuO nanoparticles and their use for decontamination of 2-chloroethyl ethyl sulfide (CEES). J. Colloid Interface Sci. 438, 102–109.

Waris, A., Din, M., Ali, A., Ali, M., Afridi, S., Baset, A., Khan, A.U., 2021. A comprehensive review of green synthesis of copper oxide nanoparticles and their diverse biomedical applications. Inorg. Chem. Commun. 123, 108369.

Xiao, X., Liu, Q.-Y., Lu, X.-R., Li, T.-T., Feng, X.-L., Li, Q., Liu, Z.-Y., Feng, Y.-J., 2017. Self-assembly of complex hollow CuS nano/micro shell by an electrochemically active bacterium *Shewanella oneidensis* MR-1. Int. Biodeterior. Biodegradation 116, 10–16.

Zarasvand, K.A., Rai, V.R., 2016. Inhibition of a sulfate reducing bacterium, *Desulfovibrio marinisediminis* GSR3, by biosynthesized copper oxide nanoparticles. 3 Biotech 6, 84.

Zhang, L., Webster, T.J., 2009. Nanotechnology and nanomaterials: promises for improved tissue regeneration. Nano Today 4, 66–80.

Zhao, K., Wang, J., Kong, W., Zhu, P., 2020. Facile green synthesis and characterization of copper nanoparticles by aconitic acid for catalytic reduction of nitrophenols. J. Environ. Chem. Eng. 8, 103517.

Zhou, N.-Q., Tian, L.-J., Wang, Y.-C., Li, D.-B., Li, P.-P., Zhang, X., Yu, H.-Q., 2016. Extracellular biosynthesis of copper sulfide nanoparticles by *Shewanella oneidensis* MR-1 as a photothermal agent. Enzym. Microb. Technol. 95, 230–235.

CHAPTER

3 Biosynthesis and characterization methods of copper nanoparticles and their applications in the agricultural sector

G. Bhagavanth Reddy[a], K. Girija Mangatayaru[a], D. Madhusudan Reddy[b], Suresh Babu Naidu Krishna[c], and Narasimha Golla[d]

[a]*Department of Chemistry, Palamuru University, Mahabub Nagar, Telangana, India,*
[b]*Department of Microbiology, Palamuru University, Mahabub Nagar, Telangana, India,*
[c]*Research Post Graduate Support, Durban University of Technology, Durban, South Africa,*
[d]*Department of Virology, Sri Venkateswara University, Tirupati, Andhra Pradesh, India*

1 Introduction

Nanoscience and nanotechnology have impacted our economy by giving noteworthy advances in various regions. The word "nano" states the dimension of the length of the order of 10^{-7} cm or 10^{-9} m. Nanoscale materials are notable as nanomaterials and nanoparticles. They are showing a profound impact on the science and technology world due to their remarkable optical, electrical, chemical, physical, magnetic, and biological properties, in comparison to their corresponding bulk substances owing to the high surface area-to-volume ratio (Ganapuram et al., 2015; Madhusudhan and Reddy, 2019; Bandi et al., 2020). Due to their distinctive properties, nanoscale materials are used in many areas such as biomedical, food, cosmetics, catalysis, sensing, electronic compounds, textiles, energy, manufacturing, biotechnology, and information technology (Bandi et al., 2018; Seku et al., 2018a; Ealias and Saravanakumar, 2017; Mousavi et al., 2018). Nanomaterials are synthesized by manipulation of materials at the nanometer scale either by scaling up the manufacturing from single groups of atoms or by refining bulk materials. The properties of nanomaterials are significantly different considerably enhanced relative to their bulk counterparts (AL-Jobory et al., 2019). Nanoparticles can be made from various materials such as metals, semiconductors, and polymers organic compounds (Ismail et al., 2018). For many decades, a few research groups have planned to develop different inorganic nanomaterials, for example, metal and metal oxide nanoparticles such as silver nanoparticles (Jaidev and Narasimha, 2010; Vaishnavi et al., 2020;

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Palithya et al., 2021) lanthanum (Saiganesh et al., 2021), neodymium (Saiganesh et al., 2021) carbon nanoparticles quantum dots, etc., for various biomedical applications (Bandi et al., 2018; Golla, 2018; Dadigala et al., 2017). Among these noble metal nanoparticles, copper nanoparticles (CuNPs) have emerged as one of the most alluring materials for present-day research in many areas because of its advantages such as unique optical electrical properties, along with corrosion resistance and good thermal conductivity (Al-Hakkani, 2020).

Copper (Cu) is a significant metal and is used in metabolic processes in living organisms (Shobha et al., 2014). It is required for crosslinking connective tissue just as in iron lipid metabolism; nonetheless, it is harmful at high exposure concentrations (Ameh and Sayes, 2019; Khodashenas and Ghorbani, 2014). Elemental Cu normally exists in nature as metallic copper in its ionic copper (Cu^{1+} or Cu^{2+}), zerovalent Cu (Cu^0), or as an engineered nanoparticle. These cupric forms instigate fluctuating degrees of harmfulness in organisms (Chauhan, 2020).

The one-of-a-kind physicochemical properties of copper make it helpful in an immense range of uses. Physical properties of copper incorporate low corrosion and high electrical thermal conductivity (Gangapuram et al., 2017). Cu is, for the most part, viewed as "inert" because it gets dissolved in acid in the presence of an oxidizing agent (Das et al., 2020). Actually, the biological function of Cu frequently includes electron transfer catalysts in many processes such as hemoglobin tissue production, protein synthesis, and carbohydrate metabolism (Ameh and Sayes, 2019). Zerovalent Cu (Cu^0) nanoparticles generally appear as different reduced Cu ions bound together in a well-ordered lattice structure and are solid and spheroidal particles in the size range of 10–100 nm. This type of CuNPs has distinctive physicochemical and biological properties than ionic copper nanoparticles. (Giannousi et al., 2017; Ameh and Sayes, 2019). The CuNPs are less toxic than silver nanoparticles because these are susceptible to aggregation oxidation, which can be due to the addition of a suitable stabilizer for capping CuNPs (Cuevas et al., 2015). The CuNPs are broadly utilized in wound dressing for their biocidal properties, as well as the catalytic process in the manufacturing industry as gas sensors, solar cells high-temperature superconductors in various industries (Shobha et al., 2014; Kasana et al., 2017). The solution of CuNP particles was implanted in transparent glass or CuNPs were supported on other solids to absorb the visible wavelength of light, offering to ascend to colors that can span the visible spectrum. These absorptions color properties of the metal are expected to plasmon excitation (Murthy et al., 2018; Zhakina and Alpysbayeva, 2020).

The bottom-up (Fig. 1) approach is mostly comprised of chemical and biological methods whose approach is much better for generating uniform particles with a distinct shape and size structure. The method is important to researchers in all fields of sciences just as those explicitly keen on developing nanoscience technology (Mukherjee et al., 2020). However, this method falls predominantly inside the domains of nanoscience technology. In nature, self-get together is regularly used to make complex structures that are restricted to relatively simple systems (Singh and Kumar, 2017).

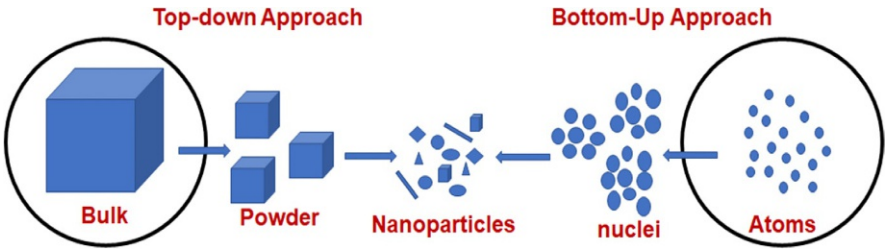

FIG. 1

Schematic representation of top-down and bottom-up approaches.

In this chapter, we represent few strategies for the synthesis of CuNPs utilizing physical, chemical, and biological properties, particularly green chemistry which has shown to be cost-effective, biocompatible simple methods. Various characterization methods and the mechanisms of particle formation are also discussed as significant, to underset the outcome of any synthetic methods. Finally, this chapter reveals the utilization of these green syntheses of CuNPs in various fields, such as, biomedical, catalytical, environment, and particularly in agriculture sector.

2 Synthesis of CuNPs

The characteristics of CuNPs mainly depend on the shape, size, and chemical environment. The properties of such materials can be studied by controlling these parameters. Several methods are in use for the synthesis of CuNPs, including physical, chemical, and biological methods. The physical methods are a moderately complex process that requires advanced instruments. The chemical techniques such as chemical reduction, thermal decomposition, microemulsion, and electrochemical are broadly utilized because of ease of control, low-cost instrument requirement, and high-quality nanoparticles. The significant impediment in the synthesis of CuNPs is that they effectively get oxidized to copper oxide after the synthesis (Santhoshkumar et al., 2019). Hence, these methods are acted in nonaqueous media under a dormant environment.

2.1 Chemical method

The method is the most widely recognized methodology in nanoparticles synthesis, being a cost-effective high yield method. Usually, the chemical synthesis of CuNPs incorporates metal ions, reducing capping agents. The chemical method process is an oxidation-reduction reaction; the reaction involves the reduction of metal ions by reducing agents such as sodium borohydride ($NaBH_4$), sodium citrate, *N*,*N*-dimethylformamide, cetyltrimethylammonium bromide, ascorbate, isopropyl alcohol, and polyol (Umer et al., 2012; Giannousi et al., 2017). Wu and Chen (2004) chemically prepared pure CuNPs by the reduction of cupric chloride with hydrazine in the presence of cetyltrimethylammonium bromide solution, and CuNP size was

found to be 5 nm. Similarly, Hashemipour et al. (2011) reported CuNP size with 30 nm by using sodium tetrahydridoborate as a reducing agent under the nitrogen atmosphere. Copper nanotubes were synthesized by using ascorbic acid polyvinylpyrrolidone as reducing and stabilizing agents, respectively, the synthesized copper nanotubes with an edge length in the range of 100 ± 25 nm. Similarly, Dang et al. (2011) also prepared less than 10 nm CuNPs by the chemical reduction of copper sulfate with sodium borohydride in water ascorbic acid as a reducing agent. Spherical CuNPs with a size 45 ± 8 nm were synthesized by employing a polyol method in an ambient environment. The CuNPs were prepared using hydrazine as reducing chitosan and as a capping agent with a size range of 35–75 nm (Usman et al., 2012).

Several reports had shown that these chemical methods include the usage of hazardous chemicals in later steps as stabilizing agent's synthetic additives, which will end up in environmental pollution. Large energy consumption, high temperature, and pressure are vast limitations of the chemical approach of synthesizing CuNPs (Ameh and Sayes, 2019).

2.2 Thermal decomposition

Thermal decomposition includes the utilization of a solvent under moderate temperature in a fixed vessel (hydrothermal autoclave) high pressure that helps the association of metal precursors during preparation. In this process water is utilized as the solvent; the strategy is called hydrothermal synthesis (Dhas et al., 1998). Spherical CuNPs of size range 4–18 nm were prepared through thermal decomposition method using $CuCl_2$, sodium oleate phenyl ether. The CuNPs of size 40 nm were synthesized by utilizing copper oxalates as a precursor (Betancourt-Galindo et al., 2014). Shah et al. (2015) reported the synthesis of CuNPs with sizes ranging from 9 to 60 nm in which water was used as a solvent under supercritical conditions. Spherical CuNP ribbon-like network of copper nanostructures was produced in the presence of a surfactant sodium dodecyl benzenesulfonate which acts as capping as well as a shape size controller (Parveen et al., 2016).

2.3 Electrochemical synthesis

Electrochemical synthesis of CuNPs is a low-cost, noticeable straightforward method for the synthesis of the controlled execution of shaped nanostructures (foils, wires, electroforms) highlighting high-index facets on the electrode surface. Electrochemical deposition includes the preparation of solid films from dissolved species by changing their oxidation states utilizing electricity (Parveen et al., 2016). Electrodeposition was applying in nanoscience since it tends to be utilized to fill three-dimensional materials at room temperature with great control of thickness morphology. The electrochemical deposition reactions happen at the interface between the electrolyte and the electrode, and the driving force of these reactions is the chemical, electrical, and potential developed in the electrolyte. Electron deposition occurs in a fragile region in front of the electrode. On account of easy operation, simple accessibility of instrument, less

contamination, and environmentally friendly process, this approach is in effect generally utilized by many scientists. Copper nanorods of size 30 nm were prepared via the controlled current electrochemical method. CuNPs were prepared with a size in the range of 3.1–11.4 nm within gel compositions of the system $CuO\text{-}SiO_2$ via electrodeposition method by applying voltage varying from 5 to 15 V. A novel electrochemical melting technique was used to prepare CuNPs (Parveen et al., 2016). Similarly, Huang developed CuNPs containing carbon films on Si substrate using electrochemical deposition approach by taking dimethylsulfoxide as carbon source acetonitrile solution of $[Cu(CH_3CN)_4]ClO_4$ as dopant at relatively low voltage. Single crystalline CuNPs with various morphologies were synthesized via the electrochemical charge-discharge approach (Huang et al., 2006). Similarly, Raja et al. (2008) reported CuNPs with 49–60 nm that were synthesized by the electroreduction method using a plating bath containing homogeneously acidified copper sulfate solution.

2.4 Microemulsion method

Microemulsion forms spontaneously at room temperature is very easy to manufacture. Microemulsion isotropic, thermodynamic stable systems composed of water, oil, and surfactant. Thermodynamic stability rather than size, is the characterizing sign of a microemulsion, despite the fact that the droplet sizes are still under 100 nm (Parveen et al., 2016). A microemulsion is a thermodynamically stable dispersion of two immiscible fluids, and the system is capped by adding surfactants. Well-dispersed CuNPs of sizes ranging 5–15 nm were synthesized by the reduction of aqueous copper chloride solution using $NaBH_4$ in the nonionic water-in-oil microemulsion (Qi et al., 1997). Khanna et al. (2009) prepared hydrophilic CuNPs using sodium formaldehyde sulfoxylate hydrazine hydrate in an aqueous medium that produced CuNPs with a size of 43 nm.

2.5 Green synthesis of CuNPs

In recent decades, there has been an extensive emphasis on the environmentally friendly synthesis of biogenic nanoparticles using biological agents, for example, plants, microorganisms, etc. Green synthesis includes the reduction of the metal ion by biological mass/extract as the resultant. The nanoparticles synthesis from green novelties is less expensive and simple and safely reduces waste (Seku et al., 2020). Furthermore, biocompatibility as the benefit of the green method than the conventional physicochemical methods indicates its viability for catalyzing reactions in aqueous media at standard pressure-temperature adaptability of the process. These nanoparticles have a few preferences in view of uniform shape and size. They eliminate toxic chemical contaminations from the environment by counteracting them or through a change in different synthetic conditions (Madhusudhan and Reddy, 2019). These nanoparticles do not interrupt the earth's biological systems; furthermore conserve their natural resources. The reduction occurred by segments accessible in biological materials, it is generally initiated by a few compounds found in the cell,

similar to amine, amide groups, phenolic, carbonyl, alkaloids, flavonoids, terpenoids, and other reducing compounds. Because of the difference in structure of these compounds, the exact mechanism of green synthesis of nanoparticles has not yet been entirely identified. Plant extract/biomass and microorganisms such as bacteria, fungi, viruses, algae, and yeast are significant biological compounds that can be used to prepare nanoparticles (Al-Hakkani, 2020).

2.5.1 Advantage of biologically synthesized nanoparticles

Nanoparticles that were prepared through the green synthetic process are free from the toxicity of by-products compared with nanoparticles derived through other methods. The green synthesis of nanoparticles is related to a few favorable circumstances, for example, biocompatible, rapid, and low-cost kinds of derived nanoparticles (Shobha et al., 2014). Moreover, there is no requirement for more capping agents. Subsequently, plant and microorganism compounds act as capping agents. Biosynthesized nanoparticles were more active because of biologically active components on the surface of prepared nanoparticles from the plants and microorganisms (Murthy et al., 2018). Many rich metabolites with pharmacological impacts are accessible and found binding to the surface of prepared nanoparticles, giving benefit through the expanded viability of the nanoparticles, particularly in therapeutic plants. Besides, the number of steps can be reduced by green synthesis. For instance, the attachment of some functional groups to the surface of nanoparticle for making them biologically active, which is an extra step for physicochemical production (Abd-Elkareem et al., 2016).

2.5.2 Green synthesis of CuNPs

The mode of usage of plant extracts for the synthesis of nanoparticles is simple, in that, the metal salt solution with a solution of extracts at various concentrations and temperature is kept under constant stirring, or under microwave irradiation or sonication for a particular time duration. The single-step reduction of metal ions to elemental metal is fast, might be done at atmospheric pressure and room temperature, such that scale-up is effectively conceivable (Din et al., 2017). The reducing agents present in the plant are secondary metabolites such as terpenoids, alkaloids, polyphenol, etc. Extracts of different plant species such as flowers, leaves, stems, and fruits, have been utilized in synthesizing CuNPs (Fig. 2). The basic green chemistry principles make a cleaner synthesis of nanoparticles. Green synthesis involves molecular tolerance mechanism metabolomics from nanoparticles (Akintelu et al., 2020). According to the recent works, it is established both high- (~ 150 kDa) and low (12–22 kDa)-molecular-weight proteins, contingent upon the nature of plant extracts, assume a significant function in the production of CuNPs from copper salts (Mukhopadhyay et al., 2018).

The general strategy used to prepare the plant-based solutions is through the selective collection of the aspect of the plant of intrigue, trailed by washing cycles to eliminate the two epiphytes necrotic plants. Therefore, it is dried for 5–10 days then powdered. The powder was dispersed in water boiled to obtain the extract, which is separated. In the end, a small number of plant extracts was added to the metal ions solution that must be reduced for the synthesis of metal nanoparticles of intrigue. This

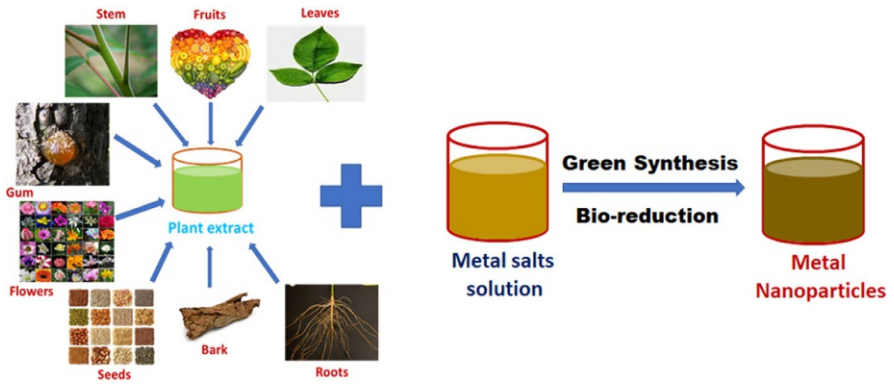

FIG. 2

Green synthesis (various plant parts) of CuNPs.

method is generally utilized in the green synthesis of CuNPs so that the reduction of ions can be monitored by the UV-Vis spectrum of the CuNPs (Sebeia et al., 2020). Different parts of plants are being employed in the formation of eco-friendly CuNPs.

Leaf extracts

Green synthesis of CuNPs with *Allium eriophyllum* Boiss leaf aqueous extract was reported and also analyzed their potential for removing bacteria and fungi, further healing of cutaneous wounds (Zhao et al., 2020). Similarly, CuNPs are prepared ranged in size from 40 to 100 nm using *Magnolia* leaf extract as a reducing stabilizing agent (Tahvilian et al., 2019). Rapid synthesis of the CuNPs has been reported when $CuSO_4$ solution contacted with leaf extract of *Brassica juncea*, *Medicago sativa*, and *Helianthus annuus* (Cioffi et al., 2005). CuNPs are synthesized from the leaf extract of *Alchornea laxiflora* (Olajire et al., 2018). The prepared CuNPs gave absorption at 364 nm, FTIR spectrum shows the Cu–O stretching vibration at 590 cm^{-1}. This demonstrates that various phytochemicals present in the extract acted as reducing stabilizing agents for the synthesis of CuNPs. TEM analysis confirmed that most of the CuNPs were spherical in shape with an average size of 3.29 ± 0.57 nm. Zhao et al. (2020) demonstrated the green synthesis approach of CuNPs with *Allium eriophyllum* Boiss leaf aqueous extract also analyzed their microbicidal activity. Green synthesis of CuNPs using *Allium saralicum* leaves extract was reported by Tahvilian et al. (2019) Rapid synthesis of the CuNPs has been reported when $CuSO_4$ solution was contacted with leaf extract of *Brassica juncea*, *Medicago sativa*, and *Helianthus annuus* (Cioffi et al., 2005). Bioreduction of activity of leaf extract of *Lantana camara* resulted in the synthesis of CuNPs in the presence of Cu^{2+} ions (Majumder, 2012). Abhiman et al. (2018) synthesized the CuNPs using the leaf extract of *Azadirachta indica* leaves, natural plant materials such as *Acalypha indica* and the CuNPs are in a spherical shape (18.9–32.09 nm) and are reported from *Prosopis cineraria* leaf extract using microwave irradiation method (Jinu et al., 2017). Table 1 summarizes the the green synthesis of CuNPs.

Table 1 Green synthesis of CuNPs.

Plant part	Plant name	Size (nm)	Shape/structure/ morphology	References
Flower	*Syzygium aromaticum*	5–40	Spherical	Rajesh et al. (2018)
	Caesalpinia pulcherrima	8–20	Spherical	Kurkure et al. (2016)
	Aloe barbadensis Miller	40	Spherical	Karimi and Mohsenzadeh (2015)
	Delonix elata	20	–	Valli and Suganya (2015)
	Anthemis xylopoda	40	–	Nasrollahzadeh et al. (2015b)
	Anthemis nobilis	18	Rectangular	Nasrollahzadeh et al. (2015a)
	Cassia fistula F.	20,000	Amorphous	Din et al. (2017)
	Broccoli	4.8	Spherical	Prasad et al. (2016)
	Aglaia elaeagnoidea	20–45	Spherical	Manjari et al. (2017)
Fruit	*Citrus medica* Linn.	33	Spherical	Cheirmadurai et al. (2014)
	Citrus limon and Turmeric curcumin	60–100	Spherical	Jayandran et al. (2015)
	Phyllanthus emblica	15–30	Flakes	Jyothi Prashanth et al. (2016)
	Psidium guajava	15–30	Flakes	Raghunandan et al. (2011)
	Citrus medica Linn.	20	Crystalline	Shende et al. (2015)
	Guava	14–30	Spherical	Din et al. (2017)
	Ripened *Duranta erecta*	76	Spherical	Ismail et al. (2019)
	Phoenix dactylifera		Spherical	Amrani et al. (2016)
	Andean blackberry	43.3	Spherical	Kumar et al. (2017)
Peel	*Citrus grandis*	22–27	Spherical	Sinha and Ahmaruzzaman (2015)
	Banana	7.3	Spherical	Ijaz et al. (2017)
	P. granatum	10–100	Spherical	Kaur et al. (2016)

Leaves	*Capparis zeylanica*	50–100	Cubical structure	Saranyaadevi et al. (2014)
	Ginkgo biloba L.	15–20	Spherical	Nasrollahzadeh and Mohammad Sajadi (2015)
	Magnolia kobus	45–110	Spherical	Lee et al. (2013)
	Pistachio	9	Crystallized nano wires	Awwad and Albiss (2015)
	Azadirachta indica	48	Cubic	Abhiman et al. (2018)
	Thymus vulgaris L.	23–94	Spherical	Issaabadi et al. (2017)
	Datura meta L.	15–20	Spherical	Parikh et al. (2014)
	Euphorbia esula L.	20–110	Spherical	Nasrollahzadeh et al. (2014)
	Plantago asiatica	17–35	Spherical	Nasrollahzadeh et al. (2017)
	Ginkgo biloba Linn.	15–20	Spherical	Nasrollahzadeh and Mohammad Sajadi (2015)
	Azadirachta indica	21.6	Spherical	Nagar and Devra (2017)
	Tilia	4.7–14	Hemispherical	Hassanien et al. (2018)
	Eclipta prostrata	31 ± 1.2	Spherical, hexagonal, cubical	Chung et al. (2017)
	Tinospora cordifolia	63.3	Spherical	Sharma et al. (2019)
	Ginkgo biloba	15–20	Spherical	Nasrollahzadeh and Mohammad Sajadi (2015)
	Green black tea	24–40	Spherical	Asghar et al. (2018)
	Bauhinia tomentosa	22–24	Spherical	Sharmila et al. (2018)
	Terminalia catappa L.	103–129	Spherical	Muthulakshmi et al. (2017)
	Aloe barbadensis	15–30	Spherical	Gunalan et al. (2012)
	Calotropis procera	46	Cylindrical	Harne et al. (2012)
	Acalypha indica	26–30	Spherical	Sivaraj et al. (2014)
	Calotropis procera	15 ± 1.9	Polydisperse spherical	Harne et al. (2012)
	Ocimum bacilicum	40–60	Spherical	Sapna Thakur (2014)
	Otostegia persica	40	Spherical	Nasrollahzadeh et al. (2016)
	Vitis vinifera	3–6	Spherical	Shaikh et al. (2016)
	Urtica	6.5		Shah et al. (2015)
	Cassia auriculata	38–43	Spherical	Valli and Geetha (2015)
	Schisandra chinensis	32		Shah et al. (2015)
	Withania somnifera	50–60	Spherical	Sapna Thakur (2014)
	Allium sativum	100	Spherical	Joseph et al. (2016)
	Ocimum bacilicum	40–60	Spherical	Sapna Thakur (2014)

Fruits

Copper nanoparticles were synthesized by green approach using fruit extract of *Ziziphus spina-christi* (L.) wild prepared CuNPs was used as an efficient adsorptive nanomaterial to remove crystal violet from aqueous solution (Khani et al., 2018). Similarly, CuNPs are synthesized using *Piper retrofractum* Vahl fruit extract. The reaction process was assisted by sonication stirring, and the reaction was monitored by varying the concentration of extract metal salts, pH, temperature, and time. The prepared CuNPs having a high uniformity with a size in the range of 2–10 nm possess spherical shapes (Amaliyah et al., 2020). For the first time, CuNPs were synthesized using the green chemistry approach by the fruit extract of *Duranta erecta*. UV-Vis spectroscopy analysis showed the SPR bat of 588 nm, the size of CuNPs was found to be 70 nm. The synthesized CuNPs were used for the reduction of organic dyes in the presence of $NaBH_4$ (Ismail et al., 2019). CuNPs are synthesized using an aqueous extract of Capparis spinosa fruit and their antibacterial activities were tested against Gram-positive and Gram-negative bacterial strains (Ebrahimi et al., 2017). Similarly, the green synthesis of CuNPs by using various fruit extracts such as *Andean blackberry*, *C. medialiin*, *C. filiformis*, *P. granatum*, and the fruit of pulp of *P. dactylifera* was reported (Shende et al., 2015; Kaur et al., 2016; Kumar et al., 2017; Zafar and Zafar, 2019).

Flower

It has been found that flower extracts have great potential for the synthesis of CuNPs. CuNPs are synthesized using an aqueous extract of the flower *Millettia pinnata*. Copper acetate was reduced by the extract of the flower *Millettia pinnata* at 60°C. UV-visible spectra suggest that the maximum absorption occurs at 384 nm. The synthesized CuNPs exhibited enhanced antioxidant and antibacterial activities (Thiruvengadam et al., 2019). The synthesis of CuNPs in copper sulfate solution using flower extract of *Eichhornia crassipes* was reported that were nearly spherical in shape with a mean diameter of 12–15 nm. Also, the H_2O_2 sensing ability of these green CuNPs was tested and the suspension of CuNPs was observed to detect the hazardous H_2O_2 instantly (Roy et al., 2019). The synthesis of CuNPs was reported by using flower extract of *Aloe vera*, which act as a reducing stabilizing agent. UV-visible spectroscopy analysis showed the SPR bat of 578 nm. The results of FESEM analysis showed that the shape of CuNPs was that CuNPs exhibited spherical shape and size of about 40 nm. FTIR spectra demonstrated that there was a thin film of proteins some secondary metabolites that cover the CuNPs (Roy et al., 2019).

Peel extracts

Ituen et al. reported the *Citrus reticulata* peel extracts mediated synthesis of CuNPs. The synthesized CuNPs were characterized by TEM analysis and it showed that CuNPs are spherical in shape, monodisperse, and their size ranges between 54 and 72 nm. The CuNPs acts as single material that inhibits both acid microbial corrosion of X80 steel (Ituen et al., 2020). CuNPs were prepared by using peel extract of *Punica granatum* as a reducing agent as well as a stabilizing agent. UV-Vis spectroscopy

studies confirmed the formation of CuNPs. The prepared CuNP size and shape were analyzed by using TEM technique and found that 15–20 nm CuNPs showed high antibacterial activity against opportunistic pathogens, that is, *Pseudomonas aeruginosa*, *Enterobacter aerogenes* MTCC 2823, *Salmonella enterica* MTCC 1253, and *Micrococcus luteus* MTCC 1809 (Kaur et al., 2016). A similar analysis was carried out for the synthesis of CuNPs using peel extracts such as banana *P. granatum* (Borah et al., 2017).

Seed extracts

Yan and coworkers demonstrated CuNPs synthesis from copper nitrate using *Nigella sativa* L. seed aqueous extract (Yan et al., 2020). The FTIR spectrum shows the presence of many antioxidant compounds with related bonds caused excellent conditions for the reduction of copper ions into CuNPs. The UV-visible spectroscopy analysis indicates the characteristic absorption peak in the range of 550–560 nm. TEM micrographs showed that the average particle size of the CuNPs is 19.5 nm (Yan et al., 2020). Similarly, CuNPs were synthesized from *Persea americana* seeds extract, which are spherical in shape and the size in the range of 42–90 nm (Girón-Vázquez et al., 2019). These CuNPs show an excellent antioxidant activity using DPPH assay against the plant pathogens including *Fusarium oxysporum*, *Aspergillus fumigatus*, and *Aspergillus niger*.

Gums

Chawla et al. (2020) reported CuNPs synthesis from copper sulfate using Gum Arabic. Gum Arabic acted as a reducing stabilizing agent, and the size of CuNPs was found 19.6–35.8 nm with polygonal prismatic shape. The Gum Arabic stabilized CuNPs showed enhanced antibacterial activity against different bacterial strains. Further CuNPs shows excellent photocatalytic activity for the degradation of methylene blue crystal violet (Chawla et al., 2020). Seku et al. (2018a, b) reported an eco-friendly novel method for CuNPs synthesis by hydrothermal processes using a carboxymethyl gum *kondagogu* as a reducing and stabilizing agent. The prepared CuNPs were stable in the air for about 30 days. The XRD results reveal that CuNPs were highly crystalline face-centered cubic structures. The TEM images noticed that the prepared CuNPs were spherical with an average size distribution of 14 ± 2 nm. The gum-capped CuNPs show enhanced antibacterial and antifungal activities against pathogenic strains.

Bud and latex nut extracts

The CuNPs were synthesized using *S. aromaticum* (clove) bud extract and FTIR spectrum showed an absorption peak range of 400–500 nm using the synthesized CuNPs indicating that the presence of various functional groups such as carboxyl, hydroxyl, amine, and alkenes amides at the various positions (Rajesh et al., 2018). The XRD studies revealed that CuNPs were highly crystalline with face-centered cubic phase, and the average size of the CuNPs was found ~15 nm. Valodkar et al. (2011) reported the extracellular synthesis of CuNPs using stem latex of a

medicinally important plant, *Euphorbia nivulia*. The CuNPs were stabilized by peptides and terpenoids present within the latex. The cytotoxicity potential of CuNPs was evaluated using MMT cell viability by extracellular lactate dehydrogenase release in cancer cell lines. Pradeep et al synthesized CuNPs from *areca* nut extract and tested antibacterial and antioxidant activities (Pradeep et al., 2019).

3 Mechanisms of CuNP biosynthesis

Eco-friendly synthesis of CuNPs by the utilization of phytochemicals offers more adaptable control over the size and shape of the CuNPs (various concentrations of metal salts extracts, reaction time, different temperature, pH). The formation of nanoparticles will be indicated by a color change of the resultant solution. The bioreduction of the copper metal ions begins immediately, and the change of the resulted mixture demonstrates the formation of CuNPs (Nasrollahzadeh and Mohammad Sajadi, 2015). Phytochemicals have a fundamental part in first reducing the copper ions afterward capping the CuNPs and the interaction of phytochemicals with Cu^{2+} and extract concentrations are involved to control the size and shape of CuNPs (Lee et al., 2013). Flavonoids, alkaloids, and carbohydrates contain polyphenolic compounds, such as menthol, salvinorin, cannabinoids, quercetin, polysaccharides, etc., which are present in various plants, such as *Hibiscus rosasinensis*, *Phyllanthus emblica*, *Dodonaea viscosa*, *Citrus medica* Linn., etc. These compounds play a key role in reducing and stabilizing the copper (Rajesh et al., 2018; Din et al., 2017; Rehana et al., 2017). Different functional groups present in the terpenoids, flavonoids, and polyphenols are responsible for the reduction of Cu^{2+}. It has been expected that –OH, –CHO, and –COOH can reduce Cu^{2+} ions to form CuNPs. During the preparation of CuNPs, copper ions are changed into elemental copper nuclei, and these nuclei are merged to obtain different shapes. During the nucleation, nuclei aggregate to form various shapes, for example, triangles, wires, rods, spheres, pentagons, and hexagons cubes. A few flavonoids can chelate the CuNPs with their carbonyl groups of carboxylic acids. Similarly, santin and quercetin are flavonoids with intense chelating action because of the presence of two functional groups participating in the carbonyl hydroxyls, and these groups chelate with CuNPs (Khodashenas and Ghorbani, 2014). Sugars such as monosaccharides, disaccharides, and polysaccharides can act as reducing and stabilizing agents.

4 Plasmonic behavior of CuNPs

Because of the expanding interest in the supply of energy, which is eco-friendly and lower cost than nuclear energy from fossil fuel, there is a requirement for a feasible, sustainable, and renewable source of energy. In this field, photovoltaic gadgets assume sunlight as a significant part of the earth's primary energy source and sunlight-based energy has been broadly concentrated as an efficient power fuel source (Parveen et al., 2016). Solar scientists around the globe are demonstrating

deep attention in plasmonic solar cells, as it exploits the nanoscale optical properties of metal and metal oxide for improving optical absorption and bringing about a general increment in cell conversion efficiency. Metal nanoparticles support localized surface plasmon resonance, which is collective oscillations of conduction electrons. The resonance wavelength of the metal nanoparticles can be tuned all through a broad spectral range by changing the shape, size, and dielectric properties of the medium. Silver and gold are most broadly utilized for plasmon solar cells on the ground because their surface plasmonic wavelength lies in the visible range. Similarly, copper also shows plasmon resonance in the visible range of the solar spectrum, which is very less expensive than silver and gold in addition to being more absorbent than gold. To make a solar cell a reasonable fuel source, catching light is essential for thin film. Plasmonic solar cell CuNPs can enhance light absorption in thin-film solar cells (Brumbaugh et al., 2014; Din and Rehan, 2017).

5 Microbial synthesis CuNPs

Biogenic synthesis of CuNPs employs microorganisms such as bacteria, algae, and fungi (Fig. 3). The Biogenic CuNPs can be produced either by bioreduction, where metal ions are chemically reduced into their stable forms due to oxidation of enzymes or by intracellular and extracellular extract of living beings. In the later process, the microorganisms are mixed with copper salts at room temperature, within a couple of minutes the reaction is completed, CuNPs are formed. Microorganisms serve as a good source for the biosynthesis of CuNPs due to their easy, cost-effective, environmental friendly biochemical diversity, and fast cultivation under normal laboratory conditions (Shobha et al., 2014; Giannousi et al., 2017).

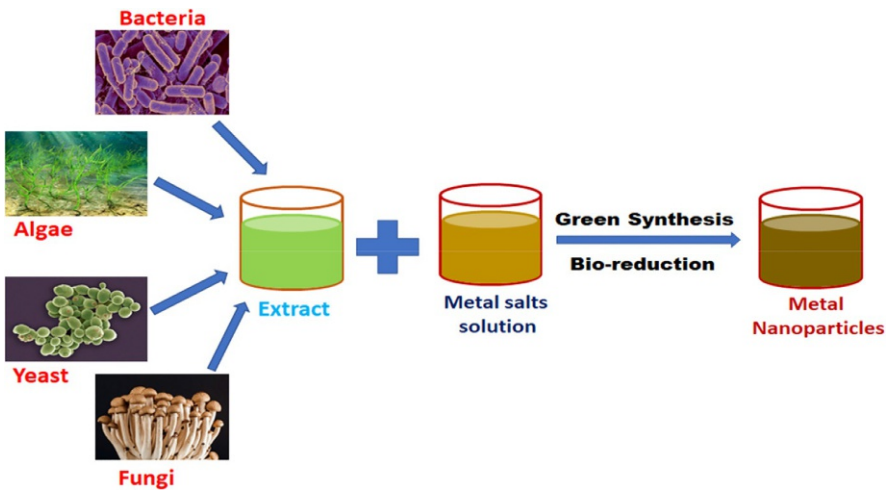

FIG. 3

Microbial synthesis of CuNPs.

5.1 Biosynthesis of CuNPs by Actinomycetes

There are general reports on the extracellular or intracellular synthesis of CuNPs by actinomycetes such as *Streptomyces griseus* and *Streptomyces capillispiralis*. Usha et al. (2010) reported that CuNPs are biosynthesized extracellularly by using *Streptomyces griseus* synthesized CuNPs showed UV-Vis absorption peak at 580 nm, indicating the formation of CuNPs. Further FTIR spectrum showed that the biogenic CuNPs bounded by various functional groups. Absorption peaks appeared at various wavenumbers indicating the presence of protein in the sample helped to identify the possible biomolecules responsible for the reduction and stabilization of bioreduced CuNPs. TEM analysis confirmed that most of the CuNPs were quasispherical in shape with average CuNP sizes ranges between 10 and 40 nm (Pradeep et al., 2019). Synthesized CuNPs were used in soil application in *P. hypolateritia* infected tea plants. Similarly, biogenic CuNPs were synthesized by using endophytic actinomycetes such as *Streptomyces capillispiralis*. A change of biomass filtrate color confirms the biosynthesized CuNPs from light blue into greenish-brown color observed in UV-Vis spectra, and it shows a characteristic peak at 600 nm. TEM analysis showed CuNPs were spherical-monodispersed shaped with sizes between 3.6 and 59 nm (Al-Hakkani, 2020). The CuNPs showed different biomedical applications against infectious microorganisms and biocontrol of phytopathogenic fungi. Hasheminya and Dehghannya (2019) reported marine endophytic actinomycetes isolated from seaweeds that were used for the synthesis of CuNPs, which were characterized by UV-Vis, FTIR, XRD, and TEM. The synthesized CuNPs showed good antibacterial activity against human pathogenic bacteria.

5.2 Fungal-mediated biosynthesis of CuNPs

The synthesis of CuNPs through fungi has attracted many researchers as this method process has an edge over the use of bacterial strains. The fungi-mediated synthesis of nanoparticles can occur by in vivo and in vitro strategies: additionally, the manifestation of mycelia offers enhanced surface area permitting fungi to secrete a higher amount of proteins than bacteria, which would profoundly increase the formation of the nanoparticles (Shnoudeh et al., 2019). A few fungi possess high intracellular metal uptake volumes, which leads to a smaller size for the particles synthesized. The formation of nanoparticles is more advantageous for mycelia because it reduces the adverse effects induced by ions. *Trichoderma koningiopsis* was used to produce spherical CuNPs that were synthesized extracellularly (Salvadori et al., 2013). These CuNPs characterized by hydroxyl carbonyl groups not only acted as reducing agents of copper salts but also functionalized the CuNPs surface contributing to making them stable. CuNPs were synthesized using white-rot fungus *Stereum hirsutum* under different pH conditions. TEM studies confirmed that the CuNPs were spherical in shape with size between 5 and 20 nm. The presence of $-NH_2$ attached to CuNPs was confirmed by

FTIR, which suggest that extracellular proteins of fungus were responsible for the stabilization of CuNPs (Cuevas et al., 2015).

5.3 Bacterial-mediated biosynthesis of CuNPs

Bacteria have an extraordinary capability to reduce copper ions into CuNPs are one of the most appropriate candidates for CuNPs synthesis due to simple handling high yield. Rather than different organisms, bacteria can be effectively formed and controlled genetically for the biomineralization of copper ions (Rai and Duran, 2011). Bacteria are regularly exposed to toxic, harsh environmental conditions resulting from high concentrations of heavy metal ions in their surroundings. Notwithstanding, they have evolved different natural defense mechanisms such as intracellular or extracellular mechanisms (Shobha et al., 2014). The bacteria can productively use these defense mechanisms for the synthesis of CuNPs for various kinds of applications. Synthesis of CuNPs has been reported by using *Pseudomonas stutzeri* bacteria through electroplating, synthesized CuNPs which were spherical in shape. CuNPs were synthesized using a copper-resistant bacterial strain *Escherichia* sp. (Shobha et al., 2014). The morphology of CuNPs was analyzed using TEM studies. It was spherical in shape with particle size ranging from 22.33 to 39 nm. FTIR studies reveal that the presence of coated proteins is involved in the capping of CuNPs. The catalytic activity was checked against azo dyes such as Congo red, direct blue-1, and reactive black-5 (Shobha et al., 2014). Similarly CuNPs with the range of 8–15 nm were synthesized using *Pseudomonas stutzeri* (Varshney et al., 2010). Another biological method has been reported for the synthesis of CuNPs using *Morganella* bacteria under an aqueous physical environment to obtain polydispersed nanoparticles (Shobha et al., 2014). Al-Hakkani (2020) reported biotransformation of CuNPs using a cell-free culture extract of metal copper-resistant bacteria *Pseudomonas fluorescens*. The biosynthesized CuNPs showed toxicity against the stored grain pest (*Tribolium castaneum*), where LC50 value was 37 ppm after 5 days of treatment (El-Saadony et al., 2020). Table 2 summarizes the microorganisms used in the synthesis of CuNPs.

6 Characterization of CuNPs

To understand the synthesis mechanism of nanoparticles and their applications in different sectors, it is essential to characterize the CuNPs. The characterization of CuNPs concludes morphology, size, structure, shape, and covering of CuNPs. There are many different techniques accessible (Fig. 4) for the characterization of CuNPs. For CuNP shape and size characterization, microscopy methods such as transmission electron microscopy (TEM), scanning electronic microscopy (SEM), and atomic force microscopy (AFM) have been commonly utilized. In this chapter, we have explored some techniques, viz., UV-visible spectroscopy, Fourier transform infrared spectroscopy (FTIR), X-ray diffraction (XRD), TEM, SEM, dynamic light scattering (DLS), and AFM.

Table 2 Microbial mediated biosynthesis of CuNPs.

Microorganism	Species name	Size (nm)	Shape/structure/morphology	References
Bacteria	*Morganella morganii*	19.2	Quasispherical	Ramanathan et al. (2011)
	Escherichia coli	15–20	Spherical	Bocarando-Chacón et al. (2020)
	Pseudomonas sp.	84–130		Shnoudeh et al. (2019)
	Pseudomonas stutzeri	8–15	Spherical	Varshney et al. (2010)
	Serratia	10–30	Polydispersed	Hasan et al. (2008)
	M. psychrotolerans, *M. morganii* RP42	20	Spherical	Ramanathan et al. (2011)
	Pseudomonas stutzeri	50–150	Spherical	Varshney et al. (2011)
	Shewanella loihica PV-4	10–16		Lv et al. (2018)
	Escherichia coli	10–40	Quasispherical	Yoon et al. (2007)
	Kocuria flava	5–30	Quasispherical	Kaur et al. (2015)
	Salmonella typhimurium	49	Spherical	Ghorbani et al. (2015)
	Shewanella oneidensis	20–40		Kimber et al. (2018)
	Morganella psychrotolerans	4–60	Irregular in shape	Pantidos and Horsfall (2020)
	Hypocrea lixii	24.5	Spherical	Salvadori et al. (2013)
	Stereum hirsutum	5–20	Spherical	Cuevas et al. (2015)
	Pseudomonas fluorescens	49	Spherical hexagonal	Shantkriti and Rani (2014)
Fungi	*Fusarium oxysporum*	93–115	Spherical	Bramhanwade et al. (2016)
	Pleurotus ostreatus fermented fenugreek	31–39	Monodisperse	El-Batal et al. (2018)
	Rhodotorula mucilaginosa	10.5	Spherical	Salvadori et al. (2014b)
	Hypocrea lixii	24.5	Spherical	Salvadori et al. (2013)
	Penicillium aurantiogriseum		Spherical	Honary et al. (2012)
	Penicillium citrinum	85–295	Spherical	Honary et al. (2012)
	Stereum hirsutum	5–20	Spherical	Cuevas et al. (2015)
	Aspergillus niger strain STA9	500		Noor et al. (2020)
	Trichoderma koningiopsis	85.7	Spherical	Salvadori et al. (2014a)
	Fusarium oxysporum	93–115	Spherical	Bramhanwade et al. (2016)

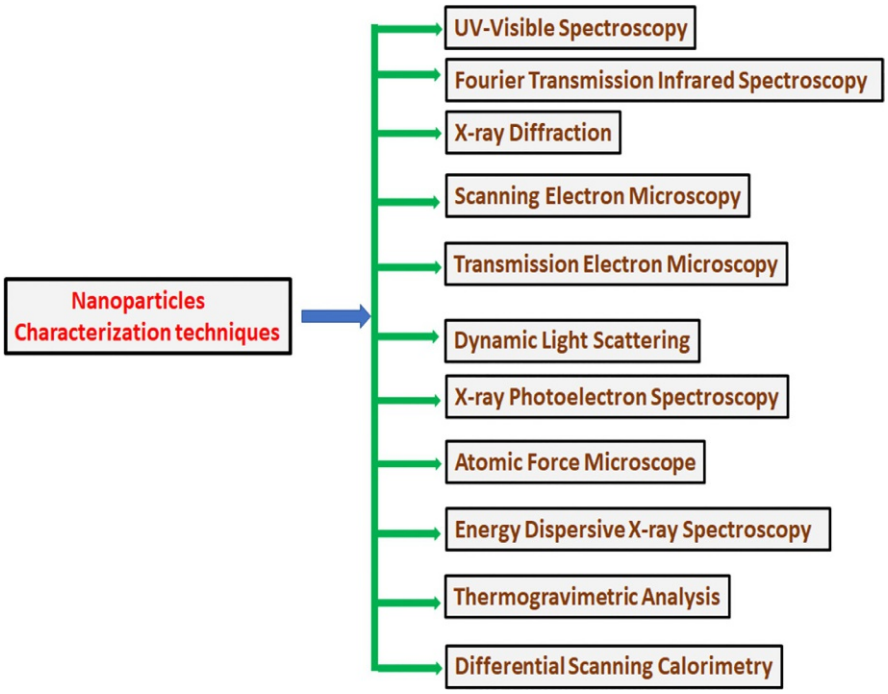

FIG. 4

Characterization technique of CuNPs.

6.1 UV-Visible spectroscopy

The applications of UV-visible spectroscopy are generally concerned with UV light (200–400 nm) and visible light (400–800 nm). UV-Vis spectra have been used to be essential characterization for the detection of synthesized CuNPs because the peak position shape of the spectra depends on particle size. Generally, CuNPs are characterized by UV-visible, especially after synthesis as the color of the reaction will change. Nagar and Devra (2017) reported the synthesis and characterization of CuNPs using *Azadirachta indica* leaf extract. The synthesized CuNPs showed the absorption peak at 560 nm, which indicates the SPR of CuNPs formed. Seku et al. (2018a, b) reported that carboxymethyl gum kondagogu-capped CuNPs showed an absorption peak at 530 nm.

6.2 FTIR analysis

FTIR measures infrared intensity vs wavelength of light, and it is used to determine the functional groups present on the surface of the nanoparticles in the presence of protein, hydroxyl, carbonyl, groups, which is a source for the biogenic synthesis (Gangapuram et al., 2018). Asghar and his colleague reported the green synthesis of

CuNPs using six different plants. The synthesized CuNPs showed an FTIR spectrum range of 500–4000 cm^{-1} designated several functional groups on the CuNPs surfaces. The FTIR spectrum showed relatively similar peaks in the following 3400–3460, 2812–2966, 2368–2378, 1625–1654, 1348–1395, 1198–1284, 1039–1091, 751–829, 542–588 cm^{-1}, characterizing the noticeable functional groups of phenolic flavonoids which are mainly responsible for the reduction of Cu^{2+} ions into CuNPs. CuNPs were synthesized flower extract of *Aloe vera* (Asghar and Asghar, 2020). The FTIR spectrum of CuNPs showed bands at 547, 1041, 1373, 1604, 2908, 3380 cm^{-1} along with other bands. The FTIR spectra reveal that there was a thin film of proteins and some secondary metabolites present on the surface of CuNPs. *Ficus religiosa*-mediated synthesized CuNPs showed an FTIR spectrum including alkaloids, flavonoids, and terpenoids (Sankar et al., 2014).

6.3 XRD studies

Crystal lattice structure and crystallite size of synthesized nanoparticles were determined by XRD analysis. Zhao et al. (2020) demonstrated the crystallinity of CuNPs *A. eriophyllum* was determined using the XRD studies. In the diffractogram, the peak positions appeared 2θ values at 43.1, 50.2, and 74.1 are indexed as (111), (200), and (220) planes, respectively, which are in good agreement with the monoclinic phase. The average crystalline size of CuNPs from *A. eriophyllum* was calculated using XRD according to the Scherrer formulae. *Azadirachta indica* leaves extract capped CuNPs show XRD peaks at 2θ = 43.5, 49.9, and 74.01 which are corresponding to (111), (200), and (220) representing a face-cantered cubic structure of copper.

6.4 TEM analysis

TEM analysis was used for the morphological analysis of nanoparticles. Their image indicates the size and shape distribution of nanoparticles in different ranges. Saranyaadevi et al. (2014) calculated the CuNP size by using TEM analysis of the particle size 50–100 nm. *Garcinia mangostana* leaf extract-mediated synthesized CuNPs were found to have a mean size of 20–25 nm confirmed by TEM studies. *S. aromaticum* are used for the synthesis of CuNPs, and the TEM characterization indicated that synthesized CuNPs were spherical and monodispersed (Subhankari and Nayak, 2013). Kaur et al. (2014) reported CuNP of size 15–20 nm. Rajesh et al. reported CuNP biosynthesized by using *Tilia* extract showed 4.7–17.4 nm size using TEM (Hassanien et al., 2018). The CuNPs has synthesized from the peel extract of *P. granatum*, size was found to be 15–20 nm and spherical in shape (Kaur et al., 2016). The XRD crystallography investigations exhibited end-centered monoclinic crystalline nature nanoparticles with 17.5 nm average size. The microscopic (AFM, SEM, TEM) analyses unveiled spherical-shaped particles with 2–69 nm size of the CuO NPs (Yugandhar et al., 2018).

6.5 SEM analysis

The SEM images demonstrated that the prepared nanoparticles were more or less uniform in size and shape. *Syzygium aromaticum*-mediated CuNPs obtained were a size of 40–50 nm by SEM studies (Rajesh et al., 2018). Similarly CuNps were synthesized by *Capparis zeylanica* plant extract and characterized their size and shape of nanoparticles with 60–100 nm (Saranyaadevi et al., 2014). Green eco-friendly CuNPs were synthesized by using an aqueous extract of the *E. caucasicum* Trautv leaves. SEM images of synthesized nanoparticles showed that spherical CuNPs were formed with a size generally less than 40 nm (Hasheminya and Dehghannya, 2019). The CuNPs were observed as spherical shape in *Garcinia mangostana* leaf (Prabhu et al., 2017) and *Malva sylvestris* leaf extracts (Benhammada and Trache, 2021), respectively.

6.6 DLS studies

DLS studies were used to find out the surface charge hydrodynamic size of nanoparticles. *C. paniculatus*-mediated synthesized CuNPs showed the negative zeta potential at − 22.2 mV; a high negative value of zeta potential specifies a strong repellent force among the particles that prevents agglomeration (Mali et al., 2020). Rajesh et al. (2018) have prepared CuNPs using *Syzygium aromaticum* bud extract. The zeta potential measurement elicits the appearance of a maximum peak at − 23.3 mV. The observed negative zeta potential, suggesting excellent stability of the CuNPs were synthesized using *Bacillus cereus*, CuNPs zeta potential confirmed the charge − 19.6 mV on the surface of CuNPs (Tiwari et al., 2016). Similarly, Rajesh et al. (2018) synthesized CuNPs from *Syzygium aromaticum* and size was calculated with 4.8 nm, whereas in *Syzygium alternifolium* extract 61.1 nm respectively (Yugandhar et al., 2018).

6.7 Atomic force microscopy (AFM)

The AFM is another technique that was used to determine the surface roughness, which is a significant aspect of the bio adhesion on bacterial surfaces. CuNPS from *Allium* synthesized using *F. vulgaris* extract that height measurements indicate that the CuNPs from *Allium* had a diameter between 45 and 50 nm (Zangeneh et al., 2019). Also, the AFM showed the formation of homogeneous distribution of CuNPs without any agglomeration. The AFM analysis of CuNPs of *Aegle marmelos Correa* showed that the biomaterial surrounding the CuNPs was agglomerated, forming distinct nanostructure (Angajala et al., 2014).

7 Applications of CuNPs

The applications of biogenic synthesized CuNPs have been progressively increased as they exhibit properties such as silver and gold nanoparticles. Silver and gold nanoparticles showed biological catalytic activity; however, these are expensive.

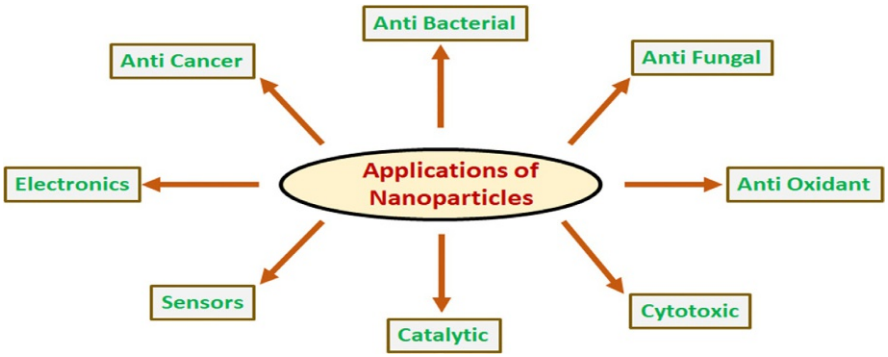

FIG. 5

Application of green-synthesized CuNPs.

Consequently, scientists have been attracted toward the CuNPs, which show excellent catalytic biological activity. This chapter has been taken into account a few applications where green-synthesized CuNPs are utilized for different biomedical, agricultural, photocatalytic, and industrial environmental applications. The key biomedical applications of biogenic synthesized CuNPs investigated here are antibacterial, antifungal, antiviral, antiparasitic, and anticancer activity (Santhoshkumar et al., 2019; Al-Hakkani, 2020). The CuNPs are applied for environmental remediation in the reduction of industrial effluents such as dyes nitro compounds (Din and Rehan, 2017). Fig. 5 showed various applications of synthesized CuNPs.

7.1 Antibacterial activity of CuNPs

Antibacterial activity CuNPs have the properties of small size, high surface-to-volume ratio, and high dispersion, which allow them to interact with the microbial surface. The high surface-to-volume ratio of CuNPs increases their interaction with microbial cell surface to carry out broad-spectrum antimicrobial activities. Chawla et al. (2020) demonstrated antimicrobial efficiency of CuNP capped with 1% gum Arabic evaluated against various pathogenic organisms. The diameter of inhibition zones around each well is evaluated. *Gum Arabic* from CuNPs showed a significant ($P < .05$) higher zone of inhibition for *Salmonella typhimurium* (27 mm) than that of other bacterial strains (Chawla et al., 2020). Punniyakotti et al. (2020) synthesized CuNPs using *Cardiospermum halicacabum* leaf extract. The synthesized CuNPs showed effective antibacterial activity against Gram-positive and Gram-negative bacterial strains. CuNPs were synthesized by using *Cissus arnotiana* plant extract, and the biosynthesized CuNPs exhibited significant antibacterial activity against the Gram-negative bacteria, *E. coli* with an inhibition zone of 22.20 ± 0.16 mm at 75 μg/mL (Rajeshkumar et al., 2019). CuNPs prepared from *Moringa oleifera* leaf extracts. The synthesized CuNPs tested antibacterial activity against *Klebsiella pneumoniae*, *Enterococcus faecalis*, *Escherichia coli*, and *Staphylococcus aureus*

(Das et al., 2020). *Capparis spinosa*-mediated synthesis of CuNPs showed their antibacterial activity compared with the Gram-negative bacteria (*Klebsiella pneumoniae* and *E. coli*) and Gram-positive bacteria (Ebrahimi et al., 2017). Similarly, CuNPs were synthesized by six plant leaf extracts such as *Azadirachta indica*, *Avicennia marina*, *Datura stramonium*, *Eucalyptus camaldulensis*, *Murraya koenigii*, and *Rosa rubiginosa* (Asghar and Asghar, 2020). The antibacterial activities of each CuNPs were found in the descending order *A. indica* > *D. stramonium* > *M. koenigii* > *R. rubiginosa* > *A. marina* > *E. camaldulensis*. Sreeju et al. (2016) reported the synthesis of CuNPs with *Psidium guava* and evaluated the dose-dependent antibacterial activity of the CuNPs against *E. coli* and *Staphylococcus aureus*. The antibacterial activities of green-synthesized CuNPs were summarized in Table 3.

7.2 Antioxidant activity of CuNPs

Human body is consistently under oxidative stress, which causes an unevenness between the free-radical antioxidants. The unevenness between antioxidants and prooxidants initiates oxidative pressure. The generation of free radicals causes infections, for example, Parkinson, autism, obesity, glomerulonephritis, Alzheimer, vasculitis, etc. Antioxidants are compounds that can restrain the creation of prooxidants radicals, defuse the free radicals, and avoid infections consequently (Joshi et al., 2019). Thiruvengadam coworkers reported the antioxidant activity of CuNPs using *Millettia pinnata* flower extract, by means of a test that used the DPPH assay. The CuNPs showed higher free-radical scavenging activity than plant extracts (Thiruvengadam et al., 2019). *Terminalia arjuna*-mediated synthesized CuNPs showed enhanced antioxidant activity. CuNPs synthesized from *Psidium guava* leave extract show antioxidant activity through DPPH, OH, and NO radical scavenging assays and greater improvement of thermal conductivity (Yallappa et al., 2013). Chung et al. (2017) examined the antioxidant activity of CuNPs assessed by DPPH free radical, using ascorbic acid as a positive control, at various concentrations. Similarly, copper nanoparticles from *Falcaria vulgaris* leaf extracts showed very good antioxidant activity (Zangeneh et al., 2019). It is concluded that an increase in concentrations increases the mean percentage inhibition values.

7.3 Antifungal activity

Asghar et al. (2018) demonstrated the antifungal activity of CuNPs synthesized with tea extract on *A. flavus*, and *A. parasiticus* fungal species. Similarly, Hassanien et al. (2018) demonstrated the antifungal activity of CuNPs against *Candida albicans* compared with the standard antifungal agent Fluconazole. The CuNPs showed an enhanced antimicrobial effect than Fluconazole. *M. oleifera* leaf extract-mediated biosynthesized CuNPs showed potent antifungal activity against *Aspergillus niger*, *Aspergillus flavus*, *Candida albicans*, and *Candida glabrata*. The results concluded that antifungal activity of CuNPs is higher than the *M. oleifera* leaf extract against *Candida albicans* and *Candida glabrata* (Das et al., 2020). Seku et al. (2018a, b) evaluated the antifungal

Table 3 Antibacterial effect of biogenic synthesized CuNPs on different microbes.

Biological entity	Test microorganisms	Method	References
Lantana camara	*E. coli*	Agar disc diffusion	Majumder (2012)
Pseudomonas sp.	*E. coli*	Agar disc diffusion	Shantkriti and Rani (2014)
Gum karaya	*E. coli*, *S. aureus*	Well-diffusion method	Padil and Černík (2013)
Fusarium oxysporum	*E. coli*	Agar disc diffusion	Bramhanwade et al. (2016)
Brassica juncea	*Fusarium oxysporum*, *Alternaria alternata*, *Curvularia lunata*, and *Phoma destructiva*	Agar disc diffusion	Nair and Chung (2015)
Zingiber officinale	*E. coli*	Zone of inhibition assay	Chitra et al. (2015)
Tridax procumbens	*E. coli*	Agar disc diffusion	Kalpana et al. (2016)
Bifurcaria bifurcata	*E. aerogenes*, *S. aureus*	Disc diffusion	Abboud et al. (2014)
Datura innoxia	*Xanthomonas oryzae* pv. *oryzae*	Disc diffusion	Din et al. (2017)
Magnolia kobus	*E. coli*	Agar disc diffusion	Lee et al. (2013)
Citrus limon and *Turmeric curcumin*	*P. aeruginosa*, *E. coli*, *S. aureus*, *B. subtilis*	Disc diffusion	Jayandran et al. (2016)
Syzygium aromaticum	*E. coli* 2065	Agar disc diffusion	Rajesh et al. (2018)
Citrus medica Linn.	*P. acnes*, *Salmonella typhi*, *K. pneumoniae*, *P. aeruginosa*, *E. coli*	Disc diffusion	Cheirmadurai et al. (2014)
Vitis vinifera	*Bacillus subtilis*, *E. coli*	Disc diffusion	Shaikh et al. (2016)
Ficus carica	*Pediococcus acidilactici*	Disc diffusion	Usman et al. (2019)
Psidium guajava	*E. coli*, *S. aureus*	Disc diffusion	Sreeju et al. (2016)
Bacopa monnieri	*E. coli*, *P. aeruginosa*	Zone of inhibition assay	Sapna Thakur (2014)

activity of carboxymethyl gum kondagogu-capped CuNPs using the agar well diffusion assay method. The antifungal activity of gum-capped CuNPs against *Aspergillus niger*, *Aspergillus oryzae*, *Candida albicans*, and *Candida glabrata* was investigated using antifungal drug miconazole used as control (Seku et al., 2018b). The CuNPs showed an excellent antifungal activity in these fungal species. The Antifungal activities of green-synthesized CuNPs were summarized in Table. 4.

7.4 Impact of CuNPs in agriculture

The utilization of nanoscience in agriculture has been prevalently hypothetical. Since it has started, it will keep on critical impact in the areas of disease detection and improvement of nutrient absorption delivery. It can improve yield by delivering pesticides for focused treatment to fight diseases (Ameh and Sayes, 2019). The effect of nanoparticles on a crop is relied upon several factors starting from composition, concentration, shape, size and properties of nanoparticles. The Metal and metal oxide nanoparticles act as mediators of DNA damage in living organisms; however, the molecular mechanisms by which damage occurs are inadequately examined (Pourakbar et al., 2020). The CuNPs are used in horticultural applications, in CuNP empowered agriculture products, for example, pesticides and fertilizers (Shobha et al., 2014). These CuNPs help in the control of microbes because of the CuNPs' capacity to bind strongly to the cell wall, release ions, and induction of leaky membranes. The uptake of CuNPs in plants relies on the species, the way of utilization, and the composition development media (Giannousi et al., 2017). Fig. 6 shows the hypothetical mechanism of functioning of nano-copper during plant development. Given these discoveries, there is an expanded chance of CuNP presentation to humans because of their utilization as either pesticides or fertilizers in agriculture (Kasana et al., 2017).

7.5 Catalytic applications of CuNPs

Metal oxide nanoparticles have been showing excellent catalytic applications due to their small size, high surface tension, which atoms more active on the surface. The field of nanocatalysis has been exceptionally dynamic in both homogeneous and heterogeneous catalysis (Reddy et al., 2015). Nanoparticles are cost-effective and can be reused as a catalyst. The use of metal nanoparticles as a catalyst has expanded dramatically over the most recent decades because of their excellent catalytic performance (Seku et al., 2018a). The possibility of utilizing small-range metal nanoparticles having different properties for various shapes makes them exceptionally alluring (Seku et al., 2019). Among them, CuNPs showed excellent catalytic applications. The reduction degradation of hazardous toxic organic dyes in wastewater has been a focal point of consideration during the past few years. Because of the biologically and chemically stable structure of dyes, it is exceptionally hard to eliminate them by regular process (Nasrollahzadeh et al., 2015c; Nasrollahzadeh and Mohammad Sajadi, 2015). Hence, the reduction of industrial dye effluents has attained great importance, both environmentally and scientifically. Nasrollahzadeh et al. (2018) evaluated the

Table 4 Antifungal effect of biogenic synthesized CuNPs.

Biological entity	Microorganisms	References
Ocimum sanctum	*Alternaria carthami*, *Colletotrichum gloeosporioides*, *Colletotrichum lindemuthianum*, *Drechslera sorghicola*, *Fusarium oxysporum* f.sp.	Muthulakshmi et al. (2017)
Citrus medica Linn.	*Fusarium culmorum*, *Fusarium oxysporum*	Shende et al. (2015)
Syzygium aromaticum	*Aspergillus niger*, *Aspergillus flavus*, *Penicillium* spp.	Rajesh et al. (2018)
Tridax procumbens	*Aspergillus niger*	Kalpana et al. (2016)
T. arjuna	*Candida albicans*, *Trichophyton rubrum*, *Chrysosporium indicum*	Yallappa et al. (2013)
Citrus limon and *Turmeric curcumin*	*Candida albicans*, *Curvularia*, *Aspergillus niger*, *Trichophyton simii*	Jayandran et al. (2015)
Allium eriophyllum Boiss	*Candida guilliermondii*, *Candida krusei*, *Candida glabrata*, *Candida albicans*	Zhao et al. (2020)
Moringa oleifera	*Aspergillus niger*, *Aspergillus flavus*, *Candida albicans*, *Candida glabrata*	Das et al. (2020)
Carboxymethyl gum kondagogu	*Candida albicans*, *Candida parapsilosis*, *Aspergillus oryzae*, and *Aspergillus niger*	Seku et al. (2018b)

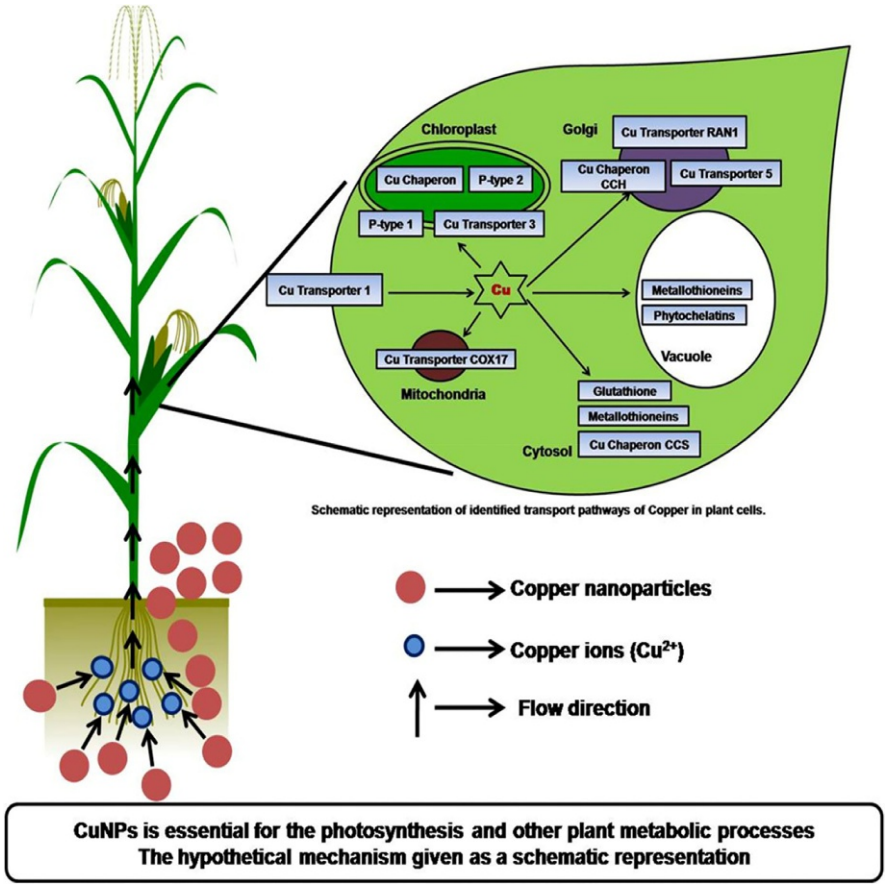

FIG. 6

Hypothetical mechanism of functioning of nano-copper during plant development.

catalytic efficiency of *Centella asiatica* L. leaf extract-mediated CuNPs. The prepared CuNPs were found to be an efficient reusable heterogeneous catalyst for the reduction of nitro compounds such as 4-nitrophenol, 2,4-dinitrophenylhydrazine, organic dyes such as rhodamine B, Congo red, and methylene blue at ambient temperature. Momeni et al. (2016) studied the catalytic activity of *Euphorbia prolifera* leaf extract-mediated CuNPs for the reduction of methylene blue and Congo red in the presence of sodium borohydride in water. It was found that the catalytic efficiency of CuNPs in the degradation of methylene blue and Congo red was unchanged after five cycles through the catalytic degradation. Issaabadi et al. (2017) reported that CuNP synthesized with *Thymus vulgaris* leaf extract showed a catalytic reduction of methylene blue and Congo red. The results showed that the CuNPs have excellent reduction as a catalyst with convenient recyclable long-term stability. *Psidium guava* leaf extract stabilized CuNPs showed catalytic activity for the degradation of the

organic effluent's nitrophenols, methyl orange, methylene blue, methyl red and eosin yellow (Khani et al., 2018). Goswami and Das (2018) reported CuNP synthesized with cellulose from the inner stem of *Hibiscus sabdariffa* by a facile method.

The synthesized CuNPs used as a catalyst in the C–N coupling reactions involved open chained as well as cyclic secondary amines. The catalyst demonstrated excellent catalytic activity (yield 82%–95%) was reused for up to six cycles (Goswami and Das, 2018). The Huisgenazide-alkyne cycloaddition is an illustrative reaction of click chemistry, particularly utilizing a copper catalyst. It produces 1,2,3-triazole, which has applications in organic chemistry and pharmaceutical biomaterials (Nasrollahzadeh and Mohammad Sajadi, 2015). Nasrollahzadeh and Mohammad Sajadi (2015) demonstrated the catalytic activity of CuNPs in the synthesis of triazole. *Ginkgo biloba* L. leaf extract stabilized CuNPs showed catalytic activity of Huisgenazide-alkyne cycloaddition of benzyl azido to phenylacetate at room temperature, which prompts to complete conversation of 1,4-disubstituted 1,5-disubstituted, and 1,2,3-triazoles.

8 Conclusions

In this chapter, we represent few strategies for the synthesis of CuNPs utilizing physical, chemical, and biological merhods. Particularly the green synthesis which has shown to be cost-effective, biocompatible, and simple to be performed at any laboratory as they offer a greater variety of potential methods and a new route of synthesis. Furthermore, the phytochemical synthesis of CuNPs is rapid reliable. It is feasible to utilize all plant parts for the synthesis of CuNPs, for example, flower, gums, root, fruits, seeds peel and also microorganism. These biological materials are enriched with biomolecules with a significant function in the reduction of copper ions. In light of this, bioreduction capacity of different biological materials is utilized in the preparation of CuNPs under different conditions. The varied range of phytochemicals, enzymes, and proteins control the shape and size of CuNPs. The mechanisms of particle formations were discussed as significant to understand the outcome of any synthetic methods. This chapter also reviews the utilization of these green-synthesized CuNPs in various fields viz., biomedical, food, and agriculture used for catalyzing and sensing..

References

Abboud, Y., Saffaj, T., Chagraoui, A., El Bouari, A., Brouzi, K., Tanane, O., Ihssane, B., 2014. Biosynthesis, characterization antimicrobial activity of copper oxide nanoparticles (CONPs) produced using brown alga extract (*Bifurcaria bifurcata*). Appl. Nanosci. 4, 571–576.

Abd-Elkareem, J.I., Bassuony, H.M., Mohammed, S.M., Fahmy, H.M., Abd-Elkader, N.R., 2016. Eco-friendly methods of copper nanoparticles synthesis. J. Bionanosci. 10, 15–37.

Abhiman, G.R., Devi, P.S., Vijayalakshmi, K.A., 2018. Green synthesis with antibacterial investigation of copper nanoparticles using *Azadirachta indica* (neem) leaf extract. Int. J. Sci. Res. Sci. Technol. 4, 697–701.

Akintelu, S.A., Folorunso, A.S., Folorunso, F.A., Oyebamiji, A.K., 2020. Green synthesis of copper oxide nanoparticles for biomedical application environmental remediation. Heliyon 6, e04508.

Al-Hakkani, M.F., 2020. Biogenic copper nanoparticles their applications: a review. SN Appl. Sci. 2, 1–20.

AL-Jobory, H.S., Hassan, K.M.A., Kareem, Z.H., Alkaim, A.F., 2019. Green synthesis of silver nanoparticles its antibacterial activity: a review. Plant Arch. 19, 2363–2367.

Amaliyah, S., Pangesti, D.P., Masruri, M., Sabarudin, A., Sumitro, S.B., 2020. Green synthesis characterization of copper nanoparticles using *Piper retrofractum* Vahl extract as bioreductor capping agent. Heliyon 6, e04636.

Ameh, T., Sayes, C.M., 2019. The potential exposure hazards of copper nanoparticles: a review. Environ. Toxicol. Pharmacol. 71, 103220.

Amrani, M.A., Srikanth, V.V.S.S., Labhsetwar, N.K., Al-Fatesh, A.S., Shaikh, H., 2016. *Phoenix dactylifera* mediated green synthesis of Cu_2O particles for arsenite uptake from water. Sci. Technol. Adv. 17, 760–768.

Angajala, G., Pavan, P., Subashini, R., 2014. One-step biofabrication of copper nanoparticles from *Aegle marmelos* correa aqueous leaf extract evaluation of its anti-inflammatory mosquito larvicidal efficacy. RSC Adv. 4, 51459–51470.

Asghar, M.A., Asghar, M.A., 2020. Green synthesized characterized copper nanoparticles using various new plants extracts aggravate microbial cell membrane damage after interaction with lipopolysaccharide. Int. J. Biol. Macromol. 160, 1168–1176.

Asghar, M.A., Zahir, E., Shahid, S.M., Khan, M.N., Asghar, M.A., Iqbal, J., Walker, G., 2018. Iron, copper silver nanoparticles: green synthesis using green black tea leaves extracts evaluation of antibacterial, antifungal aflatoxin B1 adsorption activity. LWT—Food Sci. Technol. 90, 98–107.

Awwad, A.M., Albiss, B., 2015. Biosynthesis of colloidal copper hydroxide nanowires using Pistachio leaf extract. Adv. Mater. Lett. 9, 131–137.

Bandi, R., Devulapalli, N.P., Dadigala, R., Gangapuram, B.R., Guttena, V., 2018. Facile conversion of toxic cigarette butts to N, S-codoped carbon dots their application in fluorescent film, security ink, bioimaging, sensing logic gate operation. ACS Omega 3, 13454–13466.

Bandi, R., Kannikanti, H.G., Dadigala, R., Gangapuram, B.R., Vaidya, J.R., Guttena, V., 2020. One step synthesis of hydrophobic carbon dots powder with solid state emission application in rapid visualization of latent fingerprints. Opt. Mater. 109, 110349.

Benhammada, A., Trache, D., 2021. Green synthesis of CuO nanoparticles using *Malva sylvestris* leaf extract with different copper precursors their effect on nitrocellulose thermal behavior. J. Therm. Anal. Calorim. https://doi.org/10.1007/s10973-020-10469-5.

Betancourt-Galindo, R., Reyes-Rodriguez, P.Y., Puente-Urbina, B.A., Avila-Orta, C.A., Rodríguez-Fernández, O.S., Cadenas-Pliego, G., Lira-Saldivar, R.H., García-Cerda, L.A., 2014. Synthesis of copper nanoparticles by thermal decomposition their antimicrobial properties. J. Nanomater. 9, 5.

Bocarando-Chacón, J., Vargas-Vazquez, D., Martinez-Suarez, F., Flores-Juárez, C., Cortez-Valadez, M., 2020. Surface-enhanced Raman scattering antibacterial properties from copper nanoparticles obtained by green chemistry. Appl. Phys. A 126, 1–9.

Borah, R., Saikia, E., Bora, S.J., Chetia, B., 2017. Banana pulp extract mediated synthesis of Cu_2O nanoparticles: an efficient heterogeneous catalyst for the ipso-hydroxylation of arylboronic acids. Tetrahedron Lett. 58, 1211–1215.

Bramhanwade, K., Shende, S., Bonde, S., Gade, A., Rai, M., 2016. Fungicidal activity of Cu nanoparticles against *Fusarium* causing crop diseases. Environ. Chem. Lett. 14, 229–235.

Brumbaugh, A.D., Cohen, K.A., St. Angelo, S.K., 2014. Ultrasmall copper nanoparticles synthesized with a plant tea reducing agent. ACS Sustain. Chem. Eng. 2, 1933–1939.

Chauhan, A.K., 2020. Nanomaterials in biofuels. In: Nanomaterials in Biofuels., ISBN: 978-981-13-9333-4, https://doi.org/10.1007/978-981-13-9333-4.

Chawla, P., Kumar, N., Bains, A., Dhull, S.B., Kumar, M., Kaushik, R., Punia, S., 2020. Gum arabic capped copper nanoparticles: synthesis, characterization, applications. Int. J. Biol. Macromol. 146, 232–242.

Cheirmadurai, K., Biswas, S., Murali, R., Thanikaivelan, P., 2014. Green synthesis of copper nanoparticles conducting nanobiocomposites using plant animal sources. RSC Adv. 4, 19507–19511.

Chitra, K., Manikandan, A., Moortheswaran, S., Reena, K., Antony, S.A., 2015. *Zingiber officinale* extracted green synthesis of copper nanoparticles: structural, morphological antibacterial studies. Adv. Sci. Eng. Med. 7, 710–716.

Chung, I., Rahuman, A.A., Marimuthu, S., Kirthi, A.V., Anbarasan, K., Padmini, P., Rajakumar, G., 2017. Green synthesis of copper nanoparticles using *Eclipta prostrata* leaves extract their antioxidant cytotoxic activities. Exp. Ther. Med. 14, 18–24.

Cioffi, N., Ditaranto, N., Torsi, L., Picca, R.A., De Giglio, E., Sabbatini, L., Novello, L., Tantillo, G., Bleve-Zacheo, T., Zambonin, P.G., 2005. Synthesis, analytical characterization bioactivity of Ag Cu nanoparticles embedded in poly-vinyl-methyl-ketone films. Anal. Bioanal. Chem. 82, 1912–1918.

Cuevas, R., Durán, N., Diez, M.C., Tortella, G.R., Rubilar, O., 2015. Extracellular biosynthesis of copper copper oxide nanoparticles by *Stereum hirsutum*, a native white-rot fungus from Chilean forests. J. Nanomater. https://doi.org/10.1155/2015/789089.

Dadigala, R., Bandi, R.K., Gangapuram, B.R., Guttena, V., 2017. Carbon dots Ag nanoparticles decorated g-C_3N_4 nanosheets for enhanced organic pollutants degradation under sunlight irradiation. J. Photochem. Photobiol. 342, 42–52.

Dang, T.M.D., Le, T.T.T., Fribourg-Blanc, E., Dang, M.C., 2011. Synthesis optical properties of copper nanoparticles prepared by a chemical reduction method. Adv. Nat. Sci. Nanosci. Nanotechnol. 2, 015009.

Das, P.E., Abu-Yousef, I.A., Majdalawieh, A.F., Narasimhan, S., Poltronieri, P., 2020. Green synthesis of encapsulated copper nanoparticles using a hydroalcoholic extract of *Moringa oleifera* leaves assessment of their antioxidant antimicrobial activities. Molecules 25, 555.

Dhas, N.A., Raj, C.P., Gedanken, A., 1998. Synthesis, characterization, properties of metallic copper nanoparticles. Chem. Mater. 10, 1446–1452.

Din, M.I., Rehan, R., 2017. Synthesis, characterization, applications of copper nanoparticles. Anal. Lett. 50, 50–62.

Din, M.I., Arshad, F., Hussain, Z., Mukhtar, M., 2017. Green adeptness in the synthesis stabilization of copper nanoparticles: catalytic, antibacterial, cytotoxicity, antioxidant activities. Nanoscale Res. Lett. 12, 638.

Ealias, A.M., Saravanakumar, M.P., 2017. A review on the classification, characterisation, synthesis of nanoparticles their application. IOP Conf. Ser. Mater. Sci. Eng. 263, 032019.

Ebrahimi, K., Shiravand, S., Mahmoudvand, H., 2017. Biosynthesis of copper nanoparticles using aqueous extract of *Capparis spinosa* fruit investigation of its antibacterial activity. Marmara Pharm. J. 21, 866–871.

El-Batal, A.I., Al-Hazmi, N.E., Mosallam, F.M., El-Sayyad, G.S., 2018. Biogenic synthesis of copper nanoparticles by natural polysaccharides *Pleurotus ostreatus* fermented fenugreek using gamma rays with antioxidant antimicrobial potential towards some wound pathogens. Microb. Pathog. 118, 159–169.

El-Saadony, M.T., Abd El-Hack, M.E., Taha, A.E., Fouda, M.M.G., Ajarem, J.S., Maodaa, S.N., Allam, A.A., Elshaer, N., 2020. Ecofriendly synthesis insecticidal application of copper nanoparticles against the storage pest *Tribolium castaneum*. Nanomaterials 10, 587.

Ganapuram, B.R., Alle, M., Dadigala, R., Dasari, A., Maragoni, V., Guttena, V., 2015. Catalytic reduction of methylene blue Congo red dyes using green synthesized gold nanoparticles capped by *Salmaliamal abarica* gum. Int. Nano Lett. 5, 215–222.

Gangapuram, B.R., Bandi, R., Dadigala, R., Kotu, G.M., Guttena, V., 2017. Facile green synthesis of gold nanoparticles with carboxymethyl gum karaya, selective sensitive colorimetric detection of copper (II) ions. J. Clust. Sci. 28, 2873–2890.

Gangapuram, B.R., Bandi, R., Alle, M., Dadigala, R., Kotu, G.M., Guttena, V., 2018. Microwave assisted rapid green synthesis of gold nanoparticles using *Annona squamosa* L peel extract for the efficient catalytic reduction of organic pollutants. J. Mol. Struct. 1167, 305–315.

Ghorbani, H.R., Mehr, F.P., Poor, A.K., 2015. Extracellular synthesis of copper nanoparticles using culture supernatants of *Salmonella typhimurium*. Orient. J. Chem. https://doi.org/10.13005/ojc/310165.

Giannousi, K., Pantazaki, A., Dendrinou-Samara, C., 2017. Copper-based nanoparticles as antimicrobials. in nanostructures for antimicrobial therapy: nanostructures in therapeutic. Med. Ser. 23, 515–539.

Girón-Vázquez, N.G., Gómez-Gutiérrez, C.M., Soto-Robles, C.A., Nava, O., Lugo-Medina, E., Castrejón-Sánchez, V.H., Vilchis-Nestor, A.R., Luque, P.A., 2019. Study of the effect of *Persea americana* seed in the green synthesis of silver nanoparticles their antimicrobial properties. Results Phys. 13, 102142.

Golla, N., 2018. Phytosynthesis antimicrobial studies of silver nanoparticles using *Ziziphus nummularia* leave extracts. MOJ Drug Design Dev. Ther. 2 (5), 4.

Goswami, M., Das, A.M., 2018. Synthesis of cellulose impregnated copper nanoparticles as an efficient heterogeneous catalyst for C–N coupling reactions under mild conditions. Carbohydr. Polym. 195, 189–198.

Gunalan, S., Sivaraj, R., Venckatesh, R., 2012. *Aloe barbadensis* Miller mediated green synthesis of mono-disperse copper oxide nanoparticles: optical properties. Spectrochim. Acta A Mol. 97, 1140–1144.

Harne, S., Sharma, A., Dhaygude, M., Joglekar, S., Kodam, K., Hudlikar, M., 2012. Novel route for rapid biosynthesis of copper nanoparticles using aqueous extract of *Calotropis procera* L. latex their cytotoxicity on tumor cells. Colloids Surf. B 95, 284–288.

Hasan, S.S., Singh, S., Parikh, R.Y., Dharne, M.S., Patole, M.S., Prasad, B.L.V., Shouche, Y.S., 2008. Bacterial synthesis of copper/copper oxide nanoparticles. J. Nanosci. 8, 3191–3196.

Hasheminya, S.M., Dehghannya, J., 2019. Green synthesis characterization of copper nanoparticles using *Eryngium caucasicum* Trautv aqueous extracts its antioxidant antimicrobial properties. Part. Sci. Technol. 38, 1019–1026.

Hashemipour, H., Zadeh, M.E., Pourakbari, R., Rahimi, P., 2011. Investigation on synthesis size control of copper nanoparticle via chemical reduction method. J. Phys. Sci. 6, 4331–4336.

Hassanien, R., Husein, D.Z., Al-Hakkani, M.F., 2018. Biosynthesis of copper nanoparticles using aqueous Tilia extract: antimicrobial anticancer activities. Heliyon 4, e01077.

Honary, S., Barabadi, H., Gharaei-Fathabad, E., Naghibi, F., 2012. Green synthesis of copper oxide nanoparticles using *Penicillium aurantiogriseum*, *Penicillium citrinum*, *Penicillium waksmanii*. Dig. J. Nanomater. Bios. 7, 999–1005.

Huang, L., Jiang, H., Zhang, J., Zhang, Z., Zhang, P., 2006. Synthesis of copper nanoparticles containing diamond-like carbon films by electrochemical method. Electrochem. Commun. 8, 262–266.

Ijaz, F., Shahid, S., Khan, S.A., Ahmad, W., Zaman, S., 2017. Green synthesis of copper oxide nanoparticles using *Abutilon indicum* leaf extract: antimicrobial, antioxidant photocatalytic dye degradation activities. Trop. J. Pharm. Res. 16, 743–753.

Ismail, M., Khan, M.I., Khan, S.B., Akhtar, K., Khan, M.A., Asiri, A.M., 2018. Catalytic reduction of picric acid, nitrophenols organic azo dyes via green synthesized plant supported Ag nanoparticles. J. Mol. Liq. 268, 87–101.

Ismail, M., Gul, S., Khan, M.I., Khan, M.A., Asiri, A.M., Khan, S.B., 2019. Green synthesis of zerovalent copper nanoparticles for efficient reduction of toxic azo dyes Congo red methyl orange. Green Process. Synth. 8, 135–143.

Issaabadi, Z., Nasrollahzadeh, M., Sajadi, S.M., 2017. Green synthesis of the copper nanoparticles supported on bentonite investigation of its catalytic activity. J. Clean. Prod. 142, 3584–3591.

Ituen, E., Ekemini, E., Yuanhua, L., Li, R., Singh, A., 2020. Mitigation of microbial biodeterioration acid corrosion of pipework steel using *Citrus reticulata* peels extract mediated copper nanoparticles composite. Int. Biodeter. Biodegr. 149, 104935.

Jaidev, L.R., Narasimha, G., 2010. Fungal mediated biosynthesis of silver nanoparticles, characterization antimicrobial activity. Colloids Surf. B Biointerfaces 81, 430–433.

Jayandran, M., Muhamed, M., Balasubramanian, V., 2015. Facile green synthesis of copper nanoparticles using natural reducer stabilizer an evaluation of antimicrobial activity. J. Chem. Pharm. Res. 7, 251–259.

Jayandran, M., Haneefa, M.M., Balasubramanian, V., 2016. Green synthesis, characterization antimicrobial activity studies of *Curcumin aniline* biofunctionalized copper oxide nanoparticles. Indian J. Sci. Technol. 9, 1–9.

Jinu, U., Gomathi, M., Saiqa, I., Geetha, N., Benelli, G., Venkatachalam, P., 2017. Green engineered biomolecule-capped silver copper nanohybrids using *Prosopis cineraria* leaf extract: enhanced antibacterial activity against microbial pathogens of public health relevance cytotoxicity on human breast cancer cells (MCF-7). Microb. Pathog. 105, 86–95.

Joseph, A.T., Prakash, P., Narvi, S.S., 2016. Phytofabrication characterization of copper nanoparticles using *Allium sativum* its antibacterial activity. Int. J. Sci. Eng. Technol. 4, 463–472.

Joshi, A., Sharma, A., Bachheti, R.K., Husen, A., Mishra, V.K., 2019. Plant-mediated synthesis of copper oxide nanoparticles their biological applications. In: Nanomaterials Plant Potential. Springer, pp. 221–237.

Jyothi Prashanth, G., Aishwarya, B.S., Guruprasad, R., 2016. Green synthesis of copper nanoparticles from *Phyllanthus emblica* to study its UV-protection property by *Danio Rerio* (Zebrafish) embryos. World J. Pharm. Pharm. Sci. 5, 1133–1140.

Kalpana, V.N., Chakraborthy, P., Palanichamy, V., Devi Rajeswari, V., 2016. Synthesis characterization of copper nanoparticles using *Tridax procumbens* its application in degradation of bismarck brown. Int. J. ChemTech Res. 9, 498–507.

Karimi, J., Mohsenzadeh, S., 2015. Rapid, green, eco-friendly biosynthesis of copper nanoparticles using flower extract of *Aloe vera*. Synth. React. Inorg. Met.-Org. Nano-Metal 45, 895–898.

Kasana, R.C., Panwar, N.R., Kaul, R.K., Kumar, P., 2017. Biosynthesis effects of copper nanoparticles on plants. Environ. Chem. Lett. 15, 233–240.

Kaur, R., Giordano, C., Gradzielski, M., Mehta, S.K., 2014. Synthesis of highly stable, water-dispersible copper nanoparticles as catalysts for nitrobenzene reduction. Chem. Asian J. 9, 189–198.

Kaur, H., Dolma, K., Kaur, N., Malhotra, A., Kumar, N., Dixit, P., Sharma, D., Mayilraj, S., Choudhury, A.R., 2015. Marine microbe as nano-factories for copper biomineralization. Biotechnol. Bioprocess Eng. 20, 51–57.

Kaur, P., Thakur, R., Chaudhury, A., 2016. Biogenesis of copper nanoparticles using peel extract of *Punica granatum* their antimicrobial activity against opportunistic pathogens. Green Chem. Lett. Rev. 9, 33–38.

Khani, R., Roostaei, B., Bagherzade, G., Moudi, M., 2018. Green synthesis of copper nanoparticles by fruit extract of *Ziziphus spina-christi* (L.) Willd.: application for adsorption of triphenylmethane dye antibacterial assay. J. Mol. Liq. 255, 541–549.

Khanna, P.K., More, P., Jawalkar, J., Patil, Y., Koteswar Rao, N., 2009. Synthesis of hydrophilic copper nanoparticles: effect of reaction temperature. J. Nanopart. Res. 11, 793–799.

Khodashenas, B., Ghorbani, H.R., 2014. Synthesis of copper nanoparticles: an overview of the various methods. Korean J. Chem. Eng. 31, 1105–1109.

Kimber, R.L., Lewis, E.A., Parmeggiani, F., Smith, K., Bagshaw, H., Starborg, T., Joshi, N., Figueroa, A.I., van der Laan, G., Cibin, G., Gianolio, D., Haigh, S.J., Pattrick, R.A.D., Turner, N.J., Lloyd, J.R., 2018. Biosynthesis characterization of copper nanoparticles using *Shewanella oneidensis*: application for click chemistry. Small 14, 1703145.

Kumar, B., Smita, K., Cumbal, L., Debut, A., Angulo, Y., 2017. Biofabrication of copper oxide nanoparticles using Andean blackberry (*Rubus glaucus* Benth.) fruit leaf. J. Saudi Chem. Soc. 21, S475–S480.

Kurkure, R.V., Jaybhaye, S., Sangle, A., 2016. Synthesis of copper/copper oxide nanoparticles in eco-friendly non-toxic manner from floral extract of *Caesalpinia pulcherrima*. IJRITCC 4, 363–367.

Lee, H.J., Song, J.Y., Kim, B.S., 2013. Biological synthesis of copper nanoparticles using *Magnolia kobus* leaf extract their antibacterial activity. J. Chem. Technol. Biotechnol. 88, 1971–1977.

Lv, Q., Zhang, B., Xing, X., Zhao, Y., Cai, R., Wang, W., Gu, Q., 2018. Biosynthesis of copper nanoparticles using *Shewanella loihica* PV-4 with antibacterial activity: novel approach mechanisms investigation. J. Hazard. Mater. 347, 141–149.

Madhusudhan, A., Reddy, G.B., 2019. Nanomaterials Plant Potential. pp. 111–134, https://doi.org/10.1007/978-3-030-05569-1.

Majumder, D.R., 2012. Bioremediation: copper nanoparticles from electronic-waste. IJEST 4, 4380–4389.

Mali, S.C., Dhaka, A., Githala, C.K., Trivedi, R., 2020. Green synthesis of copper nanoparticles using *Celastrus paniculatus* Willd. leaf extract their photocatalytic antifungal properties. Biotechnol. Rep. 27, 00518.

Manjari, G., Saran, S., Arun, T., Vijaya Bhaskara Rao, A., Devipriya, S.P., 2017. Catalytic recyclability properties of phytogenic copper oxide nanoparticles derived from *Aglaia elaeagnoidea* flower extract. J. Saudi Chem. Soc. 21, 610–618.

Momeni, S.S., Nasrollahzadeh, M., Rustaiyan, A., 2016. Green synthesis of the Cu/ZnO nanoparticles mediated by *Euphorbia prolifera* leaf extract and investigation of their catalytic activity. J. Colloid Interface Sci. 472, 173–179.

Mousavi, S.M., Hashemi, S.A., Ghasemi, Y., Atapour, A., Amani, A.M., SavarDashtaki, A., Babapoor, A., Arjmand, O., 2018. Green synthesis of silver nanoparticles toward bio medical applications: review study. Artif Cells Nanomed. Biotechnol. 46, 855–872.

Mukherjee, S., Dutta, S., Verma, A.S., Saha, M.K., 2020. Nanoparticle synthesis harnessing benign green routes. In: Animal Biotechnology, pp. 686–709, https://doi.org/10.1016/B978-0-12-811710-1.00038-0.

Mukhopadhyay, R., Kazi, J., Debnath, M.C., 2018. Synthesis characterization of copper nanoparticles stabilized with *Quisqualis indica* extract: evaluation of its cytotoxicity apoptosis in B16F10 melanoma cells. Biomed. Pharmacother. 97, 1373–1385.

Murthy, H.C.A., Abebe, B., Tegene Desalegn, Z., Prakash, C.H., Shantaveerayya, K., 2018. A review on green synthesis applications of Cu CuO nanoparticles. Mater. Sci. Res. India 15, 279–295.

Muthulakshmi, L., Rajini, N., Nellaiah, H., Kathiresan, T., Jawaid, M., Rajulu, A.V., 2017. Preparation properties of cellulose nanocomposite films with in situ generated copper nanoparticles using *Terminalia catappa* leaf extract. Int. J. Biol. Macromol. 95, 1064–1071.

Nagar, N., Devra, V., 2017. Green synthesis characterization of copper nanoparticles using *Azadirachta indica* leaves. Mater. Chem. Phys. 213, 44–51.

Nair, P.M.G., Chung, I.M., 2015. Study on the correlation between copper oxide nanoparticles induced growth suppression enhanced lignification in Indian mustard (*Brassica juncea* L.). Ecotoxicol. Environ. Saf. 113, 302–313.

Nasrollahzadeh, M., Mohammad Sajadi, S., 2015. Green synthesis of copper nanoparticles using *Ginkgo biloba* L. leaf extract their catalytic activity for the Huisgen [3 + 2] cycloaddition of azides alkynes at room temperature. J. Colloid Interface Sci. 457, 141–147.

Nasrollahzadeh, M., Sajadi, S.M., Khalaj, M., 2014. Green synthesis of copper nanoparticles using aqueous extract of the leaves of *Euphorbia esula* L their catalytic activity for ligand-free Ullmann-coupling reaction reduction of 4-nitrophenol. RSC Adv. 4, 47313–47318.

Nasrollahzadeh, M., Mohammad Sajadi, S., Rostami-Vartooni, A., 2015a. Green synthesis of CuO nanoparticles by aqueous extract of *Anthemis nobilis* flowers their catalytic activity for the A3 coupling reaction. J. Colloid Interface Sci. 459, 183–188.

Nasrollahzadeh, M., Sajadi, S.M., Hatamifard, A., 2015b. *Anthemis xylopoda* flowers aqueous extract assisted in situ green synthesis of Cu nanoparticles supported on natural Natrolite zeolite for N-formylation of amines at room temperature under environmentally benign reaction conditions. J. Colloid Interface Sci. 460, 146–153.

Nasrollahzadeh, M., Sajadi, S.M., Rostami-Vartooni, A., Bagherzadeh, M., Safari, R., 2015c. Immobilization of copper nanoparticles on perlite: Green synthesis, characterization catalytic activity on aqueous reduction of 4-nitrophenol. J. Mol. Catal. A Chem. 400, 22–30.

Nasrollahzadeh, M., Sajadi, S.M., Mirzaei, Y., 2016. An efficient one-pot synthesis of 1,4-disubstituted 1,2,3-triazoles at room temperature by green synthesized Cu NPs using *Otostegia persica* leaf extract. J. Colloid Interface Sci. 468, 156–162.

Nasrollahzadeh, M., Momeni, S.S., Sajadi, S.M., 2017. Green synthesis of copper nanoparticles using *Plantago asiatica* leaf extract their application for the cyanation of aldehydes using $K_4Fe(CN)_6$. J. Colloid Interface Sci. 506, 471–477.

Nasrollahzadeh, M., Sajjadi, M., Mohammad Sajadi, S., 2018. Biosynthesis of copper nanoparticles supported on manganese dioxide nanoparticles using *Centella asiatica* L. leaf extract for the efficient catalytic reduction of organic dyes nitroarenes. Chin. J. Catal. 39, 109–117.

Noor, S., Shah, Z., Javed, A., Ali, A., Hussain, S.B., Zafar, S., Ali, H., Muhammad, S.A., 2020. A fungal based synthesis method for copper nanoparticles with the determination of anticancer, antidiabetic antibacterial activities. J. Microbiol. Methods 174, 105966.

Olajire, A.A., Ifediora, N.F., Bello, M.D., Benson, N.U., 2018. Green synthesis of copper nanoparticles using *Alchornea laxiflora* leaf extract their catalytic application for oxidative desulphurization of model oil. Iran J. Sci. Technol. Trans. A Sci. 42, 1935–1946.

Padil, V.V.T., Černík, M., 2013. Green synthesis of copper oxide nanoparticles using gum karaya as a biotemplate their antibacterial application. Int. J. Nanomedicine 8, 889.

Palithya, S., Gaddam, S.A., Kotakadi, V.S., Penchalaneni, J., Golla, N., Krishna, S.B.N., Naidu, C.V., 2021. Green synthesis of silver nanoparticles using flower extracts of *Aerva lanata* their biomedical applications. Part. Sci. Technol., 1–13.

Pantidos, N., Horsfall, L., 2020. Understanding the role of SilE in the production of metal nanoparticles by *Morganella psychrotolerans* using MicroScale Thermophoresis. N. Biotechnol. 55, 1–4.

Parikh, P., Zala, D., Makwana, B.A., 2014. Biosynthesis of copper nanoparticles their antimicrobial activity. Open Access Lib. https://doi.org/10.4236/oalib.preprints.1200067.

Parveen, F., Sannakki, B., Mandke, M.V., Pathan, H.M., 2016. Copper nanoparticles: synthesis methods its light harvesting performance. Sol. Energy Mater. Sol. Cells 144, 371–382.

Pourakbar, L., Moghaddam, S.S., Popović-Djordjević, J., 2020. Synthesis of metal/metal oxide nanoparticles by green methods their applications. Sustain. Agric. Res. 41, 63–81.

Prabhu, Y.T., Venkateswara Rao, K., Sesha Sai, V., Pavani, T., 2017. A facile biosynthesis of copper nanoparticles: a micro-structural antibacterial activity investigation. J. Saudi Chem. Soc. 21, 180–185.

Pradeep, B., Hemba, P., Jagadeesh, A.K., Ramakakanavar, C.G., Nayak, S., Vaman Rao, C., 2019. Biosynthesis of copper nanoparticles from areca nut extract its antibacterial antioxidant properties. Agric. Nat. Resour. 53, 386–394.

Prasad, P.R., Kanchi, S., Naidoo, E.B., 2016. In-vitro evaluation of copper nanoparticles cytotoxicity on prostate cancer cell lines their antioxidant, sensing catalytic activity: one-pot green approach. J. Photochem. Photobiol. B 161, 375–382.

Punniyakotti, P., Panneerselvam, P., Perumal, D., Aruliah, R., Angaiah, S., 2020. Anti-bacterial anti-biofilm properties of green synthesized copper nanoparticles from *Cardiospermum halicacabum* leaf extract. Bioprocess Biosyst. Eng. 43, 1649–1657.

Qi, L., Ma, J., Shen, J., 1997. Synthesis of copper nanoparticles in nonionic water-in-oil microemulsions. J. Colloid Interface Sci. 186, 498–500.

Raghunandan, D., Mahesh, B.D., Basavaraja, S., Balaji, S.D., Manjunath, S.Y., Venkataraman, A., 2011. Microwave-assisted rapid extracellular synthesis of stable bio-functionalized silver nanoparticles from guava (*Psidium guajava*) leaf extract. J. Nanopart. Res. 13, 2021–2028.

Rai, M., Duran, N. (Eds.), 2011. Metal Nanoparticles in Microbiology. Springer Science and Business Media, https://doi.org/10.1007/978-3-642-18312-6.

Raja, M., Subha, J., Ali, F.B., Ryu, S.H., 2008. Synthesis of copper nanoparticles by electroreduction process. Mater. Manuf. Process 23, 782–785.

Rajesh, K.M., Ajitha, B., Reddy, Y.A.K., Suneetha, Y., Reddy, P.S., 2018. Assisted green synthesis of copper nanoparticles using *Syzygium aromaticum* bud extract: physical, optical antimicrobial properties. Optik 154, 593–600.

Rajeshkumar, S., Menon, S., Venkat Kumar, S., Tambuwala, M.M., Bakshi, H.A., Mehta, M., Satija, S., Gupta, G., Chellappan, D.K., Thangavelu, L., Dua, K., 2019. Antibacterial antioxidant potential of biosynthesized copper nanoparticles mediated through *Cissus arnotiana* plant extract. J. Photochem. Photobiol. B 197, 111513.

Ramanathan, R., Bhargava, S.K., Bansal, V., 2011. Biological synthesis of copper/copper oxide nanoparticles. In: Chemeca. Engineering a Better World: Sydney Hilton Hotel, NSW, Australia 1991, pp. 18–21.

Reddy, G.B., Ramakrishna, D., Madhusudhan, A., Ayodhya, D., Venkatesham, M., Veerabhadram, G., 2015. Catalytic reduction of p-nitrophenol hexacyanoferrate (III) by borohydride using green synthesized gold nanoparticles. Chin. Chem. Soc. 62, 420–428.

Rehana, D., Mahendiran, D., Kumar, R.S., Rahiman, A.K., 2017. Evaluation of antioxidant anticancer activity of copper oxide nanoparticles synthesized using medicinally important plant extracts. Biomedical 89, 1067–1077.

Roy, K., Ghosh, C.K., Sarkar, C.K., 2019. Rapid detection of hazardous H_2O_2 by biogenic copper nanoparticles synthesized using *Eichhornia crassipes* extract. Microsyst. Technol. 25, 1699–1703.

Saiganesh, S., Krishnan, T., Narasimha, G., Almoallim, H.S., Alhari, S.A., Reddy, L.V., Mallikarjuna, K., Mohammed, A., Prabhakar, V.S., 2021. Phytosynthetic fabrication of lanthanum ion-doped nickel oxide nanoparticles using *Sesbania grandiflora* leaf extract their anti-microbial properties. Crystals 11 (2), 124.

Salvadori, M.R., Lepre, L.F., Ando, R.A., Oller Do Nascimento, C.A., Corrêa, B., 2013. Biosynthesis uptake of copper nanoparticles by dead biomass of *Hypocrea lixii* isolated from the metal mine in the Brazilian Amazon region. PLoS One 8, 80519.

Salvadori, M.R., Ando, R.A., Oller Do Nascimento, C.A., Corrêa, B., 2014a. Bioremediation from wastewater extracellular synthesis of copper nanoparticles by the fungus *Trichoderma koningiopsis*. J. Environ. Sci. Health A 49, 1286–1295.

Salvadori, M.R., Ando, R.A., Oller Do Nascimento, C.A., Corrêa, B., 2014b. Intracellular biosynthesis removal of copper nanoparticles by dead biomass of yeast isolated from the wastewater of a mine in the Brazilian Amazonia. PLoS One 9, 87968.

Sankar, R., Maheswari, R., Karthik, S., Shivashangari, K.S., Ravikumar, V., 2014. Anticancer activity of *Ficus religiosa* engineered copper oxide nanoparticles. Mater. Sci. Eng. C 44, 234–239.

Santhoshkumar, J., Agarwal, H., Menon, S., Rajeshkumar, S., Kumar, S.V., 2019. A biological synthesis of copper nanoparticles its potential applications. In: Green Synthesis, Characterization Applications of Nanoparticles., ISBN: 9780081025796, pp. 199–221.

Sapna Thakur, R.R.S.S., 2014. Study the antibacterial activity of copper nanoparticles synthesized using herbal plants leaf extracts. Int. J. Bio-Technol. Res. 4, 21–34.

Saranyaadevi, K., Subha, V., Ernest Ravindran, R.S., Renganathan, S., 2014. Synthesis characterization of copper nanoparticle using *Capparis zeylanica* leaf extract. Int. J. ChemTech Res. 6, 4533–4541.

Sebeia, N., Jabli, M., Ghith, A., Saleh, T.A., 2020. Eco-friendly synthesis of *Cynomorium coccineum* extract for controlled production of copper nanoparticles for sorption of methylene blue dye. Arab. J. Chem. 13, 4263–4274.

Seku, K., Gangapuram, B.R., Pejjai, B., Kadimpati, K.K., Golla, N., 2018a. Microwave-assisted synthesis of silver nanoparticles their application in catalytic, antibacterial antioxidant activities. J. Nanostructure Chem. 8, 179–188.

Seku, K., Reddy Ganapuram, B., Pejjai, B., Mangatayaru Kotu, G., Golla, N., 2018b. Hydrothermal synthesis of copper nanoparticles, characterization their biological applications. Int. J. Nano Dimens. 9, 7–14.

Seku, K., Gangapuram, B.R., Pejjai, B., Hussain, M., Hussaini, S.S., Golla, N., Kadimpati, K.K., 2019. Eco-friendly synthesis of gold nanoparticles using carboxymethylated gum *Cochlospermum gossypium* (CMGK) their catalytic antibacterial applications. Chem 73, 1695–1704.

Seku, K., SulaimanHussaini, S., Golla, N., Mangatayaru, K.G., Sri Maha Vishnu, D., Rapolu, S., Bandi, R., Reddy, G.B., 2020. Microwave-assisted synthesis of palladium nanoparticles using *Frankincense resin* evaluation of their catalytic properties. Mater. Lett. 278, 128427.

Shah, M., Fawcett, D., Sharma, S., Tripathy, S.K., Poinern, G.E.J., 2015. Green synthesis of metallic nanoparticles via biological entities. Materials 8, 7278–7308.

Shaikh, R.R., Mirza, S.S., Sawant, M.R., Dare, S.B., 2016. Biosynthesis of copper nanoparticles using *Vitis vinifera* leaf extract its antimicrobial activity. Der Pharm. Lett. 8, 265–272.

Shantkriti, S., Rani, P., 2014. Biological synthesis of copper nanoparticles using *Pseudomonas fluorescens*. Int. J. Gynecol. Cancer 3, 31–52.

Sharma, P., Pant, S., Dave, V., Tak, K., Sadhu, V., Reddy, K.R., 2019. Green synthesis characterization of copper nanoparticles by *Tinospora cordifolia* to produce nature-friendly copper nano-coated fabric their antimicrobial evaluation. J. Microbiol. Methods 160, 107–116.

Sharmila, G., Sakthi Pradeep, R., Sandiya, K., Santhiya, S., Muthukumaran, C., Jeyanthi, J., Manoj Kumar, N., Thirumarimurugan, M., 2018. Biogenic synthesis of CuO nanoparticles using *Bauhinia tomentosa* leaves extract: characterization its antibacterial application. J. Mol. Struct. 1165, 288–292.

Shende, S., Ingle, A.P., Gade, A., Rai, M., 2015. Green synthesis of copper nanoparticles by *Citrus medica* Linn. (Idilimbu) juice its antimicrobial activity. World J. Microbiol. Biotechnol. 31, 865–873.

Shnoudeh, A.J., Hamad, I., Abdo, R.W., Qadumii, L., Jaber, A.Y., Surchi, H.S., Alkelany, S.Z., 2019. Synthesis, characterization, applications of metal nanoparticles. In: Biomaterials Bionanotechnology. Academic Press, Elsevier Inc, pp. 527–612.

Shobha, G., Moses, V., Ananda, S., 2014. Biological synthesis of copper nanoparticles its impact—a review. Int. J. Pharm. Sci. Invent. 3, 6–28.

Singh, R., Kumar, S., 2017. Green technologies environmental sustainability. J. Mater. Environ. Sci. 8, 740–757.

Sinha, T., Ahmaruzzaman, M., 2015. Biogenic synthesis of Cu nanoparticles its degradation behavior for methyl red. Mater. Lett. 159, 168–171.

Sivaraj, R., Rahman, P.K.S.M., Rajiv, P., Narendhran, S., Venckatesh, R., 2014. Biosynthesis characterization of *Acalypha indica* mediated copper oxide nanoparticles evaluation of its antimicrobial anticancer activity. Spectrochim. Acta A Mol. Biomol. Spectrosc. 129, 255–258.

Sreeju, N., Rufus, A., Philip, D., 2016. Microwave-assisted rapid synthesis of copper nanoparticles with exceptional stability their multifaceted applications. J. Mol. Liq. 221, 1008–1021.

Subhankari, I., Nayak, P., 2013. Synthesis of copper nanoparticles using *Syzygium aromaticum* (Cloves) aqueous extract by using green chemistry. World J. Nano Sci. Technol. 2, 14–17.

Tahvilian, R., Zangeneh, M.M., Falahi, H., Sadrjavadi, K., Jalalvand, A.R., Zangeneh, A., 2019. Green synthesis chemical characterization of copper nanoparticles using *Allium saralicum* leaves assessment of their cytotoxicity, antioxidant, antimicrobial, cutaneous wound healing properties. Appl. Organomet. Chem. 33, 1–16.

Thiruvengadam, M., Chung, I.M., Gomathi, T., Ansari, M.A., Gopiesh Khanna, V., Babu, V., Rajakumar, G., 2019. Synthesis, characterization pharmacological potential of green synthesized copper nanoparticles. Bioprocess Biosyst. Eng. 42, 1769–1777.

Tiwari, M., Jain, P., Chandrashekhar Hariharapura, R., Narayanan, K., Bhat, K.U., Udupa, N., Rao, J.V., 2016. Biosynthesis of copper nanoparticles using copper-resistant *Bacillus cereus*, a soil isolate. Process Biochem. 51, 1348–1356.

Umer, A., Naveed, S., Ramzan, N., Rafique, M.S., 2012. Selection of a suitable method for the synthesis of copper nanoparticles. Nano Brief Rep. Rev. 7, 1230005.

Usha, R., Prabu, E., Palaniswamy, M., Venil, C.K., Rajendran, R., 2010. Synthesis of metal oxide nano particles by *Streptomyces* species for development of antimicrobial textiles. Global J. Biotech. Biochem. 5, 153–160.

Usman, M.S., Ibrahim, N.A., Shameli, K., Zainuddin, N., Yunus, W.M.Z.W., 2012. Copper nanoparticles mediated by chitosan: synthesis characterization via chemical methods. Molecules 17, 14928–14936.

Usman, M., Ahmed, A., Yu, B., Peng, Q., Shen, Y., Cong, H., 2019. Photocatalytic potential of bio-engineered copper nanoparticles synthesized from *Ficus carica* extract for the degradation of toxic organic dye from waste water: Growth mechanism study of parameter affecting the degradation performance. Mater. Res. Bull. 120, 110583.

Vaishnavi, V., Sadasivuni, K.K., Ponnamma, D., Golla, N., 2020. Green synthesis of silver nanoparticles from *Pterocarpus santalinus* leaf broth and their antibacterial and antioxidant activities. Macromol. Symp. 392 (1), 2000079.

Valli, G., Geetha, S., 2015. Green synthesis of copper nanoparticles using *Cassia auriculata* leaves extract. Int. J. ChemTech Res. 4, 5–10.

Valli, G., Suganya, M., 2015. Biogenic synthesis of copper nanoparticles using *Delonix elata* flower extract. J. Chem. Pharm. 7, 776–779. Research article.

Valodkar, M., Nagar, P.S., Jadeja, R.N., Thounaojam, M.C., Devkar, R.V., Thakore, S., 2011. Euphorbiaceae latex induced green synthesis of non-cytotoxic metallic nanoparticle solutions: a rational approach to antimicrobial applications. Colloids Surf. A Physicochem. Eng. Asp. 384, 337–344.

Varshney, R., Bhadauria, S., Gaur, M.S., Pasricha, R., 2010. Characterization of copper nanoparticles synthesized by a novel microbiological method. JOM 62, 102–104.

Varshney, R., Bhadauria, S., Gaur, M.S., Pasricha, R., 2011. Copper nanoparticles synthesis from electroplating industry effluent. Nano Biomed. Eng. 3, 115–119.

Wu, S.H., Chen, D.H., 2004. Synthesis of high-concentration Cu nanoparticles in aqueous CTAB solutions. J. Colloid Interface Sci. 273, 165–169.

Yallappa, S., Manjanna, J., Sindhe, M.A., Satyanarayan, N.D., Pramod, S.N., Nagaraja, K., 2013. Microwave assisted rapid synthesis biological evaluation of stable copper nanoparticles using *T. arjuna* bark extract. Spectrochim. Acta A Mol. Biomol. Spectrosc. 110, 108–115.

Yan, W., Liu, Y., Mansooridara, S., Kalantari, A.S., Sadeghian, N., Taslimi, P., Zangeneh, A., Zangeneh, M.M., 2020. Chemical characterization neuroprotective properties of copper nanoparticles green-synthesized by *Nigella sativa* L. seed aqueous extract against methadone-induced cell death in adrenal phaeochromocytoma (PC12) cell line. J. Exp. Nanosci. 15, 280–296.

Yoon, K.Y., HoonByeon, J., Park, J.H., Hwang, J., 2007. Susceptibility constants of *Escherichia coli Bacillus subtilis* to silver copper nanoparticles. Sci. Total Environ. 373, 572–575.

Yugandhar, P., Vasavi, T., Rao, Y.J., Devi, P.U.M., Narasimha, G., Savithramma, N., 2018. Cost effective, green synthesis of copper oxide nanoparticles using fruit extract of *Syzygium alternifolium* (Wt.) Walp., characterization and evaluation of antiviral activity. J. Clust. Sci. 29 (4), 743–755.

Zafar, S., Zafar, A., 2019. Biosynthesis characterization of silver nanoparticles using *Phoenix dactylifera* fruits extract their in vitro antimicrobial cytotoxic effects. Open Biotechnol. J. 13, 37–46.

Zangeneh, M.M., Ghaneialvar, H., Akbaribazm, M., Ghanimatdan, M., Abbasi, N., Goorani, S., Pirabbasi, E., Zangeneh, A., 2019. Novel synthesis of *Falcaria vulgaris* leaf extract conjugated copper nanoparticles with potent cytotoxicity, antioxidant, antifungal, antibacterial, cutaneous wound healing activities under in vitro in vivo condition. J. Photochem. Photobiol. B 197, 111556.

Zhakina, A.K., Alpysbayeva, A.E., 2020. Synthesis of copper nanoparticles. In: Series Chemistry Technology, vol. 441., ISBN: 9780128223482, pp. 168–170.

Zhao, H., Su, H., Ahmeda, A., Sun, Y., Li, Z., Zangeneh, M.M., Nowrozi, M., Zangeneh, A., Moradi, R., 2020. Biosynthesis of copper nanoparticles using *Allium eriophyllum* Boiss leaf aqueous extract; characterization analysis of their antimicrobial cutaneous wound-healing potentials. Appl. Organomet. Chem., 5587.

CHAPTER

Natural gums as a sustainable source for synthesizing copper nanoparticles

4

Le Dai Vuong[a], Dao Anh Quang[b], Nguyen Huu Chuc[b], Le Van Luan[b], and Vo-Van Quoc Bao[c]

[a]School of Engineering and Technology—Hue University, Hue City, Vietnam,
[b]Hue Industrial College, Hue City, Vietnam,
[c]College of Agriculture and Forestry, Hue University, Hue City, Vietnam

1 Introduction

The application of natural gum polysaccharides, especially for fabricating nanomaterials, in different fields, including food, water, energy, biotechnology, environment, and medicine, has been of considerable research interest in recent years (Jamila et al., 2020; Padil et al., 2018). In terms of their chemical structure, natural gums belong to the class of high-molecular-weight hydrophilic compounds, including proteins, glucose, polysaccharides, minerals, and carbohydrates, that yield arabinose, mannose, galactose, glucuronic acid, rhamnose, and galacturonic acid on hydrolysis (Jamila et al., 2020). Due to their edibility, easy availability, low cost, high stability, safety for people as well as the environment, and metal biosorption properties, various synthetic and natural polymers have been previously used for the synthesis of metal nanoparticles (Jamila et al., 2020). Nanotechnology is an emerging technology that can revolutionize every field of science. The fabrication of nanoscale materials can be carried out using various approaches such as physical, chemical such as sol-gel methods, electrochemistry, chemical vapor deposition, sonochemistry, the precipitation-pyrolysis method, cathodic vacuum arc, one-step solid-state reactions, and solvothermal reactions (Bao et al., 2021; Rahman et al., 2009). However, these methods involve the use of toxic chemicals that are hazardous to environment and human health, which has encouraged the use of biological methods for the reduction and stabilization of nanoparticles (Bao et al., 2021; Chawla et al., 2020; Iravani, 2020; Wang et al., 2021). Therefore, it is necessary to develop an eco-friendly approach for the synthesis of nanomaterials. The biosynthesis of nanoparticles using natural gum polysaccharides has been suggested as a cost-effective, eco-friendly alternative to chemical and physical methods. It is considered a green technology, as it does not involve any harmful chemicals (Netala et al., 2015; Naseer et al., 2020; Wang et al., 2021). It is believed that natural gums may act both as a reducing agent and as a suitable capping agent that prevents the aggregation of nanoparticles by electrostatic or physical repulsion (Padil and Černík, 2013; Jamila et al., 2020; Naseer et al., 2020).

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Recently, copper-based nanoparticles have been gaining importance due to their applications in catalysis, printed electronics, gas sensors, dye-sensitized solar cells, paints, plastics, filters, and textiles, because of their beneficial properties, including antimicrobial activity (Kumar et al., 2017; Wang et al., 2010), and their use in producing superhigh strength materials, sensors, and catalysts (Suárez-Cerda et al., 2017). Notably, copper nanoparticles (Cu-NPs) have unique properties, which are not seen in other nanoparticles, and they are cheaper and have a high conductivity. Further, although copper and copper oxide nanoparticles are much more toxic than silver nanoparticles, copper oxide is less toxic than copper sulfate (Amorim et al., 2019).

In recent years, Cu-NPs have been prepared by integrating green chemistry approaches, including the use of a safer solvent medium and extracts and exudates of plants, algae, fungi, and bacteria (Honary et al., 2012; Jamila et al., 2020; Suárez-Cerda et al., 2017). They were prepared from the extracts of various plants such as *Hibiscus rosa-sinensis* (Subbaiya and Selvam, 2015), *Ocimum santanum* (Mallikarjuna et al., 2011; Singhal et al., 2011), *Vitis vinifira* (Angrasan and Subbaiya, 2014), *Eucalyptus* (Kolekar et al., 2015), *Cassia alata* (Jayalakshmi, 2014), *Punica granatum* (Parihar and Balekar, 2016), *Ocimum sanctum* (Shende et al., 2016), *Ginkgo biloba* (Nasrollahzadeh and Sajadi, 2015), *Citrus medicalinn* (Cheirmadurai et al., 2014), *Camellia sinensis* (Keihan et al., 2017), *Datura innoxia* (Kala et al., 2016), *Citrus limon*, *Turmeric curcumin* (Jayandran et al., 2015), *Gloriosa superba* (Gholami-Shabani et al., 2017), *Phyllanthus emblica* (Jyothi et al., 2016), *Caesalpinia pulcherrima* (Kurkure et al., 2016), *Thymus vulgaris* (Karimi and Mohsenzadeh, 2015), *Asparagus adscendens*, *Ocimum bacilicum*, *Bacopa monnieri*, *Withania somnifera* (Thakur et al., 2014), *Urtica*, *Matricaria chamomilla*, *Cinnamomum*, *Schisandra chinensis*, *Glycyrrhiza glabra*, *Inula helenium* (Shah et al., 2015), *Euphorbia esula* (Jayandran et al., 2015; Nasrollahzadeh et al., 2014), *Colocasia esculenta* and *Smithia sensitiva* (Damle et al., 2016). In particular, recently, natural gums have been used to synthesize copper nanomaterials, as they are commonly used as stabilizing and reducing agents that are low in cost with high repeatability, ease of implementation, and eco-friendly as well as safe for human. In this chapter, we discuss the use and characterization of natural gums as reducing and stabilizing agents for the biosynthesis of Cu-NPs. This is an important bio-based protocol for the green synthesis of Cu-NPs using natural gums.

2 Natural gums

Gums are hydrocolloids, which are outstanding representative eco-friendly, green biopolymers, and their derivatives have been used to synthesize many nanomaterials for a variety of applications. They are considered to be pathological products that ooze out following injury to a plant and exhibit complex structural features. They are macromolecules whose complex chemical composition depends on the type and age of the source as well as the extraction and processing methods. They can be

found in almost every biosphere on earth: in plants, animals, and many bacteria. Chemically, gums consist of carbohydrate polymers, including galactose, rhamnose, and uranic acid, and functional groups such as hydroxyl, carbonyl, and carboxyl groups with a large number of groups (-OH) repeatedly adorning the backbone of the molecule. This facilitates the formation of networking assemblies with metal ions through templating the polymeric bonds and creating multidimensional structures (Bello et al., 2017; Padil et al., 2018). Compared to other biopolymers, gum is an anionic functional group with a greater charge density. The structure of natural gum significantly affects its mechanical, thermal, rheological, optical, and film-forming properties (Saha et al., 2017).

In recent years, the function of natural gums as both reducing and stabilizing agents in nanoparticle synthesis has been extensively studied (Jamila et al., 2020; Singh et al., 2018). There is currently an interest in the development of novel eco-friendly strategies for the synthesis and biosensing of nanomaterials by integrating the green chemistry approaches with a safer solvent medium (Jamila et al., 2020). According to research results by Jamila et al. (2020), natural gums are rich sources of polysaccharides that contain a large number of derivable hydroxyl, carboxyl as well as amino groups, which are useful for Cu-NPs that could prolong the stabilization time for nanomaterials.

3 Green synthesis of copper nanoparticles by using natural gums

Nanotechnology is based on the cornerstones of nanoscience and nanotechnology, which is one of the gloriously emanating, interdisciplinary areas of research with valuable commercial applications and is an interdisciplinary field that uses the principles of chemistry, biology, physics, and engineering to design and fabricate nanoscale materials (Bao et al., 2018; Duong et al., 2017; Madhusudhan et al., 2019; Vuong et al., 2017; Wang et al., 2021). Among them, Cu-NPs are of interest in terms of both research and commercial applications. They play a very important role in many current technical fields because they exhibit shape- and size-dependent properties, which are suitable for various applications such as antimicrobial applications; catalysis; production of chemical sensors, superhigh strength materials, drug delivery systems, and filters; and medical radiographic imaging (Suárez-Cerda et al., 2017). Up to this point, researchers showed great interest in the synthesis of Cu-NPs involving different chemical and physical methods such as sol-gel methods, chemical vapor deposition, the precipitation-pyrolysis method, sonochemical and electrochemical methods, cathodic vacuum arc, solid-state reactions, and solvothermal reactions (Rahman et al., 2009). Cu-NPs are synthesized employing biological methods such as natural gums, plant extract, enzymes, and microbes because they are environmentally friendly, easily available, highly stable, cost-effective and have biosorption properties (Bao et al., 2021; Jamila et al., 2020). Green chemistry-based copper nanoscience and technologies have been used to produce sustainable

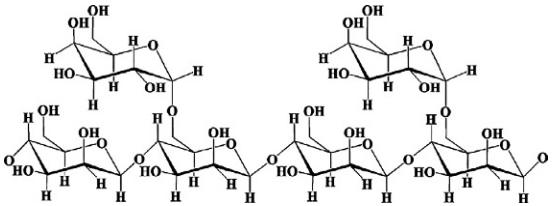
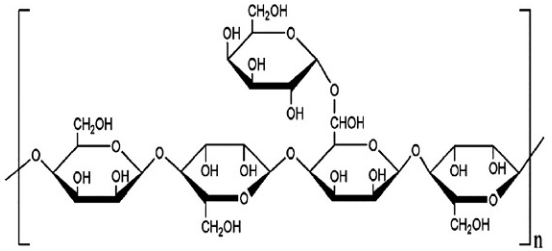
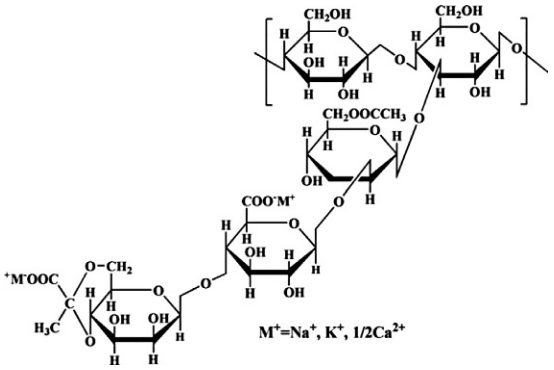
and renewable materials, to eliminate or reduce the application and formation of hazardous, unsafe, and toxic substances. Therefore, it is necessary to develop an eco-friendly approach for the synthesis of nanomaterials with the use of natural resources, nonhazardous solvents, and biodegradable and biocompatible materials via energy-reliant processes (Padil et al., 2018). Depending on the specific application, different natural gums can be used to synthesize copper nanomaterials. Natural gum hydrocolloids can be divided into three basic groups depending on their origin, structural properties, and applications. They can be derived from plants, e.g., (Pandey and Mishra, 2014), locust bean gum (Cordeiro et al., 2020), and pectin (Venkatakrishnan et al., 2014), gum arabic (GA) (Chawla et al., 2020), gum tragacanth (GT), gum karaya (GK), kondagogu gum (KG) (Padil et al., 2018), gum ghatti (GG) (Padil et al., 2016), and gum cashew (Amorim et al., 2019). In addition, alginate gum, agar gum, and carrageenan gum are derived from important seaweed polysaccharides; further, bacterial polysaccharides give xanthan gum, dextran gum, and gellan gum (Padil et al., 2018). In this section, we focus on research on the synthesis of copper nanomaterials using the natural gums mentioned above.

The important plant gums available on the market are GA, GT, GK, KG, GG (Padil et al., 2016), and GC (Amorim et al., 2019), and their chemical structures are shown in Table 1.

3.1 Biosynthesis of Cu-NPs using natural gums obtained from plant sources

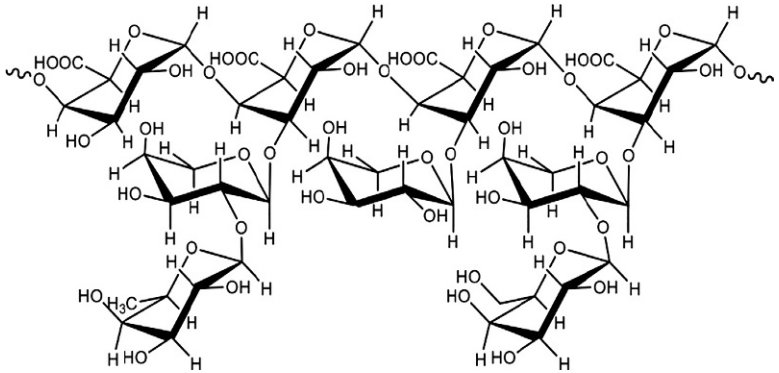
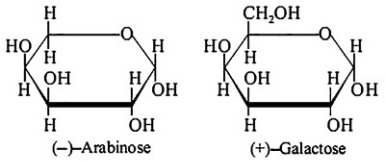
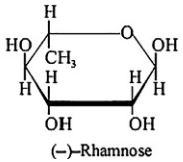
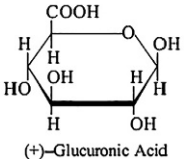
To the best of the author's knowledge, the plant-based naturally occurring gums are used as stabilizing and reducing agents for the synthesis of platinum (Venkateshaiah et al., 2019), silver (Jamila et al., 2020), gold (Madhusudhan et al., 2019), copper (Chawla et al., 2020), and palladium (Amrutham et al., 2020) nanoparticles through green synthesis. Plant gum extracts are related to the presence of several bioactive compounds as well as carbohydrates, alkaloids, polyphenols, terpenoids, glycosides, amino acids, ascorbic acid, and oxalic acid (Długosz et al., 2020). In recent years, many natural-origin materials have been used effectively as a reducing and coating mediator in the synthesis and stabilization of copper nanomaterials of various shapes and sizes by using various natural gums, as shown in Table 1. Padil and Černík (2013) reported the synthesis of CuO nanoparticles using gum karaya (size 4.8–7.8 nm), with a highly stable and significant antibacterial action. Chawla et al. (2020) synthesized Cu-NPs using L-ascorbic acid as the reducing agent, with a particle size distribution of 19.60–35.06 nm, and capped them with GA. KG is a complex and acidic polysaccharide with a high solution viscosity and gelation characteristics. Suresh et al. (2014) reported the synthesis of Cu-NPs using the natural stabilizer KG (from *Cochlospermum Gossypium*). Dong et al. (2014) have successfully fabricated Cu-NPs in aqueous solutions using copper sulfate and gum acacia. Experimental results show that the as-synthesized Cu-NPs are small, well dispersed, and spherical in shape with a narrow size distribution from 3 to 9 nm; gum acacia acts as both the reducing agent and stabilizer. According to the research results of Suresh et al.

Table 1 Chemical structures of natural gums.

No	Name	Chemical structure	References
1	Guar gum		Pandey and Mishra (2014), Wang and Wang (2013)
2	Locust bean gum		Cordeiro et al. (2020)
3	Xanthan gum		Wang and Wang (2013)

Continued

Table 1 Chemical structures of natural gums—cont'd

No	Name	Chemical structure	References
4	Tragacanth gum		Ahmad et al. (2019)
5	Gum arabic	 (–)–Arabinose (+)–Galactose  (–)–Rhamnose  (+)–Glucuronic Acid	Chawla et al. (2020), Dong et al. (2014)

(2016), water-soluble polymers increase the bulk-phase viscosity, and as a result the particles contain lower kinetic energies, leading to the eventual reduction in the number of collisions.

Some previous studies demonstrated that not only tree gum but also extracts of parts of the tree such as leaves, fruit, and root bud can be used to effectively synthesize copper nanomaterials, as shown in Table 2.

Table 2 Biosynthesis of Cu-NPs from plant sources.

Plant sources	Shape	Size	Reference
Gum karaya	Spherical	4.8–7.8 nm	Padil and Černík (2013)
Gum arabic	Spherical	3–9 nm	Dong et al. (2014)
Gum arabic	Spherical	19.6 nm	Chawla et al. (2020)
Gum kondagogu	Spherical	19 nm	Kumar et al. (2012)
Gum tragacanth	Spherical	14 nm	Seku et al. (2018), Suresh et al. (2016)
Cashew gum	Spherical	9.1 nm	Ramazani et al. (2017)
Ocimum Sanctum leaf extract	Spherical	77 nm	Amorim et al. (2019)
Ocimum Sanctum leaf extract	Nanoclusters	150–200 nm	Kulkarni and Kulkarni (2013)
Andean blackberry fruit extract	Spherical	43.3 nm	Mekala et al. (2016)
Andean blackberry leaf extract	Spherical	52.5 nm	Kumar et al. (2017)
Tomato Aqueous extract	Spherical	40–70 nm	Kumar et al. (2017)
Seedless dates extract	Spherical	78 nm	Batoool and Masood (2017)
Adhatoda vasica leaf extract	Nanoflakes	7–11 nm	Mohamed (2020)
Hibiscus Rosasinensis leaf extract	Spherical	50 nm	Bhavyasree and Xavier (2020)
Punica granatum peel extract	Spherical	15–20 nm	Subbaiya and Selvam (2015)
Cimin Grape Extract	Spherical	25–50 nm	Karimi and Mohsenzadeh (2015)
Calotropis procera leaf extract	Spherical	15 nm	Gultekin et al. (2017)
Tabernaemontana divaricate leaf extract	Spherical	46 nm	Harne et al. (2012)
Syzygium aromaticum (*Cloves*) extract	Spherical	5–40 nm	Sivaraj et al. (2014)
Asparagus adscendens leaf extract	Spherical	10–15 nm	Subhankari and Nayak (2013)
Asparagus adscendens root extract	Spherical	50–60 nm	Thakur et al. (2018)

Continued

Table 2 Biosynthesis of Cu-NPs from plant sources—cont'd

Plant sources	Shape	Size	Reference
Citrus medica fruit extract	Spherical	17–93 nm	Thakur et al. (2018)
Syzygium aromaticum bud extract	Spherical	20 nm	Nagaonkar et al. (2015)
Terminalia catappa leaf extract	Spherical	21–30 nm	Rajesh et al. (2018)
Capparis zeylanica leaf extract	Spherical	50–100 nm	Muthulakshmi et al. (2017)

Subbaiya and Selvam (2015) reported that the Cu-NPs synthesized using the *H. rosa-sinensis* leaf extract acted as an effective drug to treat lung cancer. Kulkarni and Kulkarni (2013) reported that the leaf extract of *O. sanctum* can reduce copper ions into Cu-NPs within 8–10 min. Similar research done by Mekala et al. (2016) in 2016 showed that the *O. sanctum* leaf extract acts as both reducing and capping agents. According to the research results of Karimi and Mohsenzadeh (2015) the Cu-NPs synthesized from the peel extract of *P. granatum* show high antibacterial activity against opportunistic pathogens, namely, *Micrococcus luteus*, *Pseudomonas aeruginosa*, *Salmonella enterica*, and *Enterobacter aerogenes* in vitro. Cu-NPs with an average size of 15 nm were synthesized using the *Calotropis procera* leaf extract at room temperature with continuous shaking (Harne et al., 2012). In 2014, the monodispersed copper oxide nanoparticles with a size of 46 nm were synthesized by using *Tabernaemontana divaricata* leaf extract and mixing copper sulfate to it under constant stirring (Sivaraj et al., 2014). The Cu-NPs synthesized using the *Vitis vinifera* leaf extract exhibited antibacterial activity against *Staphylococcus aureus*, *Escherichia coli*, *Klebsiella pneumonia*, *Bacillus* subtilis, and *Salmonella typhi*. Thakur et al. (2018) reported that Cu-NPs ranging in size from 5 to 15 nm were produced by using an *Asparagus adscendens* leaf extract, and Cu-NPs with a larger size (50 to 60 nm) were produced using extracts from the plant roots. The Cu-NPs synthesized using extracts from the leaves and root of *Asparagus adscendens* exhibited antibacterial activity against both gram-negative and gram-positive bacteria, such as *E. coli*, *B. subtilis*, *S. typhi*, *K. pneumonia*, and *S. aureus*. In another study for the synthesis of Cu-NPs using the *Syzygium aromaticum* bud extract, Rajesh et al. (2018) reported that the phytoconstituents present in the *S. aromaticum* bud extract were responsible for the reduction and stabilization of Cu-NPs. Moreover, the *Capparis Zeylanica* leaf extract was effectively utilized for the economical production of Cu-NPs for many pharmaceutical applications (Saranyaadevi et al., 2014).

3.2 Biosynthesis of Cu-NPs using natural gums obtained from bacterial fermentation

The mechanisms for forming copper nanomaterials from different microorganisms are different. It is believed that microorganisms capture Cu^{2+} ions from the environment and then reduce Cu^{2+} ions to Cu° nanoparticles in the presence of

enzymes generated by cell activities (Fig. 1). Various studies have suggested that the microbial synthesis of Cu-NPs occurs via different methods, including (i) growing microorganisms, (ii) the extracellular secretion from microorganisms, and (iii) the biomass from living and dead microorganisms (Kasana et al., 2016). The synthesis of Cu-NPs using bacteria and fungi is quite novel, and the use of microbial synthesis of Cu-NPs for applications in health, medicine, and agriculture is still limited. Table 2 shows that Cu-NPs with different shapes and sizes have been synthesized by using various microorganisms, both bacteria and fungi. According to review articles by Fariq et al. (2017), microorganisms like bacteria, fungi, and yeasts are most convenient for the synthesis of nanomaterials because of their high growth rate, easy cultivation, and ability to grow at ambient conditions of temperature, pH, solvent, and environmental pressure. Researchers have discovered that the production of metal nanoparticles via bacteria-mediated interactive pathways is responsible for metal ion reduction from salts of copper, e.g., copper acetate, copper chloride, copper sulfate, and copper nitrate (Fariq et al., 2017), as shown in Table 3. In 2007, Hasan et al. (Saif et al., 2008) first reported on the microbial synthesis of Cu-NPs using a Gram-negative bacterium belonging to the genus *Serratia*, isolated from the midgut of the *Stibara* species; thus, insect-produced polydispersed Cu-NPs varying from 10 to 30 nm in diameter were obtained. Cuevas et al. (2015) demonstrated that the use of the mycelium-free extract of *Stereum hirsutum* is an efficient tool for the biosynthesis of Cu-NPs, particularly in the presence of $CuCl_2$ and under neutral or basic conditions. The results of this study showed that spherical Cu-NPs with a size of 4–5 nm were created. According to Ghorbani et al. (2015), spherical Cu-NPs with the size of 40–60 nm are synthesized using the supernatant of *Salmonella typhimurium*, and the complete copper ion reduction was realized after about 40 min. In 2018,

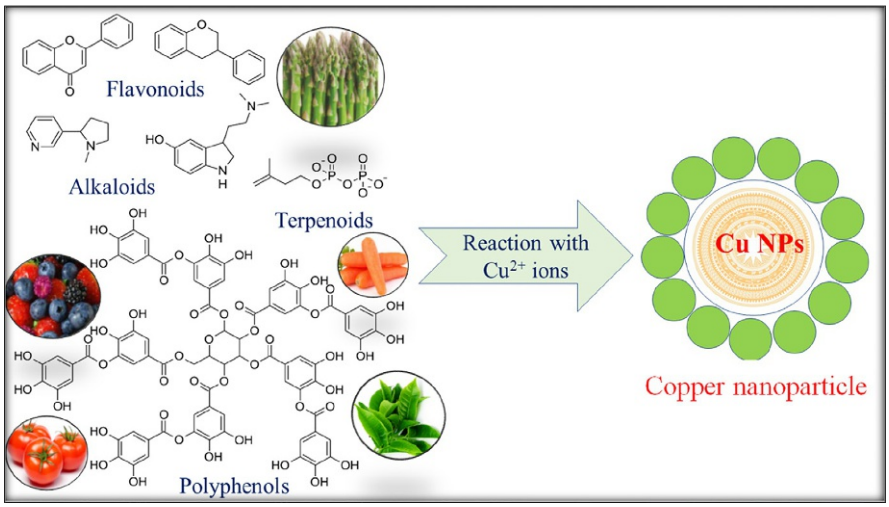


FIG. 1

Possible phytochemicals of tree extracts for copper nanoparticle synthesis.

Table 3 Biosynthesis of copper nanoparticles from microbial sources.

Microbial sources	Shape	Size	Reference
Stibara species	Spherical	10–30 nm	Saif et al. (2008)
Shewanella loihica	Spherical	10–16 nm	Lv et al. (2018)
Morganella morganii sp.	Spherical	13.5 nm	Lalitha et al. (2020)
Salmonella typhimurium	Spherical	40–60 nm	Ghorbani et al. (2015)
Pseudomonas fluorescens	Spherical, hexagonal	49 nm	Shantkriti and Rani (2014)
Stereum hirsutum	Spherical	5–20 nm	Cuevas et al. (2015)
Penicillium waksmanii	Spherical	79–179 nm	Honary et al. (2012)
Penicillium aurantiogriseum	Spherical	89–250 nm	Honary et al. (2012)
Penicillium citrinum	Spherical	85–295 nm	Honary et al. (2012)

Lv et al. (2018) used *Shewanella loihica* bacteria to successfully synthesize Cu-NPs with sizes in the range of 10–16 nm. *S. loihica* is a gram-negative facultative anaerobe capable of utilizing a broad range of electron acceptors, so the bacteria captures Cu^{2+} ions and reduces the ions to form Cu-NPs through microbial metabolisms. Thus, many researchers have reported the sustainable production of bacteria-based Cu-NPs on a large scale with limited use of toxic chemicals. However, the disadvantage in the synthesis of bacteria-based Cu-NPs is the laborious bacterial culturing processes and the limited control over their size, shape, and distribution (Fariq et al., 2017). Owing to the presence of intracellular and extracellular enzymes in the cell wall, fungi such as *Verticillium luteoalbum*, *Colletotrichum* sp., *Trichothecium* sp., *Fusarium oxysporum*, *Aspergillus oryzae*, *Alternata alternata* are capable of producing Cu-NPs (Długosz et al., 2020; Fariq et al., 2017). However, a few limitations in the synthesis of Cu-NPs using fungi have been reported, including the time-consuming and cost-intensive fabrication (Jeevanandam et al., 2016). Honary et al. (2012) used *Penicillium citrinum*, *Penicillium aurantiogriseum*, and *Penicillium waksmanii* isolated from soil to synthesize and stabilize Cu-NPs. They suggest that there is a direct correlation between the pH value, salt content, polydispersity index, and particle size (Table 2). This means that different Cu-NP sizes and shapes can be produced by a biological method by varying the content of the Cu^{2+} ions in solution, the enzymes released by fungal strains, and the solution pH.

3.3 Biosynthesis of copper film using natural gums

Biodegradable natural polymer films reinforced with metal nanoparticles have attracted significant attention in the last two decades owing to the substantial scope for their possible applications (Albrecht et al., 2006; Simon et al., 2014). Among them, copper and silver nanocomposites are promising functional materials as they have optical, catalytic, magnetic, electronic, and antimicrobial properties (Albrecht et al., 2006; Bao et al., 2018). This new type of film to keep fruits and vegetables fresh has

gained considerable interest owing to the strength of the film being comparable to that of plastic-based nonbiodegradable films. Such films are also safe for the environment as they are made of degradable materials such as agar, starch, soybean protein, chitosan, and cellulose. In 2019, Roy et al. (2019) successfully fabricated a bioactive agar-based functional composite film incorporated with Cu-NPs. Experimental results show that the biodegradable nanocomposite film reinforced with Cu-NPs exhibited distinctive antibacterial activity. Carrageenan gum is similar to agar gum and has also been used for the preparation of copper-based nanocomposite films (Oun and Rhim, 2017). According to Ben-Sasson et al. (2014), the attachment of Cu-NPs on the thin-film composite membranes resulted in significant antibacterial activity. This indicates that Cu-NPs have potential commercial applications in the prevention of food spoilage and postharvest management to minimize decay till the consignment reaches its destination.

4 Mechanism of formation and stability of copper nanoparticles

Nowadays, there are several studies on the mechanism for the formation and stability of Cu-NPs. It is well-documented that the mechanism for the fabrication of Cu-NPs involves a two-step process. It includes atom formation and then polymerization of the atom. The formation mechanism of Cu-NPs is illustrated in Fig. 2, which considers that the characteristics of the stabilizing agent affect the size and shape of the Cu-NPs. Copper (II) salt, when dissolved in water, dissociates into Cu^{2+}. Then Cu^{2+} reduces to Cu° by reduction of natural gums, forming metallic copper nuclei,

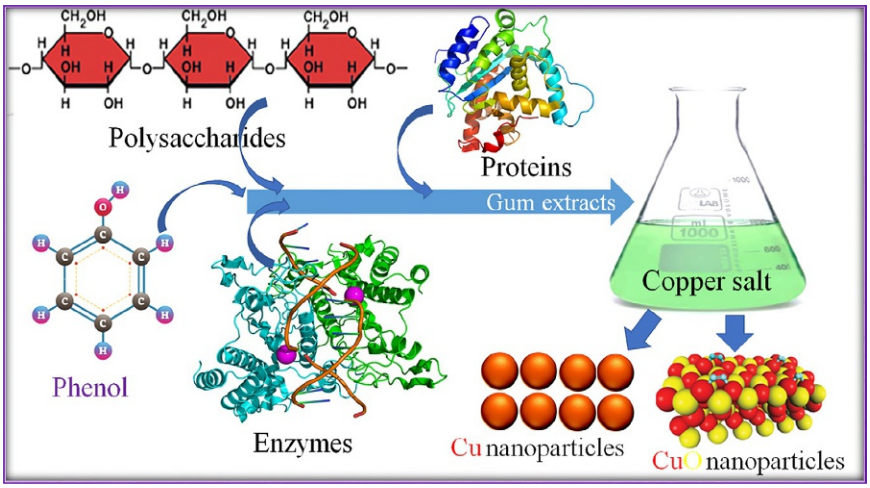


FIG. 2

Possible phytochemicals of gum extract associated with copper nanoparticle synthesis.

which initiate the growth stage (Suárez-Cerda et al., 2017). Growing Cu-NPs are stabilized through the strong association between the Cu-NP surface and O atoms of the hydroxyl and carbonyl functional groups of the natural gums.

It has been reported that the bioreduction of Cu-NPs using a combination of biomolecules found in natural gum extracts, such as phenols, lipids, vitamins, carbohydrates, amino acids, enzymes, protein molecules, organic acids, and polysaccharides, is potentially eco-friendly and economical (Jamila et al., 2020; Padil and Černík, 2013). Further, a high specificity to produce nanomaterials, as well as extended stability, can be achieved by steric or electrostatic effects (Amorim et al., 2019). The probable mechanism involved in the synthesis of Cu-NPs can be presented as follows:

$$Cu^{2+} + \text{gum extracts} \rightarrow \left[\text{Cu / gum extracts}\right]^{2+} \tag{1}$$

$$\left[\text{Cu / gum extracts}\right]^{2+} \xrightarrow{\text{heat}} \left[\text{Cu}\left(\text{OH}\right)_2 \text{ / gum extracts}\right] \tag{2}$$

$$\left[\text{Cu}\left(\text{OH}\right)_2 \text{ / gum extracts}\right] \rightarrow \text{Cu}^{\circ} \text{ / CuO / } \text{Cu}_2\text{O nanoparticles} \tag{3}$$

The formation of Cu-NPs using natural gum extracts was identified and confirmed based on the change in the color of the mixture from yellowish green to brownish black (Vuong, 2019). As suggested by Gupta et al. (2018), the synthesis of copper nanomaterials using tree gum extracts could not be regulated by enzymes because usually the extracts are heated at high temperatures during the nanoparticle synthesis process. The authors proposed that phytochemicals such as phenolic, natural sterolin, terpenoids, and flavonoids are involved in reducing and act as stabilizer agents for nanomaterials.

5 Advantages of fabrication of copper nanomaterials using natural gums

Green synthesis has led to the fabrication of many types of inorganic nanomaterials, especially Cu-NPs. Natural gums have been used for Cu-NP synthesis and have been found to be best suited for the preparation of nanomaterials with diverse morphologies and sizes. In addition, natural polymers have been used to prepare copper nanomaterials in a simple, economical, stable, and environmentally friendly manner (Fig. 3).

6 Disadvantage of fabrication of nanomaterials using natural gums

Natural gums contain excess water that can lead to the activation of enzymes and the proliferation of living organisms. Therefore, in biomimetic fabrication of Cu-NPs, it is necessary to study the effect of the gum contents on the properties and stability of the materials. This is a very important step in realizing the high antibacterial activity

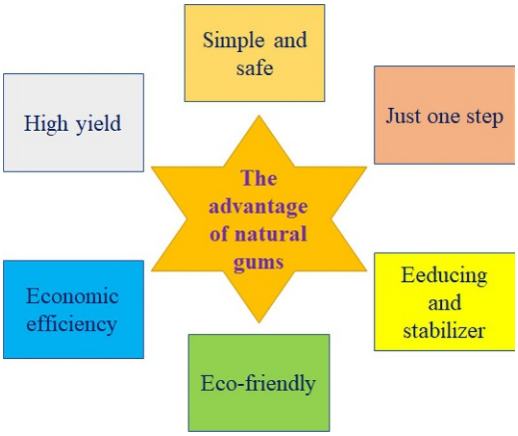


FIG. 3

Advantages of fabrication of copper nanomaterials using natural gums.

and stability of Cu-NPs. Most of the pharmacopeias have set the limit for moisture contents of natural gums at about 15.0% (Malsawmtluangi et al., 2014). Fortunately, the strong antibacterial properties of nano-copper solution reduce the growth of microorganisms.

7 Conclusion

In summary, in this chapter, the synthesis of copper nanomaterials using natural gums via "green" pathways has been explored. Natural gums have been used to prepare copper nanomaterials in a simple, economical, stable, and environmentally friendly manner. Besides, this method is an exciting addition to the large repertoire of copper nanomaterial synthesis methods. Despite the promising antimicrobial effects of the synthesized Cu-NPs, their practical application remains in the preliminary stages, which is essential to carry out thorough studies of the dosage required for plant growth and disease control for various crops.

References

Ahmad, S., Ahmad, M., Manzoor, K., Purwar, R., Ikram, S., 2019. A review on latest innovations in natural gums based hydrogels: preparations and applications. Int. J. Biol. Macromol. 136, 870–890.

Albrecht, M.A., Evans, C.W., Raston, C.L., 2006. Green chemistry and the health implications of nanoparticles. Green Chem. 8, 417–432.

Amorim, A., Mafud, A.C., Nogueira, S., Jesus, J.R., Araújo, A.R.D., Plácido, A., Brito Neta, M., Alves, M.M.M., Carvalho, F.A.A., Rufino Arcanjo, D.D., 2019. Copper nanoparticles stabilized with cashew gum: antimicrobial activity and cytotoxicity against 4T1 mouse mammary tumor cell line. J. Biomater. Appl. 34, 188–197.

Amrutham, S., Maragoni, V., Guttena, V., 2020. One-step green synthesis of palladium nanoparticles using neem gum (*Azadirachta Indica*): characterization, reduction of rhodamine 6G dye and free radical scavenging activity. Appl. Nanosci. 10, 4505–4511.

Angrasan, J., Subbaiya, R., 2014. Biosynthesis of copper nanoparticles by Vitis vinifera leaf aqueous extract and its antibacterial activity. Int. J. Curr. Microbiol. App. Sci. 3, 768–774.

Bao, V.V.Q., Vuong, L.D., Luan, L.V., 2018. Biomimetic synthesis of silver nanoparticles for preparing preservative solutions for mandarins (*Citrus Deliciosa* Tenore). Nano LIFE 8. 1850003-1850001-1850010.

Bao, V.-V.Q., Vuong, L.D., Yves, W., 2021. Synthesis of chitosan–silver nanoparticles with antifungal properties on bamboo straws. Nano Energy 10, 111–117. https://doi.org/10.1680/jnaen.20.00052.

Batoool, M., Masood, B., 2017. Green synthesis of copper nanoparticles using *Solanum lycopersicum* (tomato aqueous extract) and study characterization. J. Nanosci. Nanotechnol. Res. 1, 5.

Bello, B.A., Khan, S.A., Khan, J.A., Syed, F.Q., Anwar, Y., Khan, S.B., 2017. Antiproliferation and antibacterial effect of biosynthesized AgNPs from leaves extract of *Guiera senegalensis* and its catalytic reduction on some persistent organic pollutants. J. Photochem. Photobiol. B: Biology 175, 99–108.

Ben-Sasson, M., Zodrow, K.R., Genggeng, Q., Kang, Y., Giannelis, E.P., Elimelech, M., 2014. Surface functionalization of thin-film composite membranes with copper nanoparticles for antimicrobial surface properties. Environ. Sci. Technol. 48, 384–393.

Bhavyasree, P.G., Xavier, T.S., 2020. Green synthesis of copper oxide/carbon nanocomposites using the leaf extract of *Adhatoda vasica* Nees, their characterization and antimicrobial activity. Heliyon 6, e03323.

Chawla, P., Kumar, N., Bains, A., Dhull, S.B., Kumar, M., Kaushik, R., Punia, S., 2020. Gum arabic capped copper nanoparticles: synthesis, characterization, and applications. Int. J. Biol. Macromol. 146, 232–242.

Cheirmadurai, K., Biswas, S., Murali, R., Thanikaivelan, P., 2014. Green synthesis of copper nanoparticles and conducting nanobiocomposites using plant and animal sources. RSC Adv. 4, 19507–19511.

Cordeiro, T., Paninho, A.B., Bernardo, M., Matos, I., Pereira, C.V., Serra, A.T., Matias, A., Ventura, M.G., 2020. Biocompatible locust bean gum as mesoporous carriers for naproxen delivery. Mater. Chem. Phys. 239, 121973.

Cuevas, R., Durán, N., Diez, M.C., Tortella, G.R., Rubilar, O., 2015. Extracellular biosynthesis of copper and copper oxide nanoparticles by *Stereum hirsutum*, a native white-rot fungus from chilean forests. J. Nanomater. 2015.

Damle, S., Sharma, K., Bingi, G., Shah, H., 2016. A comparative study of green synthesis of silver and copper nanoparticles using *Smithia sensitiva* (Dabzell), *Cassia tora* (L.) and *Colocasia esculenta* (L.). Int. J. Pure App. Biosci. 4, 275–281.

Długosz, O., Chwastowski, J., Banach, M., 2020. Hawthorn berries extract for the green synthesis of copper and silver nanoparticles. Chem. Papers 74, 239–252.

Dong, C., Cai, H., Zhang, X., Cao, C., 2014. Synthesis and characterization of monodisperse copper nanoparticles using gum acacia. Phys. E Low Dimens. Syst. Nanostruct. 57, 12–20.

Duong, N.T., Vuong, L.D., Son, N.M., Van Tuyen, H., Van Chuong, T., 2017. The synthesis of TiO2 nanoparticles using sulfuric acid method with the aid of ultrasound. Nano Energy 6, 82–88.

Fariq, A., Khan, T., Yasmin, A., 2017. Microbial synthesis of nanoparticles and their potential applications in biomedicine. J. Appl. Biomed. 15, 241–248.

Gholami-Shabani, M., Gholami-Shabani, Z., Shams-Ghahfarokhi, M., Jamzivar, F., Razzaghi-Abyaneh, M., 2017. Green nanotechnology: biomimetic synthesis of metal nanoparticles using plants and their application in agriculture and forestry. Nanotechnol.: Agricul. Paradigm, 133–175.

Ghorbani, H.R., Mehr, F.P., Poor, A.K., 2015. Extracellular synthesis of copper nanoparticles using culture supernatants of *Salmonella typhimurium*. Orient. J. Chem. 31, 527–529.

Gultekin, D.D., Nadaroglu, H., Gungor, A.A., Kishali, N.H., 2017. Biosynthesis and characterization of copper oxide nanoparticles using cimin grape (*Vitis vinifera* cv.) extract. Int. J. Second. Metabol. 4, 77–84.

Gupta, M., Tomar, R.S., Kaushik, S., Mishra, R.K., Sharma, D., 2018. Effective antimicrobial activity of green ZnO nano particles of *Catharanthus roseus*. Front. Microbiol. 9, 2030.

Harne, S., Sharma, A., Dhaygude, M., Joglekar, S., Kodam, K., Hudlikar, M., 2012. Novel route for rapid biosynthesis of copper nanoparticles using aqueous extract of *Calotropis procera* L. latex and their cytotoxicity on tumor cells. Colloids Surf. B Biointerfaces 95, 284–288.

Honary, S., Barabadi, H., Gharaei-Fathabad, E., Naghibi, F., 2012. Green synthesis of copper oxide nanoparticles using *Penicillium aurantiogriseum*, *Penicillium citrinum* and *Penicillium waksmanii*. Dig. J. Nanomater. Biostruct. 7, 999–1005.

Iravani, S., 2020. Plant gums for sustainable and eco-friendly synthesis of nanoparticles: recent advances. Inorganic Nano-Metal Chem. 50, 469–488.

Jamila, N., Khan, N., Hwang, I.M., Saba, M., Khan, F., Amin, F., Khan, S.N., Atlas, A., Javed, F., Minhaz, A., 2020. Characterization of natural gums via elemental and chemometric analyses, synthesis of silver nanoparticles, and biological and catalytic applications. Int. J. Biol. Macromol. 147, 853–866.

Jayalakshmi, Y.A., 2014. Green synthesis of copper oxide nanoparticles using aqueous extract of flowers of *Cassia alata* and particles characterization. Int. J. Nanomater. Biostruct. 4, 66–71.

Jayandran, M., Haneefa, M.M., Balasubramanian, V., 2015. Green synthesis of copper nanoparticles using natural reducer and stabilizer and an evaluation of antimicrobial activity. J. Chem. Pharm. Res. 7, 251–259.

Jeevanandam, J., Chan, Y.S., Danquah, M.K., 2016. Biosynthesis of metal and metal oxide nanoparticles. Chem. Bio. Eng Rev. 3, 55–67.

Jyothi, P.G., Aishwarya, B., Guruprasad, R., 2016. Green synthesis of copper nanoparticles from *Phyllanthus emblica* and to study its uvprotection property by *Danio rerio* (zebrafish) embryos. W. J. Pharm. Sci 5, 1133–1140.

Kala, A., Soosairaj, S., Mathiyazhagan, S., Raja, P., 2016. Green synthesis of copper bionanoparticles to control the bacterial leaf blight disease of rice. Curr. Sci., 2011–2014.

Karimi, J., Mohsenzadeh, S., 2015. Rapid, green, and eco-friendly biosynthesis of copper nanoparticles using flower extract of *Aloe vera*. Synthesis and reactivity in inorganic, metal-organ. Nano-Metal Chem. 45, 895–898.

Kasana, R.C., Panwar, N.R., Kaul, R.K., Kumar, P., 2016. Copper nanoparticles in agriculture: biological synthesis and antimicrobial activity. In: Ranjan, S., Dasgupta, N., Lichtfouse, E. (Eds.), Nanoscience in Food and Agriculture. vol. 3. Springer International Publishing, Cham, pp. 129–143.

Keihan, A.H., Veisi, H., Veasi, H., 2017. Green synthesis and characterization of spherical copper nanoparticles as organometallic antibacterial agent. Appl. Organomet. Chem. 31, e3642.

Kolekar, R., Bhade, S., Kumar, R., Reddy, P., Singh, R., Pradeepkumar, K., 2015. Biosynthesis of copper nanoparticles using aqueous extract of Eucalyptus sp. plant leaves. Curr. Sci. 109, 255.

Kulkarni, V.D., Kulkarni, P.S., 2013. Green synthesis of copper nanoparticles using *Ocimum sanctum* leaf extract. Int. J. Chem. Stud. 1, 1–4.

Kumar, A., Aerry, S., Saxena, A., Mozumdar, S., 2012. Copper nanoparticulates in guar-gum: a recyclable catalytic system for the Huisgen [3 + 2]-cycloaddition of azides and alkynes without additives under ambient conditions. Green Chem. 14, 1298–1301.

Kumar, B., Smita, K., Cumbal, L., Debut, A., Angulo, Y., 2017. Biofabrication of copper oxide nanoparticles using Andean blackberry (*Rubus glaucus* Benth.) fruit and leaf. J. Saudi Chem. Soc. 21, S475–S480.

Kurkure, R.V., Jaybhaye, S., Sangle, A., 2016. Synthesis of copper/copper oxide nanoparticles in ecofriendly and non-toxic manner from floral extract of *Caesalpinia pulcherrima*. IJRITCC 4, 363–366.

Lalitha, K., Kalaimurgan, D., Nithya, K., Venkatesan, S., Shivakumar, M.S., 2020. Antibacterial, antifungal and mosquitocidal efficacy of copper nanoparticles synthesized from entomopathogenic nematode: insect–host relationship of bacteria in secondary metabolites of *Morganella morganii* sp. (PMA1). Arab. J. Sci. Eng. 45, 4489–4501.

Lv, Q., Zhang, B., Xing, X., Zhao, Y., Cai, R., Wang, W., Gu, Q., 2018. Biosynthesis of copper nanoparticles using Shewanella loihica PV-4 with antibacterial activity: novel approach and mechanisms investigation. J. Hazard. Mater. 347, 141–149.

Madhusudhan, A., Reddy, G.B., Krishana, I.M., 2019. Green synthesis of gold nanoparticles by using natural gums. In: Nanomater. Plant Potent. Springer, Cham, pp. 111–134.

Mallikarjuna, K., Narasimha, G., Dillip, G., Praveen, B., Shreedhar, B., Lakshmi, C.S., Reddy, B., Raju, B.D.P., 2011. Green synthesis of silver nanoparticles using Ocimum leaf extract and their characterization. Dig. J. Nanomater. Biostruct. 6, 181–186.

Malsawmtluangi, C., Thanzami, K., Lalhlenmawia, H., Selvan, V., Palanisamy, S., Kandasamy, R., Pachuau, L., 2014. Physicochemical characteristics and antioxidant activity of *Prunus cerasoides* D. Don gum exudates. Int. J. Biol. Macromol. 69, 192–199.

Mekala, J., Rajan, M.R., Ramesh, R., 2016. Green synthesis and characterization of copper nanoparticles using tulsi (*Ocimum sanctum*) leaf extract, PARIPEX. Indian J. Dent. Res. 5, 14–16.

Mohamed, E.A., 2020. Green synthesis of copper & copper oxide nanoparticles using the extract of seedless dates. Heliyon 6, e03123.

Muthulakshmi, L., Rajini, N., Nellaiah, H., Kathiresan, T., Jawaid, M., Rajulu, A.V., 2017. Preparation and properties of cellulose nanocomposite films with in situ generated copper nanoparticles using *Terminalia catappa* leaf extract. Int. J. Biol. Macromol. 95, 1064–1071.

Nagaonkar, D., Shende, S., Rai, M., 2015. Biosynthesis of copper nanoparticles and its effect on actively dividing cells of mitosis in *Allium cepa*. Biotechnol. Prog. 31, 557–565.

Naseer, A., et al., 2020. Biogenic and eco-benign synthesis of platinum nanoparticles (Pt NPs) using plants aqueous extracts and biological derivatives: environmental, biological and catalytic applications. J. Mater. Res. Technol. 9, 9093–9107.

Nasrollahzadeh, M., Sajadi, S.M., 2015. Green synthesis of copper nanoparticles using *Ginkgo biloba* L. leaf extract and their catalytic activity for the Huisgen [3+ 2] cycloaddition of azides and alkynes at room temperature. J. Colloid Interface Sci. 457, 141–147.

Nasrollahzadeh, M., Sajadi, S.M., Khalaj, M., 2014. Green synthesis of copper nanoparticles using aqueous extract of the leaves of *Euphorbia esula* L. and their catalytic activity for ligand-free Ullmann-coupling reaction and reduction of 4-nitrophenol. RSC Adv. 4, 47313–47318.

Netala, V.R., Kotakadi, V.S., Nagam, V., Bobbu, P., Ghosh, S.B., Tartte, V., 2015. First report of biomimetic synthesis of silver nanoparticles using aqueous callus extract of *Centella asiatica* and their antimicrobial activity. Appl. Nanosci. 5, 801–807.

Oun, A.A., Rhim, J.-W., 2017. Carrageenan-based hydrogels and films: effect of ZnO and CuO nanoparticles on the physical, mechanical, and antimicrobial properties. Food Hydrocoll. 67, 45–53.

Padil, V.V.T., Černík, M., 2013. Green synthesis of copper oxide nanoparticles using gum karaya as a biotemplate and their antibacterial application. Int. J. Nanomedicine 8, 889–898.

Padil, V.V.T., Wacławek, S., Černík, M., 2016. Green synthesis: nanoparticles and nanofibres based on tree gums for environmental applications. Ecol. Chem. Eng. S. 23, 533–557.

Padil, V.V.T., Wacławek, S., Černík, M., Varma, R.S., 2018. Tree gum-based renewable materials: sustainable applications in nanotechnology, biomedical and environmental fields. Biotechnol. Adv. 36, 1984–2016.

Pandey, S., Mishra, S.B., 2014. Catalytic reduction of p-nitrophenol by using platinum nanoparticles stabilised by guar gum. Carbohydr. Polym. 113, 525–531.

Parihar, G., Balekar, N., 2016. *Calotropis procera*: A phytochemical and pharmacological review. Thai J. Pharm. Sci. 40 (3), 115–131.

Rahman, A., Ismail, A., Jumbianti, D., Magdalena, S., Sudrajat, H., 2009. Synthesis of copper oxide nano particles by using *Phormidium cyanobacterium*. Indo. J. Chem. 9, 355–360.

Rajesh, K.M., Ajitha, B., Reddy, Y.A.K., Suneetha, Y., Reddy, P.S., 2018. Assisted green synthesis of copper nanoparticles using *Syzygium aromaticum* bud extract: physical, optical and antimicrobial properties. Optik 154, 593–600.

Ramazani, A., Taghavi, F.S., Hosseinzadeh, Z., Sadri, F., Joo, S.W., 2017. Green synthesis of magnetic copper ferrite nanoparticles using tragacanth gum as a biotemplate and their catalytic activity for the oxidation of alcohols. Iran. J. Catal. 7, 181–185.

Roy, S., Rhim, J.-W., Jaiswal, L., 2019. Bioactive agar-based functional composite film incorporated with copper sulfide nanoparticles. Food Hydrocoll. 93, 156–166.

Saha, A., Tyagi, S., Gupta, R.K., Tyagi, Y.K., 2017. Natural gums of plant origin as edible coatings for food industry applications. Crit. Rev. Biotechnol. 37, 959–973.

Saif, H.S., Singh, S., Parikh, R.Y., Dharne, M.S., Patole, M.S., Prasad, B.L.V., Shouche, Y.S., 2008. Bacterial synthesis of copper/copper oxide nanoparticles. J. Nanosci. Nanotechnol. 8, 3191–3196.

Saranyaadevi, K., Subha, V., Ravindran, R.S.E., Renganathan, S., 2014. Synthesis and characterization of copper nanoparticle using Capparis *zeylanica* leaf extract. Int. J. Chem. Tech. Res. 6, 4533–4541.

Seku, K., Reddy, G.B., Pejjai, B., Mangatayaru, K.G., Golla, N., 2018. Hydrothermal synthesis of copper nanoparticles, characterization and their biological applications. Int. J. Nano Dimens. 9, 7–14.

Shah, M., Fawcett, D., Sharma, S., Tripathy, S.K., Poinern, G.E.J., 2015. Green synthesis of metallic nanoparticles via biological entities. Materials 8, 7278–7308.

Shantkriti, S., Rani, P., 2014. Biological synthesis of copper nanoparticles using *Pseudomonas fluorescens*. Int. J. Curr. Microbiol. App. Sci. 3, 374–383.

Shende, S., Gaikwad, N., Bansod, S., 2016. Synthesis and evaluation of antimicrobial potential of copper nanoparticle against agriculturally important phytopathogens. Synthesis 1, 41–47.

Simon, S., Alcouffe, P., Espuche, E., 2014. Hybrid films of polyetherimide containing in situ grown ag, Pd, and AgPd alloy nanoparticles: synthesis route, morphology, and gas transport properties. J Polym Sci B 52, 1211–1220.

Singh, J., Dutta, T., Kim, K.-H., Rawat, M., Samddar, P., Kumar, P., 2018. 'Green' synthesis of metals and their oxide nanoparticles: applications for environmental remediation. J. Nanobiotechnol. 16, 84.

Singhal, G., Bhavesh, R., Kasariya, K., Sharma, A.R., Singh, R.P., 2011. Biosynthesis of silver nanoparticles using *Ocimum sanctum* (Tulsi) leaf extract and screening its antimicrobial activity. J. Nanopart. Res. 13, 2981–2988.

Sivaraj, R., Rahman, P.K.S.M., Rajiv, P., Salam, H.A., Venckatesh, R., 2014. Biogenic copper oxide nanoparticles synthesis using *Tabernaemontana divaricate* leaf extract and its antibacterial activity against urinary tract pathogen. Spectrochim. Acta A Mol. Biomol. Spectrosc. 133, 178–181.

Suárez-Cerda, J., Espinoza-Gómez, H., Alonso-Núñez, G., Rivero, I.A., Gochi-Ponce, Y., Flores-López, L.Z., 2017. A green synthesis of copper nanoparticles using native cyclodextrins as stabilizing agents. J. Saudi Chem. Soc. 21, 341–348.

Subbaiya, R., Selvam, M.M., 2015. Green synthesis of copper nanoparticles from Hibicus *rosasinensis* and their antimicrobial, antioxidant activities. Res. J. Pharm. Biolo. Chem. Sci 6, 1183–1190.

Subhankari, I., Nayak, P.L., 2013. Synthesis of copper nanoparticles using *Syzygium aromaticum* (Cloves) aqueous extract by using green chemistry. World J. Nano Sci. Technol. 2, 14–17.

Suresh, Y., Annapurna, S., Singh, A.K., Bhikshamaiah, G., 2014. Characterization of Kondagogu stabilized copper nanoparticles and their surface enhanced Raman scattering studies. Int. J. Nanomater. Biostruct. 4, 35–40.

Suresh, Y., Annapurna, S., Bhikshamaiah, G., Singh, A.K., 2016. Green luminescent copper nanoparticles. Conf. Ser.: Mater. Sci. Eng. 149. 012187.

Thakur, S., Rai, R., Sharma, S., 2014. Study the antibacterial activity of copper nanoparticles synthesized using herbal plants leaf extracts. Int. J. Bio-Technol. Res. 4, 21–34.

Thakur, S., Sharma, S., Thakur, S., Rai, R., 2018. Green synthesis of copper nano-particles using *Asparagus adscendens* roxb. Root and leaf extract and their antimicrobial activities. Int. J. Curr. Microbiol. App. Sci. 7, 683–694.

Venkatakrishnan, S., Veerappan, G., Elamparuthi, E., Veerappan, A., 2014. Aerobic synthesis of biocompatible copper nanoparticles: promising antibacterial agent and catalyst for nitroaromatic reduction and C–N cross coupling reaction. RSC Adv. 4, 15003–15006.

Venkateshaiah, A., Silvestri, D., Ramakrishnan, R.K., Wacławek, S., Padil, V.V.T., Černík, M., Varma, R.S., 2019. Gum kondagoagu/reduced graphene oxide framed platinum nanoparticles and their catalytic role. Molecules 24, 3643.

Vuong, L.D., 2019. Nanoparticles for the improved crop production. In: Nanotechnology for Agriculture: Crop Production & Protection. Springer, pp. 85–106.

Vuong, L.D., Luan, N.D.T., Ngoc, D.D.H., Anh, P.T., Bao, V.-V.Q., 2017. Green synthesis of silver nanoparticles from fresh leaf extract of *Centella asiatica* and their applications. Int. J. Nanosci. 16, 1650018.

Wang, Y., Biradar, A.V., Wang, G., Sharma, K.K., Duncan, C.T., Rangan, S., Asefa, T., 2010. Controlled synthesis of water-dispersible faceted crystalline copper nanoparticles and their catalytic properties. Chem. A Eur. J. 16, 10735–10743.

Wang, G., Zhao, K., Gao, C., Wang, J., Mei, Y., Zheng, X., Zhu, P., 2021. Green synthesis of copper nanoparticles using green coffee bean and their applications for efficient reduction of organic dyes. J. Environ. Chem. Eng. 9, 105331.

Wang, A., Wang, W. (2013). Gum-g-copolymers: synthesis, properties, and applications. In: Polysaccharide Based Graft Copolymers. Springer, Berlin, Heidelberg, 2013. p. 149–203.

CHAPTER

5 Role of processing parameters in solution routes for controlling size, shape, and morphology of chalcogenide nanoparticles

Sandhya Yadav and P.K. Bajpai

Advanced Material Research Laboratory, Department of Pure and Applied Physics, Guru Ghasidas Vishwavidyalaya, Bilaspur, India

1 Introduction

Inorganic metal chalcogenides have drawn considerable attention in recent decades because of their active properties. As a chalcogenide, copper sulfides (Cu_xS with $x = 1–2$) are important p-type transition metal sulfides that have been rarely investigated in comparison to other chalcogenides such as CdS or CdSe (Durga et al., 2018). Copper sulfide shows a direct band gap between 1.2 and 2.0 eV depending on the stoichiometric ratio of Cu and S (Jiao et al., 2006). Optical band gap E_g of Cu_xS increases with a decrease in the x value. An estimated optical band gap is 1.2 eV for Cu_2S, 1.75 eV for $Cu_{1.8}S$, and 2.2 eV for CuS (Basu et al., 2010; Wu et al., 2008). Copper sulfides have excellent optical and electrical properties, and its metallic conductivity transforms to a superconductor at 1.6 K (Liang and Whangbo, 1993). Copper sulfide forms compounds of variant stoichiometries from copper-rich to sulfur-rich such as Cu_2S (chalcocite), $Cu_{1.75}S$ (anilite), $Cu_{1.85}S$ (digenite), $Cu_{1.95}S$ (djurlite), and CuS (covellite), which are stable at room temperature (Premala et al., 2017). The physical and chemical properties of nanoparticles were controlled by varying their size, shape, structure, and stoichiometric compositions, which have important characteristics applicable in the field of biosensors (Pagan et al., 2015), optoelectronic devices (Zeinodin et al., 2021), solar controllers and solar radiator absorbers (Nair et al., 1991), Li-ion batteries (Zhang et al., 2019), thermoelectric cooling materials (Shen et al., 2009), catalysts (Hosseinpour et al., 2019), gas sensors (Sagade and Sharma, 2008), nanometer-scale switches (Sukamoto et al., 2003), optical filters (Chen et al., 2009), tissue imaging (Ku et al., 2012), light-emitting diodes (Zhu et al., 2004), drug delivery (Hou et al., 2017), nonlinear optical materials (Roy and Srivastava, 2006), photosensors (Husea et al., 2017), molecular imaging (Ku et al., 2012), fuel cells (Li and Nguyen, 2018), photothermal imaging (Li et al., 2010a), hydrogen peroxide

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detection (Zhang et al., 2017), supercapacitor electrodes (Jin et al., 2019; Yue et al., 2021), solar cells (Hamed and Mola, 2019; Agoro et al., 2021), etc. due to their unique optical, electrical, physical, and chemical properties.

The size-dependent optical properties are mainly attributed to changes in the optical energy band gap, which in turn influences the surface plasmon resonance of the nanomaterials. The optical band gap increases with a decrease in particle size, especially for the semiconductor nanomaterials (Karak, 2019). To study morphology control techniques and morphology-dependent properties and their potential applications, many attempts have been made to synthesize CuS nanocrystals with different morphologies such as rod-like (Liao et al., 2003), hollow sphere (Jiang et al., 2011), tubular structures (Yao et al., 2007), flower-like (Thongtem et al., 2009), urchin-like and snowflake-like patterns (Zhu et al., 2004), leaf-like (Durga et al., 2018), nanoflakes (Zhang et al., 2006), nanodisks (Senthil Kumar and Babu, 2015), nanowires (Feng et al., 2015), nanoplate (Yan et al., 2008), nanoribbons (Tan et al., 2008), microspheres (Li et al., 2007), hierarchical structures (Liu et al., 2018) etc. Various methods reported for the synthesis of CuS include solid-state reaction (Wang et al., 2006), sonochemical method (Kristl et al., 2013), coprecipitation (Yadav and Bajpai, 2017; Raj and Jaiswal, 2021), hydrothermal (Qin et al., 2005), solvothermal (Nan et al., 2006), microemulsion-template interfacial-reaction route (Jiang et al., 2011), template-assisted (Fan et al., 2003), microwave (MW) irradiation (Nafees et al., 2013), chemical vapor deposition (CVD) (Fu et al., 2020), atomic layer deposition (Schneider et al., 2016), sol-gel technique (Yadav and Bajpai, 2018), sulfuring (Chen et al., 2008), reflux condensation (Yadav et al., 2019), γ-irradiation routes (Qiao et al., 1999), polyol route (Shen et al., 2003), etc. Some synthesis routes require high temperature, high pressure, or long reaction time for the synthesis of nanoparticles, whereas some need a gaseous H_2S environment that is highly toxic and dangerous (Metcalf et al., 1982).

It is becoming a subject of interest for researchers to synthesize nanomaterials by changing various process parameters such as precursors, precursor's molar ratio, the kind of solvent, pH of the solution, reaction temperature, reaction time, surfactant/capping agent, kind of methods, etc. (Sharma and Jeevanandam, 2020).

In this chapter, we describe the effects on the formation of morphologies of copper sulfide nanostructures and the effect of processing parameters such as nature of precursors, molar ratio, reaction temperature, reaction time, reaction medium, use of capping agent, and pH value on the as-grown nanostructures in synthesis methods including coprecipitation method, refluxing method, hydrothermal/solvothermal route, MV irradiation technique, and sonochemical method, along with their various systematic applications.

2 Role of methods of synthesis in controlling the shape, size, and morphology

Various synthesis methods have been used to synthesize copper sulfide nanostructures having different compositions and phases. In this section, we briefly focus on coprecipitation, refluxing, hydrothermal/solvothermal, MV irradiation, and sonochemical

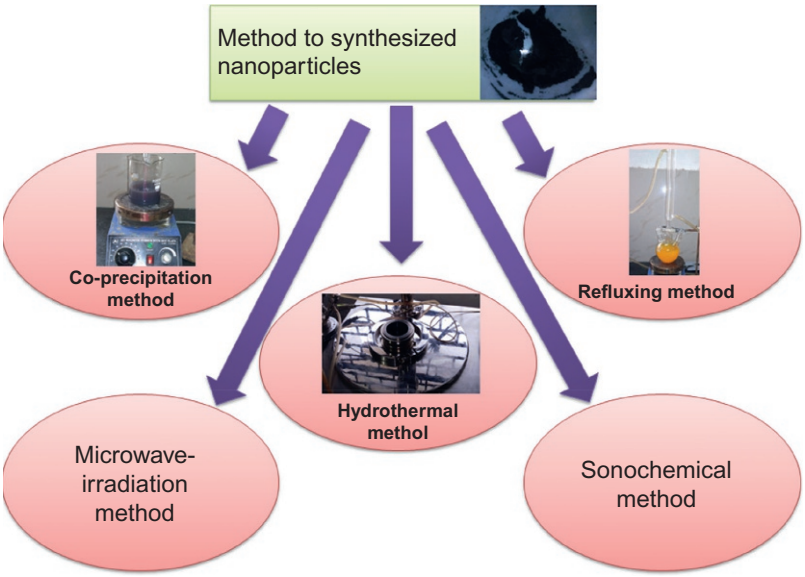

FIG. 1

Systematic diagram of different methods for the synthesis of nanoparticles.

methods and very briefly summarize the advantages and shortcomings of various methods in controlling the size, shape, and morphology. Different routes used in this chapter to synthesize nanoparticles are shown in Fig. 1.

2.1 Coprecipitation method

CuS nanoparticles have been synthesized using a coprecipitation method by a large number of researchers (Boey et al., 2007; Gautam and Mukherjee, 2006; Nath and Kalita, 2017; Nelwamondo et al., 2012; Prasanth et al., 2016; Simonescu et al., 2006, 2008; Yadav and Bajpai, 2017) due to the simple route and ease of the process. However, nucleation and growth become difficult to control in this method, which leads to multiphase growth and wide size distribution. The advantage of the coprecipitation method is that it is easy to handle, as the homogeneous mixing of reactant precipitate reduces the reaction temperature; the method is cost-effective as well. However, it is not used at high temperature and the required pressure for controlling the shape size and morphology of chalcogenide nanoparticles cannot be applied.

Attempts have been made to synthesize CuS by varying the pH of the solution using this method. Copper acetate as the copper source and sodium thiosulfate as the sulfur source were employed with a molarity ratio 1:6. CuS nanocrystals were synthesized at different pH starting with an acidic medium (pH 5.5) and basic medium (pH 11.5). In the acidic medium, a mixed phase of Cu_9S_8, CuS_2, and antlerite-$Cu_3(SO_4)(OH)_4$ were detected. CuS pure phase of covellite was obtained at pH 11.5

(Simonescu et al., 2006). The effect of pH was also reported using coprecipitation method using copper acetate and sodium thiosulfate as starting materials in molar ratio of 1:6. The pH of the solution varied from 5.5 to 9.5. At pH 5.5, mixed phases of Cu_2S and CuS_2 along with CuS were stabilized. At 6.5 pH, $Cu_{29}S_{16}$ was found with CuS; at 7.5 pH, $Cu_{29}S_{16}$ was obtained with CuS; and 8.5 pH showed CuS with some unknown peaks. At pH 9.5, a pure phase of covellite arises without any impurities (Yadav and Bajpai, 2017). CuS nanoparticles were synthesized by varying the precursors and the concentration of molecular precursors using the coprecipitation method. For the synthesis, CuCl, $CuCl_2$, and $CuSO_4$ were used as copper precursors and thiourea were used as sulfur precursors in molar ratios of 1:1 and 1:2 (Pejjai et al., 2020).

Coprecipitation method was used for the synthesis of copper sulfide capped with starch, glucose, PVA, albumin, and *Aloe vera* at room temperature (~30°C). Copper acetate $(CH_2COO)_2Cu.H_2O$) and thiourea (H_2NCSNH_2) were used as starting materials dissolved in distilled water and 3% capping agent in the molar ratio of 1:1. Nanocomposites of CuS/PVA and CuS/starch contain a mixture of $Cu_{1.96}S$, $Cu_{1.8}S$, and Cu_7S_4 having amorphous structures. The CuS/*Aloe vera* nanocomposite exhibits good crystallinity superimposed on the *A. vera* matrix (Nath and Kalita, 2017). Chitosan-capped copper sulfides were stabilized using copper acetate and thiourea as starting materials (Boey et al., 2007). Cysteine-capped CuS nanoparticles were prepared by chemical coprecipitation, and their interactions with BSA (Prasanth et al., 2016) and alanine as stabilizers capped CuS (Nelwamondo et al., 2012), water-soluble CuS nanocrystals, and nanorods (Gautam and Mukherjee, 2006). Coprecipitation method used for synthesis of CuS nanocrystals was capped with an anionic surfactant of sodium-bis(2-ethylhexyl) sulfosuccinate (Na-AOT), $Cu(CH_3COO)_2.H_2O$, and thioacetamide (TAA) used as starting materials in a molar ratio of 1:1 at 30°C. One of the advantages of this strategy is that it is an eco-friendly method (Simonescu et al., 2008).

The effect of different calcination temperatures (250, 500, and 750°C) has been also studied by the coprecipitation method. Due to the change in calcination temperature, it creates variations in crystallite size, crystal structure (hexagonal, rhombohedral, and monoclinic), texture coefficient, and lattice parameters. Grain size also increases by increasing temperature, and CuS nanoparticles transform into nonstoichiometric Cu_9S_5 at 250°C to $CuSO_4$ at 500°C, and then change into CuO (750°C) (Iqbala et al., 2020). Water-based CuS nanofluids were synthesized using a coprecipitation method that shows good electrical conductivity. It shows the highest electrical conductivity of 72.9 μS/cm with 0.0038 wt% and the optimum temperature at 55°C. It has maximum augmentation of electrical conductivity for 0.0038 wt% concentration at 2847% with the average temperature range from 30°C to 50°C, respectively (Ramalingam et al., 2020). Covellite copper sulfide nanoparticles were synthesized as an excellent Fenton-like catalyst using a facile precipitation method. CuS catalyst transformed into $Cu_{2-x}S$ and Cu_2S in dark and light conditions, respectively, through Fenton reaction. Reactive oxygen species (ROS) scavengers suggest that hydroxyl radicals are active species for degradation of cationic dyes in the dark,

whereas superoxide radicals were active species for degradation of anionic dyes in visible light. The nanoscale transformation of the catalyst facilitated the degradation activity for many cycles; on the other hand, it offered the possibility for selective and enhanced round-the-clock degradation of dyes (Raj and Jaiswal, 2021).

2.2 Refluxing method

Reflux condensation has been used to prepare nanomaterials by dissolving precursors in a solution at a high boiling point and reacting at a high temperature through refluxing.

CuS nanostructures have been synthesized by a refluxing method using copper chloride dehydrate ($CuCl_2.2H_2O$), sodium sulfide (Na_2S), and sodium thiosulfate pentahydrate as precursors, whereas polyethylene glycol (PEG) and ethylene glycol (EG) were used as solvents. CuS of different nanostructures were obtained, such as a nanoparticle-like structure with an average size of ~40 nm, a flower-like structure with a petal thickness of ~10 nm, and nanoflakes of thickness ~15 nm (Kushwah et al., 2017). The refluxing method was reported for the synthesis of CuS nanostructures by using varying precursors such as $Cu(CH_3COO)_2.H_2O$, $Cu(NO_3)_2.3H_2O$, and $CuSO_4.5H_2O$ as copper sources and CH_4N_2S, Na_2S, and $Na_2S_2O_3.5H_2O$ as sulfur sources. Obtained CuS shows different nanostructures such as tube-like structure, a cluster of nanoparticles, hexagonal plate, rectangular grains, and ball-like structures (Yadav et al., 2019). Clusters of CuS nanoparticles and sponge-like structures of CuS nanoflakes were synthesized by a refluxing method at reaction temperature of 130°C for a reaction time of 1.5–6 h using copper chloride ($CuCl_2{\cdot}4H_2O$) and TAA (CH_3CSNH_2) as precursors in deionized water to form $[Cu(CH_3CSNH_2)_2]Cl_2$ complexes. During refluxing, $[Cu(CH_3CSNH_2)_2]Cl_2$ complexes were dissociated. TAA was hydrolyzed by water to generate H_2S, which reacted with Cu^{2+} to synthesize CuS powder. For 130°C and 1.5 h refluxing, clusters of nanoparticles and nanoflakes were detected after refluxing for 4 h, and sponge-like structures of nanoflakes were achieved after 6 h of refluxing due to the crystal growth of some preferred structures (Phuruangrat et al., 2012).

The advantage of this method is that the final product has homogeneity and purity as compared to other methods, but this method is not applicable for toxic materials as well as not applicable at higher temperatures.

2.3 Hydrothermal/solvothermal method

The hydrothermal method produced inorganic chalcogenide semiconductors involving a chemical reaction between the precursors under controlled temperature and pressure in the presence of hot water. Reaction was carried out inside an autoclave, which can bear the drastic conditions of temperature and pressure.

The drawbacks encountered in other methods, including the large grain size of the product and high temperature required for the reaction, are overcome in this method. The advantages associated with hydrothermal/solvothermal method are

comparatively low-temperature requirement, reproducibility, homogeneity, and purity of the obtained product. Moreover, particle properties such as morphology and size could be controlled via hydrothermal process by adjusting the source species, reaction temperature and time, and RPM (Yang et al., 2001).

Different research groups have reported a hydrothermal method to control the shape, size, and morphology of chalcogenide nanoparticles by changing the molecular precursors, molarities of precursors, reaction temperature, time duration, and pressure. A 3D flower-like structure was obtained using Cu_2O hollow microspheres as a template via a hydrothermal route. The reaction of Cu_2O hollow spheres and TAA followed by hydrothermal treatment at 120°C for 12 h obtained 3D flower-like structures with a diameter in the range of 200–300 nm (Wu et al., 2012). CuS of various spherical, quadrate, plate-like, and tubular morphologies and sizes were obtained by adjusting the copper sources, reaction temperature, and reaction time. $Na_2S_2O_3.5H_2O$ was used as an S-precursor with a different source of Cu such as CuO, $CuSO_4.5H_2O$, and $CuCl_2.2H_2O$ at reaction temperatures 130°C–170°C for reaction times of 6–24 h (Zhang et al., 2004). CuS of different morphologies such as flower-like, nanoparticle-like, rod-like, and multilayered-like were obtained by changing the metal precursor and various reaction parameters. The flower-like morphology of CuS shows excellent electrocatalytic activity for N_2H_4 oxidation and excellent superior analytical performances (Yang et al., 2018). CuS hexagonal plates were synthesized having an edge length of 1 μm, 100-nm thickness, and ~45-nm crystallite size. It is inferred that if the reaction temperature was not highly elevated, impurities arise with CuS. Cu^{2+}:$S_2O_3^{2-}$ mole ratio plays an important role to control the amount of cyclooctasulfur (S_8). Reaction time was found to be an important parameter for impurity decomposition and increasing crystallite size and crystallinity of the CuS hexagonal plates (Auyoong et al., 2013). Different hierarchical structures like urchins and nanoplates were obtained for precursors $CuCl_2.2H_2O$, CH_4N_2S, and $Na_2S_2O_3.5H_2O$ at temperature of 150°C for a reaction time of 5 and 24 h (Saranya and Grace, 2012). Hydrothermal route has also been reported for the capping/stabilizing agent effect with chalcogenides. Copper nitrate and sodium thiosulfate are used as precursors and cetyltrimethylammonium bromide (CTAB) as a capping agent at 150°C for a reaction time of 5 and 24 h. Hexagonal nanoplates (Saranya et al., 2013) of mean plane size 75–179 nm and thickness 18–38 nm (Chu et al., 2008) have been obtained.

The solvothermal method has been reported for CuS nanomaterials with hierarchical structures in EG using $Cu(NO_3)_2.3H_2O$ as a copper source and thiourea, $Na_2S.9H_2O$, and TAA as sulfur sources for varying reaction temperatures and reaction times. Hierarchical structures of copper sulfide have applications for the fabrication of nanodevices and photocatalytic applications (Li et al., 2010b). CuS nanoparticles using EG have also been synthesized and perform photocatalytic activity having degradation rates of 97.88% using MB as a degradant (Zhou et al., 2020). 3D hierarchical CuS architectures consisting of 1D nanotubes have been synthesized by adjusting the volume ratio of aqueous solution with Cu^{2+} and MAA^- ions and ethanol. 3D hierarchical architectures show good catalytic degradation activity of about 99% of degradation of RhB in the presence of visible light and H_2O_2 within 45 min (Chai et al., 2020). Mixed solvent water and EG

have been used for the synthesis of copper sulfides such as Cu_2S, $Cu_{31}S_{16}$, $Cu_{1.8}S$, and Cu_7S_4 of morphologies of flower-like, ball-like, and irregular architectures congregated from much smaller spherical particles and nanoslices at reaction temperatures of 130°C and 160°C (Nan et al., 2006). In various nonstoichiometric phases of CuS, a mixture of Cu_7S_4-CuS and Cu_9S_5 was synthesized using copper chloride and sodium sulfide as starting materials by the solvothermal route. Tiny particles, hexagonal plates, and octahedron morphologies have been obtained by changing the ratios of precursors (Wang et al., 2013). The effect of precursors was reported by other groups of researchers using $CuCl_2$, $Cu(NO_3)_2$, and $CuSO_4$ as the copper sources and $CS(NH_2)_2$, $Na_2S_2O_3$, and Na_2S as sulfur sources via a solvothermal method. CuS of different morphologies such as spherical nanoflowers, doughnut-shaped nanospheres, and dense nanospheres were synthesized using $CuCl_2$, $Cu(NO_3)_2$, and $CuSO_4$ as the copper sources for fixed sulfur source $CS(NH_2)_2$. Typical nanoflowers and a mixture of nanoneedles, nanoparticles, and nanoplates were obtained for fixed copper source of $CuCl_2$and $Na_2S_2O_3$, and Na_2S was used as a sulfur source (Zhang et al., 2014). To achieve good indoor thermal comfort in the hot summer days, an indium-doped CuS nanocrystal was also synthesized as a novel near-infrared (NIR) shielding material for energy-efficient windows using a solvothermal method. Doping of indium ions was an effective way to improve the NIR shielding performance of CuS films (Qiang et al., 2021).

Furthermore, stoichiometries of copper sulfide were also controlled by chelating and nonchelating solvents. $Cu(NO_3)_2$ and thiourea were used as precursors, and different solvents were used, i.e., (i) ethylenediamine (En), (ii) EG, (iii) a mixed solution of 50% ethylenediamine + 50% EG, and (iv) ethanol. The reaction was operated for 12 h at reaction temperature of 130°C. Cu_2S phases were formed in the case of amine, the flower-like structure of Cu_2S crystals using ethylenediamine, and spaghetti-like crystals with an average diameter of ~0.6 μm by using EG as solvent. When ethylenediamine and EG were mixed in equal amounts, neither flower-like nor spaghetti-like morphology was detected. Spherical microparticles were observed in the case of ethanol (Gorai et al., 2005). CuS nanotubes using a microemulsion system consisting of oleic acid, water, and poly(vinylpyrrolidone) (Zhang et al., 2008) and nanorods (Ou et al., 2005) using water and alcohol solvent were prepared. Cylindrical nanostructures (Saranya et al., 2015), compactness of nanoparticles (Kundu and Pradhan, 2013), set of nanoparticles, and hierarchical spherical flower-like structures (Adhikari et al., 2017) were detected by hydrothermal/solvothermal method.

The technique also has some disadvantages such as long synthesis time and high energy consumption (Phuruangrat et al., 2013).

2.4 Microwave (MW) irradiation

The MV irradiation route holds great promise due to being faster, simpler, and highly energy-efficient (Wada et al., 2001). The advantage of this method is that it has fast molecular-level heating, which provides homogeneous and swift thermal reactions. Because of simultaneous nucleation and homogeneous heating, uniformly small particles are obtained in a large quantity (Kerner et al., 2001; Tu and Liu, 2000).

MV irradiation route has been reported for the preparation of Cu_9S_8 (20-nm diameter) and Cu_7S_4 using *N*,*N*-dimethylformamide (DMF), ethylenediamine, aqueous hydrazine, and aqueous ammonia as solvents. Dispersed rectangular particles with an average width of 30 nm and sheet-like particles were obtained if N, N-DMF, and aqueous ammonia, respectively, were used as solvents for the synthesis of Cu_9S_8. Cu_7S_4 were obtained using aqueous hydrazine as a solvent. Thus, solvents play an important role in the synthesis of nonstoichiometric copper sulfides. Reaction time and power of MW had a minor effect on the chalcogenide nanoparticles (Zhang et al., 2002). Copper sulfide Cu_9S_8 uniform nanorods with an average diameter of 5–10 nm and length 30–60 nm were reported with MV irradiation of 1% (w/v) using sodium dodecyl sulfate, copper nitrate, and TAA as starting materials (Liao et al., 2003). Various hierarchical nanostructures of CuS were synthesized using Cu and S precursors with EDTA as a complexing agent (Mu et al., 2010), and nanoparticles were synthesized via formaldehyde solution of metal ion and TAA (Liao et al., 2001) by MV irradiation route. Crystals of CuS with different morphologies such as nanorods, assemblies of nanoflakes, nanofibers, clusters of nanosized particles, and sponge-like structures were obtained from different precursors of copper and sulfur using MV irradiation (Thongtem et al., 2007). Morphologies of CuS nanostructures such as assemblies of nanoparticles into solid spheres and strip-type and leaf-like structures have resulted from different precursors of copper and sulfur in an aqueous medium by MV irradiation route in sunlight. The effect of MV power on CuS nanostructures has been probed by varying MV irradiation (2.45 G) power and time of irradiation; 160 W for 25 min, 180 W for 30 min, and 180 W power for 30 min (Nafees et al., 2012). Hollow spherical, flower-like, and tubular structures were reported by $CuCl_2.2H_2O$ and CH_3CSNH_2 used as precursors in EG using 180 W cyclic MV irradiation for 24 and 72 cycles. The irradiation for every cycle increased from 20% up to 60% (Thongtem et al., 2009). CuS microspheres are synthesized by facile MV synthesis without any template (Li et al., 2017).

MV irradiation route reported varying sized spherical shapes, utilizing $Cu(CH_3COO)_2.H_2O$ and $Na_2S_2O_3.5H_2O$ as starting materials treated under MV irradiation (2.45 GHz) at 160 and 320 W for 30 and 15 min. Power and time in MV irradiation played a vital role in the aggregate of all particles. By increasing MV time or power, aggregation kinetics could be increased and structure size changed; at low power MV irradiation, nanoparticle aggregation may not start properly due to a lesser number of collisions between nanoparticles. In this situation, when nanoparticles are unable to collide well with each other, the time of irradiation cannot greatly contribute. Appropriate optimization of power of MV irradiation and time of exposure is needed. More time and higher power quickly induce the aggregation process, and the morphology of product can be changed (Nafees et al., 2013).

2.5 Sonochemical method

The sonochemical method has been used to synthesize copper sulfides of various phases in aqueous solutions. For synthesis of CuS using this method, $Cu(CH_3COO)_2.H_2O$, $CuCl_2.2H_2O$, $CuSO_4.5H_2O$, $Cu(NO_3)_2.3H_2O$, and $Cu_2(CO_3)(OH)_2.½H_2O$ were

used as copper precursors, and thiourea, TAA, and sulfur were used as sulfur sources. EDTA monoethanolamine and triethanolamine were used as complexing agents. CuS obtained by copper acetate and thiourea shows agglomerated nanoparticles of an average diameter of 10 nm. CuS nanoparticles prepared from copper hydroxide and thiourea agglomerated into clusters with sizes of around 100 nm. Using copper carbonate and thiourea, a pure phase of covellite with an average particle size of 8.3 nm was detected. CuS synthesized without a complexing agent is a mixture of copper sulfate and copper sulfide. The crystallite sizes also depend on the complexing agent; the smallest particles were obtained in the case of using a 0.05 M aqueous EDTA solution (Kristl et al., 2013). CuS was synthesized using copper acetate and TAA in the presence of triethanolamine as a complexing agent with an average diameter of 13 nm (Wang et al., 2002). After that, CuS was prepared sonochemically in aqueous solutions from copper acetate and thiourea (Xu et al., 2006). CuS/PVA nanocomposites were also prepared in an ethylenediamine-water solution of copper acetate and sulfur under an argon flow of particle sizes ~ 165 nm and 225 nm (Kumar et al., 2002).

CuS and PrGO-CuS nanocomposite has been reported using sonochemical route. The nanocomposite was synthesized using bath-sonication (frequency: 37 kHz; power: 150 W) of graphene oxide (GO) and CuS precursors at 80°C for 60 min. FESEM confirms formation of CuS nanoplates if the synthesis is performed at 80°C. Besides this, CuS nanoparticles were formed at room temperature. CuS nanoplates on PrGO can be prepared using this method at a temperature of 80°C (Palanisamy et al., 2020). Doped and undoped CuS nanoparticles were synthesized by a sonochemical route by varying the concentration of Pb. Synthesized nanoparticles were useful for optoelectronics applications (Zeinodin et al., 2021).

Advantages of this method are uniform size distribution, a higher surface area, faster reaction time, and improved phase purity. It is extremely hard to control the temperature because ultrasonic baths usually warm up when they are in use, resulting in an inconsistent temperature. Many sonochemical reactions need to be at a certain temperature, which serves as a major disadvantage.

3 Controlling process parameters

3.1 Precursors

The counterions play a crucial role in controlling the morphology of the product. In the case of CuS synthesized using $Na_2S_2O_3.5H_2O$ as a sulfur source and CuO, $CuSO_4.5H_2O$, and $CuCl_2.2H_2O$ as different copper sources using a hydrothermal method, it is inferred that copper sources play an important role in controlling the morphology and size of nanocrystallites. CuS powders using CuO as the copper source at 150°C for 12 h consist of uniform, spherical nanoparticles with a mean size of 13 nm. CuS powders using $CuCl_2.2H_2O$ as the copper source are quadrate with the size varying from 30 to 100 nm. When $CuSO_4.5H_2O$ was used as the copper source, obtained CuS powders are composed of tubular-like structures with

diameters of 0.33–1.44 μm and lengths of 5–32 mm, as well as sphere-like particles of about 700 nm. When $CuSO_4.5H_2O$ and $CuCl_2.2H_2O$ were used as the copper sources, they are easily dissolved in water and release Cu^{2+}, which combines with $S_2O_3^{2-}$ produced upon the dissolution of $Na_2S_2O_3.5H_2O$ in water to form relatively stable complex/precipitate. Then, the formed complex/precipitate can decompose into CuS, SO_4^2, and H^+ (Zhang et al., 2004). Copper chloride ($CuCl_2{\cdot}2H_2O$), copper acetate ($Cu(CH_3COO)_2{\cdot}H_2O$), copper nitrate ($Cu(NO_3)_2{\cdot}3H_2O$), and copper sulfate ($CuSO_4{\cdot}5H_2O$) are used as copper precursors and thiourea as a sulfur source for the controlled nanostructures of flower-like, nanoparticle-like, rod-like, and multilayer-like structures, respectively, by changing the type of metal precursor using the hydrothermal method (Yang et al., 2018). Using the hydrothermal method, $Cu(NO_3)_2.3H_2O$ was taken as a copper source and thiourea (TU), TAA, and $Na_2S.9H_2O$ as sulfur sources, which explored the influence of sulfur sources on the morphologies of copper sulfide, and the pure hexagonal covellite phase of the CuS crystals was successfully synthesized. When $Na_2S.9H_2O$ was adopted, large amounts of nanoparticles were present. Large quantities of small nanorods and nanoplates were obtained by employing TAA as the sulfur source. It can be inferred that sulfur sources have great effects on the final morphologies of CuS nanomaterials due to the different release rates of S^{2-} ions in a sulfur source (Li et al., 2010b). $(CH_3COO)_2$, $CuSO_4.5H_2O$, and $CuCl_2$ as copper sources and H_2NCSNH_2, $Na_2S_2O_3.5H_2O$, and CH_3CSNH_2 as sulfur sources were used for the synthesis of CuS nano/submicron-size materials of various morphologies such as spherical, tubular, leaf-like, and strip-type structures using MV irradiation under sunlight (Nafees et al., 2012).

In the refluxing method, $Cu(CH_3COO)_2.H_2O$, $Cu(NO_3)_2.3H_2O$, and $CuSO_4.5H_2O$ as copper precursors and CH_4N_2S, $Na_2S_2O_3.5H_2O$, and Na_2S as sulfur precursors were used for the synthesis of CuS nanostructures. All precursors resulted in pure covellite except when sodium sulfide was used as a sulfur source. The morphology of nanoparticles is controlled by both sulfur precursors as well as the nature of counteranions in copper precursors. The role of sulfur precursors is mainly limited by the release rate of S^{2-} ions; in sodium sulfide, the release rate is very fast. When Na_2S is introduced into water, it dissociates into Na^+ and S^{2-} immediately, where the S^{2-} ion reacts quickly with Cu^{2+} to form CuS nuclei. Due to the high concentration of S^{2-} ions, copious amounts of CuS nuclei are created in an explosive way to form irregular CuS nanoparticles with broad size distribution. This results in uncontrolled complex formation with Cu^{2+} ions, and hence, phase formation could not be controlled resulting in mixed-phase nanoparticles (Yadav et al., 2019). By the solvothermal method, $Cu_{1.8}S$ and CuS were achieved from the Cu-Tu precursors, with Cl^-, NO_3^- and SO_4^{2-} as the counteranions in EG as the solvent. $[Cu_4(tu)_9](NO_3)_4.4H_2O$ yielded CuS when the dissociation was completed in the presence of EG in air or argon. It resulted in flower-like morphology. $Cu_{1.8}S$ was obtained when $[Cu(tu)_3]Cl$ was dissociated in the presence of air as well as argon in EG. It showed hexagonal plate-like morphology. A mixture of $Cu_{1.8}S$ and CuS was formed from the chloride ion-containing precursor and shows both these morphologies (Kumar et al., 2011).

CuS synthesized by MV hydrothermal using different sources of copper, ($Cu(CH_3COO)_2{\cdot}H_2O$, CuBr, and $CuCl_2{\cdot}2H_2O$), sulfur, (CH_3CSNH_2 and NH_2CSNH_2) and phase-pure CuS (covellite) with flower-like, nanoparticles, and nanoplates nanostructures were obtained. Using CuBr as a precursor, mixed phases of Cu_2S and CuS were detected (Phuruangrat et al., 2013), whereas using ($CuCl_2.2H_2O$, CuBr, $Cu(CH_3COO)_2.H_2O$, CH_3CSNH_2, $NH_2CSNHNH_2$, and NH_2CSNH_2) precursors of copper and sulfur, respectively, different morphologies such as assemblies of clusters of nanosized particles, nanoflakes, nanorods, nanofibers, and sponge-like structures (Thongtem et al., 2007) were reported.

A template-directed synthesis route reported CuS nanobelts and nanotubes in which $CuSO_4.5H_2O$ and $CuCl_2.2H_2O$ are used as copper precursors and $Na_2S_2O_3.5H_2O$ as a sulfur source in lyotropic liquid crystal templates. TEM revealed that these nanotubes show sheet-like morphology with inner diameters of 100–250 nm, outer diameters of 200–500 nm, and lengths up to several micrometers, while CuS nanobelts synthesized with $CuCl_2.2H_2O$ and TAA resulted in nanobelts that are very uniform with a width of about 300 nm and lengths up to several hundred micrometers (Zhu et al., 2007).

CuS nanocrystals of microspheres, nanotubes, nanoflakes, and nanoparticles synthesized by mild solution chemistry method under the same reaction conditions were reported by varying the different Cu precursors such as copper nitrate ($Cu(NO_3)_2{\cdot}3H_2O$), copper sulfate ($CuSO_4{\cdot}5H_2O$), and copper acetate ($Cu(OAc)_2{\cdot}H_2O$) for fixed sodium thiosulfate ($Na_2S_2O_3{\cdot}5H_2O$) as sulfur precursors (Kundu and Pradhan, 2014).

The coprecipitation method has been reported for the synthesis of CuS by varying copper sources as CuCl, $CuCl_2 \cdot 2H_2O$, and $CuSO_4 \cdot 7H_2O$, where CH_4N_2S was used as a sulfur source in molar ratios of 1:1 and 1:2. $C_6H_{15}NO_3$ (triethanolamine) and C_3H_8O (isopropyl alcohol) were used as complexing/chelating agents and distilled water as a solvent. CuS synthesized using CuCl and thiourea at a molar ratio of 1:2 shows a pure phase of copper sulfide, whereas molar ratio of 1:1 shows formation of mixed phases such as Cu_2O and CuS. Formation of Cu_2O indicated a partial substitution of oxygen by sulfur due to a lower concentration of S^{2-} ions in the solution. CuS nanoparticles synthesized using $CuCl_2$ and $CuSO_4$ copper sources confirmed the formation of dominant CuS phase along with minor Cu_7S_4 or Cu_2S impurity phases for the molar ratio of Cu/S ¼ 1:2. The excess thiourea partially reduced the Cu^{2+} to Cu^{+} and forms the relative stable Cu^{+}-thiourea complexes (Pejjai et al., 2020).

Fig. 2 shows scanning electron micrographs of copper sulfide synthesized by varying precursors. By varying the copper source and sulfur source, it shows different morphology. Copper sulfide nanoparticles showed a spherical shape if copper acetate and thiourea were used as precursors. Flower-like morphology was seen when copper nitrate and sodium thiosulfate were used as precursors, and its shows a cluster of nanoparticles in the case of copper sulfate pentahydrate and sodium thiosulfate used as precursors.

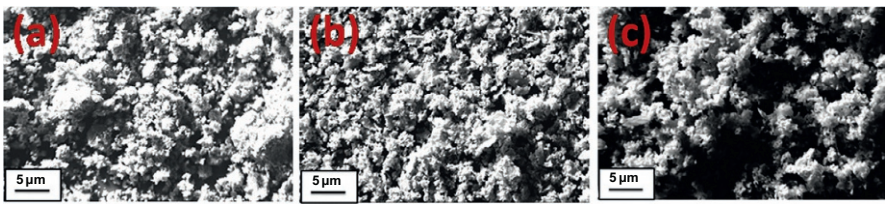

FIG. 2

Scanning electron micrographs (SEM) of different nanoparticles of copper sulfide synthesized by varying precursors: (A) Copper acetate and thiourea; (B) copper nitrate and sodium thiosulfate; (C) copper sulfate pentahydrate and sodium thiosulfate.

3.2 Molar ratio

Not just the nature of precursors, but the concentration of precursors also has a significant role in the formation of CuS nanomaterials. CuS synthesized using three different molar ratios of 1:1, 2:1, and 1:2 of $Cu(NO_3)_2$ and $Na_2S_2O_3$ precursors results in different morphologies. For molecular precursor concentration 1:1, CuS nanotubes consisting of loosely held nanoparticles were obtained; for 2:1 M ratio of precursors, both CuS nanotubes and nanoparticles were obtained, whereas for 1:2 $Cu(NO_3)_2$ and $Na_2S_2O_3$ molar ratio, mixed phase of CuS and Cu_2S were obtained (Zhang et al., 2014). In another interesting study, for CuS synthesized at molar ratios of 1, 1.25, 2, 3, 4, and 6 of precursors, the reactant molar ratio was crucial for the appearance of final crystal shape formation (Qin et al., 2005). $Cu(NO_3)_2$:$Na_2S_2O_3$ was used in molar ratios of 1:2, 1:4, and 1:6 for the synthesis of CuS. The size of the clusters obtained for the molar ratio of 1:4 and 1:6 was found to be ~1.0–2.0 mm larger than CuS obtained from precursor molar ratio of 1:2. These clusters were also found to consist of nanoparticles and nanoplates with sizes of 200–400 nm (Kundu and Pradhan, 2013). CuS formed at Cu^{2+}:$S_2O_3^{2-}$ molar ratios of 1:1, 1:1.5, 1:2.5, 1:3, and 1:5. For molar ratio of 1:1, phase natrochalcite [$NaCu_2(SO_4)(H_2O)$] with irregular plate-like morphology was detected, whereas for molar ratio of 1:1.5, pure digenite Cu_9S_5 with irregular platelet-like morphology was identified. For molar ratio of 1:2.5, 1:3 and 1:5, mixed phases of CuS and S_8 were detected. Higher Cu^{2+}:$S_2O_3^{2-}$ molar ratios identified the presence of a higher amount of S_8 (Auyoong et al., 2013). CuS, a mixture of CuS-Cu_7S_4, and Cu_9S_5 have been synthesized by adjusting the molar ratios of S^{2-} and Cu^{2+} to 1:1, 1:2, 1:3, 1:4, and 1:5 using solvothermal process, and various morphologies, such as tiny particle, hexagonal plate, and octahedron, have been detected (Wang et al., 2013).

The effects of the precursor molar ratio on the phase of copper sulfides were also investigated by varying molar ratios of Cu and sulfur precursors. For molar ratio 1/2, a mixed phase of CuS with Cu_9S_5 was obtained, and a pure phase of covellite was obtained for precursor molar ratio of 1/1. When the Cu^{2+}/S^{2-} precursor molar ratio is less (1/5–1/3), digenite Cu_9S_5 phase with large particle sizes of about 3 mm was obtained, probably due to the high concentration of S^{2-} (Luo et al., 2015). Sulfur and copper ion precursor concentration plays a very important role in the formation

of different morphologies; it is demonstrated that when the precursor ratio was 2:3, S^{2-} ions are more than Cu^{2+}; they could not aggregate with CuS in maximum dimension, so a two-dimensional structure was obtained, whereas for a 1:3 ratio, S^{2-} ions had many more ways to aggregate with Cu^{2+}, which is why spherical morphology was formed (Nafees et al., 2012). Different morphologies were obtained by changing precursors and molar ratios of the solvent. $Cu(NO_3)_2{\cdot}3H_2O$ and $Na_2S_2O_3{\cdot}5H_2O$ resulted from microspheres if water was used as a solvent. Nanotubes were seen when the precursor was the same but solvent was water and EG was a molar ratio of 1:3. At the same molar ratio, nanoflask is obtained by changing the precursors $CuCl_2$ and $Na_2S_2O_3{\cdot}5H_2O$ (Kundu and Pradhan, 2014). Copper-based sulfide nanoparticles (Cu_2S, CuS, CuO/Cu_2O/Cu_2S, Cu_2S/CuS, CuS/S) were synthesized by one-pot synthesis in PEG-400 by varying the molar ratios of Cu:S (1:0.1, 1:0.25, 1:0.5, 1:0.75, 1:1, 1:2, 1:3) using the precursors copper acetate and sublimed sulfur. By increasing sulfur content to a synthesized product, the nanoproducts change from Cu_2S (1:0.25) to CuS (1:1) and then to CuS/S (1:2). For nanoparticles synthesized at a molar ratio of copper to sulfur of 1:1, the product is irregular CuS nanoflakes with a smaller band gap value of 2.01 eV (Jiang et al., 2020). A molar ratio of Cu/S had a great influence on the phases of CuS due to changes in the kinetic release rate of sulfur. The concentration of S^{-2} ions is a crucial factor in the formation of nonstoichiometric copper sulfides. The observed Cu_7S_4 or Cu_2S minor phase was due to the partial reduction of Cu^{2+} to Cu^{+} at a high molar ratio of the sulfide source (Pejjai et al., 2020).

3.3 Reaction time

Several studies explored the role of reaction time in the synthesis of CuS nanostructures. For example, CuS synthesized using CuO as the copper source and $Na_2S_2O_3.5H_2O$ as the sulfur source at 150°C for different reaction times (12 and 24 h) resulted in different nanostructures. CuS powders derived for 12 h consist of uniform, spherical nanoparticles with a mean size of about 13 nm, while those derived for 24 h comprise mainly plate-like nanocrystallites with a size in the range of 80–220 nm, together with some rod-like nanomaterials (Zhang et al., 2004). Similarly, for different hierarchical structures like urchins, nanoplates were obtained for precursors $CuCl_2.2H_2O$, CH_4N_2S, and $Na_2S_2O_3.5H_2O$ at 150°C for a reaction time of 5 and 24 h. CuS synthesized using copper chloride and thiourea shows plate-like structures self-assembled to long cylinder-like architectures and are smaller in size for a reaction time of 24 h, which may be due to the rate of nucleation increasing at longer periods. For reaction time of 5 h, flakes are well aligned with uniform thickness ranging from 14 to 30 nm. However, the nanostructure shows impurities of unknown material for longer reaction time. In the case of thiosulfate as sulfur source for 5 h reaction time, numerous plates assembled to form sphere-like nanostructures with the thickness of each plate ranging between 18 and 64 nm, whereas for reaction time carried out for 24 h, the morphology was quite similar, but some flower-like structures were seen with petal thickness of around 75 nm (Saranya and Grace, 2012). For copper sulfide synthesized using $Cu(NO_3)_2.3H_2O$ and thiourea as copper and sulfur sources

at constant molar ratio 1:2 at 150°C, for different reaction times varying from 4, 8, 12, and 24 h, SEM images reveal that CuS microspheres composed of nanoplates or nanorods start to form at reaction time 4 h; for reaction times of 8 and 12 h, CuS microspheres aggregate with each other to form hierarchical structures. As reaction time increases to 24 h, hierarchical chain-like morphology is obtained (Li et al., 2010b). In another study, CuS was synthesized for reaction time of 15 min, 30 min, 1 h, 2 h, and 8 h, keeping other parameters such as precursor ratio $Cu(NO3)_2$:$Na_2S_2O_3$ at 1:1, temperature 70°C, and water-EG solvent ratio (1:3) fixed. For reaction time 15 and 30 min, CuS microrods are obtained with the length and diameter of the microrods in the range of 5–7 and 1–2 μm, respectively. When the reaction duration is increased to 1 h, a larger number of hexagonal-shaped microrods are found to join together forming clusters. The length and diameter of the microrods formed after 1 h of reaction are smaller in the range of 3–5 and ~1 μm, respectively. Several of these microrods are found to be hollow toward the axial end. This suggests that the initially formed solid rods are degraded at a higher rate on the axial directions than that of the lateral sides. When the reaction duration is increased to 2 h, the hexagonal tube-shaped structure emerged with a length and outer diameter in the range of 0.8–1.5 μm and 300–350 nm (200–250 nm), respectively. Similar types of tubes are obtained when the reaction duration is increased to 4 and 8 h. It has been inferred that the length and diameter of the CuS structures are reduced with increasing the reaction duration, and there is a preferential etching on the axial direction to create hollowness in the microrods producing nanotubes (Kundu and Pradhan, 2014). Auyoong et al. varied the reaction time to achieve phase pure CuS for Cu^{2+}:$S_2O_3^{2-}$ molar ratio of 1:2 at 155°C under hydrothermal synthesis. For a reaction time of 1 h, mixtures of covellite and cyclooctasulfur were detected. When reaction time was prolonged to 3 and 8 h, a pure covellite phase was obtained (Auyoong et al., 2013).

The effect of different reaction times has been studied using the hydrothermal route at fixed reaction temperature of 150°C. Reaction time of 5 h shows tubular and spherical structures. Reaction time increasing to 16 h shows the formation of self-assembled hexagons into tubules, which change into flower-like arrangements. During a further increase in reaction time up to 24 h, nanoplates self-assembled into cylindrical structures (Saranya et al., 2014).

CuS was synthesized from a stoichiometric copper chloride ($CuCl_2{\cdot}4H_2O$) and TAA (CH_3CSNH_2) by refluxing method for different reaction times at fixed reaction temperature of 130°C. Refluxing for 1.5 h results in clusters of nanoparticles, whereas nanoflakes in clusters after refluxing for 4 h and sponge-like structures of nanoflakes were achieved after 6 h refluxing (Phuruangrat et al., 2012). The role of CTAB in controlling the CuS nanostructure's morphology was studied for different reaction times. In the presence of CTAB at reaction time 20 h, it shows CuS nanoparticles with diameters of 90 nm coexist with a few nanoplates. After 24 h, large-scale homogeneous CuS nanoplates were seen. However, as the reaction was carried out for 24 h in the absence of CTAB, only CuS nanoparticles with diameters of 60 nm are formed, indicating reaction time and CTAB play important roles for the formation of morphology (Zhang and Zhang, 2008).

3.4 Reaction temperature

The role of reaction temperature has also been explored systematically to understand the factors controlling the morphology of CuS nanostructures. Copper sulfide was synthesized using $Cu(NO_3)_2.3H_2O$ and thiourea as copper and sulfur sources at a constant molar ratio of 1:2 and constant reaction time of 24 h but with varying reaction temperatures of 90, 120, 150, and 180°C. Formation of pure hexagonal covellite phases of CuS was obtained at relatively low temperatures, 90°C and 120°C. The improvement in the crystallinity is confirmed as the reaction temperature changes from 90°C to 120°C. On increasing the reaction temperature to 180°C, covellite CuS is contaminated with the digenite phase of Cu_9S_5. At 90°C, all microspheres are made up of densely packed, very thin nanoplates from 10 to 20 nm. At 120°C, all microspheres consist of sparsely packed nanoplates with a thickness from 30 to 40 nm, and the microspheres are incomplete. It has been inferred that reaction temperature is an important factor in determining not only the phase composition but also the size and morphology of the CuS nanomaterials (Li et al., 2010b). CuS was synthesized using $Cu(NO_3)_2$:$Na_2S_2O_3$ in a fixed ratio of 1:1 by varying the reaction temperature from 70°C to 120°C. Almost uniform and hexagonal shape nanotubes are found at all reaction temperatures. However, with increases in the reaction temperature from 70°C to 180°C, the length of nanotubes remains the same (~1 μm), whereas the average diameter is found to be increased to ~400 nm at 120°C and ~500 nm at 180°C from 200 nm at 70°C. It concluded that a lower reaction temperature of 70°C is suitable to grow smaller diameter CuS nanotubes (Kundu and Pradhan, 2014). Similar inferences are drawn from another report in which CuS synthesized for different reaction temperatures (120°C, 150°C, and 180°C) concluded that increasing the temperature most likely results in faster growth of crystal size (Qin et al., 2005). Pure phase covellite copper sulfide was obtained by varying the reaction temperature from 25°C up to 175°C. At reaction temperature of 25°C, mixed phases of copper sulfate [$CuSO_4$], krohnite [$NaCu_2(SO_4)(H_2O)_2$], and cyclooctasulfur [S_8] as well as covellite (CuS) were identified; increasing the reaction temperature up to 65°C, $NaCu_2(SO_4)$ $(H_2O)_2$ and $CuSO_4$ disappeared. As reaction temperature was further increased to 95°C and 125°C, the CuS phase was accompanied by S_8 phase, and finally, at 175°C, pure phase CuS was obtained (Auyoong et al., 2013). Similarly, the crucial role of the reaction temperature is demonstrated for forming CuS hollow spheres (Nafees et al., 2012).

3.5 Solvent

The reaction mediums play an important role in the synthesis and control of the shape and size of the chalcogenide nanoparticles. Alcohols such as ethylene gycol, polyethylene gycol, and benzyl alcohol have been known to act as reducing or stabilizing agents in the formation of copper sulfides (Kushwah et al., 2017). CuS nanostructures were synthesized using aqueous, alcohol (EG), and a mixture of aqueous and alcohol medium to observe their effect on the formation of CuS nanostructures. In the aqueous medium, synthesized CuS product was found with a spherical morphology of

diameter ~1 μm. These spheres are composed of agglomerated nanoplates of width and length ~100 nm and thickness ~20 nm. In a 3:1 water-EG solvent ratio, the morphology of the product remains a spherical shape, consisting of nanoplates. The average diameter of the sphere and the size of the nanoplates are reduced to ~500 nm and <100 nm, respectively. Nanoplates appear to be loosely agglomerated. Using EG as a solvent, the morphology of the product was a spherical-type with a deformed shape (Kundu and Pradhan, 2014). Oleylamine has been used as an eco-friendly solvent for the synthesis of CuS. Size and shape of the nanocrystals formed in such medium could be tuned systematically (Zhang et al., 2006).

A mixed solvent medium is found to be more effective for the synthesis of CuS nanomaterials. CuS nanomaterials were synthesized using a mixed solvent of water-butanol and water-cyclohexanol by solvothermal method wherein the water-butanol-assisted CuS sample showed high crystallinity rod-like nanostructures with an average width of the rods 40–72 nm in comparison to water-cyclohexanol-assisted CuS sample consisting of flake-like nanostructures with an average diameter ~60–80 nm (Ramamoorthy and Rajendran, 2017). CuS was synthesized in a template-free solvothermal approach to fabricating CuS nanoplate-based architectures with ethanol, EG, and DMF as the solvent. Hexagonal nanoplates with an edge length of 1 mm and a thickness of 100 nm and flower-like morphology were obtained for solvent ethanol, EG, and DMF, respectively (Li et al., 2009). In another report, CuS was synthesized using (i) ethylenediamine (En), (ii) ethyleneglycol (Eg), (iii) a mixed solution of 50% ethylenediamine + 50% ethyleneglycol, and (iv) ethanol as solvent. Monoclinic Cu_2S is achieved when ethylenediamine and a mixed solution of 50% ethylenediamine + 50% EG was used as solvent. Monoclinic Cu_2S with Cu are obtained if EG is used as a solvent. For ethanol, $Cu_{39}S_{28}$ phase were found (Gorai et al., 2005).

Solvent plays an important role to control the morphologies, for example, alkyl amines play an important role in the synthesis of CuS, with spherical, nanowire, and nanotube morphologies (Yao et al., 2007) of CuS nanostructures studied by controlling the organic and aqueous solvent ratio and their application for photocatalytic effects (Kundu and Pradhan, 2014).

3.6 pH of the solutions

The role of pH of the solution used for the synthesis of copper sulfide nanostructures has been examined. It is believed that when a higher amount of sulfur source is used, a mixed phase of copper sulfide is obtained. This may be due to the change in pH value of the solution. The effect of pH on the synthesized pure phase of copper sulfide has been reported. A molar ratio 1:6 of $Cu(CH_3COO)_2.H_2O$ and $Na_2S_2O_3.5H_2O$ has been used as a copper and sulfur source. At weak acidic pH (5.5), a mixed phase of CuS yarrowite—Cu_9S_8, CuS_2, and antlerite—$Cu_3(SO_4)(OH)_4$ was obtained. These mixed copper sulfides consist of an aggregate of small particles with an average diameter of 70–150 nm and bigger particles with an average diameter >500 nm. Small particles have a cuboidal shape and are bound in a row aggregate. The bigger

crystallites are facetates showing hexagonal plate morphology. At basic medium 11.5 pH value, only CuS was obtained. An alkali value of pH positively influences the process of nanocrystallite formation (Simonescu et al., 2006). In a simple coprecipitation method, we reported the synthesis of pure covellite CuS by varying the pH of the solution from 5.5–9.5 pH at a fixed molar ratio of 1:6. Material synthesized at 5.5 pH shows Cu_2S and CuS_2 with CuS. Increasing solution to 6.5 pH resulted in $Cu_{29}S_{16}$ with CuS; at 7.5 pH, $Cu_{29}S_{16}$ with CuS; and pH 8.5 shows CuS with some minor unknown impurities. Finally, at pH 9.5, pure phase of covellite arises without any impurities (Yadav and Bajpai, 2017).

MV irradiation method was reported for the studied effect of pH (1, 5, 9, 13) to control morphology. At a pH of 1, 50% irradiation, and 24 cycles, clusters of nanosized particles were detected. OH^- ions seem to influence their nucleation and growth. At higher pH 5 and 9, more nanosized and less plate-like particles existed. The nanosized particles began to assemble into a hollow object in the shape of a tube at pH 9. At pH 13, a number of tubes of 82–574 nm were seen (Thongtem et al., 2009).

3.7 Role of capping agents

It is noted that various surfactant, templates, or capping agents are used in chemical reactions to control the size, shape, and morphology of nanoparticles. Capping agents play critical roles to control these previously mentioned properties of nanoparticles. The use of surfactants or templates will inevitably increase the reaction complexity because of impurity in the product, and it is disadvantageous from the viewpoint of green chemistry. Surfactant is known to significantly affect the agglomeration of particles.

It was earlier reported that CTAB was used as a surfactant to reduce the agglomeration of particles. CuS was synthesized at 150°C, 180°C, and 250°C in the presence CTAB surfactant while maintaining the fixed molar ratio of the precursors [$Cu(NO_3)_2$:$Na_2S_2O_3$ = 1:2] and reaction time of 8 h. The resulting CuS nanostructures were found to be dispersed using a hydrothermal method (Kundu and Pradhan, 2013). Copper sulfide nanostructures with interesting morphologies were synthesized using CTAB as surfactant and copper nitrate and sodium thiosulfate were used as starting materials at 150°C for 5 and 24 h, respectively. The average grain size was found to be different without and with CTAB. The surfactant prevents the aggregation of the spheres, and the layer reaction time promotes the flake-like nanoplates, which self-assembled to form the nanostructures (Saranya et al., 2013). CuS nanoplates have been prepared in the presence of cation surfactant CTAB by a hydrothermal method in a solution of $CuCl_2.2H_2O$ and $Na_2S{\cdot}9H_2O$ at 180°C for 24 h. It is believed that CTAB as a capping reagent is selectively adsorbed on the different planes of CuS seeds, which help to lower the surface tension and stabilize the plates, resulting in a different growth rate of different planes to form the nanoplate structures (Zhang and Zhang, 2008). CTAB as the template used for tubular copper sulfide (CuS) microcrystal and flower-like CuS microsphere via simple hydrothermal route. At lower

concentration of CTAB, tubular structures with diameters of 1–3 μm and lengths of 7–12 μm were seen. At a higher concentration of CTAB, flower-like CuS crystals were formed (Chen et al., 2009).

Biomolecule-assisted solution route was used to synthesize Bovine Serum Albumin-conjugated copper sulfide (CuS/BSA) nanocomposites using zwitterionic surfactant BSA as a foaming and stabilizing agent. Nanoparticles are approximately spherical with a size distribution of 10–35 nm in diameter and good dispersibility, depending highly on concentration of BSA. BSA protein gives multiple binding sites for Cu^{2+}; Cu^{2+} ions can react with BSA; and the binding sites may include the –NH, –SH, –COOH, and –OH groups. Then, comparatively unstable TAA slowly hydrolyzed to release the S^{2-} ion, which reacted with Cu^{2+} ions to form CuS nuclei surrounding some special sites of BSA. As a soft template, BSA is a stable stabilizing agent and has a great effect on the monodispersal of nanoparticles by concentration-dependent BSA (Huang et al., 2010). CuS nanoparticles have been synthesized utilizing different capping molecules such as polyethyleneglycol (PEG), polyvinylpyrrolidone (PVP), and casein hydrolysate-enzymatic (CAS). Nanoparticles synthesized using PEG as a capping agent have an average size of 10 nm (Brelle et al., 2000). L-cysteine-capped nanoparticles having an average particle size of 6 nm are also reported (Prasanth et al., 2016).

Green capping material (starch, glucose, PVA, albumin, and *Aloe vera*) are also used for the synthesis of CuS at room temperature of ~30°C. The prepared nanocomposites of CuS/PVA and CuS/starch contain a mixture of copper-deficient phases such as $Cu_{1.96}S$, $Cu_{1.8}S$, and Cu_7S_4, as well as an amorphous structure of the composite materials. CuS/glucose shows nanorod-like structures while the CuS/*Aloe vera* exhibits good crystallinity superimposed on the *Aloe vera* matrix. (Nath and Kalita, 2017). *Aloe vera* acted as a good capping agent for the stabilization of CuS nanorod morphology using a green synthesis method (Nath and Kalita, 2021). Alanine-capped CuS (Nelwamondo et al., 2012) nanoparticles were also reported.

Non-ionic PVP has been used as surfactant for CuS:Ni flower-like morphologies composed of nanosheets (Wang et al., 2010) and as microspheres constituted of numerous self-organized knitted nanoribbons of ~30 nm thickness (Banerjee and Krupanidhi, 2010). Anionic surfactant sodium-bis(2-ethylhexyl) sulfosuccinate (Na-AOT) was used for synthesis of CuS nanocrystal. CuS without surfactant yielded 20–60 nm nanocrystals, while in the presence of surfactant yielded 10–30 nm nanocrystals. The particle size of CuS decreases with the surfactant concentration. Surfactant leads to obtaining dispersed nanocrystals included in the surfactant (Simonescu et al., 2008).

4 Properties

4.1 Structural properties

CuS synthesized using hydrothermal method $Cu(NO_3)_2$:$Na_2S_2O_3$ for 1:2 M ratio at 150°C and 180°C are found to be pure hexagonal CuS. Impurities arise due to presence of Cu_2S at temperature of 250°C. $Cu(NO_3)_2$ with $Na_2S_2O_3$ at molar ratio of 1:4

for reaction temperature 150°C and 180°C show orthorhombic sulfur along with CuS. Increasing the thiosulfate concentration to 1:6 CuS obtained along with sulfur at reaction temperatures 150, 180, and 210°C (Kundu and Pradhan, 2013). Pure phase of CuS was synthesized by sonochemical method. A crystallite size arises between 7 and 18 nm, and the resulting pure phase of covellite has a hexagonal phase (Kristl et al., 2013). CuS and $Cu_{1.8}S$ synthesized by successive ionic layer adsorption and reaction (SILAR) method calculated average particle size in the range of 10–10.8 nm and 5–7 nm (Balayeva et al., 2017). CuS was synthesized using sonochemical method by varying Pb concentration. As the concentration increased, crystallite size also increased (Zeinodin et al., 2021).

4.2 Surface morphology

The prepared copper sulfide was composed of uniform and regular rods with diameters ranging from 5 to 10 nm and lengths 30–50 nm (Saranya and Grace, 2012). CuS shows spherical nanoparticles with hexagonal nanoplates using hydrothermal route (Kundu and Pradhan, 2013). By the hydrothermal route, irregular plate-like and platelet-like morphology was obtained by CuS, CuS-Cu_7S_4, and Cu_9S_5 (Auyoong et al., 2013). Using the hydrothermal route, tubular structures and spheres were detected for CuS nanomaterials synthesized for reaction time 5 h, but there was not much regularity in the features. For 16 h, hexagons self-assembled into tubules, and the face of the tubule contained flower-like arrangements with the thickness of flakes ranging between 90 and 125 nm. Flower-like CuS crystal was seen consisting of an aggregation of many flake-like microcrystals, and the petal of the flower-like structures was about 95 nm in thickness. After 24 h, the formation of nanoplates self-assembled into cylindrical structures. The width of the plates is around 30–40 nm (Saranya et al., 2014). $Cu_{1.8}S$ and CuS were synthesized via solvothermal route. $Cu_{1.8}S$ showed hexagonal plate-like morphology, and flower-like morphology was seen for CuS. In the mixed phase, both $Cu_{1.8}S$ and CuS morphologies were seen (Kumar et al., 2011). Spherical nanoflowers, doughnut-shaped nanospheres, dense nanospheres, atypical nanoflowers, and the mixture of nanoneedles, nanoparticles, and nanoplates were reported as CuS nanostructures using the solvothermal technique (Zhang et al., 2014). CuS products with different flower-like, nanoparticle, and nanoplate morphologies have been synthesized by MV-hydrothermal method (Phuruangrat et al., 2013). CuS crystals of different morphologies such as nanofibers, sponge-like, clusters of nanosized particles, and assemblies of nanoflakes and nanorods structures were reported by the MV irradiation method (Thongtem et al., 2007). CuS have different nanostructures such as tube-like structures of 150–360 nm, clusters of nanoparticles with average particle size of 60 nm, hexagonal plate particle sizes 33 and 620 nm, rectangular grains with length and breadth size 80×100 nm, and ball-like structures of average diameter 70 nm, as well as big balls with average diameter 300 nm (Yadav et al., 2019).

In the coprecipitation method, CuS synthesized using precursors CuCl and thiourea showed agglomerated tiny sheet-like nanoparticles with irregular size,

whereas $CuCl_2$ or $CuSO_4$ and thiourea showed agglomerated flake-like-shaped particles (Pejjai et al., 2020). CuS synthesized using the sonochemical method shows nanoplate-like morphology with an average thickness of 26 ± 3 nm. Morphology of CuS on GO shows a spherical shape in which CuS nanoparticles anchored on the ultrathin surface of GO sheets (Palanisamy et al., 2020). CuS synthesized by varying the concentration of Pb shows nanodisks from high thickness to lower thickness, which might be due to the presence of the doping in the CuS lattice structure (Zeinodin et al., 2021).

4.3 Optical properties

The optical band gap of the synthesized CuS nanocrystals using a hydrothermal route is measured to be 1.68–1.7 eV for nanostructures, hexagonal nanoplates, and nanoparticles (Kundu and Pradhan, 2013). Solvothermal method's estimated band gap energy of CuS, CuS-Cu_4S_7, and Cu_9S_5 are 1.7, 1.8, and 0.7 eV, respectively, for morphologies such as tiny particles, hexagonal plates, and octahedrons (Wang et al., 2013). The optical band gap of the CuS nanostructures synthesized by solvothermal process was measured to be ~2.75 and 3.20 eV, respectively, for CuS synthesized using two different mixed solvents, water-butanol and water-cyclohexanol (Ramamoorthy and Rajendran, 2017). The optical energy band gaps of different nanostructures of CuS calculated 1.61, 1.93, 2.01, 1.70, and 1.82 eV for the spherical nanoflowers, doughnut-shaped nanospheres, dense nanospheres, atypical nanoflowers, and a mixture of nanoneedles, nanoparticles, and nanoplates, respectively, which were synthesized using a solvothermal method (Zhang et al., 2014). The band gaps for CuS nanoparticles obtained with different sulfur sources Na_2S and thiourea was determined as 1.7 and 1.72 eV, respectively, using the SILAR method (Balayeva et al., 2017). Microspheres have a band gap 2.08 of eV, nanotubes 2.06 eV, nanoflakes 2.16 eV, and nanoparticles 1.88 eV for nanostructures synthesized by mild solution chemistry route method (Kundu and Pradhan, 2014). A CuS nanoparticle shows a band gap of 2.021 eV, flower-like structure 3.13 eV, and nanoflask 3.211 eV (Kushwah et al., 2017). Copper sulfide synthesized using CuCl, $CuCl_2 \cdot 2H_2O$, and $CuSO_4 \cdot 7H_2O$ with fixed CH_4N_2S in molar ratio of 1:2 shows an optical band gap energy of 2.30, 2.10, and 2.05 eV, whereas a molar ratio of 1:1 shows an energy band gap of 2.25, 2.34, and 2.32 eV (Pejjai et al., 2020). Some of the CuS nanostructures have been summarized in Table 1 with their estimated optical band gap.

5 Applications

5.1 Photocatalytic degradation

Semiconductor photocatalysis technology is a method for the chemical conversion of solar energy. It received attention due to its application for water splitting and the elimination of chemical contamination (Anpo et al., 2005). Due to strong absorption in the visible region and stability under various conditions, cationic dyes like methylene blue

Table 1 Copper sulfide (CuS) nanostructures with their optical band.

Precursors		Time and temperature (°C)	Method	Nanostructures	Size (nm)	Band gap (eV)	References
Cu	**S**						
$Cu(NO_3)_2{\cdot}3H_2O$	$Na_2S_2O_3$	150°C, 24 h	Hydrothermal	Nanoflask	35 nm	1.95	Adhikari et al. (2017)
$Cu(NO_3)_2{\cdot}3H_2O$	C_2H_5NS			Nanoparticles		1.85	
$Cu(NO_3)_2{\cdot}3H_2O$	CH_4N_2S			Hierarchical spherical, flower-like	2 μm	2.16	
$CuCl_2.2H_2O$	CH_4N_2S	150°C, 5 and 24 h	Hydrothermal	Urchin-like	14–30 nm	2.21	Saranya and Grace, 2012
$CuCl_2.2H_2O$	$Na_2S_2O_3.5H_2O$			Plate-like	30–50 nm	2.18	
$Cu(NO_3)_2$	$Na_2S_2O_3$	150°C	Hydrothermal	Nanoparticles	40–100 nm	1.75	Kundu and Pradhan (2013)
$Na_2S_2O_3$	$Na_2S_2O_3$	180°C		Hexagonal nanoplates		1.68	
$CuCl_2$	$CS(NH_2)_2$	90 min, 140°C	Hydrothermal	Spherical nanoflower		1.61	Zhang et al. (2014)
$Cu(NO_3)_2$	$CS(NH_2)_2$			Doughnut-shaped nanosphere		1.93	
$CuSO_4$	$CS(NH_2)_2$			Dense nanosphere		2.01	
$CuCl_2$	$Na_2S_2O_3$			Atypical nanoflowers	1–2 μm	1.70	
$CuCl_2$	Na_2S			Mixture of nanoneedles, nanoparticles, nanoplates	100 nm	1.82	
$Cu\ (NO_3)_2{\cdot}3H_2O$	Thiourea	150°C for 24 h	Hydrothermal	Cylindrical-like structures	40–110 nm	2.08	Saranya et al. (2015)
$Cu\ (NO_3)_2{\cdot}3H_2O$	Sodium thiosulfate			Hexagonal platelets		2.08	

(MB), malachite green (MG), rhodamine B (RhB); neutral dyes like methyl red (MR); and anionic dyes such as methyl orange (MO) and eosin (E) can be used to examine their photodegradation by CuS. Various kinds of photocatalysts have been synthesized and used to convert solar energy into chemical energy to decompose materials into useful materials such as hydrocarbons (Inoue et al., 1979), as well as to remove pollutants and bacteria (Caballero et al., 2009). Various chalcogenides such as sulfides, nitrides, and oxynitrides have been investigated for visible-light or solar photocatalysis because of their interesting properties and many potential applications (Liu et al., 2010).

CuS is one of the most promising and important chalcogenide semiconductors that shows photocatalytic application. The photocatalytic performance of the hierarchical CuS structures with MB dye have been studied in the presence of hydrogen peroxide. UV–Vis spectra were applied to demonstrate photocatalytic degradation activity of MB; about 90% of the MB was degraded after 90 min (Li et al., 2010b). The catalytic activity of the synthesized CuS nanostructures was tested for MB degradation in the presence of H_2O_2 in the dark. The catalytic performance was found to be 94.5% (Kundu and Pradhan, 2014). CuS hierarchical structures were tested for their photocatalytic assessment toward 4-CP under visible light. The results showed that thiourea-assisted flower-like CuS architectures exhibited the highest degradation efficiency and depended on the surface area of the catalyst (Adhikari et al., 2017). Chemically dealloyed CuS photocatalyst was investigated for the photodegradation of azo dyes (Nie et al., 2013). Dye degradation was also performed by CuS nanofibers that were synthesized with the assistance of polyacrylonitrile (Xu et al., 2015). The photocatalytic efficiency of these copper chalcogenides depends on factors such as material design (morphology, size, and surface area), tuning optical absorption, and surface modification by doping or forming heterojunctions (Wei et al., 2013; Zhuang et al., 2012). CuS nanoparticles synthesized using solvothermal methods perform high catalytic activity for the photodegradation of MB under visible light irradiation. By adjusting the amount of H_2O_2 and catalyst, it shows a 97.88% degradation rate after 40 min reaction (Zhou et al., 2020).

The degradation rate of RhB was found to be 99.7% under visible light (Wang et al., 2013), and degradation rate was 99% in the presence of visible light and H_2O_2 within 45 min as a catalyst for 3D hierarchical CuS (Chai et al., 2020). Degradation of RhB under visible-light irradiation was also reported. CuS nanopowders consisting of a mixture of nanoneedles, nanoparticles, and nanoplates; atypical nanoflowers; and spherical nanoflowers show great degradation performances of 90% after 60 min. When doughnut-shaped nanospheres prepared from $Cu(NO_3)_2$ and $CS(NH_2)_2$ are used as the photocatalyst, the RhB degradation is 70% in 60 min. Dense CuS nanospheres prepared from $CuSO_4$ and $CS(NH_2)_2$ shows the lowest degradation rate as only 20% of the RhB is degraded (Zhang et al., 2014). CR dye is an acid-base indicator used for the application of photocatalytic degradation. CuS nanoflakes have a band gap 2.01 eV that shows 96% photodegradation of RhB in the presence of H_2O_2 in 5 min (Jiang et al., 2020). The percentage (%) degradation of the CR dye is found to be 94% and 78% of the CuS synthesized in a mixed solvent of water-cyclohexanol and water-butanol, respectively (Ramamoorthy and Rajendran, 2017).

CuS photocatalysts synthesized by the hydrothermal method revealed that catalytic process efficiency mainly depends upon the adsorption and electron transfer between the dye molecules, as the prepared CuS catalyst showed highly efficient and versatile photocatalytic activities, as well as excellent recyclability in degrading organic contaminant, i.e., nitrobenzene and 4-nitrophenol under visible light irradiation (Saranya et al., 2015).

5.2 Photothermal ablation therapy

Photothermal ablation (PTA) therapy has received much attention in the field of medicine for cancer treatment as an alternative for chemotherapy and surgery in recent years. Nanoparticles with different gold nanostructures like nanocages (Chen et al., 2007), nanoshells (Hirsch et al., 2003), and nanorods (Park et al., 2010) have been developed as a photothermal coupling agent to increase the efficacy of PTA therapy. All these plasmonic nanomaterials have strong absorption in the region of NIR ($\lambda = 700–1100$ nm) and converting optical energy into thermal energy, which enables the deposition. Various attractive nanomaterials with strong NIR absorption, such as carbon-based nanostructures (Yang et al., 2013a, b), organic dyes (Huang et al., 2014), semiconductor compounds (Wang et al., 2015), noble metal materials (Mieszawska et al., 2013), polymers (Xu et al., 2014), metal nanostructures, and copper chalcogenide semiconductors have been used for PTA therapy.

CuS has emerged as a promising photothermal coupling agent along with Au carbon nanotubes because of its advantage of low toxicity, low cost, and intrinsic NIR region absorption optical properties. The NIR absorption of CuS nanoparticles is derived from the d–d transition of Cu^{2+} ions, which gives the CuS nanoparticles the ability to resist changes in the surrounding environment and long-term light irradiation. Thus, CuS nanoparticles are increasingly employed in PTA.

Previously, thioglycolic acid-stabilized CuS NPs have been reported that demonstrated their application for photothermal destruction of tumor cells in vitro using an NIR laser beam centered at 808 nm (Li et al., 2010a). Chelator-free [^{64}Cu]CuS nanoparticles have been synthesized for PET imaging and photothermal coupling agents for PTA. These [^{64}Cu]CuS nanoparticles possess excellent stability and allow robust noninvasive micro-PET imaging. CuS nanoparticles show strong absorption in the NIR region peak at 930 nm; passive targeting prefers the tumor site, and mediated ablation of U87 tumor cells occurs upon exposure to NIR light both in vitro and in vivo after either intratumoral or intravenous injection. The combination of small diameter (~11 nm), strong NIR absorption, and integration of ^{64}Cu as a structural component makes these [^{64}Cu]CuS nanoparticles ideally suited for multifunctional molecular imaging and therapy (Zhou et al., 2010).

A hydrophilic copper sulfide-based photothermal nanoagent has been used for PTA therapy. Copper sulfide-based photothermal nanoagents were prepared by solvothermal route with the mixture of water/ethanol/PEG as the solvent for Cu/S precursor ratio of 1/1, exhibited smallest size of ~40 nm, and showed excellent hydrophilicity and the highest photoabsorption in the NIR region (Luo et al., 2015).

Albumin is widely selected as a biocompatible template for the synthesis of nanoparticles due to its abundant functional groups such as thiol, amine, and carboxyl groups. Albumin has been used as a viable drug carrier for administering chemotherapeutic drugs, so it is very attractive to develop albumin-directed CuS photothermal agents with excellent inherent biocompatibility. The synthesis of CuS nanoparticles was developed using BSA as the template, and the excellent biocompatibility and efficient photothermal therapy effects of BSA-CuS nanoparticles show great potential as an ideal photothermal agent for cancer treatment (Zhang et al., 2015).

Cysteine-coated CuS nanoparticles (Cys-CuS NPs) were synthesized as highly efficient PTT agents by a simple aqueous solution method. The Cys-CuS NPs have good biocompatibility owing to their biocompatible cysteine coating, exhibiting strong absorption in the NIR region due to the localized surface plasma resonances of valence-band free carriers. The photothermal conversion efficiency of Cys-CuS NPs reaches 38.0%, which is much higher than that of the recently reported Cu_9S_5 and $Cu_{2-x}Se$ nanocrystals. Tumor growth can be efficiently inhibited in vivo by the fatal heat arising from the excellent photothermal effect of Cys-CuS NPs at low concentration under irradiation of a 980 nm laser with a safe power density of 0.72 W cm^{-2}. Therefore, the Cys-CuS NPs have great potential as ideal photothermal agents for cancer therapy (Liu et al., 2014).

Photothermal theranostic agents have been developed with copper sulfide-ferritin nanocages (CuS − Fn NCs) by a biomimetic synthesis method for simultaneous PA/PET dual-modality imaging-guided photothermal therapy (Wang et al., 2016). Interaction of CuS nanoparticles with NIR light could generate heat, which could be harnessed for PTA of cancer cells (Li et al., 2010a). Surface plasmon-enhanced photothermal therapy for cancer treatment was investigated in vitro on PC-3 prostate cancer cells using Ag/CuS nanocomposites. The diameters of the Ag/CuS nanocomposites are in the range of 10–20 nm, and they have high absorbance in the NIR region. Ag/CuS nanocomposites can get into prostate cancer PC-3 cancer cells, which are mainly located in the cytoplasm. The treatment observations found that 5% of original Ag/CuS nanocomposites activated by a 980 nm laser at 0.6 W/cm2 can efficiently kill cancer cells. With the increase of the nanocomposite concentration or the laser output, more and more cells were killed. Compared with CuS nanoparticles, surface plasmon-enhanced Ag/CuS nanocomposites have higher efficiency for photothermal therapy (Wang et al., 2013).

5.3 Detection of H_2O_2

Hydrogen peroxide (H_2O_2) is a harmful chemical that is widely used in the field of chemical industries, pharmaceuticals, as well as food. High levels of H_2O_2 are closely associated with different types of diseases, such as cancer, and progressive neurodegenerative diseases, such as Parkinson's disease. However, appropriate detection of hydrogen peroxide is an important factor. Inorganic nanomaterials such as Ni, Fe, Cu, and their sulfides and oxides are used as biosensors and sensors due to their advantages (Zhang et al., 2017).

It was earlier reported CuS nanoparticles reduced GO-based electrochemical biosensor for the reliable detection of H_2O_2. CuS/RGO composites were synthesized as $CuCl_2$ and Na_2S aqueous solutions with PVP-protected GO (Bai and Jiang, 2013).

Copper sulfide-decorated Ca-montmorillonite (CuS-MMT) nanocomposites were synthesized using a simple and facile method. The CuS nanoparticles were formed and adsorbed on the Ca-montmorillonite surface without aggregation. The prepared CuS-MMT NPs were demonstrated to possess intrinsic peroxidase-like activity toward typical peroxidase substrates 3,3′,5,5′-tetramethylbenzidine (TMB) for H_2O_2. The CuS-MMT nanocomposites as peroxidase mimics could rapidly catalyze the oxidation of the substrate TMB in the presence of H_2O_2 (Zhang et al., 2017). Enzyme-based electrochemical biosensors have been obtained with good accuracy and sensitivity, and is applicable in the fields of medicine, chemical industries, etc. (Chen et al., 2008).

6 Conclusions

CuS chalcogenide semiconductor nanoparticles remain the center of research for their wide applications in the fields of chemical, biological, as well as medical applications. Various synthetic approaches have been successfully reviewed, and the role of various factors including synthesis methods and process parameters are critically analyzed. Nanoparticle size, shape, and morphology have been correlated with properties, and specifically, the role of various process parameters for controlling shape size and morphology are reviewed. Finally, some critical applications of chalcogenide nanoparticles of CuS are presented that demonstrate the rapid attention this important group of nanomaterials is gaining.

References

Adhikari, S., Sarkar, D., Madras, G., 2017. Hierarchical design of CuS architectures for visible light photocatalysis of 4-Chlorophenol. ACS Omega. 2, 4009–4021.

Agoro, M.A., Mbese, J.Z., Meyer, E.L., Onyenankeya, K., 2021. Electrochemical signature of CuS photosensitizers thermalized from alkyldithiocarbamato cu(II) molecular precursors for quantum dots sensitized solar cells. Mater. Lett. 285, 129191.

Anpo, M., Dohshi, S., Kitano, M., Hu, Y., Takeuchi, M., Matsuoka, M., 2005. The preparation and characterization of highly efficient titanium oxide-based photo functional materials. Annu. Rev. Mater. Res. 35, 1–27.

Auyoong, Y.L., Yap, P.L., Huang, X., Hamid, S., Abd, B., 2013. Optimization of reaction parameters in hydrothermal synthesis: a strategy towards the formation of CuS hexagonal plates. Chem. Cent. J. 7, 67.

Bai, J., Jiang, X., 2013. A facile one-pot synthesis of copper sulfide-decorated reduced graphene oxide composites for enhanced detecting of H_2O_2 in biological environments. Anal. Chem. 85, 8095–8101.

Balayeva, O.O., Azizov, A.A., Muradov, M.B., Eyvazova, G.M., Alosmanov, R.M., 2017. Influence of precursor type and concentration on the synthesis of copper sulfide nanoparticles. J. Ovonic Res. 13, 25–32.

Banerjee, N., Krupanidhi, S.B., 2010. Facile hydrothermal synthesis and observation of bubbled growth mechanism in nano-ribbons aggregated microspherical covellite blue-phosphor. Dalton Trans. 39, 9789–9793.

Basu, M., Sinha, A.K., Pradhan, M., Sarkar, S., Negishi, Y., Pal, T., 2010. Evolution of hierarchical hexagonal stacked plates of CuS from liquid−liquid interface and its photocatalytic application for oxidative degradation of different dyes under indoor lighting. Environ. Sci. Technol. 44, 6313–6318.

Boey, H.T., Tan, W.L., Abu Bakar, N.H., Abu, B.M., Ismail, J., 2007. Formation and morphology of colloidal chitosan-stabilized copper sulfides. J. Physiol. Sci. 18, 87–101.

Brelle, M.C., Torres-Martinez, C.L., McNulty, J.C., Mehra, R.K., Zhang, J.Z., 2000. Synthesis and characterization of Cu_xS nanoparticles. Nature of the infrared band and charge-carrier dynamics. Pure Appl. Chem. 72, 101–117.

Caballero, L., Whitehead, K.A., Allen, N.S., Verran, J., 2009. Inactivation of *Escherichia coli* on immobilized TiO2 using fluorescent light. J. Photochem. Photobiol. A Chem. 202, 92–98.

Chai, Z., Pan, X., Cui, F., Ma, Q., Zhang, J., Liu, M., Chen, Y., Li, L., Cui, T., 2020. Synthesis of 3D hierarchical CuS architectures consisting of 1D nanotubes for efficient photocatalysts. Mater. Lett. 275, 128168.

Chen, J.Y., Wang, D.L., Xi, J.F., Au, L., Siekkinen, A., Warsen, A., Li, Z.Y., Zhang, H., Xia, Y.N., Li, X.D., 2007. Immunogold nanocages with tailored optical properties for targeted photothermal destruction of cancer cells. Nano Lett. 7, 1318–1322.

Chen, X., Fu, C., Wang, Y., Yang, W., Evans, D.G., 2008. Direct electrochemistry and electrocatalysis based on a film of horseradish peroxides intercalated into Ni-Al layered double hydroxide nanosheets. Biosens. Bioelectron. 24, 356–361.

Chen, L.F., Yu, W., Li, Y., 2009. Synthesis and characterization of tubular CuS with flowerlike wall from a low-temperature hydrothermal route. Powder Technol. 191, 52–54.

Chu, L., Zhou, B., Mu, H., Sun, Y., Xu, P., 2008. Mild hydrothermal synthesis of hexagonal CuS nanoplates. J. Cryst. Growth 310, 5437–5440.

Durga, I.K., Rao, S.S., Reddy, A.E., Gopi, C.V.V.M., Kim, H.-J., 2018. Achieving copper sulfide leaf-like nanostructure electrode for high-performance supercapacitor and quantum-dot sensitized solar cells. Appl. Surf. Sci. 435, 666–675.

Fan, R., Wu, Y.Y., Li, D.Y., Yue, M., Majumdar, A., Yang, P.D., 2003. Fabrication of silica nanotube arrays from vertical silicon nanowire templates. J. Am. Chem. Soc. 125, 5254–5255.

Feng, C., Zhang, L., Yang, M., Song, X., Zhao, H., Jia, Z., Sun, K., Liu, G., 2015. One-pot synthesis of copper sulfide nanowires/reduced graphene oxide nanocomposites with excellent lithium-storage properties as anode materials for lithium-ion batteries. ACS Appl. Mater. Interfaces 7, 15726–15734.

Fu, Y., Li, Q., Liu, J., Jiao, Y., Hu, S., Wang, H., Xu, S., Jiang, B., 2020. In-situ chemical vapor deposition to fabricate cuprous oxide/copper sulfide core-shell flowers with boosted and stable wide-spectral region photocatalytic performance. J. Colloid Interface Sci. 570, 143–152.

Gautam, U.K., Mukherjee, B., 2006. A simple synthesis of CuS nanocrystals. Bull. Mater. Sci. 29, 1–5.

Gorai, S., Ganguli, D., Chaudhuri, S., 2005. Synthesis of copper sulfides of varying morphologies and stoichiometries controlled by chelating and nonchelating solvents in a solvothermal process. Cryst. Growth Des. 5, 875–877.

Hamed, M.S.G., Mola, G.T., 2019. Copper sulphide as a mechanism to improve energy harvesting in thin-film solar cells. J. Alloys Compd. 802, 252–258.

Hirsch, L.R., Stafford, R.J., Bankson, J.A., Sershen, S.R., Rivera, B., Price, R.E., Hazle, J.D., Halas, N.J., West, J.L., 2003. Nanoshell-mediated near-infrared thermal therapy of tumors under magnetic resonance guidance. Proc. Natl. Acad. Sci. U. S. A. 100, 13549–13554.

Hosseinpour, Z., Arefinia, Z., Hosseinpour, S., 2019. Morphology and phase control of hierarchical copper sulfide superstructures as efficient catalyst. Mater. Sci. Semicond. Process. 100, 48–55.

Hou, L., Shan, X., Hao, L., Feng, Q., Zhang, Z., 2017. Copper sulfide nanoparticle-based localized drug delivery system as an effective cancer synergistic treatment and theranostic platform. Acta Biomater. 54, 307–320.

Huang, P., Li, Z., Hu, H., Cui, D., 2010. Synthesis and characterization of bovine serum albumin-conjugated copper sulfide nanocomposites. J. Nanomater. 2010, 641545. 6 pp.

Huang, P., Rong, P., Jin, A., Yan, X., Zhang, M.G., Lin, J., Hu, H., Wang, Z., Yue, X., Li, W., Niu, G., Zeng, W., Wang, W., Zhou, K., Chen, X., 2014. Dye-loaded ferritin nanocages for multimodal imaging and photothermal therapy. Adv. Mater. 26, 6401–6408.

Husea, N.P., Divea, A.S., Gattub, K.P., Sharma, R., 2017. An experimental and theoretical study on soft chemically grown CuS thin film for photosensor application. Mater. Sci. Semicond. Process. 67, 62–68.

Inoue, T., Fujishima, A., Konishi, S., Honda, K., 1979. Photoelectrocatalytic reduction of carbon dioxide in aqueous suspensions of semiconductor powders. Nature 277, 637–638.

Iqbala, S., Shaid, N.A., Sajid, M.M., Javed, Y., Alam, M.F., Mahmood, A., Ahmad, G., Afzal, A.M., Hussain, S.Z., Ali, F., Sarwar, M., 2020. Extensive evaluation of changes in structural, chemical and thermal properties of copper sulfide nanoparticles at different calcinations temperature. J. Cryst. Growth 547, 125823.

Jiang, D., Hu, W., Wang, H., Shen, B., Deng, Y., 2011. A microemulsion-template-interfacial-reaction route to copper sulfide hollow spheres. J. Colloid Interface Sci. 357, 317–321.

Jiang, J., Jiang, Q., Deng, R., Xie, X., Meng, J., 2020. Controllable preparation, formation mechanism and photocatalytic performance of copper base sulfide nanoparticles. Mater. Chem. Phys. 254, 123504.

Jiao, S., Xu, L., Jiang, K., Xu, D., 2006. Well-defined non-spherical copper sulfide mesocages with single-c shells by shape-controlled Cu_2O crystal templating. Adv. Mater. 18, 1174–1177.

Jin, K., Zhou, M., Zhao, H., Zhai, S., Ge, F., Zhao, Y., Cai, Z., 2019. Electrodeposited CuS nanosheets on carbonized cotton fabric as flexible supercapacitor electrode for high energy storage. Electrochim. Acta 295, 668–676.

Karak, N., 2019. Fundamentals of nanomaterials and polymer nanocomposites. Nanomater. Polymer Nanocomp., 1–45.

Kerner, R., Palchik, O., Gedanken, A., 2001. Sonochemical and microwave-assisted preparations of PbTe and PbSe. A comparative study. Chem. Mater. 13, 1413–1419.

Kristl, M., Hojnik, N., Gyergyek, S., Drofenik, M., 2013. Sonochemical preparation of copper sulfides with different phases in aqueous solutions. Mater. Res. Bull. 48, 1184–1188.

Ku, G., Zhou, M., Song, S., Huang, Q., Hazle, J., Li, C., 2012. Copper sulfide nanoparticles as a new class of photoacoustic contrast agent for deep tissue imaging at 1064 nm. ACS Nano 6, 7489–7496.

Kumar, P., Gusain, M., Nagarajan, R., 2011. Synthesis of $Cu_{1.8}S$ and CuS from copper-Thiourea containing precursors; anionic (cl-, NO_3-, SO_4^{2-}) influence on the product stoichiometry. Inorg. Chem. 50, 3065–3070.

Kumar, R.V., Palchik, O., Koltypin, Yu., Diamant, Y., Gedanken, A., 2002. Sonochemical synthesis and characterization of Ag_2S/PVA and CuS /PVA nanocomposite. Ultrason. Sonochem. 9, 65–70.

Kundu, J., Pradhan, D., 2013. Influence of precursor concentration, surfactant and temperature on the hydrothermal synthesis of CuS: structural, thermal and optical properties. New J. Chem. 47, 1470–1478.

Kundu, J., Pradhan, D., 2014. Controlled synthesis and catalytic activity of copper sulfide nanostructured assemblies with different morphologies. ACS Appl. Mater. Interfaces 6, 1823–1834.

Kushwah, R., Singh, A., Anshul, A., 2017. Facile and controlled synthesis of copper sulfide nanostructures of varying morphology. J. Mater. Sci. Mater. Electron. 28, 5597–5602.

Li, Y., Nguyen, T.V., 2018. Core-shell rhodium sulfide catalyst for hydrogen evolution reaction/hydrogen oxidation reaction in hydrogen-bromine reversible fuel cell. J. Power Sources 382, 152–159.

Li, B.X., Xie, Y., Xue, Y., 2007. Controllable synthesis of CuS nanostructures from self-assembled precursors with biomolecule assistance. J. Phys. Chem. C 111, 12181–12187.

Li, F., Kong, T., Bi, W.T., Li, D.C., Li, Z., Huang, X.T., 2009. Synthesis and optical properties of CuS nanoplate-based architectures by a solvothermal method. Appl. Surf. Sci. 255, 6285–6289.

Li, Y., Lu, W., Huang, Q., Huang, M., Li, C., Chen, W., 2010a. Copper sulfide nanoparticles for photothermal ablation of tumor cells. Nanomedicine 5, 1161–1171.

Li, F., Wu, J., Qin, Q., Li, Z., Huang, X., 2010b. Controllable synthesis, optical and photocatalytic properties of CuS nanomaterials with hierarchical structures. Powder Technol. 198, 267–274.

Li, H., Wang, Y., Jiang, J., Zhang, Y., Peng, Y., Zhao, J., 2017. CuS microspheres as high-performance anode material for Na-ion batteries. Electrochim. Acta 247, 851–859.

Liang, W., Whangbo, M.H., 1993. Conductivity anisotropy and structural phase transition in Covellite CuS. Solid State Commun. 85, 405–408.

Liao, X.H., Zhu, J.J., Chen, H.Y., 2001. Microwave synthesis of nanocrystalline metal sulfides in formaldehyde solution. Mater. Sci. Eng. B 85, 85–89.

Liao, X.H., Chen, N.Y., Xu, S., Yang, S.B., Zhu, J.J., 2003. A microwave-assisted heating method for the preparation of copper sulfide nanorods. J. Cryst. Growth 252, 593–598.

Liu, Y., Kanhere, P.D., Wong, C.L., Tian, Y., Feng, Y., Boey, F., Wu, T., Chen, H., White, T.J., Chen, Z., Zhang, Q., 2010. Hydrazine hydrothermal method to synthesize three-dimensional chalcogenide framework for photocatalytic hydrogen generation. J. Solid State Chem. 183, 2644–2649.

Liu, X., Li, B., Fu, F., Xu, K., Zou, R., Wang, Q., Zhang, B., Chena, Z., Hu, J., 2014. Facile synthesis of biocompatible cysteine-coated CuS nanoparticles with high photothermal conversion efficiency for cancer therapy. Dalton Trans. 43, 11709–11715.

Liu, Y., Zhou, Z., Zhang, S., Luo, W., Zhang, G., 2018. Controllable synthesis of CuS hollow microflowers hierarchical structures for asymmetric supercapacitors. Appl. Surf. Sci. 442, 711–719.

Luo, J., Yu, N., Xiao, Z., Long, C., Macharia, D.K., Xu, W., Zhang, L., Zhu, M., Chen, Z., 2015. Simultaneous control of morphology, phase and optical absorption of hydrophilic copper sulfide-based photothermal nanoagents through cu/S precursor ratios. J. Alloys Compd. 648, 98–103.

Metcalf, H.C., Williams, J.E., Caskta, J.F., 1982. Modern Chemistry. 54 Holt Rinehart, and Winston, New York.

Mieszawska, A.J., Mulder, W.J.M., Fayad, Z.A., Cormode, D.P., 2013. Multifunctional gold nanoparticles for diagnosis and therapy of disease. Mol. Pharm. 10, 831–847.

Mu, C.F., Yao, Q.Z., Qu, X.F., Zhou, G.T., Li, M.L., Fu, S.Q., 2010. Controlled synthesis of various hierarchical nanostructures of copper sulfide by a facile microwave irradiation method. Colloid Surf. A 371, 14–21.

Nafees, M., Ali, S., Rasheed, K., Idrees, S., 2012. The novel and economical way to synthesize CuS nanomaterials of different morphologies by aqueous medium employing microwaves irradiation. Appl. Nanosci. 2, 157–162.
Nafees, M., Ali, S., Idrees, S., Rashid, K., Shafique, M.A., 2013. A simple microwave assists aqueous route to synthesis CuS nanoparticles and further aggregation to spherical shape. Appl. Nanosci. 3, 119–124.
Nair, P.K., Garcia, V.M., Fernandez, A.M., Ruiz, H.S., Nair, M.T.S., 1991. Optimization of chemically deposited Cu*x*S solar control coatings. J. Phys. D 24, 441–449.
Nan, Z., Wang, X.Y., Zhao, Z., 2006. Formation of various morphologies of copper sulfides by a solvothermal method. J. Cryst. Growth 295, 92–96.
Nath, S.K., Kalita, P.K., 2017. Effect of capping agents on the optical properties of synthesized CuS nanostructures. Mater Today Proc. 4, 3972–3978.
Nath, S.Kr., Kalita, P.K., 2021. Temperature dependent structural, optical and electrical properties of CuS nanorods in aloe vera matrix. Nano-Struct. Nano-Objects 25, 100651.
Nelwamondo, S.M.M., Moloto, M.J., Krause, R.W.M., Moloto, N., 2012. Synthesis and characterization of alanine-capped water-soluble copper sulphide quantum dots. Mater. Lett. 75, 161–164.
Nie, G., Li, Z., Lu, X., Lei, J., Zhang, C., Wang, C., 2013. Fabrication of polyacrylonitrile/CuS composite nanofibers and their recycled application in catalysis for dye degradation. Appl. Surf. Sci. 284, 595–600.
Ou, S., Xie, Q., Ma, D., Liang, J., Hu, X., Yu, W., Qian, Y., 2005. A precursor decomposition route to polycrystalline CuS nanorods. Mater. Chem. Phys. 94, 460–466.
Pagan, M., Suazo, D., Toro, N.D., Griebenow, K., 2015. Comparative study of different protein immobilization methods for the construction of an efficient nano-structured lactate oxidase-SWCNT-biosensor. Biosens. Bioelectron. 64, 138–146.
Palanisamy, S., Velmurugan, S., Yang, T.C.K., 2020. One-pot sonochemical synthesis of CuS nanoplates decorated partially reduced graphene oxide for biosensing of dopamine neurotransmitter. Ultrason. Sonochem. 66, 105043.
Park, J.H., Maltzahn, G.V., Xu, M.J., Fogal, V., Kotamraju, V.R., Ruoslahti, E., Bhatia, S.N., Sailor, M.J., 2010. Cooperative nanomaterials system to sensitize, target, and treat tumors. Proc. Natl. Acad. Sci. U. S. A. 107, 981–986.
Pejjai, B., Reddivari, M., Kotte, T.R.R., 2020. Phase controllable synthesis of CuS nanoparticles by chemical co-precipitation method: effect of copper precursors on the properties of CuS. Mater. Chem. Phys. 239, 122030.
Phuruangrat, A., Thoonchalong, P., Thongtem, S., Thongtem, T., 2012. Synthesis of CuS with different morphologies by refluxing method: nanopaticles in clusters and nanoflakes in sponge-like clusters. Chalcogenide Lett. 9, 421–426.
Phuruangrat, A., Thongtem, S., Thongtem, T., 2013. Microwave hydrothermal synthesis and characterization of copper sulfide with different morphologies. Chalcogenide Lett. 10, 359–365.
Prasanth, S., Ra, D.R., Vineesh Kumar, T.V., Thomas, R.K., Sudarsana Kumar, C., 2016. Exploring the interaction of L-cysteine capped CuS nanoparticles with bovine serum albumin (BSA): a spectroscopic study. RSC Adv. 6, 58288–58295.
Premala, E.V.A., Kannangara, Y.Y., Ratnayake, S.P., de Silva, K.M.N., 2017. Facile synthesis of colored and conducting CuS CN composite coated with CuS nanoparticles. Nanoscale Res. Lett. 507, 1–7.
Qiang, G., Xiaomei, W., Tao, H., 2021. Novel energy efficient window coating based on in doped CuS nanocrystal with enhanced NIR shielding performance. Sol. Energy 220, 1–7.
Qiao, Z.P., Xie, Y., Xu, J.G., Zhu, Y.J., Qian, Y.T., 1999. γ- radiation synthesis of the nanocrystalline semiconductors PbS and CuS. J. Colloid Interface Sci. 214, 459–461.

Qin, A.-M., Fang, Y.-P., Ou, H.D., Liu, H.-Q., Su, C.-Y., 2005. Formation of various morphologies of covellite copper sulfide submicron crystals by a hydrothermal method without surfactant. Cryst. Growth Des. 5, 855–860.

Raj, S.I., Jaiswal, A., 2021. Nanoscale transformation in CuS Fenton-like catalyst for highly selective and enhanced dye degradation. J. Photochem. Photobiol. A Chem. 410, 113158.

Ramalingam, G., Vignesh, R., Ragupathi, C., Magdalane, C.M., Kaviyarasud, K., Kennedy, J., 2020. Electrical and chemical stability of CuS nanofluids for conductivity of water soluble based nanocomposites. Surf. Interfaces 19, 100475.

Ramamoorthy, C., Rajendran, V., 2017. Synthesis and characterization of CuS nanostructures: structural, optical, electrochemical and photocatalytic activity by the hydro/ solvothermal process. Int. J. Hydrogen Energy 42, 26454–26463.

Roy, P., Srivastava, S.K., 2006. Hydrothermal growth of CuS nanowires from Cu-dithiooxamide, a novel single-source precursor. Cryst. Growth Des. 6, 1921–1926.

Sagade, A.A., Sharma, R., 2008. Copper sulphide (Cu_xS) as an ammonia gas sensor working at room temperature. Sens. Actuators B 133, 135–143.

Saranya, M., Grace, A.N., 2012. Hydrothermal synthesis of CuS nanostructures with different morphology. J. Nano Res. 18, 43–51.

Saranya, M., Santhosh, C., Augustine, S.P., Grace, A.N., 2014. Synthesis and characterisation of CuS nanomaterials using hydrothermal route. J. Exp. Nanosci. 9, 329–336.

Saranya, M., Santhosh, C., Ramachandran, R., Grace, A.N., 2013. Growth of CuS nanostructures by hydrothermal route and its optical properties. J. Nanotechnol 2014, 321571. 8 pages.

Saranya, M., Ramachandran, R., Samuel, E.J.J., Jeong, S.K., Grace, A.N., 2015. Enhanced visible light photocatalytic reduction of organic pollutant and electrochemical properties of CuS catalyst. Powder Technol. 279, 209–220.

Schneider, N., Lincot, D., Donsant, F., 2016. Atomic layer deposition of copper sulfide thin film. Thin Solid Films 600, 103–108.

Senthil Kumar, M., Babu, S.M., 2015. Synthesis and characterization of hexagonal faceted copper sulfide ($Cu_{1.8}S$) nanodisks. Mater. Sci. Semicond. Process. 40, 203–208.

Sharma, V., Jeevanandam, P., 2020. Synthesis of copper sulfide nanoparticles by thermal decomposition approach and morphology dependent peroxidase-like activity. J. Nanosci. Nanotechnol. 20, 2763–2780.

Shen, G., Chen, D., Tang, K., Liu, X., Huang, L., Qian, Y., 2003. General synthesis of metal sulfides nanocrystallines via a simple polyol route. J. Solid State Chem. 173, 232–235.

Shen, X.P., Zhao, H., Shu, H.Q., Zhou, H., Yuan, A.H., 2009. Self-assembly of CuS nanoflakes into flower-like microspheres: synthesis and characterization. J. Phys. Chem. Solid 70, 422–427.

Simonescu, C.M., Patron, L., Teodorescu, V.S., Brezeanu, M., Capatina, C., 2006. A facile chemical route to copper sulfide CuS nanocrystallites -pH effect of the morphology and the shape of them. J. Optoelectron. Adv. Mater. 8, 597–600.

Simonescu, C.M., Teodorescu, V.S., Capapina, C., 2008. Surfactant involved in copper sulfide Nanocrystallites synthesis. Rev. Chim. 59, 1327–1329.

Sukamoto, T., Sunamura, H., Kawaura, H., Hasegawa, T., Nakayama, T., Aono, M., 2003. Nanometer-scale switches using copper sulfide. Appl. Phys. Lett. 82, 3032–3034.

Tan, C.H., Lu, R., Xue, P.C., Bao, C.Y., Zhao, Y.Y., 2008. Synthesis of CuS nanoribbons templated by hydrogel. Mater. Chem. Phys. 112, 500–503.

Thongtem, T., Phuruangrat, A., Thongtem, S., 2007. Synthesis and analysis of CuS with different morphologies using cyclic microwave irradiation. J. Mater. Sci. 42, 9316–9323.

Thongtem, T., Phuruangrat, A., Thongtem, S., 2009. Formation of CuS with flower-like, hollow spherical, and tubular structures using the solvothermal-microwave process. Curr. Appl. Phys. 9, 195–200.
Tu, W., Liu, H., 2000. Continuous synthesis of colloidal metal nanoclusters by microwave irradiation. Chem. Mater. 12, 564–567.
Wada, Y., Kuramoto, H., Anand, J., Kitamura, T., Sakata, T., Mori, H., Yanagida, S., 2001. Microwave-assisted size control of CdS nanocrystallites. J. Mater. Chem. 11, 1936–1940.
Wang, H., Zhang, J.R., Zhao, X.N., Xu, S., Zhu, J.J., 2002. Preparation of copper monosulfide and nickel monosulfide nanoparticles by sonochemical method. Mater. Lett. 55, 253–258.
Wang, X., Xu, C., Zhang, Z., 2006. Synthesis of CuS nanorods by one-step reaction. Mater. Lett. 60, 345–348.
Wang, Z.H., Geng, D.Y., Zhang, Y.J., Zhang, Z.D., 2010. CuS:Ni flowerlike morphologies synthesized by the solvothermal route. Mater. Chem. Phys. 122, 241–245.
Wang, M., Xie, F., Li, W., Chen, M., Zhao, Y., 2013. Preparation of various kinds of copper sulfides in a facile way and the enhanced catalytic activity by visible light. J. Mater. Chem. A 1, 8616–8621.
Wang, S., Li, K., Chen, Y., Chen, H., Ma, M., Feng, J., Zhao, Q., Shi, J., 2015. Biocompatible PEGylated MoS_2 nanosheets: Controllable bottom up synthesis and highly efficient photothermal regression of tumor. Biomaterials 39, 206–217.
Wang, Z., Huang, P., Jacobson, O., Wang, Z., Liu, Y., Lin, L., Lin, J., Lu, N., Zhang, H., Tian, R., Niu, G., Liu, G., Chen, X., 2016. Biomineralization-inspired synthesis of copper sulfide-ferritin nanocages as cancer theranostics. ACS Nano 10, 3453–3460.
Wei, T., Liu, Y., Dong, W., Zhang, Y., Huang, C., Sun, Y., Chen, X., Dai, N., 2013. Surface-dependent localized surface plasmon resonances in CuS nanodisks. ACS Appl. Mater. Interfaces 5 (10), 473–10,477.
Wu, Y., Wadia, C., Ma, W., Sadtler, B., Alivisatos, A.P., 2008. Synthesis and photovoltaic application of copper (I) sulfide nanocrystals. Nano Lett. 8, 2551–2555.
Wu, D., Wang, Y., Zhang, C., Zhu, H., 2012. 3D Flowerlike copper sulfide nanostructures synthesized from copper (I) oxide hollow microspheres. Trans. Mat. Res. Soc. Japan 37, 119–122.
Xu, J.Z., Xu, S., Geng, J., Li, G.X., Zhu, J.J., 2006. The fabrication of hollow spherical copper sulfide nanoparticle assemblies with 2 hydroxypropyl-β-cyclodextrin as a template under sonication. Ultrason. Sonochem. 13, 451–454.
Xu, L., Cheng, L., Wang, C., Peng, R., Liu, Z., 2014. Conjugated polymers for photothermal therapy of cancer. Polym. Chem. 5, 1573–1580.
Xu, W., Zhu, S., Liang, Y., Li, Z., Cui, Z., Yang, X., Inoue, A., 2015. Nanoporous CuS with excellent photocatalytic property. Sci. Rep. 5, 18,125.
Yadav, S., Bajpai, P.K., 2017. Synthesis of copper sulfide nanoparticles: pH dependent phase stabilization. Nano-Struct. Nano-Obj. 10, 151–158.
Yadav, S., Bajpai, P.K., 2018. Effect of substrate on CuS/PVA nanocomposite thin films deposited on glass and silicon substrate. Soft Nanosci. Lett. 8, 9–19.
Yadav, S., Shrivas, K., Bajpai, P.K., 2019. Role of precursors in controlling the size, shape and morphology in the synthesis of copper sulfide nanoparticles and their application for fluorescence detection. J. Alloys Compd. 772, 579–592.
Yan, H., Wang, W., Xu, H., 2008. A micro-interface route to CuS superstructure composed of intersectional nanoplates. J. Cryst. Growth 310, 2640–2643.
Yang, S., Zavalij, P.Y., Whittingham, M.S., 2001. Hydrothermal synthesis of lithium iron phosphate cathodes. Electrochem. Commun. 3, 505–508.

Yang, C., Ma, L., Zou, X., Xiang, G., Chen, W., 2013a. Surface plasmon-enhanced Ag/CuS nanocomposites for cancer treatment Cancer. Nano 4, 81–89.
Yang, K., Feng, L.Z., Shi, X.Z., Liu, Z., 2013b. Nano-graphene in biomedicine: theranostic applications. Chem. Soc. Rev. 42, 530–547.
Yang, Z., Zhang, S., Zheng, X., Fu, Y., Zheng, J., 2018. Controllable synthesis of copper sulfide for nonenzymatic hydrazine Sensing. Sens. Actuators B 255, 2643–2651.
Yao, Z.Y., Zhu, X., Wu, C.Z., Zhang, X.J., Xie, Y., 2007. Fabrication of micrometre-scaled hierarchical tubular structures of CuS assembled by nanoflake-built microspheres using an in situ formed Cu(I) complex as a self-sacrificed template. Cryst. Growth Des. 7, 1256–1261.
Yue, X., Hu, R., Zhu, D., Qi, J., He, Y., Meng, Q., Wei, F., Ren, Y., Sui, Y., 2021. Controlled synthesis and formation mechanism of flower-like CuS/NiS microspheres for supercapacitors. Surf. Interfaces 22, 100,871.
Zeinodin, R., Jamali-Sheini, F., Cheraghizade, M., 2021. Physical properties of Pb-doped CuS nanostructures for optoelectronic applications. Mater. Sci. Semicond. Process. 123, 105501.
Zhang, Y., Qiao, Z.P., Chen, X.M., 2002. Microwave-assisted elemental-direct-reaction route to nanocrystalline copper sulfides Cu_9S_8 and Cu_7S_4. J. Solid State Chem. 167, 249–253.
Zhang, Y.C., Qiao, T., Hu, X.Y., 2004. A simple hydrothermal route to nanocrystalline CuS. J. Cryst. Growth 268, 64–70.
Zhang, H.T., Wu, G., Chen, X.H., 2006. Controlled synthesis and characterization of covellite (CuS) nanoflakes. Mater. Chem. Phys. 98, 298–303.
Zhang, X.J., Wang, G.F., Gu, A.X., Wei, Y., Fang, B., 2008. CuS nanotubes for ultrasensitive nonenzymatic glucose sensors. Chem. Commun. 45, 5945–5947.
Zhang, C., Fu, Y.Y., Zhang, X., Yu, C., Zhao, Y., Sun, S.K., 2015. BSA-directed synthesis of CuS nanoparticles as a biocompatible photothermal agent for tumorablation in vivo. Dalton Trans. 44, 13,112.
Zhang, L., Chen, M., Jiang, Y., Chen, M., Ding, Y., Liu, Q., 2017. A facile preparation of montmorillonite-supported copper sulfide nanocomposites and their application in the detection of H_2O_2. Sens. Actuators B 239, 28–35.
Zhang, Y., Li, Y., Wang, Y., Guo, R., Liu, W., Pei, H., Yin, G., Ye, D., Yu, S., Xie, J., 2019. A flexible copper sulfide @ multi-walled carbon nanotubes cathode for advanced magnesium-lithium-ion batteries. J. Colloid Interface Sci. 553, 239–246.
Zhou, M., Zhang, R., Huang, M., Lu, W., Song, S., Melancon, M.P., Tian, M., Liang, D., Li, C., 2010. A Chelator-free multifunctional [64Cu] CuS nanoparticle platform for simultaneous micro-PET/CT imaging and photothermal ablation therapy. J. Am. Chem. Soc. 132, 15,351–15,358.
Zhang, J., Zhang, Z., 2008. Hydrothermal synthesis and optical properties of CuS nanoplates. Mater. Lett. 62, 2279–2281.
Zhou, S.L., Gong, L.G., Zhao, X.Y., Liang, Q.L., Zhang, W.J., Wang, L.Y., Yu, K., Zhou, B.B., 2020. Synthesis and photocatalytic performance of copper sulfide by a simple solvothermal method. Chem. Phys. Lett. 759, 138,034.
Zhu, L., Xie, Y., Zheng, X., Liu, X., Zhou, G., 2004. Fabrication of novel urchin-like architecture and snowflake-like pattern CuS. J. Cryst. Growth 260, 494–499.
Zhu, Y., Guo, X., Jin, J., Shen, Y., Guo, X., Ding, W., 2007. Controllable synthesis of CuS nanotubes and nanobeltsusing lyotropic liquid crystal templates. J. Mater. Sci. 42, 1042–1045.
Zhuang, T.T., Fan, F.J., Gong, M., Yu, S.H., 2012. $Cu_{1.94}S$ nanocrystal seed-mediated solution-phase growth of unique Cu_2S−PbS heteronano structures. Chem. Commun. 48, 9762–9764.
Zhang, Y.Q., Zhang, B.P., Ge, Z.H., Zhu, L.F., Li, Y., 2014. Preparation by solvothermal synthesis, growth mechanism, and photocatalytic performance of CuS nanopowders. Eur. J. Inorg. Chem. 2014, 2368–2375.

PART

Plant protection

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CHAPTER

Copper-based nanopesticides 6

Aruna Jyothi Kora[a,b]

[a]*National Centre for Compositional Characterisation of Materials (NCCCM), Bhabha Atomic Research Centre (BARC), ECIL PO, Hyderabad, India,*

[b]*Homi Bhabha National Institute (HBNI), Mumbai, India*

1 Introduction

The pesticide is a chemical or biological agent which can deter, incapacitate, kill, or inhibit the pests such as insects, plant pathogens, weeds, algae, nematodes, mollusks, fishes, birds, rodents, mammals and microbes (bacteria, fungi, virus), etc.; which involve in production, processing, storage, transport, and marketing of agricultural and food commodities; wood products, animal feedstuffs, etc. The definition includes algicides, microbicides, bactericides, fungicides, viricides, slimicides, herbicides, nematicides, insecticides, insect growth regulators, termiticides, miticides, acaricides, molluscicides, piscicides, avicides, rodenticides, animal repellants, plant growth regulators, defoliants, desiccants, etc. The use of pesticides provides benefits such as improved crop yield and quality by controlling pests, plant disease vectors, and invasive species. Also, they are useful in controlling livestock and human disease vectors (Wikipedia, 2020; USEPA, 2020; Lade, 2019). In India, the import, manufacture, sale, transport, distribution, and use of insecticides is regulated by Central Insecticides Board and Registration Committee (CIBRC), Directorate of Plant Protection, Quarantine, and Storage, Ministry of Agriculture and Farmers Welfare, Government of India under Insecticides Act, 1968 and Insecticide rules, 1971. The CIBRC advises the central and state governments on technical issues of the act administration, classifies, and specifies the uses of insecticides based on toxicity and mode of application; establishes minimum intervals between the applications and harvesting; regulates the tolerance limits of insecticide residues and shelf life of insecticides (Directorate of Plant Protection, 2020).

Various compounds and complexes of copper are in use for centuries by humans for various purposes including algicide, fungicide, microbicide, antifoulant, and water purifier due to their biocidal action (Padil and Černík, 2013). While in agriculture, the copper-based inorganic compounds are widely exploited in agriculture as herbicides, algicides, fungicides, and pesticides. Copper-based macroformulations such as Bordeaux and Burgundy mixtures; cupric sulfate, cupric carbonate, copper

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oxychloride, cuprous oxide, copper-zinc chromate, copper hydroxide, organocopper, etc. are extensively used as fungicides. The Bordeaux and Burgundy mixtures were extensively used for controlling downy mildew in gardens, nurseries, vineyards, and farms. However, large dosages of these agrochemicals are needed for the effective control of phytopathogenic fungi due to their poor water solubility and resistance development. Further, the efficacy of copper compounds is enhanced by decreasing the particle size to nanodimension, leading to the higher surface for better biocidal action (Giannousi et al., 2013; Ponmurugan et al., 2016; Sidhu et al., 2017; Kanhed et al., 2014; Rai et al., 2018). The important copper-based nanostructures are copper (Cu), cupric oxide (CuO), cuprous oxide (Cu_2O), copper hydroxide $Cu(OH)_2$, and copper sulfide (CuS) nanoparticles (NPs). They gained commercial importance due to their low cost than the antimicrobial silver nanoparticles (Ag NPs), ease of synthesis, tunable size and morphologies, and multifaceted applications (Awwad and Albiss, 2015).

The current review briefly discusses the synthesis of copper-based nanomaterials and their general applications. Further, the plant protection applications of copper-based nanomaterials in agriculture fields as a bactericide, fungicide, insecticide, and nematicide are discussed in-depth, along with mechanisms involved in the biocidal action of copper-based nanomaterials.

2 Synthesis of copper-based nanomaterials

Many green biosynthetic methods using leaf extracts, flower extracts, plant gums, seaweeds, bacteria, fungi, etc. are developed for the production of copper and copper oxide nanoparticles due to their renewable, biodegradable, and nontoxic nature (Praburaman et al., 2016; Kora, 2018; Khanehzaei et al., 2014; Priyadarshini et al., 2021; Veisi et al., 2021; Paiva-Santos et al., 2021; Bukhari et al., 2021; Mondal et al., 2021). The bovine serum albumin capped copper nanoparticles (Cu NPs) were synthesized by chemical reduction with hydrazine at 50°C for 3 h (Rastogi and Arunachalam, 2013). The formation of Cu NPs is indicated from the characteristic UV-visible absorption peak at 572 nm and brick-red coloration of the synthesized copper colloidal solution (Fig. 1A). The protein capped Cu NPs showed an average particle size of 28 nm, indicated from transmission electron microscopy (TEM) image (Fig. 2A). The Cu NPs of 30–50 nm were biosynthesized using actinomycetes such as *Streptomyces griseus* (Ponmurugan et al., 2016). While, copper hydroxide ($Cu(OH)_2$) nanowires with a mean diameter of 10 nm and length of 500 nm were synthesized using *Pistachio* leaf extract (Awwad and Albiss, 2015). The gum olibanum capped copper oxide nanoparticles (CuO NPs) were produced by hydrothermal method and the CuO NPs exhibit UV-visible absorption peak at 265 nm and black coloration (Fig. 1B).

The size of the NPs ranged from 6 to 15 nm, evident from TEM picture (Fig. 2B). The CuO NPs of 60–100 nm size were prepared with aqueous spinach leaf extract (Ibrahim et al., 2018). The cuprous oxide (Cu_2O) and cupric oxide (CuO)

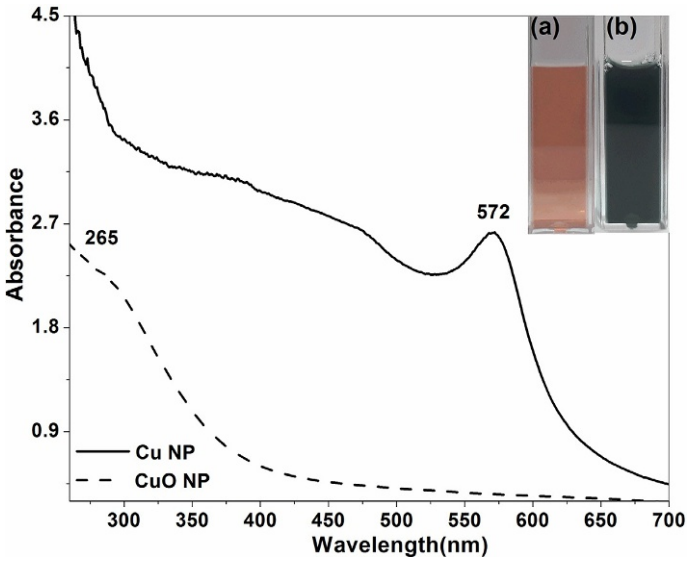

FIG. 1

The UV-visible absorption spectra of (A) bovine serum albumin capped Cu NPs and (B) gum olibanum capped CuO NPs. Inset: Corresponding coloration of (A) Cu NPs and (B) CuO NPs solutions.

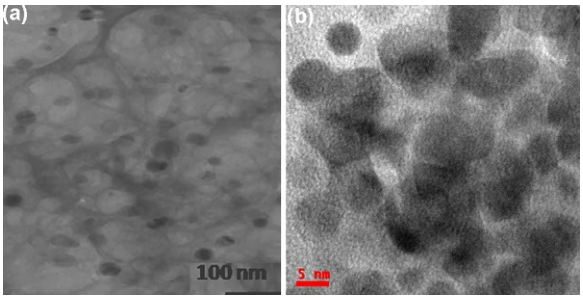

FIG. 2

The TEM images of (A) bovine serum albumin capped Cu NPs and (B) gum olibanum capped CuO NPs.

nanoparticles produced by the aqueous sol-gel process showed an average size of 31 and 32 nm, respectively (Topnani et al., 2009). The CuO NPs of 20 nm were green synthesized by leaf extract of *Aloe barbadensis* (Gunalan et al., 2012). The CuO NPs of 4.8, 5.5, and 7.8 sizes were prepared with gum karaya by colloid-thermal synthesis process at 1, 2, and 3 mM concentration of copper chloride, respectively (Padil and Černík, 2013).

3 Applications of copper-based nanomaterials

The US Environmental Protection Agency (EPA) has approved elemental copper and copper-based compounds as antimicrobials. Hence, Cu NPs and CuO NPs and nanocomposites are commercially utilized in antimicrobial paints, textiles, fabrics, medicine, agriculture, water purification (Meghana et al., 2015; Rai et al., 2018; Ighalo et al., 2021; Waris et al., 2021; Nasrollahzadeh et al., 2021; Attia et al., 2021), food packaging, etc. (Arfat et al., 2017). The compound copper oxide (CuO) is a transition metal oxide with a narrow bandgap, p-type semiconductor with monoclinic crystal structure; and employed in high-temperature superconductors, solar energy converters, field emission emitters, batteries, catalysts, gas sensors, giant magnetoresistance materials, precursors for organic-inorganic nanostructure composites, antimicrobials, antifoulants, anticancer chemotherapeutics, etc. Most importantly, they are active against pro and eukaryotes due to their ability to cross biological barriers and reach target organs (Sankar et al., 2014; Padil and Černík, 2013; Gunalan et al., 2012; Wang et al., 2021). For example, the antimicrobial, UV protecting, and self-cleaning polyester fabric was fabricated with CuO NPs of 27.5 nm size employing ash of *Seidlitzia rosmarinus* leaves and stems (Rezaie et al., 2017). The $Cu(OH)_2$ nanoparticles are utilized in the fabrication of rayon, mold inhibiting paints, ceramic colorants, a precursor for copper oxides, and as a broad-spectrum foliar fungicide (Awwad and Albiss, 2015). The properties and applications of copper-based nanomaterials toward flora and fauna are dependent on different intrinsic factors such as particle size, morphology, chemical form, oxidation state, concentration, copper ion dissolution in various media and extrinsic environmental conditions (Meghana et al., 2015; Giannousi et al., 2013).

The role of nanotechnology is vital in agriculture for secured food production in terms of plant protection for the control and management of various pests, weeds, and plant diseases caused by an array of bacterial, fungal, and viral plant pathogens. The current review is based on the applications of copper-based nanomaterials as bactericide, fungicide, insecticide, and nematicide and their biocidal mechanism is briefly discussed. The accumulation and translocation of copper-based nanopesticides in various plant parts such as roots, stems, leaves, and fruits depend upon various factors such as plant species, type, and dosage of nanopesticide; mode of application (soil, foliar), growth media (soil, hydroponics), etc. (Keller et al., 2017). The success of copper-based nanopesticides depends on its higher activity at the lower copper dosage and higher solubility and bioavailability than the conventional copper pesticides (Giannousi et al., 2013). The ease of application, enhanced stability, and activity of active formulations, efficient usage, sustained and targeted delivery and reduction in pesticide dosage; reduced toxicity toward nontargeted organisms; and beneficial biota are the key factors in sustainable agriculture, which can be addressed by nanotechnology. In addition, nanomaterials also function as gene nanocarriers and help in real-time sensing and detection of pests, insecticides, etc. (Lade, 2019).

3.1 Bactericide

The antibacterial action of Cu NPs and CuO NPs is extensively studied against environmental bacterial strains (Khatami et al., 2017), plant pathogens, urinary tract, and other human bacterial pathogens (Rezaie et al., 2017; Sutradhar et al., 2014; Sivaraj et al., 2014). The antibacterial action of copper-based nanomaterials depends on bacterial strain, particle size, and concentration (Table 1).

For example, the bactericidal action of CuO NPs of 15–30 nm size was reported against *Escherichia coli*, *Pseudomonas aeruginosa*, *Bacillus circulans*, and *Staphylococcus aureus* at 4000 μg/mL (Das et al., 2013). The Cu/Cu_2O NPs of 80 nm synthesized with *Stachys lavandulifolia* flower extract exhibited an inhibition zone of 12 mm against *P. aeruginosa* at 6300 μg/mL (Khatami et al., 2017). The CuO NPs of 50–100 nm size biosynthesized with *Piper betle* leaf extract were employed against bacterial phytopathogens, *Ralstonia solanacearum*, and *Xanthomonas axonopodis* pv. *alfalfae*. The reported inhibition zone values for the respective strains were 9 and 7 mm at 25 μg/mL (Praburaman et al., 2016). The Cu NPs and CuO NPs of 75 and 163 nm, respectively, synthesized by chemical methods were used for the control of *Xanthomonas axonopodis* pv. *punicae* (*xap*), the causative agent of bacterial blight disease in pomegranate. The minimum inhibitory concentration (MIC) values of Cu NPs and CuO NPs toward *xap* were 2.5 and 1560 μg/mL, respectively. The corresponding minimum bactericidal concentration (MBC) values were 5 and 3150 μg/mL. The foliar application of Cu NPs (400 μg/mL) exhibited a 90% and 15% reduction in disease incidence in 6-month-old plants at early and established stages of infection under polyhouse conditions, respectively. In a field study with severely infected 7-year-old plants, the postinfection foliar treatment of Cu NPs caused a 20% reduction in disease incidence (Chikte et al., 2019).

The bovine serum albumin capped Cu NPs of 28 nm showed inhibition zones of 22, 18, 16, and 28 mm toward *P. aeruginosa* 27853, *E. coli* 25922, *E. coli* 35218, and *S. aureus* 25923, respectively, at 20 μg/well (Fig. 3). The Cu NPs exhibited MBC value of 50 μg/mL toward *E. coli* 25922 (Fig. 4) (Rastogi and Arunachalam, 2013).

The karaya gum bio templated CuO NPs of 4.8 nm revealed inhibition zone values of 16.2 and 14.5 mm toward *E. coli* and *S. aureus*, respectively, at 50 μg/well. The MIC and MBC values for *E. coli* were 103 and 125 μg/mL, respectively. For *S. aureus*, the respective values were 120 and 145 μg/mL (Padil and Černík, 2013). The guar gum nanocomposite film containing 2% of silver-copper alloy nanoparticles (Ag-Cu NPs) of < 100 nm were prepared by solution casting method and exhibited 99.99% growth reduction of foodborne bacterial pathogens, *Listeria monocytogenes* and *Salmonella enterica* sv *typhimurium*, implicating its application as an active food packaging material (Arfat et al., 2017). The Cu-SiO_2 nanocomposite was formed by deposition of 10 nm-sized Cu NPs on the surface of 88 nm-sized SiO_2 nanoparticles via sol-gel method. The hybrid nanostructure with a surface area of 441.8 m^2/g demonstrated an inhibition zone of 15 mm toward *E. coli* 25922 at a dosage of 35 μg/disk (Kim et al., 2006).

Table 1 A comparison of antibacterial action of copper-based nanomaterials toward various bacterial strains, with reference to particle size and concentration.

Nanoparticles	Particle size (nm)	Target bacterial strain	Concentration	Inhibition zone (mm)	References
Cu	28	*Pseudomonas aeruginosa* 27853	20 μg/well	22	Rastogi and Arunachalam (2013)
		Escherichia coli 25922		18	
		E. coli 35218		16	
		Staphylococcus aureus 25923		28	
CuO	4.8	*E. coli*	50 μg/well	16.2	Padil and Černík (2013)
		S. aureus		14.5	
CuO	50–100	*Ralstonia solanacearum*	25 μg/mL	7	Praburaman et al. (2016)
		Xanthomonas axonopodis pv. *alfalfae*		9	
Cu/Cu_2O	80	*P. aeruginosa*	6300 μg/mL	12	Khatami et al. (2017)
$Cu\text{-}SiO_2$	10	*E. coli* 25922	35 μg/disk	15	Kim et al. (2006)

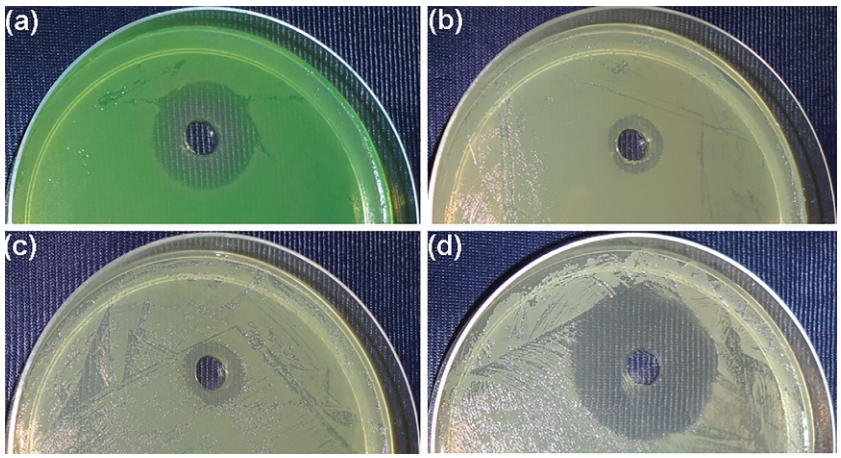

FIG. 3

The inhibition zones of (A) *P. aeruginosa* 27853, (B) *E. coli* 25922, (C) *E. coli* 35218 and (D) *S. aureus* 25923 toward protein capped Cu NPs in well diffusion assay at 20 μg/well.

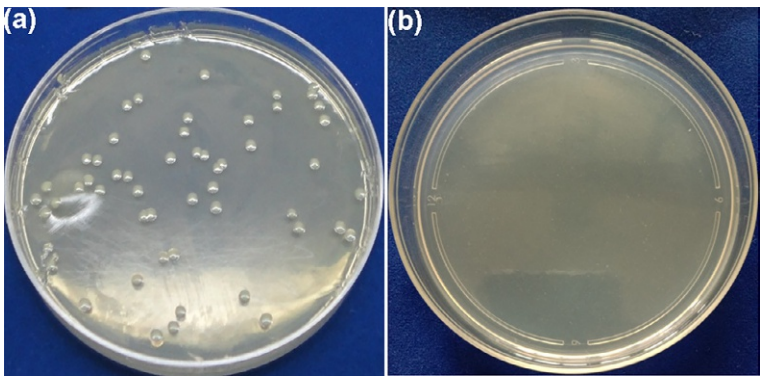

FIG. 4

The colony formation inhibition of *E. coli* 25922 at (A) 0 and (B) minimum bactericidal concentration (MBC) of 50 μg/mL of protein capped Cu NPs.

3.2 Fungicide

The nanoparticles of copper, copper oxide, and copper hydroxide are utilized as a fungicide against various phytopathogenic fungi and for the control and management of different fungal diseases in a broad range of crops such as cereals (corn, wheat), vegetables (lettuce, spinach), fruits (papaya, peach, berries), trees (pine, fir, oak, sycamore) (Table 2).

The copper-based nanofungicides may gain a market advantage over copper sulfate due to the slow release of copper ions (Keller et al., 2017). For example, Cu NPs generated by chemical reduction with a particle size in the range of

Table 2 A comparison of fungicidal action of copper-based nanomaterials toward various plant mycopathogens, with reference to particle size and concentration.

Nanoparticles	Particle size (nm)	Application	Activity against	References
Cu NPs	3–10	Antifungal agent, inhibition zones of 22, 21, 18, and 24 mm at 20 μg/disk	*Phoma destructiva*, *Curvularia lunata*, *Alternaria alternata*, *Fusarium oxysporum*	Kanhed et al. (2014)
Cu NPs	20–50	Fungicide at 45 μg/mL	*Fusarium* sp.	Viet et al. (2016)
Cu NPs	30–50	Fungicide at 2.5 μg/mL, 52.7% disease reduction	Red root rot disease in tea caused by *Poria hypolateritia*	Ponmurugan et al. (2016)
Cu NPs	33	Antifungal agent, inhibition zones of 33, 29, and 21 mm at 127 μg/disk	*F. culmorum*, *F. oxysporum*, *F. graminearum*	Shende et al. (2015)
Cu NPs	40	Antifungal agent, inhibition zone of 10 mm at 150 mg/mL	*Penicillium*	Chalandar et al. (2017)
CuO NPs	7–8	Antifungal agent, inhibition zone of 8 mm at 150 mg/mL	*Penicillium*	Chalandar et al. (2017)
CuO NPs	14	Fungicide, 60.7% reduction in infection at 277.8 μg/mL	Late blight of tomato caused by *Phytophthora infestans*	Giannousi et al. (2013)
CuO NPs	28	Antifungal agent, inhibition zones of 16, 18.3, 18, 18, and 21.2 mm at 100 μg/mL	*F. culmorum*, *F. oxysporum*, *A. niger*, *A. flavus*, *A. fumigatus*	Vanathi et al. (2016)
Cu_2O NPs	13	Fungicide, 73.5% reduction in infection at 438.7 μg/mL	Late blight of tomato caused by *P. infestans*	Giannousi et al. (2013)
Cu/Cu_2O NPs	11	Fungicide, 69.6% reduction in infection at 322.2 μg/mL	Late blight of tomato caused by *P. infestans*	Giannousi et al. (2013)
CuS NP	8	Fungicide, 100% radial growth inhibition at 15 μg/mL	*A. alternata*, *Drechserla oryzae*, *C. lunata*	Sidhu et al. (2017)
Ag/Cu NPs	20	Fungicide, 38.1% and 27% radial growth inhibition at 15 μg/mL	*A. alternata*, *Botrytis cinerea*	Ouda (2014)
Chitosan-Cu nanocomposite	2–3	Fungicide at 100 μg/mL	*S. rolfsii*, *R. solani*	Rubina et al. (2017)

Cu-chitosan NPs	150	Fungicide, 70.5% and 73.5% radial growth inhibition at 1200 μg/mL	*A. solani*, *F. oxysporum*	Saharan et al. (2015)
Cu-chitosan NPs	196	Fungicide, 89.5%, 63%, and 60.1% radial growth inhibition at 1000 μg/mL	*A. alternata*, *M. phaseolina*, *R. solani*	Saharan et al. (2013)
Thyme and dill EO encapsulated Cu NPs	100–250	Fungicide, 100% radial growth inhibition at 600 μg/mL	*Colletotrichum nymphaeae*, causative agent of anthracnose disease in strawberry and beans	Weisany et al. (2019)
Cu loaded chitosan nanogels	100–500	Antifungal agent, MIC of 75 μg/mL of Cu at 7.5 μg/mL of chitosan	*F. graminearum*	Brunel et al. (2013)

20–50 nm were evaluated as an antifungal agent against plant wilt causing fungus *Fusarium* sp. At a concentration of 450 μg/mL, 94% of fungal growth was inhibited in an incubation period of 9 days (Viet et al., 2016). The cetyltrimethylammonium bromide (CTAB) capped Cu NPs of 3–10 nm size showed inhibition zone values of 22, 21, 18, and 24 mm against the fungal plant pathogens, *Phoma destructiva*, *Curvularia lunata*, *Alternaria alternata*, and *Fusarium oxysporum* at 20 μg/disk (Kanhed et al., 2014). The actinomycetes synthesized Cu NPs of 30–50 nm caused 52.7% of reduction in red root rot disease in tea caused by the slow killing fungus *Poria hypolateritia* at a dosage of 2.5 μg/mL (Ponmurugan et al., 2016). The Cu NPs of 33 nm biosynthesized by citron juice showed inhibition zone values of 33, 29, and 21 mm against the plant pathogenic fungi, *F. culmorum*, *F. oxysporum*, and *F. graminearum* at 127 μg/disk, respectively (Shende et al., 2015).

The gum capped CuO NPs of 6–15 nm showed complete inhibition of mycelium radial growth in poisoned food technique at 100 μg/mL toward *Rhizoctonia solani*, a soil, and seed-borne fungal plant pathogen causing sheath blight disease in rice (Fig. 5). The CuO NPs of 28 nm size synthesized using leaf extract of *Eichhornia crassipes* was used for the inhibition of phytopathogenic fungi such as *Aspergillus flavus*, *A. niger*, *A. fumigatus*, *Fusarium oxysporum*, and *F. culmorum* at a concentration of 100 μg/mL, The reported inhibition zone values for the respective fungi were 16, 18.3, 18, 18, and 21.2 mm (Vanathi et al., 2016).

In another study, the Cu NPs (7–8 nm) and CuO NPs (40 nm) synthesized with chemical reduction and precipitation methods, respectively, were employed as an antifungal agent against *Penicillium* sp., the causative agent of mold green and blue disease of *Citrus* fruits. The NPs exhibited inhibition zone values of 10 and 8 mm for Cu NPs and CuO NPs at 150 mg/mL, respectively (Chalandar et al., 2017). The citrate, polyvinylpyrrolidone, and 4-aminobutyric acid capped copper sulfide nanoparticles (CuS NPs) of 8, 12, and 10 nm size were synthesized by

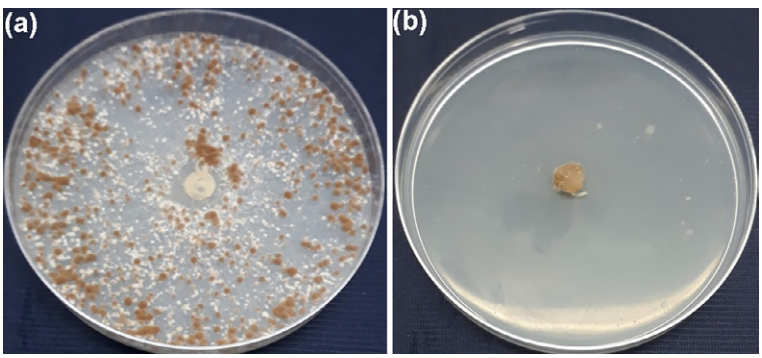

FIG. 5

The radial mycelial growth inhibition of soil and seed-borne fungal plant pathogen *R. solani* at (A) 0 and (B) 100 μg/mL of gum capped CuO NPs in poisoned food technique.

sonochemical method, respectively. They were utilized as a fungicide against agriculturally important plant pathogenic fungi, *A. alternata*, *Drechslera oryzae*, and *C. lunata* and all the NPs showed 100% radial growth inhibition toward the tested fungi at 15 μg/mL. Further, the citrate capped CuS NPs caused a significant reduction in seed rot (60%) and seedling blight (83.3%) in discolored rice seeds and enhancement in seedling vigor index (11%) at 7 μg/mL (Sidhu et al., 2017). The spherically shaped, hydrothermally synthesized Cu_2O, Cu/Cu_2O, and CuO NPs of 13, 11, and 14 nm size, capped with nonionic, biocompatible surfactants such as polysorbate 20 and polyethylene glycol 8000, respectively were tested in the field against late blight of tomato (*Lycopersicon esculentum*) caused by *Phytophthora infestans*. The necrosis of solanaceous crops (tomato, potato, brinjal, pepper) caused by the fungus is a severe problem in Mediterranean countries, affecting the yields. After 10 days of treatment, the reduction in infection (%) reached 60.7% with CuO NPs at a dosage of 277.8 μg/mL. In the case of Cu_2O NPs, the reduction in infection was 73.5% at a treatment dose of 438.7 μg/mL. While for Cu/Cu_2O NPs, the reduction was 69.6% at an application rate of 322.2 μg/mL. There was no noted phytotoxicity and permanent damage in terms of stunting, chlorosis, and bleaching in treated plants with all the copper-based nanoformulations at the tested dosage (Giannousi et al., 2013).

The Ag/Cu NPs nanocomposites of 20 nm size caused mycelial growth inhibition of 38.1% and 27% in *A. alternata* and *Botrytis cinerea* at 15 μg/mL concentration, respectively (Ouda, 2014). The Cu-chitosan nanoparticles of 196 nm size synthesized by ionic gelation showed the mycelial growth inhibition values of 89.5%, 63%, and 60.1% toward *A. alternata*, *M. phaseolina*, and *R. solani*, respectively at 1000 μg/mL concentration in poisoned food technique. At the respective concentration, the spore germination inhibition of *A. alternata* was 87.4% (Saharan et al., 2013). In another report, the Cu-chitosan nanoparticles of 150 nm showed mycelial growth inhibition of 70.5% and 73.5% toward *A. solani* and *F. oxysporum* at 1200 μg/mL, respectively. The respective in vitro spore germination inhibition values were 60.1% and 79.9%. In pot experiments, 1200 μg/mL of Cu-chitosan nanoparticles showed the percentage efficacy of disease control (PEDC) values of 87.7% in early blight and 61.1% in *Fusarium* wilt in tomato plants, confirming its growth promotion and antifungal potentialities (Saharan et al., 2015). The combined foliar application of Cu NPs (50 nm) and Se NPs (2–20 nm) at 50 and 10 μg/mL concentration, respectively, was studied in tomato crop infested by *A. solani*, the causative agent of early blight disease. The treatment caused a decrease in disease severity of the pathogen by 6%. Further, the foliar application elevated the enzymatic antioxidants and nonenzymatic compounds thereby increased the stress tolerance of tomato crops toward *A. solani* and nutraceutical characteristics of tomato fruits (Quiterio-Gutiérrez et al., 2019). The ascorbic acid reduced, 100–250 nm-sized Cu NPs were used for the encapsulation of essential oils (EO) such as thyme and dill and employed for the control of *Colletotrichum nymphaeae*, the causative agent of anthracnose disease in commercial plants such as strawberry and beans. The thyme and dill EO inhibited 100% of the mycelial growth of *C. nymphaeae* at 720 μg/mL, after 3 days of treatment. At 600 μg/mL, the Cu NPs,

thyme, and dill EO encapsulated Cu NPs completely inhibited mycelial growth. After 10 h treatment, the thyme and dill EO showed conidial germination inhibition values of 82% and 75% against *C. nymphaeae* at 1000 μg/mL, respectively. While the % spore germination inhibition values were 84.9%, 96.5%, and 87.9% for Cu NPs, thyme, and dill EO encapsulated Cu NPs at 600 μg/mL, respectively (Weisany et al., 2019). The copper-loaded chitosan nanogels with a particle size of 100–500 nm were produced by complexation. These copper-chitosan colloids showed a MIC value of 75 μg/mL of copper toward *F. graminearum*, at a chitosan concentration of 7.5 μg/mL. Thus, the strong synergistic action between chitosan and copper suggests its utilization as a biocompatible, bioactive, pH-sensitive copper-based nanopesticides (Brunel et al., 2013).

The copper-based formulations are widely used for many years for the preservation and enhancement of wood service life due to their bactericidal, fungicidal, and insecticidal activities (Semenzin et al., 2019). The CuO NPs of 30 nm size imparted high resistance to wood decay caused by a white-rot fungus, *Trametes versicolor* at 10,000 μg/mL concentration. Also, the brown-rot fungus *Gloeophyllum trabeum* was inhibited by the CuO NPs treatment and the mass loss from fungus exposed wood specimens was significantly reduced to 35% in comparison with untreated controls (65%) (Kartal et al., 2009). The tetraoctylammonium bromide stabilized Cu NPs of 3.2 nm mixed with water repellant was effective in inhibiting the biological recolonization of stone substrates (sandstone, marble, plaster) by crustose and foliose lichens for 2 years, at 220 μg/mL (Pinna et al., 2012).

3.3 Insecticide

It is reported that the metal and metal oxide nanoparticles were utilized as successful ovicides, oviposition deterrents, larvicides, pupicides, and adulticides against various mosquito species and insects (Table 3) (Benelli, 2016). The CuO NPs of 24–52.4 nm size synthesized by chemical coprecipitation method were used as an insecticide for the control and management of cotton leafworm (*Spodoptera littoralis*) which attack large scale of crops and vegetables, especially cotton (*Gossypium hirsutum*). The LC_{50}values of CuO NPs toward 2nd and 4th instar larvae were found to be 62.5 and 300 μg/mL, respectively. A mortality rate of 95% and 75% was noted for 2nd and 4th instar larvae at 1000 μg/mL, respectively. In addition, the CuO NPs exhibited photodegradation of pesticide, methomyl (Shaker et al., 2016). The CuO nanorods of 5–15 nm at 10 μg/mL caused 73.3% mortality of 2nd instar larvae of *S. littoralis*, in addition to malformation and morphological changes of larvae. The treatment resulted in oxidative stress and apoptosis through DNA damage (El-Wahab and Anwar, 2014).

The insecticidal activity of leaf extract synthesized CuO NPs of 33.8 and 68.1 nm size was studied on cotton mealybug, *Phenacoccus solenopsis* Tinsley (Hemiptera: Pseudococcidae), a polyphagous insect which feeds on economically important host plants of Cucurbitaceae, Fabaceae, and Solanaceae families. At 300 μg/mL concentration and 96 h of treatment, the respective CuO NPs showed 20% and 14%

Table 3 A comparison of insecticidal activity of copper-based nanomaterials toward various plant insect pests, with reference to particle size and concentration.

Nanoparticles	Particle size (nm)	Application	Activity against	References
CuO nanorods	5–15	Insecticide, -73.3% 2nd instar larval mortality at 10 μg/mL	Cotton leaf worm, *Spodoptera littoralis*	El-Wahab and Anwar (2014)
CuO NPs	10–70	Insecticide, 100% adult mortality at 300 μg/mL	Stored grain pest, *Tribolium castaneum*	El-Saadony et al. (2020)
CuO NPs	24–52.4	Insecticide, 95% and 75% 2nd and 4th instar larval mortality at 1000 μg/mL	*S. littoralis*	Shaker et al. (2016)
CuO NPs	33.8	Insecticide, 20% adult mortality at 300 μg/mL	Cotton mealy bug, *Phenacoccus solenopsis*	Leon-Jimenez et al. (2019)
CuO NPs	33.8	Insecticide, 14% adult mortality at 300 μg/mL	*P. solenopsis*	Leon-Jimenez et al. (2019)
Cu_2O NPs	50	Insecticide, 98% adult mortality at 5500 μg/mL	Two-spotted spider mite, *Tetranychus urticae*	Dorri et al. (2018)
Cu NPs	35–80	Insecticide, 100% larval mortality at 8 μg/mL	Malarial vector *Anopheles subpictus*, filarial vector *Culex quinquefasciatus*; and larvae of cattle tick *Rhipicephalus microplus*	Ramyadevi et al. (2011)
Cu NPs	5–20	Insecticide, 98.8% larval mortality at 5 μg/mL	*C. quinquefasciatus*	Mondal and Hajra (2016)
CuO NPs	29	Antiparasitic agent, 50% reduction in cyst viability at 0.72 μg/mL	Anthropozoonotic protozoan parasite, *Cryptosporidium parvum*	Saad et al. (2015)
CuO NPs	30	Insecticide, 50% neonatal mortality at 3.2 μg/mL	Crustacean *Daphnia magna*	Heinlaan et al. (2008)
CuO NPs	30	Insecticide, 50% larval mortality at 2.1 μg/mL	Crustacean *Thamnocephalus platyurus*	Heinlaan et al. (2008)
CuO NPs	30–50	Insecticide, 50% larval mortality at 569 μg/mL	Freshwater shredder *Allogamus ligonifer*	Pradhan et al. (2012)
CuO NPs	30–50	Insecticide, 43% adult mortality at 50 μg/mL	Euryhaline copepod, *Tigriopus japonicas*	Park et al. (2014)

mortality rates. While, the cell viabilities were found to be 38% and 30% in the viability test, respectively (Leon-Jimenez et al., 2019). The nanocomposite of copper (35 nm) such as copper-chlorophyllin (Cu-chl), copper-chlorophyllin-silver (Cu-chl/Ag), and copper-chlorophyllin-graphene (Cu-chl/Go) were tested against onion thrips, *Thrips tabaci* (L.), in an open field at 10^{-3} mL/L concentration. The onion thrips, *T. tabaci* is a vital insect pest that affects onion quality and the ability for exportation in Egypt. The thrips also act as vectors for viral (Iris yellow spot) and bacterial (bacterial center rot) diseases in onion, in addition to the spread of fungal diseases (purple blotch) during feeding. After 5 days of post foliar spray, Cu-chl, Cu-chl/Ag, and Cu-chl/Go caused 85.5%, 70.4%, and 71.8% reduction in the population of thrips, respectively (Merghany et al., 2019). The biosynthesized CuO NPs in the size range of 10–70 nm showed insecticidal action against the global stored grain pest, *Tribolium castaneum*, which causes a significant reduction in weight and nutritive quality, germination ratio, and commercial value of grains. Adult mortality of 100% was noted at 300 μg/mL of CuO NPs and the LC_{50} value was 37 μg/mL after 5 days of treatment (El-Saadony et al., 2020). The population of two-spotted spider mite, *Tetranychus urticae*, (98%) was inhibited by nanocapsules of Cu_2O NPs (50 nm) at a concentration of 5500 μg/mL, after 120 h of treatment. It is one of the major agricultural bean pests of *Phaseolus vulgaris* with a quick propagation rate, wide host range, adaptability to different environmental conditions and pesticide resistance, and heavy economic loss (Dorri et al., 2018).

The Cu NPs of 35–80 nm synthesized by polyol process were studied for their antiparasitic action toward hematophagous larvae of malarial vector *Anopheles subpictus*, filarial vector *Culex quinquefasciatus*; and larvae of the cattle tick *Rhipicephalus microplus*. The Cu NPs were able to cause 100% mortality of blood-sucking parasites at 8 μg/mL concentration within 24 h. The LC_{50} values of Cu NPs toward *A. subpictus*, *C. quinquefasciatus*, and *R. microplus* were found to be 0.95, 1.01, and 1.06 μg/mL, respectively (Ramyadevi et al., 2011). In another study, Cu NPs of 5–20 nm size synthesized with marigold and sunflower petal extracts caused 98.8% and 70% mortality of *C. quinquefasciatus* larvae after 72 h treatment at 5 μg/mL dosage, respectively (Mondal and Hajra, 2016). The larvicidal activity of CuO NPs of 16 nm synthesized using leaf extract of *Tridax procumbens* was tested against species of *Aedes aegypti* mosquito, which act as transmit vectors for dengue, chikungunya, zika, and yellow fever virus (Muthamil Selvan et al., 2018). The toxicity of CuO NPs of 30–50 nm size was tested against the larvae of freshwater shredder *Allogamus ligonifer*, a shooting moth involved in the decomposition of plant litter. The LC_{50} value was found to be 569 μg/mL, after 96 h of exposure (Pradhan et al., 2012). The CuO NPs of 30–50 nm caused 43% mortality of euryhaline copepod, *Tigriopus japonicas* at 50 μg/mL concentration and 5% salinity (Park et al., 2014). The CuO NPs of 29 nm size were used as an antiparasitic agent against the oocytes of *Cryptosporidium parvum*, an anthropozoonotic protozoan parasite that causes diarrhea in mammals. The CuO NPs caused a significant reduction for cyst viability and the LC_{50} value was found to be 0.72 μg/mL after 3 h of exposure (Saad et al., 2015). The CuO NPs of 30 nm size showed LC_{50} values of 3.2 and 2.1 μg/mL

toward crustaceans *Daphnia magna* and *Thamnocephalus platyurus*, respectively. The crustacean *D. magna* is widely used as a model, invertebrate laboratory test organism for checking and predicting the ecotoxicity of pollutants and chemicals such as pesticides, heavy metals, solvents, phenols, etc. (Heinlaan et al., 2008). The toxicity of soil-applied nanocopper was studied toward *Folsomia candida*, a common, widespread, soil-dwelling, model arthropod used for testing soil pollutants. The nanoformulation showed an EC_{50} value of 156 mg/kg, suggesting the dependence of toxicity on metal solubility and bioavailability and toxicity (Neves et al., 2019).

3.4 Nematicide

The Cu NPs of < 50 nm size biosynthesized with stem extract of a holoparasitic plant, *Orobanche aegyptiaca* was used as a nematicide against *Meloidogyne incognita*. The NPs treatment for 16 h caused 91.5% mortality of 2nd stage juveniles of *M. incognita* at 800 µg/mL under in vitro conditions. Further, the NPs exhibited ovicidal activity and showed 83% inhibition of egg hatchability at 400 µg/mL (Akhter et al., 2020). The CTAB capped, ascorbic acid-reduced Cu NPs of 100 nm size demonstrated 100% mortality of 2nd stage juveniles of *M. incognita* in soil treated with 200 µg/mL of NPs for 3 days. The root-knot nematode *M. incognita* is the most widespread and economically important soilborne parasitic/agricultural pest in the world (Mohamed et al., 2019).

4 Mechanism of copper nanomaterial biocidal action

The mechanisms involved in the biocidal action of various copper-based nanomaterials such as Cu NPs, CuO NPs, and Cu_2O NPs toward bacteria, fungi, and insects are not yet completely elucidated. The antibacterial action of copper-based nanomaterials is attributed to a series of actions such as copper ion release and penetration into bacterial membranes, reactive oxygen species (ROS) generation, oxidative stress, membrane damage, cell wall destruction, lipid peroxidation, protein oxidation, protein denaturation, cellular metabolic pathway inhibition, DNA replication inhibition, DNA degradation, and finally leading to death (Arfat et al., 2017; Rai et al., 2018). However, the precise mode of action of copper oxide (CuO and Cu_2O) nanoparticles was elucidated in a recent study. The bactericidal action of CuO and Cu_2O NPs is attributed to the contact killing mechanism via loss of cell membrane integrity and depends on the oxidation state of copper. In the case of CuO NPs, the biocidal action is due to the generation of ROS. For Cu_2O NPs, the inactivation of bacteria is through the inactivation of intracellular enzymes such as fumarase by the formation of copper (I)-peptide complex (Meghana et al., 2015). The mechanisms involved in the fungicidal action of copper-based nanomaterials are cytoplasmic loss, cytoplasmic coagulation, deformation, and destruction of fungal hyphae, which were studied in plant pathogenic fungi, *R. solani* and *S. rolfsii* (Rubina et al., 2017). The insecticidal activity of copper-based nanomaterials is attributed to the induction of

stress and membrane damage leading to distortion of lipid layers of membrane proteins (Leon-Jimenez et al., 2019). It is important to note that the biocidal action of copper nanomaterial depends on various factors such as particle size, shape, surface charge, hydrophobic, or hydrophilic nature of the nanoparticles; in addition to the cell wall and membrane composition and electrostatic interaction between cell and nanoparticles (Rai et al., 2018). However, detailed studies integrating various fields of expertise are needed to decipher the mode and mechanism of biocidal action of copper-based nanomaterials.

5 Conclusions

The pesticide applications of copper-based nanomaterials such as bactericide, fungicide, insecticide, and nematicide are discussed in detail along with the control and management of plant pests and disease and their biocidal mechanisms. Though copper-based nanopesticides are becoming popular due to their outstanding antibacterial, antifungal, and insecticidal activities, extensive studies are warranted on their environmental fate, bioavailability, forage biomass, plant mineral nutrient content, toxicity toward plant-associated nontargeted, beneficial microbes (plant growth-promoting rhizobacteria, nitrogen-fixing bacteria, mycorrhizal fungi, actinomycetes), insects, terrestrial plants, animals, humans, and another biota; microbial enzyme-mediated carbon and phosphorus cycling in soil, accumulation and induced oxidative stress in various crops, etc. (Simonin et al., 2018). Also, the required protocols and models for nanoecotoxic assessment have to be developed. Hence, formulation specific, toxicity evaluation, and risk assessment research on a case by case decide/limit its application as plant protection or phytotoxic agent (Heinlaan et al., 2008). Further, work on the combined action of copper-based nanopesticides with other chemical pesticides in the soil in terms of adsorption, dissipation, and half-life; dynamics of microbial community profiles (bacteria, fungi), etc. are envisaged (Parada et al., 2019). Also, the statutory and regulatory bodies should provide guidelines on the labeling and tracking of nanopesticides.

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References

Akhter, G., Khan, A., Ali, S.G., Khan, T.A., Siddiqi, K.S., Khan, H.M., 2020. Antibacterial and nematicidal properties of biosynthesized Cu nanoparticles using extract of holoparasitic plant. SN Appl. Sci. 2, 1268.

Arfat, Y.A., Ejaz, M., Jacob, H., Ahmed, J., 2017. Deciphering the potential of guar gum/Ag-Cu nanocomposite films as an active food packaging material. Carbohydr. Polym. 157, 65–71.

Attia, N.F., Elashery, S.E.A., Oh, H., 2021. Nanomaterials-based antibacterial textiles. In: Ehrmann, A., Nguyen, T.A., Nguyen Tri, P. (Eds.), Nanosensors and Nanodevices for Smart Multifunctional Textiles. Elsevier, pp. 135–147 (Chapter 9).

Awwad, A.M., Albiss, B., 2015. Biosynthesis of colloidal copper hydroxide nanowires using *Pistachio* leaf extract. Adv. Mater. Lett. 6, 51–54.

Benelli, G., 2016. Plant-mediated biosynthesis of nanoparticles as an emerging tool against mosquitoes of medical and veterinary importance: a review. Parasitol. Res. 115, 23–34.

Brunel, F., El Gueddari, N.E., Moerschbacher, B.M., 2013. Complexation of copper(II) with chitosan nanogels: toward control of microbial growth. Carbohydr. Polym. 92, 1348–1356.

Bukhari, S.I., Hamed, M.M., Al-Agamy, M.H., Gazwi, H.S.S., Radwan, H.H., Youssif, A.M., 2021. Biosynthesis of copper oxide nanoparticles using *Streptomyces* MHM38 and its biological applications. J. Nanomater. 2021, 6693302.

Chalandar, H.E., Ghorbani, H.R., Attar, H., Alavi, S.A., 2017. Antifungal effect of copper and copper oxide nanoparticles against *Penicillium* on orange fruit. Biosci. Biotechnol. Res. Asia 14, 279–284.

Chikte, R.G., Paknikar, K.M., Rajwade, J.M., Sharma, J., 2019. Nanomaterials for the control of bacterial blight disease in pomegranate: quo vadis? Appl. Microbiol. Biotechnol. 103, 4605–4621.

Das, D., Nath, B.C., Phukon, P., Dolui, S.K., 2013. Synthesis and evaluation of antioxidant and antibacterial behavior of CuO nanoparticles. Colloids Surf. B. Biointerfaces 101, 430–433.

Directorate of Plant Protection, Quarantine and Storage, 2020. About CIBRC. Ministry of Agriculture and Farmers Welfare (Online) http://ppqs.gov.in/divisions/cib-rc/about-cibrc. (Accessed 16 September 2020).

Dorri, H.R., Khaghani, S., Moghadam, A., Ghanbari, D., Bihamta, M.R., 2018. The effect of copper nano-capsules on the control of two spotted spider mite (*Tetranychus urticae*). J. Nanostruct. 8, 316–324.

El-Saadony, M.T., El-Hack, M.E.A., Taha, A.E., Fouda, M.M.G., Ajarem, J.S., Maodaa, S.N., Allam, A.A., Elshaer, N., 2020. Ecofriendly synthesis and insecticidal application of copper nanoparticles against the storage pest *Tribolium castaneum*. Nanomaterials 10, 1–16.

El-Wahab, R.A.A., Anwar, E.M., 2014. The effect of direct and indirect use of nanoparticles on cotton leaf worm, *Spodoptera littoralis*. Int. J. Chem. Biochem. Sci. 1, 17–24.

Giannousi, K., Avramidis, I., Dendrinou-Samara, C., 2013. Synthesis, characterization and evaluation of copper based nanoparticles as agrochemicals against *Phytophthora infestans*. RSC Adv. 3, 21743.

Gunalan, S., Sivaraj, R., Venckatesh, R., 2012. *Aloe barbadensis* Miller mediated green synthesis of mono-disperse copper oxide nanoparticles: optical properties. Spectrochim. Acta A Mol. Biomol. Spectrosc. 97, 1140–1144.

Heinlaan, M., Ivask, A., Blinova, I., Dubourguier, H.-C., Kahru, A., 2008. Toxicity of nanosized and bulk ZnO, CuO and TiO_2 to bacteria *Vibrio fischeri* and crustaceans *Daphnia magna* and *Thamnocephalus platyurus*. Chemosphere 71, 1308–1316.

Ibrahim, A.M., Munshi, G.H., Al-Harbi, L.M., 2018. Copper(II) oxide nanocatalyst preparation and characterization: green chemistry route. Bull. Natl. Res. Cent. 42, 6.

Ighalo, J.O., Sagboye, P.A., Umenweke, G., Ajala, O.J., Omoarukhe, F.O., Adeyanju, C.A., Ogunniyi, S., Adeniyi, A.G., 2021. CuO nanoparticles (CuO NPs) for water treatment: a review of recent advances. Environ. Nanotechnol. Monit. Manag. 15, 100443.

Kanhed, P., Birla, S., Gaikwad, S., Gade, A., Seabra, A.B., Rubilar, O., Duran, N., Rai, M., 2014. *In vitro* antifungal efficacy of copper nanoparticles against selected crop pathogenic fungi. Mater. Lett. 115, 13–17.

Kartal, S.N., Green, F., Clausen, C.A., 2009. Do the unique properties of nanometals affect leachability or efficacy against fungi and termites? Int. Biodeterior. Biodegrad. 63, 490–495.

Keller, A.A., Adeleye, A.S., Conway, J.R., Garner, K.L., Zhao, L., Cherr, G.N., Hong, J., Gardea-Torresdey, J.L., Godwin, H.A., Hanna, S., Ji, Z., Kaweeteerawat, C., Lin, S., Lenihan, H.S., Miller, R.J., Nel, A.E., Peralta-Videa, J.R., Walker, S.L., Taylor, A.A., Torres-Duarte, C., Zink, J.I., Zuverza-Mena, N., 2017. Comparative environmental fate and toxicity of copper nanomaterials. NanoImpact 7, 28–40.

Khanehzaei, H., Ahmad, M., Kamyar, S., Ajdari, Z., 2014. Synthesis and characterization of $Cu@Cu_2O$ core shell nanoparticles prepared in seaweed *Kappaphycus alvarezii* media. Int. J. Electrochem. Sci. 9, 8189–8198.

Khatami, M., Heli, H., Jahani, P.M., Azizi, H., Nobre, M.A.L., 2017. Copper/copper oxide nanoparticles synthesis using *Stachys lavandulifolia* and its antibacterial activity. IET Nanobiotechnol. 11, 709–713.

Kim, Y.H., Lee, D.K., Cha, H.G., Kim, C.W., Kang, Y.C., Kang, Y.S., 2006. Preparation and characterization of the antibacterial cu nanoparticle formed on the surface of SiO_2 nanoparticles. J. Phys. Chem. B 110, 24923–24928.

Kora, A.J., 2018. Plant and tree gums as renewable feedstocks for the phytosynthesis of nanoparticles: a green chemistry approach. In: Kanchi, S., Ahmed, S. (Eds.), Green Metal Nanoparticles: Synthesis, Characterization and their Applications. Scrivener Publishing LLC, USA, pp. 79–111.

Lade, B., 2019. Nanobiopesticide formulations: application strategies today and future perspectives. In: Koul, O. (Ed.), Nano-Biopesticides Today and Future Perspectives, first ed. Academic Press, pp. 179–206.

Leon-Jimenez, E., Valdez-Salas, B., Gonzalez-Mendoza, D., Tzintzuncamacho, O., 2019. Synthesis and insecticide activity of Cu-nanoparticles from *Prosopis juliflora* (Sw) DC and *Pluchea sericea* (Nutt) on *Phenacoccus solenopsis* Tinsley (Hemiptera: Pseudococcidae). Rev. Soc. Entomol. Argent. 78, 12–21.

Meghana, S., Kabra, P., Chakraborty, S., Padmavathy, N., 2015. Understanding the pathway of antibacterial activity of copper oxide nanoparticles. RSC Adv. 5, 12293–12299.

Merghany, M.M., Abdelgawad, K.F., Tawfic, G.A., Ahmed, S.S., 2019. Yield, quality and leaves anatomy structure of spring onion sprayed by nanocomposite to control *Thrips tabaci*. Plant Arch. 19, 1839–1849.

Mohamed, E.A., Elsharabasy, S.F., Abdulsamad, D., 2019. Evaluation of *in vitro* nematicidal efficiency of copper nanoparticles against root-knot nematode *Meloidogyne incognita*. South Asian J. Parasitol. 2, 1–6.

Mondal, N.K., Hajra, A., 2016. Synthesis of copper nanoparticles (CuNPs) from petal extracts of marigold (*Tagetes* sp.) and sunflower (*Helianthus* sp.) and their effective use as a control tool against mosquito vectors. J. Mosq. Res. 6, 1–9.

Mondal, A., Debnath, P., Mondal, N.K., 2021. Nanoparticles: a new tool for control of mosquito larvae. In: Bhattacharyya, S., Mondal, N.K., Platos, J., Snášel, V., Krömer, P. (Eds.), Intelligent Environmental Data Monitoring for Pollution Management. Academic Press, pp. 49–70 (Chapter 3).

Muthamil Selvan, S., Vijai Anand, K., Govindaraju, K., Tamilselvan, S., Kumar, V.G., Subramanian, K.S., Kannan, M., Raja, K., 2018. Green synthesis of copper oxide nanoparticles and mosquito larvicidal activity against dengue, zika and chikungunya causing vector *Aedes aegypti*. IET Nanobiotechnol. 12, 1042–1046.

Nasrollahzadeh, M., Akbari, R., Sakhaei, S., Nezafat, Z., Banazadeh, S., Orooji, Y., Hegde, G., 2021. Polymer supported copper complexes/nanoparticles for treatment of environmental contaminants. J. Mol. Liq. 330, 115668.

Neves, J., Cardoso, D.N., Malheiro, C., Kah, M., Soares, A.M.V.M., Wrona, F.J., Loureiro, S., 2019. Copper toxicity to *Folsomia candida* in different soils: a comparison between nano and conventional formulations. Environ. Chem. 16, 419–429.

Ouda, S.M., 2014. Antifungal activity of silver and copper nanoparticles on two plant pathogens, *Alternaria alternata* and *Botrytis cinerea*. Res. J. Microbiol. 9, 34–42.

Padil, V.V.T., Černík, M., 2013. Green synthesis of copper oxide nanoparticles using gum karaya as a biotemplate and their antibacterial application. Int. J. Nanomedicine 8, 889–898.

Paiva-Santos, A.C., Herdade, A.M., Guerra, C., Peixoto, D., Pereira-Silva, M., Zeinali, M., Mascarenhas-Melo, F., Paranhos, A., Veiga, F., 2021. Plant-mediated green synthesis of metal-based nanoparticles for dermopharmaceutical and cosmetic applications. Int. J. Pharm. 597, 120311.

Parada, J., Rubilar, O., Diez, M.C., Cea, M., Sant'ana Da Silva, A., Rodríguez-Rodríguez, C.E., Tortella, G.R., 2019. Combined pollution of copper nanoparticles and atrazine in soil: effects on dissipation of the pesticide and on microbiological community profiles. J. Hazard. Mater. 361, 228–236.

Park, J., Kim, S., Yoo, J., Lee, J.-S., Park, J.-W., Jung, J., 2014. Effect of salinity on acute copper and zinc toxicity to *Tigriopus japonicus*: the difference between metal ions and nanoparticles. Mar. Pollut. Bull. 85, 526–531.

Pinna, D., Salvadori, B., Galeotti, M., 2012. Monitoring the performance of innovative and traditional biocides mixed with consolidants and water-repellents for the prevention of biological growth on stone. Sci. Total Environ. 423, 132–141.

Ponmurugan, P., Manjukarunambika, K., Elango, V., Gnanamangai, B.M., 2016. Antifungal activity of biosynthesised copper nanoparticles evaluated against red root-rot disease in tea plants. J. Exp. Nanosci. 11, 1019–1031.

Praburaman, L., Jang, J.-S., Muthusamy, G., Arumugam, S., Manoharan, K., Cho, K.-M., Min, C., Kamala-Kannan, S., Byung-Taek, O., 2016. *Piper betle*-mediated synthesis, characterization, antibacterial and rat splenocyte cytotoxic effects of copper oxide nanoparticles. Artif. Cells Nanomed. Biotechnol. 44, 1400–1405.

Pradhan, A., Seena, S., Pascoal, C., Cássio, F., 2012. Copper oxide nanoparticles can induce toxicity to the freshwater shredder *Allogamus ligonifer*. Chemosphere 89, 1142–1150.

Priyadarshini, E., Priyadarshini, S.S., Cousins, B.G., Pradhan, N., 2021. Metal-fungus interaction: review on cellular processes underlying heavy metal detoxification and synthesis of metal nanoparticles. Chemosphere 274, 129976.

Quiterio-Gutiérrez, T., Ortega-Ortiz, H., Cadenas-Pliego, G., Hernández-Fuentes, A.D., Sandoval-Rangel, A., Benavides-Mendoza, A., Cabrera-De La Fuente, M., Juárez-Maldonado, A., 2019. The application of selenium and copper nanoparticles modifies the biochemical responses of tomato plants under stress by *Alternaria solani*. Int. J. Mol. Sci. 20, 1950.

Rai, M., Ingle Avinash, P., Pandit, R., Paralikar, P., Shende, S., Gupta, I., Biswas Jayanta, K., Da Silva Silvio, S., 2018. Copper and copper nanoparticles: role in management of insect-pests and pathogenic microbes. Nanotechnol. Rev. 7, 303–315.

Ramyadevi, J., Jeyasubramanian, K., Marikani, A., Rajakumar, G., Rahuman, A.A., Santhoshkumar, T., Kirthi, A.V., Jayaseelan, C., Marimuthu, S., 2011. Copper nanoparticles synthesized by polyol process used to control hematophagous parasites. Parasitol. Res. 109, 1403–1415.

Rastogi, L., Arunachalam, J., 2013. Synthesis and characterization of bovine serum albumin–copper nanocomposites for antibacterial applications. Colloids Surf. B: Biointerfaces 108, 134–141.

Rezaie, A.B., Montazer, M., Rad, M.M., 2017. Photo and biocatalytic activities along with UV protection properties on polyester fabric through green *in-situ* synthesis of cauliflower-like CuO nanoparticles. J. Photochem. Photobiol. B 176, 100–111.

Rubina, M.S., Vasil'kov, A.Y., Naumkin, A.V., Shtykova, E.V., Abramchuk, S.S., Alghuthaymi, M.A., Abd-Elsalam, K.A., 2017. Synthesis and characterization of chitosan–copper nanocomposites and their fungicidal activity against two sclerotia-forming plant pathogenic fungi. J. Nanostruct. Chem. 7, 249–258.

Saad, H.A., Soliman, M.I., Azzam, A.M., Mostafa, B., 2015. Antiparasitic activity of silver and copper oxide nanoparticles against *Entamoeba histolytica* and *Cryptosporidium parvum* cysts. J. Egypt. Soc. Parasitol. 45, 593–602.

Saharan, V., Mehrotra, A., Khatik, R., Rawal, P., Sharma, S.S., Pal, A., 2013. Synthesis of chitosan based nanoparticles and their *in vitro* evaluation against phytopathogenic fungi. Int. J. Biol. Macromol. 62, 677–683.

Saharan, V., Sharma, G., Yadav, M., Choudhary, M.K., Sharma, S.S., Pal, A., Raliya, R., Biswas, P., 2015. Synthesis and *in vitro* antifungal efficacy of Cu-chitosan nanoparticles against pathogenic fungi of tomato. Int. J. Biol. Macromol. 75, 346–353.

Sankar, R., Maheswari, R., Karthik, S., Shivashangari, K.S., Ravikumar, V., 2014. Anticancer activity of *Ficus religiosa* engineered copper oxide nanoparticles. Mater. Sci. Eng. C 44, 234–239.

Semenzin, E., Subramanian, V., Pizzol, L., Zabeo, A., Fransman, W., Oksel, C., Hristozov, D., Marcomini, A., 2019. Controlling the risks of nano-enabled products through the life cycle: the case of nano copper oxide paint for wood protection and nano-pigments used in the automotive industry. Environ. Int. 131, 104901.

Shaker, A.M., Zaki, A.H., Abdel-Rahim, E.F.A., Khedr, M.H., 2016. Novel CuO nanoparticles for pest management and pesticides photodegradation. Adv. Environ. Biol. 10, 274–283.

Shende, S., Ingle, A.P., Gade, A., Rai, M., 2015. Green synthesis of copper nanoparticles by *Citrus medica* Linn. (Idilimbu) juice and its antimicrobial activity. World J. Microbiol. Biotechnol. 31, 865–873.

Sidhu, A., Barmota, H., Bala, A., 2017. Antifungal evaluation studies of copper sulfide nano-aquaformulations and its impact on seed quality of rice (*Oryzae sativa*). Appl. Nanosci. 7, 681–689.

Simonin, M., Colman, B.P., Tang, W., Judy, J.D., Anderson, S.M., Bergemann, C.M., Rocca, J.D., Unrine, J.M., Cassar, N., Bernhardt, E.S., 2018. Plant and microbial responses to repeated $Cu(OH)_2$ nanopesticide exposures under different fertilization levels in an agro-ecosystem. Front. Microbiol. 9, 1769.

Sivaraj, R., Rahman, P.K.S.M., Rajiv, P., Salam, H.A., Venckatesh, R., 2014. Biogenic copper oxide nanoparticles synthesis using *Tabernaemontana divaricate* leaf extract and its antibacterial activity against urinary tract pathogen. Spectrochim. Acta A Mol. Biomol. Spectrosc. 133, 178–181.

Sutradhar, P., Saha, M., Maiti, D., 2014. Microwave synthesis of copper oxide nanoparticles using tea leaf and coffee powder extracts and its antibacterial activity. J. Nanostruct. Chem. 4, 86.

Topnani, N., Kushwaha, S., Athar, T., 2009. Wet synthesis of copper oxide nanopowder. Int. J. Green Nanotechnol. Mater. Sci. Eng. 1, M67–M73.

USEPA, 2020. Basic Information About Pesticide Ingredients. USEPA (Accessed 17 September 2020) https://www.epa.gov/ingredients-used-pesticide-products/basic-information-about-pesticide-ingredients. (Online).

Vanathi, P., Raju, R., Sivaraj, R., 2016. Synthesis and characterization of *Eichhornia*-mediated copper oxide nanoparticles and assessing their antifungal activity against plant pathogens. Bull. Mater. Sci. 39, 1165–1170.

Veisi, H., Karmakar, B., Tamoradi, T., Hemmati, S., Hekmati, M., Hamelian, M., 2021. Biosynthesis of CuO nanoparticles using aqueous extract of herbal tea (*Stachys Lavandulifolia*) flowers and evaluation of its catalytic activity. Sci. Rep. 11, 1983.

Viet, P.V., Nguyen, H.T., Cao, T.M., Hieu, L.V., 2016. *Fusarium* antifungal activities of copper nanoparticles synthesized by a chemical reduction method. J. Nanomater. 2016, 7.

Wang, R., Li, X., Nie, Z., Zhao, Y., Wang, H., 2021. Metal/metal oxide nanoparticles-composited porous carbon for high-performance supercapacitors. J. Energy Storage 38, 102479.

Waris, A., Din, M., Ali, A., Ali, M., Afridi, S., Baset, A., Ullah Khan, A., 2021. A comprehensive review of green synthesis of copper oxide nanoparticles and their diverse biomedical applications. Inorg. Chem. Commun. 123, 108369.

Weisany, W., Samadi, S., Amini, J., Hossaini, S., Yousefi, S., Maggi, F., 2019. Enhancement of the antifungal activity of thyme and dill essential oils against *Colletotrichum nymphaeae* by nano-encapsulation with copper NPs. Ind. Crop Prod. 132, 213–225.

Wikipedia, 2020. Pesticide. Wikipedia, Wikimedia Foundation, Inc. https://en.wikipedia.org/wiki/Pesticide.

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CHAPTER

Cu and Cu-based nanomaterials as nanofungicides

7

Velaphi C. Thipe, Lucas F. Freitas, Caroline S.A. de Lima, Kamila M. Nogueira, Jorge G.S. Batista, Aryel H. Ferreira, and Ademar B. Lugão

Institute for Energy and Nuclear Research, National Nuclear Energy Commission-IPEN/CNEN-SP, São Paulo, Brazil

1 Introduction

As the global demand for safe food production escalates against climate changes, it is clear that food safety and security is under great threat in modern-day civilization (Van Nguyen et al., 2020). This is exacerbated by fungal contamination with subsequent production of mycotoxins resulting in mycotoxicosis, which pose adverse harmful effects to human and animal health (Jarvis and Miller, 2005). Fungi are undesirable in food due to their degradation capacity and mycotoxins are linked to enormous economic losses as these organisms are always present in crops and grains, together with insects, and are the leading cause of stored product loss since insects tend to become spreaders of fungal spores. Conventional methods for agricultural protection against the ubiquitous fungal contamination have proven to be ineffective with high toxicity and onset of resistance attributed to fungicides (Singh et al., 2021a). New technological developments in farming techniques have used different fungicides to control fungal crop diseases and the search for new formulations is still required to circumvent the gradual increase in resistance and new strains of fungi.

We have records in history about the use of metals (e.g., copper, mercury, silver, and zinc) as disinfecting agents. During the period of the Ebers Papyrus, an Egyptian medical papyrus of herbal knowledge dating to circa 1550 BCE, utilized various copper-based constringents for treating infections (Arendsen et al., 2019). Furthermore, the Hippocratic Corpus, partially written by the great Greek physician Hippocrates, there is a mention of the use of copper-containing wound dressings and powders to treat leg ulcers and infection of fresh wounds. During the first century, in *De Medicina*, a medical writing by the Roman Aulus Cornelius Celsus, copper was regarded as an important drug to treat venereal diseases and nonhealing chronic ulcers (Walusinski, 2018). Copper was also used in the 19th century against the great European cholera epidemics. Greeks, Romans, Persians, Egyptians, and Indian ancient civilizations commonly used copper to purify water for consumption and food preservation (Nisar et al., 2019).

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The first modern use of copper in agriculture and food preservation for the control of fungi in crops dates back to 1761, when seed grains were soaked in a low-concentration copper sulfate solution; it was found to inhibit the seedborne fungi (Brauer et al., 2019). Later in the 1880s, a mixture of copper sulfate, lime, and water (Bordeaux mixture), and a mixture of copper sulfate (Burgundy mixture) were used as fungicides to spray grapes against mold, in the United States and France, respectively (Borkow and Gabbay, 2009). Since then, among the inorganic antimicrobial agents, copper compounds have been widely used in agricultural practices as a fungicide, pesticide, algaecide, herbicide, and also in livestock as disinfectants for animal husbandry purposes (Mastin and Rodgers, 2000).

Copper (Cu) is one of the most essential metal micronutrients required in very small quantities for proper protein function through coordination chemistry by plants and is used in many types of agricultural practices, particularly in organic agriculture (OA) (Chauhan et al., 2020; Da Costa et al., 2020; Malhotra et al., 2020; Rasool et al., 2021). Moreover, copper has been used as a biocide for centuries to disinfect solid surfaces, liquids, and human tissues (Borkow and Gabbay, 2004). Additionally, Cu functions as a cofactor for many enzymatic activities in plants involved in copper/zinc superoxide dismutase (Cu/ZnSOD), cytochrome-C oxidase, lysyl oxidase, tyrosinase, and dopamine hydroxylase, neuropeptide activation, connective tissue, lignin, and neurotransmitter synthesis, plastocyanin, and the ethylene receptors for the apoplastic oxidases (Da Costa et al., 2020; Lopez-Lima et al., 2021; Pilon et al., 2006). In addition, Cu is essential in plant respiration and metabolism of carbohydrates and proteins during photosynthesis, and seed production (Lopez-Lima et al., 2021; Pilon et al., 2006; Rasool et al., 2021; Yruela, 2005). Within the plant cell, Cu is required in at least six locations which include the cytosol, the endoplasmic reticulum (ER), the mitochondrial inner membrane, the chloroplast stroma, the thylakoid lumen, and the apoplast.

The main reason for the use of this metal is vastly attributed to its inherent antimicrobial properties; it was used even before the development of antibiotics to treat bacterial/fungal infections (Ingle et al., 2014). The antimicrobial properties of Cu can be exploited to control a variety of fungal and bacterial diseases (Quaranta et al., 2011; Weaver et al., 2010). Bulk Cu which is often supplied in ionic form (copper sulfate or copper hydroxide), exists in three oxidation states: Cu^0 (solid metal state); Cu^+ (cuprous ion); and Cu^{2+} (cupric ion) (Lopez-Lima et al., 2021; Malhotra et al., 2020). Cu^{2+} and Cu^+ have exhibited negative environmental effects on soil organisms (i.e., soil fauna and flora), and other symbiotic microbes such as fungal species (*Beauveria bassiana*) used as biocontrol agents against pests and insects and crop auxiliary species. This is attributed to repeated application of Cu-based pesticides resulting in Cu accumulation which oxidizes important biomolecules such as deoxyribonucleic acid, lipids, and proteins; and further exacerbated by molecular oxygen modification producing reactive oxygen species (ROS) through the Haber-Weiss and Fenton reactions, thus resulting in phytotoxicity (Hussain et al., 2021; Tegenaw et al., 2020).

Furthermore, Cu ions exhibit low stability in field conditions resulting in the formation of undesirable Cu complexes and high water solubility leading to chronic exposure to Cu which is inevitable, therefore, the recommended dietary intake of Cu for adolescents and adults is 900 µg/day which is primarily absorbed in the upper small intestine with 1/3 absorbed in the skeleton and muscle, with the median intake of Cu from food in the United States at approximately 1.0–1.6 mg/day for adult men and women (Malhotra et al., 2020; Pariona et al., 2019). The normal range of Cu in growth medium ranges between 0.05 and 0.5 ppm, with most plant tissues ranging between 3 and 10 ppm (Farid, 2015). In soil, the normal range for Cu is between 2 and 50 ppm (Da Costa et al., 2020; Rasool et al., 2021). On the other hand, in OA the use of synthetic fungicides is strictly prohibited, therefore; significant demand for alternatives is required. The objectives of this chapter are to provide an overview of (i) the use of Cu and Cu-based nanoparticles as nanofungicides in agriculture, (ii) green nanoagriculture approaches through Cu nanofungicides, (iii) provide insight on the Cu nanofungicidal mechanism of action, and (iv) highlight the ecotoxicology and safety of Cu nanofungicides.

2 Nanoagriculture

The use of nanotechnology in precision agriculture provides several benefits compared to traditional strategies in crop processes. Nanotechnology through nanocarriers have been used to deliver fertilizers, micronutrients, pest management, fungicides, herbicides, and biosensors (Chauhan et al., 2020; Duhan et al., 2017). Often methods used in agricultural areas, such as the application of chemical pesticides, has adverse effects on animals and are incredibly toxic and harmful to the environment (Damalas and Koutroubas, 2016). Their indiscriminate use increases pathogens and pest's resistance and reduces soil biodiversity by killing useful soil microbes. In addition to pesticide biomagnification, pollinators decline and destroy the natural habitat of farming, such as birds (Fischer et al., 2021; Rasool et al., 2021; Tilman et al., 2002).

There is a growing demand worldwide for food and continuous search for sustainable alternatives to increase the agricultural productivity efficiency without increasing planted area and negatively impacting the environment. Nanotechnological approaches have been proposed through several nonpersistent pesticide/fungicides formulations; including formulations based on nanomaterials for insect pests management, encapsulation of fertilizers for slow and controlled nutrients and water release, among other combinations (Bhan et al., 2018; Shang et al., 2019; Singh et al., 2021b). The use of nanotechnology through copper-based nanomaterials is a viable perspective that can effectively address various problems in crops. Copper or copper oxide nanoparticles (CuNPs and CuONPs, respectively) have excellent cytotoxic activity against a wide range of microorganisms: bacteria, fungi and viruses, including multidrug-resistant organisms (Chudobova et al., 2015; Ingle et al., 2014; Mahmoodi et al., 2018; Hai et al., 2021).

CuNPs and CuONPs present competitive advantages over other metals nanoparticles, such as silver, which also exhibit antimicrobial properties, as it is cheaper and easily available; therefore, the CuNPs/CuONPs are cost-effective (Camacho-Flores et al., 2015; Letchumanan et al., 2021). Nowadays, CuNPs and Cu alloys are also being used in many formulations and antimicrobial products such as synthetic textiles, food processing and packaging, biomedical and surgical devices, even in water purification. The reports available on antimicrobial studies of CuNPs prove its size-dependent efficacy against various pathogenic organisms in plants such as Gram-positive and Gram-negative bacteria, also to control yeast, and mold growth (Azam et al., 2012).

3 Green nanoagriculture

A recent trend in the field of nanomaterial science is "Green Nanotechnology," which is the use of nontoxic compounds for the synthesis and processing of nanomaterials in order to generate little impact on the environment for sustainably mitigating many challenges in the plant, human, and animal disease management (Singh et al., 2021a). Green nanotechnology provides a pronounced avenue for exploring the eco-friendly green synthesis for enhancing the properties of copper in a cost-effective manner, efficacious at low concentrations concomitantly reducing overt toxicity and resistance, and an additional armament of providing versatile scaffolds for the functionalization with other antimicrobial biomolecules from plants defense system (e.g., antiherbivory compounds, lectins, phytoanticipins, phytoalexins, and other defensive secondary metabolites) (Bartolucci et al., 2020; Benassai et al., 2021; Kanhed et al., 2014; Sanzari et al., 2019; Singh et al., 2021a). Green CuNPs and CuONPs can thus serve as an intervention for effective nanofungicides and growth stimulators in agriculture (Ermini and Voliani, 2021; Gámez-Espinosa et al., 2021; Malandrakis et al., 2021; Singh et al., 2021b).

Green nanotechnological approaches:

(i) Antimicrobial plant extracts and molecules used as reducing agents for the production of CuNPs and CuONPs providing a direct antagonistic effect against pathogenic fungi.

(ii) Surface modification of CuNPs and CuONPs with natural capacities of plants for resistance as plant defense stimulators to block mycotoxin production following fungal colonization.

One of such examples is demonstrated by Shiny et al. (2019), where they synthesized stable and environmentally benign CuONPs using various leaf extracts of Neem (Azadirachta indica), Pongamia (Pongamia pinnata), Lantana (Lantana camara), and extract of orange peel (Citrus reticulata). The plant extracts possess intrinsic preservative properties when coupled with biocidal properties of metallic nanoparticles such as Cu, can provide a synergistic effect as coating agents against fungi and termites, beneficial especially in timber farming and industry that produce

primary wood products (e.g., furniture and rubber) and secondary products (e.g., wood pulp for the pulp and paper industry). Their results revealed that CuONPs synthesized with L. camara produced particles sized ranging from 33 to 46 nm, while the rest produced particles > 100 nm. The size difference is correlated to the effectiveness of L. camara CuONPs that inhibited 34.44% and 100% against the tested *Oligoporus placenta* (brown rot) and *Trametes hirsuta* (white rot) fungus, respectively. Moreover, L. camara CuONPs exhibited remarkable antitermite and rubber wood preservative activity when compared to the other CuONPs.

Ray et al. (2015) tested CuNPs synthesized by sugars and vitamin C against *Rhizoctonia solani* Kuhn fungal strain and observed a dose-dependent inhibitory effect with a maximum of 98.31% inhibition at 3.55 ppm with CuNPs synthesized in dextrose. Moreover, CuNPs synthesized in dextrin or in β-cyclodextrin had a slightly lower effect, but the peak of inhibition was achieved earlier. Interestingly, nanoparticles synthesized in cyclodextrin were up to 10 times bigger than their dextrin and dextrose counterparts, but the antifungal effect seemed not to be significantly dependent on size alone. The small dextrose-CuNPs, for instance, had a greater efficacy against the fungus compared to dextrin-CuNPs, probably due to a network structure formed by dextrose which enhances the interaction with the fungus (Ray et al., 2015).

Olchowik et al. (2017) evaluated the effect of CuNPs on the growth parameters of English oak (*Quercus robur* L.) seedlings using the foliar application. The CuNPs treatment on the degree of leaves infected by powdery mildew was also investigated. In general, the authors reported no phytotoxicity, and it was worth noting that the treatment did cause some ultrastructural changes in leaf chloroplasts but not in shoot and root tissues. However, effectiveness in controlling oak powdery mildew infection was not reported. Pariona et al. (2019) reported the use of ascorbic acid as both a reducing and stabilizing agent for the synthesis of CuNPs and evaluated their antifungal activity against *Fusarium solani*, *Neofusicoccum* sp., and *Fusarium oxysporum*. Interestingly, they showed using X-ray photoelectron spectroscopy (XPS) that the produced CuNPs' surfaces are populated with different Cu species (e.g., Cu^{2+}, Cu^{+}, and Cu^{0}) and were effective against the tested pathogenic fungi (Fig. 1).

Beltrán-Partida et al. (2019) demonstrated that CuNPs with around 250 nm diameter exert dose-dependent toxicity to Candida albicans strains isolated from oral denture candidiasis. A significant antifungal activity could be observed at 250 ppm, but the minimal inhibitory concentration was found to be 500 ppm. In this case, CuNPs require a longer incubation period compared to triclosan, a standard antifungal agent, but after 500 ppm their antifungal activity is similar. After 24 h, the researchers observed that the fungi were not forming pseudohyphae, most probably because of genetic alterations caused by Cu, and the permeability of plasma membrane and cell wall was impaired (Beltrán-Partida et al., 2019). The intense accumulation of CuNPs in the cytoplasm is able to trigger oxidative stress due to the formation of hydroxyl radicals by the contact between nanoparticles and membrane proteins, and the continuous action of those nanoparticles ultimately leads to cell lysis by oxidative stress and membrane dissociation. The authors

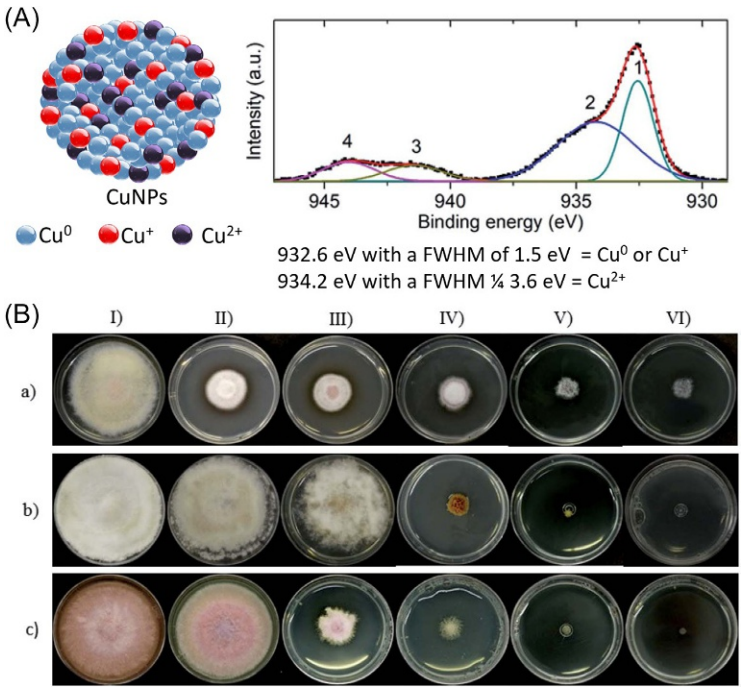

FIG. 1

Ascorbic acid CuNPs with differential Cu speciation—Cu^0, Cu^+, and Cu^{2+} (A) fitted XPS spectrum of CuNPs and (B) CuNPs antifungal activity against (a) *F. solani*, (b) *Neofusicoccum* sp. and (c) *F. oxysporum* at different concentration of CuNPs: (I) 0 (controls), (II) 0.1, (III) 0.25, (IV) 0.5, (V) 0.75, and (VI) 1.0 mg/mL of Cu-NPs.

Reproduced from Pariona, N., Mtz-Enriquez, A.I., Sánchez-Rangel, D., Carrión, G., Paraguay-Delgado, F., Rosas-Saito, G., 2019. Green-synthesized copper nanoparticles as a potential antifungal against plant pathogens. RSC Adv. 9, 18835–18843, with permission from the Royal Society of Chemistry under the Creative Commons Attribution License.

also observed that the presence of carbon and oxygen from ascorbic acid assisted in the antifungal effect of CuNPs (Beltrán-Partida et al., 2019). Wei et al. (2010) also verified that CuNPs oxidize and release Cu ions that are responsible for the oxidative stress that damages cell structures from the plasma membrane to intracellular organelles and biomolecules.

Finally, it has been demonstrated before that particles under 50 nm in diameter perform better than larger ones in terms of antimicrobial effects, especially if they are spherical (Safaei et al., 2019). Indeed, Ponmurugan et al. showed in 2016 that 2.5 ppm CuNPs (5–50 nm in diameter) reduced in 52.7% the incidence of *Poria hypolateritia*, compared to the 45.3% disease control achieved by bulk copper, although carbendazim drug performed slightly better (Ponmurugan et al., 2016). Table 1 summarizes the most important results regarding antimicrobial effects of CuNPs.

Table 1 Summarized results regarding the investigation of CuNPs antimicrobial effects.

Material characteristics	Size (nm)	Effective concentration against fungi	Summarized results	Ref.
CuNPs capped with polyvinyl-alcohol (PVA)	2–3	100% efficacy against *Corticium salmonicolor* with 7–10 ppm CuNPs	7 ppm of CuNPs were enough to inhibit the growth of *C. salmonicolor*, and spraying 10 ppm CuNPs was enough to kill most of the fungus that had already grown	Van Cao et al. (2014)
CuNPs synthesized by *Enterococcus faecalis* (extracellular method)	20–90	CuNPs (8 ppm) against *C. albicans;* 16 ppm *against Cryptococcus neoformans; and* 128 ppm for *Aspergillus niger* and *Fusarium oxysporum*	The efficacy of CuNPs was dependent on the fungus species, although the nanoparticles were more effective than regular antifungal drugs	Chavan and Kelmani (2014)
CuNPs dispersed in polymer films (PVMK, PVC, and PVDF)	~5	Excellent efficacy against *C. albicans* with 1 ppm	PVMK-CuNPs completely inhibited the yeast, while PVC- and PVDF-CuNPs were able to significantly inhibit fungal growth	Cioffi et al. (2005)
SiO-Cu and copper-doped hydroxyapatite nanopowder	3–15	14 ppm was effective against *C. albicans*	Hyperbranched polyamine/copper nanoparticles were effective against *C. albicans* even in low concentrations	Mahapatra and Karak (2009)
CuNPs stabilized with CTAB surfactant	5–10	20 μg per Kirby-Bauer standard paper disc presented good efficacy in inhibiting the growth of *Phoma destructiva, Curvularia lunata, Alternaria alternata,* and *F. oxysporum*	CuNPs provided better inhibition of the plant-infecting fungi compared to commercial fungicide, especially against *C. lunata* and *A. alternata*	Kanhed et al. (2014)
CuNPs in SDS micelles	50–70	A minimum inhibitory concentration of 3.75 ppm was achieved for *C. albicans* and *Candida parapsilosis*	CuNPs can be used as an antimicrobial agent for preventing biofilm growth and bacterial/fungal adhesion on medical materials	Kruk et al. (2015)
CuNPs stabilized with poly(acrylic acid)	15.6	Impregnation of wood with 3000 ppm was effective against *Trametes versicolor* and *Poria placenta*	Copper is a promising biocide agent for wood preservation. Its action was superior to silver in unleached wood exposed to *P. placenta*, but for leached wood, silver was superior	Pařil et al. (2017)
CuNPs stabilized with ascorbic acid	~250	Minimal Inhibitory Concentration of 500 ppm against *C. albicans*	CuNPs were able to decrease significantly the growth of *C. albicans* due to oxidative damage and cell content leakage	Beltrán-Partida et al. (2019)
Biosynthesized CuNPs	5–50	2.5 ppm of CuNPs significantly inhibited the growth of *Poria hypolateritia*	2.5 ppm could inhibit the disease in 52.7%, but Carbendazim had slightly better results (57.2% inhibition)	Ponmurugan et al. (2016)

Continued

Table 1 Summarized results regarding the investigation of CuNPs antimicrobial effects—cont'd

Material characteristics	Size (nm)	Effective concentration against fungi	Summarized results	Ref.
CuNPs synthesized in dextrose, dextrin or cyclodextrin in the presence of vitamin C.	Dextrose (6–8 nm), dextrin (5–6 nm) or cyclodextrin (50–80 nm)	3.5 ppm of CuNPs are effective against *R. solani*	The most effective CuNPs was dextrose-CuNPs (98.31% inhibition), followed by β-cyclodextrin-CuNPs (88% inhibition) and dextrin-CuNPs (84% inhibition)	Ray et al. (2015)
Alginate-CuO nanocomposite, synthesized under different conditions	37	4000 ppm of CuONPs with alginate were the most effective in inhibiting *A. niger*	Alginate-CuO nanocomposite inhibited 83.17% of *A. niger*, performing significantly better than bare CuONPs (57.24%)	Safaei et al. (2019)
CuNPs synthesized by chemical reduction (ascorbic acid)	20–50	*Fusarium* sp. were inhibited by CuNPs in a concentration-dependent manner (from 300 to 450 ppm)	The more CuNPs present in the culture medium, the smaller the fungal colonies, and the bigger the halo of inhibition. The best results were found for 450 ppm	Viet et al. (2016)
CuO nanoparticles	30	Foliar spray of CuONPs (500–1000 ppm) against *F. oxysporum* f. sp. *Niveum* to evaluate the effectiveness on suppressing *Fusarium* wilt and improving plant growth and yield	CuONPs suppressed *F. oxysporum* f. sp. *Niveum*. And yielded 39%–53% more fruits than untreated controls, moreover; polyphenol oxidase activity was elevated in plants treated with CuONPs. These results indicated that CuONPs may serve as effective delivery agent for Cu to suppress plant diseases	Elmer and White (2018)
nano-CuO synthesized extracellularly using *Streptomyces griseus*.	30–50	nano-CuO were sprayed on plants infected with *P. hypolateritia* (1.5 L/bush) and compared with treatments from bulk CuO and carbendazim. The soil and nutrient composition were also evaluated	nano-CuO increased TOC (3.5%), TN (3.6%), P (17.3%) and K (71.3%) in soil. Additionally, 2.5 ppm of CuONP—53% reduction in disease severity as compared to 45.3% and 57% reduction with bulk CuO and carbendazim, respectively	Ponmurugan et al. (2016)

CuNP, *copper nanoparticles;* CuONPs, *copper oxide nanoparticles;* PVMK, *polyvinylmethyl ketone;* PVC, *poly-(vinyl chloride);* PVDF, *polyvinylidenefluoride;* TOC, *total organic carbon;* TN, *total nitrogen;* P, *phosphorus;* K, *potassium.*

4 Mono- and/or hybrid copper nanomaterials as a fungicide

4.1 Copper nanoparticles (CuNPs)

The biosynthesis of CuNP powder using *Celastrus paniculatus* leaf extract and antifungal properties against *F. oxysporum* were explored by Mali et al. (2020). *F. oxysporum* was treated with CuNPs (0.12%, 0.18%, and 0.24%, *w*/*v* in water), $CuSO_4$ (0.1%, 1%), and plant extract. Results revealed that CuNPs showed a dose-dependent mycelia growth inhibition, with a maximum inhibition of 76.29 ± 1.52 at 0.24%, $CuSO_4$ with 20.74 ± 1, and the plant extract was not effective. This was accomplished by the flavonoid and other phenolic components in *C. paniculatus* leaf extract capping the CuNPs, resulting in a synergistic antifungal effect.

Lopez-Lima et al. (2021) demonstrated the beneficial bifunctional role of CuNPs as an effective nanofungicide and plant growth promoter against important soilborne pathogen *F. oxysporum* f. sp. *lycopersici* (FOL) that causes vascular wilt disease. Tomatoes (*Solanum lycopersicum* L.) are highly susceptible to FOL contamination. The CuNPs were produced using sodium citrate tribasic dihydrate and ascorbic acid (Pariona et al., 2019), and the antifungal activity of CuNPs and commercial copper hydroxide fungicide (Cupravit Hidro) against FOL growth was 67.3% and 15.6%, respectively, at 0.5 mg/mL. Moreover, CuNPs treatment diminished the symptoms of *Fusarium* wilt and increased the growth of tomato plants due to the increased chlorophyll content levels (from 19.3% to 28.6%) when compared to Cupravit Hidro. The authors deduced that the CuNPs effectively delivered Cu ions to the plant, while Cupravit Hidro facilitated uncontrolled Cu ion uptake, which hindered healthy plant development. Therefore, the CuNP treatment effectively provided a bifunctional approach for controlling *Fusarium* wilt and for promoting healthy tomato plant growth. The development of CuNPs/CuONPs fabricated with polymers and other metals provides enhanced antifungal properties and pathogen-induced defense mechanisms in plants for optimal protection.

Work by Van Nguyen et al. (2020) further exemplified the important role of Cu in agriculture. Seeds of the Vietnamese maize elite were treated with 4.44 ppm of CuNPs, the results suggested that CuNPs positively primed maize to regulate plant protective mechanisms associated with drought stress responses and tolerance through retaining 70% relative leaf water and enhanced superoxide dismutase (SOD) and ascorbate peroxidase (APX) enzyme activities, in addition to increased anthocyanin, chlorophyll, and carotenoid contents. Moreover, the treatment promoted maize growth, grain yield, and repression of ROS accumulation in maize under drought conditions for 21 days. This is of paramount importance in the midst of rising temperature surges attributed to global warming.

4.2 Copper nanocomposites (CuNCs)

The synergy between nanoparticulates and compounds that exhibit antimicrobial properties provide a benefit for the development of effective and enhanced fungicidal agents as hitherto incomprehensible approaches for agriculture through a myriad of

biocompatible nanofungicides (Kamli et al., 2021; Malandrakis et al., 2021; Peixoto et al., 2020). One of the major hybrid copper nanocomposite involves copper-chitosan nanoparticles due to the collective synergy beneficial for the agricultural sector as a benign innovation (Bartolucci et al., 2020; Chauhan et al., 2020; Singh et al., 2021b). Abd-Elsalam et al. (2020) developed copper-chitosan nanocomposite-based chitosan hydrogels (Cu-Chit/NCs hydrogel) and evaluated their antifungal activity against aflatoxigenic strains of *A. flavus* (high producer (HP), intermediate producer (IP), and low producer (LP)) for aflatoxin B_1 and B_2. Results showed that Cu-Chit/NCs hydrogel antifungal activity at 240 ppm was effective for 100% fungal inhibition.

El-Abeid et al. (2020) developed a potent antifungal nanocomposite composed of reduced graphene oxide nanosheet-decorated with CuONPs—(rGO-CuONPs). The produced rGO-CuONPs (5, 20, and 50 nm) treatment was compared with conventional fungicide Kocide 2000 for their antifungal activity against *F. oxysporum* affecting tomato and pepper plants. Results revealed that rGO-CuONPs at 1 ppm showed the highest levels of fungal growth inhibition rate (> 85%) due to fungal cell membrane damage compared to Kocide 2000 which was only effective at 2500 ppm but only resulted in < 69% fungal inhibition. Moreover, rGO-CuONPs drastically reduced *Fusarium* wilt and root rot diseases severity < 5% for tomato and pepper plants with no phytotoxicity as shown in Fig. 2.

Most recently, Shang et al. (2020) produced copper sulfide nanoparticles (CuSNPs; ratio of 1:1 and 1:4 Cu:S) and investigated their nanofungicidal activity compared to commercial CuONPs and Kocide 3000 against pathogenic *Gibberella fujikuroi* in rice (*Oryza sativa* L.). The authors reasoned that since sulfur is involved in abiotic and biotic stress response through induced phytohormones, its incorporation with Cu will provide enhanced antimicrobial efficiency while simultaneously minimizing environmental toxicity. Results showed that 1:4 CuSNPs at 50 ppm has increased the growth of *G. fujikuroi* by 33% compared to CuONPs which caused inhibition by 18.7%. Furthermore, both 1:1 and 1:4 CuSNPs decreased disease incidence on rice by 35.1% and 45.9%, respectively, when compared to CuONPs at 8.1%, and Kocide 3000 exhibited no disease reduction. Additionally, 1:4 CuSNPs were found to stimulate critical phytohormones (salicylic acid and jasmonic acid) production to enhance pathogen-induced defense mechanisms against *G. fujikuroi* infection.

Xin et al. (2020) developed an innovative in situ system using polysuccinimide nanoparticles (PSI-NPs) capability of scavenging Cu from Cu contaminated soils as explained by to form Cu-PSI nanocomplexes in plants to reduce Cu^{2+} phytotoxicity. This was a result of amino acids (L-aspartic acid) of PSI-NPs that provided a negatively charged surface (−20.7 mV) allowing for the chelation of positively charged Cu^{2+} ions to form the Cu-PSI nanocomplex. The reported Cu-PSI nanocomplex served as a Cu sink for effective delivery and enhanced the adsorption of Cu in the plants due to the improved seed germination and seedling growth through enhanced antioxidative enzymatic activity, and increased water and Cu uptake.

The antimicrobial activities of Ag and Cu were exploited through the production of silver-copper nanocomposites (Ag/CuNCs) using *Olax scandens* leaf extract

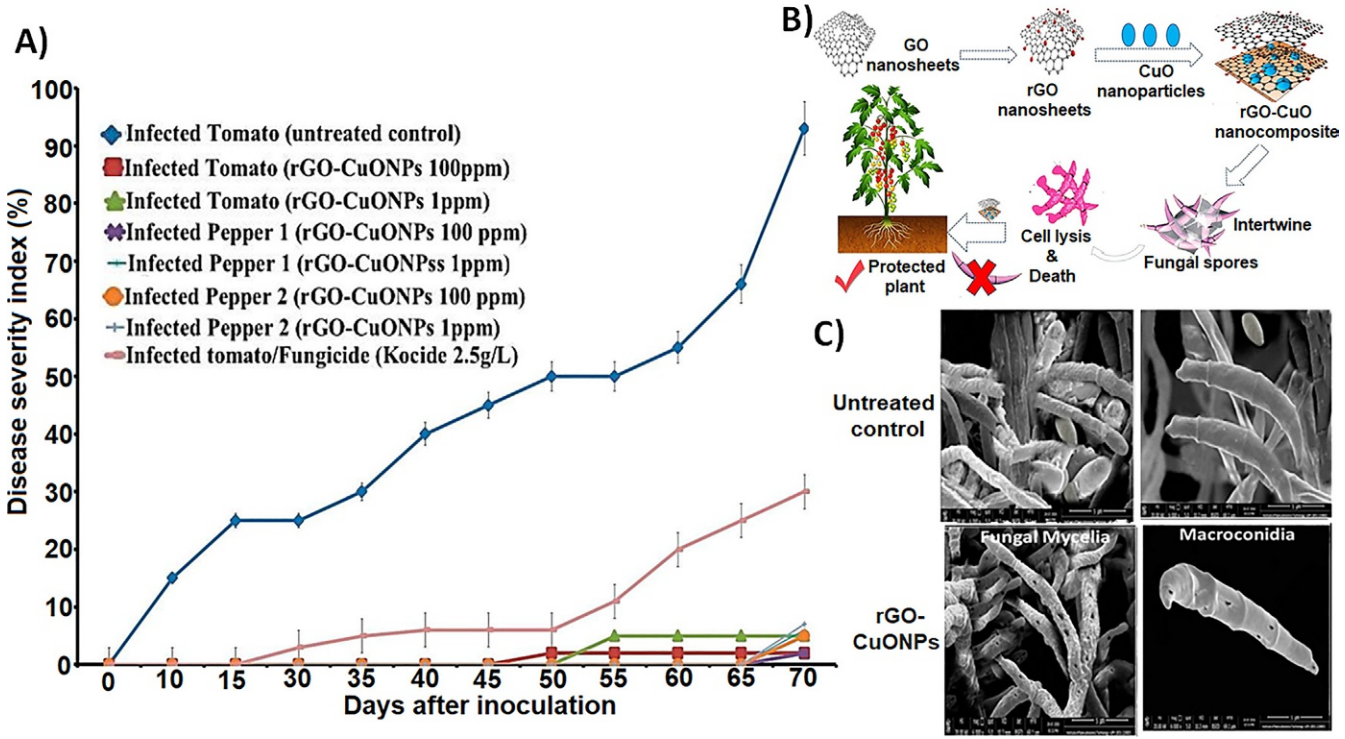

FIG. 2

Antifungal activity of rGO-CuONPs against *F. oxysporum* (A) disease severity index (%) of tomato and pepper plants with rGO-CuONPs and Kocide-3000 treatment for 70 days postinoculation; (B) schematic production of rGO-CuONPs and application for plant protection; (B) fungal inhibition growth rate of rGOCuONPs treatment; (C) SEM images of (a) untreated control and (b) rGOCuONPs interaction with fungal cells showing significant damage due to pores and irregular cavities on the cell wall surface.

Reproduced from El-Abeid, S.E., Ahmed, Y., Daròs, J.A., Mohamed, M.A., 2020. Reduced graphene oxide nanosheet-decorated copper oxide nanoparticles: a potent antifungal nanocomposite against fusarium root rot and wilt diseases of tomato and pepper plants. Nanomaterials 10, 1001. with permission from Nanomaterials under the Creative Commons Attribution License.

(Mujeeb et al., 2020). The Ag/CuNCs were composed of 33.35% Ag and 11.05% Cu to provide a bifunctional nanofungicidal activity against *F. moniliforme* and *C. albicans*. The data suggested that the minimal inhibition concentration of Ag/CuNCs was 125 ppm and 250 ppm for *F. moniliforme* and *C. albicans*, respectively. The antifungal activity was attributed to induced ROS generation by damaging cell membrane peptidoglycan, electron transport chain, protein synthesis, enzymatic degradation, and DNA damage; ultimately resulting in cell death (Hussain et al., 2021).

5 CuNPs/CuONPs nanofungicidal mechanism of action

With the emergence of pathogenic microorganisms resistant to antimicrobial drugs and an increased risk for nosocomial infections as a consequence, nanomaterials emerge as promising alternatives for pathogen control. Copper nanomaterials are already used as a fungicide, antibacterial and antifouling agents, but the mechanism of microbial growth inhibition is barely starting to be elucidated (Kruk et al., 2015). In the present day, among all metallic nanoparticles which present antimicrobial activity, silver has been the most intensively studied, and for many years the bactericidal and antifungal mechanisms of copper have been considered as the same as silver's (Ingle et al., 2014). Recent evidences show, however, that there are differences and similarities, but more studies must be performed in order to clarify the exact mechanism of CuNPs/CuONPs antifungal properties.

Copper is, indeed, known to be an effective biocide and is already available in pesticides and antifungal products, as it is capable of inhibiting the growth of various bacterial strains, algae, and fungi (Akturk et al., 2019) in a multifaceted approach but the exact mechanism is not yet fully understood. It has the advantage of being cheaper than silver and gold, therefore its use in antimicrobial products and strategies is constantly growing (Ingle et al., 2014; Van Cao et al., 2014). Besides the cost-effective property, CuNPs have the additional advantage of being easily oxidized to form more stable CuONPs, which can interact more intensively with cellular macromolecules (Ingle et al., 2014). The mechanism of action, most probably, relies on the dynamic structure of the plasma membrane from bacteria and fungi, which allow the permeation of CuNPs that release Cu^{2+} and Cu^{+} ions transported through the cell membrane via an energy-dependent transport system, thereby destabilizing the integrity of the membrane and trigger cell death pathways (Arendsen et al., 2019). Some lines of evidence also point to the toxicity of free metal ions that were dissolved from NPs attached to the plasma membrane, parallel to the oxidative stress caused by ROS generated on the nanoparticles surface (Akturk et al., 2019; Nisar et al., 2019).

In this regard, it has been observed that CuNPs can cause cell death by interacting with the DNA and disrupting the cell transcription and replication mechanism. Some proteins can lose their biological functions due to the interaction of CuNPs with their sulfhydryl groups, impairing important mechanisms (Nisar et al., 2019). Some authors hypothesized that CuNPs might exert some sort of effect on microbial

plasma membranes as a consequence of copper affinity towards amines and carboxyl groups, which are often present in the cell membrane of bacteria and fungi. Furthermore, once inside the cells, copper may form crosslinks between the DNA strands, disturbing its helical structure (Ingle et al., 2014). Parameters such as particle size and stabilizing/capping agent are paramount for the efficacy of CuNPs in eliminating microbes (Akturk et al., 2019). It is well defined that some nanoparticles with different capping agents can lead to impairment in the antioxidant defenses and metabolic mechanisms within the targeted cells; therefore, the use of biocompatible capping agents is often strongly recommended. Those compounds can increase nanoparticles stability, half-life, cellular uptake, and reduced toxicity to the plant/crop being protected (Akturk et al., 2019). The concentration of nanoparticles arriving at the target tissue is equally important (Kalatehjari et al., 2015). Regarding the size role in antimicrobial properties of metallic nanoparticles, it is likely that the smaller the size (and consequently the higher surface area per unit of volume), the more intense is the interaction with the microbial membranes.

Pařil et al. (2017) observed that copper can improve wood decay resistance in leached and unleached wood, and it is known that the efficacy is significantly dependent on the size and surface chemistry of the nanoparticles, as well as their concentration. They also found that 3003 ppm of CuNPs was ideal for inhibiting the mass loss of leached and unleached wood exposed to white-rot fungus *Tinea versicolor* and red-rot fungus *Phormosoma Placenta*. Interestingly, silver nanoparticles (AgNPs) were less effective than CuNPs against *P. Placenta.* Furthermore, the researchers also observed that the efficiency of unleached wood decreased significantly after leaching. Chang et al. (2012) summarized the possible mechanisms of toxicity towards eukaryotic cells by copper and zinc nanoparticles. They theorized that those nanoparticles can enter the cells through pores or ion channels expressed naturally in the plasma membrane due to their small size, or via endocytosis, and once inside, they interact with cytoplasmic structures and some organelles, especially the mitochondria, generating an excess ROS which will damage various important biomolecules, such as DNA and metalloproteins (Chang et al., 2012).

5.1 Molecular mechanisms

Most of the knowledge regarding the antimicrobial properties of metallic nanoparticles comes from silver, and for a long time, it was accepted that the action mechanism of copper was mostly analogous. One of the most important effects caused by AgNPs in fungi is growth inhibition, followed by cell wall damage and impaired membrane stability. Furthermore, silver ions can react with different biomolecules, with a consequent loss of function: with DNA, it can lead to base complexes that suppress the replication of the genetic material; by reacting with thiol, carboxylate, phosphate, hydroxyl, amine, imidazole, and indole groups from enzymes, silver can inhibit important metabolic pathways and lead the cell to death; when interacting with the ribosome, through the downregulation of proteins and enzymes linked to ATP production (Mukherji et al., 2012). Silver also leads to the accumulation of phosphate, mannitol, succinate, glutamine, and

proline in the interior of cells, interfering with the biochemical machinery and altering the cellular metabolism. All those effects might be due to the silver ions released in the surrounding aqueous environment, as similar findings can be observed after the administration of silver ions alone (Mukherji et al., 2012).

5.2 Copper nanoparticle-induced oxidative stress

Copper ions (Cu^{2+} and Cu^{+}) via oxidative reaction can be released from CuNPs and CuONPs, which are able to donate and accept electrons. This catalyzes the formation of ROS (hydroxyl radicals ($OH^{\bullet}$) and superoxide anions ($O_2^{\bullet-}$) that exert toxic effects on microbial cells via oxidative stress to membrane lipids (lipid peroxidation), amino acids in proteins, and nucleic acids that ultimately results in oxidative deactivation of enzymes (Arendsen et al., 2019). In bacteria, for instance, Cu^{+} and Cu^{2+} ions can interact electrostatically with peptidoglycan and other charged molecules of the cell wall. The ions undergo redox reactions at the bacterial cell surface, generating hydrogen peroxide (H_2O_2) to yield $OH^{\bullet}$ which can impair the stability of the plasma membrane. Inside the cells, copper cations can influence biochemical processes and displace metallic cofactors from binding sites in proteins, leading to their loss of function, or even bind to DNA forming double bonds and destabilizing the helical structure (Mukherji et al., 2012; Robinson et al., 2021).

One of the main suggested mechanisms for CuNPs/CuONPs antifungal action is based on cell wall disruption and intracellular toxicity after penetration. Fungal cell walls are composed mainly of a combination of glycoproteins and polysaccharides, i.e., glucan and chitin, as well as their complexes, with the basic function of protecting the cells against external stresses coming from the surrounding environment (Pinto et al., 2008). The toxicity starts with the binding of CuNPs/CuONPs on the cell wall, either by simple surface adsorption or other mechanisms, causing damage to the plasma membrane integrity. It is likely that a significant production of ROS occurs in close proximity to the membrane due to the presence of the nanoparticles, impairing the membrane dynamic equilibrium and eventually leading the fungal cell to apoptosis (Manke et al., 2013). Briefly, CuNPs and CuONPs are taken up by the cell through transport system, endocytosis and/or receptor-mediated uptake and release Cu^{2+} and Cu^{+} ions which diffuse into the cells that can interrupt mitochondrial respiratory chain and further generate additional ROS via Fenton-type and Haber-Weiss-type reactions. The CuNPs induce oxidative stress ($O_2^{\bullet-}$ and $OH^{\bullet}$) via Fenton-type reaction. CuNPs are further oxidized to CuONPs which reacts with H_2O_2 to induce $OH^{\bullet}$ via Haber-Weiss-type reaction and causes damage to nearby structures such as the mitochondria, lysosomes, endoplasmic reticulum, and ribosomes (Manke et al., 2013; Thannickal and Fanburg, 2000; Valko et al., 2006).

5.3 Copper nanoparticle-fungal cell interactions

The CuNPs can cause leakage of cellular electrolytes through disruption of cellular membrane impacted by an osmotic imbalance. As eluded above, CuNPs can release Cu^{2+} ions, besides generating an excess ROS that damage DNA and

metalloproteins (Waldron and Robinson, 2009); Cu^{2+} ions are able to compete with other essential metals such as iron ions (Fe^{2+}) catalyzed by cuproenzyme, thus preventing proteins from binding with the correct cofactor and consequently inhibiting protein function (Robinson et al., 2021; Waldron and Robinson, 2009). Finally, those nanoparticles can agglomerate close to the nuclear membrane, sometimes entering the nucleus, causing damage to the genetic material and leading the cell to death (Safaei et al., 2019).

The Cu^{+} and Cu^{2+} ions released can chelate at the active sites of certain proteins affecting their pathways and stimulant for oxidizing stress. Ma and coworkers brilliantly elucidated the biomolecular mechanisms of CuNPs, specifically C-coordinated *O*-carboxymethyl chitosan-Cu complexes (O-CSLn-Cu) against *Phytophthora capsici* Leonian, an important plant pathogen for agriculture. Using the complexes at 150 ppm, the authors were able to identify a decreased hyphal viability and an intense impairment in cell membrane integrity after 12 h of the treatment. Morphological alterations in the mycelia were also observed, i.e., shrinking and swelling or sinking and swelling (Ma et al., 2020) probably attributed to Cu ROS-mediated cell death via mitochondrial dysfunction.

When it comes to the intracellular effects, the same authors identified 1172 proteins with altered expression after the treatment: about half of them were downregulated and the other half was upregulated. Those proteins could be grouped in three main categories regarding their function: biological process (BP), cellular component (CC), and molecular function (MF) proteins. Proteins pertaining to the BP group were involved in metabolic processes, cellular processes, localization and biological regulation, while the CC group comprised proteins and protein complexes present in the membrane and in important organelles. Finally, the MF group composed of proteins linked to catalysis, binding transporter activity, structural molecules, and antioxidant capacity (Ma et al., 2020). The biological processes with significant changes comprised the acetyl-CoA biosynthetic process (Acetyl-CoA is intrinsically involved in the catabolism and anabolism of nutrients such as carbohydrates, proteins, fatty acids, and nucleic acids); metabolism of glutathione, sulfur compounds, and acetate; enzymatic activities (CoA-ligase, acetate-CoA ligase, oxidoretuctase, and 5-methyltetrahydropteroyltri-L-glutamate-dependent methyltransferase); vesicles formation and transport (Ma et al., 2020).

Furthermore, several metabolites were differentially expressed due to O-CSLn-Cu action, located in different portions of the cell: 61 dispersed in the cytoplasm, 33 confined in the mitochondria, 16 in the plasma membrane, 7 in peroxisomes, 7 in adiposome, 7 in the Golgi apparatus, 10 in the peroxisome, and 7 in the myelin sheath. All those metabolites participate in 136 different cellular pathways, and the most important are the citrate cycle, protein digestion and absorption, and metabolism of purines, alanine, aspartate, and glutamate. This result corroborates with the previous assumption that CuNPs can exert important effects on the mitochondria since it was the most affected organelle (Ma et al., 2020). The confirmation of the significant involvement of mitochondria in the growth inhibition of *P. capsici* Leonian comes with the decreased activity of α-ketoglutarase dehydrogenase complex (α-KGDHC), as well as the decreased levels of ATP and citrate caused by the treatment with O-CSLn-Cu for 12 h.

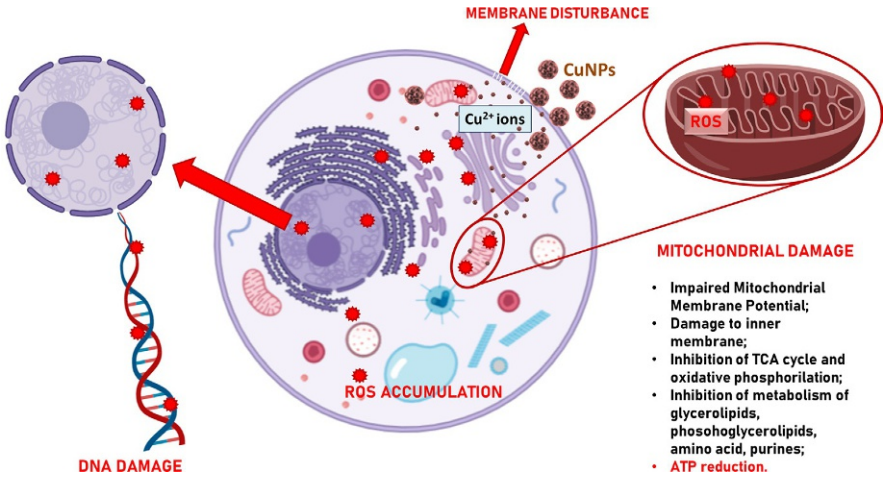

FIG. 3

Main mechanisms of CuNPs antimicrobial activity in eukaryotic cells, such as fungi: membrane disturbance, mitochondrial damage, ROS accumulation, and consequent damage to the DNA.

The low ATP levels might be further explained by a decreased citrate cycle yield, caused by the downregulation of citrate cis-aconitate, succinate, and L-malate metabolites. Furthermore, morphological alterations in those organelles could be observed, i.e., cristae disappearance and impairment of the bilayer conformation. Finally, the mitochondrial membrane potential (MMP) decreased significantly after the treatment. Mitochondria are not the sole responsible for the observed alterations, as the supplementation of ATP to normal levels was not enough to reverse the whole damage caused by the treatment (Ma et al., 2020). Once the damage to mitochondria is established, ROS can accumulate and react with important biomolecules, especially the DNA, leading the cells to death (Fig. 3). Indeed, an elevated level of ROS could be detected in *P. capsici* Leonian mycelia, corroborating the assumption that the damage to mitochondria plays a key role in the inhibition of the fungi (Fan et al., 2021; Hussain et al., 2021; Ma et al., 2020).

6 CuNPs and CuONPs ecotoxicology and safety

The increased use of nanoparticles in our daily lives even within the food chain has become the main concern to researchers and the general public, as there is still insignificant long-term data from chronic exposure and ecotoxicological profiles are still limited (Peixoto et al., 2020; Singh et al., 2021b). Humans are usually exposed to CuNPs through various indirect avenues such as dermal implants, ocular exposure, inhalation, and ingestion which can lead to their deposition in the upper and lower respiratory tract. It is imperative to comprehend CuNPs/CuONPs-plant interactions,

including uptake, mobilization, and accumulation to fully understand the ecotoxicology profile of CuNPs/CuONPs destined for environmental applications such as in agriculture used as nanofungicides against pathogenic fungal contamination and can also serve as a trace micronutrient to enhance chlorophyll, seed production, and root health (Malandrakis et al., 2021; Singh et al., 2021b). The rigorous investigations are crucial in establishing regulatory frameworks assigned to nanoparticles such as CuNPs, and CuONPs. Currently, in some European Union (EU) countries, ionic Cu is permitted for use in both conventional and organic agriculture with regulatory limits up to a maximum dose between 1.5 and 6 kg/ha/year of elemental Cu depending on the type of crops. For example, the maximum dose limit for nuts (1.5 kg/ha/year); small fruits (2), and for a majority of crops (4 kg/ha/year) (Andrivon et al., 2018). The application of Cu varieties year-by-year is based on variations in disease-pressure years. However, some EU countries such as the Netherlands and Germany have prohibited the use of Cu as crop protection agents.

Mosa et al. (2018) investigated the phytotoxicity, genotoxicity of CuNPs on cucumber (*Cucumis sativus*) plants. Results revealed that CuNPs accumulated in the plant tissues with high amounts in the roots and also caused genomic alterations (copper-zinc superoxide dismutase (Cu-Zn SOD) gene expression) in *C. sativus* attributing kg/ha/year to the phenotypical changes of decreased biomass, photosynthetic pigments (Chlorophyll a and b), and root plasma membrane damage in a concentration-dependent manner. Their results can be explained by the function of Cu as a cofactor for many enzymatic activities, and its role in plant respiration and metabolism of carbohydrates and proteins during photosynthesis. It should be noted that the CuNPs used in this study were purchased with an average size of 20 nm and no other information was disclosed regarding how the CuNPs were synthesized and what capping/stabilizing agents were used during the production of CuNPs.

Maziero et al. (2020) highlighted the importance of species-specific in vitro and in vivo ecotoxicology evaluation of nanoparticles. They evaluated the ecotoxicological profile of gum arabic protein silver nanoparticles (AgNP-GP), and they pointed out that other factors, such as the type of reducing and stabilizing agent used during the synthesis in addition to the nanoparticle size, may also influence the overall toxicity profile. Cu can be found in nature as a metallic or as an ionic element (Cu^{+} and Cu^{2+}). The use of CuNPs and CuONPs have been reported in several applications, this form of Cu has also been found in the environment. Although it is known that Cu is present in metabolic processes in humans and animals, at high concentrations and different conformations and or complexes, it may lead to toxicity. Whilst Cu is normally inert, in its ionic form it can bind with several organic substances interfering in environmental and physiological processes.

Song et al. (2014) reported that CuNPs demonstrated higher cytotoxicity against mammalian and piscine cell lines than ionic Cu^{2+}, indicating the species-specific toxicity of CuNPs. The authors emphasized the important role of the morphologies and size of CuNPs with the corresponding release of ionic Cu release attributing to the overall toxicity. Most recently, investigations of CuNPs, CuONPs, and Cu^{2+} on a variety of aquatic organisms such as zebrafish (*Danio rerio*), *Oncorhynchus mykiss*,

Apistogramma agassizi, *Poecilia reticulata*, and many more revealed that particles <50 nm at concentrations ranging from 0.1 to 50 ppm affected intestinal development through induced ionoregulatory toxicity attributed to the decrease in H^+ pump and Na^+/K^+-ATPase activity. Other effects include induced hepatitis, nephrotoxicity, with chronic exposure reported to affect reproduction.

Work by Da Costa et al. (2020) evaluated the toxicity effects between bulk Cu and CuONPs (size $= 37.5 \pm 15.0$ nm) facilitated by Cu^{2+} ions release and their effect on rice plants (*Oryza sativa*). Their inductively coupled plasma atomic emission spectroscopy (ICP-OES) measurements revealed that CuONPs and bulk Cu released ≤ 1 mg/L (0.63%) and ≤ 81 mg/L (7.79%) of Cu^{2+} ions, respectively. Treatment of the *O. sativa* showed that both CuONPs and bulk Cu caused a dose-dependent decline in CO_2 assimilation, plant growth, and photo-phosphorylation. Noticeably, the authors reported two different toxicity mechanisms; where bulk Cu was due to oxidative stress and CuONPs was caused by damage to thylakoid membrane due to NPs accumulation of nonionic form in chloroplasts without oxidative stress.

When the particle size of the CuNPs is large, the particles tend to accumulate in the lung tissue for a longer period leading to irritation and sensitization. On the other hand, when these particles are too small, they are able to move between cells or even permeate the cellular membrane or get into the blood circulation (Ameh and Sayes, 2019; Lee et al., 2016). Once in the blood circulation or the lymphatic systems, the nanoparticles may start to accumulate in other organs. This is especially worrisome for occupational workers in rubber and asphalt production industries who are extensively exposed to the emission of CuNPs. In the same way, physicochemical properties of nanoparticulated materials are what makes them very attractive to innumerous applications in the industry, these properties also have an influence on their facility in entering cells, translocating to organs and, therefore, in their toxicological behavior. There is no reference dose limit for chronic oral exposure or reference concentration for chronic inhalation exposure to CuNPs and CuONPs, which highlights the importance of developing studies and systematic methods to assess their toxicological levels. In the United States, the Environmental Protection Agency (EPA) has set maximum contaminant level for Cu is 1.3 ppm in drinking water (Ameh and Sayes, 2019; National Research Council, 2000).

Perrotta et al. (2020) investigated the consequence of the accumulation of engineered nanoparticles in freshwater using outdoor wetland mesocosm experiment for 6 months. They reported increased nutrient excretion rates of nitrogen and phosphorus which are associated with the growth and survival of consumers such as rooted macrophyte (*Egeria densa*), aquatic snails (*Physella acuta* and *Lymnaea* sp.), and eastern mosquito fish (*Gambusia holbrooki*). This was attributed to the chronic exposure due to low concentrations of Cu and AuNPs by altering the metabolism of consumers and increased consumer-mediated nutrient recycling rates as catalysts for a cascade of events that can potentially intensify eutrophication in aquatic systems.

The increase of utilizing CuNPs, CuONPs, and/or Cu nanoformulation complexes in agriculture as antifungal agents is mounting. It is imperative to clearly evaluate their life-cycle and establish regulatory limits, because when ingested via contaminated water or food (or even through breathing) at high concentrations; CuNPs has been reported to react with stomach acidic pH, approximately 84.5%

of CuNPs dissolved into Cu ions that can be rapidly absorbed, migrate through the intestines into the systemic circulation and to other organs (Ameh and Sayes, 2019; Lee et al., 2016). The prolonged exposure to airborne Cu particulates may cause diseases such as metal fume fever, impairment of gastrointestinal, respiratory, renal, and hepatic function. Some people are more sensitive to the toxicity of Cu due to genetic abnormalities, and also may manifest into Wilson's disease in adults, and in children, it can result in cirrhosis or idiopathic Cu toxicosis (Ameh and Sayes, 2019).

Adeyemi et al. (2020) studied the toxic effects of three commercially available nanomaterials: CuONPs, copper-iron oxide nanopowders, and carbon nanopowders. Usually, CuONPs are used as superconductors, sensors, or antimicrobial agents, while copper-iron oxide nanoparticles have been important in the biomedical area, for cancer targeted therapy, and as contrast agents. In vitro tests indicative of cytotoxic, genotoxic, mitochondrial disruption, and oxidative stress were carried out using human hepatoma HepG2 cell lines. The results revealed that the presence of the nanomaterials decreased the oxygen fluxes in cells when compared to controls. Moreover, elevated levels of superoxide anion, caused by the inhibition of respiration and, therefore, denoting mitochondrial dysfunction caused by the nanomaterials was reported. Results showed cytotoxicity, mutagenicity, oxidative stress, and mitochondrial impairment in cells with high concentrations of nanomaterials, in particular of CuONPs that showed to be extremely toxic.

Concerning environmental exposure, the main origin of CuNPs and CuONPs found in ecosystems comes from wastewater treatment efflux and agriculture. Some personal care products may contain CuNPs formulations and, after use, they go through wastewater into the water supply chain. In the agriculture field, CuNPs and CuONPs present in fertilizers and pesticides (Ameh and Sayes, 2019; Chibber and Shanker, 2017) can translocate into the soil, where they can be transported and transformed due to interactions with organic matters and other components within the soil and this can result in modified physicochemical properties which can lead to problem related to toxicity (Ameh and Sayes, 2019; Rasool et al., 2021). The toxicologic effects of nanoparticles are different depending on their physical properties, i.e., size, morphology, surface area, chemical composition, and solubility.

The smaller the nanoparticle provides a larger surface area considering a defined mass of material, and as a consequence, the surface reactivity with the surrounding medium (for instance, via dissolution and ion liberation) will be enhanced. The aggregation of CuNPs occurs in water according to the concentration of natural organic matter, pH, and ionic strength (Ameh and Sayes, 2019; Torres-Duarte et al., 2016). For the sedimentation process, the pH of the water and the size of the particle will be critical especially during the agricultural application of Cu nanofungicides. When Cu ions interact with other ions present in the water, changes in the capacity of CuNPs to suspend in water can be observed. Oxidation state, aggregation, pH, and natural organic matter will have an important role in the slow process of dilution of CuNPs. On the other hand, when CuNPs interact electrostatically with biopolymeric substances or even with the natural organic matter may induce stabilization and avoid particle aggregation and sedimentation (Ameh and Sayes, 2019). Table 2 shows the environmental interaction of CuNPs and CuONPs.

Table 2 Interaction of CuNPs with the environment.

Exposure medium	Species	CuNPs						
		Size (nm)	Source	Conc.	Method	Objective	Effects	Results
Terrestrial	Microorganisms (responsible for the degradation of pesticides)	40–60	Sigma-Aldrich	20 and 50 mg/L	Incubation of CuNPs and microorganisms in LB broth and mineral saline medium (MSM) media	Assess whether CuNPs in subinhibitory concentrations modify the frequency of conjugation (FC) of two conjugative catabolic plasmids (CCP)—pJP4 and pADP1	< CCP transfer; 10% reduction in FC of mating pairs; rapid release of Cu^{2+} ions (< 3 h) in a medium with a higher level of organic matter (LB)	Lower efficiency in pesticide degradation Parra et al. (2019)
	Cucumber (*Cucumis sativus*)	10–30	Hengqiu Graphene Technology (SUZHOU) Co. Ltd., Shanghai	50, 100, and 200 mg/L	Hoagland solution treatment with CuNPs in *C. sativs* for 4 days	Investigate the phytotoxicity of CuNPs in cucumber (*C. sativus*) plants hydroponically grown	Decrease in biomass by 100 and 200 mg/L; Cu accumulation in tissues with > evidence in the roots in proportion to concentration (aggregate form 80–140 nm); < chlorophyll content in proportion to concentration; > H_2O_2 and MDA levels; > H_2O_2 accumulation in the roots; > leakage of electrolytes to 50 and 200 mg/L; > SOD levels, relative gene expression of the Cu-Zn gene	Damage to the plasma membrane of the root and toxicity to the plant *C. sativus* Mosa et al. (2018)
	Wheat (*Triticum aestivum* L.)	19–47	Biosynthesis—native strain *Klebsiella pneumoniae*	25, 50, and 100 mg/kg	CuNPs were added to chromium (Cr)-rich soils (3.5 mg/kg $K_2Cr_2O_7$) for 30 days	Through biogenic CuNPs to evaluate wheat plants through Cr stress and their growth	For doses of 25 and 50 mg/kg: > root growth; > amount of biomass; > cellular antioxidant content; < H_2O_2 and MDA levels; < translocation of Cr from the soil to the roots and shoots; > amount of residual Cr in the soil, however < amount of Cr bioavailable in the soil	Cr immobilization in the soil, avoided translocation to the plant. Relieving cellular oxidative stress and contributing to healthy growth Noman et al. (2020)

Aquatic	Microorganisms (Anammox)	10–30	–	0.25–50 mg/g of suspended solid (SS)	CuNPs added to serum vials together with 10 mL of anammox biomass	Evaluate the impacts of CuNPs on anaerobic oxidation of ammonium in the sludge of granules and anammox flakes	1.25 mg/g of SS significantly inhibited the metabolic activity of anammox; 4.65 and 3.27 mg/g of SS caused 50% of the inhibition of the anammox metabolic activity for granules and flakes, respectively; 5 mg/g of SS caused severe accumulation of toxic N_2H_4 intermediate; concentrations; > 12 mg/g of SS limits the adsorption capacity of CuNPs and increases the amount of Cu^{2+} ions dissolved in water and the release of LDH	Smaller efficiency of the system anammox for the treatment of waste Zhang et al. (2017)
	Zebrafish embryos (*Danio rerio*)	25	IoLiTec, Inc. (Germany)	0.1–1 mg/L	CuNPs dispersed in egg water from 24 h	Evaluate innate immune responses of the zebra fish's dermal and intestinal system upon CuNPs exposure	For 1 mg/L: > CuNPs accumulation in the intestine and skin epithelium; alteration of chemokine *ccl20a*; increased neutrophils in the tail area; increased signal of IL1β and irg1l in the intestine and skin; reduction in the number of neuromats	Delay in embryo growth, cell death and cell extrusion of the epithelium Brun et al. (2018)

MDA, *malondialdehyde;* LDH, *lactate dehydrogenase;* IL1β, *interleukin 1 beta;* irg1l, *immunoresponsive gene 1-like.*

Taking into consideration the data presented in the studies presented in Table 2, one can notice that in certain concentrations, CuNPs can be somewhat harmful to the surrounding environment, leading to different effects and responses. However, the study by Noman et al. (2020) revealed that the interaction between CuNPs and the soil where wheat plants (*Triticum aestivum* L.) were growing generated good outcomes for the produce, compared to other studies. The authors affirm that these outcomes are due to the "green" origin and/or green production of the CuNPs. An important concern about the presence of CuNPs in the environment is the possibility of bioaccumulation in organisms, which can happen inside the cell membranes of single-cell microorganisms or in organs, systems of sea animals, and terrestrial plants. The investigations of the modifications these nanoparticles go through are paramount to understand their potential in bioaccumulation across food webs and ecotoxicity (Ameh and Sayes, 2019; Fischer et al., 2021; Singh et al., 2021b; Torres-Duarte et al., 2016).

7 Conclusion

The use of Cu nanocomplexes (i.e., CuNPs, CuONPs, and other formulations) as nanofungicides have been reported to exhibit superior antifungal activity against mycotoxigenic fungi. The use of these Cu nanocomplexes as nanofungicides provides an additional advantage over conventional fungicides, as CuNPs can be oxidized to form CuONPs, which can easily mix with polymers or macromolecules as vehicles that i7mprove their antimicrobial, chemical, physical, and mechanical properties. The CuNPs and CuONPs can also provide the chelated Cu as a micronutrient which is required in various pathways (cofactor for enzymatic reactions, metabolism, enhance chlorophyll, seed production, and root health) in plants. In addition, Cu is involved in the formation of collagen and elastin, assists in Fe absorption which enables the body to form red blood cells, and is crucial in energy production, and Cu biodistribution can be found in the brain, heart, liver, kidneys, and skeletal muscles which helps maintain healthy bones, blood vessels, nerves, and immune function. It is through this that sufficient and well-regulated amount of Cu can help prevent cardiovascular disease and osteoporosis.

It is important to consider the ecotoxicological profile of all nanoparticles used in agriculture as they become directly and indirectly with the food supply chain with a high possibility for chronic exposure to human and animal health. Cu has a numerous advantageous applications in agriculture attributed to its physiochemical factors (antimicrobial activity) and catalytic activity in water treatment which can be fed back into the agricultural system via irrigation. Additionally, Cu accumulation in soil and water body is prominent with constant usage as this can influence the toxicity of CuNPs, CuONPs, and other Cu complexes in aquatic and terrestrial organisms. However, the toxicity of the CuNPs as nanofungicides is dedicated by a number of factors such as the synthesis (reducing and/or capping agents utilized), concentrations, surrounding medium (often aqueous), dissolved organic substances/matter,

pH, temperature, and salinity which are all ascendancy of Cu ionic (Cu^{2+} and Cu^{+}) dissolution, speciation, and toxicity, in addition to the type of crop or animal being evaluated for effectiveness against fungal and mycotoxin contamination.

Green nanotechnology has provided an avenue to limit the toxicity profile with enhanced catalytic activity of Cu nanocomplexes as nanofungicides and nanopesticides in agricultural production systems or the food industry that bring unprecedented impacts, especially in developing countries. Not only does it benefit from an economic point of view but also directly or even indirectly, in the improvement of the quality of life, increased food production per cultivated area, improving the quality of agro-industrial processes, and access to new products by a greater number of consumers. Several other sectors linked to agribusiness will inevitably benefit from green nanotechnology advances with the continuous incorporation of these new technologies. The main areas that will be significantly affected are the quality and certification of agricultural products, biotechnology, agro-energy, environmental monitoring, new uses of farm products, precision agriculture, and traceability, input industry (nanofertilizers, nanopesticides), innovations in veterinary drugs, and food preservation.

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References

Abd-Elsalam, K.A., Alghuthaymi, M.A., Shami, A., Rubina, M.S., Abramchuk, S.S., Shtykova, E.V., Vasil'kov, A.Y., 2020. Copper-chitosan nanocomposite hydrogels against aflatoxigenic aspergillus flavus from dairy cattle feed. J. Fungi 6, 1–20.

Adeyemi, J.A., Machado, A.R.T., Ogunjimi, A.T., Alberici, L.C., Antunes, L.M.G., Barbosa, F., 2020. Cytotoxicity, mutagenicity, oxidative stress and mitochondrial impairment in human hepatoma (HepG2) cells exposed to copper oxide, copper-iron oxide and carbon nanoparticles. Ecotoxicol. Environ. Saf. 189, 109982.

Akturk, A., Güler, F.K., Taygun, M.E., Goller, G., Küçükbayrak, S., 2019. Synthesis and antifungal activity of soluble starch and sodium alginate capped copper nanoparticles. Mater. Res. Express 6.

Ameh, T., Sayes, C.M., 2019. The potential exposure and hazards of copper nanoparticles: a review. Environ. Toxicol. Pharmacol. 71, 103220.

Andrivon, D., Bardin, M., Bertrand, C., Brun, L., Daire, X., Fabre, F., Gary, C., Montarry, J., Nicot, P., Reignault, P., Tamm, L., Savini, I., 2018. Can Organic Agriculture Give Up Copper as a Crop Protection Product? Summary of the Scientific Assessment Report. Condens. Rep. Sci. Collect. Assess.

Arendsen, L.P., Thakar, R., Sultan, A.H., 2019. The use of copper as an antimicrobial agent in health care, including obstetrics and gynecology. Clin. Microbiol. Rev. 32, e00125–18.

Azam, A., Ahmed, A.S., Oves, M., Khan, M.S., Memic, A., 2012. Size-dependent antimicrobial properties of CuO nanoparticles against gram-positive and -negative bacterial strains. Int. J. Nanomedicine 7, 3527–3535.

Bartolucci, C., Antonacci, A., Arduini, F., Moscone, D., Fraceto, L., Campos, E., Attaallah, R., Amine, A., Zanardi, C., Cubillana-Aguilera, L.M., Palacios Santander, J.M., Scognamiglio, V., 2020. Green nanomaterials fostering agrifood sustainability. TrAC Trends Anal. Chem. 125, 115840.

Beltrán-Partida, E., Valdez-Salas, B., Valdez-Salas, E., Pérez-Cortéz, G., Nedev, N., 2019. Synthesis, characterization, and in situ antifungal and cytotoxicity evaluation of ascorbic acid-capped copper nanoparticles. J. Nanomater. 2019, 1–10.

Benassai, E., Del Bubba, M., Ancillotti, C., Colzi, I., Gonnelli, C., Calisi, N., Salvatici, M.C., Casalone, E., Ristori, S., 2021. Green and cost-effective synthesis of copper nanoparticles by extracts of non-edible and waste plant materials from Vaccinium species: characterization and antimicrobial activity. Mater. Sci. Eng. C 119, 111453.

Bhan, S., Mohan, L., Srivastava, C.N., 2018. Nanopesticides: a recent novel ecofriendly approach in insect pest management. J. Entomol. Res. 42, 263–270.

Borkow, G., Gabbay, J., 2004. Putting copper into action: copper-impregnated products with potent biocidal activities. FASEB J. 18, 1728–1730.

Borkow, G., Gabbay, J., 2009. Copper, an ancient remedy returning to fight microbial, fungal and viral infections. Curr. Chem. Biol. 3, 272–278.

Brauer, V.S., Rezende, C.P., Pessoni, A.M., De Paula, R.G., Rangappa, K.S., Nayaka, S.C., Gupta, V.K., Almeida, F., 2019. Antifungal agents in agriculture: friends and foes of public health. Biomolecules 9, 521.

Brun, N.R., Koch, B.E.V., Varela, M., Peijnenburg, W.J.G.M., Spaink, H.P., Vijver, M.G., 2018. Nanoparticles induce dermal and intestinal innate immune system responses in zebrafish embryos. Environ. Sci. Nano, 904–916. https://doi.org/10.1039/C8EN00002F.

Camacho-Flores, B.A., Martínez-Álvarez, O., Arenas-Arrocena, M.C., Garcia-Contreras, R., Argueta-Figueroa, L., De La Fuente-Hernández, J., Acosta-Torres, L.S., 2015. Copper: synthesis techniques in nanoscale and powerful application as an antimicrobial agent. J. Nanomater.

Chang, Y.-N., Zhang, M., Xia, L., Zhang, J., Xing, G., 2012. The toxic effects and mechanisms of CuO and ZnO nanoparticles. Materials (Basel) 5, 2850–2871.

Chauhan, D., Afreen, S., Talreja, N., Ashfaq, M., 2020. Chapter 8—Multifunctional copper polymer-based nanocomposite for environmental and agricultural applications. In: Multifunctional Hybrid Nanomaterials for Sustainable Agri-Food and Ecosystems. Elsevier Inc.

Chavan, D., Kelmani, C., 2014. Biosynthesis and characterization of copper nanoparticles from *Enterococcus faecalis*. Int. J. Pharma Bio Sci. 5 (4), 204–211.

Chibber, S., Shanker, R., 2017. Can CuO nanoparticles lead to epigenetic regulation of antioxidant enzyme system? J. Appl. Toxicol. 37, 84–91.

Chudobova, D., Cihalova, K., Kopel, P., Melichar, L., Ruttkay-Nedecky, B., Vaculovicova, M., Adam, V., Kizek, R., 2015. Complexes of metal-based nanoparticles with chitosan suppressing the risk of *Staphylococcus aureus* and *Escherichia coli* Infections. In: Nanotechnology in Diagnosis, Treatment and Prophylaxis of Infectious Diseases. Elsevier Inc, pp. 217–232.

Cioffi, N., Torsi, L., Ditaranto, N., Tantillo, G., Ghibelli, L., Sabbatini, L., Bleve-Zacheo, T., D'Alessio, M., Zambonin, G., Traversa, E., 2005. Copper nanoparticle/polymer composites with antifungal and bacteriostatic properties. Chem. Mater., 5255–5262. https://doi.org/10.1021/cm0505244.

Da Costa, M.V.J., Kevat, N., Sharma, P.K., 2020. Copper oxide nanoparticle and copper (II) ion exposure in *Oryza sativa* reveals two different mechanisms of toxicity. Water Air Soil Pollut. 231, 258.

Damalas, C.A., Koutroubas, S.D., 2016. Farmers' exposure to pesticides: toxicity types and ways of prevention. Toxics 4, 1.

Duhan, J.S., Kumar, R., Kumar, N., Kaur, P., Nehra, K., 2017. Nanotechnology: the new perspective in precision agriculture. Biotechnol. Rep. (Amst.) 15, 11–23.

El-Abeid, S.E., Ahmed, Y., Daròs, J.A., Mohamed, M.A., 2020. Reduced graphene oxide nanosheet-decorated copper oxide nanoparticles: a potent antifungal nanocomposite against fusarium root rot and wilt diseases of tomato and pepper plants. Nanomaterials 10, 1001.

Elmer, W., White, J., 2018. The future of nanotechnology in plant pathology. Annu. Rev. Phytopathol., 111–133. https://doi.org/10.1146/annurev-phyto-080417-050108.

Ermini, M.L., Voliani, V., 2021. Antimicrobial nano-agents: the copper age. ACS Nano 15, 6008–6029.

Fan, X., Yahia, L., Sacher, E., 2021. Antimicrobial properties of the Ag, Cu nanoparticle system. Biology (Basel) 10, 1–37.

Farid, G., 2015. Heavy metals (Cd, Ni and Pb) contamination of soils, plants and waters in Madina town of Faisalabad metropolitan and preparation of Gis based maps. Adv. Crop Sci. Technol. 04, 1–7.

Fischer, J., Evlanova, A., Philippe, A., Filser, J., 2021. Soil properties can evoke toxicity of copper oxide nanoparticles towards springtails at low concentrations. Environ. Pollut. 270, 116084.

Gámez-Espinosa, E., Deyá, C., Cabello, M., Bellotti, N., 2021. Nanoparticles synthesised from *Caesalpinia spinosa*: assessment of the antifungal effects in protective systems. Adv. Nat. Sci. Nanosci. Nanotechnol. 12.

Hai, N.T.T., Cuong, N.D., Quyen, N.T., Hien, N.Q., Hien, T.T.D., Phung, N.T.T., Toan, D.K., Huong, N.T.T., Van Phu, D., Hoa, T.T., 2021. Facile synthesis of carboxymethyl cellulose coated core/shell. Polymers (Basel) 13, 888.

Hussain, S., Amjad, M., Noreen, M., 2021. A Perspective Study on Copper Oxide Nanoparticles and Their Role in Different Fields of Biomedical Sciences.

Ingle, A.P., Duran, N., Rai, M., 2014. Bioactivity, mechanism of action, and cytotoxicity of copper-based nanoparticles: a review. Appl. Microbiol. Biotechnol. 98, 1001–1009.

Jarvis, B.B., Miller, J.D., 2005. Mycotoxins as harmful indoor air contaminants. Appl. Microbiol. Biotechnol. 66, 367–372.

Kalatehjari, P., Yousefian, M., Khalilzadeh, M.A., 2015. Assessment of antifungal effects of copper nanoparticles on the growth of the fungus Saprolegnia sp. on white fish (*Rutilus frisii* kutum) eggs. Egypt. J. Aquat. Res. 41, 303–306.

Kamli, M.R., Srivastava, V., Hajrah, N.H., Sabir, J.S.M., Hakeem, K.R., Ahmad, A., Malik, M.A., 2021. Facile bio-fabrication of Ag-Cu-Co trimetallic nanoparticles and its fungicidal activity against candida auris. J. Fungi 7, 1–21.

Kanhed, P., Birla, S., Gaikwad, S., Gade, A., Seabra, A.B., Rubilar, O., Duran, N., Rai, M., 2014. In vitro antifungal efficacy of copper nanoparticles against selected crop pathogenic fungi. Mater. Lett. 115, 13–17.

Kruk, T., Szczepanowicz, K., Stefańska, J., Socha, R.P., Warszyński, P., 2015. Synthesis and antimicrobial activity of monodisperse copper nanoparticles. Colloids Surf. B: Biointerfaces 128, 17–22.

Lee, I., Ko, J., Park, S., Moon, C., Kim, S., Heo, J., Kim, J., 2016. Comparative toxicity and biodistribution of copper nanoparticles and cupric ions in rats. Int. J. Nanomedicine 11, 2883–2900.

Letchumanan, D., Sok, S.P.M., Ibrahim, S., Nagoor, N.H., Arshad, N.M., 2021. Plant-based biosynthesis of copper/copper oxide nanoparticles: an update on their applications in biomedicine, mechanisms, and toxicity. Biomolecules 11, 564.

Lopez-Lima, D., Mtz-Enriquez, A.I., Carrión, G., Basurto-Cereceda, S., Pariona, N., 2021. The bifunctional role of copper nanoparticles in tomato: effective treatment for Fusarium wilt and plant growth promoter. Sci. Hortic. 277.

Ma, Y., Yu, H., Liu, W., Qin, Y., Xing, R., Li, P., 2020. Integrated proteomics and metabolomics analysis reveals the antifungal mechanism of the C-coordinated O-carboxymethyl chitosan Cu(II) complex. Int. J. Biol. Macromol. 155, 1491–1509.

Mahapatra, S.S., Karak, N., 2009. Hyperbranched polyamine/Cu nanoparticles for epoxy thermoset. J. Macromol. Sci. A, 296–303. https://doi.org/10.1080/10601320802637375.

Mahmoodi, S., Elmi, A., Hallaj Nezhadi, S., 2018. Copper nanoparticles as antibacterial agents. J. Mol. Pharm. Org. Process Res. 06, 1–7.

Malandrakis, A.A., Kavroulakis, N., Chrysikopoulos, C.V., 2021. Copper nanoparticles against benzimidazole-resistant *Monilinia fructicola* field isolates. Pestic. Biochem. Physiol. 173, 104796.

Malhotra, N., Ger, T.R., Uapipatanakul, B., Huang, J.C., Chen, K.H.C., Der Hsiao, C., 2020. Review of copper and copper nanoparticle toxicity in fish. Nanomaterials 10, 1–28.

Mali, S.C., Dhaka, A., Githala, C.K., Trivedi, R., 2020. Green synthesis of copper nanoparticles using Celastrus paniculatus Willd. leaf extract and their photocatalytic and antifungal properties. Biotechnol. Rep. 27, e00518.

Manke, A., Wang, L., Rojanasakul, Y., 2013. Mechanisms of nanoparticle-induced oxidative stress and toxicity. Biomed. Res. Int. 2013, 942916.

Mastin, B.J., Rodgers, J.H., 2000. Toxicity and bioavailability of copper herbicides (clearigate, cutrine-plus, and copper sulfate) to freshwater animals. Arch. Environ. Contam. Toxicol. 39, 445–451.

Maziero, J.S., Thipe, V.C., Rogero, S.O., Cavalcante, A.K., Damasceno, K.C., Ormenio, M.B., Martini, G.A., Batista, J.G.S., Viveiros, W., Katti, K.K., Karikachery, A.R., Mohandoss, D.D., Dhurvas, R.D., Nappinnai, M., Rogero, J.R., Lugão, A.B., Katti, K.V., 2020. Species-specific in vitro and in vivo evaluation of toxicity of silver nanoparticles stabilized with gum Arabic protein. Int. J. Nanomedicine 15, 7359–7376.

Mosa, K.A., El-Naggar, M., Ramamoorthy, K., Alawadhi, H., Elnaggar, A., Wartanian, S., Ibrahim, E., Hani, H., 2018. Copper nanoparticles induced genotoxicty, oxidative stress, and changes in superoxide dismutase (SOD) gene expression in cucumber (*Cucumis sativus*) plants. Front. Plant Sci. 9, 1–13.

Mujeeb, A.A., Khan, N.A., Jamal, F., Badre Alam, K.F., Saeed, H., Kazmi, S., Alshameri, A.W.F., Kashif, M., Ghazi, I., Owais, M., 2020. Olax scandens mediated biogenic synthesis of Ag-Cu nanocomposites: potential against inhibition of drug-resistant microbes. Front. Chem. 8, 1–12.

Mukherji, S., Ruparelia, J., Agnihotri, S., 2012. Antimicrobial activity of silver and copper nanoparticles. In: Cioffi, N., Rai, M. (Eds.), Nano-Antimicrobials: Progress and Prospects, pp. 1–556.

National Research Council, 2000. Copper in Drinking Water. The National Academies Press, Washington, DC.

Nisar, P., Ali, N., Rahman, L., Ali, M., Shinwari, Z.K., 2019. Antimicrobial activities of biologically synthesized metal nanoparticles: an insight into the mechanism of action. J. Biol. Inorg. Chem. 24, 929–941.

Noman, M., Shahid, M., Ahmed, T., Tahir, M., Naqqash, T., Muhammad, S., Song, F., Abid, H.M.A., Aslam, Z., 2020. Green copper nanoparticles from a native *Klebsiella pneumoniae*

strain alleviated oxidative stress impairment of wheat plants by reducing the chromium bioavailability and increasing the growth. Ecotoxicol. Environ. Saf. 192.

Olchowik, J., Bzdyk, R.M., Studnicki, M., Bederska-Błaszczyk, M., Urban, A., Aleksandrowicz-Trzcińska, M., 2017. The effect of silver and copper nanoparticles on the condition of English oak (*Quercus robur* L.) seedlings in a container nursery experiment. Forests 8, 310.

Pařil, P., Baar, J., Čermák, P., Rademacher, P., Prucek, R., Sivera, M., Panáček, A., 2017. Antifungal effects of copper and silver nanoparticles against white and brown-rot fungi. J. Mater. Sci. 52, 2720–2729.

Pariona, N., Mtz-Enriquez, A.I., Sánchez-Rangel, D., Carrión, G., Paraguay-Delgado, F., Rosas-Saito, G., 2019. Green-synthesized copper nanoparticles as a potential antifungal against plant pathogens. RSC Adv. 9, 18835–18843.

Parra, B., Tortella, G., Cuozzo, S., Martínez, M., 2019. Negative effect of copper nanoparticles on the conjugation frequency of conjugative catabolic plasmids. Ecotoxicol. Environ. Safety 169, 662–668. https://doi.org/10.1016/j.ecoenv.2018.11.057.

Peixoto, S., Henriques, I., Loureiro, S., 2020. Long-term effects of Cu(OH)2 nanopesticide exposure on soil microbial communities. Environ. Pollut. 269, 116113.

Perrotta, B.G., Simonin, M., Back, J.A., Anderson, S.M., Avellan, A., Bergemann, C.M., Castellon, B.T., Colman, B.P., Lowry, G.V., Matson, C.W., Bernhardt, E.S., King, R.S., 2020. Copper and gold nanoparticles increase nutrient excretion rates of primary consumers. Environ. Sci. Technol. 54, 10170–10180.

Pilon, M., Abdel-Ghany, S.E., Cohu, C.M., Gogolin, K.A., Ye, H., 2006. Copper cofactor delivery in plant cells. Curr. Opin. Plant Biol. 9, 256–263.

Pinto, M.R., Barreto-Bergter, E., Taborda, C.P., 2008. Glycoconjugates and polysaccharides of fungal cell wall and activation of immune system. Braz. J. Microbiol. 39, 195–208.

Ponmurugan, P., Manjukarunambika, K., Elango, V., Gnanamangai, B.M., 2016. Antifungal activity of biosynthesised copper nanoparticles evaluated against red root-rot disease in tea plants. J. Exp. Nanosci. 11, 1019–1031.

Quaranta, D., Krans, T., Santo, C.E., Elowsky, C.G., Domaille, D.W., Chang, C.J., Grass, G., 2011. Mechanisms of contact-mediated killing of yeast cells on dry metallic copper surfaces. Appl. Environ. Microbiol. 77, 416–426.

Rasool, A., John, M., Shamsul, P., 2021. Copper : uptake, toxicity and tolerance in plants and management of Cu-contaminated soil. Biometals 34, 737–759. 0123456789.

Ray, D., Pramanik, S., Mandal, R.P., Chaudhuri, S., De, S., 2015. Sugar-mediated "green" synthesis of copper nanoparticles with high antifungal activity. Mater. Res. Express 2, 105002.

Robinson, J.R., Isikhuemhen, O.S., Anike, F.N., 2021. Fungal–metal interactions: a review of toxicity and homeostasis. J. Fungi 7, 225.

Safaei, M., Taran, M., Imani, M.M., 2019. Preparation, structural characterization, thermal properties and antifungal activity of alginate-CuO bionanocomposite. Mater. Sci. Eng. C 101, 323–329.

Sanzari, I., Leone, A., Ambrosone, A., 2019. Nanotechnology in plant science: to make a long story short. Front. Bioeng. Biotechnol. 7, 120.

Shang, Y., Hasan, M.K., Ahammed, G.J., Li, M., Yin, H., Zhou, J., 2019. Applications of nanotechnology in plant growth and crop protection: a review. Molecules 24, 2558.

Shang, H., Ma, C., Li, C., White, J.C., Polubesova, T., Chefetz, B., Xing, B., 2020. Copper sulfide nanoparticles suppress Gibberella fujikuroi infection in rice (*Oryza sativa* L.) by multiple mechanisms: contact-mortality, nutritional modulation and phytohormone regulation. Environ. Sci. Nano 7, 2632–2643.

Shiny, K.S., Sundararaj, R., Mamatha, N., Lingappa, B., 2019. A new approach to wood protection: preliminary study of biologically synthesized copper oxide nanoparticle formulation as an environmental friendly wood protectant against decay fungi and termites. Maderas Cienc. Tecnol. 21, 347–356.

Singh, H., Sharma, A., Bhardwaj, S.K., Arya, S.K., Bhardwaj, N., Khatri, M., 2021a. Recent advances in the applications of nano-agrochemicals for sustainable agricultural development. Environ Sci Process Impacts 23, 213–239.

Singh, B.K., Tiwari, S., Dubey, N.K., 2021b. Essential oils and their nanoformulations as green preservatives to boost food safety against mycotoxin contamination of food commodities: a review. J. Sci. Food Agric.

Song, L., Connolly, M., Fernández-Cruz, M.L., Vijver, M.G., Fernández, M., Conde, E., de Snoo, G.R., Peijnenburg, W.J.G.M., Navas, J.M., 2014. Species-specific toxicity of copper nanoparticles among mammalian and piscine cell lines. Nanotoxicology 8, 383–393.

Tegenaw, A., Sorial, G.A., Sahle-Demessie, E., Han, C., 2020. Influence of water chemistry on colloid-size Cu-based pesticides particles: a case of Cu(OH)2 commercial fungicide/bactericide. Chemosphere 239, 124699.

Thannickal, V.J., Fanburg, B.L., 2000. Reactive oxygen species in cell signaling. Am. J. Phys. Lung Cell. Mol. Phys. 279, L1005–L1028.

Tilman, D., Cassman, K.G., Matson, P.A., Naylor, R., Polasky, S., 2002. Agricultural sustainability and intensive production practices. Nature 418, 671–677.

Torres-Duarte, C., Adeleye, A.S., Pokhrel, S., Mädler, L., Keller, A.A., Cherr, G.N., 2016. Developmental effects of two different copper oxide nanomaterials in sea urchin (*Lytechinus pictus*) embryos. Nanotoxicology 10, 671–679.

Valko, M., Rhodes, C.J., Moncol, J., Izakovic, M., Mazur, M., 2006. Free radicals, metals and antioxidants in oxidative stress-induced cancer. Chem. Biol. Interact. 160, 1–40.

Van Cao, D., Nguyen, P.P., Khuong, V.Q., Nguyen, C.K., Nguyen, X.C., Dang, C.H., Tran, N.Q., 2014. Ultrafine copper nanoparticles exhibiting a powerful antifungal/killing activity against Corticium salmonicolor. Bull. Kor. Chem. Soc. 35, 2645–2648.

Van Nguyen, D., Nguyen, H.M., Le, N.T., Nguyen, K.H., Mai, H., 2020. Copper nanoparticle application enhances plant growth and grain yield in maize under drought stress conditions. J. Plant Growth Regul.

Viet, P.V., Nguyen, H.T., Cao, T.M., Hieu, L.V., 2016. *Fusarium* antifungal activities of copper nanoparticles synthesized by a chemical reduction method. J. Nanomater. https://doi.org/10.1155/2016/1957612.

Waldron, K.J., Robinson, N.J., 2009. How do bacterial cells ensure that metalloproteins get the correct metal? Nat. Rev. Microbiol. 7, 25–35.

Walusinski, O., 2018. The scientific illusion of Victor Burq (1822–1884). Eur. Neurol. 79, 135–149.

Weaver, L., Michels, H.T., Keevil, C.W., 2010. Potential for preventing spread of fungi in air-conditioning systems constructed using copper instead of aluminium. Lett. Appl. Microbiol. 50, 18–23.

Wei, Y., Chen, S., Kowalczyk, B., Huda, S., Gray, T.P., Grzybowski, B.A., 2010. Synthesis of stable, low-dispersity copper nanoparticles and nanorods and their antifungal and catalytic properties. J. Phys. Chem. C 114, 15612–15616.

Xin, X., Zhao, F., Rho, J.Y., Goodrich, S.L., Sumerlin, B.S., He, Z., 2020. Use of polymeric nanoparticles to improve seed germination and plant growth under copper stress. Sci. Total Environ. 745.

Yruela, I., 2005. Copper in plants. Braz. J. Plant Physiol. 17, 145–156.

Zhang, Z.-Z., Xu, J.-J., Shi, Z.-J., Cheng, Y.-F., Ji, Z.-Q., Deng, R., Jin, R.-C., 2017. Short-term impacts of Cu, CuO, ZnO and Ag nanoparticles (NPs) on anammox sludge: CuNPs make a difference. Bioresource Technol. 235, 281–291. https://doi.org/10.1016/j.biortech.2017.03.135.

Further reading

Sevindik, M., 2018. Fungal factors in food products deterioration. Res. Rev.: Res. J. Biol. 6. Open Access Journals [WWW Document].

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CHAPTER

Copper-based nanostructures for plant disease management

8

Felipe Mondaca[a], Arturo I. Mtz-Enriquez[a], and Nicolaza Pariona[b]

[a]*Cinvestav-Saltillo, Ramos Arizpe, Coahuila, Mexico*

[b]*Department of Advanced Molecular Studies, The Institute of Ecology A.C. (INECOL), Xalapa, Veracruz, Mexico*

1 Introduction

Plant diseases caused by different pathogens have damaged agroecosystems since the dawn of agriculture. If plant diseases are not controlled, not only significant economic losses can occur, but also social upheaval and human live losses may succeed. For example, ca.1845, potatoes in Ireland were affected by a parasite called *Phytophthora infestans*. The epidemic was called potato late blight and lead to the death of a million people due to famine as the population was dependent on this food for their subsistence (Yoshida et al., 2013). In early 1900, *Cryphonectria parasitica* caused the disease called chestnut blight, which triggered the near extinction of *American chestnut*, a tree usually found in the Eastern United States (Anagnostakis, 1987). Another important epidemic was caused by *Bipolaris maydis*, which caused major problems of southern corn leaf blight in the United States in 1970 (Ullstrup, 1972). Therefore, pesticides have been important in attaining the desired crop protection and prevent plant diseases. Among pesticides, the main compounds are fungicides, particularly azole antifungals that are the preferred treatment owing to their relatively low cost and effectiveness against a broad range of fungi (Price et al., 2015). However, as most of these fungicides act directly on essential fungal functions and are site-specific, the target fungi can develop resistance becoming an ineffective fungicide (Leroux, 2003).

Due to their antimicrobial properties (Borkow and Gabbay, 2009) and to be part of the essential micronutrients of the plants (Printz et al., 2016), copper (Cu) compounds have been widely used as inorganic agrochemicals for crop protection and as fertilizers. However, the application of excess Cu may have negative effects on crops and environmental pollution. The copper compounds as nanoparticles (NPs) could enhance the antimicrobial properties, which may reduce the doses. In the last years, several studies have shown that Cu-based NPs are effective against different plant pathogens (Cruz et al., 2021; Hermida-Montero et al., 2019; Kanhed et al., 2014; Shende et al., 2021). Cu-based NPs offer advantages over conventional pesticides and other

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inorganics-based nanomaterials because they are cheaper than Ag and TiO_2. However, the antimicrobial properties of the Cu-based NPs, aside from the size, shape, or type of microorganism, depend on the chemical composition and oxidation state: (i) copper metal (Cu), (ii) Cu-based nanocomposites, and (iii) other nanostructures containing Cu such as copper oxides (CuO and Cu_2O), sulfates, sulfides, phosphates, etc. (Hermida-Montero et al., 2019). Additionally, the synthesis parameters such as solvents, precursors, temperature, etc. determine the antimicrobial activity of Cu-based NPs. For the application of Cu-based NPs in agriculture, the synthesis method should be eco-friendly and scalable. Among the synthesis methods to produce Cu-based NPs, chemical methods are reported as the most popular, such as hydrothermal and polyol methods (Borgatta et al., 2018). Additionally, the synthesis including microorganisms or extracts of plants has been reported (Chen et al., 2019; Kasana et al., 2017). In this chapter, new strategies to control plant diseases toward sustainable agriculture, the antimicrobial activity of Cu-based NPs against plant pathogen microorganisms (Table 1) as well as their possible mechanism are reviewed.

2 Copper-based nanostructures against plant pathogen fungi

Various Cu-based NPs have been evaluated as antifungal agents for the control of phytopathogens. Different studies have shown that the antifungal activity of these materials will depend on the crystal phase, concentration, morphology, and size. Among Cu-based NPs, Cu-NPs and CuO-NPs and Cu_2O-NPs have been mostly studied. In in vitro studies, four plant pathogenic fungi; *Phoma destructiva*, *Curvularia lunata*, *Alternaria alternata*, and *Fusarium oxysporum* have been inhibited by spherical Cu-NPs of 3–10 nm synthesized by chemical reduction (Kanhed et al., 2014). The authors showed that the fungicidal activity of the Cu-NPs depended on the fungal species; for example, *Alternaria alternata* was less susceptible to Cu-NPs and *F. oxysporum* was highly inhibited. Likewise, a study evaluated the antifungal properties of Cu-NPs of different sizes and concentrations against *Phytophthora capsica* and *F. oxysporum* and found that the growth inhibition of the fungi increased with increasing concentration and decreasing particle size. Also, the highest growth inhibition was obtained for *F. oxysporum* (Pham et al., 2019). On the other hand, the antifungal effect of different concentrations (0.1, 0.25, 0.5, 0.75, and 1 mg/mL) of Cu-NPs was reported. *F. solani* showed the highest degree of inhibition at low concentration of Cu-NPs (0.1 mg/mL), while *F. oxysporum* was inhibited at 0.25 mg/mL, and *Neofusicoccum* sp. at 0.5 mg/mL (Pariona et al., 2019). Furthermore, Cu-NPs with different concentrations of cetyltrimethylammonium bromide (an antiseptic agent) was used for the inhibition of *Fusarium* (Bramhanwade et al., 2016).

Some studies suggest the susceptibility of the fungi toward Cu-NPs which could be related to the secretion of oxalic acid by fungi. The oxalic acid is involved in buffering the fungal microenvironment, in the regulation of oxidative enzyme activity, and chelation of metals (Cessna et al., 2000; Osińska-Jaroszuk et al., 2014). Also,

Table 1 Cu-based NPs against plant pathogens.

NPs	Pathogen	Application	Disease	Crop	Reference
Cu-NPs	*Fusarium solani and Neofusicoccum* sp.	Antifungal Antifungal	Panama disease Canker and dieback	Banana plants Perennial fruit crops and trees	Pariona et al. (2019)
Cu-NPs	*F. oxysporum* f. sp. *lycopersici*	Antifungal	Vascular wilt disease	Tomato plants	Lopez-Lima et al. (2021)
Cu-NPs	*Colletotrichum capsici*	Antifungal	Anthracnose and fruit rot	Chilli crop	Iliger et al. (2021)
Mix Cu/Cu_2O-NPs	*Fusarium* sp.	Antifungal	Wilt disease	Tomato, potato, dragon fruit, watermelon plants and other cucurbits, and among others	Van Viet et al. (2016)
$Cu_3(PO_4)_2{\cdot}3H_2O$ nanosheets	*F. oxysporum* f. sp. *niveum*	Antifungal	Fusarium wilt of watermelon	Watermelon	Borgatta et al. (2018)
Copper-chitosan NPs	*Pyricularia grisea*	Antifungal	Blast disease	Finger millet plants	Sathiyabama and Manikandan (2018)
CuZn bimetallic	*Saccharomyces cerevisiae*	Antifungal	–	Tomato plants	Antonoglou et al. (2018)
Chitosan capped-copper nanobiocomposites	*Fusarium* sp., *Aspergillus* sp., *Alternaria alternata*, *Pythium* sp., and *Bacillus cereus*	Antifungal Antibacterial	–	Ginger plants	Mehta et al. (2021)
GO-Cu-NCs	*Pseudomonas syringae* pv. tomato	Antibacterial	Bacterial speck disease	Tomato plants	Li et al. (2017)
MoS_2-CuNPs	*Xanthomonas oryzae* pv. *oryzae*	Antibacterial	Bacterial leaf blight	Rice leaves	Li et al. (2020)
Gly-$Cu(OH)_2$·NPs	*Xanthomonas campestris* pv. *campestris*	Antibacterial	Cabbage black disease	Brassicas crops	Dong et al. (2020)
MV-Cu	*Xanthomonas euvesicatoria*	Antibacterial	Bacterial spot disease	Pepper	Fan et al. (2021)
MV-CuSiNG	*Xanthomonas alfalfae* and *Escherichia coli*	Antibacterial	Citrus canker disease	Citrus	Young and Santra (2014)
CuO-NPs	*Ralstonia solanacearum*	Antibacterial	Bacterial wilt	Tobacco plants	Chen et al. (2019).
Cu-NPs	*Xanthomonas axonopodis* pv. *punicae*	Antibacterial	Bacterial blight disease	Pomegranate	Mondal and Mani (2012)
CuO-NPs	*Phoma destructiva* and *Curvularia lunata*	Antibacterial	–	Black mustard	Tamil Elakkiya et al. (2021)
Cu@TWEEN20 and Cu_2O@TWEEN20 NPs	*Pseudomonas syringae*	Antibacterial	Leaf spots, cankers, and frost damage to plants	Bean plants	Gkanatsiou et al. (2019)

a study of two plant pathogenic fungi, *Botrytis cinerea* and *Alternaria alternata* exposed to microparticulate (CuO or NPs of Cu or CuO), reported that not only the overproduction of oxalic acid but also the ability of copper bioaccumulation is related to the resistance of the fungi. The authors revealed that *Botrytis cinerea* is tolerant to copper species due to their ability to biotransform Cu and CuO to Cu-oxalate (Kovačec et al., 2017). To compare the antifungal activity of different NPs, seven fungal species (*Botrytis cinerea, Alternaria alternata, Monilinia fructicola, Colletotrichum gloeosporioides, F. solani, F. oxysporum* f. sp. *radicis lycopersici*, and *Verticillium dahlia*) that cause foliar and soil-borne diseases were exposed to different NPs, namely, Cu-NPs, CuO-NPs, Ag-NPs, and ZnO-NPs. This was found that the NPs inhibited the mycelial growth for all fungal species in a dose-response manner and Cu-NPs were the most effective among the NPs, even more than CuO-NPs. Additionally, they highlight that Cu-NPs and CuO-NPs were more effective than their counterparts $Cu(OH)_2$ (Malandrakis et al., 2019). Similarly, Cu/Cu_xO-NPs synthesized in aqueous-phase were evaluated against *F. oxysporum*; it was reported that NPs with a higher ratio of Cu_2O (80%) and relatively smaller particle size (42 nm) were more effective to inhibit *F. oxysporum* than NPs containing 87% of CuO (13 nm) (Hermida-Montero et al., 2019). The great antifungal activity of the mix Cu/Cu_2O-NPs (20–50 nm) was also exhibited against *Fusarium* sp. which inhibited 93.98% of the fungal growth (Van Viet et al., 2016). Another study conducted with Cu_2O, CuO, and Cu/Cu_2O-NPs against the late blight disease on tomato plants (Caused by *Phytophthora infestans*) showed that despite all Cu-based NPs found to be effective, the efficacy of NPs was different. After 10 days of application, Cu_2O-NPs were more effective, followed by the mix Cu/Cu_2O-NPs, and finally by CuO-NPs. However, Cu/Cu_2O NPs exhibited the highest phytotoxicity in comparison with the rest of the samples, which is attributed to the presence of the Cu metal core (Giannousi et al., 2013).

The role of the morphology of copper-based NPs was studied for the control of root fungal disease in watermelon (*Citrullus lanatus*). In in vitro experiments, at a concentration of 50 and 500 mg/L, the authors found that $Cu_3(PO_4)_2{\cdot}3H_2O$ with sheet-like morphology significantly reduced the fungal biomass of *F. oxysporum* compared with CuO-NPs with irregular morphology (Borgatta et al., 2018). In the same study, they also investigated the effect of two application methods (root application and foliar spray). In vivo experiments were carried out with NPs concentrations higher (10–1000 mg/L) than those used in in vitro experiments. With 10 mg/L of $Cu_3(PO_4)_2{\cdot}3H_2O$ nanosheets were enough to repress fungal disease, while CuO-NPs needed 1000 mg/L. Other work reported that the application of CuO-NPs not only showed high efficacy against both *Fusarium* and *Verticillium* wilt but also improved the yield of tomatoes by 33% and 34% for eggplants (Elmer and White, 2016). In a greenhouse experiment, foliar application of CuO on watermelon plants reduced the *Fusarium* wilt more than other NPs (MnO, SiO, Ti, and ZnO). Additionally, treatments with CuO produced 39% more watermelon fruit (Elmer et al., 2018). On the other hand, the pathogen *F. oxysporum* f. sp. *lycopersici* that occurs in tomatoes can be treated with CuO NPs and $Cu_3(PO_4)_2{\cdot}3H_2O$ nanosheets. They also mention that

nanosheets have a better performance to improve the cultivation of fruits in plants (Ma et al., 2019). In the last year, the bifunctional role of Cu-NPs in tomato plants was reported. Globally, tomato plant is an important commercial crop that can be affected by *Fusarium* wilt disease. For that, the antifungal efficacy of Cu-NPs against vascular wilt disease which is caused by *F. oxysporum* f. sp. *lycopersici* was evaluated. In in vitro experiments at 0.5 mg/mL Cu-NPs showed higher antifungal efficacy (67.3%) than copper hydroxide. Meanwhile, with the same concentration, Cu-NPs reduced both the incidence of the *Fusarium* wilt by 68 and severity by 66.5%. Additionally, increased growth of tomato plants was observed (Lopez-Lima et al. 2021).

The comparative antifungal activities between silica and copper NPs against *Phomopsis theae* and *Poria hypolateritia* have been evaluated. Phomopsis canker and red root-rot diseases in tea plants are caused by the *Phomopsis theae* and *Poria hypolateritia*, respectively. The syntheses of the NPs were done using biocontrol agents such as *Pseudomonas fluorescens*, *Trichoderma atroviride*, and *Streptomyces griseus*. The study found that the biosynthesized copper NPs showed the highest growth inhibition for both *Poria hypolateritia* (74.76%) and *Phomopsis theae* (73.10%). Thus, the authors concluded that copper NPs have the potential for the management of diseases in tea plantations (Natesan et al., 2020). Resistance induction in finger millet plants by copper-chitosan NPs against blast disease caused by *Pyricularia grisea* was reported. The in vitro experiments showed that at 0.1 mg/mL of copper-chitosan NPs, near 80% of the radial growth was inhibited. While in vivo experiments in the application of copper-chitosan NPs as a foliar spray or as a combined (involving seed coat and foliar spray) suppress the blast disease development on finger millet plants. It was concluded that copper-chitosan NPs promoted the activity of defense enzymes, which increased the plants' protection against the blast pathogen (Sathiyabama and Manikandan, 2018). Likewise, the efficacy of the copper-chitosan NPs as antifungal was shown for *Alternaria alternata*, *Macrophomina phaseolina,* and *Rhizoctonia solani*. It was reported that copper-chitosan NPs are most effective at a concentration of 0.1% and showed 89.5%, 63.0%, and 60.1% growth inhibition for *Alternaria alternata, Macrophomina phaseolina* and *Rhizoctonia solani*, respectively (Saharan et al. 2013). Mycelial growth of *Rhizoctonia solani* and *Pythium aphanidermatum*, which are responsible for the damping-off diseases in seeds and young seedlings, were inhibited by Chitosan-coupled copper NPs (Ch-CuNPs). The in vitro study revealed that at 0.1% Ch-CuNPs, up to 94% and 98% inhibition of the growth of *Rhizoctonia solani* and *Pythium aphanidermatum,* respectively, were obtained. Also, the authors demonstrated that at 0.2% concentration of Ridomil fungicide and copper sulfate, the inhibition of the phytopathogens was lower than that obtained by Ch-CuNPs. Moreover, they showed that at $\leq$0.2%, Ch-CuNPs not only were nontoxic to chili, cowpea, and tomato plants but also promoted the growth of chili seedlings (Vanti et al., 2020). It was reported that curcumin functionalized copper NPs (Cur-CuNPs) inhibited the *F. oxysporum* f. sp. *ciceris* (FOC) growth and enhanced the chickpea wilt resistance. FOC get in through root vascular bundles provoking the wilt and death of chickpea plants. The author showed that nearly 65% of FOC fungi growth was inhibited by Cur-CuNPs in in vitro conditions. This result

was attributed to the combination of Cu^{+} ions with the curcumin in the nanoscale. Besides, the application of Cur-CuNPs on seeds enhanced the germination and growth of chickpea plants (Sathiyabama et al., 2020). Currently, there is increased research on the antifungal activity of bimetallic nanomaterials, for example, CuZn bimetallic NPs were evaluated against *Saccharomyces cerevisiae*. The investigation found that the antifungal activity of bimetallic NPs against *S. cerevisiae* was better than that of Cu-NPs. Also, to investigate the phytotoxicity of bimetallic NPs, the authors sprayed CuZn bimetallic NPs on tomato plants and analyzed the photosystem II efficiency by chlorophyll fluorescence imaging. The results showed no phytotoxic effects of CuZn bimetallic NPs on tomato plants (Antonoglou et al., 2018).

3 Copper-based nanostructures against plant pathogen bacteria

Several recent studies have reported the antimicrobial activity of Cu, CuO, and Cu_2O NPs (Azam et al., 2012; Din et al., 2017; Giannousi et al., 2017; Kanhed et al., 2014; Pariona et al., 2019); these reports have proposed the use of the Cu-based NPs as alternative pesticides for the management of plant pathogen bacteria. Most of the studies have largely been done under in vitro conditions. CuO-NPs was evaluated against *Ralstonia solanacearum*, which is responsible for the bacterial wilt in tobacco plants. Under laboratory conditions, 0.25 mg/mL of the CuO-NPs inhibited 100% of the growth of *R. solanacearum*. Meanwhile, in a greenhouse experiment, only 32.5% of disease occurrence was reported with treated CuO-NPs in comparison to the untreated samples (98.5%). The strong antibacterial activity of the CuO-NPs was attributed to the interaction of bacterial cells with NPs, which avoid biofilm formation, reduce swarming motility, and disturb ATP production (Chen et al. 2019). Another study reported the antibacterial effectiveness of CuO-NPs obtained by *Penicillium chrysogenum* filtrate utilizing copper sulfate at various gamma rays' doses. Among the phytopathogen microorganisms evaluated, *R. solanacearum* and *Erwinia amylovora* were highly inhibited by CuO-NPs (El-Batal et al. 2020). The great antibacterial activity of Cu-NPs was shown against *X. axonopodis* pv. *punicae*, which cause the bacterial blight disease in pomegranate. It was reported that the growth of *X. axonopodis* was suppressed at 0.2 mg/L of Cu-NPs, 10,000 times lower than Cu-oxychloride (Mondal and Mani, 2012).

The antibacterial activity of different nanomaterials such as Cu, CaO, CuO, MgO, and ZnO with the size of 75, 161, 163, 144, and 177 nm, respectively, have been evaluated against *X. axonopodis* pv. *punicae*. In in vitro assessment, Cu-NPs exhibited higher antimicrobial activity at lower concentrations (2.5 μg/mL) than the other NPs. The antibacterial activity of Cu-NPs was higher than the CuO-NPs. Due to the high in vitro effectiveness, the antibacterial activity of Cu-NPs was evaluated in a greenhouse, as well as in field conditions, and copper oxychloride was used as a positive control. They found that foliar application of Cu-NPs (400 μg/mL) reduced the disease by ~90% at an early stage and 15% established stage reduction in greenhouse

conditions. Meanwhile, in field condition Cu-NPs reduced the disease incidence by ~20% as compared to untreated control (Chikte et al., 2019). The effect of different Cu-based nanocomposites such as Cu@Tween20, Cu@TEG, Cu_2O@TWEEN20, and CuO@PEG1000) were evaluated on three phytopathogenic Gram-negative bacterial strains, *Erwinia amylovora*, *X. campestris,* and *Pseudomonas syringae*. In in vitro experiments, both Cu@Tween20 and Cu@TEG showed the highest inhibition % for the three evaluated bacteria, followed by Cu_2O@TWEEN20 and finally CuO@PEG1000. The authors selected Cu@TWEEN20 and Cu_2O@TWEEN20 NPs for in vivo antibacterial assays against *Pseudomonas syringae* on bean plants using the foliar method. It was demonstrated that Cu@TWEEN20 was most effective to control *Pseudomonas syringae*. It was shown the Cu-composites were more efficient antibacterial agents than Cu_2O- and CuO composites, which suggests that the oxidation state of copper is one of the main factors for the enhancement of the antimicrobial activity of the Cu-based nanocomposites (Gkanatsiou et al., 2019). Those results show the effectiveness of Cu-based NPs as bactericides.

New strategies for improving the antibacterial activity of copper-based NPs have been reported, for example, the preparation of Cu-NPs/graphene oxide nanocomposites (GO-Cu-NCs). These composites have been evaluated against *Pseudomonas syringae* pv. tomato (Pst) and its antibacterial effectiveness were compared with the bactericide Kocide 3000. The GO-Cu-NCs exhibited a 16-times higher antibacterial activity than Kocide 3000. Furthermore, for a reduction of bacterial speck below 25%, it was necessary to have 4–8 and 125–250 μg/mL of the GO-Cu-NCs and Kocide 3000, respectively. In this way, the authors showed that GO-Cu-NCs have great potential for managing crop diseases against *Pseudomonas syringae* (Li et al., 2017). To attack different bacteria at the same time, mixed-valence copper loaded silica nanogel composites (MV-CuSiNG) have been tested. Amorphous silica was used as an inert host matrix for embedding Cu in its mixed-valence states (Cu^0, Cu^{1+}, and Cu^{2+}). Minimum inhibitory concentration was used to evaluate the MV-CuSiNG, copper loaded silica nanogel (CuSiNG), $CuSO_4$, CuCl and Kocide 3000 against *X. alfalfae* and *Escherichia coli*. Their results showed that the treatments with MV-CuSiNG, a concentration of only 187.5 μg/mL Cu were used, compared to other bactericides where concentrations higher than 375 μg/mL Cu were necessary for effective inhibition. Finally, tests in greenhouse conditions for *Vinca* sp. and *Hamlin orange* were evaluated, the study showed slight phytotoxicity for the MV-CuSiNG, which indicated the potential usefulness of this composite as biocide (Young and Santra, 2014). The antibacterial effect of three Cu-based composites including Cu, Cu_2O, and CuO embedded silica matrix (MV-Cu), silica core with a shell layer of Cu nanocomposite (CS-Cu), and silica gel embedded with quaternary ammonium (NH^{4+}) with metallic Cu (FQ-Cu). These three nanocomposites have been evaluated against *X. euvesicatoria*, which cause bacterial spot disease in bell pepper. The results of the study demonstrated that the growth of *X. euvesicatoria* completely inhibited with different concentrations (100, 200, 500, and 1000 μg/mL) of CS-Cu and FQ-Cu in 1 h, meanwhile with MV-Cu (500 and 1000 μg/mL) in 24 h. In greenhouse assays, the three Cu-based composites significantly decreased disease severity in

comparison to Kocide 3000. However, CS-Cu or FQ-Cu at 500 µg/mL showed phytotoxicity to pepper plants, which mean that although MV-Cu took longer to inhibit, it is safer and more effective (Fan et al. 2021).

X. oryzae pv. *oryzae* (*X. oryzae*) is a bacterial pathovar, causing bacterial leaf blight (BLB) disease in rice. *X. oryzae* develops resistance against available antibiotics rapidly. Additionally, the antibacterial activity of Cu-NPs against *X. oryzae* has been evaluated, it was found that the size and concentration depends strongly on their antibacterial activity. The Cu-NPs of 28 nm exhibited the best antibacterial efficiency against *X. oryzae* at a concentration of 0.8 µg/mL. The authors attributed the antibacterial activity of these Cu-NPs to the increased production of reactive oxygen radicals. Furthermore, the antibacterial properties of these NPs were better than commercial antibiotic streptomycin sulfate (Majumdar et al., 2019). On the other hand, glycine-functionalized copper (II) hydroxide NPs (Gly-$Cu(OH)_2$) were reported as bactericide against *X. campestris* pv. *campestris* (Xcc), which cause the cabbage black disease in brassicas crops. The antimicrobial experiment in vitro was carried out using Kocide 3000 as a commercial control. The results showed that Gly-$Cu(OH)_2$ NPs with half concentration (100 mg/L) than Kocide 3000 (200 mg/L) suppressed the growth of Xcc. The role of glycine in copper NPs was to avoid NPs aggregation. Also, they evaluated the antibacterial efficacy of Gly-$Cu(OH)_2$ NPs against black rot disease in Chinese cabbage and tomato plants. Similarly, to the in vitro experiments, Gly-$Cu(OH)_2$·NPs showed higher efficacy diminishing the black rot disease severity than Kocide 3000. Additionally, the improved growth of Chinese cabbage and tomato plants was observed with Gly-$Cu(OH)_2$ NPs (Dong et al., 2020). Another nanocomposite reported as an excellent bactericide is the molybdenum disulfide sheets loaded with copper NPs (MoS_2-Cu-NPs). The authors evaluated the antibacterial properties of this nanocomposite against *X. oryzae* pv. *oryzae* (Xoo) in both in vitro and in vivo. The results of this investigation evidenced that MoS_2-Cu-NPs were 19.2 times more effective against Xoo cells than Kocide 3000. On the other hand, foliar application of MoS_2-Cu-NPs on rice leaves reduced the disease severity from 86.25% to 7.5%. The authors emphasized that MoS_2-CuNPs can prevent the infection of Xoo cells through the formation of the protective film and increasing the number of trichomes (45.06%) on the surface of rice leaves. Furthermore, MoS_2-CuNPs were reported to have increased chlorophyll improved the growth of rice seedlings (Li et al., 2020).

4 Possible mechanism of Cu-based NPs in plants for diseases management

Numerous researches have described the possible antimicrobial mechanism of Cu and copper oxide NPs. Most of them have attributed the antimicrobial activity to the oxidative stress induced by the generation of reactive oxygen species (ROS), which can be produced by both NPs and Cu-ions released from the NPs (Dizaj et al., 2014; Lungu et al., 2017; Slavin et al., 2017). The direct antimicrobial mechanism of Cu-based NPs against phytopathogen microorganisms has been evidenced by

various researches. Interaction of CuO-NPs on the *R. solanacearum* bacteria surface (Fig. 1D) and followed by destabilization of the cell wall and membrane (Fig. 1B and C) was observed by TEM images (Chen et al. 2019).

The latter was also observed in fungi with SEM images (Fig. 2), where the application of Cu-NPs on *F. solani* (Fig. 2B) growth cause destabilization on the cell wall with a change in their permeability and thus facilitating the entry of the NPs into the cell.

The propidium iodide (PI) staining uptake by the mycelium (Fig. 3) indicates that cell membranes of the fungi were damaged with Cu-NPs, which alter their permeability. Once inside the cells, the NPs act like a "Trojan horse" releasing metal ions. Both NPs and ions induce toxicity and oxidative stress. Consequently, it degrades several compounds and structures vital for the survival of microorganisms, such as protein inactivation, enzyme damage, and damage to genetic material such as DNA (Fig. 4).

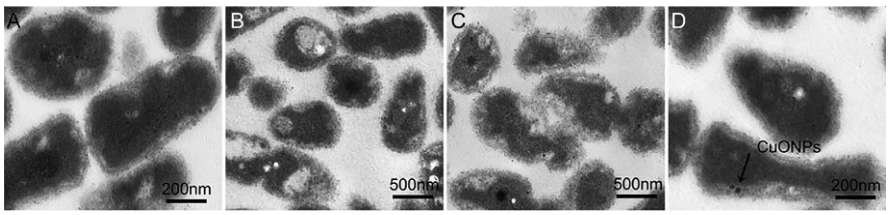

FIG. 1

TEM images of *Ralstonia solanacearum* in the presence of CuO-NPs at (A) 0, (B) 125 mg/mL, (C) 250 mg/mL, and (D) 250 mg/mL concentrations. (C) Mainly represented the damaged cell structure, and (D) mainly represented the absorption of CuO-NPs by bacterial cells (indicated by the *arrows*).

Reproduced from an open access reference: Chen, J., Mao, S., Xu, Z., Ding, W., 2019. Various antibacterial mechanisms of biosynthesized copper oxide nanoparticles against soilborne Ralstonia solanacearum. RSC Adv. 9, 3788–3799.

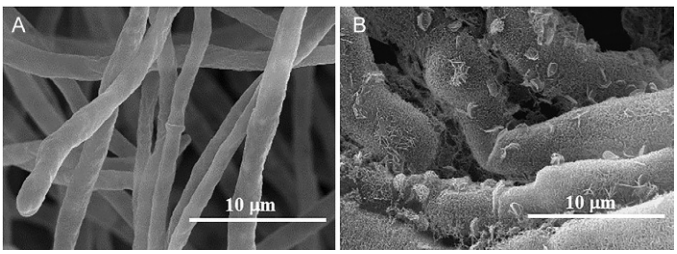

FIG. 2

SEM images of *Fusarium solani* in the presence of the Cu-NPs at (A) 0, (B) 0.5 mg/mL.

Reproduced from Pariona, N., Mtz-Enriquez, A.I., Sánchez-Rangel, D., Carrión, G., Paraguay-Delgado, F., Rosas-Saito, G., 2019. Green-synthesized copper nanoparticles as a potential antifungal against plant pathogens. RSC Adv. 9, 18835–18843.

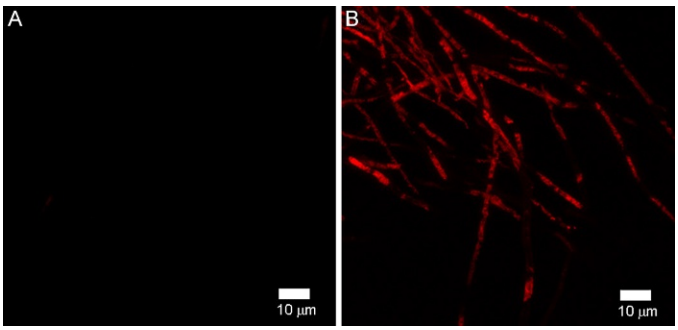

FIG. 3

The effect of Cu-NPs on the cell viability by analyzing the PI influx in *F. solani.* (A) control and (B) treatment with Cu-NPs.

Reproduced from Pariona, N., Mtz-Enriquez, A.I., Sánchez-Rangel, D., Carrión, G., Paraguay-Delgado, F., Rosas-Saito, G., 2019. Green-synthesized copper nanoparticles as a potential antifungal against plant pathogens. RSC Adv. 9, 18835–18843.

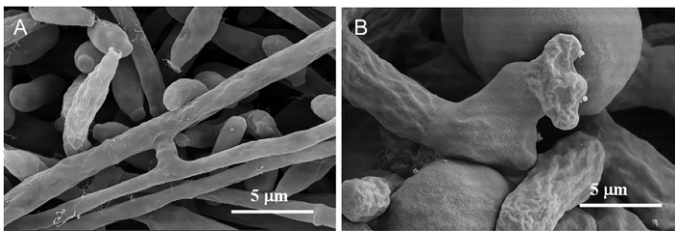

FIG. 4

SEM image of *F. oxysporum* in the presence of the Cu-NPs at (A) 0 and (B) 0.5 mg/mL.

Reproduced from Hermida-Montero, L.A., Pariona, N., Mtz-Enriquez, A.I., Carrión, G., Paraguay-Delgado, F., Rosas-Saito, G., 2019. Aqueous-phase synthesis of nanoparticles of copper/copper oxides and their antifungal effect against Fusarium oxysporum. J. Hazard. Mater. 380, 120850.

As was mentioned before, GO-Cu-NPs have presented antibacterial activity against Pst at low concentrations. The authors mentioned that graphene oxide sheets tend to nonspecifically wrap the bacteria cells, meanwhile, Cu NPs can bind to bacteria cell surfaces by electric charge difference and react with phosphorous and sulfur compounds. By TEM images, the authors show the bacteria cell death with the use of GO-Cu-NPs. Fig. 5 shows the untreated bacteria (A), the NPs adsorbed onto the cell membrane/wall (B), the NPs penetrating the bacteria cell (C), and the disorganization of the bacterial membrane and damage of the cellular structure (D). The effective penetration of the Cu-NPs and bacteria cell death was attributed to a change of cell permeability and the reaction of Cu-NPs with intercellular structure, respectively (Li et al. 2017).

On the other hand, reduced graphene oxide nanosheet decorated copper oxide nanoparticles (rGO-CuO-NPs) were fabricated, and their antifungal activity was

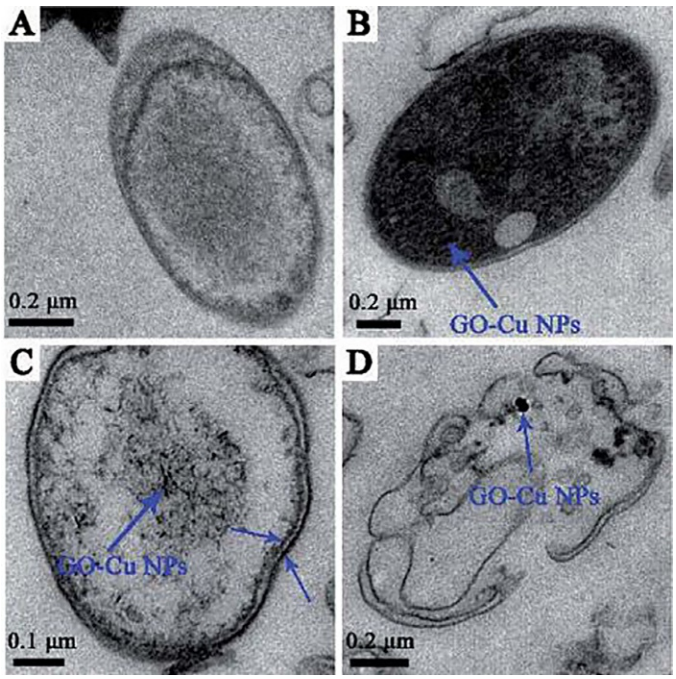

FIG. 5

TEM image of Pst bacterial cells treated with (A) sterile water, and (B–D) GO-Cu NPs.

Reproduced from an open access reference: Li, Y., Yang, D., Cui, J., 2017. Graphene oxide loaded with copper oxide nanoparticles as an antibacterial agent against: Pseudomonas syringae pv. tomato. RSC Adv. 7, 38853–38860.

evaluated against wild strains of *F. oxysporum* affecting tomato and pepper plants (El-Abeid et al., 2020). Analysis in vitro showed that rGO-CuO-NPs (at 1 mg/L) had higher antifungal activity than the fungicide Kocide 2000 (at 2.5 g/L). The TEM images (Fig. 6) show the interaction between *F. oxysporum* named FORL (isolated from tomato) and rGO-CuO-NPs. Fig. 6A and C show the intact organelles and characteristic cell wall surface of FOL spores without treatments. After rGO-CuO-NPs treatment, Fig. 6B shows adsorbed nanocomposites onto the fungal cell wall. Finally, Fig. 6D and E display how the nanocomposites are distributed in the cell cytoplasm and their interaction with cytoplasmic components.

In in vivo applications, it is possible that NPs do not require to have direct interaction with pathogens, it is because the activity of Cu-based NPs generate ROS. Additionally, ROS also play an important role in the defense responses of plants against pathogens (Orozco-Cardenas et al., 2001). This means that a second mechanism reduces the diseases in plant, and Cu-based NPs induce plant defense. In a greenhouse study, four different treatments were used to determine the importance of the application method in delivering NPs to watermelon plants (1) dipping the foliage

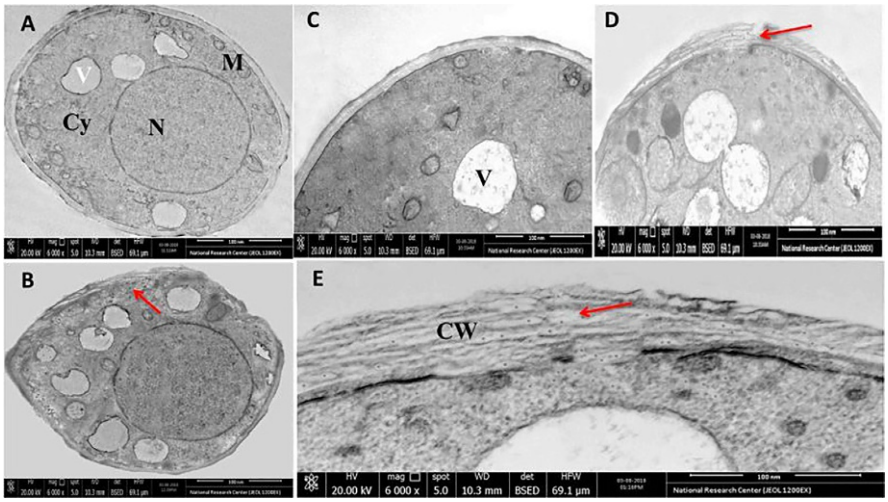

FIG. 6

Ultrastructural images obtained by TEM of (A, C) untreated and (B, D, E) rGO-CuO NP-treated FORL cells. (E) Magnified view for treated fungal cell wall layers showing the internalization of NPs and their distribution. *Red arrows* point to successful penetration of the rGO-CuO NPs in the fungal cells.

Reproduced from an open access reference: El-Abeid, S.E., Ahmed, Y., Daròs, J.A., Mohamed, M.A., 2020. Reduced graphene oxide nanosheet-decorated copper oxide nanoparticles: a potent antifungal nanocomposite against fusarium root-rot and wilt diseases of tomato and pepper plants. Nanomaterials 10, 1001.

into NPs suspensions, (2) spraying foliage with the NPs suspension (3) injecting the NPs suspensions directly into the root ball, and (4) repeated foliar application of NPs. In a broad range of amendment concentrations of $Cu_3(PO_4)_2{\cdot}3H_2O$ nanosheets and CuO-NPs against soilborne fungus *F. oxysporum* f. sp. *niveum* (Borgatta et al., 2018). The dip method application of $Cu_3(PO_4)_2{\cdot}3H_2O$ nanosheet was the most effective treatment, which was due to the homogeneity of coverage during treatment. Additionally, an increase in silicon (Si) was found in the CuO-NPs treatments, which is attributed to the important role played by CuO-NPs in plant defense. Another study also found that the combination of Cu-NPs and potassium silicate stimulate the tolerance to *Clavibacter michiganensis* in tomato plants. The foliar application of a mixture of Cu-NPs (50 mg/L) and Si (460 mg/L) was found to be the most effective in decreasing the disease severity compared to all treatments. This is attributed to the fact that the mixture of NPs promote the increase of enzymatic and nonenzymatic compounds, which are important in the defense of tomato plants, which increase the tolerance to *Clavibacter michiganensis* (Cumplido-Nájera et al. 2019). Foliar applications of $Cu_3(PO_4)_2{\cdot}3H_2O$ nanosheets and CuO-NPs on young tomato seedlings, significantly reduced the presence *Fusarium* wilt. The mechanistic insight into disease suppression is due to the application of both NPs that yielded a time-dependent transcriptional increase in three plant defense genes (pathogenesis-related genes

transcriptional activator [PTI5], polyphenol oxidase [PPO], and plant resistance protein 1A1 [PRP1A1]); particularly, $Cu_3(PO_4)_2{\cdot}3H_2O$ nanosheets improved the expression of the mentioned genes (Ma et al., 2019). Additionally, it has been reported that copper oxides damaged the cell walls of *E. coli,* which was mainly due to the formation of copper (I)/peptide complexes (for Cu_2O-NPs) and the generation of free radicals (for CuO-NPs). These conclusions were realized through enzyme assays which showed that Cu_2O NPs damage the intracellular proteins of *E. coli*. Also, it was reported that CuO NPs damaged fumarase slower than Cu_2O (Meghana et al. 2015).

5 Conclusion and future perspectives

Copper salts have been traditionally used in agriculture, however, due to their high solubility and high doses needed, copper salts may be toxic, which is an environmental concern. On the other hand, copper-based NPs have improved the antimicrobial activity at lower doses. This activity will depend on their physicochemical characteristics, which include size, surface, oxidation state, and concentration. In this regard, the synthesis of Cu-based NPs is very important to get NPs with the properties required and to maximize disease suppression. Also, the development of Cu-based NPs through eco-friendly and cost-effective synthesis methods is necessary. On the other hand, it has been reported that the antimicrobial mechanism of the Cu-based NPs direct to the microorganism is due to the oxidative stress caused by the ROS generation. However, further investigations are necessary to completely elucidate the mechanism of antimicrobial activity of Cu-based NPs in plants. Additionally, more studies over different pathogens are needed because the antimicrobial activity also could be species-dependent. Thus, Cu-based NPs are still evolving and have enormous potential applications for plant disease management. Additionally, Cu-based NPs and other nanomaterials can be used in a sustainable way for their use in agriculture for maintaining global food security.

References

Anagnostakis, S.L., 1987. Chestnut blight: the classical problem of an introduced pathogen. Mycologia 79, 23–37.

Antonoglou, O., Moustaka, J., Adamakis, I.D.S., Sperdouli, I., Pantazaki, A.A., Moustakas, M., Dendrinou-Samara, C., 2018. Nanobrass CuZn nanoparticles as foliar spray nonphytotoxic fungicides. ACS Appl. Mater. Interfaces 10, 4450–4461.

Azam, A., Ahmed, A.S., Oves, M., Khan, M.S., Memic, A., 2012. Size-dependent antimicrobial properties of CuO nanoparticles against gram-positive and -negative bacterial strains. Int. J. Nanomedicine 7, 3527–3535.

Borgatta, J., Ma, C., Hudson-Smith, N., Elmer, W., Plaza Pérez, C.D., De La Torre-Roche, R., Zuverza-Mena, N., Haynes, C.L., White, J.C., Hamers, R.J., 2018. Copper-based nanomaterials suppress root fungal disease in watermelon (*Citrullus lanatus*): role of particle morphology, composition and dissolution behavior. ACS Sustain. Chem. Eng. 6, 14847–14856.

Borkow, G., Gabbay, J., 2009. Copper, an ancient remedy returning to fight microbial, fungal and viral infections. Curr. Chem. Biol. 3, 272–278.

Bramhanwade, K., Shende, S., Bonde, S., Gade, A., Rai, M., 2016. Fungicidal activity of Cu nanoparticles against Fusarium causing crop diseases. Environ. Chem. Lett. 14, 229–235.

Cessna, S.G., Sears, V.E., Dickman, M.B., Low, P.S., 2000. Oxalic acid, a pathogenicity factor for *Sclerotinia sclerotiorum*, suppresses the oxidative burst of the host plant. Plant Cell 12, 2191–2199.

Chen, J., Mao, S., Xu, Z., Ding, W., 2019. Various antibacterial mechanisms of biosynthesized copper oxide nanoparticles against soilborne *Ralstonia solanacearum*. RSC Adv. 9, 3788–3799.

Chikte, R.G., Paknikar, K.M., Rajwade, J.M., Sharma, J., 2019. Nanomaterials for the control of bacterial blight disease in pomegranate: quo vadis? Appl. Microbiol. Biotechnol. 103, 4605–4621.

Cruz, L.F., Cruz, J.C., Carrillo, D., Mtz-Enriquez, A.I., Lamelas, A., Ibarra-Juarez, L.A., Pariona, N., 2021. In-vitro evaluation of copper nanoparticles as a potential control agent against the fungal symbionts of the invasive ambrosia beetle *Euwallacea fornicatus*. Crop Prot. 143, 105564.

Cumplido-Nájera, C.F., González-Morales, S., Ortega-Ortíz, H., Cadenas-Pliego, G., Benavides-Mendoza, A., Juárez-Maldonado, A., 2019. The application of copper nanoparticles and potassium silicate stimulate the tolerance to *Clavibacter michiganensis* in tomato plants. Sci. Hortic. (Amsterdam) 245, 82–89.

Din, M.I., Arshad, F., Hussain, Z., Mukhtar, M., 2017. Green adeptness in the synthesis and stabilization of copper nanoparticles: catalytic, antibacterial, cytotoxicity, and antioxidant activities. Nanoscale Res. Lett. 12, 2–15.

Dizaj, S.M., Lotfipour, F., Barzegar-Jalali, M., Zarrintan, M.H., Adibkia, K., 2014. Antimicrobial activity of the metals and metal oxide nanoparticles. Mater. Sci. Eng. C 44, 278–284.

Dong, H., Xiong, R., Liang, Y., Tang, G., Yang, J., Tang, J., Niu, J., Gao, Y., Zhou, Z., Cao, Y., 2020. Development of glycine-copper(ii) hydroxide nanoparticles with improved biosafety for sustainable plant disease management. RSC Adv. 10, 21222–21227.

El-Abeid, S.E., Ahmed, Y., Daròs, J.A., Mohamed, M.A., 2020. Reduced graphene oxide nanosheet-decorated copper oxide nanoparticles: a potent antifungal nanocomposite against fusarium root rot and wilt diseases of tomato and pepper plants. Nanomaterials 10, 1001.

El-Batal, A.I., El-Sayyad, G.S., Mosallam, F.M., Fathy, R.M., 2020. *Penicillium chrysogenum*-mediated mycogenic synthesis of copper oxide nanoparticles using gamma rays for in vitro antimicrobial activity against some plant pathogens. J. Clust. Sci. 31, 79–90.

Elmer, W.H., White, J.C., 2016. The use of metallic oxide nanoparticles to enhance growth of tomatoes and eggplants in disease infested soil or soilless medium. Environ. Sci. Nano 3, 1072–1079.

Elmer, W., De Latorre-Roche, R., Pagano, L., Majumdar, S., Zuverza-Mena, N., Dimkpa, C., Gardea-Torresdey, J., White, J.C., 2018. Effect of metalloid and metal oxide nanoparticles on fusarium wilt of watermelon. Plant Dis. 102, 1394–1401.

Fan, Q., Liao, Y.Y., Kunwar, S., Da Silva, S., Young, M., Santra, S., Minsavage, G.V., Freeman, J.H., Jones, J.B., Paret, M.L., 2021. Antibacterial effect of copper composites against *Xanthomonas euvesicatoria*. Crop Prot. 139, 105366.

Giannousi, K., Avramidis, I., Dendrinou-Samara, C., 2013. Synthesis, characterization and evaluation of copper based nanoparticles as agrochemicals against *Phytophthora infestans*. RSC Adv. 3, 21743–21752.

Giannousi, K., Pantazaki, A., Dendrinou-Samara, C., 2017. Copper-based nanoparticles as antimicrobials. In: Nanostructures for Antimicrobial Therapy. Nanostructures in Therapeutic Medicine Series, Elsevier Inc.

Gkanatsiou, C., Karamanoli, Menkissoglu-Spiroudi, U., Dendrinou-Samara, C., 2019. Composition effect of Cu-based nanoparticles on phytopathogenic bacteria. Antibacterial studies and phytotoxicity evaluation. Polyhedron 170, 395–403.

Hermida-Montero, L.A., Pariona, N., Mtz-Enriquez, A.I., Carrión, G., Paraguay-Delgado, F., Rosas-Saito, G., 2019. Aqueous-phase synthesis of nanoparticles of copper/copper oxides and their antifungal effect against *Fusarium oxysporum*. J. Hazard. Mater. 380, 120850.

Iliger, K.S., Sofi, T.A., Bhat, N.A., Ahanger, F.A., Sekhar, J.C., Elhendi, A.Z., Al-Huqail, A.A., Khan, F., 2021. Copper nanoparticles: green synthesis and managing fruit rot disease of chilli caused by *Colletotrichum capsici*. Saudi J. Biol. Sci. 28, 1477–1486.

Kanhed, P., Birla, S., Gaikwad, S., Gade, A., Seabra, A.B., Rubilar, O., Duran, N., Rai, M., 2014. In vitro antifungal efficacy of copper nanoparticles against selected crop pathogenic fungi. Mater. Lett. 115, 13–17.

Kasana, R.C., Panwar, N.R., Kaul, R.K., Kumar, P., 2017. Biosynthesis and effects of copper nanoparticles on plants. Environ. Chem. Lett. 15, 233–240.

Kovačec, E., Regvar, M., van Elteren, J.T., Arčon, I., Papp, T., Makovec, D., Vogel-Mikuš, K., 2017. Biotransformation of copper oxide nanoparticles by the pathogenic fungus *Botrytis cinerea*. Chemosphere 180, 178–185.

Leroux, P., 2003. Modes d'action des produits phytosanitaires sur les organismes pathogènes des plantes. Comptes Rendus Biol. 326, 9–21.

Li, Y., Yang, D., Cui, J., 2017. Graphene oxide loaded with copper oxide nanoparticles as an antibacterial agent against *Pseudomonas syringae* pv. *tomato*. RSC Adv. 7, 38853–38860.

Li, Y., Liu, Y., Yang, D., Jin, Q., Wu, C., Cui, J., 2020. Multifunctional molybdenum disulfide-copper nanocomposite that enhances the antibacterial activity, promotes rice growth and induces rice resistance. J. Hazard. Mater. 394, 122551.

Lopez-Lima, D., Mtz-Enriquez, A.I., Carrión, G., Basurto-Cereceda, S., Pariona, N., 2021. The bifunctional role of copper nanoparticles in tomato: effective treatment for Fusarium wilt and plant growth promoter. Sci. Hortic. (Amsterdam) 277, 109810.

Lungu, I.I., Holban, A.M., Ficai, A., Grumezescu, A.M., 2017. Zinc oxide nanostrucures: new trends in antimicrobial therapy. In: Nanostructures for Antimicrobial Therapy. Nanostructures in Therapeutic Medicine Series, Elsevier Inc, pp. 503–514.

Ma, C., Borgatta, J., De La Torre-Roche, R., Zuverza-Mena, N., White, J.C., Hamers, R.J., Elmer, W.H., 2019. Time-dependent transcriptional response of tomato (*Solanum lycopersicum* L.) to Cu nanoparticle exposure upon infection with *Fusarium oxysporum* f. sp. *lycopersici*. ACS Sustain. Chem. Eng. 7, 10064–10074.

Majumdar, T.D., Singh, M., Thapa, M., Dutta, M., Mukherjee, A., Ghosh, C.K., 2019. Size-dependent antibacterial activity of copper nanoparticles against *Xanthomonas oryzae* pv. *oryzae*—a synthetic and mechanistic approach. Colloids Interface Sci. Commun. 32, 100190.

Malandrakis, A.A., Kavroulakis, N., Chrysikopoulos, C.V., 2019. Use of copper, silver and zinc nanoparticles against foliar and soil-borne plant pathogens. Sci. Total Environ. 670, 292–299.

Meghana, S., Kabra, P., Chakraborty, S., Padmavathy, N., 2015. Understanding the pathway of antibacterial activity of copper oxide nanoparticles. R. Soc. Chem. Adv. 5, 12293–12299.

Mehta, M.R., Mahajan, H.P., Hivrale, A.U., 2021. Green synthesis of chitosan capped-copper nano biocomposites: synthesis, characterization, and biological activity against plant pathogens. BioNanoSci. 11, 1–11.

Mondal, K.K., Mani, C., 2012. Investigation of the antibacterial properties of nanocopper against *Xanthomonas axonopodis* pv. *punicae*, the incitant of pomegranate bacterial blight. Ann. Microbiol. 62, 889–893.

Natesan, K., Ponmurugan, P., Gnanamangai, B.M., Manigandan, V., Joy, S.P.J., Jayakumar, C., Amsaveni, G., 2020. Biosynthesis of silica and copper nanoparticles from Trichoderma, Streptomyces and Pseudomonas spp. evaluated against collar canker and red root-rot disease of tea plants. Arch. Phytopathol. Plant Prot., 1–30.

Orozco-Cardenas, M.L., Narvaez-Vasquez, J., Ryan, C.A., 2001. Hydrogen peroxide acts as a second messenger for the induction of defense genes in tomato plants in response to wounding, systemin, and methyl jasmonate. Plant Cell 13, 179–191.

Osińska-Jaroszuk, M., Wlizło, K., Szałapata, K., Jarosz-Wilkołazka, A., 2014. Correlation between the production of exopolysaccharides and oxalic acid secretion by *Ganoderma applanatum* and *Tyromyces palustris*. World J. Microbiol. Biotechnol. 30, 3065–3074.

Pariona, N., Mtz-Enriquez, A.I., Sánchez-Rangel, D., Carrión, G., Paraguay-Delgado, F., Rosas-Saito, G., 2019. Green-synthesized copper nanoparticles as a potential antifungal against plant pathogens. RSC Adv. 9, 18835–18843.

Pham, N.D., Duong, M.M., Le, M.V., Hoang, H.A., Pham, L.K.O., 2019. Preparation and characterization of antifungal colloidal copper nanoparticles and their antifungal activity against *Fusarium oxysporum* and *Phytophthora capsici*. Comptes Rendus Chim. 22, 786–793.

Price, C.L., Parker, J.E., Warrilow, A.G., Kelly, D.E., Kelly, S.L., 2015. Azole fungicides—understanding resistance mechanisms in agricultural fungal pathogens. Pest Manag. Sci. 71, 1054–1058.

Printz, B., Lutts, S., Hausman, J.-F., Sergeant, K., 2016. Copper trafficking in plants and its implication on cell wall dynamics. Front. Plant Sci. 7, 1–16.

Saharan, V., Mehrotra, A., Khatik, R., Rawal, P., Sharma, S.S., Pal, A., 2013. Synthesis of chitosan-based nanoparticles and their in vitro evaluation against phytopathogenic fungi. Int. J. Biol. Macromol. 62, 677–683.

Sathiyabama, M., Manikandan, A., 2018. Application of copper-chitosan nanoparticles stimulate growth and induce resistance in finger millet (*Eleusine coracana* Gaertn.) plants against blast disease. J. Agric. Food Chem. 66, 1784–1790.

Sathiyabama, M., Indhumathi, M., Amutha, T., 2020. Preparation and characterization of curcumin functionalized copper nanoparticles and their application enhances disease resistance in chickpea against wilt pathogen. Biocatal. Agric. Biotechnol. 29, 101823.

Shende, S., Bhagat, R., Raut, R., Rai, M., Gade, A., 2021. Myco-fabrication of copper nanoparticles and its effect on crop pathogenic fungi. IEEE Trans. NanoBioscience 20 (2), 146–153.

Slavin, Y.N., Asnis, J., Häfeli, U.O., Bach, H., 2017. Metal nanoparticles: understanding the mechanisms behind antibacterial activity. J. Nanobiotechnol. 15, 1–20.

Tamil Elakkiya, V., Meenakshi, R.V., Senthil Kumar, P., Karthik, V., Ravi Shankar, K., Sureshkumar, P., Hanan, A., 2021. Green synthesis of copper nanoparticles using Sesbania aculeata to enhance the plant growth and antimicrobial activities. Int. J. Environ. Sci. Technol.

Ullstrup, A.J., 1972. The impacts of the southern corn leaf blight epidemics of 1970-1971. Annu. Rev. Phytopathol. 10, 37–50.

Van Viet, P., Nguyen, H.T., Cao, T.M., Van Hieu, L., 2016. Fusarium antifungal activities of copper nanoparticles synthesized by a chemical reduction method. J. Nanomater. 2016, 1–7.

Vanti, G.L., Masaphy, S., Kurjogi, M., Chakrasali, S., Nargund, V.B., 2020. Synthesis and application of chitosan-copper nanoparticles on damping off causing plant pathogenic fungi. Int. J. Biol. Macromol. 156, 1387–1395.

Yoshida, K., Schuenemann, V.J., Cano, L.M., Pais, M., Mishra, B., Sharma, R., Lanz, C., Martin, F.N., Kamoun, S., Krause, J., Thines, M., Weigel, D., Burbano, H.A., 2013. The rise and fall of the *Phytophthora infestans* lineage that triggered the Irish potato famine. elife 2013, 1–25.

Young, M., Santra, S., 2014. Copper (Cu)–silica nanocomposite containing valence-engineered Cu: a new strategy for improving the antimicrobial efficacy of Cu biocides. J. Agric. Food Chem. 62, 6043–6052.

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CHAPTER

9 Cu-based nanoparticles as pesticides: Applications and mechanism of management of insect pests

Mohamed Amine Gacem[a] **and Rachid Chaibi**[a,b]

[a]*Department of Biology, Faculty of Science, University of Amar Tlidji, Laghouat, Algeria,*
[b]*Laboratory of Biological and Agronomic Sciences, Faculty of Science, University of Amar Tlidji, Laghouat, Algeria*

1 Introduction

It is well recognized that the world is facing remarkable urbanization and demographic explosion, especially in developing countries, which is not in parallel with agricultural development in these countries (Satterthwaite et al., 2010; Ehrlich and Harte, 2015). However, the Food and Agriculture Organization (FAO) noted that approximately a third of all food produced in the world (1.3 billion tons of edible food) intended for human consumption is lost and wasted each year (Ishangulyyev et al., 2019). Along with this problem caused by mismanagement by humans, the losses generated by insect pests and phytopathogens are also not negligible (Willsey et al., 2017). Faced with these serious problems, it is very important to think about and suggest solutions allowing the success of sustainable and healthy agriculture, to prevent any food shortage, especially for developing countries.

Several strategies are in place to avoid losses and increase agricultural yields. RNAi tools are among the most recommended. It eliminates harmful insects by producing resistant plant species (Christiaens et al., 2020). Alongside this molecular technique, CRISPR-Cas technology has proven its effectiveness in the fight against phytopathogens (Courtier-Orgogozo et al., 2017). However, conventional techniques are still applied, including the use of pesticides (Oesterlund et al., 2014).

Nanotechnology is currently an effective tool disseminated in almost all fields and revealing the desired success (Bayda et al., 2019). Nanoparticles are used in agriculture to stimulate growth, plant development, and ensure sustainability. Nanomaterials help to improve agricultural production by minimizing relevant losses with increased crop protection (Shang et al., 2019). They are also used as management tools for plant diseases induced by bacteria (Cai et al., 2018), viruses (Vargas-Hernandez et al., 2020), insects (Duhan et al., 2017), and phytopathogenic fungi (Hao et al., 2017). Some nanoparticles are used as nanofertilizers due to their easy absorption by plants (Rui et al., 2016).

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The majority of the nanoparticles are still expensive following their synthesis by conventional methods (Zhang et al., 2016). Unlike, CuNPs are less expensive, more available, and recommended due to their biological activities (El-Saadony et al., 2020). Otherwise, green syntheses of CuNPs are an economical and ecological alternative to fight against crop pests (Kumar et al., 2020).

The main objective of the current chapter is to reveal the importance of CuNPs in the control of insect pests in agricultural sectors. The interaction mechanism of CuNPs with the pest is also discussed. Some recommendations are noted at the end of the chapter to avoid damaging nontarget cells or inducing phytotoxicity effects.

2 Application of copper nanoparticles in agriculture and its insecticidal activity

Copper nanoparticles are used in different fields such as agriculture for improving quality and crop yield (Hernández-Hernández et al., 2019), medicine for its antioxidant, antibacterial, and anticancer properties (Mehdizadeh et al., 2020), and in the environment as a decontamination agent (Abbas et al., 2020). CuNPs are also used in other technological fields (Huang et al., 2019). Recently, extensive studies in the agricultural field have highlighted the importance of CuNPs for plant health and insect control (Fig. 1).

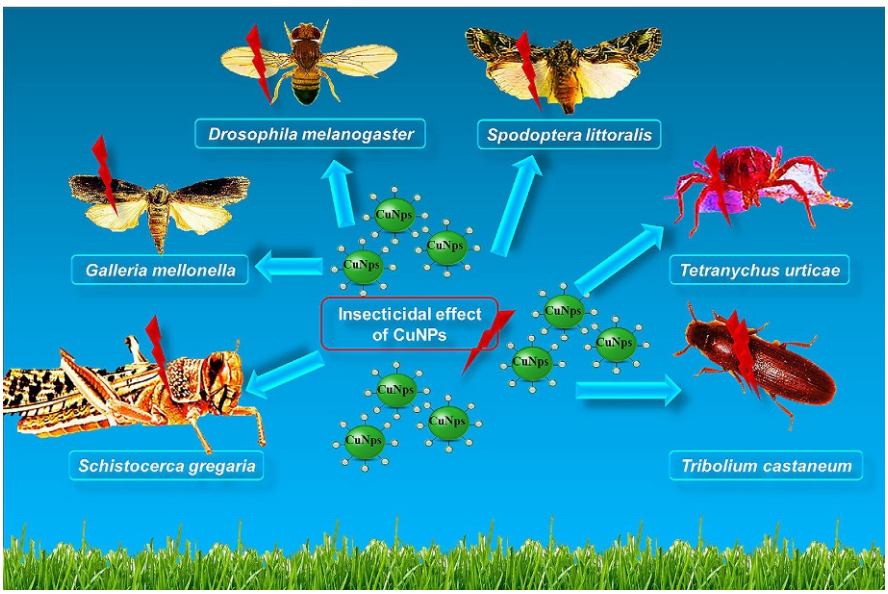

FIG. 1

Top insects managing CuNPs in the agricultural field.

Green synthesis of CuNPs show good effect against *Anopheline mosquitoes*, the highest larval mortality (100.0%) obtained with 140 and 20 ppm of *Lantana camara* extract alone or mixed with CuNPs, respectively (Hassanain et al., 2019). The above results are proved by a more recent study. The authors reported that CuNPs synthesized by *Pseudomonas fluorescens* MAL2, similar to *P. fluorescens* DSM 12442^{T}, demonstrate 100% mortality against *Tribolium castaneum* (the little mealworm) in the presence of 300 $\mu g\,mL^{-1}$ of NPs (El-Saadony et al., 2020). Green synthesis of CuONPs from the leaves of *Tridax procumbens* and evaluation of its larvicidal activities against *Aedes aegypti* revealed high mortality (Muthamil Selvan et al., 2018). The remarkable insecticidal activity of CuNPs compared to plant extracts is strongly attributed to the small particle size. The CuNPs can penetrate and cross the larval cell membrane and bind to proteins and DNA. Damage is possible after the interaction of NPs with cellular proteins and nucleic acids. Consequently, the alterations induce a rupture of the cell membrane and disrupt the driving forces of the protons. It involves a breakdown of cell functions and ultimately cell death (Parthiban et al., 2018). The insecticidal effect may also be attributed to the ability of CuNPs to cross the barrier of epithelial and endothelial cells by transcytosis (El-Saadony et al., 2020). The NPs can reach the circulatory system and attack potentially sensitive target sites such as the nervous system (Ramadan et al., 2020).

In other equally important crops, CuNPs have displayed a remarkable insecticidal effect. For example, in common bean cultivation (*Phaseolus vulgaris* L.) widely cultivated in the world, copper nanocapsules (alginate/chitosan/copper oxide nanoparticle) sprayed during the simultaneous appearance of the first flower buds demonstrated a significant reduction in the population of *Tetranychus urticae* (Dorri et al., 2018). Copper oxide NPs (CuONPs) showed high mortality rates in *Spodoptera littoralis* larvae (the cotton leafworm). NPs affect eggs laid in females and modify the sex ratio of females and males. However, the combination of CuNPs with the methomyl pesticide minimizes the toxic potency of the pesticide in the insects, the reduction of the toxic effect is due to the photodegradation of pesticide by CuNPs (Shaker et al., 2016). For other NPs, the insecticidal activity can be further enhanced by combining NPs with other chemical agents, citing as an example the combination of silver NPs with malathion. The resulting combination clearly shows its high insecticidal efficacy against *T. castaneum* (Alif Alisha and Thangapandiyan, 2019) in *Spodoptera litura*, the use of CuONPs enhances the activity of β-cypermethrin against the insect (Lu et al., 2019).

The incorporation of CuONPs and silver-doped copper oxide nanosheets into the diet of *S. littoralis* demonstrated high larval mortality. Copper NPs are more effective than doped with silver. The mortality rate is proportional to the concentration of NPs, the exposure time, and the larval stages. CuO nanostructures have a significant effect on the timing of living larval development. Deformities of pupae and malformations in adults are also recorded (Atwa et al., 2017). In *Galleria mellonella*, whose larvae are a problem for beekeepers, CuONPs induce significant oxidative stress. The accumulation of NPs in the midgut and fat body tissues of the insect larvae significantly increases the activity of glutathione S-transferase in the fat body. The CuONPs

concurrently increase catalase activity (CAT) in the midgut and fat body. However, superoxide dismutase activity (SOD) is weakened (Sezer Tuncsoy et al., 2019). In the same insect, the diets containing 10 and 100 mg L^{-1} of CuNPs induce a significantly higher increase in the total number of hemocytes, while the diets containing 1000 mg L^{-1} of CuNPs induce an opposite effect (Sezer Tuncsoy and Ozalp, 2017).

In Drosophila or vinegar fly (*Drosophila melanogaster*), CuNPs induce genotoxicity in larval hemocytes. Toxicity is characterized by DNA damage, reduced larval count, and delayed development of adult larvae (Carmona et al., 2015). In *Schistocerca gregaria*, treatment by CuNPs revealed acute toxicity. Pupal mortality is initially observed in the 4th stage of development (Ramadan et al., 2020). It should be noted that the insect mortality rate is proportional to the increase in the concentration of CuNPs and to the exposure time (El-Saadony et al., 2020). It is also noted that the nanometric level of the Cu nanoparticles is important for attenuating the targets and inducing toxicity. (Karlsson et al., 2009). Table 1 demonstrates some insecticidal effects of CuNPs.

3 Mode of interaction of copper nanoparticles against insects

Despite the recommendations encouraging the application of NPs in agriculture for pest control, knowledge of the mode and mechanism of action is essential to predict the toxicological consequences arising from the use of CuNPs as pesticides. Several types of researches have illustrated the mechanism of action of CuNPs in bacteria (Chatterjee et al., 2014; Varympopi et al., 2020; Aguilera-Correa et al., 2021). For others, they confirmed the toxicity in rats (Xu et al., 2018; Tang et al., 2018; Zhou et al., 2019). However, illustrations of the mode and mechanism of action of CuNPs against insects are strictly limited, and only a few studies have focused on possible mechanisms of action (Sezer Tuncsoy et al., 2019; Carmona et al., 2015). Due to the lack of information regarding the mechanism of action of CuNPs at the molecular level in insects, the paragraphs below discuss the most likely mechanism of toxicity by which CuNPs extinguish insects. Fig. 2 illustrates the likely mechanism of action of CuNPs against insect pests.

In general, several probable mechanisms illustrating the mode and mechanism of action of NPs against insects are accepted. Oxidative stress triggered by NPs in the target tissues is the most discussed mechanism (Angelé-Martínez et al., 2017). In addition, toxicity may also be due to the penetration of nanoparticles orally inside the digestive tract and then into the circulation (Atwa et al., 2017). As demonstrated in the intracellular space of human cells (cell line A549), CuNPs can interfere with DNA and as a result, they induce oxidative damage and DNA damage (Karlsson et al., 2009). The interaction of NPs with the membrane components is also possible, and as a consequence, it damages the membrane (Karlsson et al., 2013).

In insects, DNA is considered the primary target of CuNPs, in addition, DNA is sensitive to stress and oxidative damage. As clearly shown in human cells

Table 1 Insecticidal activity of some copper nanoparticle.

Nanoparticle	Size	Structure	Insecticidal activity against	Lethal dose	References
CuNPs	240.88 ± 62.66 nm		*Euwallacea fornicatus*		Cruz et al. (2021)
CuNPs	10–70 nm	Spherical	*Tribolium castaneum*	300 $\mu g\,mL^{-1}$	El-Saadony et al. (2020)
Cellulose/nanocrystal ZnO/CuO Nanostructure			*Anopheles stephensi*		Elfeky et al. (2020)
CuONPs	20–40 nm	Spherical	*Anopheles subpictus mosquito larvae*	80 ppm for 48 h	Velsankar et al. (2020)
CuNPs	11.5–13.5 nm	Rods in shape	*Schistocerca gregaria*		Ramadan et al. (2020)
Cu/NiNPs			*Culex quinquefasciatus*	83,96; 258.83 and 331.50 $mg\,L^{-1}$	Danbature et al. (2020)
CuNPs	11–17.8 nm	Spherical	*Anopheline mosquitoes*	20 ppm	Hassanain et al. (2019)
CuONPs	33.0 ± 8.3 nm)	Spherical	*Galleria mellonella*	10 $\mu g\,L^{-1}$.	Sezer Tuncsoy et al. (2019).
Cu_2O nano capsules	Less than 50 nm		*Tetranychus urticae*	5.5 $g\,L^{-1}$	Dorri et al. (2018)
CuONPs	16 nm	Monoclinic structure	*Aedes aegypti*	10 $mg\,mL^{-1}$	Muthamil Selvan et al. (2018)
Ag-doped CuO nanostructures	~ 10 nm		*Spodoptera littoralis*	300 mg/150 mL	Atwa et al. (2017)
CuONPs-Ag					
CuO nanostructures	24–52.4 nm		*Spodoptera littoralis*	1 $g\,L^{-1}$	Shaker et al. (2016)
CuONPs	29.84 ± 15.28 nm	Spherical	*Drosophila melanogaster*	0.24–7.5 $mg\,mL^{-1}$	Carmona et al. (2015)

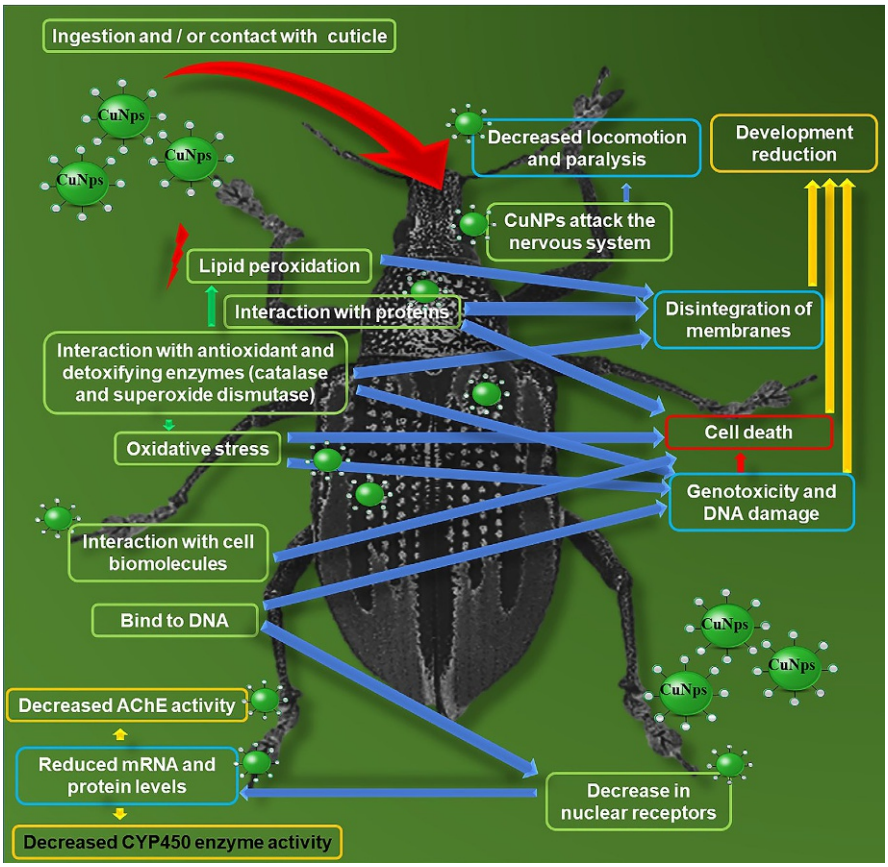

FIG. 2

Proposed mechanism of action of CuNPs against insect pests.

(alveolar epithelial cell line R3/1), CuNPs release reactive oxygen species (ROS) and induce the formation of H_2O_2 that cause cell death (Vanwinkle et al., 2009). In insects, CuNPs are well known for their genotoxic properties with several mechanisms controlling their ability to promote DNA damage. In the larval hemocytes of *D. melanogaster*, CuNPs induce remarkable toxicity. CuNPs cause dose-dependent DNA strand damage and breaks (Carmona et al., 2015). Oxidative stress is proposed as the main mechanism of the alteration. The ROS generated in the intracellular environment potentially cause oxidative damage to DNA by a radical attack (Ahamed et al., 2010). DNA damage is also possible by interaction with malondialdehyde formed by the breakdown of lipid peroxidation products. In *D. melanogaster* treated with CuNPs, the induction of oxidative stress via lipid peroxidation is not an intrinsic characteristic effect of CuNPs, but it is attributed to copper (Carmona et al., 2015). In the human lung epithelial cell line (A549), cells surviving the actions of CuNP demonstrated cell cycle arrest. The blocked cell cycle is attributed to Cu ions released by CuNPs in the medium (Hanagata et al., 2011).

CuNPs can alter the activities of antioxidant enzymes. As demonstrated in *G. mellonella* larvae exposure to CuNPs, the accumulation of copper in the midgut and fat body of the larvae causes a reduction of SOD in the fat body. However, CAT activity increases in the midgut and fat body. For glutathione S-transferase, an increase is noted in the fat body, while for acetylcholinesterase (AChE), a decrease is noted in the midgut (Sezer Tuncsoy et al., 2019). In *S. gregaria*, treatment with copper NPs also induced a decrease in the enzymatic activity of AChE (Ramadan et al., 2020). The affinity of copper for sulfur-donor groups may induce AChE inhibition by binding to its thiol residues (Gomes et al., 2011). Treatment of *S. littoralis* larvae (2nd instar) by CuNPs resulted in malformations and morphological changes through adsorption of nanoparticles. Low levels of SOD are also noted (Abd El Wahab and Anwar, 2014). During the study of the enzymatic activity in *Daphnia magna*, the glutathione content and the activities of CAT and SOD are inhibited when the insect was exposed to CuNPs (Liu et al., 2014). This strongly suggests that the destabilization of the cellular functionalities is due to the strong oxidative stress induced by CuNPs.

CuNPs can reach the nervous system and induce severe toxicities. As demonstrated in *S. gregaria*, CuNPs cause paralysis, decreased locomotion, and tremors of the abdominal segments (Ramadan et al., 2020). The previous result suggests that excessive copper levels can be harmful to the nervous system (Gromadzka et al., 2020). Otherwise, astrocytes can accumulate copper oxide nanoparticles and copper ions. When the accumulation exceeds the threshold tolerated by the cells, accelerated production of ROS is noted (Bulcke and Dringen, 2016). The gradual accumulation of copper causes brain damage and neurological symptoms. In rat astrocytes, the excess copper decreases the activity of glutathione reductase and increases the activity of nitric oxide. The destabilization of enzymatic activities aggravates oxidative stress (Scheiber et al., 2014), and causes a severe loss of cell viability (Joshi et al., 2019). CuNPs also induce mitochondrial dysfunctions and plasma membrane disintegration (Minocha and Mumper, 2012).

4 Proposal delivery systems to improve the insecticidal effect of copper nanoparticles

To breed high crops production capable of meeting global food needs, and ensuring food safety, conventional crop protection practices require large amounts of fungicides, herbicides, and insecticides. Under certain conditions, chemicals are unable to attenuate crucial targets and therefore ineffective control is noted (Hawkins et al., 2018). Conventional practices increase expenditure in agricultural production and the depletion of environmental ecosystems by pollution (Pham et al., 2011; Zhang et al., 2019), without neglecting the deleterious effects of pesticides on human health (Damalas and Eleftherohorinos, 2011). In this regard, the preparation of active ingredients at a minimum effective concentration capable of reaching active sites and attenuating targets is essential to ensure better protection of crops against pests (Vega-Vásquez et al., 2020). The development of a new phytosanitary formulation capable of protecting crops against phytopathogens and pests has long been a major

concern for agricultural research. The use of nanoparticles as pesticides is one of the new formulations that nanotechnology is trying to bring out and apply in the field.

Nanoparticles must be delivered to the target in an intact state. In this regard, the encapsulation technique is promising, because it reduces the total amount of NP used in pest control. In addition, encapsulation of NPs is a recommended technique, it also reduces the use of pesticides and the cost of agricultural production. Encapsulation facilitates the persistence of NPs in root zones or inside plants without compromising their efficiency by limiting their solubility in water (Prasad et al., 2017; Sampathkumar et al., 2020; Vega-Vásquez et al., 2020).

Halloysite nanotubes are tubular clay nanomaterials of natural origin. They are used in a variety of applications, such as environmental sciences, wastewater treatment, dye removal, nanoelectronics, and nanocomposite fabrication (Satish et al., 2019). Encapsulation of NPs in halloysites capsules may be cost-effective and efficient. As demonstrated by Kim et al., Halloysites show sustained release of active ingredients. In their studies, the prevention of Indian fly (*Plodia interpunctella*) to spoil food is prevented by applying clove oil encapsulated in halloysite and polyethyleneimine nanotubes, the result demonstrated a slow and controlled release of oil (Kim et al., 2016). Copper nanoparticles incorporated into halloysite nanotubes have shown good antibacterial activity against *Escherichia coli* (Ding et al., 2014). Unfortunately, no studies have been performed against insects.

Silica nanostructures have entomotoxic effects against cotton worms (*S. littoralis*). The nanostructures cause extreme dehydration due to damage in the cuticular insect barrier (Ayoub et al., 2017). The application of these nanostructures as fertilizers and insecticides against *Sitophilus oryzae*, *Rhizopertha dominica*, *T. castaneum*, and *Orizaephilus surinamenisis* demonstrated improved maize growth, meanwhile, NPs are considered potent unconventional pesticides (El-Naggar et al., 2020). Silica can support copper nanoparticles with a strong dispersion (Huang et al., 2008). Maniprasad and Santra formed a complex nanostructure of Silica shell that accommodate copper. The resulting structure was highly monodispersing and more effective as an antibacterial agent (Maniprasad and Santra, 2012). Copper ions (Cu^{2+}) chelated mesoporous silica nanoparticles are recommended for the control of azoxystrobin release. The control is done by the coordination bonding interaction between copper ions and azoxystrobin (Xu et al., 2020). Treatment of contaminated soil with green copper nanoparticles improves the growth of wheat plants by decreasing the acropetal Cd translocation in the treated wheat (Noman et al., 2020). The incorporation of silica nanoparticles and copper nanoparticles is probably more effective against crop pests.

Chitosan has significant insecticidal activity (Said et al., 2011). It allows the encapsulation of the active ingredients and therefore form new and more powerful biocides against pathogens and plant pests. Chitosan allows bioavailability and well-controlled release of NPs. Encapsulation of active products in chitosan nanotransporters protects plants against the toxic effect of active products and minimizes negative impacts (Maluin and Hussein, 2020). The incorporation of chitosan with CuNPs improves antimicrobial activity (Jayaramudu et al., 2019), Cu nanoparticles

encapsulated in alginate and chitosan revealed good inhibitory activity against *T. urticae* (Dorri et al., 2018). In *Eleusine coracana* Gaertn, the application of copper-chitosan nanoparticles as a blast disease controller by foliar spray increases yield and inhibits disease development (Sathiyabama and Manikandan, 2018). Field application of copper and chitosan nanoparticles improves the growth and yield of maize and controls Curvularia leaf spot (CLS) disease (Choudhary et al., 2017). The innovation of techniques for controlling the delivery systems of insecticide NPs allows for "precision agriculture," which targets only crop protection without affecting water and soil (Duhan et al., 2017).

5 Toxicity and a beneficial effect of CuNPs for nontarget cells

The limited knowledge about terrestrial and aquatic ecotoxicology of CuNPs, and even their side effects on human and plant health, which are not yet discussed, require many concerns that remain to be deepened and illustrated before the use of CuNPs in the field. The field of nanoparticles and transgenic plants has undergone a remarkable development in recent decades, while the interaction between NPs and transgenic plants has not yet been well studied, which requires systematic studies to reveal the unintended impacts. In transgenic Bt cotton and conventional cotton, CuNPs inhibited growth, development, nutrient content, and concentrations of indole-3-acetic acid and abscisic acid. The images obtained by electron microscopy show that CuNPs form aggregates in the epidermis of conventional cotton leaves, whereas in transgenic cotton, NPs reach the leaf cells by endocytosis. NPs have also been identified in the outer epidermis of the root and in the intercellular spaces of conventional and transgenic cotton (Van et al., 2016). However, depending on the applied concentration, CuNPs can cause phytotoxic effects. A recent study demonstrated that the low concentrations ($40\,\mu g\,mL^{-1}$) of copper NPs (~ 6.6 nm) synthesized by the green method does not affect or enhance the growth of *Lactuca sativa* seedlings, whereas, at higher concentrations, an inhibition of seed germination and radicle growth was observed. The high NPs concentrations also induced a decrease in total antioxidant activities. At concentration $\leq 20\,\mu g\,mL^{-1}$ of CuNPs, beneficial effects characterized by improved plant growth are obtained (Pelegrino et al., 2020).

Further in-depth studies are underway. The results clearly showed that high concentrations of NP inhibit seed germination and early growth of rice plants (*Oryza sativa*) (Wang et al., 2020). Phytotoxicity is probably induced by the accumulation of copper in the cells and severe oxidative damage generated by the formation of ROS (Shaw and Hossain, 2013). An exposure concentration greater than $10\,mg\,L^{-1}$ of CuNPs leads to deleterious effects in the germination of *Raphanus sativus* seeds (Singh and Kumar, 2019), the exposure of *Spinacia oleracea* to a concentration of $1.2\times10^{-2}\,mol\,kg^{-1}$ of soil induces a reduction of 36% of plant biomass (Singh and Kumar, 2020).

Foliar application of copper nanoparticles (250 mg L^{-1}) to tomatoes grown under salt stress reduced salt damage. Also, foliar application of CuNPs increased performance and improved the Na^+/K^+ ratio. In addition, the level of phenols and the enzymatic activity of phenylalanine ammonia-lyase, ascorbate peroxidase, glutathione peroxidase, SOD, and CAT were increased, suggesting that foliar spraying of tomatoes by CuNPs improves tolerance to salt stress (Pérez-Labrada et al., 2019). The same beneficial effects are observed with the application of CuNPs in peppers grown under salt stress. NPs ameliorated the content of bioactive compounds in fruits (González-García et al., 2021). The application of CuNPs also generates beneficial effects by increasing enzymatic and nonenzymatic compounds and reducing the severity of *Alternaria solani* in tomatoes (Quiterio-Gutiérrez et al., 2019). Another study found that NPs increase crop yield while also improving antioxidant enzymes and vitamin C (Hernández-Hernández et al., 2019). However, the interactions of CuNPs with the tissues and cellular DNA of plants can be harmful. The sensitivity of bell pepper (*Capsicum annum* L.) to the harmful effects of CuNPs depends on the applied concentrations (Rawat et al., 2018). The accumulation of NPs leads to the formation of ROS and induces changes in proteins, cellulose, and carbohydrates (Ahmed et al., 2018).

The harmful effects of CuNPs are strongly related to the applied dose. Exposure of *Solanum lycopersicum* and *Brassica oleracea* plants to 100 and 500 mg L^{-1} of CuNPs resulted in a decrease in the chlorophyll and sugar content in both plants, while 10 mg L^{-1} of NPs lightly increased the pigment and sugar content in the tomato plants. High concentrations of NPs cause lipid peroxidation (Singh et al., 2017). In spring barley (*Hordeum sativum* distichum), CuNPs affect germination rate, root length, and transpiration rate. Changes have also been identified in cell organelles (plastids, mitochondria), starch granules, protoplasm, and membranes (Rajput et al., 2018). In order to ensure a healthy diet, it is advisable to determine the potential risk of consuming plants contaminated with CuNPs.

6 Conclusion and future perspectives

The failure of conventional plans to control crop damage caused by insect pests has prompted researchers to adopt new farm management plans. Several scientific studies have demonstrated the effectiveness of CuNPs in the control of insect pests. CuNPs damage vital cells and lead to the death of the insect. However, several studies have also shown that the massive use of CuNPs negatively affects the metabolism of the plant and its yield. Further studies are needed to fully elucidate the toxicity of CuNPs in nontarget cells. Otherwise, the insecticidal activity of CuNPs encourages their use in biological control with new formulations. The new formulations can also lead to minimizing the excessive use of pesticides and their toxicity problems.

References

Abbas, S., Nasreen, S., Haroon, A., Ashraf, M.A., 2020. Synthesis of silver and copper nanoparticles from plants and application as adsorbents for naphthalene decontamination. Saudi. J. Biol. Sci. 27, 1016–1023.

Abd El Wahab, R.A., Anwar, E.M., 2014. The effect of direct and indirect use of nanoparticles on cotton leaf worm, *Spodoptera littoralis*. Int. J. Chem. Biol. Sci. 1, 17–24.

Aguilera-Correa, J.J., Esteban, J., Vallet-Regí, M., 2021. Inorganic and polymeric nanoparticles for human viral and bacterial infections prevention and treatment. Nano 111, 137.

Ahamed, M., Siddiqui, M.A., Akhtar, M.J., Ahmad, I., Pant, A.B., Alhadlaq, H.A., 2010. Genotoxic potential of copper oxide nanoparticles in human lung epithelial cells. Biochem. Biophys. Res. Commun. 396, 578–583.

Ahmed, B., Khan, M.S., Musarrat, J., 2018. Toxicity assessment of metal oxide nanopollutants on tomato (*Solanum lycopersicon*): A study on growth dynamics and plant cell death. Environ. Pollut. 240, 802–816.

Alif Alisha, A.S., Thangapandiyan, S., 2019. Comparative bioassay of silver nanoparticles and malathion on infestation of red flour beetle *Tribolium castaneum*. JoBAZ 80, 1–10.

Angelé-Martínez, C., Nguyen, K.V., Ameer, F.S., Anker, J.N., Brumaghim, J.L., 2017. Reactive oxygen species generation by copper(II) oxide nanoparticles determined by DNA damage assays and EPR spectroscopy. Nanotoxicology 11, 278–288.

Atwa, A., Salah, N., Khafagi, W., Al-Ghamdi, A., 2017. Insecticidal effects of pure and silver-doped copper oxide nanosheets on *Spodoptera littoralis* (Lepidoptera: *Noctuidae*). Canad. Entomol. 149, 677–690.

Ayoub, H.A., Khairy, M., Rashwan, F.A., Abdel-Hafez, H.F., 2017. Synthesis and characterization of silica nanostructures for cotton leafworm control. J. Nanostruct. Chem. 7, 91–100.

Bayda, S., Adeel, M., Tuccinardi, T., Cordani, M., Rizzolio, F., 2019. The history of nanoscience and nanotechnology: from chemical-physical applications to nanomedicine. Molecules 25, 112.

Bulcke, F., Dringen, R., 2016. Handling of copper and copper oxide nanoparticles by astrocytes. Neurochem. Res. 41, 33–43.

Cai, L., Chen, J., Liu, Z., Wang, H., Yang, H., Ding, W., 2018. Magnesium oxide nanoparticles: effective agricultural antibacterial agent against *Ralstonia solanacearum*. Front. Microbiol. 9, 790.

Carmona, E.R., Inostroza-Blancheteau, C., Obando, V., Rubio, L., Marcos, R., 2015. Genotoxicity of copper oxide nanoparticles in *Drosophila melanogaster*. Mutat. Res. Genet. Toxicol. Environ. Mutagen. 791, 1–11.

Chatterjee, A.K., Chakraborty, R., Basu, T., 2014. Mechanism of antibacterial activity of copper nanoparticles. Nanotechnology 25, 135101.

Choudhary, R.C., Kumaraswamy, R.V., Kumari, S., Sharma, S.S., Pal, A., Raliya, R., Biswas, P., Saharan, V., 2017. Cu-chitosan nanoparticle boost defense responses and plant growth in maize (*Zea mays* L.). Sci. Rep. 7, 9754.

Christiaens, O., Niu, J., Nji Tizi Taning, C., 2020. RNAi in insects: A revolution in fundamental research and pest control applications. Insects 11, 415.

Courtier-Orgogozo, V., Morizot, B., Boëte, C., 2017. Agricultural pest control with CRISPR-based gene drive: time for public debate: Should we use gene drive for pest control? EMBO Rep. 18, 878–880.

Cruz, L.F., Cruz, J.C., Carrillo, D., Mtz-Enriquez, A.I., Lamelas, A., Ibarra-Juarez, L.A., Pariona, N., 2021. In-vitro evaluation of copper nanoparticles as a potential control agent against the fungal symbionts of the invasive ambrosia beetle *Euwallacea fornicatus*. Crop Prot. 143, 105564.

Damalas, C.A., Eleftherohorinos, I.G., 2011. Pesticide exposure, safety issues, and risk assessment indicators. Int. J. Environ. Res. Public Health 8, 1402–1419.

Danbature, W.L., Shehu, Z., Mai, A.J., Magaji, B., Adam, M.M., Bunu, M.A., 2020. Green synthesis, characterization and larvicidal activity of Cu/Ni bimetallic nanoparticles using fruit extract of Palmyra palm. Int. J. Chem. Mater. Res. 8, 20–25.

Ding, X., Wang, H., Chen, W., Liua, J., Zhang, Y., 2014. Preparation and antibacterial activity of copper nanoparticle/halloysite nanotube nanocomposites via reverse atom transfer radical polymerization. RSC Adv. 4, 41993–41996.

Dorri, H.R., Khaghani, S.H., Moghadam, A., Ghanbari, D., Bihamta, M.R., 2018. The effect of copper nano-capsules on the control of two spotted spider mite (*Tetranychus urticae*). J. Nanostruct. 8, 316–324.

Duhan, J.S., Kumar, R., Kumar, N., Kaur, P., Nehra, K., Duhan, S., 2017. Nanotechnology: the new perspective in precision agriculture. Biotechnol. Rep. 15, 11–23.

Ehrlich, P.R., Harte, J., 2015. Opinion: to feed the world in 2050 will require a global revolution. Proc. Natl. Acad. Sci. U. S. A. 112, 14743–14744.

Elfeky, A.S., Salem, S.S., Elzaref, A.S., Owda, M.E., Eladawy, H.A., Saeed, A.M., Awad, M.A., Abou-Zeid, R.E., Fouda, A., 2020. Multifunctional cellulose nanocrystal /metal oxide hybrid, photo-degradation, antibacterial and larvicidal activities. Carbohydr. Polym. 230, 115711.

El-Naggar, M.E., Abdelsalam, N.R., Fouda, M., Mackled, M.I., Al-Jaddadi, M., Ali, H.M., Siddiqui, M.H., Kandil, E.E., 2020. Soil application of nano silica on maize yield and its insecticidal activity against some stored insects after the post-harvest. Nano 10, 739.

El-Saadony, M.T., Abd El-Hack, M.E., Taha, A.E., Fouda, M., Ajarem, J.S., Maodaa, S.N., Allam, A.A., Elshaer, N., 2020. Ecofriendly synthesis and insecticidal application of copper nanoparticles against the storage pest *Tribolium castaneum*. Nano 10, 587.

Gomes, T., Pinheiro, J.P., Cancio, I., Pereira, C.G., Cardoso, C., Bebianno, M.J., 2011. Effects of copper nanoparticles exposure in the mussel *Mytilus galloprovincialis*. Environ. Sci. Technol. 45, 9356–9362.

González-García, Y., Cárdenas-Álvarez, C., Cadenas-Pliego, G., Benavides-Mendoza, A., Cabrera-de-la-Fuente, M., Sandoval-Rangel, A., Valdés-Reyna, J., Juárez-Maldonado, A., 2021. Effect of three nanoparticles (Se, Si and Cu) on the bioactive compounds of bell pepper fruits under saline stress. Plan. Theory 10, 217.

Gromadzka, G., Tarnacka, B., Flaga, A., Adamczyk, A., 2020. Copper dyshomeostasis in neurodegenerative diseases-therapeutic implications. Int. J. Mol. Sci. 21, 9259.

Hanagata, N., Zhuang, F., Connolly, S., Li, J., Ogawa, N., Xu, M., 2011. Molecular responses of human lung epithelial cells to the toxicity of copper oxide nanoparticles inferred from whole genome expression analysis. ACS Nano 5, 9326–9338.

Hao, Y., Cao, X., Ma, C., Zhang, Z., Zhao, N., Ali, A., Hou, T., Xiang, Z., Zhuang, J., Wu, S., Xing, B., Zhang, Z., Rui, Y., 2017. Potential applications and antifungal activities of engineered nanomaterials against gray mold disease agent *Botrytis cinerea* on rose petals. Front. Plant Sci. 8, 1332.

Hassanain, N.A.E.H., Shehata, A.Z., Mokhtar, M.M., Shaapan, R.M., Hassanain, M.A.L.H., Zaky, S., 2019. Comparison between insecticidal activity of *Lantana camara* extract and its synthesized nanoparticles against *Anopheline mosquitoes*. Pak. J. Biol. Sci. 22, 327–334.

Hawkins, N.J., Bass, C., Dixon, A., Neve, P., 2018. The evolutionary origins of pesticide resistance. Biol. Rev. Camb. Philos. Soc. 94, 135–155.
Hernández-Hernández, H., Quiterio-Gutiérrez, T., Cadenas-Pliego, G., Ortega-Ortiz, H., Hernández-Fuentes, A.D., Cabrera de la Fuente, M., Valdés-Reyna, J., Juárez-Maldonado, A., 2019. Impact of selenium and copper nanoparticles on yield, antioxidant system, and fruit quality of tomato plants. Plan. Theory 8, 355.
Huang, Z., Cui, F., Kang, H., Chen, J., Zhang, X., Xia, C., 2008. Highly dispersed silica-supported copper nanoparticles prepared by precipitation-gel method: A simple but efficient and stable catalyst for glycerol hydrogenolysis. Chem. Mater. 20, 5090–5099.
Huang, S., Wang, Y., Shen, S., Tang, Y., Yu, A., Kang, B., Silva, S., Lu, G., 2019. Enhancing the performance of polymer solar cells using solution-processed copper doped nickel oxide nanoparticles as hole transport layer. J. Colloid Interface Sci. 535, 308–317.
Ishangulyyev, R., Kim, S., Lee, S.H., 2019. Understanding food loss and waste-why are we losing and wasting food? Foods 8, 297.
Jayaramudu, T., Varaprasad, K., Pyarasani, R.D., Reddy, K.K., Kumar, K.D., Akbari-Fakhrabadi, A., Mangalaraja, R.V., Amalraj, J., 2019. Chitosan capped copper oxide/copper nanoparticles encapsulated microbial resistant nanocomposite films. Int. J. Biol. Macromol. 128, 499–508.
Joshi, A., Thiel, K., Jog, K., Dringen, R., 2019. Uptake of intact copper oxide nanoparticles causes acute toxicity in cultured glial cells. Neurochem. Res. 44, 2156–2169.
Karlsson, H.L., Gustafsson, J., Cronholm, P., Möller, L., 2009. Size-dependent toxicity of metal oxide particles- -a comparison between nano- and micrometer size. Toxicol. Lett. 188, 112–118.
Karlsson, H.L., Cronholm, P., Hedberg, Y., Tornberg, M., De Battice, L., Svedhem, S., Wallinder, I.O., 2013. Cell membrane damage and protein interaction induced by copper containing nanoparticles- -importance of the metal release process. Toxicology 313, 59–69.
Kim, J., Park, N.H., Na, J.H., Han, J., 2016. Development of natural insect-repellent loaded halloysite nanotubes and their application to food packaging to prevent *Plodia interpunctella* infestation. J. Food Sci. 81, E1956–E1965.
Kumar, B., Smita, K., Debut, A., Cumbal, L., 2020. Andean Sacha Inchi (*Plukenetia Volubilis* L.) leaf-mediated synthesis of Cu_2O nanoparticles: A low-cost approach. Bioengineering 7, 54.
Liu, J., Fand, D., Wang, L., Shi, L., Ding, J., Chen, Y., Shen, S., 2014. Effects of ZnO, CuO, Au, and TiO_2 nanoparticles on *Daphnia magna* and early life stages of zebrafish danio rerio. Environ. Prot. Eng. 40, 139–149.
Lu, K., Li, W., Cheng, Y., Ni, H., Chen, X., Li, Y., Tang, B., Sun, X., Li, Y., Liu, T., Qin, N., Chen, D., Zeng, R., Song, Y., 2019. Copper exposure enhances *Spodoptera litura* larval tolerance to β-cypermethrin. Pestic. Biochem. Physiol. 160, 127–135.
Maluin, F.N., Hussein, M.Z., 2020. Chitosan-based agronanochemicals as a sustainable alternative in crop protection. Molecules 25, 1611.
Maniprasad, P., Santra, S., 2012. Novel copper (Cu) loaded core-shell silica nanoparticles with improved Cu bioavailability: synthesis, characterization and study of antibacterial properties. J. Biomed. Nanotechnol. 8, 558–566.
Mehdizadeh, T., Zamani, A., Abtahi Froushani, S.M., 2020. Preparation of cu nanoparticles fixed on cellulosic walnut shell material and investigation of its antibacterial, antioxidant and anticancer effects. Heliyon. 6, e03528.
Minocha, S., Mumper, R.J., 2012. Effect of carbon coating on the physico-chemical properties and toxicity of copper and nickel nanoparticles. Small 8, 3289–3299.

Muthamil Selvan, S., Vijai Anand, K., Govindaraju, K., Tamilselvan, S., Kumar, V.G., Subramanian, K.S., Kannan, M., Raja, K., 2018. Green synthesis of copper oxide nanoparticles and mosquito larvicidal activity against dengue, zika and chikungunya causing vector *Aedes aegypti*. IET. Nanobiotechnology 12, 1042–1046.

Noman, M., Ahmed, T., Hussain, S., Niazi, M., Shahid, M., Song, F., 2020. Biogenic copper nanoparticles synthesized by using a copper-resistant strain *Shigella flexneri* SNT22 reduced the translocation of cadmium from soil to wheat plants. J. Hazard. Mater. 398, 123175.

Oesterlund, A.H., Thomsen, J.F., Sekimpi, D.K., Maziina, J., Racheal, A., Jørs, E., 2014. Pesticide knowledge, practice and attitude and how it affects the health of small-scale farmers in Uganda: a cross-sectional study. Afr. Health Sci. 14, 420–433.

Parthiban, E., Manivannan, N., Ramanibai, R., Mathivanan, N., 2018. Green synthesis of silver-nanoparticles from *Annona reticulata* leaves aqueous extract and its mosquito larvicidal and anti-microbial activity on human pathogens. Biotechnol. Rep. 21, e00297.

Pelegrino, M.T., Kohatsu, M.Y., Seabra, A.B., Monteiro, L.R., Gomes, D.G., Oliveira, H.C., Rolim, W.R., de Jesus, T.A., Batista, B.L., Lange, C.N., 2020. Effects of copper oxide nanoparticles on growth of lettuce (*Lactuca sativa* L.) seedlings and possible implications of nitric oxide in their antioxidative defense. Environ. Monit. Assess. 192, 232.

Pérez-Labrada, F., López-Vargas, E.R., Ortega-Ortiz, H., Cadenas-Pliego, G., Benavides-Mendoza, A., Juárez-Maldonado, A., 2019. Responses of tomato plants under saline stress to foliar application of copper nanoparticles. Plan. Theory 8, 151.

Pham, M.H., Sebesvari, Z., Tu, B.M., Pham, H.V., Renaud, F.G., 2011. Pesticide pollution in agricultural areas of Northern Vietnam: case study in Hoang Liet and Minh Dai communes. Environ. Pollut. 159, 3344–3350.

Prasad, R., Bhattacharyya, A., Nguyen, Q.D., 2017. Nanotechnology in sustainable agriculture: recent developments, challenges, and perspectives. Front. Microbiol. 8, 1014.

Quiterio-Gutiérrez, T., Ortega-Ortiz, H., Cadenas-Pliego, G., Hernández-Fuentes, A.D., Sandoval-Rangel, A., Benavides-Mendoza, A., Cabrera-de la Fuente, M., Juárez-Maldonado, A., 2019. The application of selenium and copper nanoparticles modifies the biochemical responses of tomato plants under stress by *Alternaria solani*. Int. J. Mol. Sci. 20, 1950.

Rajput, V., Minkina, T., Fedorenko, A., Sushkova, S., Mandzhieva, S., Lysenko, V., Duplii, N., Fedorenko, G., Dvadnenko, K., Ghazaryan, K., 2018. Toxicity of copper oxide nanoparticles on spring barley (*Hordeum sativum distichum*). Sci. Total Environ. 645, 1103–1113.

Ramadan, A.F., Abol-Noor, K.M.A., Elshiekh, A., Aboghalia, A., El-Shafiey, S.N., 2020. Responses of desert locust *Schistocerca gregaria* (Orthoptera: *Acrididae*) to treatment with chemically synthesized zinc and copper oxides nanoparticle. Egypt. J. Plant Protect. Res. Inst. 3, 339–345.

Rawat, S., Pullagurala, V.L.R., Hernandez-Molina, M., Sun, Y., Niu, G., Hernandez-Viezcas, J.A., Peralta-Videa, J.R., Gardea-Torresdey, J.L., 2018. Impacts of copper oxide nanoparticles on bell pepper (*Capsicum annum* L.) plants: a full life cycle study. Environ. Sci: Nano. 5, 83–95.

Rui, M., Ma, C., Hao, Y., Guo, J., Rui, Y., Tang, X., Zhao, Q., Fan, X., Zhang, Z., Hou, T., Zhu, S., 2016. Iron oxide nanoparticles as a potential iron fertilizer for peanut (*Arachis hypogaea*). Front. Plant Sci. 7, 815.

Said, S.M., El-Sayed, S.M., Farid, H.E.A., Abozid, M.M., 2011. Insecticidal effect of chitosan prepared by different chemical processing sequences against *Galleria melleonella*. Az. J. Pharm. Sci. 43, 123–132.

Sampathkumar, K., Tan, K.X., Loo, S., 2020. Developing nano-delivery systems for agriculture and food applications with nature-derived polymerse. iScience 23, 101055.
Sathiyabama, M., Manikandan, A., 2018. Application of copper-chitosan nanoparticles stimulate growth and induce resistance in finger millet (*Eleusine coracana* Gaertn.) plants against blast disease. J. Agric. Food Chem. 66, 1784–1790.
Satish, S., Tharmavaram, M., Rawtani, D., 2019. Halloysite nanotubes as a nature's boon for biomedical applications. Nanobiomedicine 6. 1849543519863625.
Satterthwaite, D., McGranahan, G., Tacoli, C., 2010. Urbanization and its implications for food and farming. Philos. Trans. R. Soc. Lond. B Biol. Sci. 365, 2809–2820.
Scheiber, I.F., Mercer, J.F., Dringen, R., 2014. Metabolism and functions of copper in brain. Prog. Neurobiol. 116, 33–57.
Sezer Tuncsoy, B., Ozalp, P., 2017. Effects of copper oxide nanoparticles on hemocytes of *Galleria mellonella*. Toxicol. Lett. 280, S187.
Sezer Tuncsoy, B., Tuncsoy, M., Gomes, T., Sousa, V., Teixeira, M.R., Bebianno, M.J., Ozalp, P., 2019. Effects of copper oxide nanoparticles on tissue accumulation and antioxidant enzymes of *Galleria mellonella* L. Bull. Environ. Contam. Toxicol. 102, 341–346.
Shaker, A.M., Zaki Elham, A.H., Abdel-Rahim, F., Khedr, M.H., 2016. Novel CuO nanoparticles for pest management and pesticides photodegradation. Adv. Environ. Biol. 10, 274–283.
Shang, Y., Hasan, M.K., Ahammed, G.J., Li, M., Yin, H., Zhou, J., 2019. Applications of nanotechnology in plant growth and crop protection: A review. Molecules 24, 2558.
Shaw, A.K., Hossain, Z., 2013. Impact of nano-CuO stress on rice (*Oryza sativa* L.) seedlings. Chemosphere 93, 906–915.
Singh, D., Kumar, A., 2019. Assessment of toxic interaction of nano zinc oxide and nano copper oxide on germination of *Raphanus sativus* seeds. Environ. Monit. Assess. 191, 703.
Singh, D., Kumar, A., 2020. Quantification of metal uptake in *Spinacia oleracea* irrigated with water containing a mixture of CuO and ZnO nanoparticles. Chemosphere 243, 125239.
Singh, A., Singh, N.B., Hussain, I., Singh, H., 2017. Effect of biologically synthesized copper oxide nanoparticles on metabolism and antioxidant activity to the crop plants *Solanum lycopersicum* and *Brassica oleracea* var. *botrytis*. J. Biotechnol. 262, 11–27.
Tang, H., Xu, M., Shi, F., Ye, G., Lv, C., Luo, J., Zhao, L., Li, Y., 2018. Effects and mechanism of nano-copper exposure on hepatic cytochrome P450 enzymes in rats. Int. J. Mol. Sci. 19, 2140.
Van, N.L., Ma, C., Shang, J., Rui, Y., Liu, S., Xing, B., 2016. Effects of CuO nanoparticles on insecticidal activity and phytotoxicity in conventional and transgenic cotton. Chemosphere 144, 661–670.
Vanwinkle, B.A., de Mesy Bentley, K.L., Malecki, J.M., Gunter, K.K., Evans, I.M., Elder, A., Finkelstein, J.N., Oberdörster, G., Gunter, T.E., 2009. Nanoparticle (NP) uptake by type I alveolar epithelial cells and their oxidant stress response. Nanotoxicology 3, 307–318.
Vargas-Hernandez, M., Macias-Bobadilla, I., Guevara-Gonzalez, R.G., Rico-Garcia, E., Ocampo-Velazquez, R.V., Avila-Juarez, L., Torres-Pacheco, I., 2020. Nanoparticles as potential antivirals in agriculture. Agriculture 10, 444.
Varympopi, A., Dimopoulou, A., Theologidis, I., Karamanidou, T., Kaldeli Kerou, A., Vlachou, A., Karfaridis, D., Papafotis, D., Hatzinikolaou, D.G., Tsouknidas, A., Skandalis, N., 2020. Bactericides based on copper nanoparticles restrain growth of important plant pathogens. Pathogens 9, 1024.
Vega-Vásquez, P., Mosier, N.S., Irudayaraj, J., 2020. Nanoscale drug delivery systems: from medicine to agriculture. Front. Bioeng. Biotechnol. 8, 79.

Velsankar, K., Aswin Kumar, R.M., Preethi, R., Muthulakshmi, V., Sudhahar, S., 2020. Green synthesis of CuO nanoparticles via Allium sativum extract and its characterizations on antimicrobial, antioxidant, antilarvicidal activities. J. Environ. Chem. Eng. 8, 104123.

Wang, W., Liu, J., Ren, Y., Zhang, L., Xue, Y., Zhang, L., He, J., 2020. Phytotoxicity assessment of copper oxide nanoparticles on the germination, early seedling growth, and physiological responses in *Oryza sativa* L. Bull. Environ. Contam. Toxicol. 104, 770–777.

Willsey, T., Chatterton, S., Cárcamo, H., 2017. Interactions of root-feeding insects with fungal and oomycete plant pathogens. Front. Plant Sci. 8, 1764.

Xu, M., Tang, H., Zhou, X., Chen, H., Dong, Q., Zhang, Y., Ye, G., Shi, F., Lv, C., Jing, B., He, C., Zhao, L., Li, Y., 2018. Effects and mechanisms of sub-chronic exposure to copper nanoparticles on renal cytochrome P450 enzymes in rats. Environ. Toxicol. Pharmacol. 63, 135–146.

Xu, C., Shan, Y., Bilal, M., Xu, B., Cao, L., Huang, Q., 2020. Copper ions chelated mesoporous silica nanoparticles via dopamine chemistry for controlled pesticide release regulated by coordination bonding. Chem. Eng. J. 395, 125093.

Zhang, X.F., Liu, Z.G., Shen, W., Gurunathan, S., 2016. Silver nanoparticles: synthesis, characterization, properties, applications, and therapeutic approaches. Int. J. Mol. Sci. 17, 1534.

Zhang, J., Wang, J., Zhou, X., 2019. Farm machine use and pesticide expenditure in maize production: health and environment implications. Int. J. Environ. Res. Public Health 16, 1808.

Zhou, X., Zhao, L., Luo, J., Tang, H., Xu, M., Wang, Y., Yang, X., Chen, H., Li, Y., Ye, G., Shi, F., Lv, C., Jing, B., 2019. The toxic effects and mechanisms of nano-cu on the spleen of rats. Int. J. Mol. Sci. 20, 1469.

CHAPTER

Copper nanomaterials for pesticide detection

10

Alexsandra Valério[a], Danielle Maass[b], Lidiane Maria de Andrade[c], Dachamir Hotza[a], Débora de Oliveira[a], and Cristiano José de Andrade[a]

[a]*Department of Chemical Engineering and Food Engineering (EQA), Federal University of Santa Catarina (UFSC), Florianópolis, Brazil*

[b]*Institute of Science and Technology (ICT), Federal University of São Paulo (UNIFESP), São José dos Campos, Brazil*

[c]*Department of Chemical Engineering. University of São Paulo (USP), São Paulo, Brazil*

1 Introduction

Climate changes have been imposing unprecedented challenges on global agricultural systems. Advanced nanotechnology is emerging as a handy tool for increasing crop production, assuring sustainability, and improving food security. Agricultural production is enhanced by using nanotechnology techniques that boost the efficiency of inputs and diminish relevant losses. Nanomaterials offer a wider specific surface area to fertilizers and pesticides.

Pesticides are often misused in the endeavor to increase agricultural productivity. Thus, it is crucial to advance technologically on the accurate detection methods of pesticides (e.g., novel methods, portability, sensibility, precision, speed, among others) (Burrati et al., 2021).

In this sense, fluorescent, colorimetric, and electrochemical nanosensors for monitoring a wide range of pesticides have been attracting great interest recently due to their economical, efficient, user-friendly, easy to operate, rapid, and sensitive detection in comparison to the traditional techniques (Burrati et al., 2021; Chen et al., 2021; Choi, 2021; Li et al., 2021; Wang et al., 2020).

These sensors can be based on metallic nanoparticles such as copper nanoparticles (CuNPs). CuNPs play an essential role in several areas, such as optics, electronics, and antimicrobial applications. Currently, there is a great diversity of inorganic nanoparticles that present unique properties as a function of composition, morphology, size, shape, geometry, homogeneity, and surface area. Inorganic nanoparticles can be applied to distinct areas, including agriculture. The control of the size, form, and consequently the properties of the CuNPs are dependent on the synthesis parameters.

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Chen et al. (2021) proposed a Cu^{2+}-g-C_3N_4 nanosheet probe as a novel fluorescent and calorimetric dual-response sensor using malathion pesticide as a model. The authors obtained lower detection limits for fluorescence and calorimetric probes of 6.798 and 1.497 nM, respectively, indicating a reliable and high sensitivity alternative, when compared with traditional methods.

To detect organophosphorus pesticide, which is highly neurotoxic and a severe threat to food safety, CuNP-based aptasensors have been developed. A label-free and enzyme-free fluorescent aptasensor for detecting acetamiprid based on AT-rich dsDNA-templated CuNPs showed a sensitive and selective fluorescence enhancement acetamiprid, reaching a detection limit of 2.37 nM (Fan et al., 2019). An aptasensor based on one step coelectrodeposition of aptamer and GO-CuNP nanocomposite for organophosphorus pesticide showed a detection limit of 0.003 nM for profenofos, 0.3 nM for phorate, 0.03 nM for isocarbophos, and 0.3 nM for omethoate (Fu et al., 2019). Another aptasensor using Fe_3O_4@GO and AT-TWJ DNA stabilized CuNPs as a background reducer and fluorescent signal, respectively, was developed and presented a sensitive and specific isocarbophos pesticide detection with a detection limit of 3.38 nM (Fan et al., 2020).

Setznagl and Cesarino (2020) determined glyphosate, a herbicide widely used, in water. They evaluated a glassy carbon electrode modified with reduced graphene oxide and CuNPs. Due to the Cu^0 to Cu^{2+} oxidation process, the authors verified that a decrease of 30 mV of the anodic peak decreases linearly with small glyphosate additions. In conclusion, the electrode can be used to quantify the pesticide content, achieving a linear response in the range of 0.1–1.1 $\mu mol\,L^{-1}$ with a detection limit of 0.19 $\mu mol\,L^{-1}$.

This chapter aims to highlight recent findings on copper nanomaterials for pesticide detection, including physical and chemical techniques for producing CuNPs and the nonconventional biological synthesis of CuNPs, which comprises bacteria, fungi, yeast, and plants (including algae). Then it describes the applications of CuNPs in agriculture with a focus on pesticides.

2 Copper nanoparticles production

2.1 Chemical synthesis

CuNPs have been synthesized by several chemical techniques that are based on the control of morphology, size, shape, geometry, homogeneity, and surface area. In this sense, the most critical parameters to be considered are the molar ratio, temperature, pH, and agitation speed (Kidwai et al., 2007; Miao and Wang, 2007; Sarwar et al., 2021; Tamilvanan et al., 2014).

Two different approaches can be carried out to synthesize CuNPs: top-down (physical methods) and bottom-up (chemical methods). In the top-down approach, the precursor is larger than the nanoparticles, and it is necessary to reduce the size down to nanoscale through mechanical processes. Contrariwise, in the bottom-up approach, the precursors, such as atoms or molecules, are smaller than the target nanostructures. Fig. 1 shows the physical and chemical routes for CuNP synthesis.

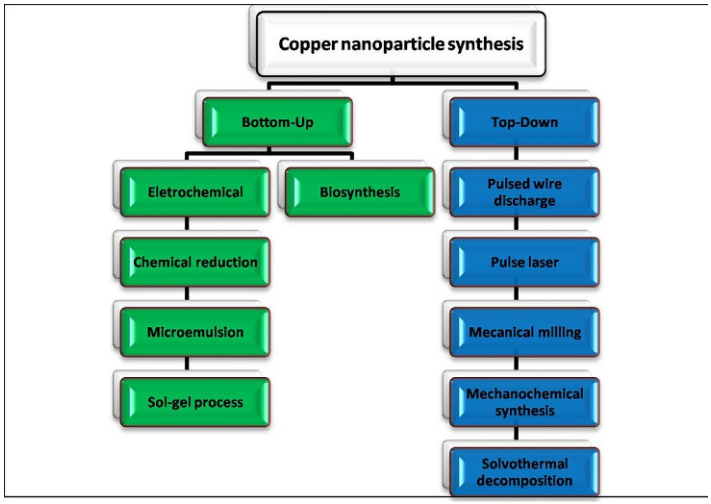

FIG. 1

Classification of CuNP synthesis techniques.

Microemulsion (microemulsion, reverse microemulsion, and bicontinuous) (Egorova and Revina, 2000; Pileni and Lisiecki, 1993; Solanki et al., 2010), electrochemical (Dorozhko et al., 2021; Kadam, 2016; Raja, 2008) and chemical reduction (Dan et al., 2021; Hashemipour et al., 2011; Narayanan and Sakthivel, 2010) are the most feasible techniques for synthesizing CuNP production. Thus, microemulsification, electrochemical and chemical reduction are briefly described below.

2.1.1 Microemulsification

Microemulsions are colloidal dispersions in which two liquids initially immiscible (water and oil) coexist in one phase due to the presence of a surfactant. Thus, microemulsions consist of a system formed by an aqueous, polar phase, an organic phase (usually oil, a nonpolar compound), and an optically stable surfactant (composed of a nonpolar hydrocarbon tail and a polar head). The surfactant forms an interfacial film, separating the polar and nonpolar phases. Different microstructures, from spherical drops or a bicontinuous phase (Eriksson, 2004; Malik et al., 2012; Pileni et al., 1999), can be formed depending on the oil-water ratio and also on the nonpolar and polar balance of the surfactant, as shown in Fig. 2, according to the Winsor classification (Sanchez-Dominguez et al., 2012).

In excess of oil, the oil-in-water microemulsion is formed, and the surfactant-rich water phase and the oil phase coexist (Fig. 2, I) (Sanchez-Dominguez et al., 2012). Water solubilized in the nucleus forms a water pool and the aggregates that present W (water/surfactant molar ratio) > 15 are named microemulsions (Luisi et al., 1986).

A bicontinuous phase (Fig. 2, III) is rich in surfactant and coexists with both excesses of water and oil phases in comparable amounts (three-phase system). Nevertheless, the surfactants do not have defined self-aggregation forms and can

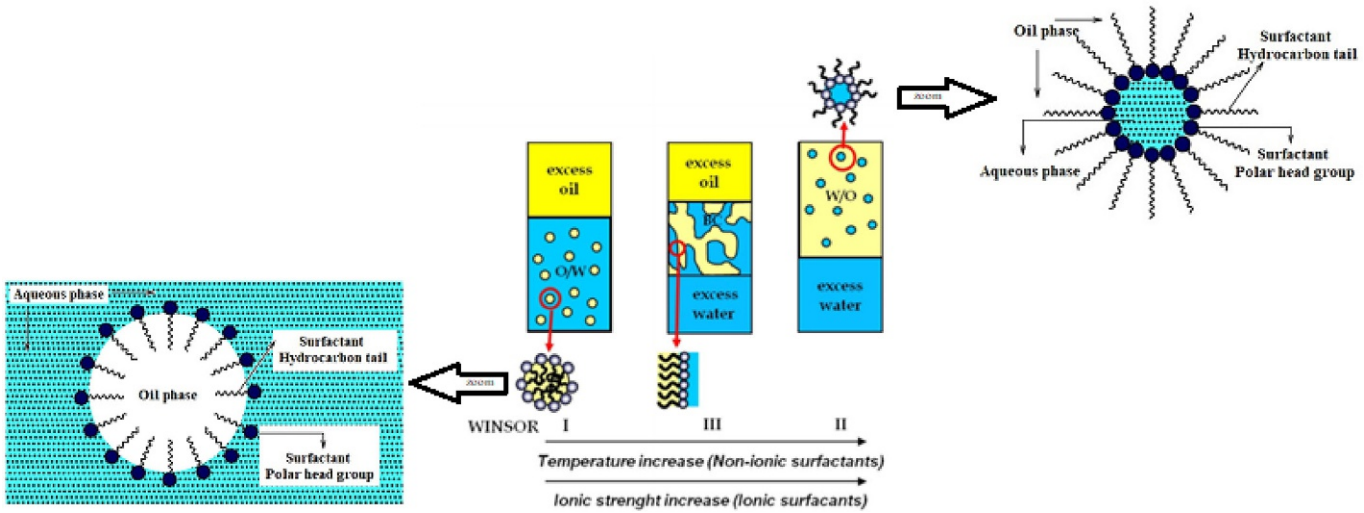

FIG. 2

Winsor classification of microemulsion equilibrium.

turn reversibly from one type to another (Eriksson, 2004; Malik et al., 2012; Pileni et al., 1999; Sanchez-Dominguez et al., 2012).

The microemulsion water-in-oil (Fig. 2, II), also known as reverse microemulsion, is formed when the concentration of the organic phase is much higher, which is surfactant-rich. The reverse microemulsion produces small spheroidal aggregates (in minimal quantities of water or the absence of water) (Eriksson, 2004; Malik et al., 2012; Pileni, 1989; Pileni et al., 1999; Sanchez-Dominguez et al., 2012). In the absence of water, the aggregates formed are exceedingly small. On the other hand, the presence of water induces large aggregates. If the aggregates present a water surfactant molar ratio (W) higher than 15, they are named reserve micelles (Luisi et al., 1986). Reverse microemulsion can be defined as a water-in-oil microemulsion. In this case, polar head groups of surfactants are attracted by the aqueous phase and directed toward the inside, and the polar phase (hydrocarbon) is attracted by the non-aqueous phase and directed toward the outside.

The mechanism for CuNP synthesis through microemulsifation consists of dissolved precursors in oil nanodroplets in an oil/water microemulsion stabilized by a hydrophilic surfactant.

The reverse microemulsification (water-in-oil) consists of two microemulsions, one containing the copper precursor and the other containing the precipitating agent. After the contact, due to the droplet collisions and coalescence, they will form a precipitate as nanoparticles in the microemulsion droplets' interior. The mechanism of nanoparticle synthesis by this method is shown in Fig. 3.

Microemulsification enables controlling the particle size at the nanoscale (up to 100 nm) (Richard et al., 2017), geometry, morphology, homogeneity, and surface area to obtain nearly monodispersed nanoparticles (Hu et al., 2009; Pileni, 2003; Sanchez-Dominguez et al., 2012). Moreover, oil/water synthesis, compared to water/oil synthesis, is more environmentally friendly since water is the predominant phase (Sanchez-Dominguez et al., 2012) (Fig. 4).

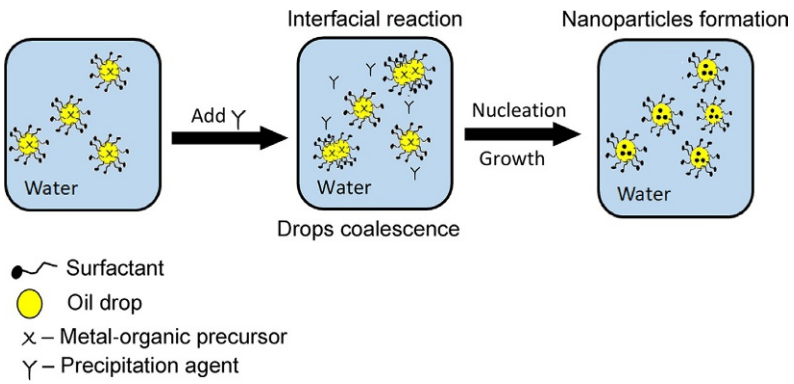

FIG. 3

Synthesis of nanoparticles by interfacial oil-in-water microemulsification.

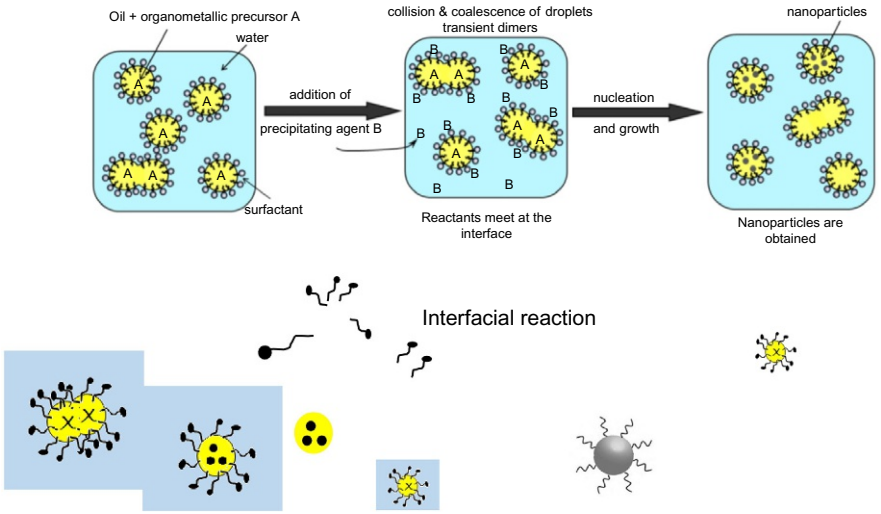

FIG. 4

Mechanism of nanoparticle synthesis by reverse microemulsification—Water-in-oil.

2.1.2 Electrochemical methods

There are many electrochemical methods to produce CuNPs, such as electrochemical milling, electrodeposition, electrochemical dissolution, hybrid electrochemical, thermal electrochemical (Anand et al., 2015; Zhang et al., 2005). Electrochemical deposition is one of the most promising nanoparticle synthesis techniques since it is noncomplex (operationally), low-cost, and easily scalable (Wei and Liu, 2017; Zhou et al., 2004).

The electrochemical method, which has been widely used to reduce metal ions, is based on an electrical current between cathodic and anodic electrodes separated for an electrolytic solution (Ghorbani, 2015).

The nucleation of nanoparticles occurs on the cathodic surface (metal, semiconductor, and polymers), producing various sizes and shapes of nanostructured particles (Nichols et al., 1995; Ortega, 2000; Zhou et al., 2004).

Regarding particle size, higher current densities lead to smaller CuNP sizes, for instance, from 35 to 110 nm (Xu et al., 2010). Besides, nanoparticles yield can be enhanced at higher temperatures; however, narrow-size distribution is often observed (Zhang and Hua, 2014).

Capping agents are also essential in the production of CuNPs by the electrochemical method. Ben Aissa et al. (2015) used oleylamine to synthesize anisotropic triangles, whereas Ko et al. (2009) used dodecylbenzene sulfonic acid and poly(vinylpyrrolidone) to produce nanoparticles in cubic, multipod, and pyramidal shapes. On the other hand, Wei and Liu (2017) studied agent capping (trisodium citrate—$Na_3C_6H_5O_7{\cdot}2H_2O$) to reduce deposited crystal aggregation. The authors described that the appropriate ratio of agent capping and $CuSO_4$ (precursor) contributed

to a good dispersity of cubes crystals formed. Besides, higher negative potential, higher nucleation, and smaller particles are observed. Kodaei and Karegar, 2021 studied polyvinyl pyrrolidone (PVP) and cetyltrimethylammonium bromide (CTAB) as double capping agents and concluded that these capping agents alone cannot be effective, but using these together is promising on the polyindole conductivity/stability.

2.1.3 Chemical reduction

Chemical reduction is one of the most important methods for CuNP synthesis. Chemical processes usually include a reduction of copper salt in various solvents (ethanol, methanol, water, acetonitrile, cyclohexane), reducing agents (polyols, sodium borohydride, hydrazine, ascorbic acid), and capping agents (polyethylene glycol and poly(vinylpyrrolidone)) (Chandra et al., 2014; Dang et al., 2011; Ghorbani, 2015). Parameters such as the concentration of metal ions, the type of reductant, time, pH, and temperature, among others, are often correlated to nucleation (Han and Kim, 2009).

Alzahrani (2016) reported the synthesis of CuNPs that show a wide range of sizes and shapes by chemical reduction of copper nitrate, isopropyl alcohol (IPA—reducing agent), and CTAB (capping agent) aiming the application in a nonenzymatic sensor for H_2O_2 and antibacterial agents. When the capping agent was used at high concentrations, CuNPs of size 16, 23, and 37 nm and hexagonal shape were produced. Nevertheless, when high concentrated copper nitrate was used, a spherical shape was observed. It was also reported that the electrocatalytic activities were strongly dependent on the microstructure of CuNPs, concerning sizes and shapes. The best ratio was 1:2 (CTAB: $Cu(NO_3)_2$).

Khan et al. (2016) studied starch-stabilized CuNPs. The chemical reduction (to copper) took place in an aqueous medium. Interestingly, starch was used instead of gases (usually CO or H_2) to protect against oxidation and control the nanoparticles' growth. The reduction of Cu ions was carried out by ascorbic acid (reducing agent), which has a weak reducing property, producing nonaggregated CuNPs due to the low reaction driving force. They reached an average size of ~28 nm.

The chemical copper reduction by sodium borohydride in the presence of polyacrylate produced CuNPs of 14 nm (Prucek et al., 2009), whereas Chatterjee et al. (2012) obtained CuNPs of size 50–60 nm by using a simple method with $CuCl_2$ as a reducing agent and gelatin as a stabilizer. Similarly, Cheng et al. (2017) synthesized CuNPs of $Cu(OH)_2$ as the precursor, L-ascorbic acid as reducing agent, polyvinyl pyrrolidone and diethylene glycol as a capping agent and a solvent, respectively. The authors achieved CuNPs of 140 nm which was stored at room temperature for 3 months without oxidation. Fig. 5 shows an example of a chemical reduction method for CuNP synthesis.

Therefore, the first approach for CuNP synthesis can be carried out by chemical reduction due to its technological simplicity, high efficiency, and low environmental impact. When applying the chemical reduction technique, it is easy to control the size and size dispersion by parameters such as stabilizer to precursor and reducing agent to precursor ratios.

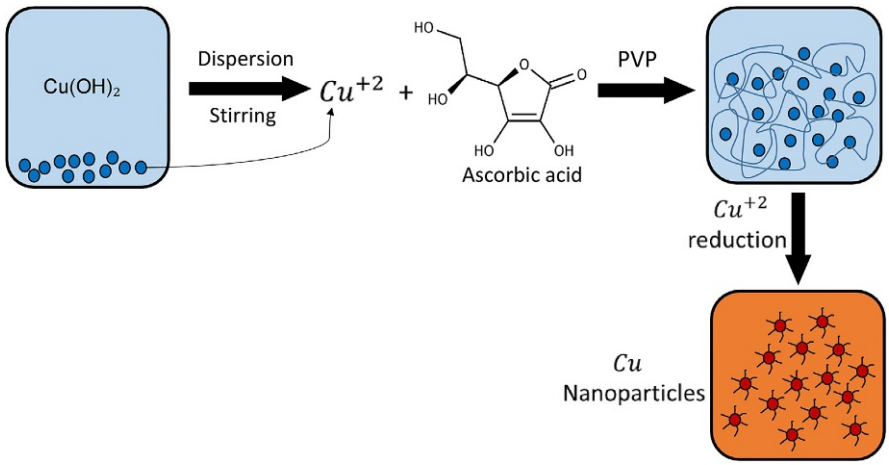

FIG. 5

Schematic diagram of CuNP synthesis by chemical reduction using hydroxide of copper as a precursor—Ascorbic acid as reducing agent—Polyvinyl pyrrolidone as a capping agent and diethylene glycol as a solvent.

2.2 Biological synthesis

As already mentioned, CuNP production can be carried out by physical-chemical techniques. However, these chemical methods are environmentally harmful (Anil Kumar et al., 2007; Bansal et al., 2005; Varshney et al., 2012). An eco-friendly alternative method to chemical routes is biological synthesis, in which bacteria, fungi, actinomycetes, yeast, plants, human cell lines, and biocompatible agents can produce metal nanoparticles, which can act both as reducing and capping agents (Table 1) (Narayanan and Sakthivel, 2010; Shobha et al., 2014).

Biosynthesis of metal nanoparticles is considered a newly emerging technique of nanobiotechnology. It comprises a single step, bottom-up approach, which leads to stable and monodispersible metal nanoparticles. Biosynthesized metal nanoparticles often show exquisite and unique morphologies (Narayanan and Sakthivel, 2010; Tiwari et al., 2016). The bottom-up approach is also known as an anabolic approach. The formation of final nanoparticles involves the activation and coalescence of smaller particles into larger particles (nucleation by Ostwald ripening) and the termination phase. This building block scheme affects the nanoparticles' shape and size (Vaid et al., 2020).

The extensive range of biomolecules available for the production of metal nanoparticles is undoubtedly a significant advantage (Narayanan and Sakthivel, 2011). Nonetheless, biological methods have some drawbacks, such as high time-consuming and inherent difficulty controlling the size distribution, shape, and crystallinity (Narayanan and Sakthivel, 2010).

Table 1 Biogenic synthesis of CuNPs.

	Specie	Shape	Diameter (nm)	Copper source	Reference
Bacteria	Actinomycetes[a]	Spherical	198	$Cu.SO_4$	Nabila and Kannabiran (2018)
	Shewanella loihica	Spherical	6–20	$Cu{\cdot}Cl_2$	Lv et al. (2018)
	Pseudomonas sp.	–	84–130	e-waste	Majumder (2012)
Fungus	*Penicillium aurantiogriseum*	Spherical	91–250	$Cu{\cdot}SO_4$	Honary et al. (2012)
	Penicillium citrinum		85–295		
	Penicillium waksmani		79–179		
	Hypocrea lixii	Spherical	24.5	$Cu{\cdot}Cl_2$	Salvadori et al. (2013)
	Fusarium oxysporum	–	93–115	e-waste	Majumder (2012)
	Aspergillus flavus	Spherical	5–12	$Cu{\cdot}SO_4$	Shende et al. (2021)
Yeast	*Rhodotorula mucilaginosa*	Spherical	10.5	$Cu{\cdot}Cl_2$	Salvadori et al. (2014)
Algae	*Botryococcus braunii*	Cubical and spherical	10–70	$Cu{\cdot}(CH_3COO)_2$	Arya et al. (2018)
	Macrocystis pyrifera	Spherical	2–50	$CuSO_4$	Araya-Castro et al. (2021)
Plant	*Syzygium aromaticum*	Spherical	20	$Cu{\cdot}(CH_3COO)_2$	Rajesh et al. (2018)
	Lantana camara	Spherical	20	e-waste	Majumder (2012)
	Pronus domestic	Spherical	10	$Cu{\cdot}Cl_2$	Tovar-Corona et al. (2018)
	Ocimum tenuiflorum	Spherical	22.09	$CuSO_4$	Ramadhan et al. (2019)
	Eucalyptus globulus	Nanowires	From 14–20 to 160–400	$Cu{\cdot}Cl_2$	Pinto et al. (2019)

[a] *Actinomycete, (order Actinomycetales), any member of a heterogeneous group of gram-positive, generally anaerobic bacteria noted for a filamentous and branching growth pattern that results, in most forms, in an extensive colony, or mycelium.*

Over the last few decades, both prokaryote and eukaryote cells have been investigated for their biosorption and bioreduction properties. It is worth noting that toxic metal ions are chemically changed to nontoxic metal salts during these bioprocesses. In addition, intracellular and extracellular metabolites can produce metal nanoparticles (Nangia et al., 2009; Narayanan and Sakthivel, 2010). Usually, the biological synthesis of metal nanoparticles involves two biomolecules: a reducing agent and a capping agent that stabilizes the nanoparticles at the nanoscale (Tiwari et al., 2014).

To the best of our knowledge, the interaction between metabolites and metals for the production of metal nanoparticles is not fully understood (Varshney et al., 2012). In this sense, there are many more scientific reports on gold and silver, but not on copper (Tiwari et al., 2014). Thus, the mechanisms of CuNP synthesis by bacteria, fungi, yeasts, and plants (including algae) will be briefly presented:

2.2.1 Bacteria-based synthesis

The biosynthesis of metal nanoparticles by bacteria is especially advantageous due to the high growth rate, facility to handle, and amenability to genetic manipulation to overproduce biomass or enzymes. Another advantage is the microbial resistance to heavy metals toxicity, which leads to efflux of heavy metal ions from the cell in an energy-dependent membrane-associated enzymatic action (Khare et al., 2019; Narayanan and Sakthivel, 2010). Thus, the bacteria cells can either reduce or precipitate out soluble toxic inorganic ions into insoluble, nontoxic metal aggregation. Moreover, the large-scale production bacterial system is devoid of toxic chemicals, involves simple downstream processing, and can be easily scaled up (Khare et al., 2019).

Biosynthesis of CuNPs may occur using either bacteria whole cells or cell-free supernatant obtained from the bacteria growth medium. Furthermore, reports are using both Gram-positive and Gram-negative bacteria (Shobha et al., 2014). Hereinafter, some reports on CuNP synthesis using bacteria will be briefly presented.

Nabila and Kannabiran (2018) reported the biosynthesis of CuNPs mediated by actinomycetes. Actinomycetes are considered an efficient candidate for the biosynthesis of metal NPs since their nanoparticles exhibit high stability and polydispersity (Nabila and Kannabiran, 2018; Składanowski et al., 2017). The biosynthesis was carried out using the cell-free supernatant obtained from actinomycetes growth medium mixed with an aqueous solution of copper sulfate ($CuSO_4$), heated at 100°C for 15 min (Nabila and Kannabiran, 2018). The average size of the biosynthesized NPs was found to be 198 nm. According to the authors, this is owing to the polydispersity of the synthesized CuNPs.

The Gram-negative bacteria *Pseudomonas stutzeri* were applied in the synthesis of CuNPs using electroplating wastewater as a precursor. The bacterial strain produced cubical CuNPs with an average size ranging from 50 to 150 nm (Varshney et al., 2012). Another Gram-negative bacterium belonging to the genus *Serratia* was used to promote the synthesis of polydispersed CuNPs of size 10–30 nm. The bacteria whole cells were added to flasks containing distilled water and $CuSO_4$ (Saif Hasan et al., 2008).

Whole cells of *Shewanella loihica* were used to produce CuNPs successfully. The biosynthesis process was carried out by mixing bacterium cells with a broth medium containing a $CuCl_2$ solution. Most of the synthesized CuNPs were attached to the bacterial cell surfaces, suggesting that extracellular Cu (II) bioreduction mainly contributed to this process. The size distribution ranged from 6 to 20 nm (Lv et al., 2018). The whole cells of *Escherichia coli* proved to be an interesting alternative to produce CuNPs. *Escherichia coli* cells were incubated with an aqueous solution of $CuSO_4$ for 42 h, 28°C, and 150 rpm (Singh et al., 2010).

Usha et al. (2010) reported the extracellular production of CuONPs from *Streptomyces* sp. The CuONPs of size 100–150 nm showed antimicrobial properties (i.e., textiles for hospital use to prevent or minimize infection with pathogenic bacteria).

Quasispherical CuNPs of size 10–40 nm were produced by the bacterium *Morganella morganii* using an aqueous solution of $CuSO_4$ as a precursor (Ramanathan et al., 2013).

Cell-free supernatants from *Pseudomonas fluorescens* (Shantkriti and Rani, 2014) and *Salmonella typhimurium* (Ghorbani, 2015) were used to synthesize CuNPs. Another cell-free supernatant of nonpathogenic *Pseudomonas aeruginosa* culture was used to promote the biosynthesis of CuNPs of size 110.9 nm (average). The flask containing cell-free supernatant and an equal volume of $CuSO_4$ solution was kept in an orbital shaker at 45°C and 200 rpm (Tiwari et al., 2016).

2.2.2 Fungi-based synthesis

The synthesis of metallic nanoparticles using fungi is a simple and economically viable downstream processing, which can be easily scaled up since fungi secrete a broad spectrum of enzymes (Priyadarshini et al., 2021; Shobha et al., 2014; Varshney et al., 2012).

Penicillium aurantiogriseum, *Penicillium citrinum*, and *Penicillium waksmanii* isolated from soil were used for extracellular synthesis of CuNPs. CuONPs with 79–295 nm were produced using an aqueous solution of $CuSO_4$ as a precursor (Honary et al., 2012). Dead biomass of *Hypocrea lixii* (isolated from a metal mine in the Brazilian Amazon region) and *Trichoderma koningiopsis* produced spherical CuNPs of size 24.5 and 87.5 nm, respectively (Salvadori et al., 2013). The white-rot fungus *Stereum hirsutum* was applied in the biosynthesis of CuNPs using three different copper salts ($CuCl_2$, $CuSO_4$, and $Cu(NO_3)_2$). The CuNPs and CuONPs obtained were mainly spherical (size between 5 and 20 nm). *Fusarium oxysporum* synthesized CuNPs of size 84–130 nm from integrated circuits present on electronic boards (Majumder, 2012).

2.2.3 Yeast-based synthesis

Eukaryotes such as yeasts, fungi, and plants have been used to synthesize different metallic nanoparticles (Bharde et al., 2005; Lang and Schüler, 2006). Yeasts have a remarkable capacity for bioleaching metals from mineral ores (He et al., 2008; Kröger et al., 1999).

Interestingly, the dead biomass of the yeast *Rhodotorula mucilaginosa* (isolated from the wastewater of a mine in the Brazilian Amazonia) promoted intracellular biosynthesis of CuNPs. The synthesized nanoparticles were mainly spherical, with 10.5 nm (Salvadori et al., 2014).

2.2.4 Algae-based synthesis

Algae are a diverse group in the plant kingdom explored for efficiently synthesizing metallic highly stable nanoparticles (Ramaswamy et al., 2016; Varshney et al., 2012).

The algae-based synthesis of metallic nanoparticles is relatively simple. Briefly, algae accumulate metal cations within their cellular matrix, and subsequently the bioactive components reduce the cations to form nanoparticles. When the biosynthesis process occurs intracellularly, the formation of metallic nanoparticles can be often visualized with the naked eye and further evidenced by optical and electron microscopes. Nevertheless, the extracellular algae-based production of metallic nanoparticles is usually investigated. In extracellular biosynthesis, biomolecules secreted by algae into the culture medium promote the algae-based synthesis process (Rahman et al., 2020). In fact, the bioremediation process was the precursor to biosynthesis using algae, since the stage of metallic nanoparticles accumulation within the cell wall corresponds to biosorption, and the intracellular stage of reducing cations and forming nanoparticles is analogous to the process of bioaccumulation (Dahoumane et al., 2017; Rahman et al., 2020).

Generally, the biosynthesis process using algae may refer to: (i) algae culture in order to increase the cell density; (ii) cells are harvested and subsequently used in the biosynthesis process; (iii) occasionally, the cells are harvested from their culture medium by centrifugation or filtration and redispersed in distilled, deionized water or added directly into an aqueous solution containing metallic salts; (iv) cells can also be disrupted, to liberate the biocompounds present inside the cell, and the extract is used to synthesize the nanoparticles. Some biosynthesis processes are carried out with whole algae cells concurrently to the cultivation stage, where cells are expected to continue their metabolism, photosynthesis, and growth (Dahoumane et al., 2016; Rahman et al., 2020). Thus, many factors affect the synthesis yield, morphology, and stability of nanoparticles. Some of the main factors include algae/biomass concentration, light intensity, incubation time, pH of the reaction medium, precursor ion concentration, and temperature (Khare et al., 2019; Rahman et al., 2020).

A little information on the use of algae to produce CuNPs is available (Abboud et al., 2014). Ramaswamy et al. (2016) reported the synthesis of CuONPs from the brown seaweed *Sargassum polycystum* using copper sulfate as a precursor. Usually, biocompounds present in seaweed cells (e.g., bromophenols, carotenoids, flavonoids, polysaccharides, tannins, and phenolic acids) exhibit different biological activities and are indirectly responsible for the synthesis of CuNPs. Thus, Ramaswamy et al. (2016) applied the aqueous extraction from *Sargassum polycystum* to synthesize metallic nanoparticles.

Aqueous extract from *Bifurcaria bifurcate*, a brown alga, was used to produce CuNPs of size 5–45 nm (Abboud et al., 2014; Kasana et al., 2017). The synthesis of

CuO and Cu_2O nanoparticles was accomplished using a cell-free extract of the brown alga and $CuSO_4$ aqueous solution, under stirring, to 100–120°C (Abboud et al., 2014; Dahoumane et al., 2017). The cyanobacterium *Phormidium* sp. was used to produce quasispherical CuO and Cu_2O nanoparticles of 10–40 nm. The biosynthesis occurred using whole cells of the cyanobacterium dispersed in an aqueous solution of $CuSO_4$ and incubated for 42 h at 28°C (Dahoumane et al., 2017). Arya et al. (2018) reported the synthesis of CuNPs using the aqueous extract of *Botryococcus braunii*, a green alga, and an aqueous solution of $Cu_2(OAc)_4$. The biosynthesis was accomplished by trickling the aqueous extract into a flask containing the $Cu_2(OAc)_4$. The flask was vigorously stirred and incubated for 24 h at 100°C.

2.2.5 Plant-based synthesis

Since the early 1900s, plants have been used for the production of metallic nanoparticles. It is a straightforward, easily scalable, and eco-friendly method (Khare et al., 2019; Shobha et al., 2014). A wide variety of phytochemicals can act as reducing agents and thus assist the nanoparticle synthesis. Different concentrations and combinations of these reducing agents lead to infinite (virtually) sizes and shapes of metallic nanoparticles (Khare et al., 2019; Kumar and Yadav, 2009). The size, shape, and stability of metallic nanoparticles are related to the concentration of phytochemicals in plant extract, metal salts' concentration, pH, contact (reaction) time, and temperature, among others. Usually, metallic nanoparticles' biosynthesis using plant extracts is carried out by phytoextracts (usually aqueous extracts) with an aqueous solution of metal salts with optimized reaction volumes and ratios (Dwivedi and Gopal, 2010; Khare et al., 2019). Currently, there are numerous reports on the exploitation of phytoextracts, exudates, inactivated plant tissue, gums, and other parts of plants to synthesize CuNPs (Shobha et al., 2014).

Rajesh et al. (2018) reported the synthesis of CuNPs using the *Syzygium aromaticum* (clove) bud extract, where spherical CuNPs of ~20 nm were obtained. CuNPs were synthesized by cyanidine-*O*-3-glucoside (obtained from the skin of *Pronus domestic*—red plum) using a solution of $CuCl_2$ as the precursor. Quasispherical CuNPs of 10 nm were obtained (Tovar-Corona et al., 2018). Three-dimensional (3D) CuONPs having flowerlike morphology were obtained using a leaf extract of *Ficus benghalensis*, where the nanoflowers presented a size range from 250 nm to 2.5 µm (Agarwal et al., 2016). CuNPs of size 122.7 nm (average) were biosynthesized using the *Ocimum sanctum* plant leaf extract as a reducer and also as a stabilizer (Patel et al., 2016). Well-dispersed copper nanowires, with lengths ranging from 5 to dozens of micrometers and average diameters ranging between 44 and 145 nm, were obtained using an aqueous plant extract (*Eucalyptus globulus*) (Pinto et al., 2019). Crystalline CuONPs of 15–30 nm were synthesized by *Aloe vera* extract (Gunalan et al., 2012). The extract of henna leaves was used as a reducing and capping agent in the phytosynthesis of CuNPs, which present average sizes between 27 and 45 nm (Cheirmadurai et al., 2014). *Centella asiatica* (L.) leaf extracts were used to produce CuONPs of size 2–5 µm (Devi and Singh, 2014). *Syzygium aromaticum*, *Tabernaemontana divaricate*, *Vitis vinifera*, and fruit juice of *Citrus medica* were used to fabricate CuNPs

of size 5–93 nm (Kasana et al., 2017). Jayalakshmi and Yogamoorthi (2014) reported the stable water-soluble CuNP synthesized using an aqueous flower extract of *Cassia alata* L. of size 110–280 nm. Similarly, the *Gloriosa superba* L. plant extract resulted in spherical CuONPs with 5–10 nm using $Cu(NO_3)_2$ as a precursor (Naika et al., 2015). Stable CuNPs of size 40–100 nm were produced using the plant leaf extract of *Magnolia kobus* as a reducing agent and an aqueous solution of $CuSO_4$ as a precursor (Lee et al., 2013). Stable and uniform CuNPs of ~20 nm were produced using a complex Cu-soybeans extract (Guajardo-Pacheco et al., 2010). Černík and Thekkae Padil (2013) described the production of CuONPs of 4.8 nm using gum karaya, a natural, nontoxic hydrocolloid, as a reduction agent and $CuCl_2$ as a precursor. Ruku (*Ocimum tenuiflorum*) leaf extract was used as a capping agent in the biosynthesis of spherically shaped CuNPs of 22.09 nm (Ramadhan et al., 2019). Elakkiya et al. (2021) showed that the CuNPs synthesized by the *Sesbania aculea* leaf extract can enhance plant growth and antimicrobial activities.

3 Copper nanoparticles applications in agriculture: Focus on pesticides

In agriculture, CuNPs are finding many applications and have attracted a great deal of attention from all over the world due to their broad-spectrum application mainly as an antimicrobial agent (Shang et al., 2019). In this sense, regarding challenges for pesticide detection, CuNPs can be used as a remarkable tool in nanomaterial engineering, that is, it is the cutting-edge track of research that supports the development of a high-tech detection mechanism.

In recent years, some authors have reported the use of DNA-templated copper nanoparticles (DNA-CuNPs) as biosensors, by a simple and rapid preparation, with high efficiency and low biological toxicity (Chen et al., 2016; Qing et al., 2019; Song et al., 2019). DNA-templated CuNPs as a fluorescent probe were reported by Fan et al. (2019), who demonstrated that the developed strategy has promising application potential for acetamiprid assay in food safety fields. The authors reported a label-free and enzyme-free sensor for sensitive assay of acetamiprid using AT-rich dsDNA-templated copper nanoparticles.

A nonenzymatic electrochemical system based on CuONPs for detecting phenolic compounds and pesticides in real samples was reported by Pino et al. (2016). The authors have shown that CuONPs are a reliable sensor system with an improved analytical performance that would be useful as an alternative to enzyme-based inhibition sensors. In addition, it was reported that the developed system promoted an AT-rich dsDNA/CuNPs with strong fluorescence, offering a turn-on detection of acetamiprid.

The use of nonenzymatic processes is advantageous since it overcomes some limitations related to long incubation steps and easy denaturation. It occurs since temperature sensitivity restricts these biosensor applications (Bagheri et al., 2017; Gu et al., 2020; Nsibande and Forbes, 2016).

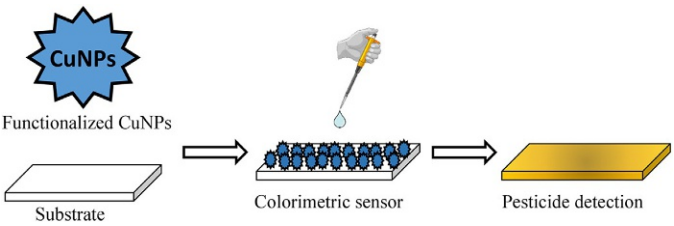

FIG. 6

Representation of the main colorimetric detection of pesticide by functionalized CuNPs on substrate.

An advance in nanoparticles' field to detect pesticides associated with the colorimetric sensor has attracted attention in the last years. It provides an excellent alternative for detecting residual pesticides with high precision and speed (Singh et al., 2020). In Fig. 6, the mechanism behind these analytical techniques is illustrated.

Kirk and Andreescu (2019) described a low-cost sensor with simplified user operation based on polyethyleneimine (PEI), a potent chelator for Cu^{2+} ions. The sensor was based on colorimetry (color change), which showed high sensitivity in pesticide detection Ghoto et al. (2019) conducted a study using CuNPs, coated with cetyltrimethylammonium bromide as a colorimetric probe, for sensing dithiocarbamate ziram zineb, and maneb pesticides in the environment and juice samples. When in the presence of the pesticides, the sensor changed color from reddish wine to yellow. Similarly, Fu et al. (2013) reported a highly sensitive colorimetric detection of organophosphate pesticides based on Cu (I)-catalyzed click chemistry as the colorimetric signal.

According to Zamora-Sequeira et al. (2019), when compared with the traditional techniques for environmental control, biosensors based on CuNPs can be considered a faster, simpler, low-cost, and more sensitive manner for pesticide determination. On the other hand, even with a low-cost and easy operation, Ghoto et al. (2019) mention that one of the significant problems in utilizing CuNPs in sensor applications is their susceptibility to oxidation when exposed to air.

To overcome this matter, biopolymeric matrices as chitosan (Ali et al., 2018; Ramachandraiah and Hong, 2021; Puente et al., 2021) and proteins (Bagheri et al., 2017; Asdagh et al., 2021; Gómez-Guillén and Montero, 2021) can be used to design metallic nanoparticles. According to Bakhsh et al. (2019), this sort of matrix can be employed simultaneously to recognize and complete the select pesticide reduction. Thus, the modification and functionalization of CuNPs with ligands and the use of a stable matrix are powerful tools to improve the sensitivity and selectivity of copper-based colorimetric sensors.

4 Conclusion and perspectives

Innovation is essential in modern agriculture. In this sense, the detection of pesticides associated with colorimetric sensors has attracted increased attention. These sensors

can be based on metal and oxide nanoparticles, including copper and copper oxide. For the chemical synthesis of CuNPs and CuONPs, the most feasible techniques are microemulsification, electrochemical and chemical reductions due to their easy control, high simplicity, and possible scalability. However, CuNPs and CuONPs can also be produced biologically from algae, bacteria, fungi, yeasts, and plants. When compared to the chemical synthesis of CuNPs, biological production is eco-friendly and produces smaller and unique CuNPs. It is worth noting that purification strategies of the biologically synthesized CuNPs should be investigated. An interesting alternative is to apply the CuNP microemulsification using bioactive molecules, a chemical-biological approach. Regarding the colorimetric sensors for pesticides, a significant drawback is related to the susceptibility of CuPs to oxidation. In this regard, chitosan and proteins can be applied to these colorimetric sensors to reduce oxidation. In addition, these biopolymers can enhance the recognition of a specific pesticide.

References

Abboud, Y., Saffaj, T., Chagraoui, A., El Bouari, A., Brouzi, K., Tanane, O., Ihssane, B., 2014. Biosynthesis, characterization and antimicrobial activity of copper oxide nanoparticles (CONPs) produced using brown alga extract (*Bifurcaria bifurcata*). Appl. Nanosci. 4, 571–576.

Agarwal, M., Singh Bhadwal, A., Kumar, N., Shrivastav, A., Raj Shrivastav, B., Pratap Singh, M., Zafar, F., Mani Tripathi, R., 2016. Catalytic degradation of methylene blue by biosynthesised copper nanoflowers using *F. benghalensis* leaf extract. IET Nanobiotechnol. 10, 321–325.

Ali, F., Khan, S.B., Kamal, T., Alamry, K.A., Bakhsh, E.M., Asiri, A.M., Sobahi, T.R.A., 2018. Synthesis and characterization of metal nanoparticles templated chitosan-SiO_2 catalyst for the reduction of nitrophenols and dyes. Carbohydr. Polym. 192, 217–230.

Alzahrani, E., 2016. Synthesis of copper nanoparticles with various sizes and shapes: application as a superior non-enzymatic sensor and antibacterial agent. Int. J. Electrochem. Sci. 11 (6), 4712–4723.

Anand, V., Harshavardhan, Srivastava, V.C., 2015. Synthesis and characterization of copper nanoparticles by electrochemical method: effect of pH. J. Nano Res. 31, 81–92.

Anil Kumar, S., Abyaneh, M.K., Gosavi, S.W., Kulkarni, S.K., Pasricha, R., Ahmad, A., Khan, M.I., 2007. Nitrate reductase-mediated synthesis of silver nanoparticles from $AgNO_3$. Biotechnol. Lett. 29, 439–445.

Araya-Castro, K., Chao, T.-Z., Durán-Vinet, B., Cisternas, C., Ciudad, G., Rubilar, O., 2021. Green synthesis of copper oxide nanoparticles using protein fractions from an aqueous extract of brown algae *Macrocystis pyrifera*. Processes 9 (1), 78.

Arya, A., Gupta, K., Chundawat, T.S., Vaya, D., 2018. Biogenic synthesis of copper and silver nanoparticles using green alga *Botryococcus braunii* and its antimicrobial activity. Bioinorg. Chem. Appl. 2018, 1–9.

Asdagh, A., Sani, I.K., Pirsa, S., Amiri, S., Shariatifar, N., Eghbaljoo-Charehgheshlaghi, H., Shabahang, Z., Taniyan, A., 2021. Production and characterization of nanocomposite film based on whey protein isolated/copper oxide nanoparticles containing coconut essential oil and paprika extract. J. Polym. Environ. 29, 335–349.

Bagheri, H., Afkhami, A., Khoshsafar, H., Hajian, A., Shahriyari, A., 2017. Protein capped Cu nanoclusters-SWCNT nanocomposite as a novel candidate of high-performance platform for organophosphates enzymeless biosensor. Biosens. Bioelectron. 89, 829–836.

Bakhsh, E.M., Ali, F., Khan, S.B., Marwani, H.M., Danish, E.Y., Asiri, A.M., 2019. Copper nanoparticles embedded chitosan for efficient detection and reduction of nitroaniline. Int. J. Biol. Macromol. 131, 666–675.

Bansal, V., Rautaray, D., Bharde, A., Ahire, K., Sanyal, A., Ahmad, A., Sastry, M., 2005. Fungus-mediated biosynthesis of silica and titania particles. J. Mater. Chem. 15, 2583.

Ben Aissa, M.A., Tremblay, B., Andrieux-Ledier, A., Maisonhaute, E., Raouafi, N., Courty, A., 2015. Copper nanoparticles of well-controlled size and shape: a new advance in synthesis and self-organization. Nanoscale 7, 3189–3195.

Bharde, A., Wani, A., Shouche, Y., Joy, P.A., Prasad, B.L.V., Sastry, M., 2005. Bacterial aerobic synthesis of nanocrystalline magnetite. J. Am. Chem. Soc. 127, 9326–9327.

Burrati, L., Ciotta, E., Matteis, D., Prosposito, P., 2021. Metal nanostructures for environmental pollutant detection based on fluorescence. Nanomaterials 11 (2), 276.

Černík, M., Thekkae Padil, V.V., 2013. Green synthesis of copper oxide nanoparticles using gum karaya as a biotemplate and their antibacterial application. Int. J. Nanomedicine 8, 889–898.

Chandra, S., Kumar, A., Tomar, P.K., 2014. Synthesis and characterization of copper nanoparticles by reducing agent. J. Saudi Chem. Soc. 18, 149–153.

Chatterjee, A.K., Sarkar, R.K., Chattopadhyay, A.P., Aich, P., Chakraborty, R., Basu, T., 2012. A simple robust method for synthesis of metallic copper nanoparticles of high antibacterial potency against E. *coli*. Nanotechnology 23, 085103.

Cheirmadurai, K., Biswas, S., Murali, R., Thanikaivelan, P., 2014. Green synthesis of copper nanoparticles and conducting nanobiocomposites using plant and animal sources. RSC Adv. 4, 19507.

Chen, J., Ji, X., Tinnefeld, P., He, Z., 2016. Multifunctional dumbbell-shaped DNA-templated selective formation of fluorescent silver nanoclusters or copper nanoparticles for sensitive detection of biomolecules. ACS Appl. Mater. Interfaces 8, 1786–1794.

Chen, Y., Zhu, Y., Zhao, Y., Wang, J., Li, M., 2021. Fluorescent and colorimetric dual-response sensor based on copper (II)-decorated graphitic carbon nitride nanosheets for detection of toxic organophosphorus. Food Chem. 345, 128560.

Cheng, C., Li, J., Shi, T., Yu, X., Fan, J., Liao, G., Li, X., Cheng, S., Zhong, Y., Tang, Z., 2017. A novel method of synthesizing antioxidative copper nanoparticles for high performance conductive ink. J. Mater. Sci. Mater. Electron. 28, 13556–13564.

Choi, S.K., 2021. Nanomaterial-enabled sensors and therapeutic platforms for reactive organophosphates. Nanomaterials 11 (1), 224.

Dahoumane, S.A., Mechouet, M., Alvarez, F.J., Agathos, S.N., Jeffryes, C., 2016. Microalgae: an outstanding tool in nanotechnology. Bionature 1, 196–201.

Dahoumane, S.A., Mechouet, M., Wijesekera, K., Filipe, C.D.M., Sicard, C., Bazylinski, D.A., Jeffryes, C., 2017. Algae-mediated biosynthesis of inorganic nanomaterials as a promising route in nanobiotechnology—a review. Green Chem. 19, 552–587.

Dan, H., Song, Y., Xu, Y., Gao, Y., Kong, W., Huang, Y., Yue, Q., Gao, B., 2021. Green synthesis of Cu nanoparticles supported on straw-graphene composite for catalytic reduction of p-nitrophenol. J. Clean. Prod. 283, 124578.

Dang, T.M.D., Le, T.T.T., Fribourg-Blanc, E., Dang, M.C., 2011. Synthesis and optical properties of copper nanoparticles prepared by a chemical reduction method. Adv. Nat. Sci. Nanosci. Nanotechnol. 2, 015009.

Devi, H.S., Singh, T.D., 2014. Synthesis of copper oxide nanoparticles by a novel method and its application in the degradation of methyl orange. Adv. Electron. Electr. Eng. 4, 83–88.

Dorozhko, E.V., Gashevskay, A.S., Korotkova, E.I., Barek, J., Vyskocil, V., Eremin, S.A., Galunin, E.V., Saqib, M., 2021. A copper nanoparticle-based electrochemical immunosensor for carbaryl detection. Talanta 228, 122174.

Dwivedi, A.D., Gopal, K., 2010. Biosynthesis of silver and gold nanoparticles using *Chenopodium album* leaf extract. Colloids Surf. A Physicochem. Eng. Asp. 369, 27–33.

Egorova, E., Revina, A., 2000. Synthesis of metallic nanoparticles in reverse micelles in the presence of quercetin. Colloids Surf. A Physicochem. Eng. Asp. 168, 87–96.

Elakkiya, V.T., Meenakshi, R.V., Kumar, P.S., Karthik, V., Shankar, K.R., Sureshkumar, P., Hanan, A., 2021. Green synthesis of copper nanoparticles using *Sesbania aculeata* to enhance the plant growth and antimicrobial activities. Int. J. Environ. Sci. Technol. 18 (2).

Eriksson, S., 2004. Preparation of catalysts from microemulsions and their applications in heterogeneous catalysis. Appl. Catal. A Gen. 265, 207–219.

Fan, K., Kang, W., Qu, S., Li, L., Qu, B., Lu, L., 2019. A label-free and enzyme-free fluorescent aptasensor for sensitive detection of acetamiprid based on AT-rich dsDNA-templated copper nanoparticles. Talanta 197, 645–652.

Fan, K., Yang, R., Zhao, Y., Zang, C., Miao, X., Qu, B., Lu, L., 2020. A fluorescent aptasensor for sensitive detection of isocarbophos based on AT-rich three-way junctions DNA templated copper nanoparticles and Fe_3O_4@GO. Sensors Actuators B Chem. 321, 128515.

Fu, G., Chen, W., Yue, X., Jiang, X., 2013. Highly sensitive colorimetric detection of organophosphate pesticides using copper catalyzed click chemistry. Talanta 103, 110–115.

Fu, J., An, X., Yao, Y., Guo, Y., Sun, X., 2019. Electrochemical aptasensor based on one step co-electrodeposition of aptamer and GO-CuNPs nanocomposite for organophosphorus pesticide detection. Sensors Actuators B Chem. 287, 503–509.

Ghorbani, H.R., 2015. Extracellular synthesis of copper nanoparticles using culture supernatants of *Salmonella typhimurium*. Orient. J. Chem. 31, 527–529.

Ghoto, S.A., Khuhawar, M.Y., Jahangir, T.M., 2019. Applications of copper nanoparticles for colorimetric detection of dithiocarbamate pesticides. J. Nanostructure Chem. 9, 77–93.

Gómez-Guillén, M.C., Montero, M.P., 2021. Enhancement of oral bioavailability of natural compounds and probiotics by mucoadhesive tailored biopolymer-based nanoparticles: a review. Food Hydrocoll. 118, 106772.

Gu, C., Wang, Q., Zhang, L., Yang, P., Xie, Y., Fei, J., 2020. Ultrasensitive non-enzymatic pesticide electrochemical sensor based on HKUST-1-derived copper oxide @ mesoporous carbon composite. Sensors Actuators B Chem. 305, 127478.

Guajardo-Pacheco, M.J., Morales-Sánchez, J.E., González-Hernández, J., Ruiz, F., 2010. Synthesis of copper nanoparticles using soybeans as a chelant agent. Mater. Lett. 64, 1361–1364.

Gunalan, S., Sivaraj, R., Venckatesh, R., 2012. *Aloe barbadensis Miller* mediated green synthesis of mono-disperse copper oxide nanoparticles: Optical properties. Spectrochim. Acta A Mol. Biomol. Spectrosc. 97, 1140–1144.

Han, K.N., Kim, N.S., 2009. Challenges and opportunities in direct write technology using nano-metal particles. KONA Powder Particle J. 27, 73–83.

Hashemipour, H., Zadeh, M.E., Pourakbari, R., Rahimi, P., 2011. Investigation on synthesis and size control of copper nanoparticle via electrochemical and chemical reduction method. Int. J. Phys. Sci. 6, 4331–4336.

He, S., Zhang, Y., Guo, Z., Gu, N., 2008. Biological synthesis of gold nanowires using extract of *Rhodopseudomonas capsulata*. Biotechnol. Prog. 24, 476–480.

Honary, S., Barabadi, H., Gharaei-Fathabad, E., Naghibi, F., 2012. Green synthesis of copper oxide nanoparticles using *Penicillium aurantiogriseum*, *Penicillium citrinum* and *Penicillium waksmanii*. Dig. J. Nanomater. Biosctructures. 7, 999–1005.

Hu, A., Yao, Z., Yu, X., 2009. Phase behavior of a sodium dodecanol allyl sulfosuccinic diester/n-pentanol/methyl acrylate/butyl acrylate/water microemulsion system and preparation of acrylate latexes by microemulsion polymerization. J. Appl. Polym. Sci. 113, 2202–2208.

Jayalakshmi, A., Yogamoorthi, 2014. Green synthesis of copper oxide nanoparticles using aqueous extract of flowers of *Cassia alata* and particles characterisation. J. Nanomater. Biostruct. 4, 66–71.

Kadam, S.L., 2016. Synthesis and characterization of copper nanoparticles by using electrochemical method. Int. J. Sci. Eng. Res. 7, 1067–1069.

Kasana, R.C., Panwar, N.R., Kaul, R.K., Kumar, P., 2017. Biosynthesis and effects of copper nanoparticles on plants. Environ. Chem. Lett. 15, 233–240.

Khan, A., Rashid, A., Younas, R., Chong, R., 2016. A chemical reduction approach to the synthesis of copper nanoparticles. Int. Nano Lett. 6, 21–26.

Khare, T., Oak, U., Shriram, V., Verma, S.K., Kumar, V., 2019. Biologically synthesized nanomaterials and their antimicrobial potentials. In: Verma, S.K., Das, A.K. (Eds.), Comprehensive Analytical Chemistry: Engineered Nanomaterials and Phytonanotechnology: Challenges for Plant Sustainability. Elsevier, Amsterdam, pp. 263–289.

Kidwai, M., Mishra, N.K., Bansal, V., Kumar, A., Mozumdar, S., 2007. Cu-nanoparticle catalyzed $_O$-arylation of phenols with aryl halides via Ullmann coupling. Tetrahedron Lett. 48, 8883–8887.

Kirk, K.A., Andreescu, S., 2019. Easy-to-use sensors for field monitoring of copper contamination in water and pesticide-sprayed plants. Anal. Chem. 91, 13892–13899.

Ko, W.-Y., Chen, W.-H., Cheng, C.-Y., Lin, K.-J., 2009. Architectural growth of Cu nanoparticles through electrodeposition. Nanoscale Res. Lett. 4, 1481–1485.

Kodaei, M.M., Karegar, M., 2021. Synthesis and characterization of copper nanoparticles stabilized with polyvinyl pyrrolidone and its performance on the conductivity and stability of polyindole. J. Iran. Chem. Soc. 18, 863–872.

Kröger, N., Deutzmann, R., Sumper, M., 1999. Polycationic peptides from diatom biosilica that direct silica nanosphere formation. Science 286, 1129–1132.

Kumar, V., Yadav, S.K., 2009. Plant-mediated synthesis of silver and gold nanoparticles and their applications. J. Chem. Technol. Biotechnol. 84, 151–157.

Lang, C., Schüler, D., 2006. Biogenic nanoparticles: production, characterization, and application of bacterial magnetosomes. J. Phys. Condens. Matter. 18, S2815–S2828.

Lee, H.-J., Song, J.Y., Kim, B.S., 2013. Biological synthesis of copper nanoparticles using *Magnolia kobus* leaf extract and their antibacterial activity. J. Chem. Technol. Biotechnol. 81, 1971–1977.

Li, L., Lin, D., Yang, F., Xiao, Y., Yang, L., Yu, S., Jiang, C., 2021. Gold nanoparticle-based peroxyoxalate chemiluminescence system for highly sensitive and rapid detection of thiram pesticides. ACS Appl. Nano Mater. 4 (4), 3932–3939.

Luisi, P.L., Magid, L.J., Fendler, J.H., 1986. Solubilization of enzymes and nucleic acids in hydrocarbon micellar solution. Crit. Rev. Biochem. 20, 409–474.

Lv, Q., Zhang, B., Xing, X., Zhao, Y., Cai, R., Wang, W., Gu, Q., 2018. Biosynthesis of copper nanoparticles using *Shewanella loihica* PV-4 with antibacterial activity: novel approach and mechanisms investigation. J. Hazard. Mater. 347, 141–149.

Majumder, D.R., 2012. Bioremediation: copper nanoparticles from electronic-waste. Int. J. Eng. Sci. Technol. 4, 4380–4389.
Malik, M.A., Wani, M.Y., Hashim, M.A., 2012. Microemulsion method: a novel route to synthesize organic and inorganic nanomaterials. Arab. J. Chem. 5, 397–417.
Miao, T., Wang, L., 2007. Immobilization of copper in organic–inorganic hybrid materials: a highly efficient and reusable catalyst for the Ullmann diaryl etherification. Tetrahedron Lett. 48, 95–99.
Nabila, M.I., Kannabiran, K., 2018. Biosynthesis, characterization and antibacterial activity of copper oxide nanoparticles (CuO NPs) from actinomycetes. Biocatal. Agric. Biotechnol. 15, 56–62.
Naika, H.R., Lingaraju, K., Manjunath, K., Kumar, D., Nagaraju, G., Suresh, D., Nagabhushana, H., 2015. Green synthesis of CuO nanoparticles using *Gloriosa superba* L. extract and their antibacterial activity. J. Taibah Univ. Sci. 9, 7–12.
Nangia, Y., Wangoo, N., Goyal, N., Shekhawat, G., Suri, C.R., 2009. A novel bacterial isolate Stenotrophomonas maltophilia as living factory for synthesis of gold nanoparticles. Microb. Cell Factories 8, 39.
Narayanan, K.B., Sakthivel, N., 2010. Biological synthesis of metal nanoparticles by microbes. Adv. Colloid Interf. Sci. 156, 1–13.
Narayanan, K.B., Sakthivel, N., 2011. Green synthesis of biogenic metal nanoparticles by terrestrial and aquatic phototrophic and heterotrophic eukaryotes and biocompatible agents. Adv. Colloid Interf. Sci. 169, 59–79.
Nichols, R.J., Schröer, D., Meyer, H., 1995. An *in-situ* scanning probe microscopy study of copper electrodeposition on conductive polypyrrole. Electrochim. Acta 40, 1479–1485.
Nsibande, S.A., Forbes, P.B.C., 2016. Fluorescence detection of pesticides using quantum dot materials—a review. Anal. Chim. Acta 945, 9–22.
Ortega, J., 2000. Electrodeposition of copper on poly(o-aminophenol) modified platinum electrode. Thin Solid Films 360, 159–165.
Patel, B.H., Channiwala, M.Z., Chaudhari, S.B., Mandot, A.A., 2016. Biosynthesis of copper nanoparticles; its characterization and efficacy against human pathogenic bacterium. J. Environ. Chem. Eng. 4, 2163–2169.
Pileni, M.P., 1989. Structure and Reactivity in Reverse Micelles. Elsevier, Amsterdam.
Pileni, M.P., 2003. Nanocrystals: fabrication, organization and collective properties. C. R. Chim. 6, 965–978.
Pileni, M.P., Lisiecki, I., 1993. Nanometer metallic copper particle synthesis in reverse micelles. Colloids Surf. A Physicochem. Eng. Asp. 80, 63–68.
Pileni, M.P., Ninham, B.W., Gulik-Krzywicki, T., Tanori, J., Lisiecki, I., Filankembo, A., 1999. Direct relationship between shape and size of template and synthesis of copper metal particles. Adv. Mater. 11, 1358–1362.
Pino, F., Mayorga-Martinez, C.C., Merkoçi, A., 2016. High-performance sensor based on copper oxide nanoparticles for dual detection of phenolic compounds and a pesticide. Electrochem. Commun. 71, 33–37.
Pinto, R.J.B., Lucas, J.M.F., Silva, F.M., Girão, A.V., Oliveira, F.J., Marques, P.A.A.P., Freire, C.S.R., 2019. Bio-based synthesis of oxidation resistant copper nanowires using an aqueous plant extract. J. Clean. Prod. 221, 122–131.
Priyadarshini, E., Priyadarshini, S.S., Cousins, B.G., Pradhan, N., 2021. Metal-fungus interaction: review on cellular processes underlying heavy metal detoxification and synthesis of metal nanoparticles. Chemosphere 274, 129976.

Prucek, R., Kvítek, L., Panáček, A., Vančurová, L., Soukupová, J., Jančík, D., Zbořil, R., 2009. Polyacrylate-assisted synthesis of stable copper nanoparticles and copper(I) oxide nanocubes with high catalytic efficiency. J. Mater. Chem. 19, 8463–8469.

Puente, C., Sánchez-Domínguez, M., Brosseau, C.L., López, I., 2021. Silver-chitosan and gold-chitosan substrates for surface-enhanced Raman spectroscopy (SERS): effect of nanoparticle morphology on SERS performance. Mater. Chem. Phys. 260, 124107.

Qing, Z., Bai, A., Xing, S., Zou, Z., He, X., Wang, K., Yang, R., 2019. Progress in biosensor based on DNA-templated copper nanoparticles. Biosens. Bioelectron. 137, 96–109.

Rahman, A., Kumar, S., Nawaz, T., 2020. Biosynthesis of nanomaterials using algae. In: Yousuf, A. (Ed.), Microalgae Cultivation for Biofuels Production. Elsevier, Amsterdam, pp. 265–279.

Raja, M., 2008. Production of copper nanoparticles by electrochemical process. Powder Metall. Met. Ceram. 47, 402–405.

Rajesh, K.M., Ajitha, B., Reddy, Y.A.K., Suneetha, Y., Reddy, P.S., 2018. Assisted green synthesis of copper nanoparticles using *Syzygium aromaticum* bud extract: physical, optical and antimicrobial properties. Optik 154, 593–600.

Ramachandraiah, K., Hong, G.-P., 2021. Polymeric nanomaterials for the development of sustainable plant food value chains. Food Biosci. 41, 100978.

Ramadhan, V.B., Ni'mah, Y.L., Yanuar, E., Suprapto, S., 2019. Synthesis of copper nanoparticles using *Ocimum tenuiflorum* leaf extract as capping agent. Int. Conf. Sci. Appl. Sci. 020067.

Ramanathan, R., Field, M.R., O'Mullane, A.P., Smooker, P.M., Bhargava, S.K., Bansal, V., 2013. Aqueous phase synthesis of copper nanoparticles: a link between heavy metal resistance and nanoparticle synthesis ability in bacterial systems. Nanoscale 5, 2300–2306.

Ramaswamy, S.V.P., Narendhran, S., Sivaraj, R., 2016. Potentiating effect of ecofriendly synthesis of copper oxide nanoparticles using brown alga: antimicrobial and anticancer activities. Bull. Mater. Sci. 39, 361–364.

Richard, B., Lemyre, J.-L., Ritcey, A.M., 2017. Nanoparticle size control in microemulsion synthesis. Langmuir 33, 4748–4757.

Saif Hasan, S., Singh, S., Parikh, R.Y., Dharne, M.S., Patole, M.S., Prasad, B.L.V., Shouche, Y.S., 2008. Bacterial synthesis of copper/copper oxide nanoparticles. J. Nanosci. Nanotechnol. 8, 3191–3196.

Salvadori, M.R., Lepre, L.F., Ando, R.A., Oller do Nascimento, C.A., Corrêa, B., 2013. Biosynthesis and uptake of copper nanoparticles by dead biomass of *hypocrea lixii* isolated from the metal mine in the Brazilian Amazon region. PLoS One 8, e80519.

Salvadori, M.R., Ando, R.A., Oller do Nascimento, C.A., Corrêa, B., 2014. Intracellular biosynthesis and removal of copper nanoparticles by dead biomass of yeast isolated from the wastewater of a mine in the Brazilian Amazonia. PLoS One 9, e87968.

Sanchez-Dominguez, M., Aubery, C., Solans, C., 2012. New trends on the synthesis of inorganic nanoparticles using microemulsions as confined reaction media. In: Smart Nanoparticles Technology, pp. 195–220.

Sarwar, N., Humayoun, U.B., Kumar, M., Zaidi, S.F.A., Yoo, J.H., Ali, N., Jeong, D.I., Lee, J.H., Yoon, D.H., 2021. Citric acid mediated green synthesis of copper nanoparticles using cinnamon bark extract and its multifaceted applications. J. Clean. Prod. 292, 125974.

Setznagl, S., Cesarino, I., 2020. Copper nanoparticles and reduced graphene oxide modified a glassy carbon electrode for the determination of glyphosate in water samples. Int. J. Environ. Anal. Chem., 1–13.

Shang, Y., Hasan, M.K., Ahammed, G.J., Li, M., Yin, H., Zhou, J., 2019. Applications of nanotechnology in plant growth and crop protection: a review. Molecules 24, 2558.

Shantkriti, S., Rani, P., 2014. Biological synthesis of copper nanoparticles using *Pseudomonas fluorescens*. Int. J. Curr. Microbiol. Appl. Sci. 3, 374–383.
Shende, S., Bhagat, R., Raut, R., Rai, M., Gade, A., 2021. Myco-fabrication of copper nanoparticles and its effect on crop pathogenic fungi. IEEE Trans. Nanobiosci. 20 (2), 146–153.
Shobha, G., Moses, V., Ananda, S., 2014. Biological synthesis of copper nanoparticles and its impact. Int. J. Pharm. Sci. Invent. 3, 6–28.
Singh, A.V., Patil, R., Anand, A., Milani, P., Gade, W.N., 2010. Biological synthesis of copper oxide nano particles using *Escherichia coli*. Curr. Nanosci. 6, 365–369.
Singh, R., Kumar, N., Mehra, R., Kumar, H., Singh, V.P., 2020. Progress and challenges in the detection of residual pesticides using nanotechnology based colorimetric techniques. Trends Environ. Anal. Chem. 26, e00086.
Składanowski, M., Wypij, M., Laskowski, D., Golińska, P., Dahm, H., Rai, M., 2017. Silver and gold nanoparticles synthesized from *Streptomyces* sp. isolated from acid forest soil with special reference to its antibacterial activity against pathogens. J. Clust. Sci. 28, 59–79.
Solanki, J.N., Sengupta, R., Murthy, Z.V.P., 2010. Synthesis of copper sulphide and copper nanoparticles with microemulsion method. Solid State Sci. 12, 1560–1566.
Song, Q., Chen, C., Yu, W., Yang, L., Zhang, K., Zheng, J., Du, X., Chen, H., 2019. *In situ* formation of DNA-templated copper nanoparticles as fluorescent indicator for hydroxylamine detection. RSC Adv. 9, 25976–25980.
Tiwari, M., Narayanan, K., Thakar, M.B., Jagani, H.V., Venkata Rao, J., 2014. Biosynthesis and wound healing activity of copper nanoparticles. IET Nanobiotechnol. 8, 230–237.
Tamilvanan, A., Balamurugan, K., Ponappa, K., Kumar, B.M., 2014. Copper nanoparticles: synthetic strategies, properties and multifunctional application. Int. J. Nanosci. 13, 1430001.
Tiwari, M., Jain, P., Chandrashekhar Hariharapura, R., Narayanan, K., Bhat, U., Udupa, N., Rao, J.V., 2016. Biosynthesis of copper nanoparticles using copper-resistant *Bacillus cereus*, a soil isolate. Process Biochem. 51, 1348–1356.
Tovar-Corona, A., Lobo-Sánchez, M.A., Herrera-Perez, J.L., Zanella, R., Rodriguez-Mora, J.I., Vázquez-Cuchillo, O., 2018. Green synthesis of copper (0) nanoparticles with cyanidine-$_O$-3-glucoside and its strong antimicrobial activity. Mater. Lett. 211, 266–269.
Usha, R., Prabu, E., Palaniswamy, M., Venil, C.K., Rajendran, R., 2010. Synthesis of metal oxide nano particles by *Streptomyces* sp. for development of antimicrobial textiles. Global J. Biotechnol. Biochem. 5, 153–160.
Vaid, P., Raizada, P., Saini, A.K., Saini, R.V., 2020. Biogenic silver, gold and copper nanoparticles—a sustainable green chemistry approach for cancer therapy. Sustain. Chem. Pharm. 16, 100247.
Varshney, R., Bhadauria, S., Gaur, M.S., 2012. A review: biological synthesis of silver and copper nanoparticles. Nano Biomed. Eng. 4.
Wang, W., Wang, X., Cheng, N., Luo, Y., Lin, Y., Xu, W., Du, D., 2020. Recent advances in nanomaterials-based electrochemical (bio) sensors for pesticide detection. TRAC-Trend. Anal. Chem. 132, 116041.
Wei, C., Liu, Q., 2017. Shape-, size-, and density-tunable synthesis and optical properties of copper nanoparticles. CrystEngComm 19, 3254–3262.
Xu, J., Chen, J., Yang, S., Zhang, L., Lu, J., 2010. Effects of current density on copper nanoparticle prepared by electrochemical method. Int. J. Nanopart. 3, 93.
Zamora-Sequeira, R., Starbird-Pérez, R., Rojas-Carillo, O., Vargas-Villalobos, S., 2019. What are the main sensor methods for quantifying pesticides in agricultural activities? A review. Molecules 24, 2659.

Zhang, Q.B., Hua, Y.X., 2014. Electrochemical synthesis of copper nanoparticles using cuprous oxide as a precursor in choline chloride–urea deep eutectic solvent: nucleation and growth mechanism. Phys. Chem. Chem. Phys. 16, 27088–27095.

Zhang, D.W., Chen, C.H., Zhang, J., Ren, F., 2005. Novel electrochemical milling method to fabricate copper nanoparticles and nanofibers. Chem. Mater. 17, 5242–5245.

Zhou, X.J., Harmer, A.J., Heinig, N.F., Leung, K.T., 2004. Parametric study on electrochemical deposition of copper nanoparticles on an ultrathin polypyrrole film deposited on a gold film electrode. Langmuir 20, 5109–5113.

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CHAPTER

Copper nanomaterials for eliminating the risk of mycotoxins

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Velaphi C. Thipe[a,b], Jorge G.S. Batista[a], and Ademar B. Lugão[a]

[a]*Institute for Energy and Nuclear Research, National Nuclear Energy Commission-IPEN/CNEN-SP, São Paulo, Brazil*

[b]*Department of Radiology, School of Medicine, University of Missouri-Columbia, Missouri, United States*

1 Introduction

Mycotoxins are low molecular weight secondary metabolites produced by mycotoxigenic fungi, which often contaminate agricultural products (Brunel et al., 2013). Mycotoxins are ubiquitous and caused by *Aspergillus*, *Penicillium*, *Fusarium*, *Alternaria*, and *Cladosporium* genera. Mycotoxins are difficult to eradicate and causes serious agricultural losses thereby directly affecting growing crops intended for market—gross domestic product (GDP) of a country. For many years, this has become a global grand challenge impacted by increasing global population, loss of arable land, and gruesome reality of the consequences of climate change.

This is exacerbated by the toxicity and health problems associated with the consumption of mycotoxin contaminated foods and feeds contaminated by mycotoxin. The most prevalent and major mycotoxins include aflatoxins (AFs), fumonisins (FBs), patulin, ochratoxins (OT), zearalenone (ZEA), and trichothecenes including deoxynivalenol (DON) and T-2 toxin found in food, posing unpredictable and ongoing food safety and security problems worldwide. Some of these mycotoxins [e.g., aflatoxin B1 (AFB_1), citrinin, fumonisin B1 (FB_1), ochratoxin A (OTA), patulin, T-2 toxin, and ZEA] have been reported to cause neoplasia (cancer) in humans and animals, in addition to kidney, gastrointestinal, urogenital, vascular, and neurological diseases. This is attributed to the chemical nature of some mycotoxins being highly liposoluble, where they can easily be absorbed from the gastrointestinal and respiratory tract into the blood stream, thereby dissimilating throughout the body and other organs (e.g., liver and kidneys) (Adam et al., 2017; Çelik, 2019).

It is important to acknowledge that multiple contaminations are possible as a single fungus (such as *A. parasiticus*, *A. Flavus*, and *F. graminearum*) can produce several kinds of mycotoxins within one type of food or feed ingredient; therefore, several types of mycotoxins can be present in the same food or feed ingredient—multicontamination. Exposure of farm animals (mainly cattle, pigs, and poultry) to

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mycotoxins through ensiled by-product feed is poorly regulated and detailed. This negligence can carryover residual mycotoxins in animals' products, thereby resulting in an indirect dietary exposure to humans through the consumption of contaminated animal products (such as eggs for poultry, milk for mammals, and meat). The objectives of this chapter are to provide insight on (i) the significant role of copper (Cu) and Cu-based nanomaterials fungicides for reducing mycotoxin contamination, (ii) Cu antifungal activity against mycotoxigenic fungi, and (iii) the future recommendations for Cu nanofungicides for an intricate understanding of the comprehensive regulatory framework for their utilization in agriculture, food, and feed sectors.

2 Copper fungicides

The primary efforts for eliminating the risk of mycotoxins have involved the use of fungicides against fungal manifestation as an indirect approach in preventing mycotoxin contamination. The use of fungicides has been the first defense strategy against mycotoxigenic fungi, these fungicides are classified as either systemic or nonsystemic. Systemic fungicides are absorbed into the plants, while nonsystemic fungicides do not translocate into the crops being protected but merely acting upon the protection of the plant's surface against fungal colonization. Conventional fungicides exhibit a number of challenges such as (i) ineffectiveness overtime amid the onset of fungicide resistance, (ii) limitation on fungi, as they are not effective against bacteria, nematodes, or viral diseases, and (iii) highly toxicity on plants and the overall environment.

Moreover, commonly employed fungicides are not approved for use in organic farming. One of the major alternatives is the utilization of copper (Cu) fungicides, which included copper sulfate ($CuSO_4$) also known as bluestone due its color and copper derivatives (Bordeaux mixture: $CuSO_4$ and lime water and Burgundy mixture: $CuSO_4$ and sodium carbonate). Copper is recognized as a potent antimicrobial metal with a comprehensive control, and some Cu-based fungicides are classified into both inorganic and organic fungicides are approved for organic farming practices (Adisa et al., 2019; Brunel et al., 2013; Sidhu et al., 2017). Copper-based fungicides are categorized as copper hydroxide fungicide (COH), copper oxychloride fungicide (COC), and copper oxide fungicide (COX) and their application can be through suspension concentrate, wettable powder, and water granule. According to the market analysis by MarketWatch (2021), in 2020, the global Cu fungicide market was valued at 796.6 million USD and is expected to grow at a compound annual growth rate (CAGR) of 4.0% (during 2021–26 forecast) to reach 1051.5 million USD by the end of 2026.

The use of Cu is also beneficial because it is much cheaper, less toxic than its counterpart silver (Ag), and have been reported to be effective against a variety of pathogenic fungi (*A. carbonarius*, *A. fumigatus*, *A. niger*, *Alternaria solani*, *F. expansum*, etc.) (Khamis et al., 2017; Nath et al., 2019). Oziengbe and Osazee (2012) reported on the effectiveness of $CuSO_4$ against *Colletorichum gleosporioides*, which causes Anthracnose in mango fruit (*Mangifera indica*). The results revealed that $CuSO_4$ at 0.8 parts per million (ppm) significantly reduced the growth of *C. gleosporioides* and induced potent defense reactions in mango fruit.

Besides, Cu is one of the most essential micronutrient metals/minerals required by plants, animals, and humans (Tang et al., 2019). For plant's growth and development, the concentration of Cu ranges between 0.05 and 0.5 ppm, with most tissues (e.g., vascular, dermal, and ground tissue cells) between 3 and 10 ppm (Adisa et al., 2019). Furthermore, Cu participates in various physiological processes such as the formation of chlorophyll and photosynthesis assisting in plant respiration and metabolism of carbohydrates and proteins. Some of the enzymatic reactions use Cu as a cofactor, this includes activation of many metalloproteins and those involved in lignin synthesis (Fig. 1). The source of Cu for plants is essentially from fertilizers and several fungicides, which contain Cu as their active ingredient. Foods that contribute a majority of Cu consumed by animals and humans, include three major dietary sources; that is, seafood (e.g., oysters and other shellfish), organ meats (e.g., kidneys and liver), and dark leafy greens, whole grains, legumes (e.g., beans and lentils), nuts, potatoes, and dried fruits (e.g., prunes, cocoa, and black pepper). Cu as a nutritional dietary supplement in animal feeds is categorized as "generally recognized as safe" (GRAS) according to the US Food and Drug Administration (USFDA) and the European Food Safety Authority (EFSA) Panel on Additives and Products or Substances used in Animal Feed (FEEDAP Panel) (He et al., 2019).

In humans, the adult body contains between 1.4 and 2.1 mg of Cu per kilogram of body weight (kg/bw), hence a healthy human weight of 60 kg contains approx. 0.1 g of Cu. For humans and animals, Cu is found in the liver, brain, heart, kidneys, and skeletal muscle, it assists in maintaining various physiological and metabolic processes (absorption of iron), promotes strong and healthy bones (collagen), ensures proper nervous system homeostasis, and plays a role in energy production. However, this small amount is essential to the overall well-being of humans. In agriculture, the consistent use and effectiveness of these Cu fungicides poses several challenges such as toxicity to plants, where the Cu accumulates in the roots and restricts root growth by burning the root tips and thereby causing excess lateral root growth; and Cu build up in sediments and cause long-term soil contamination (Konappa et al., 2021; Nath et al., 2019; Tegenaw et al., 2015).

Therefore, Cu impairs nutrient deficiency, chlorosis, resulting in hyperaccumulator plants and, in more severe cases, tissue necrosis and plant/crop death. The high amounts of Cu through Cu fungicides have been reported to affect crop productivity and yield, in addition to the onset of fungicide resistance from mycotoxigenic fungi (Gogos et al., 2012). Excess Cu can compete with plant uptake of iron (Fe) and sometimes molybdenum (Mo) or zinc (Zn), which are equally essential for the plant's growth and development. Moreover, Cu compounds can leach from the agricultural application into aquatic environments via groundwater and can threaten aquatic species and other organisms; thus, posing a serious environmental hazard.

To minimize the abovementioned challenges, researchers are constantly searching for alternatives to optimize Cu fungicides with limited to no toxicity effects, thereafter. Chelated Cu complexes (e.g., copper-8-quinolinolate) are known to be nonreactive with other chemical constituents in an aqueous medium. Young et al. (2016) evaluated the potential fungicidal activity of Cu^{2+} complexation with

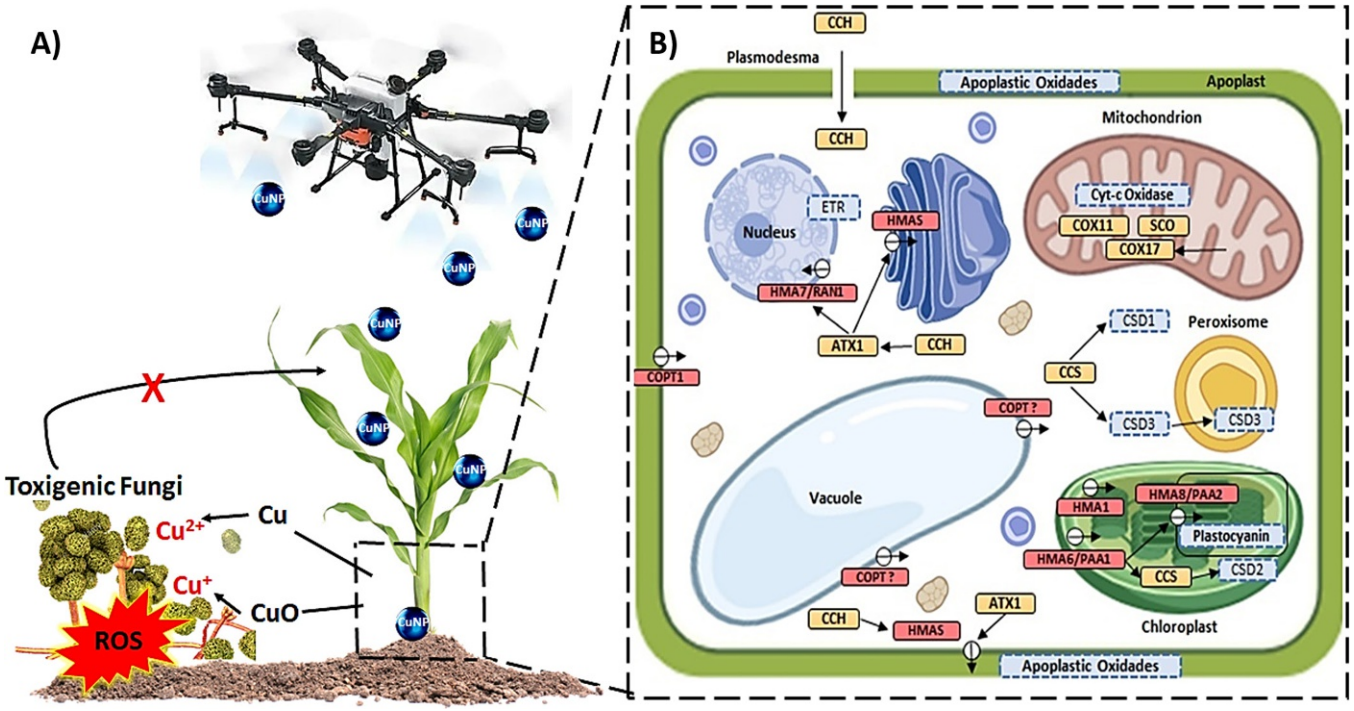

FIG. 1

The pivotal role Cu plays in agriculture (A) antifungal activity of Cu nanoformulations through the release of $Cu2^{+}$ and Cu^{+} ions and the generation of reactive oxygen species (ROS) and (B) Cu, cofactor functionality for a variety of enzymatic reactions. Cu participates and/or linked with proteins (*blue*), transporters (*rose*), and Cu-metallo chaperones (*orange*).

salicylaldehyde benzoylhydrazone (SBH) for Cu^{2+} release against pathogenic fungi thereby minimizing their propensity of producing mycotoxins. Their experiment compared commercial DuPont Kocide 3000 [active ingredient: $Cu(OH)_2$], Kocide 3000/SBH mixtures, and Cu^{2+}-SBH complex for their fungicidal effectiveness. Results revealed that the Cu^{2+}-SBH complex improved Cu^{2+} delivery at low concentrations compared to Kocide 3000 and Kocide 3000/SBH mixtures, this can be a strategy to mitigate the environmental impact of Cu fungicides. Most recently, work by Melendez et al. (2020) from 15 farms in New Jersey, United States that used Cu fungicides (e.g., cuprous oxide and copper hydroxide) using soil analysis reported elevated soil Cu levels, which resulted from Cu accumulation with the potential to become toxic to sensitive crops and impact soil health.

3 Nanotechnology: Nano-Cu significance in mycotoxin and environment

Nanotechnology has rendered precise capability is revolutionizing every field and industry it influences from biomedical to agricultural applications, the latter being agri-nanotechnology, providing a potential to cope with food production, safety, and security against fungal and mycotoxin manifestations (Adisa et al., 2019; Agrimonti et al., 2021; Castro-Mayorga et al., 2020; Konappa et al., 2021; Mishra et al., 2017; Tanwar and Sushil, 2019). Nanomaterials, because of their captivating properties are considered new chemical entities from their bulk counterparts. In agriculture, the pronounced use of nanomaterials especially Ag, Cu, Fe, and Zn-based nanoformulations has been on nanofertilizers and nanopesticides for the protection against mycotoxigenic fungi and other pathogenic organisms with subsequent increase in crop productivity and health (Abd-Elsalam et al., 2019; Adisa et al., 2019; Agrimonti et al., 2021; Castro-Mayorga et al., 2020). The lack of science-based regulatory frameworks for nanomaterials has made it difficult to regulate the use of nanomaterials (Dimitrijevic et al., 2015; Mishra et al., 2017). Table 1 shows the commercial Cu nanoformulations utilized in agriculture.

In a recent literature review by Zhang et al. (2020), the authors describe the need to develop methods for the identification of mycotoxins and mycotoxins masked by means of separation with greater efficiency and biorecognition molecules with greater specificity and sensitivity. The development of standard detection methods using nanomaterials provides an ultrasensitive and multiplexed detection system for multiple mycotoxins in a single test is paramount. Masked mycotoxins are difficult to detect with conventional standards due to their biotransformation. To date, many Cu nanomaterials and nanocomposites have been promoted as antifungal agents; however, there is an urgent need to develop multifunctional nanocomposites able to detect small concentrations of mycotoxins simultaneously with the added functionality of adsorption and detoxification with limited to no ecotoxicity.

Work by Song et al. (2018) utilized dsDNA [ochratoxin A (OTA)-aptamer]-templated CuNPs as label-free fluorescence indicators in biosensor for sensitive

Table 1 Current commercial Cu nanoformulations utilized in agriculture.

Commercial names	Manufacturers	Current status and legislation compliance	Nanomaterial composition	Application and function
Saula Drip 10-40-10	Bio Nano Technology, Giza, Egypt	Commercialized	Minor elements, (iron, zinc, manganese, **Cu**, boron) NPs	Nanofertilizer, fertilizer
NANOCU		Commercialized	Nano **Cu**, adjuvants and chelating materials	Nanopesticides, fungicide and bactericide
ZENGA		Commercialized	**Cu**, Mitalaxil, Mancozeb	Nanopesticides, fungicide, and bactericide
NovaLand-Nano	Land Green & Technology Co., Ltd., Taiwan	Commercialized	Microelements as Mn, **Cu**, Fe, Zn, Mo, N NPs	Nanofertilizer, fertilizer

detection of OTA. Where the dsDNA serves as the template for CuNP synthesis exhibiting high fluorescence quantum yield and in the presence of OTA, aptamer forms an OTA-aptamer, and many dsDNA-templated CuNPs are degraded into mononucleotides by the RecJf exonuclease (single-stranded DNA-specific exonuclease) resulting in low fluorescence. The system had a low detection limit (LOD) of 5 parts per billion (ppb). Recent similar work by Chen et al. (2021) developed and investigated a highly specific and ultrasensitive assay that used copper monosulfide nanoparticles (CuSNPs) conjugated to an anti-OTA antibody (CuS-AbNPs) as fluorescent probes for the specific and sensitive detection of OTA in coffee, corn, and soybean samples. The fluorescent probe detected Cu^{2+} dissolution/release; briefly, OTA present in the sample binds with CuS-AbNPs which causes the release of Cu^{2+}, thereby activating the Cu^{2+} fluorescent probe. Results revealed that the assay can detect 0.1–100 ppb OTA with LOD of 0.001 ppb and a detection time of 170 min. This provides the opportunity for OTA quantification for food safety, quality assurance/control, and exemplifies the vast application of CuNPs for the detection of mycotoxins (Alghuthaymi et al., 2021).

In agriculture, a vast majority of Cu nanomaterials are used as antimicrobial agents has provided beneficial advantages over their bulk Cu counterparts (Abd-Elsalam et al., 2019; Chellaram et al., 2014) to produce more healthy foods without mycotoxin contamination (Dimitrijevic et al., 2015). This is through the antimicrobial activity of Cu nanomaterials is attributed by the release of Cu^{2+} and Cu^{+} ions and their ease functionalization via encapsulation of bioactive compounds resulting in improved food storage, increased shelf life correlating to protection against fungal contamination and mycotoxins, thus improved food safety and security (Nath et al., 2019).

There are several Cu-based fungicidal products in the market which lack significant information (e.g., chemical composition, mineral speciation, toxicological data, and surface chemistry and reactivity) which is critical for accurately evaluating the ecotoxicological risks associated with these products (Jesmin and Chanda, 2020; Nile et al., 2020). Tegenaw et al. (2015) examined Cu-based fungicidal products (product A and B) and reference compounds (metallic Cu, Cu_2O, CuO, $CuCl_2$, and aqueous Cu^{2+}) to evaluate their mineral speciation and particle size, which correlate to their potential environmental implications (Keller et al., 2017). Their results revealed that product A and B contained 360 and 310 g of Cu kg^{-1}, respectively, which was attributed to the presence of cornetite [$Cu_3(PO_4)_2$], malachite [$Cu_2CO_3(OH)_2$], spertiniite [$Cu(OH)_2$], and tenorite (CuO).

Mineral speciation analysis revealed that product A, dominant Cu species was spertiniite and product B was dominated by tenorite (approx. 30%, < 450 nm). Product A and B had Cu nanoparticles that were 90 and 25 nm in size, respectively. Furthermore, product B had a higher toxicological impact than all the tested samples, attributed to their size compared to product A. Under environmental parameters (e.g., background electrolytes, ionic strength, and pH), both products were impacted. The authors also highlighted the importance of the charge-driven stability (electrostatics) of the nanomaterials, which is a proxy for predicting their fate and mobility within the environment. Results also pointed out that CuO was found to pose more

risks than other Cu species, because of their genotoxic potential. The consensus of the work suggests that the type of chemical speciation used in the nanofungicide formulations must be also taken into consideration together with other factors such as type of synthesis, particle size, stability, and reactivity, which dictates the overall ecotoxicology of the nanofungicides (Jesmin and Chanda, 2020).

Another study by Maqsood et al. (2020) evaluated the antifungal activity of CuNPs against *A. niger*. Their results showed maximum inhibitory effect at 1.5% of CuNP concentration. In addition, Kolackova et al. (2021) evaluated the delivery of different Cu-based fungicides [CuO, $CuSO_4$, Cu-EDTA, CuO-nanopowder (< 50 nm)] using superabsorbent polymers on the effects of foliar application for nutritional characteristics (i.e., percentage of ash, crude protein, crude fat and crude fiber, acid detergent fiber, ash-free neutral detergent fiber, lignin, cellulose, and starch) and effects against mycotoxin (DON and T-2 toxin) contamination on wheat kernel. Their results revealed that the highest nutritional content was observed with treatment of Cu-nano, while all treatments were effective at controlling DON and T-2 toxin production. It is imperative to restrict mycotoxins in the food chain without affecting quality/nutritional characteristics of food, and the environment such as microbes in soil and water (Agrimonti et al., 2021; Jesmin and Chanda, 2020).

The University of California Center on the Environmental Implications of Nanotechnology conducted a systematic empirical study of the potential risks of CuNPs used in agriculture as fungicidal agents (Keller et al., 2017). The study focused on six Cu-based materials: (i) nano-Cu (nCu), (ii) micro-Cu (μCu), (iii) nano-CuO (nCuO), (iv) micro-CuO (μCuO), (v) CuPro ($nCu(OH)_2$-a), and (vi) Kocide 3000 ($nCu(OH)_2$-b). The results from the study revealed > 95% of Cu released accumulates to potentially toxic levels (> 0.5 ppm) into the environment entered the soil and aquatic sediments, and Cu^{2+} even at low concentrations exhibited higher toxicity especially in aquatic organisms, especially freshwater daphnids and marine amphipods which are more susceptible to CuNP toxicity than terrestrial plants as shown in Fig. 2. El-Abeid et al. (2020) demonstrated the use of graphene oxide nanosheet-decorated CuONPs (rGO-CuONPs) against *F. oxysporum*. Results revealed comparative antifungal activity of rGO-CuONPs was effective at 1 ppm without any phytotoxicity, while conventional fungicide Kocide 2000 was at 2500 ppm.

Shah and Mraz (2020) reported that 20 ppb of CuNPs or 100 ppb of $CuSO_4$ exposed to juvenile rainbow trout (*Oncorhynchus mykiss*) caused organ injuries (gill, gut, liver, kidney, brain, and muscle) according to the pathological findings. A review by Malhotra et al. (2020) summarized the toxicity of metallic Cu, CuNPs, and CuONPs on various fish species, data related to their toxicity are still limited. The results are contradictory where some studies reported CuNPs to be less toxic than $CuSO_4$, while others reported otherwise. Interestingly, Fadl et al. (2020) reported on the binding affinity of CuONPs and hydrated sodium aluminum silicate nanoparticles (HSCASNPs) as adsorbents at 500 ppm for OTA in Nile tilapia fish fed on OTA contaminated diet. Collectively, these results provide insight on the environmental risk predictions to assess impacts, and approaches to mitigate the toxicity of Cu nanoformulations while promoting beneficial uses of Cu-nanofungicides.

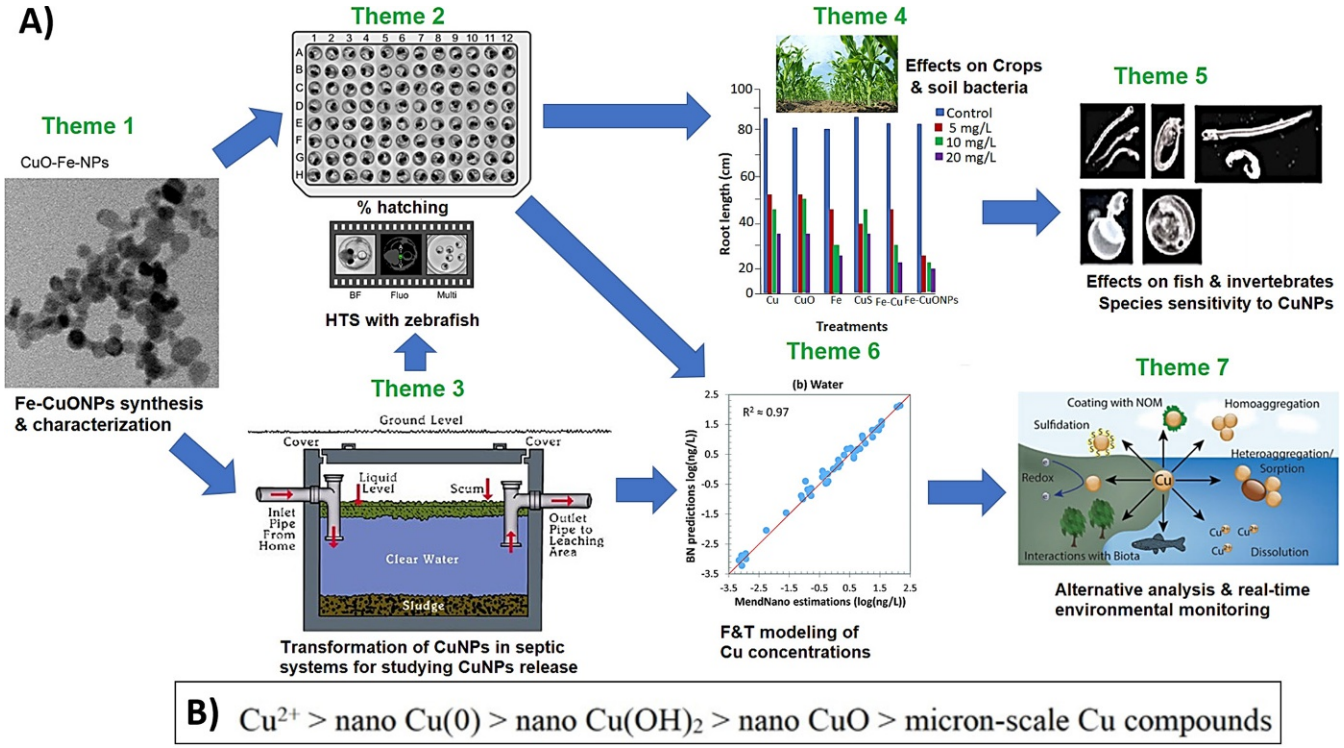

FIG. 2

Copper nanoparticles (CuNPs) lifecycle (A) Theme 1: acquisition and characterization of the Cu particles, followed by distribution of the characterized materials to other themes; Theme 2: high throughput screening, which served to design and prioritize studies in Themes 4 (terrestrial toxicity) and Theme 5 (aquatic toxicity). In parallel, Theme 3 conducted life cycle material flow analyses to determine likely release estimates, exposure concentrations, and doses for use in Themes 4 and 5. Exposure and toxicological data were transferred to Theme 6 to model risk based on expected concentrations/doses and hazards. Theme 7 conducted alternative analyses workshops for copper in paints. The project outcomes were (1) release estimates for various CuNP applications; (2) assessment of likely exposure pathways and concentrations; and (3) ranking of toxicity of different species of CuNPs, micron-scaled Cu particles, and Cu salts and (B) comparative toxicity of CuNPs, μ-scaled Cu particles and Cu salts.

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Table 2 Antifungal activity of $NCuS_{1-3}$ and standard fungicide (Captan).

	A. alternata		*D. oryzae*		*C. lunata*	
Treatments	**ED_{50}**	**ED_{90}**	**ED_{50}**	**ED_{90}**	**ED_{50}**	**ED_{90}**
$NCuS_1$	6.7	9.6	8.0	10.0	8.0	10.5
$NCuS_2$	8.3	11.0	7.0	9.5	11.5	14.0
$NCuS_3$	5.5	8.3	5.0	7.0	6.0	8.0
Captan[a]	240	430	250	390	270	400

[a] *Standard fungicide (*N*-trichloromethyl-thio-4-cyclohexene-1,2-dicarboximide), ED_{50}, effective dose at 50% fungal inhibition, ED_{90}, effective dose at 90% fungal inhibition.*

Sidhu et al. (2017) developed copper sulfide nano-aquaformulation ($NCuS_{1–3}$) with different capping agents for their antifungal activity against *Alternaria alternata*, *Drechslera oryzae*, and *Curvularia lunata* and their impact on seed quality of rice grains (*Oryzae sativa*). The NCuS, naked CuS (no stabilizing agent); $NCuS_1$, stabilized with polyvinyl pyrrolidone (PVP); $NCuS_2$, stabilized with 4-aminobutyric acid (GABA); and $NCuS_3$, stabilized with trisodium citrate and their average size range of 14, 12, 10, and 8 nm, respectively. Antifungal activity results are summarized in Table 2 (adapted from Sidhu et al., 2017) and $NCuS_3$ at 7 ppm for 2 h significantly reduced seed rot and seedling blight, favorable effect to accelerate seed germination and seedling growth.

On the other hand, green nanotechnology provides pronounced strategies to circumvent the challenges experienced with conventional Cu fungicides (Tanwar and Sushil, 2019). This can be done through the green synthesis of copper sulfate, copper, and copper oxide nanoparticles ($CuSO_4$-NPs, CuNPs, and CuONPs, respectively) using bioactive constituents from plants. Ideally, this would produce Cu nanofungicides with high efficacy at low concentrations, stability, low cost, biocompatibility, and concomitantly low ecotoxicity to crops, animals, humans, and the overall ecosystem (Jesmin and Chanda, 2020; Mishra et al., 2017; Tegenaw et al., 2015). Cu nanofungicides would provide a multifarious approach with armaments potential as nanofertilizers for enhanced plant/crop growth stimulation while proffering plant/crop protection from mycotoxins (Konappa et al., 2021).

4 Cu antifungal activity

The activity of Cu nanomaterials as antimicrobial agents is attributed through the electrostatic forces exerted by Cu^{2+} ions on the outer plasma membrane composed of lipopolysaccharide, eliciting significant permeability thus affecting several essential membrane-dependent protein transport systems (e.g., ATP-powered pumps, channel proteins, and transporters). Cu-induced disruption of membrane integrity inevitably results in cellular death, thereby reducing fungal growth eliminating the risk of mycotoxins (Borkow and Gabbay, 2009). The Cu^{2+} ions released from Cu

nanofungicides impose structural conformational changes in protein folding resulting in inhibition or impaired biological activities, thus leads to substantial protein alterations and cleavage (e.g., Cu^{2+} can result in the inactivation of the vaccinia H1-related tyrosine phosphatase and stoichiometric concentrations of Cu ions can inhibit HIV-1 protease activity) (Kim et al., 2000).

Furthermore, Cu ions can intercalate with DNA, causing helical structure deformation and denaturation and this is a result of guanine-specific covalent binding affinity of Cu^{2+} ions facilitating a Cu^{2+}-induced oxidative DNA damage. DNA damage is further intensified by repeated cyclic redox reactions through the generation of reactive oxygen species (ROS), where Cu^{2+} and Cu^{+} catalyze H_2O_2 to hydroxyl radicals (•OH) through the Fenton oxidation reaction (Dimitrijevic et al., 2015). The redox Cu^{2+} and Cu^{+} are responsible for preventing the germination of fungal spores thereby eliminating the risks of mycotoxin manifestation (Gogos et al., 2012). It is worth noting that once Cu nanofungicides (> 95% of Cu) applied in the field to mitigate mycotoxigenic fungal contamination, it takes approximately hours to weeks for their oxidization, dissolving, and forming chemical speciation of CuS and other insoluble Cu complexes depending on the soil, water chemistry (e.g., alkalinity, salinity, organic matter content, presence of sulfide, and other complexing ions) is released into the environment enters soil and aquatic sediments (Keller et al., 2017).

5 Green Cu nanofungicides

The synthetic repertoire of Cu nanoparticles is very challenging due to the rapid oxidation of CuNPs to CuONPs. Several green synthetic routes have been reported, this includes chitosan-Cu (Chit-Cu) nanogels and nanohydrogels complexation for inhibiting *F. graminearum* through the synergistic effect of chitosan and Cu (Alghuthaymi et al., 2021; Atiq et al., 2020). This provides a platform for the generation of biodegradable nanofungicides. Brunel et al. (2013) developed Chit-Cu^{2+} nanohydrogels as a biocompatible, bioactive, and pH-sensitive system for Cu^{2+} release against *F. graminearum*. They reported that at optimum conditions, the optimal adoption of Cu^{2+} (300 mg) was complexed to 1 g of chitosan via neutralized amino groups. The authors revealed that the slow release of Cu^{2+} was facilitated through two mechanisms as shown in Fig. 3.

The announced benefit of the Chit-Cu^{2+} nanohydrogels which include the ease in the complexation of chitosan with Cu^{2+} ions provides a thermodynamically favorable reservoir for slow Cu^{2+} release; chitosan has been reported to demonstrate antimicrobial activity, and is also known to be a plant growth promoter. Taken together with antimicrobial and biological activity of Cu, Chit-Cu^{2+} nanohydrogels provide a culminating synergistic complementary antifungal repertoire against mycotoxigenic fungi, subsequently eliminating the risk of mycotoxins.

Maize (*Zea mays* L.) is one of the major staple crop worldwide surpassing wheat and rice; however, it is susceptible to different fungal (*A. flavus*, *F. verticillioides*,

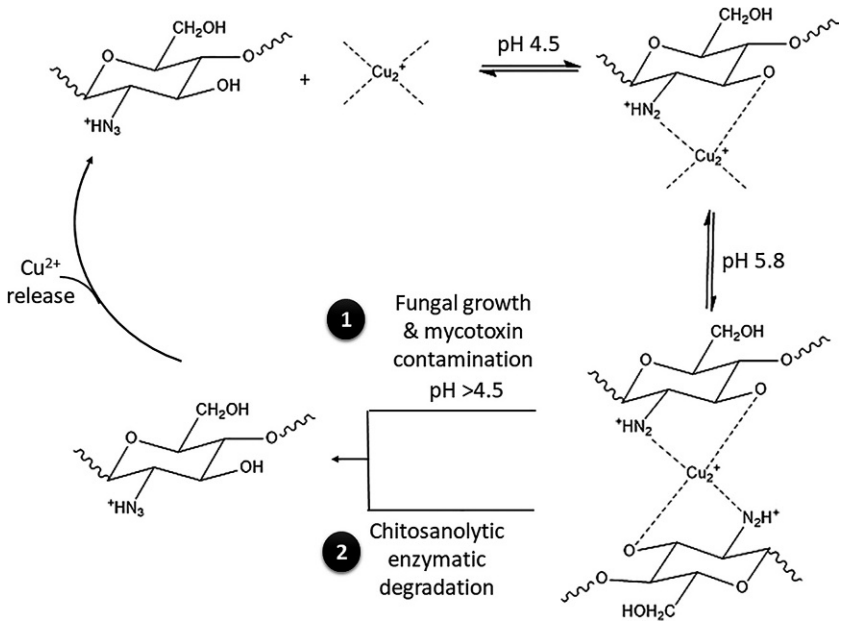

FIG. 3

Mechanism of Cu^{2+} complexation with chitosan and the release of Cu^{2+} through (1) acidification caused by fungal growth and mycotoxin contamination which aided the protonation of the amino groups, concomitantly releasing the bound Cu^{2+} from chitosan and (2) chitosanolytic enzymatic degradation of chitosan nanogels by fungal growth which causes a release of bound Cu^{2+}.

and *F. graminearum*) contamination both in field and during storage; therefore, is prone to multimycotoxins such as AFB_1, FBs, and DON contamination (Giorni et al., 2019). Choudhary et al. (2017) developed biodegradable chitosan-Cu nanoparticles (Chit-CuNPs) to enhanced innate immunity and plant growth stimulate activities of maize against various fungal diseases like curvularia leaf spot (CLS) disease caused by *Curvularia lunata*, which can also be applicable for eliminating mycotoxin contamination.

The developed Chit-Cu nanocomplex generated a well-coordinated synergy between chitosan and Cu, allowing for dynamic bioactivities of chitosan and Cu to be realized using cofactor functionality of various enzymes engaged in electron transport and redox reactions. Their findings revealed that the Chit-CuNPs were formed through CN bonding, with pH- and time-dependent Cu release facilitated by the protonation and deprotonation of the amino group of chitosan. At pH 4.5, Cu release was rapidly release from the nanocomplex, whereas at pH > 4.5 a gradual and persistent Cu release was observed. Their results revealed that the Chit-CuNPs were through C–N bonding with the pH- and time-dependent release of Cu facilitated by protonation and deprotonation of the amino group of chitosan, at pH < 4.5

expedited Cu release and pH > 4.5 resulted in slow and sustained release of Cu, corroborating the results repeated by Brunel et al. (2013). In addition, Chit-CuNPs enhanced plant defense responses through increased superoxide dismutase (SOD), peroxidase (POD), polyphenol oxidase, (PPO), and phenylalanine ammonia-lyase (PAL) activities (Fig. 4).

Pariona et al. (2019) synthesized CuNP fungicide using ascorbic acid and evaluated their antifungal activity against *F. solani*, *Neofosicoccum* sp., and *F. oxysporum.* Their results revealed that CuNPs induced mycelium morphological change through cell membrane damage and intracellular ROS generation. The utilization of green nanotechnology using phytochemicals from plants or crops susceptible to fungal and mycotoxin contamination to produce nanoformulations as nanomicrobicidal agents for synergistic protection will be an effective benign strategy. This notion was demonstrated by Ponmurugan et al. (2016), where they synthesized CuNP synthesized extracellularly using *Streptomyces griseus* to evaluate their antifungal activity against *Poria hypolateritia*, which causes red root-rot disease in tea plants. Their CuNPs were compared with widely used commercial systemic fungicide carbendazim and bulk Cu to assess their effectiveness as fungicide and soil quality after treatment. The results showed that the produced CuNPs were < 50 nm, fungicidal activity was recorded at 57.2% for carbendazim, followed by 52.7% at 2.5 ppm for CuNPs, and 45.3% bulk Cu.

Abd-Elsalam et al. (2020) developed a nanocomposite hydrogel composed of copper and chitosan (Cu-Chit/NC hydrogel) prepared by metal vapor synthesis (MVS). This study demonstrated the antifungal activity of the nanocomposite hydrogel against aflatoxigenic strains of *A. Flavus*, at 240 ppm attributed by the inactivation of *A. flavus* mycelia growth, subsequently reducing the production of AFs. The results demonstrate that Cu-Chit/NCS hydrogel is an innovative nano-biopesticide that can be used not only as an effective fungicide against plant pathogens but also as an effective agent for the management of toxigenic fungi in food and feed.

Carbendazim showed superior activity, however, CuNPs in addition to the fungicidal activity provided maximum leaf yield and improved soil macronutrients (total organic carbon, total nitrogen, phosphorus, and potassium) compared to the other treatments. In another study by Devipriya and Roopan (2017) produced 30 nm CuONPs synthesized using *Cissus quadrangularis* and evaluated their antifungal activity against *A. niger* and *A. flavus*, well-known mycotoxigenic fungi; notorious for producing aflatoxins and ochratoxins. The CuONPs exhibited better antifungal activity (> 80% inhibition at 500 ppm) against *A. niger* and *A. flavus*, while carbendazim showed 40% at 500 ppm. This knowledge provides a clear indication of the importance of developing benign Cu nanofungicides for agricultural practices against mycotoxigenic fungi and other pathogenic organisms that pose significant challenges in food safety and security.

Asghar et al. (2020) conducted a study comparing the antimicrobial activity of three different metallic nanoparticles (Ag, Cu, and Fe) synthesized via green chemistry using leaf extracts of *Syzygium cumini.* Results revealed that AgNPs showed

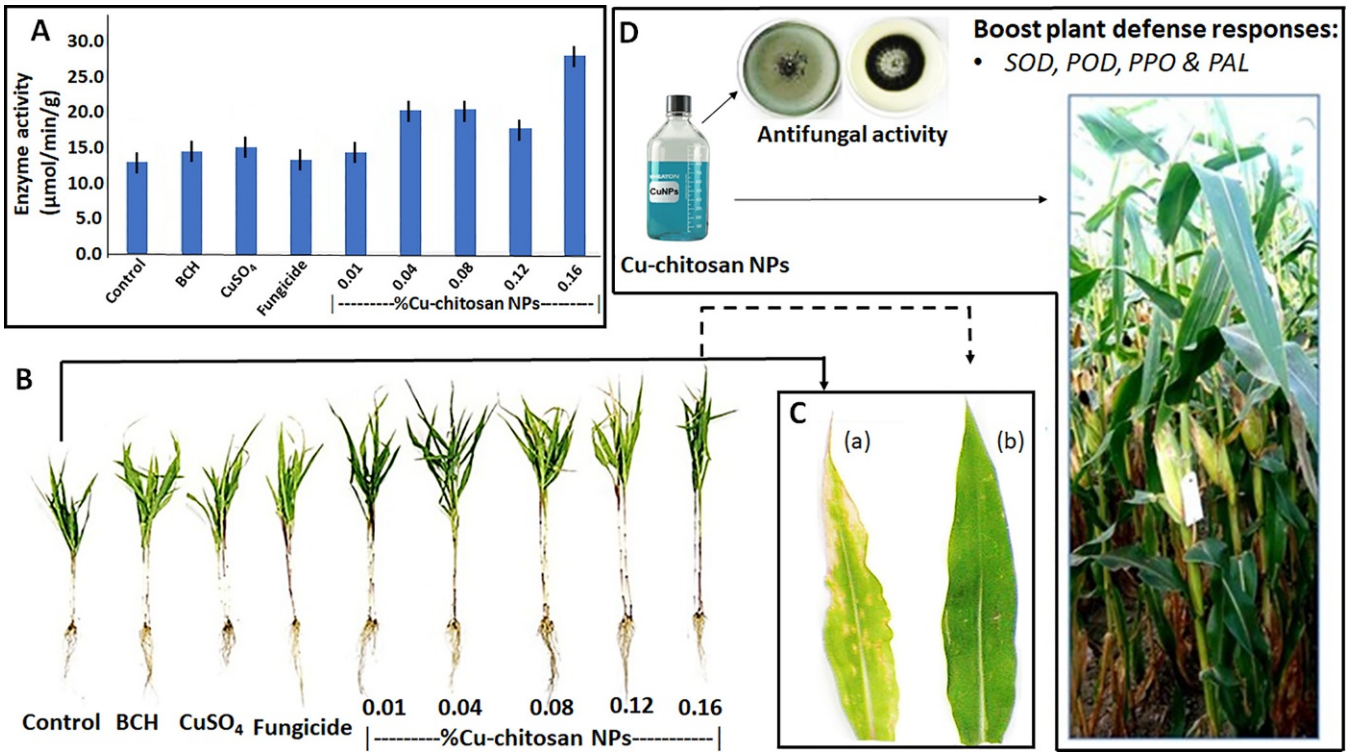

FIG. 4

Chitosan-Cu nanoparticles (Chit-CuNPs) antifungal and plant growth activities (A) effect of Chit-CuNPs on enzymes (SOD, POD, PAL, PPO) activity, (B) plant growth effects of Chit-CuNP treatment, (C) CLS disease symptoms on maize plant leaf (a) necrotic lesions in control, (b) no lesions on Chit-CuNPs (0.16%) treated leaf, and (D) in-field translational application model of Chit-CuNPs for enhanced defense responses and plant growth in maize.

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excellent antimicrobial activities against methicillin and vancomycin resistance bacterial strains *Staphylococcus aureus* and aflatoxigenic fungi *A. flavus* and *A. parasiticus*. Additionally, the production of AFs was significantly inhibited by the treatments, with AFB_1 adsorption capability on NPs observed in the following order FeNPs > CuNPs > AgNPs. Thus, metallic NPs obtained by green nanotechnology can be used with AF adsorbent and provide a promising avenue for the detoxification of AFB_1 in human food and animal feed.

Researchers have developed a method of mycogenic synthesis of zinc oxide (ZnO) and copper oxide (CuO) nanoparticles using *Penicillium chrysogenum* (Mohamed et al., 2020). The synthetic route for the production was facilitated by secreted extracellular proteins related to nitrate reductase during fungal growth. The produced ZnONPs and CuONPs exhibited increased antimicrobial activity against Gram-positive and Gram-negative bacteria, antibiofilm effects, and phytopathogenic fungal strains (*F. solani*, *F. oxysporum*, *Sclerotium sclerotia*, and *A. terreus*). Results showed that CuONPs antifungal activity was stronger than ZnONPs at 10 mg/mL. The CuONPs and ZnONPs were also effective *A. solani*, *A. niger*, *F. oxysporum*, *Pythium ultimum*, and *A. alternata*. The proposed mechanism of activity of nanomaterials to inhibit fungal growth was multifunctional through affecting cell functions, causing morphological changes in fungal hyphae, preventing the expansion of conidia and conidiophores, and consequently, leading to cell death.

Pérez-de León et al. (2020) investigated the comparative antifungal and antifumonigenic activities between CuNPs (2.5 ± 0.3 nm) and AgNPs (17 ± 1.5 nm) obtained by the chemical reduction method. Results revealed that both these nanoparticles exhibited antifungal activity against *F. verticillioides*, at 125 and 75 ppm for CuNPs and AgNPs, respectively. Antifumonigenic activity of CuNPs, completely inhibited FB_1 production at ≥ 100 ppm, while AgNPs only suppressed FB_1 biosynthesis at ≥ 20 ppm. The authors suggest that the activity of treatment with CuNPs and AgNPs occurred due to changes caused in the structure of the hyphae, such as the interference in mycelial growth, loss of contour and uniformity of the hyphae, and rupture of the hyphae, resulting in a significant reduction in the biosynthesis of FB_1. It is worth noting, since AgNPs were performed better than CuNPs, CuNPs for agricultural applications are more superior than AgNPs because of its added advantage of being an essential micronutrient for plant growth promoter.

Researchers have developed an innovative approach using sucrose as a carbon source to obtain copper oxide nanocomposites (CuO/C) with a particle size of 50 nm (Roopan et al., 2019). The antifungal activities of the CuO/C nanocomposite were evaluated against *A. niger* and *A. flavus*. Antifungal activity of CuO/C nanocomposite at 1000 ppm, inhibited *A. flavus* and *A. niger* by 70% and 90%, respectively. Another study by Safaei et al. (2019) developed an alginate-CuO bionanocomposite and evaluated the antifungal activity against *A. niger*. Although the efficacy against the production of mycotoxins has not been evaluated, the alginate-CuO nanocomposite produced by green synthesis has demonstrated satisfactory antifungal efficacy, in addition to biocompatibility for biomedical, pharmaceutical, nutritional, agricultural, and environmental applications.

6 Future recommendations for Cu nanofungicides

The development and production of Cu nanofungicides require a comprehensive understanding of the multitude of the tripartite interactions of Cu nanoparticles with plant, soil, and soil microbes in order to assess and govern reliable ecotoxicology risk assessments and risk management factors of Cu nanofungicides destined for agricultural applications for effective protection against mycotoxigenic fungal contamination. It is only through this notion that sufficient scientific evidences would provide the basis of legislative frameworks, regulatory entities [e.g., USFDA, Food and Agriculture Organization (FAO), US Environmental Protection Agency (USEPA), Organization for Economic Cooperation and Development (OECD), International Standard Organization (ISO), and Registration, Evaluation, Authorization and Restriction of Chemicals (REACH)] for specific guidelines and provisions bestowing Cu nanofungicides utilization for agriculture, food, and feed sectors (Fig. 5). The intricate understanding of the comparative environmental fate and ecotoxicology of Cu nanomaterials interactions for eliminating the overall risk of mycotoxicology.

7 Conclusion

The use of Cu nanoformulation produced through green nanotechnology provides a remarkable strategy to reduce the amount of Cu introduced into agroecosystems, thus limiting ecotoxicological risks but still providing significant Cu for antifungal activity and micronutrient as a cofactor required by plants to facilitate a cascade of essential pathways. Albeit benefits have been since with the utilization of Cu

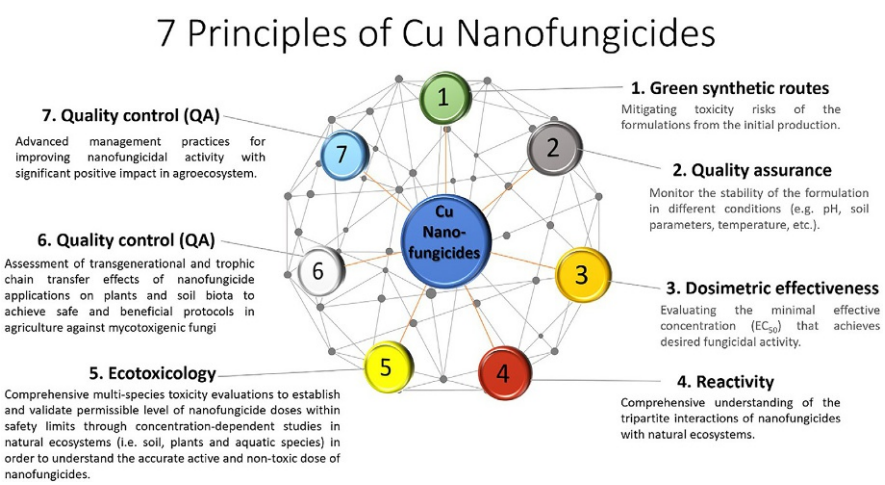

FIG. 5

The seven principles of the production, assessment, and application of Cu nanofungicides for eliminating mycotoxin contamination and other agricultural pathogens.

nanofungicides over conventional fungicides. It is imperative to invest in the understanding of the ecotoxicology of the Cu nanoformulation lifecycle. The architectural design of Cu nanofungicides can influence the physiochemical and fungicidal/fungistatic properties attributed by bioavailability and cupric ion release as a function of antifungal activity and overall toxicity profile. To avert toxicity, it is important to consider green nanotechnologies and dosimetric calculations. This amalgamation of a green sustainable nanotechnology will result in enhanced fungicidal activity thereby eliminating the risk of mycotoxins with improved crop/food productivity and management without imposing ecotoxicological, nano-phytotoxicity effects in agroecosystems (crops, soil), animal, and human.

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References

Abd-Elsalam, K.A., El-Naggar, M.A., Ghannouchi, A., Bouqellah, N.A., 2019. Nanomaterials and ozonation: safe strategies for mycotoxin management. In: Nanomycotoxicology: Treating Mycotoxins in the Nano Way. Elsevier Inc., https://doi.org/10.1016/B978-0-12-817998-7.00013-6.

Abd-Elsalam, K.A., Alghuthaymi, M.A., Shami, A., Rubina, M.S., Abramchuk, S.S., Shtykova, E.V., Vasil'kov, A.Y., 2020. Copper-chitosan nanocomposite hydrogels against aflatoxigenic *Aspergillus flavus* from dairy cattle feed. J. Fungi 6 (3), 1–20. https://doi.org/10.3390/jof6030112.

Adam, M.A.A., Tabana, M.Y., Musa Binti, K., Sandai Anak, D., 2017. Effects of different mycotoxins on humans, cell genome and their involvement in cancer (review). Oncol. Rep. 37 (3), 1321–1336. https://doi.org/10.3892/or.2017.5424.

Adisa, I.O., Pullagurala, V.L.R., Peralta-Videa, J.R., Dimkpa, C.O., Elmer, W.H., Gardea-Torresdey, J.L., White, J.C., 2019. Recent advances in nano-enabled fertilizers and pesticides: a critical review of mechanisms of action. Environ. Sci. Nano 6 (7), 2002–2030. https://doi.org/10.1039/c9en00265k.

Agrimonti, C., Lauro, M., Visioli, G., 2021. Smart agriculture for food quality: facing climate change in the 21st century. Crit. Rev. Food Sci. Nutr. 61 (6), 971–981. https://doi.org/10.1080/10408398.2020.1749555.

Alghuthaymi, M.A., Rajkuberan, C., Rajiv, P., Kalia, A., Bhardwaj, K., Bhardwaj, P., Abd-Elsalam, K.A., Valis, M., Kuca, K., 2021. Nanohybrid antifungals for control of plant diseases: current status and future perspectives. J. Fungi 7 (1), 1–20. https://doi.org/10.3390/jof7010048.

Asghar, M.A., Zahir, E., Asghar, M.A., Iqbal, J., Rehman, A.A., 2020. Facile, one-pot biosynthesis and characterization of iron, copper and silver nanoparticles using *Syzygium cumini* leaf extract: As an effective antimicrobial and aflatoxin B1 adsorption agents. PLoS One 15 (7), e0234964. https://doi.org/10.1371/journal.pone.0234964.

Atiq, M., Naeem, I., Sahi, S.T., Rajput, N.A., Haider, E., Usman, M., Shahbaz, H., Fatima, K., Arif, E., Qayyum, A., 2020. Nanoparticles: a safe way towards fungal diseases. Arch. Phytopathol. Plant Protect., 1–12. https://doi.org/10.1080/03235408.2020.1792599.

Borkow, G., Gabbay, J., 2009. Copper, an ancient remedy returning to fight microbial, fungal and viral infections. Curr. Chem. Biol. 3 (3), 272–278. https://doi.org/10.2174/187231309789054887.

Brunel, F., El Gueddari, N.E., Moerschbacher, B.M., 2013. Complexation of copper(II) with chitosan nanogels: toward control of microbial growth. Carbohydr. Polym. 92 (2), 1348–1356. https://doi.org/10.1016/j.carbpol.2012.10.025.

Castro-Mayorga, J.L., Cabrera-Villamizar, L., Balcucho-Escalante, J., Fabra, M.J., López-Rubio, A., 2020. Applications of nanotechnology in agry-food productions. Nanotoxicity, 319–340. https://doi.org/10.1016/b978-0-12-819943-5.00015-4.

Çelik, K., 2019. The efficacy of mycotoxin-detoxifying and biotransforming agents in animal nutrition. In: Nanomycotoxicology: Treating Mycotoxins in the Nano Way, pp. 271–284, https://doi.org/10.1016/B978-0-12-817998-7.00012-4.

Chellaram, C., Murugaboopathi, G., John, A.A., Sivakumar, R., Ganesan, S., Krithika, S., Priya, G., 2014. Significance of nanotechnology in food industry. APCBEE Procedia 8 (Caas 2013), 109–113. https://doi.org/10.1016/j.apcbee.2014.03.010.

Chen, R., Sun, Y., Huo, B., Zhao, X., Huang, H., Li, S., Bai, J., Liang, J., Gao, Z., 2021. A copper monosulfide-nanoparticle-based fluorescent probe for the sensitive and specific detection of ochratoxin A. Talanta 222, 121678. https://doi.org/10.1016/j.talanta.2020.121678.

Choudhary, R.C., Kumaraswamy, R.V., Kumari, S., Sharma, S.S., Pal, A., Raliya, R., Biswas, P., Saharan, V., 2017. Cu-chitosan nanoparticle boost defense responses and plant growth in maize (*Zea mays* L.). Sci. Rep. 7 (1), 1–11. https://doi.org/10.1038/s41598-017-08571-0.

Devipriya, D., Roopan, S.M., 2017. *Cissus quadrangularis* mediated ecofriendly synthesis of copper oxide nanoparticles and its antifungal studies against *Aspergillus niger*, *Aspergillus flavus*. Mater. Sci. Eng. C 80, 38–44. https://doi.org/10.1016/j.msec.2017.05.130.

Dimitrijevic, M., Karabasil, N., Boskovic, M., Teodorovic, V., Vasilev, D., Djordjevic, V., Kilibarda, N., Cobanovic, N., 2015. Safety aspects of nanotechnology applications in food packaging. Proc. Food Sci. 5, 57–60. https://doi.org/10.1016/j.profoo.2015.09.015.

El-Abeid, S.E., Ahmed, Y., Daròs, J.A., Mohamed, M.A., 2020. Reduced graphene oxide nanosheet-decorated copper oxide nanoparticles: a potent antifungal nanocomposite against fusarium root rot and wilt diseases of tomato and pepper plants. Nanomaterials 10 (5). https://doi.org/10.3390/nano10051001.

Fadl, S.E., El-Shenawy, A.M., Gad, D.M., El Daysty, E.M., El-Sheshtawy, H.S., Abdo, W.S., 2020. Trial for reduction of Ochratoxin A residues in fish feed by using nano particles of hydrated sodium aluminum silicates (NPsHSCAS) and copper oxide. Toxicon 184 (May), 1–9. https://doi.org/10.1016/j.toxicon.2020.05.014.

Giorni, P., Bertuzzi, T., Battilani, P., 2019. Impact of fungi co-occurrence on mycotoxin contamination in maize during the growing season. Front. Microbiol. 10, 1265. https://www.frontiersin.org/article/10.3389/fmicb.2019.01265.

Gogos, A., Knauer, K., Bucheli, T.D., 2012. Nanomaterials in plant protection and fertilization: current state, foreseen applications, and research priorities. J. Agric. Food Chem. 60 (39), 9781–9792. https://doi.org/10.1021/jf302154y.

He, X., Deng, H., Hwang, H.M., 2019. The current application of nanotechnology in food and agriculture. J. Food Drug Anal. 27 (1), 1–21. https://doi.org/10.1016/j.jfda.2018.12.002.

Jesmin, R., Chanda, A., 2020. Restricting mycotoxins without killing the producers: a new paradigm in nano-fungal interactions. Appl. Microbiol. Biotechnol. 104 (7), 2803–2813. https://doi.org/10.1007/s00253-020-10373-w.

Keller, A.A., Adeleye, A.S., Conway, J.R., Garner, K.L., Zhao, L., Cherr, G.N., Hong, J., Gardea-Torresdey, J.L., Godwin, H.A., Hanna, S., Ji, Z., Kaweeteerawat, C., Lin, S., Lenihan, H.S., Miller, R.J., Nel, A.E., Peralta-Videa, J.R., Walker, S.L., Taylor, A.A., et al., 2017. Comparative environmental fate and toxicity of copper nanomaterials. NanoImpact 7, 28–40. https://doi.org/10.1016/j.impact.2017.05.003.

Khamis, Y., Hashim, A.F., Margarita, R., Alghuthaymi, M.A., Abd-Elsalam, K.A., 2017. Fungicidal efficacy of chemically-produced copper nanoparticles against *Penicillium digitatum* and *Fusarium solani* on citrus fruit. Philipp. Agric. Sci. 100 (1), 69–78.

Kim, J.-H., Cho, H., Ryu, S.-E., Choi, M.-U., 2000. Effects of metal ions on the activity of protein tyrosine phosphatase VHR: highly potent and reversible oxidative inactivation by Cu^{2+} ion. Arch. Biochem. Biophys. 382 (1), 72–80. https://doi.org/10.1006/abbi.2000.1996.

Kolackova, I., Gruberova, H.A., Kratochvil, O., Baholet, D., Skladanka, J., Jancar, J., Skarpa, P., 2021. Effect of foliar copper-containing superabsorbent polymers on nutritional characteristics and mycotoxin contamination of wheat kernel. Acta Univ. Agric. Silvic. Mendel. Brun. 69 (1), 71–78. https://doi.org/10.11118/ACTAUN.2021.007.

Konappa, N., Krishnamurthy, S., Arakere, U.C., Chowdappa, S., Akbarbasha, R., Ramachandrappa, N.S., 2021. Nanofertilizers and nanopesticides: recent trends, future prospects in agriculture. In: Jogaiah, S., Singh, H.B., Fraceto, L.F., de Lima, R. (Eds.), Woodhead Publishing Series in Food Science, Technology and Nutrition. Woodhead Publishing, pp. 281–330, https://doi.org/10.1016/B978-0-12-820092-6.00012-4 (Chapter 12).

Malhotra, N., Ger, T.R., Uapipatanakul, B., Huang, J.C., Chen, K.H.C., Der Hsiao, C., 2020. Review of copper and copper nanoparticle toxicity in fish. Nanomaterials 10 (6), 1–28. https://doi.org/10.3390/nano10061126.

Maqsood, S., Qadir, S., Hussain, A., Asghar, A., Saleem, R., Zaheer, S., Nayyar, N., 2020. Antifungal properties of copper nanoparticles against *Aspergillus niger*. Sch. Int. J. Biochem. 03 (04), 87–91. https://doi.org/10.36348/sijb.2020.v03i04.002.

MarketWatch, 2021. Copper Fungicides Market 2021: Analytical Overview, Key Players, Growth Factors, Demand, Market Size, Trends and Forecast to 2026 with Top Countries Data. The Expresswire. https://www.marketwatch.com/press-release/copper-fungicides-market-2021-analytical-overview-key-players-growth-factors-demand-market-size-trends-and-forecast-to-2026-with-top-countries-data-2021-03-21.

Melendez, M.V., Heckman, J.R., Murphy, S., D'amico, F., 2020. New Jersey farm soil copper levels resulting from copper fungicide applications. HortTechnology 30 (2), 268–272. https://doi.org/10.21273/HORTTECH04494-19.

Mishra, S., Keswani, C., Abhilash, P.C., Fraceto, L.F., Singh, H.B., 2017. Integrated approach of agri-nanotechnology: challenges and future trends. Front. Plant Sci. 8 (April), 1–12. https://doi.org/10.3389/fpls.2017.00471.

Mohamed, A.A., Abu-Elghait, M., Ahmed, N.E., Salem, S.S., 2020. Eco-friendly mycogenic synthesis of ZnO and CuO nanoparticles for in vitro antibacterial, antibiofilm, and antifungal applications. Biol. Trace Elem. Res. https://doi.org/10.1007/s12011-020-02369-4.

Nath, A., Molnár, M.A., Albert, K., Das, A., Bánvölgyi, S., Márki, E., Vatai, G., 2019. Agrochemicals from nanomaterials—synthesis, mechanisms of biochemical activities and applications. Compr. Anal. Chem. 84, 263–312. https://doi.org/10.1016/bs.coac.2019.04.004.

Nile, S.H., Baskar, V., Selvaraj, D., Nile, A., Xiao, J., Kai, G., 2020. Nanotechnologies in food science: applications, recent trends, and future perspectives. Nano-Micro Lett. 12 (1). https://doi.org/10.1007/s40820-020-0383-9. Springer, Singapore.

Oziengbe, E.O., Osazee, J.O., 2012. Antifungal activity of copper sulphate against *Colletotrichum gloeosporioides*. J. Asian Sci. Res. 2 (12), 835–839. http://aessweb.com/past-issue.php?id=5003%0Ahttps://www.cabdirect.org/cabdirect/abstract/20133089771.

Pariona, N., Mtz-Enriquez, A.I., Sánchez-Rangel, D., Carrión, G., Paraguay-Delgado, F., Rosas-Saito, G., 2019. Green-synthesized copper nanoparticles as a potential antifungal against plant pathogens. RSC Adv. 9 (33), 18835–18843. https://doi.org/10.1039/c9ra03110c.

Pérez-de León, A., Plasencia, J., Vázquez-Durán, A., Méndez-Albores, A., 2020. Comparison of the in vitro antifungal and anti-fumonigenic activities of copper and silver nanoparticles against *Fusarium verticillioides*. J. Clust. Sci. 31 (1), 213–220. https://doi.org/10.1007/s10876-019-01638-0.

Ponmurugan, P., Manjukarunambika, K., Elango, V., Gnanamangai, B.M., 2016. Antifungal activity of biosynthesised copper nanoparticles evaluated against red root-rot disease in tea plants. J. Exp. Nanosci. 11 (13), 1019–1031. https://doi.org/10.1080/17458080.2016.1184766.

Roopan, S.M., Devi Priya, D., Shanavas, S., Acevedo, R., Al-Dhabi, N.A., Arasu, M.V., 2019. CuO/C nanocomposite: synthesis and optimization using sucrose as carbon source and its antifungal activity. Mater. Sci. Eng. C 101, 404–414. https://doi.org/10.1016/j.msec.2019.03.105.

Safaei, M., Taran, M., Imani, M.M., 2019. Preparation, structural characterization, thermal properties and antifungal activity of alginate-CuO bionanocomposite. Mater. Sci. Eng. C 101, 323–329. https://doi.org/10.1016/j.msec.2019.03.108.

Shah, B.R., Mraz, J., 2020. Advances in nanotechnology for sustainable aquaculture and fisheries. Rev. Aquac. 12 (2), 925–942. https://doi.org/10.1111/raq.12356.

Sidhu, A., Barmota, H., Bala, A., 2017. Antifungal evaluation studies of copper sulfide nanoaquaformulations and its impact on seed quality of rice (*Oryzae sativa*). Appl. Nanosci. 7 (8), 681–689. https://doi.org/10.1007/s13204-017-0606-7.

Song, C., Hong, W., Zhang, X., Lu, Y., 2018. Label-free and sensitive detection of Ochratoxin A based on dsDNA-templated copper nanoparticles and exonuclease-catalyzed target recycling amplification. Analyst 143 (8), 1829–1834. https://doi.org/10.1039/c8an00158h.

Tang, H., Xu, M., Luo, J., Zhao, L., Ye, G., Shi, F., Lv, C., Chen, H., Wang, Y., Li, Y., 2019. Liver toxicity assessments in rats following sub-chronic oral exposure to copper nanoparticles. Environ. Sci. Eur. 31 (1). https://doi.org/10.1186/s12302-019-0214-0.

Tanwar, A., Sushil, 2019. Role and effects of nanotechnology used in pesticides and agriculture field. AIP Conf. Proc. 2142 (August). https://doi.org/10.1063/1.5122581.

Tegenaw, A., Tolaymat, T., Al-Abed, S., El Badawy, A., Luxton, T., Sorial, G., Genaidy, A., 2015. Characterization and potential environmental implications of select Cu-based fungicides and bactericides employed in U.S. markets. Environ. Sci. Technol. 49 (3), 1294–1302. https://doi.org/10.1021/es504326n.

Young, D., Avila-Adame, C., Webster, J., Olson, B., Ouimette, D., 2016. Enhancing the Efficacy of Copper Fungicides Through Synergism with Salicylaldehyde Benzoylhydrazones. VIII. Modern Fungicides and Antifungal Compounds, vol. VII Deutsche Phytomedizinische Gesellschaft, Braunschweig, ISBN: 978-3-941261-15-0, pp. 273–278.

Zhang, X., Li, G., Wu, D., Liu, J., Wu, Y., 2020. Recent advances on emerging nanomaterials for controlling the mycotoxin contamination: from detection to elimination. Food Front. 1 (4), 360–381. https://doi.org/10.1002/fft2.42.

CHAPTER

12 Application of copper-based nanomaterials against parasitic nematodes

Sharba Kausar
Department of Microbiology, Jawaharlal Nehru Medical College, Aligarh Muslim University, Aligarh, Uttar Pradesh, India

1 Introduction

Nematodes are also called roundworms that occur as parasites in animals and plants and are also present as free-living forms in soil, water, etc. From the research point of view, all the three categories of nematodes are important due to their agricultural, medicinal, and veterinary importance and used as a test organism in toxicological studies to test the biocompatibility of different compounds. Nematodes as phytopathogens cause a loss in productivity and quality of agriculture crops and horticultural turnout (Lopes-Caitar et al., 2019; Shekoohi et al., 2021). Animal parasitic nematodes cause debilitating diseases with a significant rate of morbidity and mortality in animals and humans around the world (Salikin et al., 2020). There are chemical and biological control strategies to overcome the effects of these parasites but due to survival of environmental stages, reinfection of the host occurs. In addition, mass drug administration of anthelmintics and regular use of nematicides increased the development of resistance against them in animal and plant-parasitic nematodes, respectively. Reduction in the use of some nematicides for protecting the environment becomes a significant hindrance toward parasite control programs (Holden-Dye and Walker, 2014).

The application of nanotechnology toward agriculture pest management has overcome the risk of environmental pollution by replacing chemical nematicides with metal nanoparticles, which reduces the risk of active chemicals entering the agroecosystem. Nanotechnology also helps in plant health management such that it improves solubility, delivery, and more lasting residual activity of agrichemicals and longer residual activity (Elmer et al., 2018). In plant disease management, copper nanoparticles (CuNPs) played a significant role which came into the limelight in 2013 when plant foliage exposed to CuO, Cu_2O, and Cu/Cu_2O nanocomposites and their effects was compared with the conventional registered fungicides to control late

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blight disease. In addition to this, copper is an essential plant nutrient that plays a pivotal role in growth and in the defense mechanism of plants against diseases. The three most important proteins secreted during the plant defense mechanism against pathogen attack are plastocyanins, peroxidases, and multi-Cu oxidases, which require copper as a prerequisite material (Elmer et al., 2018). This chapter summarizes the different approaches used in the synthesis of copper nanoparticles, involvement of CuNPs in plant disease management as a potential nematicide against phytonematodes, and as an anthelmintic drug against animal parasitic nematodes, their mechanism of action against the nematode. The major application of *Caenorhabditis elegans* as a test organism used in the field of toxicology is discussed with a focus on neurotoxicity, genotoxicity, and environmental toxicology associated with CuNPs.

2 Synthesis of nanoparticles

The most common ways to synthesize NPs include two approaches: the top-down approach that includes the physical method and the bottom-up approach comprises the chemical and biological methods (Bali et al., 2006) (Fig. 1).

2.1 Top-down (physical) approach

In this approach, techniques like cutting, grinding, and scratching are involved to convert bulk material into nanosize dimensions (nanoparticles) without atomic-level control (Rodgers, 2006).

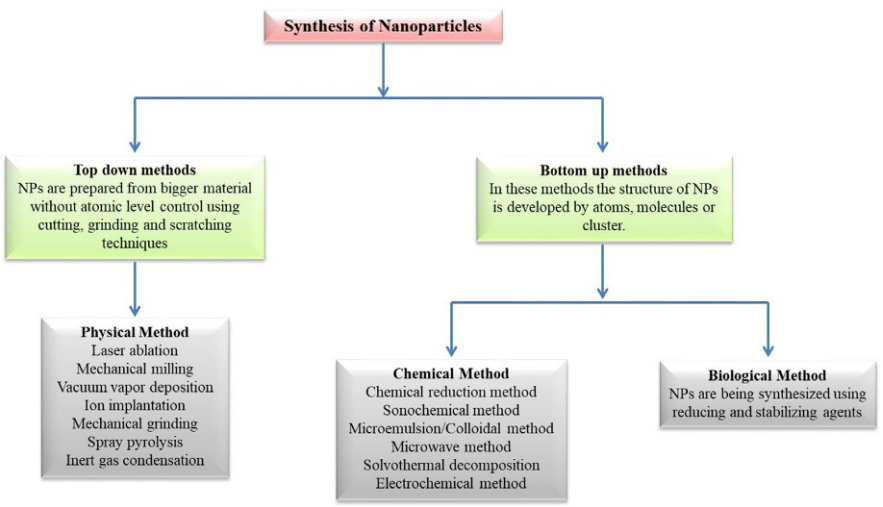

FIG. 1

Schematic representation of nanoparticle synthesis.

2.1.1 Physical method

Physical strategies for the synthesis of NPs are laser (pulse) ablation (Wu et al., 2004), vacuum vapor deposition (Lisiecki and Pileni, 1993), pulsed wire discharge (PWD) (Zhou et al., 2008), and mechanical milling (Tanori et al., 1997). These methods are economically very expensive as they require sophisticated equipment, require radiations for heating, and consume high power and expensive chemicals to synthesize nanoparticles (Khandel et al., 2018).

2.2 In the bottom-up approach

In the bottom-up approach, the structure of NPs is produced by atoms, molecules, or a cluster. Under this approach, NPs are formed by two methods: chemical and biological.

2.2.1 Chemical methods

In this method, metal ions are reduced by using chemicals in the solution. Depending on the reaction mixture condition, small clusters of metals ions are formed either by aggregation or nucleation. Hydrazine hydrogen and sodium borohydride are some of the reducing agents (Egorova and Revina, 2000) and cellulose, natural rubber, chitosan, and copolymer micelles are some of the stabilizing agents used in the reduction of metal ions. Organic solvents such as ethane, dimethyl, formaldehyde, toluene, and chloroform are also needed during this process due to the hydrophobic nature of chemicals. Chemical reduction (Song et al., 2004), microemulsion (colloidal) procedures (Kapoor and Mukherjee, 2003), nonchemical reduction (Huang, 1997), electrochemical (Mott et al., 2007), microwave-assisted (Panigrahi et al., 2006), and hydrothermal (Janafi et al., 2000) methods are the processes used for the synthesis of NPs that come under chemical methodology. During the formation of NPs, some toxic chemicals as by-products are also produced because of which NPs synthesized from these methods are not applicable for medical purposes. To reduce the toxicity risk associated with both the physical and chemical methods, biological methods of NP synthesis are applied in the research field (Patel et al., 2015).

2.2.2 Biological method

The biogenic synthesis of nanoparticles (NPs) involves two steps. Firstly, metal ions are reduced by bioreduction (Mukunthan and Balaji, 2012). In this process, metal ions reduction is aligned with enzyme oxidation to produce stable and inert metal NPs (Deplanche et al., 2010; Mukunthan and Balaji, 2012). The second step involves biosorption of metal ions by getting attached to the peptides of cell wall automatically without energy input and forms stable metal NPs (Yong et al., 2002). Biologically synthesized NPs have a well-defined shape and size as compared with the NPs obtained from physical and chemical methods (Azizi et al., 2013). NPs produced from microorganisms are nontoxic, eco-friendly, biocompatible, and scalable and have medicinal applications. But because of the high cost of maintaining high aseptic conditions during the synthesis of NPs, much emphasis is turned toward the use of plants for the production of NPs (Park et al., 2011; Dhuper et al., 2012; Sajadi et al., 2016).

Plant-based synthesis has an advantage over other forms of synthesis as it does not require toxic chemicals, high temperature or pressure, and is much cheaper as compared with other methods, and from this method one can produce NPs on a mass level (Shankar et al., 2004). Green synthesis of NPs has gained much attention as it has both antioxidant and reducing properties which help in the reduction of NPs (Abd El-Rahman and Mohammad, 2014).

Previously, many reports have been carried out to discover green methods for the production of metal NPs (Raveendran et al., 2003; Iravani and Zolfaghari, 2013; Mittal et al., 2013). More attention is shifted toward the production of copper (CuNPs) using plant extracts to obtain the advantages of this method. A detailed analysis of precursors, plants, and characterization techniques used in the synthesis of CuNPs is summarized in Table 1.

3 Metal nanoparticles for nematode management

There are various plant management strategies followed in our agriculture system to control pathogenic nematodes, such as biological, chemical, etc. Use of chemical nematicides are effective but causes environmental disturbances due to their biomagnification. A nanotechnology-based management system against phytonematodes provide drug carriers, drug targeting and releasing system that can enhance the standard of life and world's thrift (Safeena and Zakeel, 2020). Application of nanoparticles (NPs) as nematicides proved the most effective and progressive approach toward plant disease management. Direct application of NPs to soil or seed or foliage not only protects the plants from the attack of different pathogens, but also their applications significantly affect the symbionts, solubilizers, as well as NPs act as a carrier for concentrated intermediates of various pesticides and insecticides. Therefore, the role of NPs in the plant disease management system is divided into two. Firstly, they can be used directly against nematodes, and secondly they can be used in nematicide formulations (Thakur and Shirkot, 2017).

Metal-based nanomaterials such as silver, gold, copper, titanium, zinc and their oxides (Gogos et al., 2012; Kah and Hofmann, 2014; Mishra and Singh, 2015; Malerba and Cerana, 2016; Rafique et al., 2017; Sadeghi et al., 2017; Kim et al., 2018a), carbon NPs (Shojaei et al., 2019), and NPs used as nanocarriers, like silica (Barik et al., 2008; Mody et al., 2014), chitosan (Li et al., 2011; Kashyap et al., 2015; Malerba and Raffaella, 2018), solid lipid nanoparticles (SLN) (Ekambaram et al., 2012; Borel and Sabliov, 2014), and layered double hydroxide (LDH) (Xu et al., 2006; Bao et al., 2016; Mitter et al., 2017) NPs have been employed for controlling plant diseases. Some reports demonstrated the enhancement of plant resistance to pathogens by the application of various nanosized products such as silica (Suriyaprabha et al., 2014), nanosized glucans, and chitosan (Egusa et al., 2015; Anusuya and Sathiyabama, 2015). A similar mechanism of action was induced by selenium and chitosan-based NPs in tomato and pinewood against nematodes and other phytopathogens, respectively (Liang et al., 2018; Udalova et al., 2018).

Table 1 Summarizes different precursors, plants used in the synthesis of CuNPs along with characterization techniques.

S.No.	Precursor	Plants	Plant parts	Size of nanoparticles	Shape of nanoparticles	Characterization techniques	References
1	Copper sulfate ($CuSO_4$)	*Capparis zeylanica*	Leaves	50–100 nm	Cubical structure	UV-visible spectroscopy, FTIR, XRD, SEM, EDX, and TEM	Saranyaadevi et al. (2014)
2	Copper nitrate ($CuNO_3$)	*Hibiscus rosasinensis*	Leaves	–	–	UV-visible spectroscopy, FT-IR, and TEM	Subbaiya (2015)
3	Copper sulfate ($CuSO_4$)	*Syzygium aromaticum*	Flower	14–50 nm	Spherical and granular nature	UV-visible spectroscopy, XRD, TEM, and SEM	Subhankari and Nayak (2013a)
4	Copper (II) sulfate pentahydrate ($CuSO_4{\cdot}5H_2O$)	*Ocimum sanctum*	Leaves	77 nm	–	XRD and FTIR	Kulkarni and Kulkarni (2013)
5	Copper (II) sulfate pentahydrate ($CuSO_4{\cdot}5H_2O$)	*Datura meta* L.	Leaves	15–20 nm	Spherical	UV-visible spectroscopy, particle size analyzer (PSA), TEM, EDX, and FTIR	Parikh et al. (2014)
6	Copper sulfate ($CuSO_4$)	*Camellia sinensis*	Fruit	–	–	UV-visible spectroscopy	Kundu (2013)
7	Copper chloride ($CuCl_2$)	*Citrus limon*	Fruit	60–100 nm	Nearly spherical	UV-visible spectroscopy, FTIR, XRD, SEM, and TEM	Jayandran et al. (2015)
8	Copper chloride ($CuCl_2$)	Papaya	Leaves	20 nm	Nearly spherical and crystalline	UV-visible spectroscopy, Absorption spectrometer, XRD, FTIR, SEM, and TEM	Suresh et al. (2014)
9	Copper (II) sulfate pentahydrate ($CuSO_4{\cdot}5H_2O$)	*Citrus medica* Linn.	Fruit	20 nm	Crystalline	UV-visible spectroscopy, NPs tracking and analysis system (NTA), and XRD	Shende et al. (2015)
10	Copper sulfate ($CuSO_4$)	*Vitis vinifera*	Leaves	–	–	UV-visible spectroscopy and FTIR	Angrasan and Subbaiya (2014)
11	Copper sulfate ($CuSO_4$)	*Nerium oleander*	Leaves	–	–	UV-visible spectroscopy and FTIR	Gopinath et al. (2014)
12	Copper sulfate ($CuSO_4$)	*Euphorbia esula* L.	Leaves	20–110 nm	Spherical	UV-visible spectroscopy, XRD, FTIR, and TEM	Nasrollahzadeh et al. (2014)

Continued

Table 1 Summarizes different precursors, plants used in the synthesis of CuNPs along with characterization techniques—cont'd

S.No.	Precursor	Plants	Plant parts	Size of nanoparticles	Shape of nanoparticles	Characterization techniques	References
13	Cupric chloride dihydrate ($CuCl_2{\cdot}2H_2O$)	Pistachio	Leaves	9 nm	Crystallized nanowires with 10 nm diameter	XRD, FTIR, and SEM	Awwad and Albiss (2015)
14	Cupric chloride dehydrate ($CuCl_2{\cdot}2H_2O$)	*Malva sylvestris*	Leaves	14 nm	Spherical	XRD, FTIR, and SEM	Awwad et al. (2015)
15	Copper sulfate ($CuSO_4$)	*Albizia lebbeck*	Leaves	100 nm	Roughly spherical	UV-visible spectroscopy, SEM, TEM, EDS, and XRD	Jayakumarai et al. (2015)
16	Copper (II) sulfate pentahydrate ($CuSO_4{\cdot}5H_2O$)	*Artabotrys odoratissimus*	Leaves	135 nm	–	Particle size analysis (PSA)	Kathad and Gajera (2014)
17	Copper (II) sulfate pentahydrate ($CuSO_4{\cdot}5H_2O$)	*Magnolia kobus* L.	Leaves	37–110 nm	Spherical	UV-visible spectroscopy, inductively coupled plasma spectrometry (ICP), EDS, XPS, and HRTEM	Lee et al. (2013)
18	Cupric chloride dihydrate ($CuCl_2{\cdot}2H_2O$)	*Ginkgo biloba* Linn.	Leaves	15–20 nm	Spherical	UV-visible spectroscopy, TEM, EDS, and FTIR	Nasrollahzadeh and Sajadi (2015)
19	Copper acetate Cu $(CH_3COO)_2$	*Calotropis procera* L.	Latex	15 ± 1.7 nm	Polydispers spherical	XRD, FTIR, TEM, and EDAX	Harne et al. (2012)
20	Cupric chloride dihydrate ($CuCl_2{\cdot}2H_2O$)	*Psidium guajava* L.	Leaves	13.13 ± 0.19 nm	–	UV-visible spectroscopy	Kote et al. (2014)
21	Copper (II) acetate ($Cu(CH_3COO)_2H_2O$)	*Aloe vera* F.	Flower	40 nm	Spherical	UV-visible spectroscopy, field emission scanning electron microscopy (FESEM), and FTIR	Karimi and Mohsenzadeh (2015)
22	Copper sulfate ($CuSO_4$)	*Cinnamum*, *Inula*, *Chamomilla*, *Urtica*, *Glycyrrhiza*, *Schizandra*	Leaves, flower, and roots	18.17–91.28 nm	–	UV-visible spectroscopy and DLS	Mussabayeva et al. (2014)

23	Copper sulfate ($CuSO_4$)	*Eucalyptus* sp. L.	Leaves	38.62 nm	–	UV-visible spectroscopy, FTIR, XRD, and SEM	Kolekar et al. (2015)
24	Copper sulfate ($CuSO_4$)	*Zingiber officinale*	Rhizome	40 and 25 nm	–	UV-visible spectroscopy and XRD	Subhankari and Nayak (2013b)
25	Copper sulfate ($CuSO_4$)	Soy beans	Seeds	20 nm	Spherical	UV-visible spectroscopy, TEM, and DLS	Guajardo-Pacheco et al. (2010)
26	Copper (II) sulfate pentahydrate ($CuSO_4{\cdot}5H_2O$)	*Bacopa monnieri*	Leaves	20–50 nm	Spherical	UV-visible spectroscopy, FTIR, and HRTEM	Thakur et al. (2014)
27	Copper (II) sulfate pentahydrate ($CuSO_4{\cdot}5H_2O$)	*Ocimum bacilicum*	Leaves	40–60 nm	Spherical	UV-visible spectroscopy, FTIR, and HRTEM	Thakur et al. (2014)
28	Copper (II) sulfate pentahydrate ($CuSO_4{\cdot}5H_2O$)	*Asparagus adscendens*	Leaves	10–15 nm	Spherical	UV-visible spectroscopy, FTIR and HRTEM	Thakur et al. (2014)
29	Copper (II) sulfate pentahydrate ($CuSO_4{\cdot}5H_2O$)	*Withania somnifera*	Leaves	50–60 nm	Spherical and ring pattern	UV-visible spectroscopy, FTIR, and HRTEM	Thakur et al. (2014)
30	Copper sulfate ($CuSO_4$)	*Phyllanthus emblica* (gooseberry)	Fruit	15–30 nm	FCC structure	UV-visible spectroscopy, FTIR, XRD, SEM, and EDAX	Caroling et al. (2015a)
31	Cupric chloride dihydrate ($CuCl_2{\cdot}2H_2O$)	*Gum karaya*	Gum	4.8 ± 1.6 nm	Spherical	XRD, FTIR, TEM, SEM, and XPS	Padil and Černík (2013)
32	Copper sulfate ($CuSO_4$)	*Gymnema sylvestre*	Leaves	65–302 nm	Spherical	UV-visible spectroscopy, FTIR, and SEM	Heera et al. (2015)
33	Copper sulfate ($CuSO_4$)	Guava	Fruit	15–30 nm	Spherical	UV-visible spectroscopy; FTIR, XRD, SEM, TEM, and EDAX	Caroling et al. (2015b)
34	Copper sulfate ($CuSO_4$)	*Cassia fistula* F.	Flower	20,000 nm	Amorphous	UV-visible spectroscopy, FTIR, XRD, and SEM	Valli and Suganya (2015)

Continued

Table 1 Summarizes different precursors, plants used in the synthesis of CuNPs along with characterization techniques—cont'd

S.No.	Precursor	Plants	Plant parts	Size of nanoparticles	Shape of nanoparticles	Characterization techniques	References
35	Copper (II) sulfate pentahydrate ($CuSO_4 \cdot 5H_2O$)	*Ocimum tenuiflorum* L.	Leaves	72 nm	Hexagonal wurtzite crystal structure	UV-visible spectroscopy, XRD, FTIR, SEM, and EDAX	Vennila and Nithya (2015)
36	Cupric chloride dihydrate ($CuCl_2 \cdot 2H_2O$)	*Otostegia persica*	Leaves	40 nm	Spherical	UV-visible spectroscopy, XRD, FTIR, and TEM	Nasrollahzadeh et al. (2016a)
37	Cupric chloride dihydrate ($CuCl_2 \cdot 2H_2O$)	*Thymus vulgaris* L.	Leaves	30 nm	FCC structure	UV-visible spectroscopy, XRD, FTIR, TEM, EDS, TGA, and DTA	Nasrollahzadeh et al. (2016b)
38	Copper chloride ($CuCl_2$)	*Anthemis nobilis*	Flower	18 nm	Rectangular structures	UV-visible spectroscopy, XRD, FTIR, SEM, and EDS	Nasrollahzadeh et al. (2015a)
39	Copper chloride ($CuCl_2$)	*Anthemis xylopoda*	Flower	40 nm		UV-visible spectroscopy, TEM, FESEM, and EDS	Nasrollahzadeh et al. (2015b)
40	Copper sulfate ($CuSO_4$)	*Orobanche aegyptiaca*	Stem	50 nm	Spherical structure	UV-visible spectroscopy, XRD, FTIR, SEM, EDX, TEM	Akhter et al. (2020)

Recently, researches were carried out on the biological synthesis of metal-based NPs using plant extracts to obtain less toxic and eco-friendly NPs. Earlier, it was reported in various researches that plant extracts have nematicidal and nematostatic properties (Nour El-Deen and Darwish, 2011; Cromwell et al., 2014; Nour El-Deen et al., 2014; Khan et al., 2017; Singh et al., 2017). Ardakani (2013), Kim et al. (2010), and Nazir et al. (2019) performed researches that revealed the toxicity of silver, silicon oxide, Platinum and titanium oxide against the root-knot nematode *Meloidogyne incognita* under greenhouse conditions. Silver nanoparticles (AgNPs) have proved to be one of the most effective nanomaterials against phytonematodes. Lim et al. (2012) have reported an increase in oxidative stress in the nematode cells when exposed to AgNPs. Nassar (2016) has analyzed the nematicidal effect of AgNPs associated with rugby (AgNPs-rugby) synthesized from the *Urtica urens* extract against eggs and second-stage larvae of *M. incognita*. The AgNP-rugby showed 11-fold more nematicidal activity as compared with the plant extract in ethyl acetate (least toxic) and in petroleum ether (highly toxic). In another research, a comparative study was conducted between AgNPs synthesized from an aqueous solution of ginger extract (*Zingiber officinale*) and sodium borohydride to analyze their nematicidal effect separately. AgNPs synthesized from ginger extract showed a significant nematicidal effect against *M. incognita* by reducing the number of galls and egg mass which resulted in the improved growth of tomato (El-Deen and El-Deeb, 2018). Nematicidal activity of AgNPs synthesized from the aqueous extract of the cyanobacterium, Nostoc sp. PCC7524 was assessed against *M. javanica* and their influence on faba bean growth was also measured. The cyanobacterium-based Ag-NPs showed a biostimulant effect on faba bean growth and makes them expedient to control *M. javanica* (Hamed et al., 2019). AgNPs synthesized from *Senna siamea* were used against *M. incognita* infesting *Trachyspermum ammi*. A significant increase in plant growth, biochemical characteristics, and a rise in antioxidant enzymes was observed in *T. ammi* when it was treated with 50 ppm AgNPs 1 week before the inoculation of *M. incognita*. However, plants treated with 100 ppm AgNPs showed a reduction in the number of galls, egg masses, and root-knot indices. The outcome of this work suggested that AgNPs synthesized from *S. siamea* can be used as a nematicide to overcome nematode manifestations (Danish et al., 2021). The research was conducted by Abbassy et al. (2017) to evaluate the nematicidal activities of crude leaf extracts of *Conyza dioscoridis*, *Melia azedarach*, and *Moringa oleifera* plant in different solvents and the AgNPs synthesized from these plant leaf extracts in different solvents against eggs and second-stage juveniles (J2s) of *M. incognita*. The AgNPs showed potential nematicidal activity toward eggs and second-stage juveniles (J2s) which was five times as high as compared with the nematicidal activity of crude plant extracts alone. The study also revealed that the toxicity of all the plant extracts is dependent on their concentrations. Both forms of the extract of *C. dioscoridis* (crude and AgNPs) showed the highest nematicidal activity with a low LC50 value. Similarly, AgNPs synthesized from *Ulva lactuca* and *Turbinaria turbinata* have been applied separately to *Solanum melongena* to control the effect of root-knot nematode *M. javanica*. Both the synthesized AgNPs proved effective at 12.75 mg/100 mL

against the nematode activity in eggplant. Also, to study their phytotoxicity, experiments were conducted on eggplant DNA using random amplified polymorphic DNA (RAPD) and expressed sequence tag (EST) markers which showed a modified DNA of eggplant depending on their concentrations, whereas the overall growth rate of the eggplants was remarkably improved without causing any phytotoxicity to the plants (Abdellatif et al., 2016). Kalaiselvi et al. (2019) investigated the nematicidal effect of AgNPs synthesized from the latex extract of *Euphorbia tirucalli* against the eggs and second-stage juveniles (J2) of root-knot nematode *M. incognita* and the in-planta trials of Et-AgNPs at different concentrations to study their action in protecting the tomato plant. The observations showed that Et-AgNPs were highly toxic at all concentrations to J2 and suppressed the population of nematodes by inhibiting egg hatching. However, the results of in-planta trials indicated a significant decrease in the nematode infestation on tomato roots after their treatment with Et-AgNPs and it also provided a positive impact on plant growth.

The effect of AgNPs as a nematicide was investigated against the rice root-knot nematode, *M. graminicola*, on *Oryza sativa* through various experimental conditions like water and sand screening in lab and glasshouse experiments using a soilless system, autoclaved soil, and naturally infested soil. The results revealed 100% mortality of the nematode at 0.1 μg/mL and 2 μg/mL of AgNPs after 12 and 24 h of incubation during water and sand screening tests, respectively. In the soilless system of glasshouse experiments, 1 μg/mL concentration of AgNPs significantly suppressed the root gall formation in rice crop, whereas in the field soil assay the effective concentration of AgNPs was 3 μg/mL, which was much lower than the value of 150 μg/mL as reported earlier in the literature. No adverse effect was observed on plant growth (Baronia et al., 2020). Ghareeb et al. (2020) investigated the nematicidal effect of the freshwater green macroalga *Cladophora glomerata* aqueous extract and AgNPs biosynthesized from it against *M. javanica* on tomato plants. Expression profiling of poly phenol oxidase (PPO), peroxidase (POX), and phenylalanine ammonia-lyase (PAL) was carried out to determine the plant response toward biosynthesized AgNPs using Quantitative Real-Time PCR (Q-PCR). Biosynthesized AgNPs exhibited a high mortality of juveniles (J2) and inhibited egg hatching of *M. javanica*, and a significant reduction was observed in egg masses, gall numbers, females per root system. The expressions of the three enzymes were increased after 14 days of nematode inoculation which later improved after the treatment of the plant with biosynthesized AgNPs. Therefore, it was concluded that *C. glomerata* synthesized AgNPs can be used as a potential nematicide against plant-parasitic nematodes.

Another report was conducted to study the eco-nematicidal effect of microcrystalline cellulose (MCC) embedded Ag-NPs against *M. incognita*. The highest mortality (M%) (40.36 ± 1.15%) was detected at 20 ppm of AgNPs after 24 h incubation. The investigation concluded that AgNPs can be used as an eco-nematicide for nematodes with the approved dose of 20–40 ppm (Fouda et al., 2020). Recently, the combined effect of β-aminobutyric acid (BABA) and AgNPs synthesized from the aqueous leaf extract of *Malva sylvestris* was tested on *Solanum melongena* infected with *M. javanica* in vitro. The results obtained showed a 51.6% and 55.9% decrease

in reproduction factor with 4 and 8 eggs (cm^3 soil)$^{-1}$ in infected plants treated with BABA (1 mM) and AgNPs, respectively. Hence, the outcomes of the research revealed that the combination of BABA and AgNPs reduced the damage of *S. melongena* caused by *M. javanica* (Shekoohi et al., 2021).

Thakur and Shirkot (2017) and Thakur et al. (2018) demonstrated the nematicidal effect of gold nanoparticles (GNPs) against *M. incognita* infested tomato plants, which showed no toxic effect on growth and development of tomato plants. Gold and Silver NPs possess excellent nematicidal activity which provided an alternative to be used over high-risk synthetic nematicides or inconsistent biological control agents. Biweekly application of doses ($ 90.4 mg/m^2) of gold and silver NPs was required to achieve effective field efficacy for the root-knot nematode (Kalimuthu et al., 2008; Kalishwaralal et al., 2008; Zhang et al., 2005; Saifuddin et al., 2009; Law et al., 2008; Parikh et al., 2008). A study was conducted to scrutinize the effect of ionic strength on the ecotoxicity of AgNPs to *C. elegans*, transferred by AgNP-treated *Escherichia coli*. The results showed enhanced reproductive toxicity, neurotoxicity and it also increased the oxidative stress in *C. elegans*, which proved the toxic effect of ionic strength (Yang et al., 2018).

Ma et al. (2018) selected *C. elegans* as a test organism to study the comparative toxicity of food additives, bulk TiO_2, and nanosized P25. The results revealed the high toxicity rate in the body of the nematode due to the accumulation of the three products. Khan et al. (2021) assessed the nematicidal potential of chitosan in combination with chopped leaves of *Argemone mexicana* L., *Achyranthes aspera* L., and *Ricinus communis* L. against infestation caused by *M. incognita* on carrot under both in vitro and in vivo conditions. Maximum mortality of Infectious stage (J2s) of *M. incognita* and highest inhibition in egg hatching were detected at 2500 ppm of chitosan after 36 h incubation. However, pots treated with 1 g chitosan and 30 g of chopped leaves of all the three tested botanicals showed a significant reduction in pathological parameters and enhanced plant growth and photosynthetic characteristics of carrot. This study suggested the synergistic effect of all the three botanicals in enhancing the nematicidal effect of chitosan against *M. incognita* on carrot as compared to chitosan alone.

Kucharska et al. (2011) investigated the pathogenic effect of gold nanoparticles (GNPs) on entomopathogenic nematodes (*Steinernema feltiae*). The rate of larval mortality along with the time duration at different concentrations of GNPs determined the effectiveness of GNPs against the larvae of the nematode. Toxicity analysis was performed on *C. elegans* using GNPs. Analysis revealed that the 11-nm GNPs showed higher toxicity in *C. elegans* as compared with 150 nm (Gonzalez-Moragas et al., 2017). Hu et al. (2018) investigated the effect of size-tunable GNPs with or without the 11-mercaptoundecanoic acid (MUA) coating using *C. elegans* as a test organism. Both the nanoparticles were found to be absorbed inside the whole organism. Besides, they affected the growth of axons, the body size, mobility, and brood size of the nematode. Bosch et al. (2018) measured the toxicity related to the engineered nanogold (nAu) particles on *C. elegans* and found that at high concentration, nAu causes gonadal damage, whereas no effect was observed on

the growth of the organism. Kim et al. (2010) assessed the antioxidant property of platinum nanoparticles in *C. elegans*. As a result, platinum nanoparticles showed protection against oxidative stress and helped in extending the life span of the nematode.

Toxicity analysis was also performed on ZnO NPs (PinnacleAF ZnO NP suspension) over an aqueous solution of zinc chloride ($ZnCl_2$) against *C. elegans* (Ma et al., 2009). The comparative effect of toxicity of ZnO NPs and $ZnCl_2$ was measured based on experimental parameters like lethality, behavior, reproduction, and transgene expression of the transgenic strain of *C. elegans*. The results revealed no significant difference in the toxicity caused by ZnO NPs and $ZnCl_2$ against the free-living nematode *C. elegans*. The toxicity of zinc oxide nanoparticles (ZnO NPs) and the bulk counterpart was analyzed in two free-living nematode species belonging to different life strategies: *Xiphinema vuittenezi*, a K-strategist plant-feeder nematode and *Panagrellus redivivus*, an r-strategist bacterivor nematode. Both ZnO NPs and the bulk exhibited a dose-response effect on the mortality of *P. redivivus*. However, ZnO NPs showed higher toxicity on the mortality of *X. vuittenezi* (Hrács et al., 2018). Dong et al. (2018) worked to investigate the combined effect of nanopolystyrene particles and titanium dioxide nanoparticles (TiO_2-NPs) at environmentally suitable concentrations on *C. elegans*. The toxicity of TiO_2-NPs (1 μg/L) increased in wild-type nematodes in the form of decreased locomotion and enhancement in intestinal oxidative stress when exposed to nanopolystyrene particles (1 μg/L).

The toxicity of Fe_3O_4, ZnO, and TiO_2 NPs was evaluated by measuring their effect on the survival of entomopathogenic nematodes and their growth inhibition effect on the nematode symbiotic bacteria. No significant toxicity was observed; all the metal oxides had less influence on the survival of entomopathogenic nematodes and growth of nematode symbiotic bacteria. Therefore, the study notified the tolerance of entomopathogenic nematodes and their bacterial partner toward the toxic effect of all the metal oxide NPs (Makirita et al., 2020).

Toxicity analysis using *C. elegans* as test organisms was conducted to determine the aquatic toxicity of Magnetic nanoparticles (MNPs). *C. elegans* was chronically exposed to concentrations that are suitable to the environment. The effect was measured based on mobility, mortality, growth, fertility, and gene expression at different concentrations (10–200 mg/L) of MNPs. The results indicated no significant effect of MNPs on the mortality, growth, and gene expression of *C. elegans*, whereas correlation was observed between the concentration of MNPs and fertility in *C. elegans* (Marimon-Bolívar et al., 2019).

C. elegans was used as a model organism to clarify the in vivo oral toxicity of silica nanoparticles (SiO_2 NPs) and also to assess their effect on the reproductive system. The results obtained showed that it has no significant effect on the nematode survival but affects the movement, development, and reproduction of nematodes. Mostly, SiO_2 NPs affect the nematode fecundity rate (Zhang et al., 2020). Li et al. (2020) conducted toxicity analysis between nanopolystyrene and three metal oxide nanoparticles (NPs) (Al_2O_3-NPs, TiO_2-NPs, and SiO_2-NPs) using *C. elegans* as a test organism. After exposure from L1 to adult, nanopolystyrene (10–100 μg/L)

reduced brood size and induced germline apoptosis; it also decreased the locomotory behavior of the nematode, enhanced oxidative stress, and activated the mitochondrial unfolded protein response (mt UPR). From the results, it was concluded that while nanopolystyrene can induce higher toxicity than SiO_2-NPs, it was less toxic as compared with Al_2O_3-NPs or TiO_2-NPs. Recently, Zhang et al. (2021) evaluated the toxicity and possible mechanism of pristine Al_2O_3 NPs (p-Al_2O_3), lipophilic (o-Al_2O_3) and hydrophilic (w-Al_2O_3) modifications of Al_2O_3 NPs, both in vitro and in vivo, on *C. elegans* at different concentrations. In o-Al_2O_3 NPs, exposed *C. elegans* damaged of intestinal membrane was observed with the increased intestinal permeability. Cytotoxicity analysis measured high levels of ROS in o-Al_2O_3 NPs (100 μg/mL) as compared with p-Al_2O_3 and w-Al_2O_3 due to which the cell undergo apoptosis. Transcriptome sequencing and RT-qPCR data proved that the toxicity of o-Al_2O_3 NPs was highly related to cell membrane damage and intracellular redox imbalance.

4 Copper-based nanomaterials as nematicides and antiparasitic drugs and their characterization

Nematodes are the most abundant metazoans on this planet that have been reported from all terrains of all the continents. They are free living as well as parasitic, living in both plants and animals. Parasitic nematodes are most important because they severely affect their host, thereby causing significant economic loss. The animal parasitic nematodes cause several debilitating diseases in humans, livestock, and other domestic animals (Shakya and Yadav, 2020). The treatment and control of animal parasitic nematode infection is primarily dependent on anthelmintic drugs. But due to continuous treatment with the drugs against the parasitic nematodes, they become resistant. Therefore, to overcome drug resistance, we need to develop new drug formulations to improve the effectiveness of anthelmintics. Recently, nanoparticles have been used as drug adjuvants to increase their effectiveness which helps to overcome drug resistance. Zafar et al. (2016) used CuO nanoparticles as an adjuvant to improve the effectiveness of albendazole against the filarial worm.

Plant-parasitic nematodes are usually managed by spraying chemical nematicides, employing primitive methods, and by cultivating phytonematode-resistant crops. Recently, nanotechnology has been employed in agriculture management to control phytonematodes and other microorganisms. Nanotechnology-based agricultural management systems to control phytonematodes include drug carriers and a controllable drug targeting and releasing system (Khot et al., 2012; Mattos et al., 2017; Iavicoli et al., 2016; De Oliveira et al., 2016; Liu et al., 2016; Yamamoto and Kuroda, 2016; Wang et al., 2017; Shen et al., 2017; Nakamura et al., 2017). Generally, root-knot nematode *Meloidogyne* and cyst nematodes (*Heterodera* and *Globodera*) are the most harmful sedentary endoparasites that cause maximum damage to agricultural crop yields (Oka et al., 2000). The effect of CuNPs on the mortality of "entomopathogenic nematodes (EPNs)" *Steinernema feltiae* was investigated by

Kucharska et al. (2014). The results confirmed that the mortality of nematodes was correlated with the increasing concentrations of CuNPs and the length of exposure of *Steinernema larvae* to CuNPs. Mohamed et al. (2019) performed a similar in vitro experiment to study the effect of CuNPs against *M. incognita.* A 100% mortality of nematodes was observed at 0.2 g/L of CuNP concentration. Additionally, some researches were carried out which showed that Cu NPs have the most potent nematicidal activity as compared with silicon carbide NPs (Al Banna et al., 2018) and AgNPs (Taha Entsar, 2016).

Anderson et al. (2018) focused their research to study the mechanism through which plants modify themselves by increasing their resistance to plant pathogens during the implementation of nanoparticles. They discovered that nanoparticles (CuO and ZnO) alter the interkingdom cell signaling processes which are important for the production of a crop. Gkanatsiou et al. (2019) evaluated the role of copper/iron-based nanoparticles ($CuFeO_2$ NPs, CuFe NPs) as bioactive agents against the root-knot nematode *Meloidogyne* spp., along with the plant enhancement properties on the nematode infested host plant. CuFe NPs was found to be the most effective revealing/exhibiting the lowest EC_{50} value at 0.03 μg ai g/soil. A positive effect of CuFe NPs was recorded toward tomato plants with an increase in root weight and rise in shoot length. Nematicidal and ovicidal properties of CuNPs biosynthesized from the extract of the holoparasitic plant *Orobanche aegyptiaca* were reported against *M. incognita* in vitro (Akhter et al., 2020). Recently, Tauseef et al. (2021) investigated the nematicidal effect of copper oxide nanoparticles (CuO NPs) against the second-stage juveniles (J2S) of the root-knot nematode *M. incognita* under in vitro and in-planta conditions. Scanning electron micrograph analysis was performed on CuO NPs-treated J2S which revealed a crinkled and distorted cuticle. During in-planta trials, the effect of CuONPs was measured based on the morphology, yield, and biochemical characteristics of infected *Vigna unguiculata* L. *Gomti* (cowpea). Plants sprayed with 100 ppm of CuO NPs showed a healthy growth with a reduction in nematode parameters in comparison with the infected plant.

5 Toxicity analysis of copper-based nanomaterials using nematodes as test organism

There are some nematodes, namely *Caenorhabditis elegans*, entomopathogenic nematodes, etc., which are used as test organisms to study the nanosafety and toxicity effect of nanoparticles on other nontargeted organisms in the surroundings of the treatment area (Meyer et al., 2010; Kim et al., 2012, 2018b; Taha and Abo-Shady, 2016; Ma et al., 2018; Wu et al., 2019). Mostly, *C. elegans* is used as a test organism due to its shorter life cycle, a high degree of similarity to higher organisms, and low cost of maintenance. This organism is used in mechanistic and high-throughput screening approaches, due to its ability to self-fertilize and generate a large number of offspring along with the complex tissue system, which is ideal to carry out nanotoxicological multiple endpoint experiments (Kumar and Suchiang, 2020).

Studies related to the reporter gene such as green fluorescence protein (GFP) and microRNAs in *C. elegans* have provided the discovery of different biomarkers to carry out toxicological research (Kumar and Suchiang, 2020). Gao et al. (2008) investigated the bioaccumulation and toxicological effect of engineered copper nanoparticles (ECuNPs) on *C. elegans*. By using radiation microbeam synchrotron X-ray fluorescence (m-SRXRF) they identified the nanoparticle distribution inside the body of nematode. The mapping result revealed the degree of toxicity that occurred against *C. elegans*.

Mashock et al. (2016) quantified the inhibitory effects of both copper oxide nanoparticles (CuONPs) and copper sulfate on the three wild strains of *C. elegans* along with the Bristol N2 laboratory strain at various toxicological endpoints (including nematode reproduction, feeding behavior, and average body length) to elucidate their biological effects. All the strains showed greater sensitivity to CuONPs than to copper sulfate, as observed by the reduction of average body length, feeding behavior, and reproduction rate. About 10% of the nematode population showed neurotoxicity (degeneration of dopaminergic neurons) after exposure to CuONPs. It was also predicted that the development of tolerance toward the CuONPs in nematodes indicates mutations in both the divalent-metal transporters, smf-1 and smf-2, which determined the involvement of both the transporters in the copper-induced neurodegeneration process. Therefore, the results highlighted that the toxicity of CuONPs toward the nematodes through their specific effect on the average body length and feeding behavior of nematode and copper ion-specific effect was detected through neurodegeneration. Jones et al. (2019) used *C. elegans* as a test organism to demonstrate simultaneous ptychography and XFM on whole intact animal specimens with areas approaching 0.1 mm, imaged as the largest single area in a continuous scan to date. A study was performed on *C. elegans* to discover the lasting effects of cubic Cu_2O nanoparticles by keeping a check on the defecation rate and difference in the size of nematode. A decrease in the defecation rate and size was observed in the nematode exposed to cubic Cu_2O nanoparticles exposed nematode; hence, this study highlighted the toxic effect of metal oxides on the environment (Zizzo, 2020).

The in vivo transgenerational toxicity was detected in parental CuO NPs exposed to the nematode *C. elegans*, which is caused by epigenetic regulation due to the exposure of parental CuO NPs (Wei et al., 2020). You et al. (2020) used near-infrared (NIR) light to dual-promote the CuAAC reaction of a biocompatible heterogeneous copper nanocatalyst through photodynamic and photothermal effects in *C. elegans* to determine the antitumor efficacy.

6 Mechanism of action of copper-based nanomaterials against nematodes

Through some studies, it was found that copper nanomaterials enter through the cell membrane and into the cell and cause oxidative stress due to the generation of reactive oxygen species (ROS) that leads to DNA damage, apoptosis, cytotoxicity, and unregulated cell signaling (Sarfraz et al., 2020).

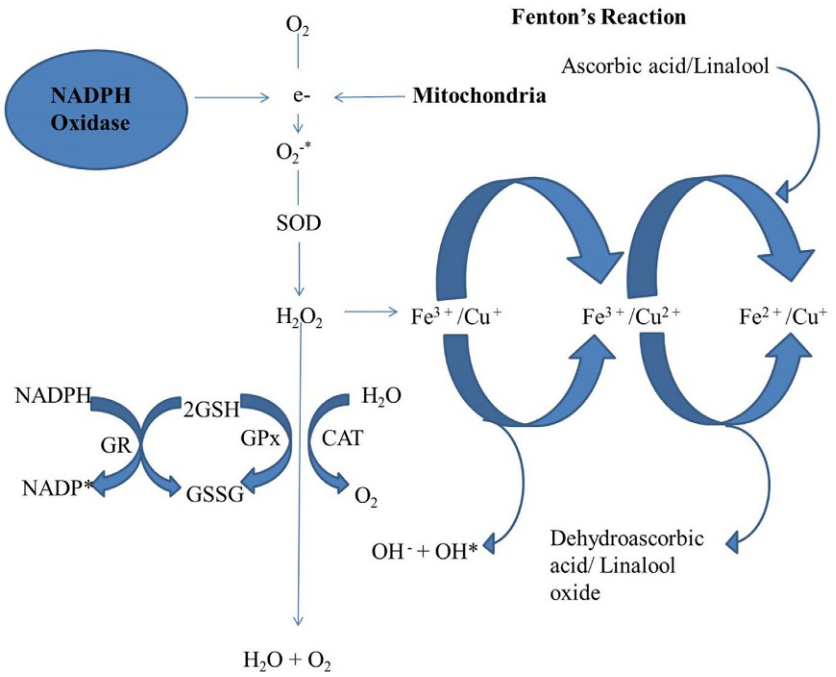

FIG. 2

Mechanism of ROS generation: Schematic diagram showing the formation of superoxide free radical (O_2-*) by NADPH oxidase and mitochondria. This O_2-* converted to hydrogen peroxide (H_2O_2) by antioxidant enzyme superoxide dismutase (SOD). The H_2O_2 is converted to water (H_2O) and oxygen (O_2) by other antioxidant enzymes such as catalase (CAT), glutathione reductase (GR), glutathione peroxidase (GPx). The released H_2O_2 reacts with the transition metal ion, which gives rise to hydroxyl free radical (OH*) and the oxidized metal ion in the Fenton reaction. The product of Fenton reaction is very toxic to biological molecules, hence generating ROS.

ROS is produced by all the cells to maintain their intracellular activity (Aust et al., 1993; Mignolet-Spruyt et al., 2016). ROS results from the high production of free radicals of oxygen. There are various neutralizing enzymes called antioxidants such as SOD, catalase, GPx, GSH (Baek and An, 2011) that help in converting these free radicals into water and oxygen (Fig. 2). But due to exposure to nanomaterials, the rate of oxidative stress increases, which results in an imbalance between ROS generation and its neutralization by antioxidant enzymes (Thannickal and Fanburg, 2000). This high oxidative stress in the cell leads to harmful effects on biomolecules like proteins, nucleic acids, and lipids (Ray et al., 2012). ROS generates signaling molecules which lead to apoptosis, and ultimately the cell dies (Guzik and Harrison, 2006; Bedard and Krause, 2007; Storz, 2011; Coso et al., 2012).

Copper nanomaterials act as a catalyst and enhance ROS formation through Fenton reactions or the Haber-Weiss reaction, which produces a hydroxyl radical

(Aust et al., 1993; Thannickal and Fanburg, 2000; Halliwell and Gutteridge, 2015; Mignolet-Spruyt et al., 2016). Copper nanoparticles (CuNPs) interact with the cell membrane and are transported into the cell by endocytosis. CuNPs start intracellular ROS generation by the catalysis of free radical reaction in mitochondria. The mitochondrial membrane is depolarized and the NADPH enzyme is activated due to interference in the electron transport chain caused by CuNPs (Xia et al., 2006). Copper nanomaterials block the electron transport chain and increase oxygen-free radicals, leading to oxidative stress in the cell (Nel et al., 2006). Moreover, in the ROS-dependent mechanism, immune cells are also activated by nanoparticle exposure via NADPH oxidase (NOX) activation (Risom et al., 2005). Free radicals produced by nanoparticles reduced the glutathione (GSH) into glutathione disulfide, leading to oxidative stress in cells (Rahman, 2007; Fenoglio et al., 2008). The cells antioxidant defense system activates when exposed to a low level of CuNPs, and thereby controls the oxidative stress in the cell. In contrast, the antioxidant system is overwhelmed by exposure to a high level of CuNPs, which leads to inflammation and cytotoxicity. Oxidative stress leads to apoptosis, DNA damage, cytotoxicity, and unregulated cell signaling (Nel et al., 2006; Xia et al., 2008; Zhu et al., 2013). Hydroxyl free radical generated by nanoparticles combined with DNA and yield 8-hydroxyl-2-deoxyguanosine (8-OHdG), which has been widely used as a biomarker to measure oxidative stress caused by DNA damage (Valavanidis et al., 2009). Antifilarial activity of CuO nanoparticles combined with albendazole was studied by Zafar et al. (2016). CuO nanoparticles showed a synergistic apoptotic effect with albendazole against the nematode parasite *Setaria cervi* by ROS generation which causes oxidative stress and ultimately lead to the death of the parasite. Fig. 3 represents the mechanism through which Copper nanoparticles enter the host cell (nematode) and causes its death.

7 Conclusion

In the field of agriculture, management nanotechnology plays a significant role in reducing the damage caused by phytonematodes. The use of copper nanoparticles in agriculture to control soil and plant nematodes reduces the use of chemicals and helps in reducing the bioaccumulation of harmful residues of pesticides. Further steps should be taken to incorporate nanotechnology into phytopathology at the field level in natural conditions so that our agriculture provides us fruitful production and helps in strengthening the world's health and wealth. In the field of drug discovery, copper nanoparticles have also proved very effective against parasitic nematodes. Copper nanoparticles are used as adjuvants to various anthelmintic drugs to increase their efficacy, reduce the drug resistance rate by providing more than one drug target site, and also reduce the drug inhibitory concentration which minimizes the side effects of anthelmintic drugs. Further studies have to be conducted to design nano-drug formulations using copper nanoparticles to fight against parasitic nematode infection along with their mode of action.

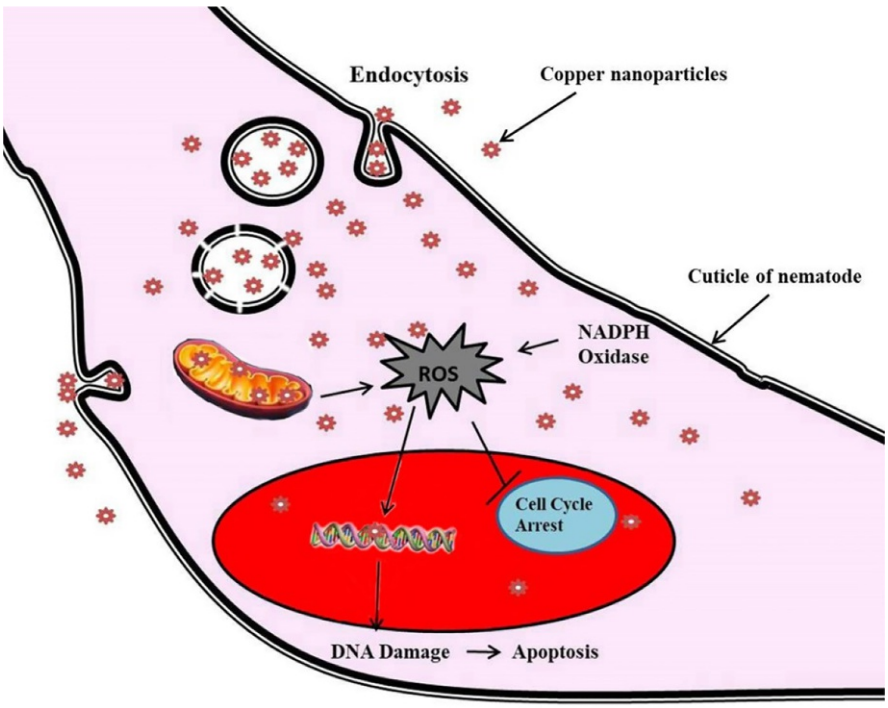

FIG. 3

Diagrammatic representation of the mechanism of action of copper nanoparticles. Copper nanoparticles enter the nematode through endocytosis and produce ROS which arrests the cell cycle arrest and causes DNA damage; ultimately, the nematode dies due to apoptosis.

References

Abbassy, M.A., Abdel-Rasoul, M.A., Nassar, A.M., Soliman, B.S., 2017. Nematicidal activity of silver nanoparticles of botanical products against root-knot nematode, *Meloidogyne incognita*. Arch. Phytopathol. Plant Protect. 50 (17–18), 909–926.

Abd El-Rahman, A.F., Mohammad, T.G.M., 2014. Green synthesis of silver nanoparticle using *Eucalyptus globulus* leaf extract and its antibacterial activity. J. Appl. Sci. Res. 9 (10), 6437–6440.

Abdellatif, K.F., Abdelfattah, R.H., Mostafa El-Ansary, M.S., 2016. Green nanoparticles engineering on root-knot nematode infecting eggplants and their effect on plant DNA modification. Iran. J. Biotechnol. 14 (4), 250–259. https://doi.org/10.15171/ijb.1309.

Akhter, G., Khan, A., Ali, S.G., Khan, T.A., Siddiqi, K.S., Khan, H.M., 2020. Antibacterial and nematicidal properties of biosynthesized Cu nanoparticles using extract of holoparasitic plant. SN Appl. Sci. 2, 1268.

Al Banna, L., Salem, N., Ghrair, A., Habash, S., 2018. Impact of silicon carbide nanoparticles on hatching and survival of soil nematodes *Caenorhabditis elegans* and *Meloidogyne incognita*. Appl. Ecol. Environ. Res. 16 (3), 2651–2662.

Anderson, A.J., Joan, E.M., Astrid, R.J., David, W.B., 2018. CuO and ZnO nanoparticles modify interkingdom cell signaling processes relevant to crop production. J. Agric. Food Chem. 66, 6513–6524.

Angrasan, J., Subbaiya, R., 2014. Biosynthesis of copper nanoparticles by *Vitis vinifera* leaf aqueous extract and its antibacterial activity. Int. J. Curr. Microbiol. App. Sci. 3 (9), 768–774.

Anusuya, S., Sathiyabama, M., 2015. Protection of turmeric plants from rhizome rot disease under field conditions by β-D-glucan nanoparticle. Int. J. Biol. Macromol. 77, 9–14.

Ardakani, A.S., 2013. Toxicity of silver, titanium and silicon nanoparticles on the root-knot nematode, *Meloidogyne incognita*, and growth parameters of tomato. Nematology 15 (6), 1–7.

Aust, S., Chignell, C.F., Bray, T.M., Kalyanaraman, B., Mason, R.P., 1993. Free radicals in toxicology. Toxicol. Appl. Pharmacol. 120 (2), 168–178.

Awwad, A.M., Albiss, B., 2015. Biosynthesis of colloidal copper hydroxide nanowires using pistachio leaf extract. Adv. Mater. Lett. 6 (1), 51–54.

Awwad, A., Albiss, B., Salem, N., 2015. Antibacterial activity of synthesized copper oxide nanoparticles using *Malva sylvestris* leaf extract. SMU Med. J. 2 (1), 91–101.

Azizi, S., Ahmad, M., Mahdavi, M., Abdolmohammadi, S., 2013. Preparation, characterization, and antimicrobial activities of ZnO nanoparticles/cellulose nanocrystal nanocomposites. Bioresources 8, 1841–1851.

Baek, Y.W., An, Y.J., 2011. Microbial toxicity of metal oxide nanoparticles (CuO, NiO, ZnO, and Sb_2O_3) to *Escherichia coli*, *Bacillus subtilis*, and *Streptococcus aureus*. Sci. Total Environ. 409 (8), 1603–1608.

Bali, R., Razak, N., Lumb, A., Harris, A.T., 2006. The synthesis of metallic nanoparticles inside live plants. In: Proceedings of the International Conference on Nanoscience and Nanotechnology, pp. 224–227.

Bao, W., Wang, J., Wang, Q., O'Hare, D., Wan, Y., 2016. Layered double hydroxide nanotransporter for molecule delivery to intact plant cells. Sci. Rep. 6, 26738.

Barik, T., Sahu, B., Swain, V., 2008. Nanosilica—from medicine to pest control. Parasitol. Res. 103, 253–258.

Baronia, R., Kumar, P., Singh, S.P., Walia, R.K., 2020. Silver nanoparticles as a potential nematicide against *Meloidogyne graminicola*. J. Nematol. 52.

Bedard, K., Krause, K.H., 2007. The NOX family of ROS-generating NADPH oxidases: physiology and pathophysiology. Physiol. Rev. 87 (1), 245–313.

Borel, T., Sabliov, C., 2014. Nanodelivery of bioactive components for food applications: types of delivery systems, properties, and their effect on ADME profiles and toxicity of nanoparticles. Annu. Rev. Food Sci. Technol. 5, 197–213.

Bosch, S., Botha, T.L., Jordaan, A., Maboeta, M., Wepener, V., 2018. Sublethal effects of ionic and nanogold on the nematode *Caenorhabditis elegans*. J. Toxicol. 2018, 6218193.

Caroling, G., Vinodhini, E., Ranjitham, A.M., Shanthi, P., 2015a. Biosynthesis of copper nanoparticles using aqueous *Phyllanthus embilica* (gooseberry) extract-characterisation and study of antimicrobial effects. Int. J. Nano. Chem. 1, 53–63.

Caroling, G., Priyadharshini, M.N., Vinodhini, E., Ranjitham, A.M., Shanthi, P., 2015b. Biosynthesis of copper nanoparticles using aqueous guava extract-characterisation and study of antibacterial effects. Int. J. Pharm. Bio Sci. 5, 25–43.

Coso, S., Harrison, I., Harrison, C.B., Vinh, A., Sobey, C.G., Drummond, G.R., Williams, E.D., Selemidis, S., 2012. NADPH oxidases as regulators of tumor angiogenesis: current and emerging concepts. Antioxid. Redox Signal. 16 (11), 1229–1247.

Cromwell, W.A., Yang, J., Starr, J.L., Jo, Y.K., 2014. Nematicidal effects of silver nanoparticles on rootknot nematode in Bermuda grass. J. Nematol. 46 (3), 261–266.

Danish, M., Altaf, M., Robab, M.I., Shahid, M., Manoharadas, S., Hussain, S.A., Shaikh, H., 2021. Green synthesized silver nanoparticles mitigate biotic stress induced by *Meloidogyne incognita* in *Trachyspermum ammi* (L.) by improving growth, biochemical, and antioxidant enzyme activities. ACS Omega 6, 11389–11403.

De Oliveira, J.L., Campos, E.V., Bakshi, M., Abhilash, P.C., Fraceto, L.F., 2016. Application of nanotechnology for the delivery to intact plant cells. Sci. Rep. 6, 6.

Deplanche, K., Caldelari, I., Mikheenko, I.P., Sargent, F., Macaskie, L.E., 2010. Involvement of hydrogenases in the formation of highly catalytic Pd(0) nanoparticles by bioreduction of Pd(II) using *Escherichia coli* mutant strains. Microbiology 156, 2630–2640.

Dhuper, S., Panda, D., Nayak, P.L., 2012. Green synthesis and characterization of zero valent iron nanoparticles from the leaf extract of *Mangifera indica*. Nano Trends J. Nanotechnol. Appl. 13, 16–22.

Dong, S., Qu, M., Rui, Q., Wang, D., 2018. Combinational effect of titanium dioxide nanoparticles and nanopolystyrene particles at environmentally relevant concentrations on nematode *Caenorhabditis elegans*. Ecotoxicol. Environ. Saf. 161, 444–450.

Egorova, E.M., Revina, A.A., 2000. Synthesis of metallic nanoparticles in reverse micelles in the presence of quercetin (article). Colloids Surf. A Physicochem. Eng. Asp. 168 (1), 87–96.

Egusa, M., Matsui, H., Urakami, T., Okuda, S., Ifuku, S., Nakagami, H., Kaminaka, H., 2015. Chitin nanofiber elucidates the elicitor activity of polymeric chitin in plants. Front. Plant Sci. 6, 1098.

Ekambaram, P., Sathali, A.A.H., Priyanka, K., 2012. Solid lipid nanoparticles: a review. Sci. Rev. Chem. Commun. 2, 80–102.

El-Deen, A.N., El-Deeb, B.A., 2018. Effectiveness of silver nanoparticles against root-knot nematode, *Meloidogyne incognita* infecting tomato under greenhouse conditions. J. Agric. Sci. 10 (2), 148–156.

Elmer, W., Ma, C., White, J., 2018. Nanoparticles for plant disease management. Curr. Opin. Environ. Sci. Health 6, 66–70.

Fenoglio, I., Corazzari, I., Francia, C., Bodoardo, S., Fubini, B., 2008. The oxidation of glutathione by cobalt/tungsten carbide contributes to hard metal-induced oxidative stress. Free Radic. Res. 42 (8), 437–745.

Fouda, M.M., Abdelsalam, N.R., Gohar, I.M.A., Hanfy, A.E., Othman, S.I., Zaitoun, A.F., Allam, A.A., Morsy, O.M., El-Naggar, M., 2020. Utilization of high throughput microcrystalline cellulose decorated silver nanoparticles as an eco-nematicide on root-knot nematodes. Colloids Surf. B Biointerfaces 188, 110805.

Gao, Y., Liu, N., Chen, C., Luo, Y., Li, Y., Zhang, Z., Zhao, Y., Zhao, B., Atsuo Iida, A., Chai, Z., 2008. Mapping technique for biodistribution of elements in a model organism, *Caenorhabditis elegans*, after exposure to copper nanoparticles with microbeam synchrotron radiation X-ray fluorescence. J. Anal. At. Spectrom 23, 1121–1124.

Ghareeb, R.Y., Alfy, H., Fahmy, A.A., Ali, H.M., Abdelsalam, N.R., 2020. Utilization of *Cladophora glomerata* extract nanoparticles as eco-nematicide and enhancing the defense responses of tomato plants infected by *Meloidogyne javanica*. Sci. Rep. 10 (1), 1–15.

Gkanatsiou, C., Ntalli, N., Menkissoglu-Spiroudi, U., Dendrinou-Samara, C., 2019. Essential metal-based nanoparticles (copper/iron NPs) as potent nematicidal agents against *Meloidogyne spp*. J. Nanotechnol. Res. 1 (2), 044–058.

Gogos, A., Knauer, K., Bucheli, T.D., 2012. Nanomaterials in plant protection and fertilization: current state, foreseen applications, and research priorities. J. Agric. Food Chem. 60, 9781–9792.

Gonzalez-Moragas, L., Berto, P., Vilches, C., Quidant, R., Kolovou, A., Santarella-Mellwig, R., Schwab, Y., Stürzenbaum, S., Roiga, A., Laromaine, A., 2017. In vivo testing of gold nanoparticles using the *Caenorhabditis elegans* model organism. Acta Biomater. 53, 598–609.

Gopinath, M., Subbaiya, R., Selvam, M.M., Suresh, D., 2014. Synthesis of copper nanoparticles from *Nerium oleander* leaf aqueous extract and its antibacterial activity. Int. J. Curr. Microbiol. App. Sci. 3 (9), 814–818.

Guajardo-Pacheco, M.J., Morales-Sánchez, J., Gonzalez-Hernandez, J., Ruiz, F., 2010. Synthesis of copper nanoparticles using soybeans as a chelant agent. Mater. Lett. 64, 1361–1364.

Guzik, T.J., Harrison, D.G., 2006. Vascular NADPH oxidases as drug targets for novel antioxidant strategies. Drug Discov. Today 11 (11–12), 524–533.

Halliwell, B., Gutteridge, J.M., 2015. Free Radicals in Biology and Medicine. Oxford University Press, USA.

Hamed, S.M., Hagag, E.S., Abd El-Raouf, N., 2019. Green production of silver nanoparticles, evaluation of their nematicidal activity against *Meloidogyne javanica* and their impact on growth of faba bean. Beni-Suef Univ. J. Basic Appl. Sci. 8 (1), 1–12.

Harne, S., Sharma, A., Dhaygude, M., Joglekar, S., Kodam, K., Hudlikar, M., 2012. Novel route for rapid biosynthesis of copper nanoparticles using aqueous extract of *Calotropis procera L.* latex and their cytotoxicity on tumor cells. Colloids Surf. B Biointerfaces 95, 284–288.

Heera, P., Shanmugam, S., Ramachandran, J., 2015. Green synthesis of copper nanoparticle using *Gymnema sylvestre* by different solvent extract. Int. J. Curr. Res. Acad. Rev. 3, 268–275.

Holden-Dye, L., Walker, R.J., 2014. Anthelmintic drugs and nematicides: studies in *Caenorhabditis elegans*. In: The C. elegans Research Community (Ed.), WormBook. WormBook, https://doi.org/10.1895/wormbook.1.143.2.

Hrács, K., Sávoly, Z., Seres, A., Kiss, L.V., Papp, I.Z., Kukovecz, Á., Záray, G., Nagy, P., 2018. Toxicity and uptake of nanoparticulate and bulk ZnO in nematodes with different life strategies. Ecotoxicology 27 (8), 1058–1068.

Hu, C.C., Wu, G.H., Lai, S.F., Shanmugam, M.M., Hwu, Y., Wagner, O.I., Yen, T.J., 2018. Toxic effects of size-tunable gold nanoparticles on *Caenorhabditis elegans* development and gene regulation. Sci. Rep. 8, 15245.

Huang, H., 1997. Synthesis, characterization and nonlinear optical properties of copper nanoparticles. Langmuir 13, 172–175.

Iavicoli, I., Leso, V., Beezhold, D.H., Shvedova, A.A., 2016. Nanotechnology in agriculture: opportunities. Int. J. Mol. Sci. 17 (7), 996.

Iravani, S., Zolfaghari, B., 2013. Green synthesis of silver nanoparticles using *Pinus eldarica* bark extract. Biomed. Res. Int. 2013, 1.

Janafi, N.R., Wangl, Z.L., Sau, T.K., 2000. Seed-mediated growth method to prepare cubic copper nanoparticles. Curr. Sci. 79, 1367–1370.

Jayakumarai, G., Gokulpriya, C., Sudhapriya, R., Sharmila, G., Muthukumaran, C., 2015. Phytofabrication and characterization of monodisperse copper oxide nanoparticles using *Albizia lebbeck* leaf extract. Appl. Nanosci. 5, 1017–1021.

Jayandran, M., Haneefa, M., Balasubramanian, V., 2015. Green synthesis of copper nanoparticles using natural reducer and stabilizer and an evaluation of antimicrobial activity. J. Chem. Pharm. Res. 7 (2), 251–259.

Jones, M.W.M., Phillips, N.W., Abbey, B., Hare, D.J., van Riessen, G.A., Vine, D.J., de Jonge, M.D., McColl, G., 2019. Simultaneous nanostructure and chemical imaging of intact whole nematodes. Chem. Commun. (Camb) 55 (8), 1052–1055.

Kah, M., Hofmann, T., 2014. Nanopesticide research: current trends and future priorities. Environ. Int. 63, 224–235.

Kalaiselvi, D., Mohankumar, A., Shanmugam, G., Nivitha, S., Sundararaj, P., 2019. Green synthesis of silver nanoparticles using latex extract of *Euphorbia tirucalli*: a novel approach for the management of root knot nematode, *Meloidogyne incognita*. Crop Prot. 117, 108–114.

Kalimuthu, K., Babu, R.S., Venkataraman, D., Mohd, B., Gurunathan, S., 2008. Biosynthesis of silver nanocrystals by *Bacillus licheniformis*. Colloids Surf. B Biointerfaces 65, 150–153.

Kalishwaralal, K., Deepak, V., Ramkumarpandian, S., Nellaiah, H., Sangiliyandi, G., 2008. Extracellular biosynthesis of silver nanoparticles by the culture supernatant of *Bacillus licheniformis*. Mater. Lett. 62, 4411–4413.

Kapoor, S., Mukherjee, T., 2003. Photochemical formation of copper nanoparticles in poly (N-vinylpyrrolidone). Chem. Phys. Lett. 370, 83–87.

Karimi, J., Mohsenzadeh, S., 2015. Rapid, green, and eco-friendly biosynthesis of copper nanoparticles using flower extract of *Aloe vera*. Synth. React. Inorg. Met.-Org. Chem. 45, 895–898.

Kashyap, P.L., Xiang, X., Heiden, P., 2015. Chitosan nanoparticle based delivery systems for sustainable agriculture. Int. J. Biol. Macromol. 77, 36–51.

Kathad, U., Gajera, H., 2014. Synthesis of copper nanoparticles by two different methods and size comparison. Int. J. Pharm. Bio Sci. 5, 533–540.

Khan, A., Mohd, A., Moh, T., Bushra, R., Kavita, P., Mansoor, A.S., 2017. Phytochemical investigation, nematostatic and nematicidal potential of weeds extract against the root-knot nematode *Meloidogyne incognita in vitro*. Asian J. Biol. Sci. 10, 38–46.

Khan, A., Tariq, M., Ahmad, F., Mennan, S., Khan, F., Asif, M., Nadeem, H., Ansari, T., Shariq, M., Siddiqui, M.A., 2021. Assessment of nematicidal efficacy of chitosan in combination with botanicals against *Meloidogyne incognita* on carrot. Acta Agric. Scand. B Soil Plant Sci. 71, 1–12.

Khandel, P., Yadaw, R.K., Soni, D.K., Kanwar, L., Shahi, S.K., 2018. Biogenesis of metal nanoparticles and their pharmacological applications: present status and application prospects. JNSC 8, 217–254.

Khot, L.R., Sankaran, S., Majaa, J.M., Ehsania, R., Schuster, E.W., 2012. Applications of nanomaterials in agricultural production and crop protection. Crop Prot. 35, 64–67.

Kim, J., Shirasawa, T., Miyamoto, Y., 2010. The effect of TAT conjugated platinum nanoparticles on lifespan in a nematode *Caenorhabditis elegans* model. Biomaterials 22, 5849–5854.

Kim, S.W., Nam, S.H., An, Y.J., 2012. Interaction of silver nanoparticles with biological surfaces of *Caenorhabditis elegans*. Ecotoxicol. Environ. Saf. 77, 64–70.

Kim, D.Y., Kadam, A., Shinde, S., Saratale, R.G., Patra, J., Ghodake, G., 2018a. Recent developments in nanotechnology transforming the agricultural sector: a transition replete with opportunities. J. Sci. Food Agric. 98 (3), 849–864.

Kim, S.W., Moon, J., An, Y.J., 2018b. Matricidal hatching can induce multi-generational effects in nematode *Caenorhabditis elegans* after dietary exposure to nanoparticles. Environ. Sci. Pollut. Res. 25, 36394–36402.

Kolekar, R., Bhade, S., Kumar, R., Reddy, P., Singh, R., Pradeepkumar, K., 2015. Biosynthesis of copper nanoparticles using aqueous extract of *Eucalyptus sp*. plant leaves. Curr. Sci. 109, 255.

Kote, J.R., Mulani, R.M., Kadam, A.S., Solankar, B.M., 2014. Anti-mycobacterial activity of nanoparticles from *Psidium guajava* L. J. Microbiol. Biotechnol. Res. 4 (5), 14–17.

Kucharska, K., Pezowicz, E., Tumialis, D., Kucharski, D., Zajde, B., 2014. Nanoparticles of copper and entomopathogenic nematodes *Steinernema feltiae* (Filipjev, 1934) in reducing the number of the lesser mealworm beetle *Alphitobius diaperinus* (panzer, 1797). Anim. Sci. 53, 29–35.

Kucharska, K., Tumialis, D., Pezowicz, E., Skrzecz, I., 2011. The effect of gold nanoparticles on the mortality and pathogenicity of entomopathogenic nematodes from Owinema biopreparation. Insect Pathogens and Entomopathogenic Nematodes. vol. 66 IOBC/WPRS Bulletin, pp. 347–349.

Kulkarni, V.D., Kulkarni, P.S., 2013. Green synthesis of copper nanoparticles using *Ocimum Sanctum* leaf extract. Int. J. Chem. Stud. 1 (3), 01–04.

Kumar, S., Suchiang, K., 2020. *Caenorhabditis elegans*: evaluation of nanoparticle toxicity. In: Siddhardha, B., Dyavaiah, M., Kasinathan, K. (Eds.), Model Organisms to Study Biological Activities and Toxicity of Nanoparticles. Springer, pp. 333–369.

Kundu, S., 2013. Biological Synthesis of Copper/Copper Oxide Nanoparticles and Their Characterization (Master of Technology thesis). Food Technology and Biochemical Engineering Department Jadavpur University, Kolkata, pp. 1–31.

Law, N., Ansari, S., Livens, F.R., Renshaw, J.C., Lloyd, J.R., 2008. The formation of nanoscale elemental silver particles via enzymatic reduction by *Geobacter sulfurreducens*. Appl. Environ. Microbiol. 74, 7090–7093.

Lee, H.J., Song, J.Y., Kim, B.S., 2013. Biological synthesis of copper nanoparticles using *Magnolia kobus* leaf extract and their antibacterial activity. J. Chem. Technol. Biotechnol. 88, 1971–1977.

Li, M., Huang, Q., Wu, Y., 2011. A novel chitosan-poly (lactide) copolymer and its submicron particles as imidacloprid carriers. Pest Manag. Sci. 67, 831–836.

Li, D., Ji, J., Yuan, Y., Wang, D., 2020. Toxicity comparison of nanopolystyrene with three metal oxide nanoparticles in nematode *Caenorhabditis elegans*. Chemosphere 245, 125625.

Liang, W., Yu, A., Wang, G., Zheng, F., Jia, J., Xu, H., 2018. Chitosan-based nanoparticles of avermectin to control pine wood nematodes. Int. J. Biol. Macromol. 112, 258–263.

Lim, D.H., Jang, J., Kim, S., Kang, T., Lee, K., Choi, I.H., 2012. The effects of sub-lethal concentrations of silver nanoparticles on inflammatory and stress genes in human macrophages using cDNA microarray analysis. Biomaterials 33, 4690–4699.

Lisiecki, I., Pileni, M.P., 1993. Synthesis of copper metallic clusters using reverse micelles as microreactors. J. Am. Chem. Soc. 115, 3887–3896.

Liu, B.X., Wang, Y., Yang, F., Wang, X., Shen, H., Cui, H.X., Wu, D.C., 2016. Construction of a controlled release delivery system for pesticides using biodegradable PLA-based microcapsules. Colloids Surf. B Biointerfaces 144, 38–45.

Lopes-Caitar, V.S., Pinheiro, J.B., Marcelino-Guimarães, F.C., 2019. Nematodes in horticulture: an overview. J. Hortic. Sci. Crop Res. 1 (1), 105.

Ma, H., Bertsch, P.M., Glenn, T.C., Kabengi, N.J., Williams, P.L., 2009. Toxicity of manufactured zinc oxide nanoparticles in the nematode *Caenorhabditis elegans*. Environ. Toxicol. Chem. 28, 1324–1330.

Ma, W., Saccardo, A., Roccatano, D., 2018. Modular assembly of proteins on nanoparticles. Nat. Commun. 9, 1489.

Makirita, W.E., Yong, L., He, N., Mbega, E.R., Chacha, M., Li, X., Zhang, F., 2020. Effects of nanoparticles of metal oxides on the survival of the entomopathogenic nematode: *Steinernema carpocapsae*. J. Nanosci Nanotechnol. 20, 1434–1439.

Malerba, M., Cerana, R., 2016. Chitosan effects on plant systems. Int. J. Mol. Sci. 17 (7), 996.

Malerba, M., Raffaella, C., 2018. Recent advances of chitosan applications in plants. Polymers 10, 118.

Marimon-Bolívar, W., Tejeda-Benítez, L.P., Núñez-Avilés, C.A., De De Léon-Pérez, D., 2019. Evaluation of the in vivo toxicity of green magnetic nanoparticles using *Caenorhabditis elegans* as a biological model. Environ. Nanotechnol. Monit. Manag. 12, 100253.

Mashock, M.J., Zanon, T., Kappell, A.D., Petrella, L.N., Andersen, E.C., Hristova, K.R., 2016. Copper oxide nanoparticles impact several toxicological endpoints and cause neurodegeneration in *Caenorhabditis elegans*. PLoS One 11 (12), E0167613.

Mattos, B.D., Tardy, B.L., Magalhães, W.L.E., Rojas, O.J., 2017. Controlled release for crop and wood protection: recent progress toward sustainable and safe nanostructured biocidal systems. J. Control. Release 28, 139–150.

Meyer, J.N., Lord, C.A., Yang, X.Y., Turner, E.A., Badireddy, A.R., 2010. Intracellular uptake and associated toxicity of silver nanoparticles in *Caenorhabditis elegans*. Aquat. Toxicol. 100 (2), 140–150.

Mignolet-Spruyt, L., Xu, E., Idänheimo, N., Hoeberichts, F.A., Mühlenbock, P., Brosché, M., Van Breusegem, F., Kangasjärvi, J., 2016. Spreading the news: subcellular and organellar reactive oxygen species production and signalling. J. Exp. Bot. 67 (13), 3831–3844.

Mishra, S., Singh, H., 2015. Biosynthesized silver nanoparticles as a nanoweapon against phytopathogens: exploring their scope and potential in agriculture. Appl. Microbiol. Biotechnol. 99, 1097–1107.

Mittal, A.K., Chisti, Y., Banerjee, U.C., 2013. Synthesis of metallic nanoparticles using plant extracts. Biotechnol. Adv. 31, 346–356.

Mitter, N., Worrall, E.A., Robinson, K.E., Li, P., Jain, R.G., Taochy, C., Fletcher, S.J., Carroll, B.J., Lu, G.Q., Xu, Z.P., 2017. Clay nanosheets for topical delivery of RNAi for sustained protection against plant viruses. Nat. Plants 3, 16207.

Mody, V.V., Cox, A., Shah, S., Singh, A., Bevins, W., Parihar, H., 2014. Magnetic nanoparticle drug delivery systems for targeting tumor. Appl. Nanosci. 4, 385–392.

Mohamed, E.A., Elsharabasy, S.F., Abdulsamad, D., 2019. Evaluation of in vitro nematicidal efficiency of copper nanoparticles against root-knot nematode *Meloidogyne incognita*. South Asian J. Parasitol. 2 (1), 1–6.

Mott, D., Galkowski, J., Wang, L., Luo, J., Zhong, C.J., 2007. Synthesis of size controlled and shaped copper nanoparticles. Langmuir 23, 5740–5745.

Mukunthan, K.S., Balaji, S., 2012. Cashew apple juice (*Anacardium occidentale* L.) speeds up the synthesis of silver nanoparticles. Int. J. Nanotechnol. 4, 71–79.

Mussabayeva, B., Murzagulova, K., Kasymova, Z., Aripzhanova, Z., Orazzhanova, L., Koizhaiganova, M., 2014. Preparation of silver and copper nanoparticles in plant extracts. Bothalia J. 44 (12), 558–568.

Nakamura, K., Matsubara, H., Akagi, S., Sarashina, T., Ejiri, K., Kawakita, N., Yoshida, M., Miyoshi, T., Watanabe, A., Nishii, N., Ito, H., 2017. Nanoparticle-mediated drug delivery system for pulmonary arterial hypertension. J. Clin. Med. 6 (5), 48.

Nasrollahzadeh, M., Sajadi, S.M., 2015. Green synthesis of copper nanoparticles using *Ginkgo biloba L.* leaf extract and their catalytic activity for the Huisgen [3 + 2] cycloaddition of azides and alkynes at room temperature. J. Colloid Interface Sci. 457, 141–147.

Nasrollahzadeh, M., Sajadi, S.M., Khalaj, M., 2014. Green synthesis of copper nanoparticles using aqueous extract of the leaves of *Euphorbia esula* L and their catalytic activity for ligand-free Ullmann-coupling reaction and reduction of 4-nitrophenol. RSC Adv. 4, 47313–47318.

Nasrollahzadeh, M., Sajadi, S.M., Rostami-Vartooni, A., 2015a. Green synthesis of CuO nanoparticles by aqueous extract of *Anthemis nobilis* flowers and their catalytic activity for the A^3 coupling. J. Colloid Interface Sci. 459, 183–188.

Nasrollahzadeh, M., Sajadi, S.M., Hatamifard, A., 2015b. *Anthemis xylopoda* flowers aqueous extract assisted in situ green synthesis of cu nanoparticles supported on natural Natrolite zeolite for N-formylation of amines at room temperature under environmentally benign reaction conditions. J. Colloid Interface Sci. 460, 146–153.

Nasrollahzadeh, M., Sajadi, S.M., Mirzaei, Y., 2016a. An efficient one-pot synthesis of 1,4-disubstituted 1,2,3-triazoles at room temperature by green synthesized Cu NPs using *Otostegia persica* leaf extract. J. Colloid Interface Sci. 468, 156–162.

Nasrollahzadeh, M., Sajadi, S.M., Rostami-Vartooni, A., Hussin, S.M., 2016b. Green synthesis of CuO nanoparticles using aqueous extract of *Thymus vulgaris L.* leaves and their catalytic performance for N-arylation of indoles and amines. J. Colloid Interface Sci. 466, 113–119.

Nassar, A.M.K., 2016. Effectiveness of silver nanoparticles of extracts of *Urtica urens* (Urticaceae) against root-knot nematode *Meloidogyne incognita*. Asian J. Nematol. 5, 14–19.

Nazir, K., Mukhtar, T., Javed, H., 2019. In vitro effectiveness of silver nanoparticles against root-knot nematode (*Meloidogyne incognita*). Pak. J. Zool. 51 (6).

Nel, A., Xia, T., Mädler, L., Li, N., 2006. Toxic potential of materials at the nanolevel. Science 311 (5761), 622–627.

Nour El-Deen, A.H., Darwish, H., 2011. Nematicidal activity of certain Egyptian weeds and bald cypress callus extracts against *Meloidogyne incognita* infecting eggplant under greenhouse conditions. Egypt. J. Agronematol. 10 (2), 242–254.

Nour El-Deen, A.H., Cseh, E., Darwesh, H.Y., 2014. Evaluation of certain Hungarian plant extracts for their nematicidal properties against root-knot nematode, *Meloidogyne incognita in-vitro*. Int. J. Adv. Res. 2 (8), 443–448.

Oka, Y., Nacar, S., Putievsky, E., Ravid, U., Yaniv, Z., Spiegel, Y., 2000. Nematicidal activity of essential oils and their components against the root-knot nematode. Phytopathology 90, 710–715.

Padil, V.V.T., Černík, M., 2013. Green synthesis of copper oxide nanoparticles using gum karaya as a biotemplate and their antibacterial application. Int. J. Nanomedicine 8, 889–898.

Panigrahi, S., Kundu, S., Ghosh, S.K., Nath, S., Praharaj, S., Basu, S., Pal, T., 2006. Selective one-pot synthesis of copper nanorods under surfactantless condition. Polyhedron 25, 1263.

Parikh, R.Y., Singh, S., Prasad, B.L., Patole, M.S., Sastry, M., Shouche, Y.S., 2008. Extracellular synthesis of crystalline silver nanoparticles and molecular evidence of silver resistance from *Morganella sp.*: towards understanding biochemical synthesis mechanism. ChemBioChem 9, 1415–1422.

Parikh, P., Zala, D., Makwana, B.A., 2014. Biosynthesis of copper nanoparticles and their antimicrobial activity. Open Access Library PrePrints 1, 1–15.

Park, Y., Hong, Y.N., Weyers, A., Kim, Y.S., Linhardt, R.J., 2011. Polysaccharides and phytochemicals: a natural reservoir for the green synthesis of gold and silver nanoparticles. IET Nanobiotechnol. 5, 69–78.

Patel, V., Berthold, D., Puranik, P., Gantar, M., 2015. Screening of cyanobacteria and microalgae for their ability to synthesize silver nanoparticles with antibacterial activity. Biotechnol. Rep. 5, 112–119.

Rafique, M., Sadaf, I., Rafique, M.S., Tahir, M.B., 2017. A review on green synthesis of silver nanoparticles and their applications. Artif. Cells Nanomed. Biotechnol. 45, 1272–1291.

Rahman, K., 2007. Studies on free radicals, antioxidants, and co-factors. Clin. Interv. Aging 2 (2), 219–236.

Raveendran, P., Fu, J., Wallen, S.L., 2003. Completely "green" synthesis and stabilization of metal nanoparticles. J. Am. Chem. Soc. 125, 13940–13941.

Ray, P.D., Huang, B.W., Tsuji, Y., 2012. Reactive oxygen species (ROS) homeostasis and redox regulation in cellular signaling. Cell. Signal. 24 (5), 981–990.

Risom, L., Møller, P., Loft, S., 2005. Oxidative stress-induced DNA damage by particulate air pollution. Mutat. Res. 592 (1–2), 119–137.

Rodgers, P., 2006. Top down, bottom up. Nat. Nanotechnol. 5, 17.
Sadeghi, R., Rodriguez, R.J., Yao, Y., Kokini, J.L., 2017. Advances in nanotechnology as they pertain to food and agriculture: benefits and risks. Annu. Rev. Food Sci. Technol. 8, 467–492.
Safeena, M.I.S., Zakeel, M.C.M., 2020. Nanobiotechnology-driven management of phytonematodes. In: Ansari, R., Rizvi, R., Mahmood, I. (Eds.), Management of Phytonematodes: Recent Advances and Future Challenges. Springer, Singapore.
Saifuddin, N., Wong, C.W., Nuryasumira, A.A., 2009. Rapid biosynthesis of silver nanoparticles using culture supernatant of bacteria with microwave irradiation. Eur. J. Chem. 6, 61–70.
Sajadi, S.M., Nasrollahzadeh, M., Maham, M., 2016. Aqueous extract from seeds of *Silybum marianum L.* as a green material for preparation of the Cu/Fe_3O_4 nanoparticles: a magnetically recoverable and reusable catalyst for the reduction of nitroarenes. J. Colloid Interface Sci. 469, 93–98.
Salikin, N.H., Nappi, J., Majzoub, M.E., Suhelen Egan, S., 2020. Combating parasitic nematode infections, newly discovered antinematode compounds from marine epiphytic bacteria. Microorganisms 8 (12), 1963.
Saranyaadevi, K., Subha, V., Ravindran, R.E., Renganathan, S., 2014. Synthesis and characterization of copper nanoparticle using *Capparis zeylanica* leaf extract. Int. J. ChemTech Res. 6 (10), 4533–4541.
Sarfraz, S., Javed, A., Mughal, S.S., Bashir, M., Rehman, A., Parveen, S., Khushi, A., Khan, M.K., 2020. Copper oxide nanoparticles: reactive oxygen species generation and biomedical applications. Int. J. Comput. Theor. Chem. 8 (2), 40–46.
Shakya, S., Yadav, B.C., 2020. Screening of anti-nematode potential through inhibition of egg hatching in plant-parasitic nematode *Meloidogyne javanica*. Curr. Bot. 11, 93–98.
Shankar, S.S., Rai, A., Ahmad, A., Sastry, M., 2004. Rapid synthesis of Au, Ag, and bimetallic Au core-Ag shell nanoparticles using neem (*Azadirachta indica*) leaf broth. J. Colloid Interface Sci. 275, 496–502.
Shekoohi, S.S., Charehgani, H., Abdollahi, M., Rajabi, H.R., 2021. Combined effect of β-aminobutyric acid and silver nanoparticles on eggplants, *Solanum melongena*, infected with *Meloidogyne javanica*. Nematology 1 (aop), 1–16.
Shen, Y., Wang, Y., Zhao, X., Sun, C., Cui, B., Gao, F., Zeng, Z., Cui, H., 2017. Preparation and physicochemical characteristics of thermo-responsive Emamectin benzoate microcapsules. Polymers 9 (9), 418.
Shende, S., Ingle, A.P., Gade, A., Rai, M., 2015. Green synthesis of copper nanoparticles by *Citrus medica* Linn. (Idilimbu) juice and its antimicrobial activity. World J. Microbiol. Biotechnol. 31 (6), 865–873.
Shojaei, T.R., Salleh, M.A.M., Tabatabaei, M., Hossein, M., Aghbashlo, M., Rashid, S.A., Tan, T., 2019. Applications of nanotechnology and carbon nanoparticles in agriculture. In: Rashid, S.A., et al. (Eds.), Agriculture Synthesis, Technology and Applications of Carbon Nanomaterials. Elsevier, Amsterdam, pp. 247–277.
Singh, N.G., Anil, K., Sewak, R., Vinod, K., 2017. Evaluation of nematicidal activity of ethanolic extracts of medicinal plants to *Meloidogyne incognita* (Kofoid and white) Chitwood under lab conditions. Int. J. Pure Appl. Biosci. 5 (1), 827–831.
Song, X., Sun, S., Zhang, W., Yin, Z., 2004. A method for the synthesis of spherical copper nanoparticles in the organic phase. J. Colloid Interface Sci. 273, 463–469.
Storz, P., 2011. Forkhead homeobox type O transcription factors in the responses to oxidative stress. Antioxid Redox Signal 14 (4), 593–605.
Subbaiya, M.M.S.R., 2015. Green synthesis of copper nanoparticles from *Hibicus rosasinensis* and their antimicrobial, antioxidant activities. Res. J. Pharm., Biol. Chem. Sci. 6, 1183–1190.

Subhankari, I., Nayak, P., 2013a. Synthesis of copper nanoparticles using *Syzygium aromaticum* (cloves) aqueous extract by using green chemistry. World J. Nano Sci. Technol. 2, 14–17.

Subhankari, I., Nayak, P., 2013b. Antimicrobial activity of copper nanoparticles synthesised by ginger (*Zingiber officinale*) extract. World J. Nano Sci. Technol. 2 (1), 10–13.

Suresh, Y., Annapurna, S., Bhikshamaiah, G., Singh, A., 2014. Copper nanoparticles: green synthesis and characterization. Int. J. Sci. Eng. Res. 5 (3), 156–160.

Suriyaprabha, R., Karunakaran, G., Kavitha, K., Yuvakkumar, R., Rajendran, V., Kannan, N., 2014. Application of silica nanoparticles in maize to enhance fungal resistance. IET Nanobiotechnol. 8, 133–137.

Taha, E.H., Abo-Shady, N.M., 2016. Effect of silver nanoparticles on the mortality pathogenicity and reproductivity of entomopathogenic nematodes. Int. J. Zool. Res. 12, 47–50.

Taha Entsar, H., 2016. Nematicidal effects of silver nanoparticles on root-knot nematodes (*Meloidogyne incognita*) in laboratory and screenhouse. J. Plant Prot. Pathol. 7 (5), 333–337.

Tanori, J., Gulik-Krzywicki, T., Pileni, M.P., 1997. Phase diagram of copper(II) bis(2-ethylhexyl)sulfosuccinate, $Cu(AOT)_2$-isooctane-water. Langmuir 13 (4), 632–638.

Tauseef, A., Gupta, J., Rehman, A., Uddin, I., 2021. Differential response of cowpea towards the CuO nanoparticles under *Meloidogyne incognita* stress. S. Afr. J. Bot. 139, 175–182.

Thakur, R.K., Shirkot, P., 2017. Potential of biogold nanoparticles to control plant pathogenic nematodes. J. Bioanal. Biomed. 9 (4), 220–222.

Thakur, S., Rai, R., Sharma, S., 2014. Study the antibacterial activity of copper nanoparticles synthesized using herbal plants leaf extracts. Int. J. Bio-Technol. Res. 4, 21–34.

Thakur, R.K., Dhirta, B., Shirkot, P., 2018. Studies on effect of gold nanoparticles on *Meloidogyne incognita* and tomato plants growth and development. bioRxiv. https://doi.org/10.1101/428144.

Thannickal, V.J., Fanburg, B.L., 2000. Reactive oxygen species in cell signaling. Am. J. Physiol. Lung Cell. Mol. Physiol. 279 (6), L1005–L1028.

Udalova, Z.V., Folmanis, G.E., Khasanov, F.K., Zinovieva, S.V., 2018, September. Selenium nanoparticles—an inducer of tomato resistance to the root-knot nematode *Meloidogyne incognita* (Kofoid et white, 1919) Chitwood 1949. Dokl. Biochem. Biophys. 482 (1), 264–267. Pleiades Publishing.

Valavanidis, A., Vlachogianni, T., Fiotakis, C., 2009. 8-Hydroxy-2′-deoxyguanosine (8-OHdG): a critical biomarker of oxidative stress and carcinogenesis. J. Environ. Sci. Health C 27 (2), 120–139.

Valli, S., Suganya, M., 2015. Green synthesis of copper nanoparticles using *Cassia fistula* flower extract. J. Biol. Innov. 4, 162–170.

Vennila, S., Nithya, T., 2015. Green synthesis of copper, silver nanoparticles using *Ocimum tenuiflorum* leaf extract. World J. Pharm. Res. 5 (1), 257–265.

Wang, L., Hu, C., Shao, L., 2017. The antimicrobial activity of nanoparticles: present situation and prospects for the future. Int. J. Nanomedicine 12, 1227–1249.

Wei, C., Yen, P., Chaikritsadakarn, A., Huang, C., Chang, C., Liao, V.H., 2020. Parental CuO nanoparticles exposure results in transgenerational toxicity in *Caenorhabditis elegans* associated with possible epigenetic regulation. Ecotoxicol. Environ. Saf. 203, 111001.

Wu, Z., Jiang, H., Sun, Q., Guo, H., Yang, H., Gong, Q., 2004. Micro-ablation at the front and rear surfaces of a fused silica window by using a femtosecond laser pulse in air. J. Opt. A: Pure Appl. Opt. 6 (7), 671.

Wu, T., Xu, H., Liang, X., Tang, M., 2019. *Caenorhabditis elegans* as a complete model organism for biosafety assessments of nanoparticles. Chemosphere 221, 708–726.

Xia, T., Kovochich, M., Brant, J., Hotze, M., Sempf, J., Oberley, T., Sioutas, C., Yeh, J.I., Wiesner, M.R., Nel, A.E., 2006. Comparison of the abilities of ambient and manufactured nanoparticles to induce cellular toxicity according to an oxidative stress paradigm. Nano Lett. 6 (8), 1794–1807.

Xia, T., Kovochich, M., Liong, M., Mädler, L., Gilbert, B., Shi, H., Yeh, J.I., Zink, J.I., Nel, A.E., 2008. Comparison of the mechanism of toxicity of zinc oxide and cerium oxide nanoparticles based on dissolution and oxidative stress properties. ACS Nano 2 (10), 2121–2134.

Xu, Z., Zeng, Q., Lu, M., Yu, A., 2006. Inorganic nanoparticles as carriers for efficient cellular delivery. Chem. Eng. Sci. 61, 1027–1040.

Yamamoto, E., Kuroda, K., 2016. Colloidal mesoporous silica nanoparticles. Bull. Chem. Soc. Jpn. 89, 501–539.

Yang, Y., Xu, G., Xu, S., Chen, S., Xu, A., Wu, L., 2018. Effect of ionic strength on bioaccumulation and toxicity of silver nanoparticles in *Caenorhabditis elegans*. Ecotoxicol. Environ. Saf. 165, 291–298.

Yong, P., Rowson, A.N., Farr, J.P.G., Harris, I.R., Mcaskie, L.E., 2002. Bioaccumulation of palladium by *Desulfovibriode sulfuricans*. J. Chem. Technol. Biotechnol. 55, 593–601.

You, Y., Cao, F., Zhao, Y., Deng, Q., Sang, Y., Li, Y., Dong, K., Ren, J., Qu, X., 2020. Near-infrared light dual-promoted heterogeneous copper nanocatalyst for highly efficient bioorthogonal chemistry in vivo. ACS Nano 14, 4178–4187.

Zafar, A., Ahmad, I., Ahmad, A., Ahmad, M., 2016. Copper (II) oxide nanoparticles augment antifilarial activity of Albendazole: in vitro synergistic apoptotic impact against filarial parasite *Setaria cervi*. Int. J. Pharm. 501 (1–2), 49–64.

Zhang, H., Li, Q., Lu, Y., Sun, D., Lin, X., Deng, X., He, N., Zheng, S., 2005. Biosorption and bioreduction of diamine silver complex by *Corynebacterium*. J. Chem. Technol. Biotechnol. 80, 285–290.

Zhang, F., You, X., Zhu, T., Gao, S., Wang, Y., Wang, R., Yu, H., Qian, B., 2020. Silica nanoparticles enhance germ cell apoptosis by inducing reactive oxygen species (ROS) formation in *Caenorhabditis elegans*. J. Toxicol. Sci. 45 (3), 117–129.

Zhang, S., Chu, Q., Zhang, Z., Xu, Y., Mao, X., Zhang, M., 2021. Responses of *Caenorhabditis elegans* to various surface modifications of alumina nanoparticles. Environ. Pollut. 271, 116335.

Zhou, R., Wu, X., Hao, X., Rao, W., Li, H., Zhou, F., 2008. Influences of surfactants on the preparation of copper nanoparticles by electron beam irradiation. Nucl. Instrum. Methods Phys. Res. B 266 (4), 599–603.

Zhu, X., Hondroulis, E., Liu, W., Li, C., 2013. Biosensing approaches for rapid genotoxicity and cytotoxicity assays upon nanomaterial exposure. Small 9 (9–10), 1821–1830.

Zizzo, J., 2020. Toxicity effects of Cubic Cu_2O nanoparticles on defecation rate and length in *C. elegans*. Biomed. Res. Ther. 7 (10), 4045–4051.

PART

Plant science

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CHAPTER

13 Impact of copper-based nanoparticles on economically important plants

Josef Jampílek[a,b] and Katarína Kráľová[c]

[a]*Department of Analytical Chemistry, Faculty of Natural Sciences, Comenius University, Bratislava, Slovakia*

[b]*Department of Chemical Biology, Faculty of Science, Palacký University, Olomouc, Czech Republic*

[c]*Institute of Chemistry, Faculty of Natural Sciences, Comenius University, Bratislava, Slovakia*

1 Introduction

The green revolution over the period 1960–2000 pronouncedly contributed to the development of high-yield varieties of cereal grains and large increases in crop production (Evenson and Gollin, 2003; Den Herder et al., 2010). However, intensification of agriculture over the years was also accompanied by excessive use of fertilizers and pesticides and monoculture cropping of a few crop cultivars, which caused serious environmental problems, including the breakdown of resistance and the degradation of soil fertility, environmental pollution, and decline in biodiversity (Gahukar, 1992; Swaminathan, 2006; Kesavan and Malarvannan, 2010).

Therefore, there is a need for an evergreen revolution enabling to achieve productivity without causing ecological harm, which would be less dependent on chemical and more on biological inputs (Kesavan and Malarvannan, 2010), whereby using a sustainable intensification approach in agricultural systems increased yields without an adverse environmental impact and the conversion of additional nonagricultural land could be achieved (Pretty and Bharucha, 2014; Fraceto et al., 2016). Moreover, considering the ongoing climate change, increased attention could be devoted to improving crop tolerance to abiotic and biotic stresses (Jampílek and Kráľová, 2019a, 2021; Jampílek et al., 2020; Kráľová and Jampílek, 2021).

One of the ways to reduce fertilizer and pesticide doses, while maintaining the same effect, is to use them in the form of nanoparticles (NPs)/nanoformulations. The US National Nanotechnology Initiative (2004) defined nanotechnology in 2004 as "the understanding and control of matter at dimensions of roughly 1–100 nanometers, where unique phenomena enable novel applications." Hence, nanoscale materials showing the same chemical composition as microscale/bulk ones usually have

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different physical and chemical properties and also a distinct impact on the environment, including living organisms (Gupta and Xie, 2018; Jeevanandam et al., 2018; Pikula et al., 2020). Moreover, by using nanoscale formulations, the controlled release and targeted delivery of active ingredients can be achieved. Therefore, they are frequently used not only in agriculture as fertilizers, herbicides, insecticides, or fungicides (Jampílek and Kráľová, 2015, 2017a,b, 2018a, 2019a,b,c, 2020a,b; Jampílek et al., 2019a, 2020; Kráľová and Jampílek, 2021), but also in medicine (Jampílek and Kráľová, 2017c, 2018b, 2019d,e,f,g; Jampílek et al., 2019a,b,c), the food industry (Jampílek and Kráľová, 2015, 2018c; Jampílek et al., 2019a,c), or as adsorbents or catalysts (Jampílek and Kráľová, 2020c,d).

NPs can be taken up by roots, where they are adsorbed foremost at the root surface, followed by their uptake, and subsequently via inter/intracellular movements to achieve the plant tissues. On the other hand, at foliar treatment with NPs, these enter the plant through stomata, trichomes, and cuticles. A size exclusion limit of 40–50 nm was reported to be the main restriction for penetration of NPs into plant tissues, and NPs translocation and accumulation inside the cells (e.g., González-Melendi et al., 2008; Taylor et al., 2014); however, the uptake of NPs is also affected by the chemical nature and morphology of the applied NPs (Ma et al., 2010; Raliya et al., 2016). Depending on the chemical nature and applied NPs concentration, stimulation or inhibition of seed germination and plant development can be observed, whereby the response to NPs application also depends on individual plant species (Masarovičová et al., 2014; Jampílek and Kráľová, 2019a,b; Khan et al., 2019).

Metal-based NPs can be prepared via chemical ways or by green synthesis using extracts of plants or microorganisms as reducing and capping agents (Husen and Siddiqi, 2014; Singh et al., 2016; Kasana et al., 2017; Rafique et al., 2017), whereby the eco-friendly synthesis of NPs using plant extracts was found to have advantages over using bacteria and fungi (Al-Hakkani, 2020). The biological activity of phytosynthesized CuNPs and CuO NPs is usually higher compared to NPs prepared by chemical methods due to capping compounds on the NP surface, and therefore the use of such NPs is favorable not only in agricultural practice but also in the medicine or food industry. Plant leaf extracts that have been used for the phytosynthesis of CuNPs, CuO NPs, Cu_2O NPs, or copper quantum dots include, for example, *Arachis hypogaea* (Ramesh et al., 2011), *Moringa oleifera* (Das et al., 2020), *Curcuma longa* (Jayarambabu et al., 2020), *Mangifera indica* (Rani et al., 2020), *Psidium guajava* (Singh et al., 2019), *Camellia sinensis* (Ahmed et al., 2019), *Terminalia belerica* (Akhter et al., 2019), *Syzygium alternifolium* (Yugandhar et al., 2019), *Aloe vera* (Kumar et al., 2015), *Morus alba* (Singh et al., 2017), and *Vitis vinifera* (Angrasan and Subbaiya, 2014).

The beneficial effects of copper as an essential element for plant growth were described already in 1931 by Sommer (1931). On the other hand, by the end of the 19th century, Millardet found that the mixture of $CuSO_4$ with lime (popularly known as Bordeaux mixture) can be used for effective control of destructive fungal disease, the downy mildew of grapes (*Plasmopara viticola*) (Millardet, 1885), and the early history of copper fungicides was presented by Johnson (1935). Copper

bioavailability, uptake, toxicity, and tolerance in plants were overviewed by Shabbir et al. (2020) and Kumar et al. (2021).

The beneficial and adverse effects of nanoscale CuNPs, CuO NPs, and copper nanocompositions on plants were reported by many researchers (e.g., Keller et al., 2017; Masarovičová and Kráľová, 2013; Masarovičová et al., 2014; Jampílek and Kráľová, 2019a,b; Rai et al., 2018; Rajput et al., 2019a; Wu et al., 2020), and in the following sections the impact of these NPs on economically important food crops, including cereals and vegetables needed for healthy human nutrition, will be discussed in detail, with particular emphasis on wheat and rice, which provide the most global human per capita energy (526 and 544 kcal per capita) (Fogler, 2014).

However, nanosized Cu/CuO particles could also contribute indirectly to improved food crop yield when applied in plant protection management as insecticides, fungicides, or bactericides. Formulations of several metal-based NPs were reported to show significant insecticidal activity (Jampílek et al., 2020). The role of Cu and CuNPs in the management of insect-pests and pathogenic microbes was discussed by Rai et al. (2018). CuO NPs applied at low concentrations increased the expression of the exogenous gene encoding the *Bacillus thuringiensis* (Bt) toxin protein in leaves and roots of transgenic plants, thereby contributing to increased Bt cotton insect resistance (Van et al., 2016). CuNPs green synthesized using the leaf extract of *Prosopis juliflora* and *Pluchea sericea* showing sizes 33.8 and 68.10 nm and zeta potentials of − 69.7 mV for *P. juliflora* and − 53.9 mV for *P. sericea*, respectively, exhibited considerable toxicity against the cotton mealybug, *Phenacoccus solenopsis*, a major pest of cotton crops (Leon-Jimenez et al., 2019). CuO NPs were reported to exhibit a fast entomotoxic effect against the cotton leafworm (*Spodoptera littoralis*) with an LC_{50} of 232.75 mg/L after 3 days (Ayoub et al., 2018). CuO NPs phytofabricated using *Punica granatum* peels extract showed insecticidal activity against the green peach aphid (*Myzus persicae*) (Ghidan et al., 2016). CuO NPs which were applied in the artificial diet to the honeycomb moth *Galleria mellonella* induced some physiological changes in the protein, glycogen, and lipid content of the midgut and fat body of larvae (Sezer Tuncsoy and Ozalp, 2016). Investigation of trophic transfer of $Cu(OH)_2$ nanomaterials by tobacco hornworms (*Manduca sexta*) feeding on surface-treated tomato leaves showed that first-instar larvae were more susceptible to the toxicity of $Cu(OH)_2$ nanowire and commercial fungicide Kocide 3000 (containing as active ingredient nanoneedles of $Cu(OH)_2$NPs) than second-instar larvae (Li et al., 2019).

Plant diseases caused by harmful fungi and bacteria also represent a serious threat for crop development and yields and, in particular, plant pathogenic fungi cause great economic and ecological problems worldwide (Jampílek and Kráľová, 2015, 2017b, 2018a, 2020a,b; Pariona et al., 2019). The use of nanoscaled metal-based fungicides and bactericides in crop protection can significantly reduce the damages caused by these noxious pests, and due to the excellent antifungal and antibacterial properties of Cu, attention was also devoted to the use of Cu-based NPs in crop protection, for example, against *Fusarium* sp. (Bramhanwade et al., 2016; Kasana et al., 2016; Elmer et al., 2018; Pariona et al., 2019; Perez et al., 2020), *Alternaria* sp. (Banik and Perez-de-Luque, 2017; Sidhu et al., 2017; Quiterio-Gutierrez et al., 2019),

Curvularia sp. (Choudhary et al., 2017; Sidhu et al., 2017), *Phytophthora infestans* (Giannousi et al., 2013; Kasana et al., 2016), *Xanthomonas euvesicatoria* (Fan et al., 2021), *Rhizoctonia solani* (Vanti et al., 2020), *Pythium aphanidermatum* (Vanti et al., 2020), or *Pseudomonas syringae* (Banik and Perez-de-Luque, 2017).

The finding that excess Cu can modulate emissions of N_2O, which is a greenhouse gas, by soybean root nodules, causing a decrease of nitrate and nitrite reductase activities and simultaneously increasing nitrous oxide reductase activity, can be exploited in an effective strategy for N_2O mitigation (Tortosa et al., 2020).

This chapter presents a comprehensive overview focused on the impact of Cu-based NPs on economically important crops, including cereals, legumes, and some other important vegetables crucial for healthy human nutrition. The beneficial effect of Cu-based NPs used as fertilizers on the growth and development of crops is analyzed and the effectiveness of Cu-based NPs applied as nanoherbicides or nanofungicides and nanobactericides for crop protection and to control plant diseases is discussed. The benefits of green synthesized Cu-based NPs using plant extracts over those fabricated using chemical methods are outlined. Attention is devoted to the effects of particle size on the biological activity of Cu-based NPs and a comparison of their effectiveness with those of their bulk counterparts is performed as well. Mechanisms of action of Cu-based NPs, with particular emphasis on nano specific toxicity, are highlighted as well.

2 Copper as nutrient and toxicant

Micronutrients, e.g., B, Cu, Fe, Mn, Mo, Ni, and Zn, are involved in all metabolic and cellular functions. Some of them are redox-active and function as catalytically active cofactors in enzymes, whereas others have enzyme-activating functions or fulfill a structural role in stabilizing proteins (Haensch and Mendel, 2009). The involvement of micronutrients in plant metabolism, nutrient regulation, reproductive growth, chlorophyll (Chl) synthesis, production of carbohydrates, fruit and seed development, etc. ensures healthy development and growth of plants (Tripathi et al., 2015).

Copper is an essential nutrient for plants and in appropriate amount it is indispensable for normal plant development and growth. It plays crucial roles in photosynthetic and respiratory electron transport chains, in ethylene sensing, cell wall metabolism, oxidative stress protection, and biogenesis of the molybdenum cofactor (Yruela, 2009). Several enzymes, e.g., amine oxidase, catechol oxidase, hexose oxidase, indole 2,3-dioxygenase, L-ascorbate oxidase, laccase, polyphenol oxidase (PPO), superoxide dismutase (SOD), and tyrosinase, use copper as a cofactor in their catalysis (Maksymiecz, 1997; Yruela, 2005). Moreover, copper is a constituent of plastocyanine (PC), a carrier of photosynthetic electron transport (PET), which transfers electrons from the cytochrome b_6f (cyt b_6f) complex to P_{700}, the primary donor of photosystem (PS) I, whereby in the PSI-PC binding site the reduced electron carriers are situated in the lumen side of the PSI (Caspy et al., 2020). PC is a

β-sheet protein with a Cu atom acting as the redox center, which is coordinated to four amino acid residues [for structure of PC refer to Gross (2013)]. Copper is also a part of cytochrome oxidase (also known as complex IV), a transmembrane protein in the inner mitochondrial membrane, which is the terminal enzyme in the respiratory chain and reduces molecular oxygen to water (Mansilla et al., 2018). The structure of cytochrome oxidase in the inner mitochondrial membrane is shown in Cytochrome oxidase (2020). Consequently, Cu deficiency can alter essential functions in plant metabolism resulting in an adverse impact on plant growth (Yruela, 2009; Rehman et al., 2019). On the other hand, the uptake of some important nutrients such as Fe, Zn, Ca, and Mn can be inhibited by Cu (e.g., Amri et al., 2017; Roy et al., 2017; Hippler et al., 2018), resulting finally in impaired plant growth and yield.

Direct effects of copper resulting in the beneficial impact of Cu on crops such as improved germination and plant growth, improved photosynthesis, or enhanced production of valuable secondary metabolites could be obtained using Cu-based compounds such as nanopriming agents or fertilizers/nutrients, which could also pronouncedly contribute indirectly to healthy food crop growth and yield when applied as pesticides (herbicides, insecticides, fungicides, or bactericides) (Fig. 1). Moreover, the application of low concentrations of Cu, whether in bulk or a nano-sized form, can elicit the enhancement of defense responses reflected in the increase in ascorbate peroxidase (APX) expression (Valdes et al., 2020). On the other hand, excess copper has a detrimental impact on plants and is reflected mainly in the inhibition of germination, plant growth, Chl synthesis, photosynthesis, nutrient uptake and transpiration, induction of oxidative stress accompanied by the increased formation of reactive oxygen species (ROS), membrane damage, and genotoxicity (Fig. 2). Due to the fluctuation of environmental metal ion concentrations from low to high toxic levels, the plants evolved mechanisms to cope with such phenomena (DalCorso

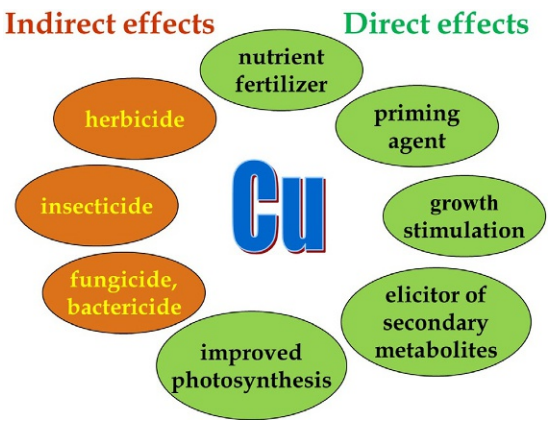

FIG. 1

Direct and indirect effects of copper improving growth, yield, and nutritional quality of crops.

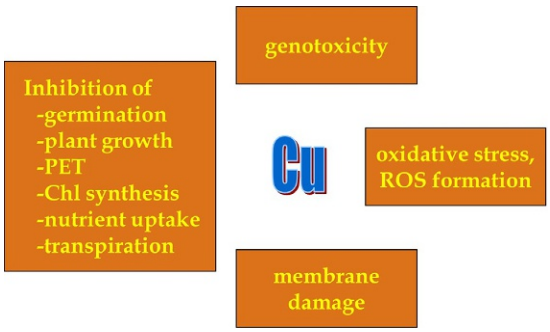

FIG. 2

Adverse effects of excess copper on crops.

et al., 2014). Hormesis, i.e., biphasic dose-response relationship at application of low and high doses of bioactive compounds (Agathokleous et al., 2020), was also observed at treatments of crops with bulk Cu (e.g., Li et al., 2020; Gomes et al., 2020).

The influence of high and low levels of metal ions such as Co, Cu, Fe, Mn, Mo, Ni, and Zn that are beneficial for plant growth and development on plants was analyzed by Arif et al. (2016) and Tolaymat et al. (2017). The adverse effects of metals on plants are reflected in the inhibition of germination, plant growth, Chl synthesis, photosynthesis, transpiration, membrane damage, and genotoxicity (e.g., Maksymiecz, 1997; Yruela, 2005; Masarovičová et al., 2010; Kráľová et al., 2019). Seneviratne et al. (2019) overviewed the findings related to heavy metal-induced oxidative stress on seed germination and seedling development, and the impact of excess Cu on the growth and physiology of important food crops was comprehensively discussed by Adrees et al. (2015). Copper accumulates primarily in roots and is characterized with low translocation from roots to shoots, whereby this translocation can be greatly improved in the presence of chelating compounds (e.g., Johnson et al., 2009; Yeh et al., 2015; Kráľová and Masarovičová, 2008). For example, ethylenediaminetetraacetic acid (EDTA) was able to enhance the Cu amount accumulated by plants allocated to the shoots of *Matricaria recutita* treated with 24 and 60 μmol/L EDTA to 45% and 59%, respectively, compared to 5.2% and 4.8%, respectively, observed in untreated plants. This extremely high translocation of Cu at EDTA application could be connected with the large value of the Cu-EDTA stability constant (log K_1 = 18.8) (Kráľová and Masarovičová, 2008). However, it could be emphasized that the accumulation of toxic metals in the edible parts of crops/plants used for food and feed in levels exceeding the permitted levels represents a risk due to the adverse impact on the health of humans and animals (Gall et al., 2015; Clemens and Ma, 2016).

2.1 Toxicity of Cu^{+}/Cu^{2+} ions and induction of oxidative stress

Copper is a transition metal that has two common oxidation numbers, Cu^{+} and Cu^{2+}. In an aqueous medium, Cu^{2+} shows higher stability than Cu^{+} due to the greater charge

density compared to the Cu^+ ion and consequently forms much stronger bonds releasing more energy. On the other hand, the Cu^+ ions are unstable in an aqueous solution and disproportionate to give Cu^{2+} and Cu.

Based on the classification of metals according to their ionic and covalent bonding tendencies and donor-atom preference of metals, Cu^{2+} belongs to the group of borderline (intermediate) metal ions (Nieboer et al., 1999) with its covalent index $(\chi_m)^2 r$ of 3.0 reflecting the relative ability of the metal to form covalent versus ionic bonds and ionic index (z^2/r) of 5.4 expressing an effective measure of ionic interactions (where z is the ion charge, χ_m is the Pauling electronegativity, and r is the ionic radius corresponding to the most common coordination number). Borderline metals (metal ions) are characterized by an ambivalent affinity for all three donor atoms, i.e., oxygen, nitrogen, and sulfur, in contrast to oxygen donor atom seekers belonging to metals of class A (e.g., macronutrients such as K^+ and Ca^{2+}) or nitrogen and sulfur seekers belonging to metals of class B (e.g., Hg^{2+}, Ag^+, Cu^+). Metal toxicity increases in the following order: type A < intermediate < type B.

As mentioned above, the toxic effects of Cu^+ and Cu^{2+} ions are predominantly connected with the induction of oxidative stress accompanied by the enhanced formation of ROS. Due to the one-electron difference between Cu^+ and Cu^{2+} or Cu^{2+} and Cu^{3+}, copper can stimulate radical reactions and under appropriate conditions, it can interact with superoxide radical ($O_2^{\bullet -}$):

$$Cu^{2+} + O_2^{\bullet -} \rightarrow Cu^+ + O_2$$

$$H^+ + Cu^+ + HOO^{\bullet} \rightarrow Cu^{2+} + H_2O_2$$

$$O_2^{\bullet -} + Cu^+ + H_2O \rightarrow Cu^{2+} + HO^- + HOO^-$$

Copper via changing its oxidation state catalyzes the conversion of two $O_2^{\bullet -}$ radicals and two H^+ to H_2O_2 and O_2 (Halliwell and Gutteridge, 2015).

The production of extremely toxic oxygen free radicals ($^{\bullet}OH$ and $^{\bullet}OOH$) catalyzed by copper ions (similarly to iron ions) results in oxidative stress causing damage to DNA, lipids, proteins, or other molecules (Halliwell and Gutteridge, 1984). To biologically relevant ROS belong superoxide anion radicals ($O_2^{\bullet -}$), hydroxyl radicals ($^{\bullet}OH$), singlet oxygen ($^1O_2$), and H_2O_2, whereby the primary ROS, $O_2^{\bullet -}$, is generated by the one-electron reduction of molecular oxygen catalyzed by nicotinamide adenine dinucleotide phosphate (NADPH) oxidase and further reduction of oxygen can result in either H_2O_2 or $^{\bullet}OH$ via dismutation, and the metal-catalyzed Fenton reaction, respectively (Manke et al., 2013; Fu et al., 2014). Due to oxidative stress, membrane damage resulting in electrolyte leaching, lipid peroxidation, protein denaturation, carbohydrate oxidation, pigment breakdown, an impairment of enzymatic activity and DNA damage are observed (Yruela, 2005; Pandey et al., 2009; Fu et al., 2014; Dutta et al., 2018; Mosa et al., 2018).

The adverse impact of Cu-induced oxidative stress on plant growth and yield was described by several researchers (e.g., Rastogi et al., 2017; Saleem et al., 2020). To mitigate the negative effects of Cu-induced oxidative stress, plants activate the

antioxidative defense systems resulting in enhanced activity of antioxidant enzymes such as SOD, catalase (CAT), peroxidase (POD), APX and increased content of non-enzymatic antioxidants such as glutathione (GSH) (e.g., Shaw and Hossain, 2013; Da Costa and Sharma, 2016; Yasmeen et al., 2017; Ogunkunle et al., 2018; Perez-Labrada et al., 2019). Moreover, metallothioneins and phytochelatins function as essential detoxifying components able to detoxify plants from poisoning with toxic metals (Cobbett, 2000; Panda et al., 2016; Rodrigo et al., 2016).

2.2 Impact of Cu^{2+} ions on plant photosynthetic apparatus

Copper ions are extremely toxic to the photosynthetic apparatus of algae and vascular plants (Maksymiecz, 1997; Yruela, 2005; Masarovičová et al., 2010; Kráľová et al., 2019). They inhibit photosynthetic electron transport (PET) and several sites of Cu^{2+} action in the PET chain were determined. In photosystem (PS) II, the researchers reported the site of Cu^{2+} action directly in protein D1 (Vavilin et al., 1995), between the redox active tyrosine Y_Z and primary electron donor of PSII, P_{680} (e.g., Renganathan and Bose, 1989), directly in Y_Z (Schröder et al., 1994), in both tyrosine intermediates, Y_Z and Y_D (Kráľová et al., 1994; Šeršeň et al., 1996, 1997), in the manganese cluster on the donor side of PSII (Kráľová et al., 1994; Šeršeň et al., 1996, 1997), in redox active quinones Q_A and Q_B on the acceptor side of PSI (Yruela et al., 1991, 1992, 1993), on both sides of PSII, namely in Y_Z and in Q_A and Q_B (Renger et al., 1993; Jegerschöld et al., 1995), in nonheme Fe^{2+} in PSII resulting in a displacement of iron ions (Jegerschöld et al., 1999), in cytochrome b_{559} in the PSII thylakoids (Burda et al., 2002, 2006) or in the antenna Chl of PSII (Lidon et al., 1993). The other researchers situated the site of Cu^{2+} action in PSI without precise localization (Bohner et al., 1980; Samuelsson and Öquist, 1980), in ferredoxin (Fd) on the acceptor side of PSI (Shoi et al., 1978) or in cytochrome *b* on the donor side of PSI (Singh and Singh, 1987). The abovementioned sites of Cu^{2+} action in the PET chain can be seen in Fig. 3. However, it could be mentioned that Cu^{2+} ions can also interact directly with the thylakoid membranes (Szalontai et al., 1999) and modify the lipid composition in PSII (Quartacci et al., 2000).

However, according to Lidon and Henriques (1991), the prevailing toxic effect of Cu in hydroponically cultivated rice (*Oryza sativa* L.) plants was reflected in the reduced activity of ribulose-1,5-bisphosphate carboxylase/oxygenase (Rubisco) resulting subsequently in a restriction of the overall photosynthetic activity and impaired Rubisco activity together with a considerable reduction of Chl ($a + b$) content after Cu application was observed in oats plants grown in the field (Moustakas et al., 1994). The adverse impact of Cu on the activity of chloroplast enzyme Rubisco and phosphoribulokinase in vitro could be explained by the inactivation of the thiol groups (Stiborová et al., 1986; Mysliwa-Kurdziel et al., 2004).

Cu^{2+} applied at a dose of 5 μM was found to inhibit the phosphoenolpyruvate carboxylase from maize in vivo and in vitro, while the same dose of Cu^{2+} showed a time-dependent activation of Rubisco from barley (Stiborová et al., 1986).

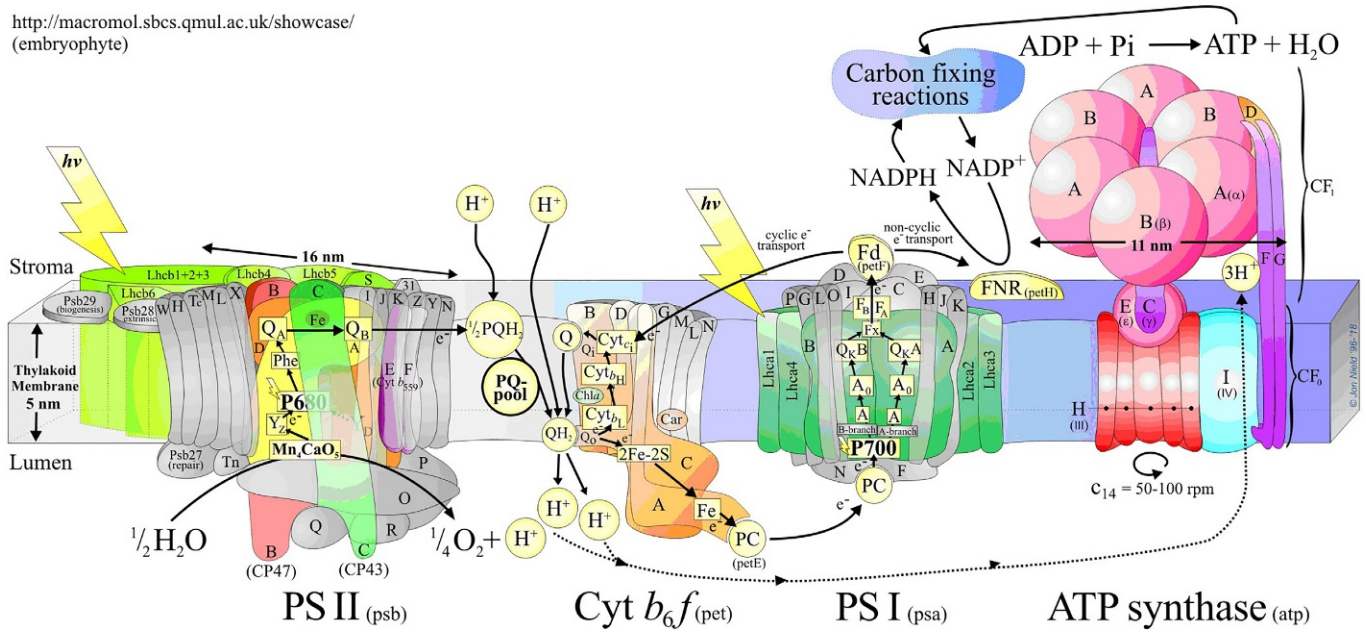

FIG. 3

Structures of photosystem II, complex cytochrome b_6f, photosystem I and ATP synthase.

Courtesy Jon Nield, Principal Research Fellow in the School of Biological and Chemical Sciences, The Queen Mary University of London.

Beneficial impacts on contents and activities of Rubisco and Rubisco activase, which were reduced by application of excess Cu to tobacco (*Nicotiana tabacum*) plants grown in vitro, were observed with the application of sodium nitroprusside [a nitric oxide (NO) donor], suggesting its protective role in the regulation of plant responses to toxic Cu levels (Khairy et al., 2016). Pronouncedly reduced values of the specific Rubisco activity due to the inhibition of de novo Rubisco synthesis were also observed in the leaves of three Slovak autochthonous oak species: *Quercus cerris* L., *Q. robur* L., and *Q. dalechampii* L. stemming from forest stands, which were exposed to acid rain as well as other pollution sources containing toxic metals, including Cu (Konečná et al., 1989). In a Cu-tolerant species, *Elsholtzia splendens*, exposed to 100 μM $CuSO_4$ for 3 and 6 days, the estimated leaf proteins were mainly degraded fragments of Rubisco and antioxidative protein (Li et al., 2009). A decline in Rubisco activity was also observed in *Salvinia natans* plants showing high metal accumulating capacity, including Cu, whereby its impaired photosynthetic potential was connected primarily with changes in the carbon assimilation efficiency and only minor variations in primary photochemical activities and photophosphorylation potential were observed (Dhir et al., 2011).

3 Impact of copper-based nanoparticles on cereals

Cereals are annual plants, generally of the gramineous family, yielding grains used for food, feed, seed, and industrial purposes, e.g., ethanol production, and it has been recommended that the denomination of "cereal crops" could be limited to crops harvested for dry grain only, excluding crops harvested green for forage, silage, grazing, etc. Besides, the dominant nutrient elements, i.e., carbohydrates, mainly starches, cereal crops, also contain a modest amount of protein and little fat and are characterized by low moisture content (FAO, 2020a).

Human consumption accounted for 78% of total rice production in 2009, compared with 64% for wheat and 14% for maize (Ricepedia, 2020). Wheat production and global cereal markets are expected to remain balanced and comfortable despite concerns about the impact of COVID-19 in 2020. The world forecast for cereal use for 2019–20 has risen slightly to 2722 million tons now, indicating an increase of 33 million tons (1.2%) from 2018 to 2019 (FAO 2020b).

3.1 *Triticum aestivum*

Wheat plays an outstanding role in feeding the human population and improving global food security because it contributes to c. 20% of the total dietary calories and proteins worldwide (Shiferaw et al., 2013). The FAO's world wheat production forecast for 2020 remains unchanged in April 2020, with preliminary expectations still indicating an output of 763 million tons, a comparable level to the outturn in 2019 (FAO 2020b).

In an experiment performed in agar media, CuNPs inhibited the growth of *Phaseolus radiatus* and *Triticum aestivum* plants showing the 2-d median effective concentrations of 335 and 570 mg/L, respectively, the mung bean being more sensitive to CuNPs than *T. aestivum*, whereby the toxic impact of CuNPs was due to the nano specific toxicity of NPs because the release of Cu^{2+} ions from CuNPs was negligible. Cu bioaccumulation increased with increasing CuNP concentration and agglomeration of particles was observed in the cells (Lee et al., 2008).

The biogeochemistry of Cu in the rooting zone of the plant was found to affect the impact of CuO NPs on crop production. *T. aestivum* cv. Dolores plants cultivated for 10 days in sand deficient in Fe, Zn, Mn, and Cu essential elements needed for optimum plant growth, which were supplemented with CuO NPs (0–300 mg Cu/kg), were characterized by increased root exudation at higher CuO NPs doses. The exudate contained 2-deoxymugineic acid (DMA), a Cu-complexing phytosiderophore contributing to the higher dissolution of the CuO NPs. At application of low doses in the dissolved CuO NPs, Cu-citrate complexes prevailed, while at high doses dominated the complexes with DMA. Moreover, at treatment of *T. aestivum* plants with CuO NPs, dose-dependent decreases in Fe, Ca, Mg, Mn, and K both in roots and shoots were observed (McManus et al., 2018). $Cu_2O/Cu(OH)_2$ NPs (2.11 ± 0.64 nm) coated with sulfated polysaccharides extracted from *Avicennia marina* leaves applied to the soil promoted the growth of wheat plants and enhanced the total Chl and carotenoids by 49.76% and 70%, respectively (Essa et al., 2020).

To evaluate the impact of the solubility of Cu-based NPs on Cu uptake and NP association with plant roots, Spielman-Sun et al. (2018) investigated hydroponically cultivated wheat seedlings, which were exposed to 1 mg/L Cu-based NPs showing different solubilities, namely CuO NPs, CuS NPs, and $Cu(OH)_2$ NPs, for 1 h and then transferred them to a Cu-free medium for 48 h. They found that in contrast to $Cu(OH)_2$ NPs characterized by higher solubility and showing a higher Cu uptake after 1 h of exposure, less soluble copper NPs, CuO NPs and CuS NPs were more persistent on the roots and were able to deliver Cu to plant leaves over the 48 h depuration period, suggesting that by tuning the solubility of NPs a long-term slow delivery of micronutrients to plants could be achieved.

A comparison of the effect of 15.6 μM CuNPs and an equivalent dose of Cu^{2+} on the root morphology, physiology, and gene transcription levels of wheat showed that treatment with CuNPs caused a decrease of the root growth rate by c. 60% but promoted the formation of lateral roots, likely due to the increased nitrogen uptake and auxin accumulation in lateral roots; however, only one gene was downregulated to about 50% of the control. On the other hand, exposure to Cu^{2+} resulted in the expression of four of the genes involved in the positive regulation of cell proliferation and negative regulation of programmed cell death decreased to 50% compared to control; a 2.17-fold increase in methane dicarboxylic aldehyde accumulation and a $> 50\%$ decrease in antioxidant enzyme activities compared to control indicated high oxidative stress. Induction of the synthesis of proline acting as an antioxidant induced by CuNPs, which was able to scavenge the excess ROS, contributed to the alleviation of oxidative stress (Zhang et al., 2018).

At the exposure of stress-tolerant wheat seedlings to CuNPs of 10 nm, the abundance of proteins related to photosynthesis and tetrapyrrole synthesis was decreased, resulting in reduced levels of assimilation pigments (Chl*a*, Chl*b*, total Chl), and consequently the rate of photosynthesis and carbon assimilation decreased as well. On the other hand, an abundance of proteins related to glycolysis and the tricarboxylic acid cycle was increased in the presence of CuO NPs, which attenuated the negative impact of CuO NPs on photosynthesis and plant growth (Yasmeen et al., 2018). Oxidative stress of wheat plants grown in sand and exposed to CuO NPs (< 50 nm) at a dose of 500 mg Cu/kg causing increased ROS generation was reflected in enhanced lipid peroxidation and oxidized glutathione in roots and decreased the Chl content in shoots, while higher POD and CAT activities were estimated in roots (Dimkpa et al., 2012). After 14 days of incubation of CuO NPs with wheat planted in the sand, their nominal sizes of < 50 nm increased to approx. 317 nm and their negative surface charge of − 27.0 mV was reduced by the presence of plants to − 19.8 mV. On the other hand, plants did not affect the surface charge of the CuO microparticles (MPs). Plant growth was found to increase dissolution of CuO NPs as well as CuO MPs in the sand from < 0.3 mg/kg to c. 1.0 mg/kg resulting in reduced wheat root length by approx. 60%. In wheat, plants treated with CuO NPs and CuO MPs Cu accumulated in the shoots in the form of CuO and Cu(I)-sulfur complexes. The NPs having a smaller particle size exhibited greater root toxicity (Dimkpa et al., 2013). Sharm and Uttam (2017) used nondestructive, sensitive, and advanced spectroscopic probes, laser-induced fluorescence, and attenuated total reflectance Fourier transform infrared spectroscopy to investigate the impact of CuO NPs (10–800 mg/L) on wheat seedlings and found that with the increasing CuO NPs concentration, a decrease of the Chl content and pronounced changes in the content and conformation of cell wall polysaccharides were observed; treatment with doses of 500–800 mg/L CuO NPs increased the pectin content as well. Moreover, an increase of the amide I and amide II contents and lignin content in the leaves as well as lipid peroxidation was estimated at an exposure of wheat seedlings to CuO NPs, and the overall results suggested a phytotoxic impact of CuO NPs on wheat seedlings.

Treatment of wheat seedlings with 0.01 g/L CuO NPs resulted in the improvement of germination capacity by 14.5% and a twofold increase in the root and stem length compared to the control. Application of 0.001–0.1 g/L of CuO NPs was able to inhibit *Alternaria solani* mycelium development and spore germination by 34%–50%, although treatment with $CuCl_2{\cdot}6H_2O$ was more efficient (Zakharova et al., 2019). On the other hand, CuO NPs which aged 28 days before wheat planting showed an increased toxic effect on plants reflected in the reduced maximal length of roots. On the other hand, in the rhizosphere soil, greater pH increase was observed at application of aged CuO NPs compared to fresh ones (0.6 pH units vs 0.4 pH units), which reduced the dissolution of CuO NPs and exudates from roots increased soluble Cu in pore water. $CaCl_2$ extractable Cu concentrations corresponding to the most soluble fractions of total soil Cu increased in the rhizosphere soil compared to bulk soil, from 1.8 to 6.2 mg/kg at exposure to fresh CuO NPs and from 3.4 to 5.4 mg/kg at treatment with aged CuNPs (Gao et al., 2018). The phytotoxicity of CuO NPs on germination

and growth of wheat could be efficiently reduced by the application of biochar, and the presence of the 3% wt biochar in the hydroponic culture system completely suppressed the adverse impact of CuO NPs on plant growth up to 500 mg/L CuO NPs. By the application of biochar, a 3.7–7.8- and 3.3–4.9-fold reduction in the Cu content of shoots and roots, respectively, could be achieved. The lower toxicity of CuO NPs to wheat seedlings was due to the reduced Cu^{2+} and CuO NPs entry into plant cells caused by the adsorption of Cu^{2+} and space shield by biochar (Sima et al., 2017).

Investigation of the impact of CuO NPs (0.8–63.5 g/L) on *Triticum vulgare* seedlings during 1–72 h showed that the number of dead cells in seedlings increased by 5%–15% compared to control; a 4.5–8.9-fold higher Cu uptake in the leaves and a 5–9.7-fold higher Cu uptake in roots were observed compared to control, whereby increased ROS levels in roots by 27.6% were estimated as well. Moreover, the addition of CuO NPs to the medium at doses of 3.2–63.5 g/L resulted in DNA fragmentation and a rise of the fragments < 3000 bp on 51.4%–62.8% (Korotkova et al., 2017).

Treatment of wheat plants grown in the sand with CuO NPs at doses > 10 mg Cu/kg caused inhibition of root elongation, root hair proliferation, and shortening of the zones of division and elongation, whereby epidermal cells in the compressed root tip showed an abnormal shape but a general increase in epidermal cell death was not estimated. Changes in root morphology due to the presence of CuO NPs were likely connected with the release of Cu from dissolution at the root surface. On the other hand, CuO NPs did not change the accumulation of NO required for root hair formation. Because the supply of exogenous indole-3-acetic acid (IAA) through the tryptophan metabolism by the root-colonizing bacterium, *Pseudomonas chlororaphis* O6, also results in the suppression of root elongation and proliferation of root hair formation, it could be assumed that the Cu levels achieved at the dissolution of the CuO NPs in the rhizosphere were able to modify IAA distribution resulting in root shortening, while permitted NO cell signaling to stimulate root hair proliferation (Adams et al., 2017).

Presowing soaking of wheat seeds in 0.5% and 1% solutions of nanocomposites consisting of citrate chelate NPs of Ag and Cu promoted the growth of leaves and mass accumulation of 6–7-day-old sprouts and resulted in the improved photochemistry efficiency of PSII and Rubisco activity in leaves leading to a pronounced rise in the intensity of photosynthetic processes. In a field experiment, the foliar treatment of wheat plants infected with mycoplasma *Acholeplasma laidlawii* using a 1% solution of this nanocomposite was able to suppress the adverse impact of mycoplasma resulting in a considerable increase in the percentage of full grains, while at foliar application of nanocomposite solution on intact wheat plants a weak phytotoxic effect was observed (Patyka et al., 2017).

Colonization of wheat roots by the bacterium *P. chlororaphis* O6 protected roots from growth inhibition at exposure to CuO NPs, although ROS accumulation in roots induced with CuO NPs was only slightly affected. However, the extent of expression of some genes associated with plant responses to stress induced by root exposure to CuO NPs as well as the levels of citric and malic acids chelating Cu^{2+} ions in

the rhizosphere solution were reduced by *P. chlororaphis* O6 bacterial colonization. Consequently, lower levels of soluble Cu in the rhizosphere solution and reduced Cu loads into leaves were observed (Wright et al., 2016).

Based on the proteomic and physiological analyses of wheat seeds exposed to 25 ppm CuNPs, it was found that they improved stress tolerance in wheat plants by increasing the number of proteins related to starch degradation, glycolysis and the tricarboxylic acid cycle, and in CuNP-treated wheat seeds, increased sugar content, SOD activity, and Cu content were estimated (Yasmeen et al., 2017). The investigation of the long-term impact of CuO NPs applied at doses of 50 and 500 mg/kg on wheat growth showed that the NPs inhibited the growth and development of grains, reduced pronouncedly the Fe and Zn content in grains, while increasing the Cu content by 18.84%–30.45% compared with the control. Moreover, treatment with CuO NPs resulted in reduced levels of the essential amino acids isoleucine, leucine, threonine, and histidine suggesting that CuO NPs affected the nutritional quality of wheat grains (Wang et al., 2019a).

3.2 *Oryza sativa*

Rice is the staple food of more than 3.5 billion people providing > 20% of their daily calories, whereby rice provided 19% of global human per capita energy and 13% of per capita protein in 2009. Although rice protein ranks high in nutritional quality among cereals, its protein content is modest (Ricepedia, 2020).

Da Costa and Sharma (2016) investigated the impact of CuO NPs on growth, morphology, photosynthesis, and antioxidant response in *Oryza sativa* and found that higher CuO NPs concentrations inhibited the germination rate, root and shoot length, and biomass of rice. CuO NPs accumulation in the cells, especially in the chloroplasts, and a lower number of thylakoids per granum were estimated. Increased levels of malondialdehyde (MDA) and proline and elevated expression of APX and SOD suggested CuO NPs-induced oxidative stress in rice plants. With increasing CuO NPs concentration, the photosynthetic rate, transpiration rate, stomatal conductance, maximal quantum yield of PSII photochemistry, and Chl contents showed a decrease, whereby at 1000 mg CuO NPs/L complete loss of PSII photochemical quenching was observed.

Peng et al. (2017) investigated the fate and transformation of CuO NPs in the soil-rice system during the life cycle of rice plants and found that exposure of plants at the maturation stage to 1000 mg/kg of CuO NPs pronouncedly reduced the redox potential by 202.75 mV but enhanced electrical conductivity by 497.07 mS/cm compared to controls. It was observed that at application of high CuO NPs concentration, the plant growth was accompanied by the reduction of CuO NPs bioavailability in the soil; however, after drying-wetting cycles, it showed a considerable increase. The higher adverse impact of CuO NPs on plant growth compared to bulk CuO particles was reflected in a strong decline of the fresh weight of grains (up to 6.51% of controls). CuO NPs were translocated from the soil to the chaff and stimulated the Cu accumulation in the aleurone layer of rice but could not reach the polished rice.

The germination percentage of rice seeds was pronouncedly reduced under stress induced by CuO NPs (< 50 nm particle size), root cells lost viability, and a decline in carotenoid levels was observed as well. In a 7- and 14-day experiment, it was shown that despite considerable increase of APX activity at treatment with 1.0 and 1.5 mM CuO NPs, the scavenging of all H_2O_2 produced due to CuO NP-induced stress did not occur, and even an increase in glutathione reductase (GR) activity, increased ratio of GSH in its reduced and oxidized state (GSH/GSSG), and proline accumulation did not provide sufficient protection against oxidative stress-induced damages (Shaw and Hossain, 2013).

On the other hand, a beneficial impact on the germination and growth parameters of rice seedlings was observed at treatment of discolored paddy seeds with 7 µg/mL of citrate capped CuS nanoformulation for 2 h, which also ensured a considerable reduction in seed rot and seedling blight (Sidhu et al., 2017). Rice seedlings exposed to 5, 10, 20, and 50 µM CuO NPs showed improved growth reflected in a higher fresh and dry weight and length, higher levels of total Chl, carotenoids, and protein contents, increased Chl*a* fluorescence parameters such as PSII maximum quantum yield (F_v/F_m) and photochemical quenching (qP) as well as higher amounts of Ca, Mg, Na, and K. On the other hand, treatment with doses of 100, 200, and 500 µM of CuO NPs was found to be phytotoxic due to the enhanced accumulation of Cu and oxidative stress (Tiwari et al., 2019).

High CuO NPs concentrations (50 and 100 mg/L) attenuated the adverse effect of 10 mg/kg of As on the number of root branches of rice seedlings (Liu et al., 2018a). Treatment with CuO NPs improved the Cu uptake in rice seedlings and seedling growth in the presence of As, and the interaction of CuO NPs and As affected the mature plant dry biomass, panicle number, panicle emergence, total grain weight, average grain weight, and several other panicle parameters, whereby CuO NPs reduced the As accumulation in dehusked grains. It was stated that the accelerated heading stage by CuO NPs may contribute to a shortening of the life cycle of rice plants, thereby reducing the As accumulation in grains (Liu et al., 2018b). The combined application of 1 mg/L As(V) with 100 mg/L CuO NPs to hydroponically cultivated rice plants resulted in a 45% reduction of As(V) in roots, while the combined application of As(III) or As(V) with CuO NPs reduced the Cu concentration in roots of *Oryza sativa* L. by 40% and 50%, respectively, but did not affect the Cu content in rice roots when Cu(II) was used. Consequently, it could be stated that the interactions between As and Cu were significantly affected by the initial oxidation state of As (Wang et al., 2019b). Liu et al. (2018c) overviewed the environmental behavior and phytotoxicity of CuO NPs and As, including the interaction of CuO NPs with As in the environment.

3.3 *Zea mays*

Maize (*Zea mays* L.) is the third leading crop of the world after rice and wheat. It is a source of nutrition as well as phytochemical compounds. The maize kernel contains several vitamins (C, E, K, B1, B2, B3, B5, B6, and B9 (folic acid)), Se, and K, which is usually deficient in an average human diet (Shah et al., 2016).

In maize plants cultivated in soil for 42 days and exposed to CuO NPs at a dose of 500 mg Cu/kg, the observed plant growth inhibition was slightly weaker compared to $CuSO_4$, Cu accumulated in roots with minor translocation to shoots, enzyme activities on the rhizoplane were slightly inhibited by CuO NPs, and they were positively related to soil pH and negatively correlated with diethylenetriaminepentaacetic acid (DTPA)-extractable and exchangeable Cu. It was found that the toxicity of CuO NPs to plants and microbes predominantly depended on the gradually released bioavailable Cu (Pu et al., 2019).

Maize root exudates pronouncedly inhibited CuO NPs aggregation regardless of the ionic strength and electrolyte type, and the critical coagulation concentration of CuO NPs in the presence of NaCl increased from 30 to 125 mM, while in the presence of $CaCl_2$ it increased from 4 to 20 mM. The greater impact on the reduction of aggregation exhibited a higher molecular weight (MW) fraction (> 10 kDa) of root exudates, while the lower MW fraction (< 3 kDa) of root exudates mostly stimulated the CuO NP dissolution. Cu accumulation in plant root tissues was enhanced with root exudates. Root exudates were found to increase Cu accumulation in maize roots and enhanced CuO NPs toxicity for *Zea mays* plants (Shang et al., 2019).

A dose of 150 and 200 mg/L CuO NPs showing a size < 50 nm and a surface area of 29 m^2/g completely inhibited the germination of maize seeds and treatment with 100 mg/L CuO NPs showed similar or greater toxicity than 150 and 200 mg/L Cu in bulk form. In 8 days of experiment, both CuO NPs and bulk CuO particles considerably suppressed photosynthetic pigments, shoot and root lengths of maize plants, and increased soluble proteins and total antioxidants in a dose-dependent manner achieving c. 200% of control at treatment with 150 mg/L CuO and approx. 200%–300% of control at exposure to 100 mg/L CuO NPs; reducing power activity increased fourfold compared to control at application of 150 mg/L CuO and 100 mg/L CuO NPs, respectively. Moreover, at 100 mg/L CuO NPs, an eightfold increase of SOD compared with control was observed (El-Shazoly and Amro, 2019).

Foliar treatment of 3-week-old maize plants lasting 7 days with 100 mg $Cu(OH)_2$ NPs resulted in considerably reduced Chl content and biomass up to 17%–20%, upregulation of K and P by 14% and 13%, respectively, a pronounced increase of gene expression of POD1 and glutathione *S*-transferase (GST) 1 by 42.6% and 71.8%, respectively, and elevated levels (by 24%–122%) of phenylalanine, tyrosine, 4-hydroxycinnamic acid, and the total phenolic content suggested the essential role of phenolic acids in antioxidant defense (Zhao et al., 2017a).

Maize plants exposed to CuNPs (< 50 nm) in hydroponium or via foliar application increased the plant growth by 51% compared to control suggesting that they can enter the plant cells through the roots and leaves as well. Both ways of application of CuNPs had a pronounced impact on the activity of glucose-6-phosphate dehydrogenase and it was found that CuNPs affected the pentose phosphate pathway of maize plants. At application of increasing CuNP concentration, the bioaccumulation showed an increase and agglomeration of particles was observed in the cells (Adhikari et al., 2016).

Although CuO NPs did not affect maize seed germination, their phytotoxic effect at doses of 25–2000 mg/L on maize plants was found to be concentration-dependent and was connected mainly with the nano specific toxicity, and application of the highest tested Cu concentration resulted in 95.73% inhibition of root elongation (Yang et al., 2015).

Treatment of maize plants with Cu-chitosan (CS) NPs stimulated Chl synthesis and some production characteristics such as plant height, stem diameter, root length, and root number in pot experiments, while in a field experiment increased plant height, ear length, ear weight/plot, grain yield/plot, and 100 grain weight were observed. Moreover, Cu-CS NPs were able to control the *Curvularia* leaf spot disease of maize by mimicking the natural elicitation of the plant defense and antioxidant system for disease protection reflected in higher activities of SOD and POD and defense enzymes PPO and phenylalanine ammonia-lyase (PAL) (Choudhary et al., 2017). Exposure to 0.04%–0.12% Cu-CS NPs enhanced germination percentage, shoot and root length, root number, seedling length, fresh and dry weight, and seed vigor index of maize as compared to water, $CuSO_4$, and bulk CS treatments and induced the activities of α-amylase and protease enzymes accompanied by decreased starch and protein contents in germinating seeds. It could be suggested that the growth-stimulating effect of Cu-CS NPs was connected with their ability to mobilize the reserved food, primarily starch, through the higher activity of α-amylase. Moreover, a beneficial effect of Cu-CS NPs on seedling growth was also reflected in 16-fold higher Cu-CS NP concentration causing a growth inhibition of maize seedlings compared to $CuSO_4$ (0.16% vs 0.01%) (Saharan et al., 2016).

3.4 *Hordeum vulgare*

Barley (*Hordeum vulgare* L.) is the fourth most important cereal crop of the world after wheat, maize, and rice. It is of major commercial importance as a cereal grain used as fodder crop and for malting in beer and whiskey production (Vasanthan and Hoover, 2009).

In soils freshly spiked with various Cu compounds, the toxicity to barley measured with seedling root elongation decreased in the following order: $Cu(OAc)_2$ > CuO NPs > bulk CuO, and in soils aged for 90 days the differences in toxicity among tested compounds became smaller (Qiu and Smolders, 2017).

High CuO NPs concentrations showed toxic effects on the ultrastructure of chloroplasts, plastoglobules, and starch granules of hydroponically cultivated barley plants, which were reflected in lower counts of plastoglobule and starch granule in chloroplast and increased size of plastoglobule and chloroplast compared to control, whereby swollen starch granules and scattered thylakoids were estimated as well (Rajput et al., 2019b). The CuO NPs were reported to inhibit the germination rate, root and shoot lengths, maximal quantum yield of PSII, and transpiration rate of hydroponically cultivated barley plants, and they also affected stomatal aperture, root morphology and metaxylem size, and caused changes in cellular organelles, plastoglobules, starch granules, protoplasm, and membranes, whereby the formation of

electron-dense materials in the intercellular space of cells of CuO NPs-treated plants was estimated as well. Exposure to CuO NPs also pronouncedly enhanced the Cu contents of plant roots and shoots, which were 5.7- and 6.4-folds higher than those observed in control plants (Rajput et al., 2018). Treatment of barley plants with CuO NPs (< 50 nm; 0.5–1.5 mM) showed a dose-dependent decrease in shoot and root growth and a pronounced reduction of the performance index parameter irrespective of the stress level. Under CuO NP-induced stress lasting 10 or 20 days, the increased flavonol level and APX activity were not able to reduce H_2O_2 levels and impaired collaborative action of dehydroascorbate reductase and monodehydroascorbate reductase (MDHR) in treated leaves, resulting in an impaired ability for efficient enzymatic recycling of dehydroascorbic acid into ascorbic acid. Moreover, CuO NPs treatment caused a pronounced reduction in the GSH/GSSG ratio and increased GR activity in barley leaves treated with 1.0 and 1.5 mM CuO NPs was not able to protect the seedlings from oxidative damages (Shaw et al., 2014).

Presowing treatment of barley seeds with zerovalent CuNPs introduced in a mixture of Na-carboxymethyl cellulose and polyethylene glycol (PEG) 400 polymers increased the germination rate and sprout ability, the green mass and root mass of plants, whereby an increase in grain yield by 4.1% and a 2.2% decrease in moisture content in comparison with the control moisture content was observed (Olkhovskaya et al., 2019).

3.5 *Sorghum bicolor*

Sorghum (*Sorghum bicolor*) is a grass species cultivated for its grain, which is used for food for humans, animal feed, and ethanol production. Due to its great drought tolerance, it is a predominant cereal grain in semiarid regions of the world (Rooney, 2016). Treatment of *S. bicolor* L. and *Vigna unguiculata* L. seedlings with CuO NPs showing sizes < 100 nm using a dose of 750 mg/kg of seed improved germination, while application of 1250 mg of CuO NPs/kg seed resulted in reduced seed germination (Maity et al., 2018). The growth of the sorghum seedlings supplemented with 1 ppm CuNPs and Cu^{2+} pronouncedly decreased compared to control, CuNPs being more toxic than Cu^{2+}. Both CuNPs and Cu^{2+} decreased the specific activity of oxalate oxidase and H_2O_2 content but increased total oxalate content in shoots harvested at day 10 of germination, suggesting decreased oxalate oxidase activity in plants treated with CuNPs and Cu^{2+} (Aggarwal et al., 2020).

3.6 *Eleusine coracana* Gaertn

Finger millet (*Eleusine coracana* Gaertn.) is a cereal crop grown in the arid and semiarid areas of Africa and Asia. It contains a very high Ca content and is rich in iron and fiber, whereby its energy content is better than that of other cereals (Gupta et al., 2017). Finger millet plants treated with Cu-CS NPs, either foliar or via combined application (seed coat and foliar spray), were characterized by improved growth and increased yield, whereby at application of the combined method not only yield increase

of approx. 89% achieved, but also approx. 75% protection of treated plants against *Pyricularia grisea* pathogen was observed compared to infected control plants. The suppression of blast disease was connected with increased levels of defense enzymes in finger millet plants treated with Cu-CS NPs (Sathiyabama and Manikandan, 2018).

4 Impact of copper-based nanoparticles on vegetables

Vegetables play an important role in providing essential vitamins, minerals, and dietary fiber to the world feeding populations in both developed and developing countries. The FAO estimated that the world production of vegetables over 3 years (1993–95) was 489 million tons (FAO, 2003).

4.1 Legumes

Legume refers to any plant from the *Fabaceae* family that would include its leaves, stems, and pods, while a pulse is an edible seed from a legume plant. Considering the importance of pulses in food production and nutritional diversity in the effort to eradicate hunger and malnutrition, the 68th UN General Assembly declared 2016 the International Year of Pulses under the banner "nutritious seeds for a sustainable future" (UN General Assembly, 2014; Foyer et al., 2016). Grain legumes have an inherent capacity for symbiotic atmospheric nitrogen fixation, thus reducing the application of nitrogen fertilizers (Foyer et al., 2016). They provide fiber, protein, carbohydrate, B vitamins, Fe, Cu, Mg, Mn, Zn, and P (Polak et al., 2015).

4.1.1 Glycine max

The most widely planted and highest-yielding grain legume is soybean (*Glycine max* L.), which is one of the five major crops (Foyer et al., 2016). Its seeds are a source of protein, oil, and nutraceuticals and due to the content of the isoflavones and folic acid, soybean can be used for healthy food applications (Tidke et al., 2015).

Treatment of soybean seeds with CuNPs stimulated the germination rate and the growth of primary roots and enhanced the root mitotic index compared to control, while the growth of primary leaves during the first 60 h was not affected (Hoe et al., 2018). Mustafa and Komatsu (2017) in their review paper discussed the soybean response mechanism at the morphological, physiological, and proteomic levels mediated by engineered metal-based NPs, including CuO NPs. In a laboratory experiment, an increase in the germination rate of soybean (Vietnamese species DT-51) seeds treated with zerovalent nanocrystalline Cu powder was estimated compared to control (65% vs 55%), while in the field experiment increases in the Chl index and the number of nodules and increased crop yield up to 16% were observed when compared with control plants (Ngo et al., 2014).

Exposure of *Glycine max* L. grown in a half-strength Murashige and Skoog (MS) medium supplemented with 500 mg/L of CuO NPs pronouncedly reduced the shoot growth, weight, and total Chl content, while considerably higher H_2O_2 levels, POD activity, and lignin contents in roots were observed already from the concentration

of 100 mg/L, and ROS generation in roots and lignification of root cells showed a concentration-dependent increase. Upregulation in the expression levels of POD2, POD4, and POD7 genes in the presence of CuO NPs was estimated as well (Nair and Chung, 2014).

Application of the mixed ZnO NPs (2 mg Zn/kg), CuO NPs (1 mg Cu/kg), and B (1 mg B/kg) in soil specifically promoted shoot growth (47%), flower formation (63%), shoot biomass (34%), shoot N (53%) and K (42%) accumulation in *Glycine max* plants, while omission of individual elements from the mixtures evoked significant responses of soybean plants. Based on the comparison with the effects achieved with the mixture of respective bulk metal oxides, it was found that nanoscale microelements played a more significant role in evoking plant responses than did the bulk microelements (Dimkpa et al., 2019).

4.1.2 *Phaseolus vulgaris, Vigna radiata, Vigna unguiculata*

The common bean (*Phaseolus vulgaris* L.) is a nutritionally and economically important food crop providing nutrients including carbohydrates, elevated levels of proteins, dietary fiber, minerals, and vitamins as well as various polyphenolic compounds (Hayat et al., 2014). The mung bean (*Vigna radiata* L.) contains elevated protein levels (14.6–33.0 g/100 g) and Fe (5.9–7.6 mg/100 g), antioxidants such as polyphenols and carotenoids, and fiber (Dahiya et al., 2015), and the cowpea (*Vigna unguiculata* L.) is considered as an important nutritional food due to enhanced levels of high-quality plant proteins and carbohydrates, relatively low fat content, and a complementary amino acid pattern (Jayathilake et al., 2018).

Seeds of *P. vulgaris* plants cultivated to maturity (90 days) in soil amended with CuNPs (50 or 100 mg/kg) showed enhanced Cu accumulation and a pronouncedly lower Fe content compared with untreated seeds, and at combined treatment of bean plants with 100 mg/kg of CuNPs and 10 μM of kinetin, a 11.6% reduction in Mg content was observed (Apodaca et al., 2018). The growth of roots in green bean was inhibited by 46%, while the growth of shoot was stimulated due to exposure to CuO NPs (Bai et al., 2020).

Polymer-encapsulated CuNPs improved PET, photophosphorylation, and the carbon assimilatory pathway in mung bean chloroplasts, and in CuNPs-treated plants higher pigment contents and activities of antioxidant enzymes as well as elevated nitrogen assimilation were observed compared to plants exposed to $CuSO_4$ (Pradhan et al., 2015). *Vigna radiata* L. seedlings cultivated for 21 days in a half-strength MS medium supplemented with 200 and 500 mg/L CuO NPs pronouncedly reduced the shoot length and biomass, while a considerable reduction in root length and biomass was observed at exposure to 20–500 mg/L CuO NPs. Application of 100, 200, and 500 mg/L CuNPs resulted in a pronounced reduction of total Chl content and a considerable increase in proline content, although without a significant impact on carotenoid levels. At exposure to CuNPs (20–500 mg/L), a concentration-dependent increase in ROS generation in roots was observed and a pronounced increase in H_2O_2 content and lipid peroxidation in roots was estimated for treatment with CuO NPs ranging from 100 to 500 mg/L, which was accompanied by modulations in

the expression of SOD, CAT, and APX genes. Excess lignification of CuNP-treated mung bean root cells was estimated as well (Nair et al., 2014). The 2-d median effective concentration for mung bean exposed to CuNPs using a plant agar test was estimated at 335 mg/L, whereby increasing concentration of CuNPs resulted in enhanced bioaccumulation, and agglomeration of particles in the cells. For toxic effects of CuNPs, nonspecific toxicity was found to be responsible (Lee et al., 2008).

Vigna unguiculata (cowpea) plants exposed to CuNPs (25 nm or 60–80 nm) at doses of 125–1000 mg/kg for 65 days showed higher APX and GR activities in leaves and roots compared to control, and increased CAT activity in roots but reduced SOD activity in both leaves and roots, suggesting an organ-specific response of antioxidant enzymes to CuNPs. Application of 25 nm CuNPs at doses of 500–1000 mg/kg increased the MDA content in leaves by c. 8.4%, while at treatment with 60–80 nm of CuNPs a 52.8% increase of MDA levels in roots was estimated. Moreover, increased Cu bioaccumulation in seeds of treated plants by at least 250% was observed (Ogunkunle et al., 2018).

4.1.3 Pisum sativum, Cajanus cajan

The common pea (*Pisum sativum* L.) has a similar protein structure to *Glycine max* resulting in similar functional properties; however, it contains fewer allergenic factors than soybean and from the nutritional aspect, it could be an effective soybean substitute (Fischer et al., 2020). The nutritional bioactive compounds and other health benefits of the pigeon pea (*Cajanus cajan* L.) were overviewed by Talari and Shakappa (2018). Increased Fe levels in seeds by 42% were estimated when *P. sativum* plants were cultivated in soil amended with 100 mg/kg of CuO NPs and 100 μM IAA, while the coapplication of 50 mg/kg of CuO NPs and 100 μM IAA reduced the boron content and coapplication of CuO NPs with 10 μM IAA did not affect the production or nutritional quality of *P. sativum* seeds (Ochoa et al., 2018). *P. sativum* plants grown to full maturity in soil amended with CuO NPs (10–100 nm) at a dose of 50 mg/kg increased the pod Fe and Ni contents by 258% and 325%, respectively; however, the exogenous application of IAA (10 and 100 μM) combined with CuO NPs reduced the number of plants and pod biomass (Ochoa et al., 2017). Treatment of pigeon pea plants with 20 ppm of CuNPs with sizes 20–30 nm pronouncedly increased the height, root length, fresh and dry weight, and performance index of seedlings due to the growth stimulating activity of CuNPs (Shende et al., 2017).

4.1.4 Arachis hypogaea

The peanut (*Arachis hypogaea* L.) is one of the most widely consumed proteins and energy-rich legumes globally containing phytonutrients such as resveratrol, isoflavonoids, phenolic acids, and phytosterols (Toomer, 2018). Rui et al. (2018) studied the impact of CuO NPs applied at doses of 50 and 500 mg/kg on peanuts in a full life cycle study (145 days). Application of 500 mg/kg of CuO NPs reduced the fresh shoot biomass and 1000-grain weight by 44% and 31%, respectively, as compared to the control and treatment with 50 and 500 mg/kg of CuO NPs caused a 36.2% and 21.1% reduction in the total amino acid content, while in grains of plants treated with these

CuNPs doses the resveratrol content increased to 1.8 and 2.3 mg/kg, respectively, and Cu contents in grains increased in a dose-dependent manner suggesting that CuO NPs could alter the peanut crop yield and its nutritional quality. Suresh et al. (2016) used Fourier-transform infrared spectroscopy (FTIR) and multivariate analysis to study the potential variation in biochemical constituents of peanut plant leaves affected by presoaking peanut seeds in the suspension of CuO NPs and bulk CuO. Principal component analysis (PCA) carried out to explain the total variance in the secondary structure of protein content in peanut plant leaves showed that principal component 1 (PC1) accounted for 63.50% variation in the secondary structure of a protein, whereas principal component 2 (PC2) accounted for 29.56%. However, presoaking of seeds with CuNP suspension did not pronouncedly affect the growth of plants.

4.1.5 *Cicer arietinum*

Chickpea (*Cicer arietinum* L.) is an important pulse crop containing besides carbohydrates and proteins of high quality all essential amino acids (except sulfur-containing amino acids), dietary fibers and it is rich in linoleic and oleic acids as well as important vitamins such as riboflavin, niacin, thiamin, folate and the vitamin A precursor, β-carotene (Jukanti et al., 2012). In an in vivo experiment, the CS-Cu NPs applied at a dose of 100 μg/mL to potted chickpea (*Cicer arietinum* L.) plants infested with *Fusarium oxysporum* f. sp. *ciceri* reduced the disease by 46.67% and stimulated the growth of plants as compared to untreated plants (Kaur et al., 2018). A dispersion of CuNP-grown carbon nanofibers showing a size of 95 nm and enabling controlled release of the CuNPs was dispersed in *Cicer arietinum* seed-containing water by Ashfaq et al. (2017). A pronouncedly enhanced water uptake capacity, germination rate, shoot and root lengths, and Chl and protein contents as well as effective translocation of CuNPs from the root to the shoot of the plants were observed in the plants treated with this nanoformulation. In the chickpea seedlings grown in a half-strength MS medium supplemented with CuO NPs (50–500 mg/L) reduced shoot and root growth, high ROS generation and high lipid peroxidation level were observed accompanied by increases in POD enzyme activity and lignin content. CuO NPs increased the number of xylem vessels and enhanced their lignification. Considerable upregulation of the CuZn-SOD gene at exposure to CuO NPs was observed only in roots, while the expression of the CAT gene was pronouncedly high under 50, 100, and 200 mg/L of CuO NPs, and the expression levels of the APX gene in plant organs were not affected (Nair and Chung, 2015a).

4.2 Gourds

Gourd is occasionally used to describe crop plants like pumpkins or cucumbers in the family *Cucurbitaceae*.

4.2.1 *Cucumis sativus*

Cucumber (*Cucumis sativus* L.) belonging to the family *Cucurbitaceae* is consumed in different ways like vegetable and salads and contains various phytochemicals having pharmacological activities such as tannins, cardiac glycosides, terpenoids,

carbohydrates, resins, saponins, and phytosterols, and cucumber fruits contain alkaloids, flavonoids, glycosides, steroidal terpenes, and phyllobatamines (Sahu and Sahu, 2015).

At the exposure of cucumber plants to nanoscale Cu pesticide, dose-dependent changes in concentrations of antioxidants were estimated, whereby 10 antioxidants were pronouncedly depleted at ROS scavenging and protecting plants from oxidative damage, while levels of a further 3 antioxidants were upregulated, signaling activation of the defense system (Huang et al., 2019). On the other hand, CuNPs can activate physiological and biochemical processes during seed germination and when applied at concentrations of 0.1–10 g/ha could function as regulators of the cucumber sprouts growth and development (Polischuk et al., 2018).

In cucumber plants exposed to CuNPs (200–800 mg/kg soil) and harvested in 60 days, 13 amino acids were upregulated (tyrosine level increased even 11.0-fold after exposure to 800 mg/kg of CuNPs) suggesting an active defense response of the cucumber plants to CuNP-induced stress (Huang et al., 2018). Exposure of hydroponically cultivated cucumber plants to CuNPs (10–30 nm) adversely affected plant biomass and reduced levels of Chl*a* and Chl*b* in a concentration-dependent manner, caused damage to the root plasma membrane resulting in enhanced electrolyte leakage as well as a considerable rise in H_2O_2 and MDA contents. Treatment with CuNPs also induced Cu-Zn SOD gene expression and caused genomic alterations in *C. sativus*, whereby Cu accumulated predominantly in roots (Mosa et al., 2018). Exposure of cucumber plants at early development stages cultivated in hydroponium to 10 and 20 mg/L of CuNPs affected the uptake of some micro- and macronutrients (e.g., Na, P, S, Mo, Zn, and Fe), and considerable metabolic changes in leaves and root exudates were observed. An active defense mechanism against CuNP-induced stress performed by the root exudates metabolic changes resulted in sequestration/exclusion of Cu/CuNPs due to the upregulation of amino acids, while reduced mobilization of Cu ions was achieved by downregulation of citric acid; ROS suppression was reached by ascorbic acid upregulation, and upregulation of phenolic compounds improved the antioxidant system (Zhao et al., 2016a). Exposure of cucumber plants to CuNPs caused the perturbation of Fe uptake in leaves, while treatment with 400 and 800 mg/kg of CuNPs resulted in enhanced Ca, K, S, P, Zn and Mg levels in fruits. Due to treatment with CuNPs, proline, glycine, valine, pelargonic acid, arachidic acid, xylose, and benzoic acid were upregulated, while citric acid, myo-inositol, ornithine, and 1-kestose were downregulated, whereby the galactose metabolism and the tricarboxylic acid cycle were mainly changed, suggesting that C and N metabolism was perturbed by CuNPs (Zhao et al., 2016b). *Cucumis sativus* L. seedlings grown in a semisolid half-strength MS medium supplemented with 50–500 mg/L of CuO NPs for 15 days were characterized with a pronouncedly reduced shoot and root growth and biomass, increased xylogenesis, lignin content, and reduced mitochondrial membrane potential. Exposure to CuNPs resulted in a concentration-dependent increase in ROS generation and MDA levels, and considerable modulation in the expression of genes related to oxidative stress and lignin biosynthesis (Nair and Chung, 2015b).

In contrast to Cu^{2+} ions, which caused leaf chlorosis symptoms in cucumber plants cultivated in artificial media, $Cu(OH)_2$ nanopesticide did not affect the photosynthetic pigment production; however, its foliar application induced considerable changes in the mRNA levels of antioxidant and detoxification-related genes: SOD, glutathione peroxidase (GPX), GPX4, MDAR, POD, and WRKY6 were upregulated, while cytosolic APX (cAPX) was downregulated and decreased transcript production of a stress-related gene (DNAJ) was observed as well. Similar results were also obtained with $CuSO_4$ application suggesting that most of the responses were due to the released Cu^{2+} ions (Zhao et al., 2017b). CuO NPs were found to cause a much stronger inhibition of cucumber root elongation than bulk CuO. Using SELDI-TOF MS analysis, 34 differentially expressed proteins were estimated in cucumber seeds treated with CuO NPs. A comparison of the expression patterns with those estimated at seeds treated with bulk CuO showed that they significantly differed at least in 9 proteins, and a 5977-*m*/*z* protein was denoted as the most suitable biomarker for determining phytotoxicity by CuO NPs. Moreover, variability in the modes of inhibitory action on cucumber seeds and roots was observed (Moon et al., 2014). CuO NPs and CuO MPs supplemented at a dose of 1000 mg CuO/kg were found to be toxic to microbes and plants in the soil ecosystem, whereby the inhibition of the soil enzyme activity and plant biomass was higher at CuO NPs application (Kim et al., 2013). On the other hand, CuO NPs did not considerably affect the diversity and metabolic profiles of the prokaryotic community in the pecan tree (*Carya illinoinensis*) rhizospheric soil, suggesting the suitability of nanosized CuO particles to be used for Cu delivery to Cu-poor soils (Salas-Leiva et al., 2021).

Treatment of hydroponically cultivated cucumber plants with $CuFe_2O_4$ NPs (0.04–5 ppm) showing a crystallite size of 30.7 nm increased the fresh weight and protein content of plants and pronouncedly enhanced SOD and POD activities in roots and shoots as well as the uptake of Fe and Cu (Abu-Elsaad and Hameed, 2019).

4.2.2 *Cucurbita pepo*

Cucurbita pepo L. is widely used as food and in folk medicine due to the contents of medicinally important phytoconstituents belonging mainly to cucurbitosides, multiflorane-type triterpenoids, carotenoids, ent-kaurane-type diterpene, and cucurbitaglycosides (Perez Gutierrez, 2016). Zucchini plants cultivated in a 1:1 (v/v) potting mix native soil mixture amended with CuNPs or CuO NPs for 3 weeks were characterized with pronouncedly higher Cu concentrations in the root, stem, and leaves compared to control without an adverse impact on plant growth or Chl production. In the root tissues of CuO NPs-treated plants, the activity of APX was reduced by at least 45%, while CAT activity showed a decrease by 78% and 80% compared to control when plants were treated with 50 and 200 mg/kg, respectively, while the activity of APX and CAT in the leaves was not affected. However, treatment with CuNPs or CuO NPs resulted in reduced Zn and B accumulation in the roots (Tamez et al., 2019). Bulk Cu particles, as well as CuNPs, exhibited phytotoxic effects to zucchini plants reflected in reduced growth and transpiration by 60%–70% compared to control. The Cu^{2+} concentration in solutions applied for the treatment was 1.4–4.4-fold higher in

bulk than in NP amended solutions. Using humic acid at a dose of 50 mg/L Cu^{2+} resulted in complete mitigation of the toxicity caused by bulk Cu due to a dramatic decrease of Cu^{2+} content, while a 1.4–2.9-fold increase of Cu^{2+} ions in solutions containing CuNPs was observed (Musante and White, 2012). Exposure of zucchini seeds to 1000 mg/L CuNPs caused a reduction of emerging root length by 77% and 64% compared to control and seeds exposed to bulk Cu particles. At application of CuNPs, biomass reduction by 90% compared to control plants was observed, and it was found that half the observed phytotoxicity originated from the elemental NPs (Stampoulis et al., 2009). Combined treatment of *Cucurbita pepo* L. plants grown in vermiculite with La_2O_3 NPs and CuO NPs using doses of 500 mg/L resulted in 2–5-fold higher Cu uptake suggesting a complete deregulation of Cu uptake (Pagano et al., 2017).

4.2.3 *Citrullus lanatus*

Watermelon (*Citrullus lanatus*) is a plant species in the family *Cucurbitacae* containing bioactive compounds such as triterpenes, sterols, vitamins, cucurbitacin, and minerals and its seeds contain considerable amounts of protein, fat, vitamins, and minerals (Gupta et al., 2018). CS-polyvinyl alcohol (PVA) hydrogel with absorbed CuNPs applied to grafted watermelon plants (cv. 'Jubilee') was reported to increase stoma width, primary stem length, and root length by 7%, 8%, and 14%, respectively (Gomez et al., 2017). Leaves of young watermelon plants sprayed with CuNPs (500–1000 μg/mL; 1–2 mL per plant) planted in a potting mix infested with *Fusarium oxysporum* f. sp. *niveum* increased the biomass or yield compared to controls; an increase of fruit yields was achieved and CuO NP showed excellent antifungal activity as well. Moreover, strong upregulation of PPO and PRI genes in watermelon roots in CuO NP-treated plants infested with *F. oxysporum* f. sp. *niveum* was observed (Elmer et al., 2018).

4.3 Leafy vegetables

Leafy vegetables are grown or harvested primarily for the consumption of their leafy parts, either raw or cooked.

4.3.1 *Lactuca sativa*

Lettuce (*Lactuca sativa* L.) is considered the most important vegetable in the group of leafy vegetables and is almost exclusively used as a fresh vegetable in salads (Křístková et al., 2008). Lettuce is low in calories, fat, and sodium and it contains several minerals and fiber as well as bioactive compounds such as folate, β-carotene, lutein, and phenolics (Kim et al., 2016). The impact of low CuNPs (< 50 ppm) concentration on the germination of lettuce (*Lactuca sativa*) seeds in a water medium was found to be only slightly more toxic than that of Cu^{2+} ions (Liu et al., 2016). CuNPs and CuO NPs, as well as the respective bulk compounds and commercial preparations of CuPRO 2005 and Kocide 3000, applied at doses of 10 and 20 mg/L, pronouncedly reduced the root length of lettuce plants, increased APX activity in roots, and decreased the P and Fe content in lettuce shoots (Hong et al., 2015).

Hydroponically grown 18-day-old lettuce plants, which were treated with core-shell Cu/CuO NPs (10 and 20 mg/L), reduced the water content, root length, and dry biomass of the plants; Cu/CuO NPs treatments increased CAT activity but decreased APX activity; the plants accumulated pronouncedly more Cu in roots compared to treatment with Cu^{2+} and contained considerably higher levels of Cu, Al, and S but less Mn, P, Ca, and Mg compared to control (Trujillo-Reyes et al., 2014).

Treatment of *Lactuca sativa* plants cultivated in soil with CuO NPs and CuO MPs at doses of 200 and 400 mg Cu/kg soil for 60 days resulted in increased Cu accumulation in plant roots, while the shoot Cu content was practically unchanged and oxidative stress was not observed. In contrast to CuO MPs, which did not affect the shoot biomass, at application of CuO NPs it increased by 16.3%–19.1%, which could be connected with modification in the photosynthesis system of lettuce accompanied by increased transpiration rate and higher stomatal conductance (Wang et al., 2019c).

Treatments of lettuce plants with 16 nm CuO NPs at doses of 0.8–798.9 mg Cu/L resulted in dose-dependent increases in root diameter up to + 52%, while no effect was observed with application of $CuCl_2$ and hydraulic conductivity of the root system exposed to 16 and 45 nm CuO NP (798.9 mg Cu/L) showed a 46% decrease compared to control. Considering the root thickening and reduction of root hydraulic conductivity due to treatment with CuO NPs, it could be suggested that these NPs could compromise root water transport and thus crop performance (Margenot et al., 2018). Exposure of lettuce and cabbage plants via leaves to CuO NPs (10 or 250 mg per plant) lasting 15 days resulted in foliar uptake of 3773 mg Cu/kg d.w. for lettuce and 4448 mg Cu/kg d.w. for cabbage. Treated plants were characterized by decreased weight, net photosynthesis level, and water content, and necrotic Cu-rich areas were situated close to deformed stomata containing CuO NPs. Based on the translocation of Cu from leaves to roots, Cu speciation biotransformation in leaf tissues as well as CuO NP transfer rate from leaves to roots achieving 7.8–242 μg/day, the involvement of CuO NPs in plant Cu regulation processes was suggested (Xiong et al., 2017). CuO NPs of c. 6.6 nm green synthesized using green tea extract when used at doses < 40 μg/mL did not affect or even enhance seed germination, but doses at the concentration range of 40–300 μg/mL inhibited seed germination and root growth ranging from 35% to 75%. Increasing CuO NP concentrations resulted in enhanced levels of nitrite and *S*-nitrosothiols in roots and reduced SOD and total antioxidant activities. The obtained results suggested the involvement of nitric oxide signaling in the phytotoxic effects induced by a high concentration of CuO NPs (Pelegrino et al., 2020).

After foliar spraying of *L. sativa* plants with $Cu(OH)_2$ NPs (1050–2100 mg/L) for 1 month, 97%–99% of Cu (1353–2501 mg/kg) was found to be sequestered in the leaves and only 1%–3% (17.5–56.9 mg/kg) was translocated to root tissues through phloem loading. However, $Cu(OH)_2$ NPs were able to alter metabolite levels of lettuce leaves, caused disturbances in the tricarboxylic acid cycle and some amino acid-related biological pathways, considerably reduced contents of antioxidants such as *cis*-caffeic acid, chlorogenic acid, 3,4-dihydroxycinnamic acid and dehydroascorbic acid, while nicotianamine acting as a Cu chelator showed a 12–27-fold

increase compared to the control, suggesting that it can be involved in the detoxification mechanism. The enhanced tolerance and alleviation of oxidative stress can also contribute to the upregulation of polyamines (spermidine and putrescine) and potassium (Zhao et al., 2016c). In 24-day-old lettuce plants grown in soil and exposed via the leaves to $Cu(OH)_2$ NPs (1050 and 1555 mg/L) for 1 month, the Cu concentrations estimated in leaves and vascular and photosynthetic tissues were 823–1111 and 1353–2008 mg/kg, respectively, and an increase of K concentration in leaves by 6%–7% and by 21%–28% in vascular and photosynthetic tissues was observed as well. Moreover, exposure to $Cu(OH)_2$ NPs reduced the total antioxidant capacity of lettuce plants by 20%–23% and up- and downregulation of a number of amino acids, especially 4-hydroxybutyric acid (GABA), showing that a 50% decrease could affect the overall nutritional value of lettuce leaves (Zhao et al., 2016d).

4.3.2 *Spinacia oleracea*

Spinach (*Spinacia oleracea* L.) is a nutrient-rich leafy vegetable containing at least 13 different flavonoids that function as antioxidants, vitamin K, and carotenoids (Bunea et al., 2008; Roberts and Moreau, 2016). Irrigation of spinach plants with water containing 1000 mg/L of CuO NPs till 11 weeks resulted in a reduction in root length (16%), shoot length (22%), total weight (37%), Chl (18%), and carotenoids (46%), while at the application of low CuNP concentration (10 mg/L) pronounced toxic effects on growth and uptake of metal ion were not observed (Singh and Kumar, 2016).

4.4 *Solanum lycopersicum*

Tomato (*Solanum lycopersicum* L.) is the second most important vegetable crop in the world after potato, and although tomatoes are fruits, they are considered as vegetables. Tomatoes are one of the major food sources of carotenoids, providing an estimated 80% of the daily intake of lycopene, and of folate, ascorbic acid, flavonoids, α-tocopherol, and potassium in the western diet (Bramley, 2000; Willcox et al., 2003; Erba et al., 2013). Tomato seedlings were grown on an MS medium supplemented with CuNPs (79 nm), ZnNPs (54 nm), and FeNPs (27 nm) instead of corresponding metal salts, whereby pronouncedly improved seedling parameters such as root length, root activity, and seed germination were observed compared to plants cultivated in standard MS medium (Chen et al., 2020). CuNPs of 50 nm applied twice during the development of tomato plants using doses of 50–500 mg/L resulted in the production of fruits with greater firmness. The fruits of treated plants had increased content of vitamin C, lycopene, and a higher 2,2′-azino-bis(3-ethylbenzothiazoline-6-sulfonic acid) (ABTS) antioxidant capacity compared to the control, showed a decrease in the activities of APX and GPX, and pronouncedly increased activities of SOD and CAT (Lopez-Vargas et al., 2018). The beneficial impact of CuNPs applied via foliar spray to tomato plants under salt stress on the accumulation of bioactive compounds such as total phenols, β-carotene, and vitamin C was also reported previously by Hernandez-Fuentes et al. (2017). Treatment of tomato plants with CuNPs

absorbed on CS hydrogels at 100 mg CuNPs/kg applied to the substrate before transplantation at doses of 0.015–0.3 g/L showed a beneficial impact on the morphological, production characteristics and nutritional quality of tomato (Juarez-Maldonado et al., 2016). Cu-CS NPs applied at doses of 0.08%–0.12% stimulated tomato seed germination, seedling length, fresh and dry weight. In pot experiments, treatments with 0.12% Cu-CS NPs were able to achieve a high percentage efficacy of disease control in tomato plants, namely 87.7% and 61.1% in early blight and *Fusarium* wilt, respectively (Saharan et al., 2015). Copper-based nanoparticles tested in the field on tomato plants against *Phytophthora infestans* were found to be more effective than the trade agrochemicals and their use was accompanied by no deleterious effect on plants (Giannousi et al., 2013).

CS-PVA hydrogels and CuNPs improved the growth of *S. lycopersicum* plants and stimulated the expression of jasmonic acid (JA) and SOD genes under salt stress, suggesting that they can mitigate this abiotic stress via the regulation of oxidative and ionic stress (Hernandez-Hernandez et al., 2018). Treatment with CuNPs (0.02, 0.2, 2, and 10 mg applied to the substrate) encapsulated in CS-PVA hydrogels increased the numbers of leaves and clusters, fresh biomass of roots, and dry biomass of stem-leaves and roots of the tomato plants as well as the soluble solid content, titratable acidity, lycopene content, and total antioxidant capacity in the fruits. An optimum dose of 10 mg CuNPs applied to the substrate for the growth and yield of tomato was able to increase the stem diameter and dry biomass of stem leaves and roots by 13% and 30%, respectively, and the yield by 17%. On the other hand, using a dose of 0.02 mg CuNPs, an increase of the lycopene content by 37% and the total antioxidant capacity of the fruit by 10% was observed, suggesting the enhanced nutraceutical quality of the tomato fruits (Hernandez Hernandez et al., 2017).

Using the foliar application of CuNPs (250 mg/L) to tomato plants exposed to 50 mM NaCl, the damage caused by salt stress was attenuated, which was reflected in the increased performance and improved Na^+/K^+ ratio. CuNPs were found to increase the levels of phenols in the leaves as well as the content of ascorbic acid, GSH, and phenols by 7.8% in the fruit compared to control due to the higher Cu content in the tissues of salt-stressed plants; enhanced activities of PAL, APX, GPX, SOD, and CAT in leaves were observed as well (Perez-Labrada et al., 2019). The combined application of CuNPs and K_2SiO_3 improved activities of SOD, PAL, GPX, and APX and concentrations of GSH and total phenols in the leaves of tomato plants as well as activities of the PAL and GPX enzymes and lycopene and β-carotene content in the fruits and increased the tolerance of tomato plants to *Clavibacter michiganensis*, which resulted in the reduction of yield loss due to this phytopathogen by 16.1% (Cumplido-Najera et al., 2019).

Combined foliar treatment of tomato plants infected by *Alternaria solani* with high doses of CuNPs and SeNPs induced the activities of SOD, APX, GPX, and PAL in the leaves and GPX in the fruit; increased levels of Chl*a*, Chl*b*, and total Chls in leaves; enhanced contents of ascorbic acid, GSH, phenols, and flavonoids in fruits were estimated as well, whereby the disease severity caused by *A. solani* in tomato plants was reduced (Quiterio-Gutierrez et al., 2019). *S. lycopersicum* plants

cultivated in sand supplemented with 100 and 500 mg/L of CuO NPs (20–40 nm) prepared using the *Morus alba* leaf extract showed a pronounced decrease in total Chls and sugar contents, while at application of 10 mg/L CuO NPs a minor increase of Chl and sugar content was observed. An increase of lipid peroxidation, electrolyte leakage, and antioxidant enzyme activity as well as $O_2^{\bullet-}$ and H_2O_2 formation in leaves with increasing CuNP concentration was estimated, and at application of 500 mg/L CuNPs the deposition of lignin in roots was also observed (Singh et al., 2017).

4.5 *Daucus carota*—A root vegetable

Daucus carota is a root vegetable with an enlarged fleshy taproot, eaten as a raw vegetable or cooked, which contains alkaloids, carbohydrates, chlorogenic acid, flavonoids, phenols, essential oils, terpenoids, and coumarin (Al-Snafi, 2017). A greater reduction in the shoot biomass of carrot (*Daucus carota*) was observed when plants are grown in the sand amended with Cu^{2+} compared to treatment with CuO NPs. Cu accumulation in taproot was restricted to the taproot periderm and was higher at treatment with Cu^{2+}. Similarly, the translocation to shoots was greater for Cu^{2+}-treated plants compared to CuO NPs-treated plants, whereby plants exposed to CuO NPs were characterized by reduced Cu accumulation in the edible tissues of carrot (Ebbs et al., 2016a). Peeling carrots were found to reduce the projected dietary intake by 1–2 orders of magnitude for both CuO NPs and Cu^{2+}-treated carrots grown in sand (Ebbs et al., 2016b). Application of 16 nm CuO NP exhibited a dose-dependent increase in the root diameter of the carrot seedling (+ 26%) but did not affect the hydraulic conductivity of the root system, and no Cu was observed in xylem sap (Margenot et al., 2018).

5 Conclusions

Staple crops such as cereals and pulses, which are consumed in large quantities, serve as a major source of energy and nutrients. However, ongoing climate change connected with not only prolonged drought periods and temperature increases but also with erratic rainstorms, floods, and increasing areas affected by salinization together with a high degree of environmental pollution due to anthropogenic activity and the progressive extension of pests have adverse impact on agriculture. Therefore, to ensure sufficient healthy food for the increasing human population, it is necessary to apply effective fertilizers and pesticides with controlled release and targeted delivery of active compounds in agricultural production. For this purpose, nanoparticles/nanoformulations achieving the same or better effect than their bulk counterparts at using lower doses are suitable. Nanoscaled formulations of copper micronutrient, which are used as nanofertilizers and supply this essential mineral in required amounts to crops, effectively improve the growth and development of the crops. On the other hand, nanosized copper compounds are used in crop protection due to their effective antibacterial and antifungal activities, and therefore it is necessary to estimate the

optimum dose able to kill harmful bacteria and fungi but not adversely affecting the food crops and showing no adverse impact on the environment. Similarly, for copper-based nanoherbicides, a species-specific herbicidal activity is required that avoids damage to food crops. Therefore, it is favorable to apply copper-based biopesticides, i.e., copper-based nanoparticles or nanoformulations, containing a biologically active constituent of natural origin, e.g., chitosan, which can improve their efficiency without an adverse impact on the environment and nontarget organisms. It could be emphasized that in agricultural practice, it is advantageous to prefer the application of green synthesized copper nanoparticles fabricated using plant extracts as reducing and capping agents, which, apart from the fact that they were prepared without the use of dangerous chemicals, also usually exhibit improved biological activity due to capping compounds on their surface.

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References

Abu-Elsaad, N.I., Hameed, R.E.A., 2019. Copper ferrite nanoparticles as nutritive supplement for cucumber plants grown under hydroponic system. J. Plant Nutr. 42 (14), 1645–1659.

Adams, J., Wright, M., Wagner, H., Valiente, J., Britt, D., Anderson, A., 2017. Cu from dissolution of CuO nanoparticles signals changes in root morphology. Plant Physiol. Biochem. 110, 108–117.

Adhikari, T., Sarkar, D., Mashayekhi, H., Xing, B.S., 2016. Growth and enzymatic activity of maize (*Zea mays* L.) plant: solution culture test for copper dioxide nano particles. J. Plant Nutr. 39 (1), 102–118.

Adrees, M., Ali, S., Rizwan, M., Ibrahim, M., Abbas, F., Farid, M., Zia-ur-Rehman, M., Irshad, M.K., Bharwana, S.A., 2015. The effect of excess copper on growth and physiology of important food crops: a review. Environ. Sci. Pollut. Res. 22 (11), 8148–8162.

Agathokleous, E., Kitao, M., Calabrese, E.J., 2020. Hormesis: highly generalizable and beyond laboratory. Trends Plant Sci. 25 (11), 1076–1086.

Aggarwal, V., Prashant, A., Malik, J., Chaudhary, D., Jaiwal, P.K., Pundir, C.S., 2020. Influence of chemically synthesized copper nanoparticles and cupric ions on oxalate oxidation system in germinating *Sorghum* grain. Indian J. Exp. Biol. 58 (1), 58–63.

Ahmed, A., Usman, M., Liu, Q.Y., Shen, Y.Q., Yu, B., Cong, H.L., 2019. Plant mediated synthesis of copper nanoparticles by using *Camelia sinensis* leaves extract and their applications in dye degradation. Ferroelectrics 549 (1), 61–69.

Akhter, S.M.H., Mohammad, F., Ahmad, S., 2019. *Terminalia belerica* mediated green synthesis of nanoparticles of copper, iron and zinc metal oxides as the alternate antibacterial agents against some common pathogens. Bionanoscience 9 (2), 365–372.

Al-Hakkani, M.F., 2020. Biogenic copper nanoparticles and their applications: a review. SN Appl. Sci. 2 (3), 505.
Al-Snafi, A.E., 2017. Nutritional and therapeutic importance of *Daucus carota*—a review. IOSR J. Pharm. 7 (2), 72–88.
Amri, B., Ben Kaab, S., Gouia, H., Martino, E., Collina, S., 2017. Copper-induced changes in nutrient uptake, enzymatic and non-enzymatic antioxidant systems in horehound (*Marrubium vulgare* L.). Bot. Sci. 95 (3), 565–575.
Angrasan, J.K.V.M., Subbaiya, R., 2014. Biosynthesis of copper nanoparticles by *Vitis vinifera* leaf aqueous extract and its antibacterial activity. Int. J. Curr. Microbiol. Appl. Sci. 3 (9), 768–774.
Apodaca, S.A., Medina-Velo, I.A., Lazarski, A.C., Flores-Margez, J.P., Peralta-Videa, J.R., Gardea-Torresdey, J.L., 2018. Different forms of copper and kinetin impacted element accumulation and macromolecule contents in kidney bean (*Phaseolus vulgaris*) seeds. Sci. Total Environ. 636, 1534–1540.
Arif, N., Yadav, V., Singh, S., Singh, S., Ahmad, P., Mishra, R.K., Sharma, S., Tripathi, D.K., Dubey, N.K., Chauhan, D.K., 2016. Influence of high and low levels of plant-beneficial heavy metal ions on plant growth and development. Front. Environ. Sci. 4, 69.
Ashfaq, M., Verma, N., Khan, S., 2017. Carbon nanofibers as a micronutrient carrier in plants: efficient translocation and controlled release of Cu nanoparticles. Environ. Sci. Nano 4 (1), 138–148.
Ayoub, H.A., Khairy, M., Elsaid, S., Rashwan, F.A., Abdel-Hafez, H.F., 2018. Pesticidal activity of nanostructured metal oxides for generation of alternative pesticide formulations. J. Agric. Food Chem. 66 (22), 5491–5498.
Bai, T.H., Wang, Y.Y., Adeel, M., Hao, Y., Tan, W.M., Rui, Y.K., 2020. Effects of nanoparticles on seed germination and seedling growth. Fresenius Environ. Bull. 29 (1), 339–345.
Banik, S., Perez-de-Luque, A., 2017. In vitro effects of copper nanoparticles on plant pathogens, beneficial microbes and crop plants. Span. J. Agric. Res. 15 (2), e1005.
Bohner, H., Böhme, H., Böger, P., 1980. Reciprocal formation of plastocyanin and cytochrome *c*-553 and the influence of cupric ions on photosynthetic electron transport. Biochim. Biophys. Acta 592, 103–112.
Bramhanwade, K., Shende, S., Bonde, S., Gade, A., Rai, M., 2016. Fungicidal activity of Cu nanoparticles against *Fusarium* causing crop diseases. Environ. Chem. Lett. 14 (2), 229–235.
Bramley, P.M., 2000. Is lycopene beneficial to human health? Phytochemistry 54, 233–236.
Bunea, A., Andjelkovic, M., Socaciu, C., Bobis, O., Neacsu, M., Verhr, T., Camp, J.V., 2008. Total and individual carotenoids and phenolic acids content in fresh, refrigerated and processed spinach (*Spinacia oleracea* L.). Food Chem. 108 (2), 649–656.
Burda, K., Kruk, J., Strzalka, K., Schmid, G.H., Kruse, O., 2002. Stimulation of oxygen evolution in photosystem II by copper (II) ions. Z. Naturforsch. C: J. Biosci. 57, 853–857.
Burda, K., Kruk, J., Strzalka, K., Stanek, J., Schmid, G.H., Kruse, O., 2006. Mösbauer studies of Cu(II) ions interaction with the non-heme iron and cytochrome *b*559 in a *Chlamydomonas reinhardtii* PS I minus mutant. Acta Phys. Pol. A 109, 237–247.
Caspy, I., Borovikova-Sheinker, A., Klaiman, D., Shokolnisky, Y., Nelson, N., 2020. The structure of a triple complex of plant photosystem I with ferredoxin and plastocyanin. Nat. Plants 6, 1300–1305.
Chen, Y., Lu, J.Y., Liu, M., Li, H.S., Sun, Q., Nechitaylo, G.S., Bogoslovskaya, O.A., Olkhovskaya, I.P., Glushchenko, N.N., 2020. Tomato response to metal nanoparticles introduction into the nutrient medium. IET Nanobiotechnol. 14 (5), 382–388.

Choudhary, R.C., Kumaraswamy, R.V., Kumari, S., Sharma, S.S., Pal, A., Raliya, R., Biswas, P., Saharan, V., 2017. Cu-chitosan nanoparticle boost defense responses and plant growth in maize (*Zea mays* L.). Sci. Rep. 7, 9754.

Clemens, S., Ma, J.F., 2016. Toxic heavy metal and metalloid accumulation in crop plants and foods. Annu. Rev. Plant Biol. 67, 489–512.

Cobbett, C.S., 2000. Phytochelatins and their roles in heavy metal detoxification. Plant Physiol. 123, 825–832.

Cumplido-Najera, C.F., Gonzalez-Morales, S., Ortega-Ortiz, H., Cadenas-Pliego, G., Benavides-Mendoza, A., Juarez-Maldonado, A., 2019. The application of copper nanoparticles and potassium silicate stimulate the tolerance to *Clavibacter michiganensis* in tomato plants. Sci. Hortic. 245, 82–89.

Cytochrome oxidase, 2020. ChemistryLibreTexts. California State University, USA. https://chem.libretexts.org/Courses/Saint_Marys_College_Notre_Dame_IN/CHEM_342%3A_Bio-inorganic_Chemistry/Readings/Metals_in_Biological_Systems_(Saint_Mary%27s_College)/Cytochrome_Oxidase.

Da Costa, M.V.J., Sharma, P.K., 2016. Effect of copper oxide nanoparticles on growth, morphology, photosynthesis, and antioxidant response in *Oryza sativa*. Photosynthetica 54 (1), 110–119.

Dahiya, P.K., Linnemann, A.R., Van Boekel, M.A.J.S., Khetarpaul, N., Grewal, R.B., Nout, M.J.R., 2015. Mung bean: technological and nutritional potential. Crit. Rev. Food Sci. Nutr. 55 (5), 670–688.

DalCorso, G., Manara, A., Piasentin, S., Furini, A., 2014. Nutrient metal elements in plants. Metallomics 6 (10), 1770–1788.

Das, P.E., Abu-Yousef, I.A., Majdalawieh, A.F., Narasimhan, S., Poltronieri, P., 2020. Green synthesis of encapsulated copper nanoparticles using a hydroalcoholic extract of *Moringa oleifera* leaves and assessment of their antioxidant and antimicrobial activities. Molecules 25 (3), 555.

Den Herder, G., Van Isterdael, G., Beeckman, T., De Smet, I., 2010. The roots of a new green revolution. Trends Plant Sci. 15 (11), 600–607.

Dhir, B., Sharmila, P., Saradhi, P.P., Sharma, S., Kumar, R., Mehta, D., 2011. Heavy metal induced physiological alterations in *Salvinia natans*. Ecotoxicol. Environ. Saf. 74 (6), 1678–1684.

Dimkpa, C.O., McLean, J.E., Latta, D.E., Manangon, E., Britt, D.W., Johnson, W.P., Boyanov, M.I., Anderson, A.J., 2012. CuO and ZnO nanoparticles: phytotoxicity, metal speciation, and induction of oxidative stress in sand-grown wheat. J. Nanopart. Res. 14 (9), 1125.

Dimkpa, C.O., Latta, D.E., McLean, J.E., Britt, D.W., Boyanov, M.I., Anderson, A.J., 2013. Fate of CuO and ZnO nano- and microparticles in the plant environment. Environ. Sci. Technol. 47 (9), 4734–4742.

Dimkpa, C.O., Singh, U., Bindraban, P.S., Adisa, I.O., Elmer, W.H., Gardea-Torresdey, J.L., White, J.C., 2019. Addition-omission of zinc, copper, and boron nano and bulk oxide particles demonstrate element and size-specific response of soybean to micronutrients exposure. Sci. Total Environ. 665, 606–616.

Dutta, S., Mitra, M., Agarwal, P., Mahapatra, K., De, S., Sett, U., Roy, S., 2018. Oxidative and genotoxic damages in plants in response to heavy metal stress and maintenance of genome stability. Plant Signal. Behav. 13 (8), e1460048.

Ebbs, S.D., Bradfield, S.J., Kumar, P., White, J.C., Musante, C., Ma, X.M., 2016a. Accumulation of zinc, copper, or cerium in carrot (*Daucus carota*) exposed to metal oxide nanoparticles and metal ions. Environ. Sci. Nano 3 (1), 114–126.

Ebbs, S.D., Bradfield, S.J., Kumar, P., White, J.C., Musante, C., Ma, X.M., 2016b. Projected dietary intake of zinc, copper, and cerium from consumption of carrot (*Daucus carota*) exposed to metal oxide nanoparticles or metal ions. Front. Plant Sci. 7, 188.

Elmer, W., De La Torre-Roche, R., Pagano, L., Majumdar, S., Zuverza-Mena, N., Dimkpa, C., Gardea-Torresdey, J., White, J.C., 2018. Effect of metalloid and metal oxide nanoparticles on Fusarium wilt of watermelon. Plant Dis. 102 (7), 1394–1401.

El-Shazoly, R.M., Amro, A., 2019. Comparative physiological and biochemical effects of CuO NPs and bulk CuO phytotoxicity onto the maize (*Zea mays*) seedlings. Global NEST J. 21 (3), 276–289.

Erba, D., Casiraghi, M.C., Ribas, A., Cáceres, R., Marfà, O., Castellari, M., 2013. Nutritional value of tomatoes (*Solanum lycopersicum* L.) grown in greenhouse by different agronomic techniques. J. Food Compos. Anal. 31 (2), 245–251.

Essa, H.L., Abdelfattah, M.S., Marzouk, A.S., Guirguis, H.A., El-Sayed, M.M.H., 2020. Nanoformulations of copper species coated with sulfated polysaccharide extracts and assessment of their phytotoxicity on wheat (*Triticum aestivum* L.) seedlings in seed germination, foliar and soil applications. Appl. Sci. 10 (18), 6302.

Evenson, R.E., Gollin, D., 2003. Assessing the impact of the Green Revolution, 1960 to 2000. Science 300 (5620), 758–762.

Fan, Q.R., Liao, Y.Y., Kunwar, S., Da Silva, S., Young, M., Santra, S., Minsavage, G.V., Freeman, J.H., Jones, J.B., Paret, M.L., 2021. Antibacterial effect of copper composites against *Xanthomonas euvesicatoria*. Crop Prot. 139, 105366.

FAO, 2003. Handling and Preservation of Fruits and Vegetables by Combined Methods for Rural Areas Technical Manual. FAO Agricultural Services Bulletin 149. http://www.fao.org/documents/pub_dett.asp?pub_id=126311&lang=en.

FAO, 2020a. Crops Statistics—Concepts, Definitions and Classifications. http://www.fao.org/economic/the-statistics-division-ess/methodology/methodology-systems/crops-statistics-concepts-definitions-and-classifications/en/.

FAO, 2020b. Ample Supplies to Help Shield Food Markets From the COVID-19 Crisis. https://doi.org/10.4060/ca8445en.

Fischer, E., Cachon, R., Cayot, N., 2020. *Pisum sativum* vs *Glycine max*, a comparative review of nutritional, physicochemical, and sensory properties for food uses. Trends Food Sci. Technol. 95, 196–204.

Fogler, T., 2014. The Next Green Revolution. National Geographic Magazine. https://www.nationalgeographic.com/foodfeatures/green-revolution/.

Foyer, C.H., Lam, H.M., Nguyen, H.T., 2016. Neglecting legumes has compromised human health and sustainable food production. Nat. Plants 2, 16112.

Fraceto, L.F., Grillo, R., de Medeiros, G.A., Scognamiglio, V., Rea, G., Bartolucci, C., 2016. Nanotechnology in agriculture: which innovation potential does it have? Front. Environ. Sci. 4, 20.

Fu, P.P., Xia, Q.S., Hwang, H.M., Ray, P.C., Yu, H.T., 2014. Mechanisms of nanotoxicity: generation of reactive oxygen species. J. Food Drug Anal. 22, 64–75.

Gahukar, R.T., 1992. Green-revolution in food crops—an Indian experience. Outlook Agric. 21 (2), 129–136.

Gall, J.E., Boyd, R.S., Rajakaruna, N., 2015. Transfer of heavy metals through terrestrial food webs: a review. Environ. Monit. Assess. 187 (4), 201.

Gao, X., Avellan, A., Laughton, S., Vaidya, R., Rodrigues, S.M., Casman, E.A., Lowry, G.V., 2018. CuO nanoparticle dissolution and toxicity to wheat (*Triticum aestivum*) in rhizosphere soil. Environ. Sci. Technol. 52 (5), 2888–2897.

Ghidan, A.Y., Al-Antary, T.M., Awwad, A.M., 2016. Green synthesis of copper oxide nanoparticles using *Punica granatum* peels extract: effect on green peach aphid. Environ. Nanotechnol. Monit. Manag. 6, 95–98.

Giannousi, K., Avramidis, I., Dendrinou-Samara, C., 2013. Synthesis, characterization and evaluation of copper based nanoparticles as agrochemicals against *Phytophthora infestans*. RSC Adv. 3 (44), 21743–21752.

Gomes, D.G., da Cunha, L.S., Oliveira, H.C., 2020. Dose-dependent dual effect of soil copper on the initial development of *Glycine max* (L.) Merr. cv. BRS 257 seedlings. Bull. Environ. Contam. Toxicol. 105 (4), 553–558.

Gomez, H.G., Godina, F.R., Ortiz, H.O., Mendoza, A., Torres, V.R., De la Fuente, M.C., 2017. Use of chitosan-PVA hydrogels with copper nanoparticles to improve the growth of grafted watermelon. Molecules 22 (7), 1031.

González-Melendi, P., Fernández-Pacheco, R., Coronado, M.J., Corredor, E., Testillano, P.S., Risueño, M.C., Marquina, C., Ibarra, M.R., Rubiales, D., Pérez-de-Luque, A., 2008. Nanoparticles as smart treatment-delivery systems in plants: assessment of different techniques of microscopy for their visualisation in plant tissues. Ann. Bot. 101, 187–195.

Gross, E.L., 2013. Plastocyanin. In: Lennarz, W.J., Lane, M.D. (Eds.), Encyclopedia of Biological Chemistry, second ed. Academic Press, Elsevier, pp. 530–532.

Gupta, R., Xie, H., 2018. Nanoparticles in daily life: applications, toxicity and regulations. J. Environ. Pathol. Toxicol. Oncol. 37 (3), 209–230.

Gupta, S.M., Arora, S., Mirza, M., Pande, A., Lata, C., Puranik, S., Kumar, J., Kumar, A., 2017. Finger millet: a "certain" crop for an "uncertain" future and a solution to food insecurity and hidden hunger under stressful environments. Front. Plant Sci. 8, 643.

Gupta, A., Singh, A., Prasad, R., 2018. A review on watermelon (*Citrullus lanatus*) medicinal seeds. J. Pharmacogn. Phytochem. 7 (3), 2222–2225.

Haensch, R., Mendel, R.R., 2009. Physiological functions of mineral micronutrients (Cu, Zn, Mn, Fe, Ni, Mo, B, Cl). Curr. Opin. Plant Biol. 12 (3), 259–266.

Halliwell, B., Gutteridge, J.M.C., 1984. Oxygen toxicity, oxygen radicals, transitions metals and disease. Biochem. J. 219, 1–14.

Halliwell, B., Gutteridge, J.M.C., 2015. Redox chemistry: the essentials. In: Free Radicals in Biology & Medicine, fifth ed. Oxford University Press, pp. 30–76.

Hayat, I., Ahmad, A., Masud, T., Ahmed, A., Bashir, S., 2014. Nutritional and health perspectives of beans (*Phaseolus vulgaris* L.): an overview. Crit. Rev. Food Sci. Nutr. 54 (5), 580–592.

Hernandez Hernandez, H., Benavides-Mendoza, A., Ortega-Ortiz, H., Hernandez-Fuentes, A.D., Juarez-Maldonado, A., 2017. Cu nanoparticles in chitosan-PVA hydrogels as promoters of growth, productivity and fruit quality in tomato. Emir. J. Food Agr. 29 (8), 573–580.

Hernandez-Fuentes, A.D., Lopez-Vargas, E.R., Pinedo-Espinoza, J.M., Campos-Montiel, R.G., Valdes-Reyna, J., Juarez-Maldonado, A., 2017. Postharvest behavior of bioactive compounds in tomato fruits treated with Cu nanoparticles and NaCl stress. Appl. Sci. 7 (10), 980.

Hernandez-Hernandez, H., Juarez-Maldonado, A., Benavides-Mendoza, A., Ortega-Ortiz, H., Cadenas-Pliego, G., Sanchez-Aspeytia, D., Gonzalez-Morales, S., 2018. Chitosan-PVA and copper nanoparticles improve growth and overexpress the SOD and JA genes in tomato plants under salt stress. Agronomy 8 (9), 175.

Hippler, F.W.R., Boaretto, R.M., Dovis, V.L., Quaggio, J.A., Azevedo, R.A., Mattos, D., 2018. Oxidative stress induced by Cu nutritional disorders in *Citrus* depends on nitrogen and calcium availability. Sci. Rep. 8, 1641.

Hoe, P.T., Mai, N.C., Lien, L.Q., Ban, N.K., Minh, C.V., Chau, N.H., Buu, N.Q., Hien, D.T., Van, N.T., Hien, L.T.T., Linh, T.T.M., 2018. Germination responses of soybean seeds to Fe, ZnO, Cu and Co nanoparticle treatments. Int. J. Agric. Biol. 20 (7), 1562–1568.

Hong, J., Rico, C.M., Zhao, L.J., Adeleye, A.S., Keller, A.A., Peralta-Videa, J.R., Gardea-Torresdey, J.L., 2015. Toxic effects of copper-based nanoparticles or compounds to lettuce (*Lactuca sativa*) and alfalfa (*Medicago sativa*). Environ. Sci. Process Impacts 17 (1), 177–185.

Huang, Y.X., Li, W.W., Minakova, A.S., Anumol, T., Keller, A.A., 2018. Quantitative analysis of changes in amino acids levels for cucumber (*Cucumis sativus*) exposed to nano copper. Nanoimpact 12, 9–17.

Huang, Y.X., Adeleye, A.S., Zhao, L.J., Minakova, A.S., Anumol, T., Keller, A.A., 2019. Antioxidant response of cucumber (*Cucumis sativus*) exposed to nano copper pesticide: quantitative determination via LC-MS/MS. Food Chem. 270, 47–52.

Husen, A., Siddiqi, K.S., 2014. Phytosynthesis of nanoparticles: concept, controversy and application. Nanoscale Res. Lett. 9, 229.

Jampílek, J., Kráľová, K., 2015. Application of nanotechnology in agriculture and food industry, its prospects and risks. Ecol. Chem. Eng. 22, 321–361.

Jampílek, J., Kráľová, K., 2017a. Nanomaterials for delivery of nutrients and growth-promoting compounds to plants. In: Prasad, R., Kumar, M., Kumar, V. (Eds.), Nanotechnology: An Agricultural Paradigm. Springer, Singapore, pp. 177–226.

Jampílek, J., Kráľová, K., 2017b. Nanopesticides: preparation, targeting and controlled release. In: Grumezescu, A.M. (Ed.), Nanotechnology in the Agri-Food Industry, Vol. 10—New Pesticides and Soil Sensors. Elsevier, London, UK, pp. 81–127.

Jampílek, J., Kráľová, K., 2017c. Nano-antimicrobials: activity, benefits and weaknesses. In: Ficai, A., Grumezescu, A.M. (Eds.), Nanostructures in Therapeutic Medicine, Vol. 2—Nanostructures for Antimicrobial Therapy. Elsevier, Amsterdam, pp. 23–54.

Jampílek, J., Kráľová, K., 2018a. Benefits and potential risks of nanotechnology applications in crop protection. In: Abd-Elsalam, K.A., Prasad, R. (Eds.), Nanobiotechnology Applications in Plant Protection, Nanotechnology in the Life Sciences. Springer International Publishing AG, pp. 189–246.

Jampílek, J., Kráľová, K., 2018b. Application of nanobioformulations for controlled release and targeted biodistribution of drugs. In: Sharma, A.K., Keservani, R.K., Kesharwani, R.K. (Eds.), Nanobiomaterials: Applications in Drug Delivery. CRC Press, Warentown, pp. 131–208.

Jampílek, J., Kráľová, K., 2018c. Nanomaterials applicable in food protection. In: Rai, R.V., Bai, J.A. (Eds.), Nanotechnology Applications in Food Industry. CRC Press/Taylor & Francis Group, Boca Raton, pp. 75–96.

Jampílek, J., Kráľová, K., 2019a. Beneficial effects of metal- and metalloid-based nanoparticles on crop production. In: Panpatte, D.G., Jhala, Y.K. (Eds.), Nanotechnology for Agriculture. Springer Nature, Singapore, pp. 161–219.

Jampílek, J., Kráľová, K., 2019b. Impact of nanoparticles on photosynthesizing organisms and their use in hybrid structures with some components of photosynthetic apparatus. In: Prasad, R. (Ed.), Plant Nanobionics, Nanotechnology in the Life Sciences. Springer Nature Switzerland AG, pp. 255–332.

Jampílek, J., Kráľová, K., 2019c. Nanobiopesticides in agriculture: state of the art and future opportunities. In: Koul, O. (Ed.), Nano-Biopesticides Today and Future Perspectives. Elsevier Inc, pp. 397–447.

Jampílek, J., Kráľová, K., 2019d. Natural biopolymeric nanoformulations for brain drug delivery. In: Keservani, R.K. (Ed.), Nanocarriers for Brain Targeting, Principles and Applications. Apple Academic Press, Taylor & Francis, pp. 131–203.

Jampílek, J., Kráľová, K., 2019e. Recent advances in lipid nanocarriers applicable in the fight against cancer. In: Grumezescu, A.M. (Ed.), Nanoarchitectonics in Biomedicine. Elsevier Inc, pp. 219–294.

Jampílek, J., Kráľová, K., 2019f. Nanotechnology-based formulations for drug targeting to the central nervous system. In: Keservani, R.K., Sharma, A.K. (Eds.), Nanoparticulate Drug Delivery Systems. Apple Academic Press, Taylor & Francis, pp. 151–220.

Jampílek, J., Kráľová, K., 2019g. Nanoformulations: a valuable tool in the therapy of viral diseases attacking humans and animals. In: Rai, M., Jamil, B. (Eds.), Nanotheranostics. Springer Nature Switzerland AG, pp. 137–178.

Jampílek, J., Kráľová, K., 2020a. Impact of nanoparticles on toxigenic fungi. In: Rai, M., Abd-Elsalam, K.A. (Eds.), Nanomycotoxicology, Treating Mycotoxins in the Nano Way. Academic Press, Elsevier, pp. 309–348.

Jampílek, J., Kráľová, K., 2020b. Nanocomposites: synergistic nanotools for management of mycotoxigenic fungi. In: Rai, M., Abd-Elsalam, K.A. (Eds.), Nanomycotoxicology, Treating Mycotoxins in the Nano Way. Academic Press, Elsevier, pp. 349–383.

Jampílek, J., Kráľová, K., 2020c. Potential of nanoscale carbon-based materials for remediation of pesticide-contaminated environment. In: Abd-Elsalam, K.A. (Ed.), Carbon Nanomaterials for Agri-food and Environmental Applications. Elsevier, pp. 359–399.

Jampílek, J., Kráľová, K., 2020d. Preparation of nanocomposites from agricultural waste and their versatile applications. In: Abd-Elsalam, K.A. (Ed.), Multifunctional Hybrid Nanomaterials for Sustainable Agri-food and Ecosystems. Elsevier, pp. 51–98.

Jampílek, J., Kráľová, K., 2021. Nanoparticles for improving and augmenting plant functions. In: Jogaiah, S., Singh, H.B., Fraceto, L.F., De Lima, R. (Eds.), Advances in Nano-Fertilizers and Nano-Pesticides in Agriculture. A Smart Delivery System for Crop Improvement. Woodhead Publishing, Elsevier, pp. 171–227.

Jampílek, J., Kráľová, K., Campos, E.V.R., Fraceto, L.F., 2019a. Bio-based nanoemulsion formulations applicable in agriculture, medicine, and food industry. In: Prasad, R. (Ed.), Nanobiotechnology in Bioformulations, Nanotechnology in the Life Sciences. Springer Nature Switzerland AG, pp. 33–84.

Jampílek, J., Kráľová, K., Novák, P., Novák, M., 2019b. Nanobiotechnology in neurodegenerative diseases. In: Rai, M., Yadav, A. (Eds.), Nanobiotechnology in Neurodegenerative Diseases. Springer Nature, Switzerland, pp. 65–138.

Jampílek, J., Kos, J., Kráľová, K., 2019c. Potential of nanomaterial applications in dietary supplements and foods for special medical purposes. Nanomaterials 9, 296.

Jampílek, J., Kráľová, K., Fedor, P., 2020. Bioactivity of nanoformulated synthetic and natural insecticides and their impact on environment. In: Fraceto, L.F., de Castro, S.S.V.L., Grillo, R., Avila, D., Caixeta, O.H., Lima, R. (Eds.), Nanopesticides—From Research and Development to Mechanisms of Action and Sustainable Use Agriculture. Springer Nature Switzerland AG, pp. 165–225.

Jayarambabu, N., Akshaykranth, A., Rao, T.V., Rao, K.V., Kumar, R.R., 2020. Green synthesis of Cu nanoparticles using *Curcuma longa* extract and their application in antimicrobial activity. Mater. Lett. 259, 126813.

Jayathilake, C., Visvanathan, R., Deen, A., Bangamuwage, R., Jayawardana, B.C., Nammi, S., Liyanage, R., 2018. Cowpea: an overview on its nutritional facts and health benefits. J. Sci. Food Agric. 98 (13), 4793–4806.

Jeevanandam, J., Barhoum, A., Chan, Y.S., Dufresne, A., Danquah, M.K., 2018. Review on nanoparticles and nanostructured materials: history, sources, toxicity and regulations. Beilstein J. Nanotechnol. 9, 1050–1074.

Jegerschöld, C., Arellano, J.B., Schröder, W.P., van Kan, P.J.M., Barón, M., Styring, S., 1995. Cu(II) inhibition of the electron transfer through photosystem II studied by EPR spectroscopy. Biochemistry 34, 12747–12754.

Jegerschöld, C., MacMillan, F., Lubitz, W., Rutherford, A.W., 1999. Effects of copper and zinc ions on photosystem II studied by EPR spectroscopy. Biochemistry 38, 12439–12445.

Johnson, G.F., 1935. The early history of copper fungicides. Agric. Hist. 9 (2), 67–79.

Johnson, A., Gunawardana, B., Singhal, N., 2009. Amendments for enhancing copper uptake by *Brassica juncea* and *Lolium perenne* from solution. Int. J. Phytoremediation 11 (3), 215–234.

Juarez-Maldonado, A., Ortega-Ortiz, H., Perez-Labrada, F., Cadenas-Pliego, G., Benavides-Mendoza, A., 2016. Cu nanoparticles absorbed on chitosan hydrogels positively alter morphological, production, and quality characteristics of tomato. J. Appl. Bot. Food Qual. 89, 183–189.

Jukanti, A.K., Gaur, P.M., Gowda, C.L., Chibbar, R.N., 2012. Nutritional quality and health benefits of chickpea (*Cicer arietinum* L.): a review. Br. J. Nutr. 108 (Suppl. 1), S11–S26.

Kasana, R.C., Panwar, N.R., Kaul, R.K., Kumar, P., 2016. Copper nanoparticles in agriculture: biological synthesis and antimicrobial activity. In: Rajnan, S., Dasgupta, N., Lichtfouse, E. (Eds.), Nanoscience in Food and Agriculture 3. Sustainable Agriculture Reviews, vol. 23. Springer, pp. 129–143.

Kasana, R.C., Panwar, N.R., Kaul, R.K., Kumar, P., 2017. Biosynthesis and effects of copper nanoparticles on plants. Environ. Chem. Lett. 15 (2), 233–240.

Kaur, P., Duhan, J.S., Thakur, R., 2018. Comparative pot studies of chitosan and chitosan-metal nanocomposites as nano-agrochemicals against Fusarium wilt of chickpea (*Cicer arietinum* L.). Biocatal. Agric. Biotechnol. 14, 466–471.

Keller, A.A., Adeleye, A.S., Conway, J.R., Garner, K.L., Zhao, L., Cherr, G.N., Hong, J., Gardea-Torresdey, J.L., Godwin, H.A., Hanna, S., Ji, Z., Kaweeteerawat, C., Lin, S., Lenihan, H.S., Miller, R.J., Nel, A.E., Peralta-Videa, J.R., Walker, S.L., Taylor, A.A., Torres-Duarte, C., Zink, J.I., Zuverza-Mena, N., 2017. Comparative environmental fate and toxicity of copper nanomaterials. NanoImpact 7, 28–40.

Kesavan, P.C., Malarvannan, S., 2010. Green to evergreen revolution: ecological and evolutionary perspectives in pest management. Curr. Sci. 99 (7), 908–914.

Khairy, A.I.H., Oh, M.J., Lee, S.M., Kim, D.S., Roh, K.S., 2016. Nitric oxide overcomes Cd and Cu toxicity in *in vitro*-grown tobacco plants through increasing contents and activities of rubisco and rubisco activase. Biochim. Open 2, 41–51.

Khan, M.R., Adam, V., Rizvi, T.F., Zhang, B.H., Ahamad, F., Josko, I., Zhu, Y., Yang, M.Y., Mao, C.B., 2019. Nanoparticle-plant interactions: two-way traffic. Small 15 (37), 1901794.

Kim, S., Sin, H., Lee, S., Lee, I., 2013. Influence of metal oxide particles on soil enzyme activity and bioaccumulation of two plants. J. Microbiol. Biotechnol. 23 (9), 1279–1286.

Kim, M.J., Moon, Y.Y., Tou, J.C., Mou, B.Q., Waterland, N.L., 2016. Nutritional value, bioactive compounds and health benefits of lettuce (*Lactuca sativa* L.). J. Food Compos. Anal. 49, 19–34.

Konečná, B., Frič, F., Masarovičová, E., 1989. Ribulose-1,5-bisphosphate carboxylase activity and protein content in pollution damaged leaves of three oaks species. Photosynthetica 23 (4), 566–574.

Korotkova, A.M., Lebedev, S.V., Gavrish, I.A., 2017. The study of mechanisms of biological activity of copper oxide nanoparticle CuO in the test for seedling roots of *Triticum vulgare*. Environ. Sci. Pollut. Res. 24 (11), 10220–10233.

Králová, K., Jampílek, J., 2021. Nanotechnology as effective tool for improved crop production under changing climatic conditions. In: Sarma, H., Joshi, S.J., Prasad, R., Jampílek, J. (Eds.), Biobased Nanotechnology for Green Applications. Springer Nature, Switzerland, pp. 463–512.

Králová, K., Masarovičová, E., 2008. EDTA-assisted phytoextraction of copper, cadmium and zinc using chamomile plants. Ecol. Chem. Eng. A 15 (3), 213–220.

Králová, K., Šeršeň, F., Blahová, M., 1994. Effects of Cu(II) complexes on photosynthesis in spinach chloroplasts. Aqua(aryloxyacetato)copper(II) complexes. Gen. Physiol. Biophys. 13, 483–491.

Králová, K., Masarovičová, E., Jampílek, J., 2019. Plant responses to stress induced by toxic metals and their nanoforms. In: Pessarakli, M. (Ed.), Handbook of Plant and Crop Stress, fourth ed. Taylor and Francis, CRC, Boca Raton, pp. 479–522.

Křístková, E., Doležalová, I., Lebeda, A., Vinter, V., Novotná, A., 2008. Description of morphological characters of lettuce (*Lactuca sativa* L.) genetic resources. Hortic. Sci. 35 (3), 113–129.

Kumar, P.P.N.V., Shameem, U., Kollu, P., Kalyani, R.L., Pammi, S.V.N., 2015. Green synthesis of copper oxide nanoparticles using *Aloe vera* leaf extract and its antibacterial activity against fish bacterial pathogens. Bionanoscience 5 (3), 135–139.

Kumar, V., Pandita, S., Sidhu, G.P.S., Sharma, A., Khanna, K., Kaur, P., Bali, A.S., Setia, R., 2021. Copper bioavailability, uptake, toxicity and tolerance in plants: a comprehensive review. Chemosphere 262, 127810.

Lee, W.M., An, Y.J., Yoon, H., Kweon, H.S., 2008. Toxicity and bioavailability of copper nanoparticles to the terrestrial plants mung bean (*Phaseolus radiatus*) and wheat (*Triticum aestivum*): plant agar test for water-insoluble nanoparticles. Environ. Toxicol. Chem. 27 (9), 1915–1921.

Leon-Jimenez, E., Valdez-Salas, B., Gonzalez-Mendoza, D., Tzintzun-Camacho, O., 2019. Synthesis and insecticide activity of Cu-nanoparticles from *Prosopis juliflora* (Sw) DC and *Pluchea sericea* (Nutt.) on *Phenacoccus solenopsis* Tinsley (Hemiptera: Pseudococcidae). Rev. Soc. Entomol. Argent. 78 (2), 12–21.

Li, F., Shi, J.Y., Shen, C.F., Chen, G.C., Hu, S.P., Chen, Y.X., 2009. Proteomic characterization of copper stress response in *Elsholtzia splendens* roots and leaves. Plant Mol. Biol. 71 (3), 251–263.

Li, J.R., Rodrigues, S., Tsyusko, O.V., Unrine, J.M., 2019. Comparing plant-insect trophic transfer of Cu from lab-synthesised nano-$Cu(OH)_2$ with a commercial nano-$Cu(OH)_2$ fungicide formulation. Environ. Chem. 16 (6), 411–418.

Li, J.H., Qiu, Y., Zhao, Q.J., Chen, D.L., Wu, Z.P., Peng, A.A., Niazi, N.K., Trakal, L., Sakrabani, R., Gao, B., Wang, H.L., Wu, W.D., 2020. Lead and copper-induced hormetic effect and toxicity mechanisms in lettuce (*Lactuca sativa* L.) grown in a contaminated soil. Sci. Total Environ. 741, 140440.

Lidon, F.C., Henriques, F.S., 1991. Limiting step on photosynthesis of rice plants treated with varying copper levels. J. Plant Physiol. 138, 115–118.

Lidon, F.C., Ramalho, J., Henriques, F.S., 1993. Copper inhibition of rice photosynthesis. J. Plant Physiol. 142, 12–17.

Liu, R.Q., Zhang, H.Y., Lal, R., 2016. Concentrations on lettuce (*Lactuca sativa*) seed germination: nanotoxicants or nanonutrients? Water Air Soil Pollut. 227 (1), 42.

Liu, J., Dhungana, B., Cobb, G.P., 2018a. Copper oxide nanoparticles and arsenic interact to alter seedling growth of rice (*Oryza sativa japonica*). Chemosphere 206, 330–337.

Liu, J., Simms, M., Song, S., King, R.S., Cobb, G.P., 2018b. Physiological effects of copper oxide nanoparticles and arsenic on the growth and life cycle of rice (*Oryza sativa japonica* 'Koshihikari'). Environ. Sci. Technol. 52 (23), 13728–13737.

Liu, J., Dhungana, B., Cobb, G.P., 2018c. Environmental behavior, potential phytotoxicity, and accumulation of copper oxide nanoparticles and arsenic in rice plants. Environ. Toxicol. Chem. 37 (1), 11–20.

Lopez-Vargas, E.R., Ortega-Ortiz, H., Cadenas-Pliego, G., Romenus, K.D., Fuente, M.C., Benavides-Mendoza, A., Juarez-Maldonado, A., 2018. Foliar application of copper nanoparticles increases the fruit quality and the content of bioactive compounds in tomatoes. Appl. Sci. 8 (7), 1020.

Ma, X., Geisler-Lee, J., Deng, Y., Kolmakov, A., 2010. Interactions between engineered nanoparticles (ENPs) and plants: phytotoxicity, uptake and accumulation. Sci. Total Environ. 408, 3053–3061.

Maity, A., Natarajan, N., Pastor, M., Vijay, D., Gupta, C.K., Wasnik, V.K., 2018. Nanoparticles influence seed germination traits and seed pathogen infection rate in forage sorghum (*Sorghum bicolour*) and cowpea (*Vigna unguiculata*). Indian J. Exp. Biol. 56 (6), 363–372.

Maksymiecz, W., 1997. Effect of copper on cellular processes in higher plants. Photosynthetica 34 (3), 321–342.

Manke, A., Wang, L.Y., Rojanasakul, Y., 2013. Mechanisms of nanoparticle-induced oxidative stress and toxicity. Biomed. Res. Int. 2013, 942916.

Mansilla, N., Racca, S., Gras, D.E., Gonzalez, D.H., Welchen, E., 2018. The complexity of mitochondrial complex IV: an update of cytochrome c oxidase biogenesis in plants. Int. J. Mol. Sci. 19 (3), 662.

Margenot, A.J., Rippner, D.A., Dumlao, M.R., Nezami, S., Green, P.G., Parikh, S.J., McElrone, A.J., 2018. Copper oxide nanoparticle effects on root growth and hydraulic conductivity of two vegetable crops. Plant Soil 431 (1–2), 333–345.

Masarovičová, E., Kráľová, K., 2013. Metal nanoparticles and plants. Ecol. Chem. Eng. S 20 (1), 9–22.

Masarovičová, E., Kráľová, K., Šeršeň, F., 2010. Plant responses to toxic metal stress. In: Pessarakli, M. (Ed.), Handbook of Plant and Crop Stress, third ed. Taylor and Francis, CRC, Boca Raton, pp. 595–634.

Masarovičová, E., Kráľová, K., Zinjarde, S.S., 2014. Metal nanoparticles in plants. Formation and action. In: Pessarakli, M. (Ed.), Handbook of Plant and Crop Physiology, third ed. Taylor and Francis, CRC, Boca Raton, pp. 683–731.

McManus, P., Hortin, J., Anderson, A.J., Jacobson, A.R., Britt, D.W., Stewart, J., McLean, J.E., 2018. Rhizosphere interactions between copper oxide nanoparticles and wheat root exudates in a sand matrix: influences on copper bioavailability and uptake. Environ. Toxicol. Chem. 37 (10), 2619–2632.

Millardet, P.A., 1885. Traitement du mildiou par le mélange de sulphate de cuivre et de chaux. J. Agric. Prat. 2, 707–710.

Moon, Y.S., Park, E.S., Kim, T.O., Lee, H.S., Lee, S.E., 2014. SELDI-TOF MS-based discovery of a biomarker in *Cucumis sativus* seeds exposed to CuO nanoparticles. Environ. Toxicol. Pharmacol. 38 (3), 922–931.

Mosa, K.A., El-Naggar, M., Ramamoorthy, K., Alawadhi, H., Elnaggar, A., Wartanian, S., Ibrahim, E., Hani, H., 2018. Copper nanoparticles induced genotoxicty, oxidative stress, and changes in superoxide dismutase (SOD) gene expression in cucumber (*Cucumis sativus*) plants. Front. Plant Sci. 9, 872.

Moustakas, M., Lanaras, T., Symeonidis, L., Karataglis, S., 1994. Field-grown *Avena sativa* under copper and lead stress. Photosynthetica 30, 389–396.

Musante, C., White, J.C., 2012. Toxicity of silver and copper to *Cucurbita pepo*: differential effects of nano and bulk-size particles. Environ. Toxicol. 27 (9), 510–517.

Mustafa, G., Komatsu, S., 2017. Nanoparticles mediated soybean response mechanism at morphological, physiological, and proteomic level. Curr. Proteomics 14 (1), 3–12.

Mysliwa-Kurdziel, B., Prasad, M.N.V., Strzalka, K., 2004. Photosynthesis in heavy metal stressed plants. In: Prasad, M.N.V. (Ed.), Heavy Metal Stress in Plants: From Biomolecules to Ecosystems, second ed. Springer, Berlin, pp. 46–181.

Nair, P.M.G., Chung, I.M., 2015a. A mechanistic study on the toxic effect of copper oxide nanoparticles in soybean (*Glycine max L.*) root development and lignification of root cells. Biol. Trace Elem. Res. 162 (1–3), 342–352.

Nair, P.M.G., Chung, I.M., 2015b. Biochemical, anatomical and molecular level changes in cucumber (*Cucumis sativus*) seedlings exposed to copper oxide nanoparticles. Biologia 70 (12), 1575–1585.

Nair, P.M.G., Chung, I.M., 2015a. Changes in the growth, redox status and expression of oxidative stress related genes in chickpea (*Cicer arietinum* L.) in response to copper oxide nanoparticle exposure. J. Plant Growth Regul. 34 (2), 350–361.

Nair, P.M.G., Kim, S.H., Chung, I.M., 2014. Copper oxide nanoparticle toxicity in mung bean (*Vigna radiata* L.) seedlings: physiological and molecular level responses of in vitro grown plants. Acta Physiol. Plant. 36 (11), 2947–2958.

Ngo, Q.B., Dao, T.H., Nguyen, H.C., Tran, X.T., Van Nguyen, T., Khuu, T.D., Huynh, T.H., 2014. Effects of nanocrystalline powders (Fe, Co and Cu) on the germination, growth, crop yield and product quality of soybean (Vietnamese species DT-51). Adv. Nat. Sci. Nanosci. Nanotechnol. 5 (1), 015016.

Nieboer, E., Fletcher, G.G., Thomassen, Y., 1999. Relevance of reactivity determinants to exposure assessment and biological monitoring of the elements. J. Environ. Monit. 1, 1–14.

Ochoa, L., Medina-Velo, I.A., Barrios, A.C., Bonilla-Bird, N.J., Hernandez-Viezcas, J.A., Peralta-Videa, J.R., Gardea-Torresdey, J.L., 2017. Modulation of CuO nanoparticles toxicity to green pea (*Pisum sativum* Fabaceae) by the phytohormone indole-3-acetic acid. Sci. Total Environ. 598, 513–524.

Ochoa, L., Zuverza-Mena, N., Medina-Velo, I.A., Flores-Margez, J.P., Peralta-Videa, J.R., Gardea-Torresdey, J.L., 2018. Copper oxide nanoparticles and bulk copper oxide, combined with indole-3-acetic acid, alter aluminum, boron, and iron in *Pisum sativum* seeds. Sci. Total Environ. 634, 1238–1245.

Ogunkunle, C.O., Jimoh, M.A., Asogwa, N.T., Viswanathan, K., Vishwakarma, V., Fatoba, P.O., 2018. Effects of manufactured nano-copper on copper uptake, bioaccumulation and enzyme activities in cowpea grown on soil substrate. Ecotoxicol. Environ. Saf. 155, 86–93.

Olkhovskaya, I.P., Bogoslovskaya, O.A., Yablokov, A.G., Glushchenko, N.N., 2019. Spring barley yield after presowing seed treatment with metal nanoparticles. Nanotechnol. Russ. 14 (1–2), 55–61.

Pagano, L., Pasquali, F., Majumdar, S., De la Torre-Roche, R., Zuverza-Mena, N., Villani, M., Zappettini, A., Marra, R.E., Isch, S.M., Marmiroli, M., Maestri, E., Dhankher, O.M., White, J.C., Marmiroli, N., 2017. Exposure of *Cucurbita pepo* to binary combinations of engineered nanomaterials: physiological and molecular response. Environ. Sci. Nano 4 (7), 1579–1590.

Panda, S.K., Choudhury, S., Patra, H.K., Tuteja, N., 2016. Heavy-metal-induced oxidative stress in plants: physiological and molecular perspectives. In: Gill, S.S. (Ed.), Abiotic Stress Response in Plants. Wiley-VCH, pp. 221–236.

Pandey, N., Pathak, G.C., Pandey, D.K., Pandey, R., 2009. Heavy metals, Co, Ni, Cu, Zn and Cd, produce oxidative damage and evoke differential antioxidant responses in spinach. Braz. J. Plant Physiol. 21 (2), 103–111.

Pariona, N., Mtz-Enriquez, A.I., Sanchez-Rangel, D., Carrion, G., Paraguay-Delgado, F., Rosas-Saito, G., 2019. Green-synthesized copper nanoparticles as a potential antifungal against plant pathogens. RSC Adv. 9 (33), 18835–18843.

Patyka, V.P., Huliaieva, H.B., Tokovenko, I.P., Maksin, V.I., Kaplunenko, V.G., 2017. Physiological effect of citrate chelate nanoparticles on plants of wheat. Agric. Sci. Pract. 4 (2), 28–36.

Pelegrino, M.T., Kohatsu, M.Y., Seabra, A.B., Monteiro, L.R., Gomes, D.G., Oliveira, H.C., Rolim, W.R., de Jesus, T.A., Batista, B.L., Lange, C.N., 2020. Effects of copper oxide nanoparticles on growth of lettuce (*Lactuca sativa* L.) seedlings and possible implications of nitric oxide in their antioxidative defense. Environ. Monit. Assess. 192 (4), 232.

Peng, C., Xu, C., Liu, Q.L., Sun, L.J., Luo, Y.M., Shi, J.Y., 2017. Fate and transformation of CuO nanoparticles in the soil-rice system during the life cycle of rice plants. Environ. Sci. Technol. 51 (9), 4907–4917.

Perez Gutierrez, R.M., 2016. Review of *Cucurbita pepo* (pumpkin) its phytochemistry and pharmacology. Med. Chem. 6 (1), 012–021.

Perez, C.D.P., De La Torre-Roche, R., Zuverza-Mena, N., Ma, C.X., Shen, Y., White, J.C., Pozza, E.A., Pozza, A.A.A., Elmer, W.H., 2020. Metalloid and metal oxide nanoparticles suppress sudden death syndrome of soybean. J. Agric. Food Chem. 68 (1), 77–87.

Perez-Labrada, F., Lopez-Vargas, E.R., Ortega-Ortiz, H., Cadenas-Pliego, G., Benavides-Mendoza, A., Juarez-Maldonado, A., 2019. Responses of tomato plants under saline stress to foliar application of copper nanoparticles. Plants 8 (6), 151.

Pikula, K., Chaika, V., Zakharenko, A., Markina, Z., Vedyagin, A., Kuznetsov, V., Gusev, A., Park, S., Golokhvast, K., 2020. Comparison of the level and mechanisms of toxicity of carbon nanotubes, carbon nanofibers, and silicon nanotubes in bioassay with four marine microalgae. Nanomaterials 10 (3), 485.

Polak, R., Phillips, E.M., Campbell, A., 2015. Legumes: health benefits and culinary approaches to increase intake. Clin. Diab. 33 (4), 198–205.

Polischuk, S.D., Churilov, G.I., Borychev, S.N., Byshov, N.V., Nazarova, A.A., 2018. Nanopowders of cuprum, cobalt and their oxides used in the intensive technology for growing cucumbers. Int. J. Nanotechnol. 15 (4–5), 352–369.

Pradhan, S., Patra, P., Mitra, S., Dey, K.K., Basu, S., Chandra, S., Palit, P., Goswami, A., 2015. Copper nanoparticle (CuNP) nanochain arrays with a reduced toxicity response: a biophysical and biochemical outlook on *Vigna radiata*. J. Agric. Food Chem. 63 (10), 2606–2617.

Pretty, J., Bharucha, Z.P., 2014. Sustainable intensification in agricultural systems. Ann. Bot. 114 (8), 1571–1596.

Pu, S.Y., Yan, C., Huang, H.Y., Liu, S., Deng, D.L., 2019. Toxicity of nano-CuO particles to maize and microbial community largely depends on its bioavailable fractions. Environ. Pollut. 255 (Part 2), 113248.

Qiu, H., Smolders, E., 2017. Nanospecific phytotoxicity of CuO nanoparticles in soils disappeared when bioavailability factors were considered. Environ. Sci. Technol. 51 (20), 11976–11985.

Quartacci, M.F., Pinzino, C., Sgherri, C.L.M., Dalla Vecchia, F., Navari-Izzo, F., 2000. Growth in excess copper induces changes in the lipid composition and fluidity of PSII-enriched membranes in wheat. Physiol. Plant. 108, 87–93.

Quiterio-Gutierrez, T., Ortega-Ortiz, H., Cadenas-Pliego, G., Hernandez-Fuentes, A.D., Sandoval-Rangel, A., Benavides-Mendoza, A., Cabrera-de la Fuente, M., Juarez-Maldonado, A., 2019. The application of selenium and copper nanoparticles modifies the biochemical responses of tomato plants under stress by *Alternaria solani*. Int. J. Mol. Sci. 20 (8), 1950.

Rafique, M., Shaikh, A.J., Rasheed, R., Tahir, M.B., FaiqBakhat, H., Rafique, M.S., Rabbani, F., 2017. A review on synthesis, characterization and applications of copper nanoparticles using green method. Nano 12 (4), 1750043.

Rai, M., Ingle, A.P., Pandit, R., Paralikar, P., Shende, S., Gupta, I., Biswas, J.K., da Silva, S.S., 2018. Copper and copper nanoparticles: role in management of insect-pests and pathogenic microbes. Nanotechnol. Rev. 7 (4), 303–315.

Rajput, V., Minkina, T., Fedorenko, A., Sushkova, S., Mandzhieva, S., Lysenko, V., Duplii, N., Fedorenko, G., Dvadnenko, K., Ghazaryan, K., 2018. Toxicity of copper oxide nanoparticles on spring barley (*Hordeum sativum* distichum). Sci. Total Environ. 645, 1103–1113.

Rajput, V., Minkina, T., Ahmed, B., Sushkova, S., Singh, R., Soldatov, M., Laratte, B., Fedorenko, A., Mandzhieva, S., Blicharska, E., Musarrat, J., Saquib, Q., Flieger, J., Gorovtsov, A., 2019a. Interaction of copper-based nanoparticles to soil, terrestrial and aquatic systems: critical review of the state of the science and future perspectives. Rev. Environ. Contam. Toxicol. 252, 51–96.

Rajput, V.D., Minkina, T., Fedorenko, A., Mandzhieva, S., Sushkova, S., Lysenko, V., Duplii, N., Azarov, A., Chokheli, V., 2019b. Destructive effect of copper oxide nanoparticles on ultrastructure of chloroplast, plastoglobules and starch grains in spring barley (*Hordeum sativum*). Int. J. Agric. Biol. 21 (1), 171–174.

Raliya, R., Franke, C., Chavalmane, S., Nair, R., Reed, N., Biswas, P., 2016. Quantitative understanding of nanoparticle uptake in watermelon plants. Front. Plant Sci. 7, 1288.

Ramesh, C., HariPrasad, M., Ragunathan, V., 2011. Effect of *Arachis hypogaea* L. leaf extract on Barfoed's solution; Green synthesis of Cu_2O nanoparticles and its antibacterial effect. Curr. Nanosci. 7 (6), 995–999.

Rani, H., Singh, S.P., Yadav, T.P., Khan, M.S., Ansari, M.I., Singh, A.K., 2020. In-vitro catalytic, antimicrobial and antioxidant activities of bioengineered copper quantum dots using *Mangifera indica* (L.) leaf extract. Mater. Chem. Phys. 239, 122052.

Rastogi, A., Zivcak, M., Sytar, O., Kalaji, H.M., He, X.L., Mbarki, S., Brestic, M., 2017. Impact of metal and metal oxide nanoparticles on plant: a critical review. Front. Chem. 5, 78.

Rehman, M., Liu, L.J., Wang, Q., Saleem, M.H., Bashir, S., Ullah, S., Peng, D.X., 2019. Copper environmental toxicology, recent advances, and future outlook: a review. Environ. Sci. Polut. 26 (18), 18003–18016.

Renganathan, M., Bose, S., 1989. Inhibition of primary photochemistry of photosystem II by copper in isolated pea chloroplasts. Biochim. Biophys. Acta 974, 247–253.

Renger, G., Gleiter, H.M., Haag, E., Reifarth, F., 1993. Photosystem II: thermodynamics and kinetics of electron transport from Q_A to $Q_B(Q_B^*)$ and deletrious effects of copper (II). Z. Naturforsch. 48c, 234–240.

Ricepedia, 2020. The Global Staple. http://ricepedia.org/rice-as-food/the-global-staple-rice-consumers.

Roberts, J.L., Moreau, R., 2016. Functional properties of spinach (*Spinacia oleracea* L.) phytochemicals and bioactives. Food Funct. 7 (8), 3337–3353.

Rodrigo, M.A.M., Anjum, N.A., Heger, Z., Zitka, O., Vojtech, A., Pereira, E., Kizek, R., 2016. Role of phytochelatins in redox caused stress in plants and animals. In: Shanker, A.K., Shanker, C. (Eds.), Abiotic and Biotic Stress in Plants: Recent Advances and Future Perspectives. InTech, Rijeka, Croatia, https://doi.org/10.5772/62160.

Rooney, W.L., 2016. Sorghum: production and improvement practices. In: Wrigley, C., Corke, H., Seetharaman, K., Faubion, J. (Eds.), second ed. Encyclopedia of Food Grains, vol. 4. Elsevier, pp. 201–206.

Roy, S.K., Cho, S.W., Kwon, S.J., Kamal, A.H.M., Lee, D.G., Sarker, K., Lee, M.S., Xin, Z.G., Woo, S.H., 2017. Proteome characterization of copper stress responses in the roots of sorghum. Biometals 30 (5), 765–785.

Rui, M.M., Ma, C.X., White, J.C., Hao, Y., Wang, Y.Y., Tang, X.L., Yang, J., Jiang, F.P., Ali, A., Rui, Y.K., Cao, W.D., Chen, G.C., Xing, B.S., 2018. Metal oxide nanoparticles alter peanut (*Arachis hypogaea* L.) physiological response and reduce nutritional quality: a life cycle study. Environ. Sci. Nano 5 (9), 2088–2102.

Saharan, V., Sharma, G., Yadav, M., Choudhary, M.K., Sharma, S.S., Pal, A., Raliya, R., Biswas, P., 2015. Synthesis and in vitro antifungal efficacy of Cu-chitosan nanoparticles against pathogenic fungi of tomato. Int. J. Biol. Macromol. 75, 346–353.

Saharan, V., Kumaraswamy, R.V., Choudhary, R.C., Kumari, S., Pal, A., Raliya, R., Biswas, P., 2016. Cu-chitosan nanoparticle mediated sustainable approach to enhance seedling growth in maize by mobilizing reserved food. J. Agric. Food Chem. 64 (31), 6148–6155.

Sahu, T., Sahu, J., 2015. *Cucumis sativus* (cucumber): a review of its pharmacological activity. J. Appl. Pharm. Res. 3 (1), 4–9.

Salas-Leiva, J., Salas-Leiva, D.E., Tovar-Ramirez, D., Herrera-Perez, G., Tarango-Rivero, S., Luna-Velasco, A., Orrantia-Borunda, E., 2021. Copper oxide nanoparticles slightly affect diversity and metabolic profiles of the prokaryotic community in pecan tree (*Carya illinoinensis*) rhizospheric soil. Appl. Soil Ecol. 157, 103772.

Saleem, M.H., Fahad, S., Khan, S.U., Din, M., Ullah, A., Sabagh, A.E., Hossain, A., Llanes, A., Liu, L.J., 2020. Copper-induced oxidative stress, initiation of antioxidants and phytoremediation potential of flax (*Linum usitatissimum* L.) seedlings grown under the mixing of two different soils of China. Environ. Sci. Pollut. Res. 27, 5211–5221.

Samuelsson, G., Öquist, G., 1980. Effects of copper chloride on photosynthetic electron transport and chlorophyll-protein complexes of *Spinacia oleracea*. Plant Cell Physiol. 21, 445–454.

Sathiyabama, M., Manikandan, A., 2018. Application of copper-chitosan nanoparticles stimulate growth and induce resistance in finger millet (*Eleusine coracana* Gaertn.) plants against blast disease. J. Agric. Food Chem. 66 (8), 1784–1790.

Schröder, W.P., Arellano, J.B., Bittner, T., Barón, M., Eckert, H.J., Renger, G., 1994. Flash-induced absorption spectroscopy studies of copper interaction with photosystem II in higher plants. J. Biol. Chem. 269, 32865–32870.

Seneviratne, M., Rajakaruna, N., Rizwan, M., Madawala, H.M.S.P., Ok, Y.S., Vithanage, M., 2019. Heavy metal-induced oxidative stress on seed germination and seedling development: a critical review. Environ. Geochem. Health 41 (4), 1813–1831.

Šeršeň, F., Kráľová, K., Blahová, M., 1996. Photosynthesis of *Chlorella vulgaris* as affected by diaqua(4-chloro-2-methyl-phenoxyacetato)copper(II) complex. Biol. Plant. 38, 71–75.

Šeršeň, F., Kráľová, K., Bumbálová, A., Švajlenová, O., 1997. The effect of Cu(II) ions bound with tridentate Schiff base ligands upon the photosynthetic apparatus. J. Plant Physiol. 151 (3), 299–305.

Sezer Tuncsoy, B., Ozalp, P., 2016. Toxic effects of copper oxide nanoparticles in midgut and fat body of *Galleria mellonella* (Lepidoptera: Pyralidae). Toxicol. Lett. 258, 270.

Shabbir, Z., Sardar, A., Shabbir, A., Abbas, G., Shamshad, S., Khalid, S., Natasha, Murtaza, G., Dumat, C., Shahid, M., 2020. Copper uptake, essentiality, toxicity, detoxification and risk assessment in soil-plant environment. Chemosphere 259, 127436.

Shah, T.R., Prasad, K., Kumar, P., 2016. Maize—a potential source of human nutrition and health: a review. Cogent Food Agric. 2 (1), 1166995.

Shang, H.P., Guo, H.Y., Ma, C.X., Li, C.Y., Chefetz, B., Polubesova, T., Xing, B.S., 2019. Maize (*Zea mays* L.) root exudates modify the surface chemistry of CuO nanoparticles: altered aggregation, dissolution and toxicity. Sci. Total Environ. 690, 502–510.

Sharm, S., Uttam, K.N., 2017. Rapid analyses of stress of copper oxide nanoparticles on wheat plants at an early stage by laser induced fluorescence and attenuated total reflectance Fourier transform infrared spectroscopy. Vib. Spectrosc. 92, 135–150.

Shaw, A.K., Hossain, Z., 2013. Impact of nano-CuO stress on rice (*Oryza sativa* L.) seedlings. Chemosphere 93 (6), 906–915.

Shaw, A.K., Ghosh, S., Kalaji, H.M., Bosa, K., Brestic, M., Zivcak, M., Hossain, Z., 2014. Nano-CuO stress induced modulation of antioxidative defense and photosynthetic performance of Syrian barley (*Hordeum vulgare* L.). Environ. Exp. Bot. 102, 37–47.

Shende, S., Rathod, D., Gade, A., Rai, M., 2017. Biogenic copper nanoparticles promote the growth of pigeon pea (*Cajanus cajan* L.). IET Nanobiotechnol. 11 (7), 773–781.

Shiferaw, B., Smale, M., Braun, H.J., Duveiller, E., Reynolds, M., Muricho, G., 2013. Crops that feed the world 10. Past successes and future challenges to the role played by wheat in global food security. Food Secur. 5 (3), 291–317.

Shoi, Y., Tamai, H., Sasa, T., 1978. Inhibition of photosystem II in green alga, *Ankistrodesmus falcatus* by copper. Physiol. Plant. 44, 434–438.

Sidhu, A., Barmota, H., Bala, A., 2017. Antifungal evaluation studies of copper sulfide nanoaquaformulations and its impact on seed quality of rice (*Oryzae sativa*). Appl. Nanosci. 7 (8), 681–689.

Sima, X.F., Shen, X.C., Fang, T., Yu, H.Q., Jiang, H., 2017. Efficiently reducing the plant growth inhibition of CuO NPs using rice husk-derived biochar: experimental demonstration and mechanism investigation. Environ. Sci. Nano 4 (8), 1722–1732.

Singh, D., Kumar, A., 2016. Impact of irrigation using water containing CuO and ZnO nanoparticles on *Spinach oleracea* grown in soil media. Bull. Environ. Contam. Toxicol. 97 (4), 548–553.

Singh, D.P., Singh, S.P., 1987. Action of heavy metals on Hill activity and O_2 evolution in *Anacystis nidulants*. Plant Physiol. 83, 12–14.

Singh, P., Kim, Y.J., Zhang, D.B., Yang, D.C., 2016. Biological synthesis of nanoparticles from plants and microorganisms. Trends Biotechnol. 34 (7), 588–599.

Singh, A., Singh, N.B., Hussain, I., Singh, H., 2017. Effect of biologically synthesized copper oxide nanoparticles on metabolism and antioxidant activity to the crop plants *Solanum lycopersicum* and *Brassica oleracea* var. *botrytis*. J. Biotechnol. 262, 11–27.

Singh, J., Kumar, V., Kim, K.H., Rawat, M., 2019. Biogenic synthesis of copper oxide nanoparticles using plant extract and its prodigious potential for photocatalytic degradation of dyes. Environ. Res. 177, 108569.

Sommer, A.L., 1931. Copper as an essential for plant growth. Plant Physiol. 6 (2), 339–345.

Spielman-Sun, E., Lombi, E., Donner, E., Avellan, A., Etschmann, B., Howard, D., Lowry, G.V., 2018. Temporal evolution of copper distribution and speciation in roots of *Triticum aestivum* exposed to CuO, $Cu(OH)_2$, and CuS nanoparticles. Environ. Sci. Technol. 52 (17), 9777–9784.

Stampoulis, D., Sinha, S.K., White, J.C., 2009. Assay-dependent phytotoxicity of nanoparticles to plants. Environ. Sci. Technol. 43 (24), 9473–9479.

Stiborová, M., Doubravová, M., Leblová, S., 1986. A comparative study of the effect of heavy metal ions on ribulose-1,5-bisphosphate carboxylase and phosphoenol pyruvate carboxylase. Biochem. Physiol. Pflanz. 181, 373–379.

Suresh, S., Karthikeyan, S., Jayamoorthy, K., 2016. FTIR and multivariate analysis to study the effect of bulk and nano copper oxide on peanut plant leaves. J. Sci. Adv. Mater. Dev. 1 (3), 343–350.

Swaminathan, M.S., 2006. An evergreen revolution. Crop Sci. 46 (5), 2293–2303.

Szalontai, B., Horvath, L.I., Debreczeny, M., Droppa, M., Horvath, G., 1999. Molecular rearrangements of thylakoids after heavy metal poisoning, as seen by Fourier transform infrared (FTIR) and electron spin resonance (ESR) spectroscopy. Photosynth. Res. 61, 241–252.

Talari, A., Shakappa, D., 2018. Role of pigeon pea (*Cajanus cajan* L.) in human nutrition and health: a review. Asian J. Dairy Food Res. 37, 212–220.

Tamez, C., Hernandez-Molina, M., Hernandez-Viezcas, J.A., Gardea-Torresdey, J.L., 2019. Uptake, transport, and effects of nano-copper exposure in zucchini (*Cucurbita pepo*). Sci. Total Environ. 665, 100–106.

Taylor, A.F., Rylott, E.L., Anderson, C.W., Bruce, N.C., 2014. Investigating the toxicity, uptake, nanoparticle formation and genetic response of plants to gold. PLoS One 9, e93793.

Tidke, S.A., Ramakrishna, D., Kiran, S., Kosturkova, G., Ravishankar, G.A., 2015. Nutraceutical potential of soybean: review. Asian J. Clin. Nutr. 7, 22–32.

Tiwari, P.K., Shweta, Sing, A.K., Singh, V.P., Prasad, S.M., Ramawat, N., Tripathi, D.K., Chauhan, D.K., Rai, A.K., 2019. Liquid assisted pulsed laser ablation synthesized copper oxide nanoparticles (CuO-NPs) and their differential impact on rice seedlings. Ecotoxicol. Environ. Saf. 176, 321–329.

Tolaymat, T., Genaidy, A., Abdelraheern, W., Dionysiou, D., Andersen, C., 2017. The effects of metallic engineered nanoparticles upon plant systems: an analytic examination of scientific evidence. Sci. Total Environ. 579, 93–106.

Toomer, O.T., 2018. Nutritional chemistry of the peanut (*Arachis hypogaea*). Crit. Rev. Food Sci. Nutr. 58 (17), 3042–3053.

Tortosa, G., Pacheco, P.J., Hidalgo-Garcia, A., Granados, A., Delgado, A., Mesa, S., Bedmar, E.J., Delgado, M.J., 2020. Copper modulates nitrous oxide emissions from soybean root nodules. Environ. Exp. Bot. 180, 104262.

Tripathi, D.K., Singh, S., Singh, S., Mishra, S., Chauhan, D.K., Dubey, N.K., 2015. Micronutrients and their diverse role in agricultural crops: advances and future prospective. Acta Physiol. Plant. 37 (7), 139.

Trujillo-Reyes, J., Majumdar, S., Botez, C.E., Peralta-Videa, J.R., Gardea-Torresdey, J.L., 2014. Exposure studies of core-shell Fe/Fe_3O_4 and Cu/CuO NPs to lettuce (*Lactuca sativa*) plants: are they a potential physiological and nutritional hazard? J. Hazard. Mater. 267, 255–263.

U.S. National Nanotechnology Initiative, 2004. The National Nanotechnology Initiative Strategic Plan. https://www.nano.gov/sites/default/files/pub_resource/nni_strategic_plan_2004.pdf.

UN General Assembly, 2014. Resolution adopted by the General Assembly on 20 December 2013. https://undocs.org/en/A/RES/68/231.

Valdes, C., Cota-Ruiz, K., Flores, K., Ye, Y.Q., Hernandez-Viezcas, J.A., Gardea-Torresdey, J.L., 2020. Antioxidant and defense genetic expressions in corn at early-developmental stage are differentially modulated by copper form exposure (nano, bulk, ionic): nutrient and physiological effects. Ecotoxicol. Environ. Saf. 206, 111197.

Van, N.L., Ma, C.X., Shang, J.Y., Rui, Y.K., Liu, S.T., Xing, B.S., 2016. Effects of CuO nanoparticles on insecticidal activity and phytotoxicity in conventional and transgenic cotton. Chemosphere 144, 661–670.

Vanti, G.L., Masaphy, S., Kurjogi, M., Chakrasali, S., Nargund, V.B., 2020. Synthesis and application of chitosan-copper nanoparticles on damping off causing plant pathogenic fungi. Int. J. Biol. Macromol. 156, 1387–1395.

Vasanthan, T., Hoover, R., 2009. Barley starch: production, properties, modification and uses. In: BeMiller, J., Whistker, R. (Eds.), Starch, Chemistry and Technology, third ed. Elsevier, pp. 601–628.

Vavilin, D.V., Polynov, V.A., Matorin, D.N., Venediktov, P.S., 1995. The sublethal concentrations of copper stimulate photosystem II photoinhibition in *Chlorella pyrenoidosa*. J. Plant Physiol. 146, 609–614.

Wang, Y.Y., Jiang, F.P., Ma, C.X., Rui, Y.K., Tsang, D.C.W., Xing, B.S., 2019a. Effect of metal oxide nanoparticles on amino acids in wheat grains (*Triticum aestivum*) in a life cycle study. J. Environ. Manag. 241, 319–327.

Wang, X.X., Sun, W.J., Ma, X.M., 2019b. Differential impacts of copper oxide nanoparticles and copper(II) ions on the uptake and accumulation of arsenic in rice (*Oryza sativa*). Environ. Pollut. 252 (Part B), 967–973.

Wang, Y.J., Lin, Y.J., Xu, Y.W., Yin, Y., Guo, H.Y., Du, W.C., 2019c. Divergence in response of lettuce (var. *ramosa* Hort.) to copper oxide nanoparticles/microparticles as potential agricultural fertilizer. Environ. Pollut. Bioavailab. 31 (1), 80–84.

Willcox, J.K., Catignani, G.L., Lazarus, S., 2003. Tomatoes and cardiovascular health. Crit. Rev. Food Sci. Nutr. 43, 1–18.

Wright, M., Adams, J., Yang, K., McManus, P., Jacobson, A., Gade, A., McLean, J., Britt, D., Anderson, A., 2016. A root-colonizing pseudomonad lessens stress responses in wheat imposed by CuO nanoparticles. PLoS One 11 (10), e0164634.

Wu, F., Harper, B.J., Crandonb, L.E., Harper, S.L., 2020. Assessment of Cu and CuO nanoparticle ecological responses using laboratory small-scale microcosms. Environ. Sci. Nano 7, 105–115.

Xiong, T.T., Dumat, C., Dappe, V., Vezin, H., Schreck, E., Shahid, M., Pierart, A., Sobanska, S., 2017. Copper oxide nanoparticle foliar uptake, phytotoxicity, and consequences for sustainable urban agriculture. Environ. Sci. Technol. 51 (9), 5242–5251.

Yang, Z.Z., Chen, J., Dou, R.Z., Gao, X., Mao, C.B., Wang, L., 2015. Assessment of the phytotoxicity of metal oxide nanoparticles on two crop plants, maize (*Zea mays* L.) and rice (*Oryza sativa* L.). Int. J. Environ. Res. Public Health 12 (12), 15100–15109.

Yasmeen, F., Raja, N.I., Razzaq, A., Komatsu, S., 2017. Proteomic and physiological analyses of wheat seeds exposed to copper and iron nanoparticles. Biochim. Biophys. Acta Proteins Proteomics 1865 (1), 28–42.

Yasmeen, F., Raja, N.I., Ilyas, N., Komatsu, S., 2018. Quantitative proteomic analysis of shoot in stress tolerant wheat varieties on copper nanoparticle exposure. Plant Mol. Biol. Rep. 36 (2), 326–340.

Yeh, T.Y., Lin, C.L., Lin, C.F., Chen, C.C., 2015. Chelator-enhanced phytoextraction of copper and zinc by sunflower, Chinese cabbage, cattails and reeds. Int. J. Environ. Sci. Technol. 12, 327–340.

Yruela, I., 2005. Copper in plants. Braz. J. Plant Physiol. 17 (1), 147–156.

Yruela, I., 2009. Copper in plants: acquisition, transport and interactions. Funct. Plant Biol. 36 (5), 409–430.

Yruela, I., Montoya, G., Alonso, P.J., Picorel, R., 1991. Identification of the pheophytin-Q_A-Fe domain of the reducing side of the photosystem II as the Cu(II) inhibitory binding site. J. Biol. Chem. 266, 22847–22850.

Yruela, I., Montoya, G., Picorel, R., 1992. The inhibitory mechanism of Cu(II) on the photosystem II electron transport from higher plants. Photosynth. Res. 33, 227–233.

Yruela, I., Alonso, P.J., De Zarate, I.O., Montoya, G., Picorel, R., 1993. Precise location of the Cu(II) inhibitory binding site in higher plant and bacterial photosynthetic reaction centers as probed by light induced absorption changes. J. Biol. Chem. 268, 1684–1689.

Yugandhar, P., Vasavi, T., Shanmugam, B., Devi, P.U.M., Reddy, K.S., Savithramma, N., 2019. Biofabrication, characterization and evaluation of photocatalytic dye degradation efficiency of *Syzygium alternifolium* leaf extract mediated copper oxide nanoparticles. Mater. Res. Express 6 (6), 065034.

Zakharova, O., Kolesnikov, E., Shatrova, N., Gusev, A., 2019. The effects of CuO nanoparticles on wheat seeds and seedlings and *Alternaria solani* fungi: in vitro study. In: Gusev, A. (Ed.), International Jubilee Scientific and Practical Conference Innovative Directions of Development of the Forestry Complex. IOP Conference Series-Earth and Environmental Science, vol. 226, p. 012036.

Zhang, Z.Y., Ke, M.J., Qu, Q., Peijnenburg, W.J.G.M., Lu, T., Zhang, Q., Ye, Y.Z., Xu, P.F., Du, B.B., Sun, L.W., Qian, H., 2018. Impact of copper nanoparticles and ionic copper exposure on wheat (*Triticum aestivum* L.) root morphology and antioxidant response. Environ. Pollut. 239, 689–697.

Zhao, L.J., Huang, Y.X., Hu, J., Zhou, H.J., Adeleye, A.S., Keller, A.A., 2016a. ^{1}H NMR and GC-MS based metabolomics reveal defense and detoxification mechanism of cucumber plant under nano-Cu stress. Environ. Sci. Technol. 50 (4), 2000–2010.

Zhao, L.J., Huang, Y.X., Zhou, H.J., Adeleye, A.S., Wang, H.T., Ortiz, C., Mazer, S.J., Keller, A.A., 2016b. GC-TOF-MS based metabolomics and ICP-MS based metallomics of cucumber (*Cucumis sativus*) fruits reveal alteration of metabolites profile and biological pathway disruption induced by nano copper. Environ. Sci. Nano 3 (5), 1114–1123.

Zhao, L.J., Ortiz, C., Adeleye, A.S., Hu, Q.R., Zhou, H.J., Huang, Y.X., Keller, A.A., 2016c. Metabolomics to detect response of lettuce (*Lactuca sativa*) to $Cu(OH)_2$ nanopesticides: oxidative stress response and detoxification mechanisms. Environ. Sci. Technol. 50 (17), 9697–9707.

Zhao, L., Huang, Y., Hannah-Bick, C., Fulton, A.N., Keller, A.A., 2016d. Application of metabolomics to assess the impact of $Cu(OH)_2$ nanopesticide on the nutritional value of lettuce (*Lactuca sativa*): enhanced Cu intake and reduced antioxidants. NanoImpact 3–4, 58–66.

Zhao, L.J., Hu, Q.R., Huang, Y.X., Keller, A.A., 2017a. Response at genetic, metabolic, and physiological levels of maize (*Zea mays*) exposed to a $Cu(OH)_2$ nanopesticide. ACS Sustain. Chem. Eng. 5 (9), 8294–8301.

Zhao, L.J., Hu, Q.R., Huang, Y.X., Fulton, A.N., Hannah-Bick, C., Adeleye, A.S., Keller, A.A., 2017b. Activation of antioxidant and detoxification gene expression in cucumber plants exposed to a $Cu(OH)_2$ nanopesticide. Environ. Sci. Nano 4 (8), 1750–1760.

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CHAPTER

14 Copper-based nanoparticles in soil: Uptake, bioaccumulation, toxicity, and biotransformation in plants

Clement O. Ogunkunle[a,b], Mariam A. Akanbi-Gada[a,c], Stephen Oyedeji[a], and Mayank Varun[d]

[a]*Environmental Biology unit, Department of Plant Biology, Faculty of Life Sciences, University of Ilorin, Ilorin, Nigeria,*
[b]*Department of Plant Biology, Osun State University, Osogbo, Nigeria,*
[c]*Department of Biological Sciences, Kwara State University, Malete, Nigeria,*
[d]*Department of Botany, Hislop College, Nagpur, Maharashtra, India*

1 Introduction

Nanoparticles (NPs) refer to minute materials of size between 1 and 100 nm. However, several definitions of nanomaterials and different variants of their classification appear in the literature (Klaine et al., 2008). They can be grouped based on their properties, shapes, or sizes into fullerenes, metal NPs, ceramic NPs, and polymeric NPs (Khan et al., 2019). Metal NPs have attracted great scientific interest due to their distinctive optical, electrical, and physicochemical properties owing to their morpho-functional characteristics including size, shape, crystallinity, and structure (Srivastava and Dwivedi, 2018). This has consequently led to their potential use in a wide range of applications in areas such as molecular diagnostics, electronics, catalysis, drug delivery, soil nanoremediation, antimicrobial agents, and biosensor (Castro et al., 2014; Ogunkunle et al., 2021). NPs have gained great utility in agro-environment in the recent decades due to their various applications (Ranjan et al., 2021). In recent times, the production of metal NPs has increased in a bid to meet the increasing demands and applications. The global market for metal NPs indicated that the production of metal oxide NPs reached about 1.7 million metric tons in 2020 (Rajput et al., 2019). The entry of nanoparticle into the environment can be categorized into natural and anthropogenic ones. Natural sources include dust, sand storms, muddled waters, aerosols, forest fires, volcanic bursts, and forest fires, as well as biological objects such as viruses, products of vital functions, films, colloids, etc. (Krichevskii, 2010). Copper (Cu) is an essential micronutrient required for the

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adequate growth of plants. It is involved in various physiological processes. It exists in multiple oxidative states (Cu^{2+}, Cu^{+}) in vivo (Yruela, 2005). It acts as a structural component in proteins and is also involved in photosynthetic, respiration, oxidative stress responses, cell wall metabolism, and hormone signaling (Marschner, 1995; Raven et al., 1999; Solymosi and Bertrand, 2012). Toxicity level of Cu varies depending on the organism. Humans are mandated to not exceed 1–2 mg/L Cu in their drinking water (OJEC, 1998; EPA, 2003), while animals and plants experience toxic effects at concentrations as low as 10 μg/L (EPA, 2007).

Among metal NPs, copper-based NPs (Cu-NPs) have attracted greater interest when compared to other metal NPs of silver, gold, and platinum due to their high surface/volume ratio, improved size, shape, and oxidation resistance (Tamilvanan et al., 2014). Cu-NPs are spherical blackish-brown metal NPs with a size in the range 30–70 nm and characterized by high surface area, and usually obtained in either pure, dispersed, or carbon-coated form (Khan and Jameel, 2018). Owing to their minute sizes, Cu-NPs have a much higher surface area than "bulk" Cu particles per unit weight and correspondingly exhibit broad range of specialized properties including catalytic, mechanical, optical, electrical, and thermal conduction properties with high toxicity potential (Srivastava and Dwivedi, 2018; Rajput et al., 2019) and great semiconductive and antimicrobial properties (Keller et al., 2017; Shi et al., 2018). And in fact, Cu particles have been reported to portend greater phytotoxicity in nano-sized particles than macro-sized particles, especially CuO (Burachevskaya et al., 2021). Nanomaterials and their application in various industrial uses result in greater pollution of the environment by nanoparticles (NPs) (Corredor et al., 2009). Despite the vast researches on Cu and Cu-based NPs, their fate and toxicity to biota are still poorly understood. Consequently, many households, industries, and farm holdings use Cu-based NPs without an adequate understanding of their environmental implications (Hortin, 2017). These NPs find their way into the environment through various means, but at present, the bulk of the releases are linked to its applications as antifouling paints in aquatic ecosystems (Adeleye et al., 2016), food preservatives (Maniprasad et al., 2015), fertilizers and pesticides in agriculture (Gardea-Torresdey et al., 2014), antibacterial coat in textiles (Majumder and Neogi, 2016), biosolids in wastewater treatment systems (Lazareva and Keller, 2014), and personal care that may pose concern over time (Keller et al., 2017). This chapter describes the uptake processes of Cu-based nanoparticles in plants, documents the phytotoxic responses in plants, and biotransformation in plant tissues to increase the understanding of copper phytotoxicity.

2 Uptake, translocation, and bioaccumulation in plants

Studies have shown that Cu-based NPs can be taken up by plants' roots and translocated to aboveground biomass (Shi et al., 2014; Ogunkunle et al., 2017, 2018; AlQuraidi et al., 2019). The processes of uptake, translocation, and bioaccumulation in plant species are influenced by plant species type, particle size, particle shape, and particle stability among others (Rico et al., 2011; Mukherjee et al., 2016; Rajput et al., 2018; Abreeq et al., 2020). Cu-NPs can get in contact with plants through

several routes, vis-à-vis direct application, contaminated soil/sediments, accidental release from industries, atmospheric fallouts, or via smart agriculture involving the use of nanopesticides and nanofertilizers. For interaction to exist between Cu-NPs and plant tissue, NPs must be internalized into plant cells. The first entry route of Cu-NPs in plants is the root uptake viz-à-viz root tips, rhizodermis/cortex, lateral root junction, and wounds (Wang et al., 2016a; Ruttkay-Nedecky et al., 2017). Plant cells are known to be negatively charged, hence the ability to transport positively charged compounds into the cells via the apoplastic pathway. Cu-based NPs can also penetrate cells via the cell walls and cell membranes of roots and later enter the xylem (vascular bundle) through the symplastic pathways (Fig. 1). The particles can later be translocated along with the stem tissues to leaves (Lopez-Lima et al., 2021) and possibly fruits (Ma et al., 2010; Ma et al., 2015). To overcome the hurdle

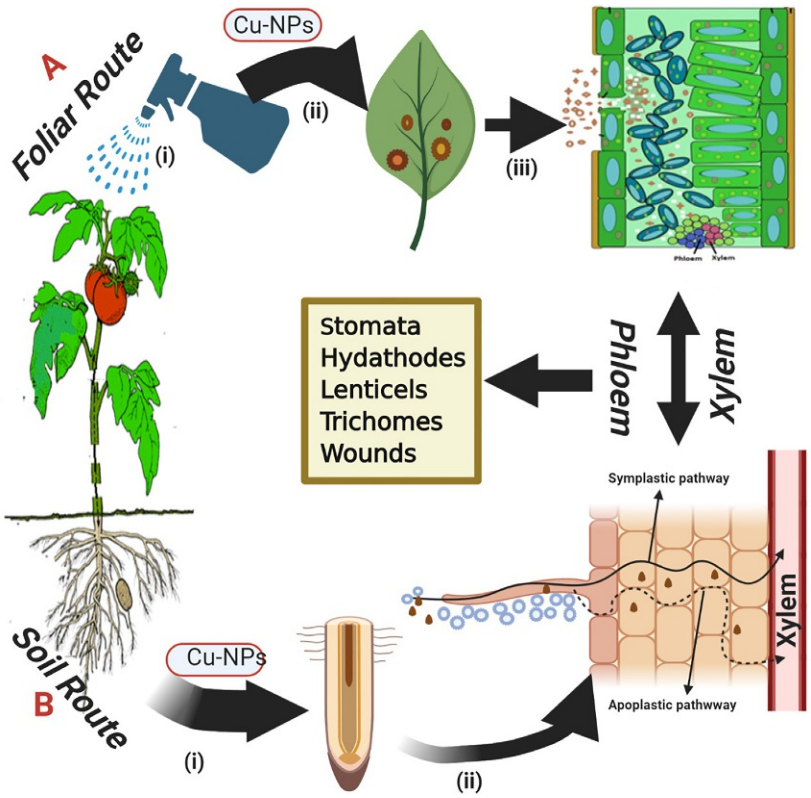

FIG. 1

Entry routes of copper-based nanoparticles (Cu-NPs) into plants. (A) Entry through foliar deposition (i) Cu-NPs depositions on leaf lamina and (ii) penetration into mesophylls (palisade and spongy) and transport into vascular tissues and (B) entry through root uptake from soil (i) penetration into root hairs and (ii) movement in root tissues into xylem via the apoplastic and symplastic pathways.

of crossing into intact cells in plants, Cu-based NPs must move through the pores on the cell walls/membranes. Findings have shown that Cu-NPs must first be passively integrated through the apoplastic pathway in the endodermis to get across to the stele from the root hairs (Tripathi et al., 2016). Carpita and Gibeaut (1993) asserted that cell walls are a porous network of polysaccharide fiber matrices that allow water molecules and solutes to enter via the pores. These pores on cell walls are usually of size range 3–8 nm and can only allow Cu-NPs that are much smaller than the pores to pass through the plasma membrane leaving out the larger particles outside the cells (Navarro et al., 2008). However, it is also possible for larger Cu-NPs to create new large-sized pores that can allow the internalization of larger NPs. At times, there must be a dissolution of Cu-based nanoparticles to release Cu ions for uptake to take place by roots of the plant (Keller et al., 2017).

Another route of uptake of Cu-based NPs in plants is the foliar route either from atmospheric depositions or intentional application as nanopesticides and nanofertilizers. The pathway of leaf-shoot-root involves the penetration of NPs into the stomata or its entrapment by the cuticle, and subsequent movement into the stems and eventual translocation into roots via the phloems (Hong et al., 2014; Wang et al., 2021). In foliar entry route, nanoparticles may get access into plant cells through cuticles, epidermis, stomata, trichomes, hydathodes, lenticels, and wounds (Wang et al., 2016a; Ruttkay-Nedecky et al., 2017), and transport to shoot and roots (Fig. 1). However, in most cases of foliar application, larger amounts of Cu are bioaccumulated in fruits or/and leaves with a small portion transported to the roots via the phloem (Rajput et al., 2019). In *Cucumis sativus* (cucumber) exposed to foliar application of *n*CuO and nano-Cu at 50, 100, and 200 mg/L from 3 weeks till fruiting, significant Cu accumulation in leaves was observed. However, Cu was not significantly accumulated in roots and fruits. Contrarily for nano-Cu (*n*Cu), root tissues presented significant translocation of Cu (Hong et al., 2016). Similarly, a small amount of Cu (17–56 mg/kg) was transported and found in roots of cucumber exposed to Cu-based nanopesticides (Zhao et al., 2016b). In a study by Keller and coauthors where lettuce, collard green, and kale were exposed to nano-CuO through a foliar application, CuO in the nano-form was detected in the leaves by *SP*-inductively coupled plasma-mass spectroscopy (Keller et al., 2018). In the study of Xiong et al. (2017), lettuce and cabbage were exposed to CuO-NPs by foliar application and found that significant amounts of Cu were accumulated in leaves and about 1% translocated to the roots. In a recent study by Xiong et al. (2021a, b), Cu level in leaves of lettuce after foliar application of CuO-NPs reached up to 63,500 mg/kg, while ~525 mg/kg was found in roots.

Nanoparticles (metal/metal oxide) can translocate to stem and leaf (shoot) tissues after uptake in soil (Rico et al., 2011; Miralles et al., 2012). In most times, the NPs could be translocated in nano-forms, dissociated into ions (reduced state in many instances), or transformed into crystal forms of different sizes and shapes (Majumdar et al., 2012). The propensity of translocation in plants varies from species to species. For instance, Hong et al. (2016) reported 3%–5% of Cu was translocated from root to shoot in alfalfa exposed to 20 mg/L *n*CuO, whereas lettuce translocated between 0.5% and 0.6% to aboveground tissue. However, several studies have confirmed that

plant species bioaccumulate greater amounts of Cu-NPs in the roots than the shoots (Ogunkunle et al., 2018; AlQuraidi et al., 2019). Bioaccumulation of Cu in roots of plant exposed to Cu-NPs seemed to reduce as concentration gradient increase in medium, possibly presenting a strategy to reduce severity of toxicity in the roots. This was observed by Da Costa and Sharma (2015) in rice plants, where a 76-fold increment of Cu content was observed in roots biomass exposed to 100 mg/L while Cu content was only ~ 9-fold at 1000 mg/L. The bioaccumulation of Cu-NPs in plants has also been described to be dependent on transportation process within plant's tissues (Ahmed et al., 2018a). The bioaccumulation of Cu-NPs in cells, cytoplasm, and cortical cells was proposed to be influenced by the xylem- and phloem-based transport systems in two-directional pathways in the roots (Rajput et al., 2019). Wang et al. (2012) found that *n*CuO was transported in maize plants via both the xylem and phloem, evidently confirming that Cu-NPs can be translocated to aboveground biomass after uptake. Wang et al. (2016b) also found out that *n*CuO of size range between 20 and 40 nm were able to penetrate the cells of *Zea mays* and got translocated through the xylem.

3 Mechanism of phytotoxicity

The mechanism of toxicity of Cu-NPs in plant cells is not a straightforward process. However, several authors have proposed mechanisms of interaction and toxicity of Cu-NPs in plants (Dietz and Herth, 2011; Rico et al., 2011; Wang et al., 2016a; Rai et al., 2018). The reported mechanisms of phytotoxicity of Cu-NPs are schematically presented in Fig. 2. The process involves the dissolution and potential release of toxic

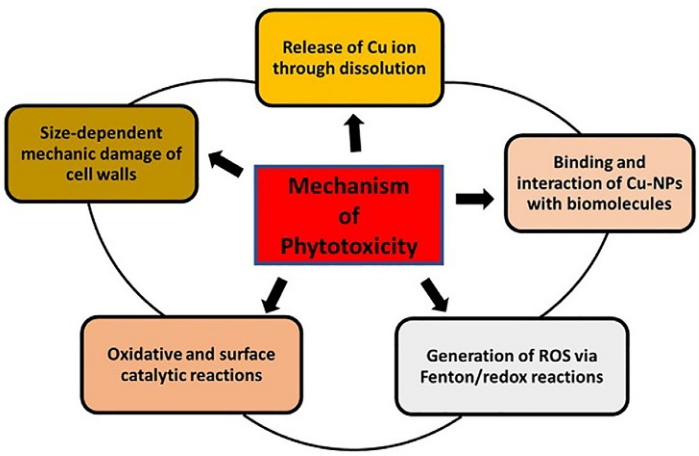

FIG. 2

Proposed schematic representation of mechanisms of phytotoxicity of Cu-based NPs in plant cells.

Cu ions from Cu-NPs before entrance into cells. Tang et al. (2016) have reported that the release of Cu^{2+} ions from nano-CuO contributed to partial toxicity of nano-CuO in *Arabidopsis thaliana* (Tang et al., 2016). Another proposed process of toxicity is the binding of Cu-NPs and interaction with biomolecules such as the DNA, protein, etc. by either noncovalent or covalent mechanisms (Atha et al., 2012; Sharifi et al., 2012). This scenario was demonstrated by Peng et al. (2015) when 40 nm CuO-NPs were translocated to shoots from rice roots, and also found that dissolved Cu^{2+} was mainly complexed with citrate, cysteine, and phosphate ligands. The excess generation of ROS through reduction-oxidation and the Fenton reaction which is always catalyzed by Fe^{2+} is another mechanism of Cu-NPs toxicity in plant cells (Wang et al., 2016a). Zhao et al. (2012) also proposed oxidation and catalysis of surface biomolecules by Cu-NPs as another toxicity mechanism in plants, while size-dependent mechanical damage of cell walls and cell membranes by nanoparticles was proposed (Asli and Neumann, 2009).

4 Factor affecting phytotoxicity of Cu-based NPs in plants

The propensity of nanoparticles to be taken up by plant's roots or pass-through stomata in leaves (via foliar contact), to overcome cell barriers and interact with intracellular structures depend on the particle size and surface reactivity. These attributes greatly contribute to the potential for toxicity (Kovacic and Somanathan, 2010; Kumari et al., 2009). Several key factors are responsible for the phytotoxicity of Cu-based NPs to plants, and among the factors are plant species type, particle size, and concentration. Several reports in literature reported that phytotoxicity of Cu-based NPs is species dependent in plants. For instance, *n*CuO was reported to be toxic to duckweeds at concentrations as low as 1 mg/L (Shi et al., 2011) whereas it was only toxic to buckwheat at 4000 mg/L (Lee et al., 2013), showing that plant species is an important role in the toxicity. Lee et al. (2008) also revealed that mungbean was more sensitive to nano-Cu than wheat due to the difference in root anatomy as xylem structure depicts speed of water transport, and also presents different uptake kinetics for nano-Cu particles in plants (Ma et al., 2010). Another important factor influencing the magnitude of toxicity of Cu-NPs to plant species is the dose (concentration). Several researchers have opined to the linear relationship between the toxic response of plants and concentration gradient of Cu-NPs. For instance, Ogunkunle and coauthors found out that nano-Cu concentrations from 250 to 1000 mL/L produced increased phytotoxic responses in *Vigna unguiculata* grown on soil medium (Ogunkunle et al., 2018, 2019). In another study, a linear relationship between increasing nano-Cu doses and toxicity potential of NPs in tissues of bean and wheat plants was observed in agar medium by Lee et al. (2008), and in *Oryza sativa* grown in soil medium (Da Costa and Sharma, 2015). Studies have also shown that another important indicator of phytotoxicity level of Cu-NPs to plants is the particle size (Barrena et al., 2009). For instance, Ogunkunle et al. (2018) observed that toxicity of nano-Cu of < 25 to *Vigna unguiculata* was not only organ dependent but also particle

size dependent. Phytotoxicity of Cu-NPs may be depended on the dissolved Cu ions released or on the particle size of the nanoparticles. Investigation into the phytotoxicity of Cu NPs to *Phaseolus radiatus* and *Triticum aestivum* showed that acute phytotoxicity to root growth was mainly due to NPs and not the metallic ions released after dissolution (Lee et al., 2008). Recently, it has been found that the strength of light spectra to plants exposed to CuO-NPs can also influence NP-phytotoxicity due to the photocatalytic and photodynamic properties. A study with *Brassica nigra* seeds grown in vitro on CuO-NP-supplemented media with exposure to different spectral lights showed significant alteration in shoot and root length with different levels of toxicity expression (Zia et al., 2021). In addition, the state of Cu-based nanomaterial can also influence the degree of toxicity in plants. Rawat et al. (2021) found that weathered CuO-NPs (35-d soil-aged NPs) in soil imposed greater toxicity to spinach foliar health compared to fresh CuO-NPs in a full life cycle study.

4.1 Phytotoxicity at the morpho-physiological level

Studies have demonstrated that CuO-NPs adversely affect plant growth and development as altered photosynthesis, and enhanced reactive oxygen species (ROS) accumulation always result in exposed plants (e.g., Xiong et al., 2021a). Morpho-physiological changes are the first observed phytotoxicity responses in plant species, and the toxic effects are mostly expressed in Cu-NPs at high doses (concentrations) irrespective of medium type (Table 1). Copper-based NPs could impair the general growth and development of plant species by first altering photosynthetic processes, nutrients uptake, modify morphology and anatomy of cells/tissues, affect timing of senescence, flowering, and fruiting in relation to concentration level and particle size (Tripathi et al., 2016). There is plethora of reports of phytotoxicity of Cu-NPs to plants as evidenced in the endpoint-germination rate, and root and shoot elongation of seedlings. Zhao et al. (2016a) provided evidence that cucumber plants exposed to Cu-NPs (10 and 20 mg/L) in hydroponic solution decreased root length and root biomass as a consequence of Cu-NPs phytotoxicity. In another study with laboratory-prepared Cu-NPs at < 50 ppm in a water medium, seeds of *Lactuca sativa* showed reduced germination and root elongation (Liu et al., 2016). In another study, Yang et al. (2015) showed evidence of CuO-NPs phytotoxicity to *Zea mays* and *Oryza sativa*. The authors found out that *n*CuO at the concentration of 2000 mg/L significantly inhibited root elongation (~ 96% for maize and ~ 97% for rice), and the shoot length was also reduced by ~ 31% in maize. Zuverza-Mena et al. (2015) reported that nano-Cu reduced shoot elongation at 80 mg/kg by 11%–12%, while nano-Cu reduced seedling growth of wheat at 335 and 570 mg nano-Cu/L (Lee et al., 2008). Da Costa and Sharma (2015) also reported reduction in germination rate of *Oryza sativa*. Lettuce (*Lactuca sativa*) and alfalfa (*Medicago sativa*) were exposed to *n*CuO and nano-Cu in hydroponic media for 15 days. Exposure to 20 mg/L *n*CuO or nano-Cu resulted in the least root length in both plants (Hong et al., 2015). Photosynthesis is the most important process in plants and the major target of Cu-NPs toxicity. Da Costa and Sharma (2015) used the transmission electron micrograph to assess the

Table 1 Overview of phytotoxicity of Cu-NPs on photosynthetic and morpho-physiological parameters of plant species.

Plant species	Type; size (nm)	Concentrations	Growth medium	Period	Endpoint	Response	References
Cucurmis sativum	*n*Cu	10 and 20 mg/L	Hydroponic solution	NA	Root length Root biomass	Reduction Reduction	Zhao et al. (2016a)
Elodea densa	*n*CuO; 30 nm	0.25–5.0 mg/L	H_2O	3 days	Photosynthetic rate	Reduction	Nekrasova et al. (2011)
Lactuca sativa	CuO-NPs	0–1000 mg/L	Soil; foliar-applied	15 days	Chlorophylls *a*, *b* and total chlorophyll	Reduction	Xiong et al. (2021a)
Lactuca sativa	CuO-NPs; 40–200 nm	0–1000 mg/L	Soil; foliar-applied	15 days	Root growth	Reduction	Xiong et al. (2021b)
Landoltia punctata	*n*CuO; 43 nm	1.0 mg/L	Hoagland solution	10 days	Leaf chlorophylls	Reduction	Shi et al. (2011)
Landoltia punctata	*n*CuO; 70 nm	0.1–10.0 g/L	Fresh H_2O inorganic medium	7 days	Leaf chlorophylls	Reduction	Lalau et al. (2015)
Elsholtzia splendens	*n*CuO; 49 nm	100–1000 mg/L	Hydroponic culture	14 days	Leaf chlorophylls	Reduction	Shi et al. (2014)
Triticum aestivum	*n*CuO; < 50 nm	500 mg/kg	Sand matrix	14 days	Shoot chlorophylls	Reduction	Dimkpa et al. (2012)
Solanum lycopersicum	CuO-NPs	0–4000 μg/mL	Petri dishes	NA	Germination	Reduction	Khaldari et al. (2021)
Oryza sativa	*n*CuO; < 50 nm	100–1000 mg/L	Hoagland solution	6 days	Germination Photosynthetic rate Transpiration rate	Inhibition Reduction Reduction	Da Costa and Sharma (2015)

Brassica juncea	*n*CuO; < 50 nm	100–500 mg/L	Murashige and Skoog medium	14 days	Germination Total chlorophyll Carotenoids	Inhibition Reduction Reduction	Nair and Chung (2015)
Cucurbita pepo	*n*Cu; < 50 nm	1000 mg/L	NA		Biomass mass	Reduction	Stampoulis et al. (2009)
Raphanus sativus	*n*CuO; 100 nm	1000 mg/L	Petri dish	6 days	Root elongation Shoot elongation	Inhibition Inhibition	Atha et al. (2012)
Coriandrum sativum	*n*Cu; NA	200–800 mg/L	Hydroponic solution	7 days	Root elongation	Inhibition	AlQuraidi et al. (2019)
Lolium perenne	*n*CuO; < 100 nm	1000 mg/L	Petri dish	6 days	Root elongation Shoot elongation	Inhibition Inhibition	Atha et al. (2012)
Phaseolus radiatus	*n*Cu; NA	800 mg/L	Agar medium	NA	Shoot elongation	Inhibition	Lee et al. (2008)
Cucurbita pepo	*n*CuO; NA	NA	Not available	NA	Shoot elongation	Inhibition	Musante and White (2012)
Glycine max	*n*CuO; < 50 nm	100–600 mg/L	Petri dishes	5 days	Root elongation	Inhibition	Adhikari et al. (2016)
Zea mays	*n*CuO; 20–40 nm	10–100 mg/L	Hydroponic solution	15 days	Root elongation	Inhibition	Wang et al. (2012)
Oryza sativa	*n*CuO; < 50 nm	0.5–1.5 nM	Suspension	14 days	Seed germination	Reduction	Shaw and Hossain (2013)
Lactuca sativa	*n*CuO; < 10 nm	0.2 and 300 μg/mL	Suspension	7 days	Seed germination	35%–75% inhibition	Pelegrino et al. (2020)

Continued

Table 1 Overview of phytotoxicity of Cu-NPs on photosynthetic and morpho-physiological parameters of plant species—cont'd

Plant species	Type; size (nm)	Concentrations	Growth medium	Period	Endpoint	Response	References
Cucumis sativus	*n*CuO; NA	100–600 mg/L	Petri dishes	7 days	Seed germination and root elongation	Inhibition	Moon et al. (2014)
Triticum aestivum	*n*Cu	0.0–0.06 mg/mL	Petri dishes	7 days	Root and shoot elongation	Inhibition	Essa et al. (2020)
Zea mays	*n*CuO; < 50 nm	2000 mg/L	Deionized H_2O	5 days	Root elongation	Inhibition	Yang et al. (2015)
Hordeum vulgare	CuO-NPs	17, 35, and 70 mg/L	Hydroponic solution	14 days	Shoot and root	Reduction in length	Petrova et al. (2021)
Glycine max	CuO-NPs	0–10 mg/L	Suspension	48 h	Root growth	Inhibition	Liu et al. (2021)
Daucus carota	*n*Cu; 25–55 nm	10–1000 mg/L	Coarse sand	91 days	Root biomass	Dose-dependent reduction	Ebbs et al. (2016)
Raphanus sativus	*n*CuO; NA	10–1000 mg/kg	NA	NA	Root and shoot length	Dose-dependent reduction	Singh and Kumar (2018)
Triticum aestivum	*n*CuO; NA	500 mg/kg	NA	NA	Root length	Reduction	Gao et al. (2018)

toxic effect of *n*CuO on photosynthetic apparatus of *Oryza sativa*. The authors found a distortion in the thylakoid membranes and also swelling of the intra-thylakoidal space at exposure dose of 1000 mg/L. AlQuraidi et al. (2019) also reported that nano-Cu portend toxicity to *Coriandrum sativum* by affecting the rate of photosynthetic activity and decrease chlorophyll contents in the leaves. Another endpoint of toxicity of Cu-NPs to plant species is the biomass and yield level. Lee et al. (2008) have reported that seedlings of bean and wheat presented about 40% reduction in the biomass of studied species when exposed to 200 mg/L and 80% reduction at 1000 mg/L. Similarly, a 90% reduction in biomass of *Cucurbita pepo* was observed at exposure concentration of 1000 mg *n*CuO (50 nm) (Stampoulis et al., 2009) in mungbean plants, reduction in general growth was reported at concentrations up to 1000 mg/L (Lee et al., 2008). Da Costa and Sharma (2015) also reported that fresh biomass of *Oryza sativa* shoots exposed to 1000 mg/L *n*CuO was reduced by 31% in relation to control. Biomass of *Coriandrum sativum* was also reduced after exposure to nano-Cu at 200–800 mg/L in hydroponic solution (AlQuraidi et al., 2019).

4.2 Phytotoxicity at the biochemical level

It is a known fact in nanotoxicology that metal-based nanoparticles portend phytotoxicity potential to plant species but the mechanisms of action of these NPs are still unclear and vaguely understood (Mukherjee et al., 2016). However, it has been scientifically proved that Cu-based NPs induce oxidative stress in plants by compromising membrane integrity, thereby leading to damage of cells at both organelle and molecular levels. In the process of energy generation by plants for day-to-day activities, oxygen (O_2) is utilized. Generally, O_2 of ground state are reduced to H_2O and reactive oxygen species (ROS) viz-à-viz the singlet oxygen ($^1O_2$), superoxide (O_2^-), hydroxyl ion (OH^-), and hydrogen peroxide (H_2O_2) (Gill and Tuteja, 2010; Sharma et al., 2012). These ROS are generated from the several electron transfer reactions in plants or through mechanism of energy transfer. ROS may also be partly generated as by-products during metabolic processes in chloroplasts of plants and when overproduced, they can result into deterioration of chlorophyll (Rico et al., 2015; Ma et al., 2015). In addition, mode of actions of ROS in plants also depends solely on the species type of ROS and target organs in cellular organelles of plants. The overproduction of ROS in plants always triggers the activation of defense mechanisms in order to combat subsequent effect of ROS. Antioxidant enzymes such as the superoxide dismutase (SOD), catalase (CAT), POD (peroxidase), guaiacol peroxidase (GPX), and ascorbate peroxidase (APX) are generally altered or modulated in response to changes in ROS production (Du et al., 2016). An overview of the effects of Cu-based NPs on level of ROS, antioxidant enzymes, and consequent oxidative damage in plant species are summarized in Table 2.

Studies have shown that *n*CuO have the potential to induce ROS, alter activity of antioxidant enzymes, and subsequently lead to increased malondialdehyde (MDA) that result in significant oxidative stress in rice (Da Costa and Sharma, 2015), soybean (Nair and Chung, 2014a), wheat (Dimkpa et al., 2012), and *Arabidopsis thaliana*

Table 2 Overview of phytotoxicity of Cu-NPs on biochemical and genetic parameters of plant species.

Plant species	Type; size (nm)	Concentration	Growth medium	Period	Endpoint	Response	References
Raphanus sativus	*n*CuO; 100 nm	200–1000 mg/L	NA	NA	DNA	Damage to DNA	Atha et al. (2012)
Vigna unguiculata	*n*Cu; < 25 nm	500–1000 mg/L	Soil	49 days	Shoot	Reduced protein content	Ogunkunle et al. (2017)
					Root	Reduced Co and Fe	
Vigna unguiculata	*n*Cu; < 25 nm; 60–80 nm	0–1000 mg/L	Soil	65 days	Root and leaf	Increased APX and GR activities SOD reduced	Ogunkunle et al. (2018)
Lactuca sativa	CuO-NPs; 40–200 nm	0–1000 mg/L	Soil; foliar-applied	15 days	Leaf	Mn, K, and Ca decreased	Xiong et al. (2021a, b)
Gossypium hirsutum	*n*CuO; 30 nm	10–1000 mg/L	Nutrient solution	10 days	Root	Reduced uptake of B, Mo, Mn, Mg, Zn, and Fe	Le Van et al. (2016)
Glycine max	CuO-NPs	0–10 mg/L	Suspension	48 h	Root	Decrease in mitotic index	Liu et al. (2021)
Oryza sativa	*n*CuO; < 50 nm	0.5–1.5 Mm	Hydroponic solution	14 days	Leaf	Increased MDA Increased APX and GR activities	Shaw and Hossain (2013)
Glycine max	*n*CuO; < 50 nm	100–500 mg/L	Murashige and Skoog medium	14 days	Root	Significant increase in H_2O_2 and POD	Nair and Chung (2014a)
Arabidopsis thaliana	*n*CuO; < 30 nm	100 mg/L	Murashige and Skoog medium	21 days	Root and leaf	Dose-dependent increase of O_2^- and H_2O_2	Nair and Chung (2014b)
Triticum aestivum	*n*CuO; < 50 nm	100–5000 mg/L	Sand matrix	14 days	Root	Increased MDA Higher POD and CAT activities	Dimkpa et al. (2012)

Cucumis sativus	*n*Cu; < 50 nm	100–1000 mg/L	Hoagland solution	5 days	Root	Increased SOD, CAT, and POD activities	Kim et al. (2012)
Capsicum annum	*n*CuO	500 mg/kg	NA	NA	Leaf	Reduction of Zn content (55%)	Rawat et al. (2018)
					Fruit	Reduction of Zn content (47%)	
Oryza sativa	*n*CuO; < 50 nm	62.5–250 mg/L	Hydroponic solution	7 days	Leaf	Reduced CAT and SOD	Yang et al. (2020)
Oryza sativa	*n*CuO; < 50 nm	62.5–250 mg/L	Hydroponic solution	7 days	Root	Increased SOD	Yang et al. (2020)
Glycine max	*n*CuO; 25–250 nm	50–500 mg/kg	Soil medium	120 days	Leaf	Increased SOD and CAT	Yusefi-Tanha et al. (2020)
Oryza sativa	NA	62.5–250 mg/L	Hydroponic solution	7 days	Shoot	Increased MDA	Yang et al. (2020)
Solanum lycopersicon	*n*CuO	0.2–2.0 mg/kg	NA	NA	Root	Cu accumulation (341.6 mg/kg)	Ahmed et al. (2018b)
					Shoot	Cu accumulation (146.9 mg/kg)	

(Nair and Chung, 2014b). Similarly, CuNPs were reported to induce reduction of CAT activity in alfalfa (Hong et al., 2015) and inhibited activity of APX in Indian mustard (Nair and Chung, 2015). The biochemical responses to toxicity of Cu-based NPs in plants seemed to depend on plants species and particle size. Ogunkunle and coauthors exposed *Vigna unguiculata* plants to nano-Cu of different particle sizes (< 25 and 60–80 nm) through soil medium. The authors found that APX and GR activities were promoted in leaf and root tissues in response to the nano-Cu types, whereas activity of SOD activity was reduced. The authors proposed that the phytotoxic response of antioxidant enzymes in cowpea to Cu-based NPs was species dependent (Ogunkunle et al., 2018). The same authors also reported that particle size of nano-Cu also played a key role in severity of toxicity to the cowpea plants. Species of Cu-NPs may also present different enzyme response based on plant's organ. Alfalfa (*Medicago sativa*) exposed to 10 mg/L *n*CuO exhibited a considerable change in catalase activity in both root and shoot tissues as a toxic response while at 5 mg/L *n*Cu$(OH)^{2-}$, catalase was affected only in the roots (Lee et al., 2008). Recently, AlQuraidi et al. (2019) exposed *Coriandrum sativum* to nano-Cu at concentrations of 200, 400, and 800 mg/L via Hoagland solutions for 7 days. The authors found that nano-Cu generated significant amounts of H_2O_2 in the roots, and consequently caused a twofold magnitude of MDA concentration in shoot and root tissues compared to control. Cu-based nanoparticles can also cause alteration in mineral contents of plant species as phytotoxicity response. In a study, 18-day-old hydroponically grown *Lactuca sativa* seedlings were treated with *n*CuO at 10 and 20 mg/L. The results indicated increased CAT activity and reduced APX activity in the roots in addition to a significant alteration in the nutritional quality of the lettuce in which concentrations of Cu, S, and Al, while P, Ca, Mn, and Mg were increased (Trujillo-Reyes et al., 2014).

4.3 Phytotoxicity at the genetic level

Several authors have described the uptake and internalization of metal-based NPs in plants as a smart delivery strategy due to the fact that the major point of target after internalization is the genome (genes or DNAs) of cells (Siddiqui et al., 2015). Metal-based NPs portend potentials to induce both cytotoxic and genotoxic effects on plant cells (Ghosh et al., 2017; Pramanik et al., 2018b; Kumbhakar et al., 2019). In many instances, the effects may lead to significant consequences that could confer heritable changes to plants (Kumbhakar et al., 2016). However, few studies have demonstrated the cytotoxicity and genotoxicity of (Cu-NPs) in plant species (Table 2), and up till date, little studies have addressed the molecular basis of phytotoxic role of Cu-NPs in plant species. Oxidative stress is a major toxic impact of Cu-NPs in plants which may present damage to the DNA or gene mutations. Oxidatively induced damages to plants' DNA structure from Cu-based NPs toxicity involves damages to DNA bases by induction of oxygen-derived radicals attack, majorly the hydroxyl radical on purine and pyrimidine bases in the nucleotide chains or on intact DNA duplex via the heterocyclic DNA (Atha et al., 2012). This form of oxidatively induced DNA damages may be cytotoxic or genotoxic. For instance, Atha et al. (2012) revealed that

CuO nanoparticles can impose genotoxicity in radish seedlings by inducing significant increase in accumulation of DNA lesions (220%, 260%, and 450%, respectively) for 7,8-dihydro-8-oxoguanine; 2,6-diamino-4-hydroxy-5-formamidopyrimidine; and 4,6-diamino-5-formamidopyrimidine at 1000 mg/L concentration. Such toxic effects on DNA via DNA lesions, especially in mitochondrion, chloroplast, or nucleus have been reported to be usually initiated by $^{*}OH$ species (Aruoma et al., 1991). Cu ions from metal nanoparticles can potentially dissolve from its nanoparticles form and initiate oxidative burst in terrestrial plant species, especially during seed germination to generate radicals such as O_2^-, H_2O_2, and $^{*}OH$ via the Fenton reaction (Halliwell and Gutteridge, 2007; Stampoulis et al., 2009). However, in the case of *n*CuO toxicity to radish seedling, the significant accumulated DNA damage as observed in the amounts of DNA lesions was not solely attributed to Cu ions alone, particle size was reported to have contributed to the significant DNA damage (Atha et al., 2012). The damage to plant DNA by *n*CuO is known to be via direct redox interactions, and *n*CuO can promote oxidation of several biomolecules indirectly in plants in order to generate $^{\bullet}OH$ that is capable of DNA damage by diffusion-controlled pace (Atha et al., 2012). In perennial ryegrass (*Lolium perenne*) seedlings, Atha and coauthors reported that *n*CuO induced damages to the DNA by accumulating significant amounts of DNA lesions at 1000 mg/L, though at lesser amounts when compared to radish. However, NP-induced DNA damage observed in perennial ryegrass was also significant at the lowest concentration of 10 mg/L for all lesions (7,8-dihydro-8-oxoguanine; 2,6-diamino-4-hydroxy-5-formamidopyrimidine; and 4,6-diamino-5-formamidopyrimidine).

The variation in the toxic responses of plants to Cu-based NPs has brought about the concern of significant and measurable molecular factors needed to determine or observe differences in nanoparticles phytotoxicity in plant species (Atha et al., 2012). Pramanik et al. (2018a) reported that *n*CuO induced cytological aberrations in both mitotic and meiotic cells (tripolarity, irregular chromosomal separation, laggards, and bridges) of *Coriandrum sativum* as comparable to conventional mutagen. These aberrations indicate that the consequences of *n*CuO genotoxicity in plants can be a transferrable trait that can be passed to the next generation. In another study, AlQuraidi et al. (2019) utilized the random amplified polymorphic DNA (RAPD) to assess the phytotoxicity of nano Cu to genomes of *Coriandrum sativum* using several sets of primers (OPA-01, OPA-02, OPA-06, and OPA-07). At 400 and 800 mg/L nano-Cu concentrations, roots of *C. sativum* exhibited the absence of band at 1000 bps (Fig. 3), showing that the nano-Cu caused significant changes in genome of *C. sativum* plants.

5 Biotransformation of Cu-based nanoparticles in plants

Biotransformation of NPs has been reported to be a plant-specific phenomenon (Rajput et al., 2019), which can either be a process for toxification or detoxification. In a study by Peng et al. (2015), it was revealed that *n*CuO rice epidermis

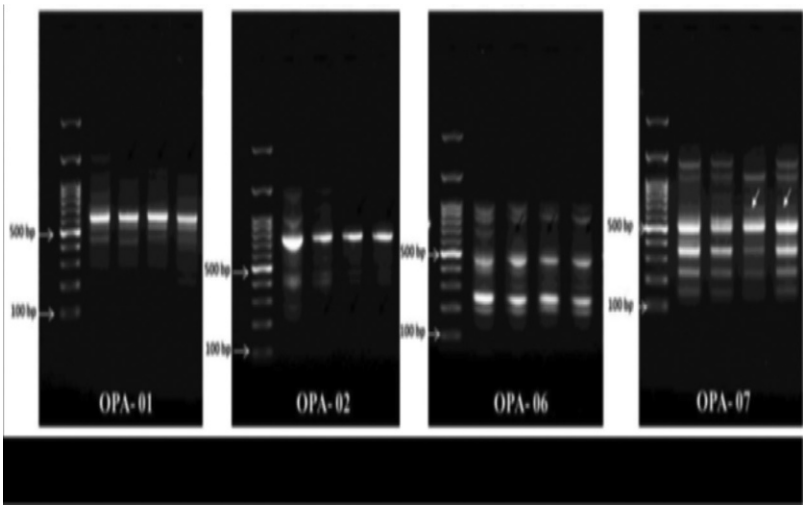

FIG. 3

Random amplified polymorphic DNA (RAPD) of *Coriandrum sativum* plants exposed to 200, 400, and 800 mg/L of Cu-NPs at 7 days. The *white arrows* indicate the disappearance and appearance of bands between control and treated plants.

Reproduced with permission from AlQuraidi, A.O., Mosa, K.A., Ramamoorthy, K., 2019. Phytotoxic and genotoxic effects of copper nanoparticles in coriander (Coriandrum sativum—Apiaceae). Plan. Theory 8(1), 19. https://doi.org/10.3390/plants8010019 with copyright permission granted by the authors (2019).

was reduced to Cu(I), which is highly redox active and portends serious toxicity to the rice plant even at small concentration. Wang et al. (2012) also reported the biotransformation evidence (reduction) of the NPs from Cu(II) to Cu(I) in maize. Ogunkunle et al. (2016, 2019) studied the biotransformation of Cu ions in roots of cowpea plants exposed to nano-Cu at 1000 mg/kg using X-ray absorption near-edge structure (XANES) and discovered the speciation of Cu to Cu^{2+} in plants' roots as against the Cu^{1+} in nano-Cu applied to the soil. The authors also proposed that the Cu^{2+} in roots could be bound to ligands such as histidine as depicted in Fig. 4. Xiong et al. (2017) used electron paramagnetic resonance (EPR) to investigate the speciation of *n*CuO foliar applied to lettuce leaves. The result of EPR spectroscopy suggested the occurrence of electron transfer that involved Mn with Cu(II) reduced to Cu(I), which depicts indirectly the CuO-NP-induced oxidative stress. A similar reduction of Cu^{2+} to Cu^{1+} in plants was also observed in soil-cultivated rice and maize (Wang et al., 2012; Peng et al., 2017). Most studies that reported the speciation of *n*CuO in plants revealed that Cu ions are always reduced to Cu^{1+} from Cu^{2+} and this reduction process always present severe toxicity to plant species. Under + 1 oxidation state in Cu ions, there is always the potential to bind to small molecules such as oxygen or components of cells like the sulfhydryl, carboxyl, imidazole groups

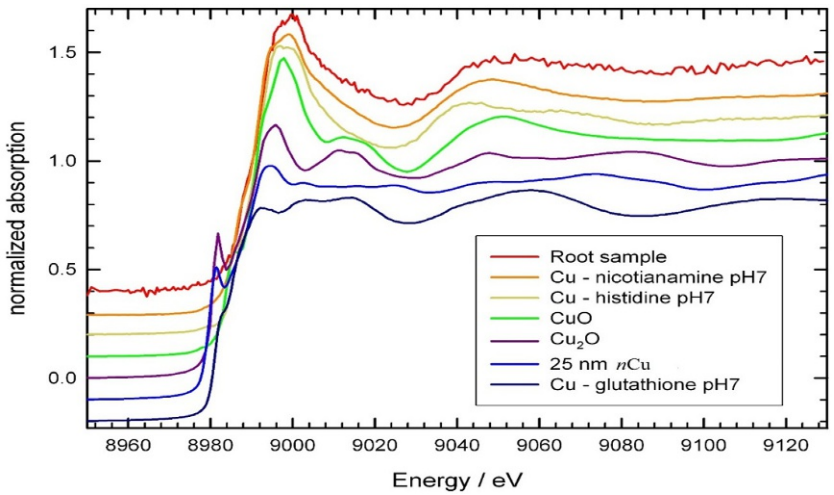

FIG. 4

Cu-K edge XANES of Cu-nicotianamine, Cu-histidine, Cu-glutathione, CuO, Cu_2O, the nano-Cu sample, and root samples of cowpea grown in 1000 mg *n*Cu/kg.

Reproduced with permission from Ogunkunle, C.O., Bornmann, B., Wagner, R., Fatoba, P.O., Frahm, R., Luezenkirchen-Hecht, D., 2019. Copper uptake, tissue partitioning and biotransformation evidence by XANES in cowpea (Vigna unguiculata L) grown in soil amended with nano-sized copper particles. Environ. Nanotechnol. Monit. Manag. 12. Elsevier. Available online at: https://doi.org/10.1016/j.enmm.2019.100231 with copyright permission granted by Elsevier (2019).

of proteins, or the DNA causing activity change (Faisal et al., 2013). In a study by Shi and coauthors on Cu-tolerant plant—*Elsholtzia splendens* exposed to 1000 mg *n*CuO/L under hydroponic conditions, the authors found that there was no biotransformation. The Cu species were found in roots and shoots were predominantly *n*CuO when Cu K-edge XANES was applied to unravel the speciation and suggest *E. splendens* may have evolved the strategy as Cu-tolerant plants to tolerate the toxicity. The toxicity threshold of Cu species has been highlighted to follow the pattern—Cu^{2+} > *n*Cu > *n*CuO ~ $n\text{Cu(OH)}_2$ > μCu ~ μCuO (Keller et al., 2017). In most instances of speciation of Cu-based NPs, plants tend to detoxify Cu ions from NPs by sulfidation process to be tolerant. Wang et al. (2013) investigated the transformations of *n*CuO in a biological medium and found that *n*CuO underwent sulfidation process which was considered as a natural detoxification mechanism. In a similar study, Dimkpa et al. (2012) exposed *n*CuO to wheat plants via sand matrix and found a similar transformation of CuO to Cu(I)-sulfide complexes, suggesting wheat plants biotransformed *n*CuO top reduce severity of toxicity. The transformation of Cu(II) to Cu(I) in plants has been ascribed to the involvement of reducing sugars in the roots (Huang et al., 2017; Servin et al., 2017).

6 Conclusion

Phytotoxicity of Cu-NPS could be considered as an important issue. Various studies have confirmed that Cu-based NPs have a different fate in soil and subsequent uptake by plants. Uptake, translocation, and accumulation in plants are dependent on some factors including plant species, morphology and chemical nature of NPs, and nature of soil/sediments. The entry of Cu-NPs into the plant system could either be via root or foliage/shoot, while root entry occurs by apoplastic and/or symplastic routes depending on the target destination. Foliar application of Cu-NPs has been shown to increase Cu levels in fruits in some species. The action of Cu-NPs on plant systems has been linked to its dissolution and transformation through redox process and combination with plant biomolecules to generate ROS. It has been highlighted that the phytotoxic effects Cu-NPs are largely dependent on the plant species, particle size, and concentration. Impairment of germination, pigmentation, growth, and yield as well as inducement of ROS production has been documented. Nano-Cu have been shown to alter genomic sequence in plants, thereby posing a significant threat to plant diversity. Although some plant species have developed a natural mechanism to detoxify Cu-NPs, the transformation mechanism comes with a cost as an energy that would have been used for photosynthesis is channeled for the purpose. Moreover, not all plants have developed mechanisms to detoxify and transform Cu-NPs, hence the need for advocacy to control target release of Cu-NPs to reduce soil contamination and protect plant species. Further, more research on the interaction of NPs (Cu-NPs) with soil and plant is still needed to better analyze and predict toxicity of metal-based NPs for their sustainable applications.

References

Abreeq, F., Shikha, S., Sheo, M.P., 2020. Interaction between copper oxide nanoparticles and plants: uptake, accumulation and phytotoxicity. In: Hayat, S., Pichtel, J., Faizan, M., Fariduddin, Q. (Eds.), Sustainable Agricultural Reviews 41 (Nanotechnology for Plant Growth and Development). Springer Nature, Switzerland, https://doi.org/10.1007/978-3-030-33996-8.

Adeleye, A.S., Oranu, E.A., Tao, M., Keller, A.A., 2016. Release and detection of nanosized copper from a commercial antifouling paint. Water Res. 102, 374–382.

Adhikari, T., Sarkar, D., Mashayekhi, H., Xing, B.S., 2016. Growth and enzymatic activity of maize (*Zea mays* L.) plant: solution culture test for copper dioxide nano particles. J. Plant Nutr. 39 (1), 99–115.

Ahmed, B., Khan, M.S., Saquib, Q., Al-Shaeri, M., Musarrat, J., 2018a. Interplay between engineered nanomaterials (ENMs) and edible plants: a current perspective. In: Faisal, M., Saquib, Q., Alatar, A.A., Al-Khedhairy, A.A. (Eds.), Phytotoxicity of Nanoparticles. Springer, Cham, pp. 63–102.

Ahmed, B., Khan, M.S., Musarrat, J., 2018b. Toxicity assessment of metal oxide nano-pollutants on tomato (*Solanum lycopersicon*): a study on growth dynamics and plant cell death. Environ. Pollut. 240, 802–816.

AlQuraidi, A.O., Mosa, K.A., Ramamoorthy, K., 2019. Phytotoxic and genotoxic effects of copper nanoparticles in coriander (*Coriandrum sativum*—Apiaceae). Plan. Theory 8 (1), 19. https://doi.org/10.3390/plants8010019.

Aruoma, O.I., Halliwell, B., Gajewski, E., Dizdaroglu, M., 1991. Copper-ion-dependent damage to the bases in DNA in the presence of hydrogen peroxide. Biochem. J. 273, 601–604.

Asli, S., Neumann, P.M., 2009. Colloidal suspensions of clay or titanium dioxide nanoparticles can inhibit leaf growth and transpiration via physical effects on root water transport. Plant Cell Environ. 32, 577–584.

Atha, D.H., Wang, H., Petersen, E.J., Cleveland, D., Holbrook, R.D., Jaruga, P., Dizdaroglu, M., Xing, B., Nelson, B.C., 2012. Copper oxide nanoparticle mediated DNA damage in terrestrial plant models. Environ. Sci. Technol. 46 (3), 1819–1827.

Barrena, R., Casals, E., Colan, J., Font, X., Sanchez, A., Puntes, V., 2009. Evaluation of the ecotoxicology of model nanoparticles. Chemosphere 75 (7), 850–857.

Burachevskaya, M., Minkina, T., Mandzhieva, S., Bauer, T., Nevidomskaya, D., Shuvaeva, V., Shushkova, S., Kizilkaya, R., Gulser, C., Rajput, V., 2021. Transformation of copper oxide and copper oxide nanoparticles in the soil and their accumulation by *Hordeum sativum*. Environ. Geochem. Health 43, 1655–1672.

Carpita, N.C., Gibeaut, D.M., 1993. Structural models of primary cell walls in flowering plants: consistency of molecular structure with the physical properties of the walls during growth. Plant. J. 31, 1–30.

Castro, L., Blázquez, M.L., Muñoz, J.A., Gonzalez, F.G., Ballester, A., 2014. Mechanism and applications of metal nanoparticles prepared by bio-mediated process. Rev. Adv. Sci. Eng. 3, 1–18.

Corredor, E., Testillano, P.S., Coronado, M.J., Melendi, P.G., Pacheco, R.F., Marquina, C., Ibarra, M.R., de la Fuente, J.M., Rubiales, D., de -Luque, A.P., Risueno, M.C., 2009. Nanoparticle penetration and transport in living pumpkin plants: *in situ* subcellular identification. BMC Plant Biol. 9, 45.

Da Costa, M.V., Sharma, P.K., 2015. Effect of copper oxide nanoparticles on growth, morphology, photosynthesis, and antioxidant response in *Oryza sativa*. Photosynthetica 54 (1), 110–119. https://doi.org/10.1007/s11099-015-0167-5.

Dietz, K.J., Herth, S., 2011. Plant nanotoxicology. Trends Plant Sci. 16, 582–589.

Dimkpa, C.O., McLean, J.E., Latta, D.E., Manangón, E., Britt, D.W., Johnson, W.P., Boyanov, M.I., Anderson, A.J., 2012. CuO and ZnO nanoparticles: phytotoxicity, metal speciation, and induction of oxidative stress in sand-grown wheat. J. Nanopart. Res. 14 (9), 1–15.

Du, W., Tan, W., Peralta-Videa, J.R., Gardea-Torresdey, J.L., Ji, R., Yin, Y., Guo, H., 2016. Interaction of metal oxide nanoparticles with higher terrestrial plants: physiological and biochemical aspects. Plant Physiol. Biochem. https://doi.org/10.1016/j.plaphy.2016.04.024.

Ebbs, S.D., Bradfield, S.J., Kumar, P., White, J.C., Musante, C., Ma, X., 2016. Accumulation of zinc, copper, or cerium in carrot (*Daucus carota*) exposed to metal oxide nanoparticles and metal ions. Environ. Sci. Nano 3, 114–126.

EPA, 2003. National Primary Drinking Water Standards. EPA Agency. EPA-816-F-03-016.

EPA, 2007. Aquatic Life Ambient Freshwater Quality Criteria—Copper Revision. EPA Agency. EPA-822-F07-001.

Essa, H.L., Abdelfattah, M.S., Marzouk, A.S., Guirguis, H.A., El-Sayed, M.M.H., 2020. Nanoformulations of copper species coated with sulfated polysaccharide extracts and assessment of their phytotoxicity on wheat (*Triticum aestivum* L.) seedlings in seed germination, foliar and soil applications. Appl. Sci. 10, 6302. https://doi.org/10.3390/app10186302.

Faisal, M., Saquib, Q., Alatar, A.A., Al-Khedhairy, A.A., Hegazy, A.K., Musarrat, J., 2013. Phytotoxic hazards of NiO-nanoparticles in tomato: a study on mechanism of cell death. J. Hazard. Mater. 250-251, 318–332.

Gao, X., Avellan, A., Laughton, S., Vaidya, R., Rodrigues, S.M., Casman, E.A., et al., 2018. CuO nanoparticle dissolution and toxicity to wheat (*Triticum aestivum*) in rhizosphere soil. Environ. Sci. Technol. 52, 2888–2897.

Gardea-Torresdey, J.L., Rico, C.M., White, J.C., 2014. Trophic transfer, transformation, and impact of engineered nanomaterials in terrestrial environments. Environ. Sci. Technol. 48 (5), 2526–2540.

Ghosh, B., Datta, A.K., Pramanik, A., Kumbhakar, D.V., Das, D., Paul, R., Biswas, J., 2017. Mutagenic effectivity of cadmium sulphide and copper oxide nanoparticles on some physiological and cytological attributes of *Lathyrus sativus* L. Cytologia 82, 267–271.

Gill, S.S., Tuteja, N., 2010. Reactive oxygen species and antioxidant machinery in abiotic stress tolerance in crop plants. Plant Physiol. Biochem. 48 (12), 909–930.

Halliwell, B., Gutteridge, J.M.C., 2007. Free Radicals in Biology and Medicine. Oxford University Press, New York.

Hong, J., Peralta-Videa, J.R., Rico, C., Sahi, S., Viveros, M.N., Bartonjo, J., Zhao, L.J., Gardea-Torresdey, J.L., 2014. Evidence of translocation and physiological impacts of foliar applied CeO_2 nanoparticles on cucumber (*Cucumis sativus*) plants. Environ. Sci. Technol. 48, 4376–4385.

Hong, J., Rico, C.M., Zhao, L., Adeleye, A.S., Keller, A.A., Peralta-Videa, J.R., Gardea-Torresdey, J.L., 2015. Toxic effects of copper-based nanoparticles or compounds to lettuce (*Lactuca sativa*) and alfalfa (*Medicago sativa*). Environ. Sci. Process. Impacts 17 (1), 177–185.

Hong, J., Wang, L., Sun, Y., Zhao, L., Niu, G., Tan, W., Rico, C.M., Peralta-Videa, J.R., Gardea-Torresdey, J.L., 2016. Foliar applied nanoscale and microscale CeO_2 and CuO alter cucumber (*Cucumis sativus*) fruit quality. Sci. Total Environ. 563, 904–911.

Hortin, J.M., 2017. Behavior of Copper Oxide Nanoparticles in Soil Pore Waters as Influenced by Soil Characteristics, Bacteria and Wheat Roots (Master of Science Thesis). Utah State University, Logan, UT.

Huang, Y., Zhao, L., Keller, A.A., 2017. Interactions, transformations, and bioavailability of nanocopper exposed to root exudates. Environ. Sci. Technol. 51, 9774–9783.

Keller, A.A., Adeleye, A.S., Conway, J.R., Garner, K.L., Zhao, L., Cherr, G.N., Hong, J., Gardea-Torresdey, J.L., Godwin, H.A., Hanna, S., Ji, Z., Kaweeteerawat, C., Lin, S., Lenihan, H.S., Miller, R.J., Nel, A.E., Peralta-Videa, J.R., Walker, S.L., Taylor, A.A., Torres-Duarte, C., Zink, J.I., Zuverza-Mena, N., 2017. Comparative environmental fate and toxicity of copper nanomaterials. NanoImpact 7, 28–40.

Keller, A.A., Huang, Y., Nelson, J., 2018. Detection of nanoparticles in edible plant tissues exposed to nano copper using single particle ICP-MS. J. Nanopart. Res. 20, 101.

Khaldari, I., Naghavi, M.R., Motamedi, E., 2021. Synthesis of green and pure copper oxide nanoparticles using two plant resources via solid-state route and their phytotoxicity assessment. RSC Adv. 11, 3346–3353. https://doi.org/10.1039/D0RA09924D.

Khan, N.T., Jameel, N., 2018. Copper nanoparticles-synthesis and applications. Acta Sci. Pharm. Sci. 2 (12), 41–43.

Khan, I., Saeed, K., Khan, I., 2019. Nanoparticles: properties, applications and toxicities. Arab. J. Chem. 12 (7), 908–931.

Kim, S., Lee, S., Lee, I., 2012. Alteration of phytotoxicity and oxidant stress potential by metal oxide nanoparticles in *Cucumis sativus*. Water Air Soil Pollut. 223 (5), 2799–2806.

Klaine, S.J., Alvarez, P.J.J., Batley, G.E., Fernandes, T.F., Handy, R.D., Lyon, D.Y., Mahendra, S., McLaughlin, M.J., Lead, J.R., 2008. Nanomaterials in the environment: behavior, fate, bioavailability, and effects. Environ. Toxicol. Chem. 27 (9), 1825–1851.

Kovacic, P., Somanathan, R., 2010. Biomechanisms of nanoparticles (toxicants, antioxidants and therapeutics): electron transfer and reactive oxygen species. J. Nanosci. Nanotechnol. 10, 1–12.

Krichevskii, G.E., 2010. Nanotechnologies: dangers and risks. Inspecting principles for nanotechnologies and nanomaterials. Nanotekhnol. Okhrana Zdorov'ya 2 (3), 4.

Kumari, M., Mukherjee, A., Chadrasekaran, N., 2009. Genotoxicity of silver nanoparticle in *Allium cepa*. Sci. Total Environ. 407, 5243–5246.

Kumbhakar, D.V., Datta, A.K., Mandal, A., Das, D., Gupta, S., Ghosh, B., Halder, S., Dey, S., 2016. Effectivity of copper and cadmium sulphide nanoparticles in mitotic and meiotic cells of *Nigella sativa* L. (black cumin)–can nanoparticles act as mutagenic agents? J. Exp. Nano. Sci. 11, 823–839.

Kumbhakar, D.V., Das, D., Ghosh, B., Pramanik, A., Gupta, S., Datta, A.K., 2019. Phyto-nano interaction—an insight to the phenomenon. In: Raliya, R. (Ed.), Nanoscale Engineering in Agricultural Management. CRC Press, Boca Raton, FL.

Lalau, C.M., de Almeida Mohedano, R., Schmidt, É.C., Bouzon, Z.L., Ouriques, L.C., dos Santos, R.W., da Costa, C.H., Vicentini, D.S., Matias, W.G., 2015. Toxicological effects of copper oxide nanoparticles on the growth rate, photosynthetic pigment content, and cell morphology of the duckweed *Landoltia punctata*. Protoplasma 252 (1), 221–229.

Lazareva, A., Keller, A.A., 2014. Estimating potential life cycle releases of engineered nanomaterials from wastewater treatment plants. ACS Sustain. Chem. Eng. 2 (7), 1656–1665.

Le Van, N., Ma, C.X., Shang, J.Y., Rui, Y.K., Liu, S.T., Xing, B.S., 2016. Effects of CuO nanoparticles on insecticidal activity and phytotoxicity in conventional and transgenic cotton. Chemosphere 144, 661–670.

Lee, W.M., An, Y.J., Yoon, H., Kweon, H.S., 2008. Toxicity and bioavailability of copper nanoparticles to the terrestrial plants mung bean (*Phaseolus radiatus*) and wheat (*Triticum aestivum*): plant gar test for water-insoluble nanoparticles. Environ. Toxicol. Chem. 27, 1915–1921.

Liu, R.Q., Zhang, H.Y., Lal, R., 2016. Effects of stabilized nanoparticles of copper, zinc, manganese, and iron oxides in low concentrations on lettuce (*Lactuca sativa*) seed germination: nanotoxicants or nanonutrients? Water Air Soil Pollut. 227, 1–14.

Lee, S., Chung, H., Kim, S., Lee, I.S., 2013. The genotoxic effect of ZnO and CuO nanoparticles on early growth of buckwheat, *Fagopyrum esculentum*. Water 224. https://doi.org/10.1007/s11270-013-1668-0.

Liu, C., Yu, Y., Liu, H., Xin, H., 2021. Effect of different copper oxide particles on cell division and related genes of soybean roots. Plant Physiol. Biochem. 163, 205–214.

Lopez-Lima, D., Mitz-Enriquez, A.I., Carrion, G., Basurto-Cereceda, S., Pariona, N., 2021. The bifunctional role of copper nanoparticles in tomato: effective treatment for Fusarium wilt and plant growth promoter. Sci. Hortic. 277, 109810. https://doi.org/10.1016/j.scienta.2020.109810.

Ma, X., Geiser-Lee, J., Deng, Y., Kolmakov, A., 2010. Interactions between engineered nanoparticles (ENPs) and plants: phytotoxicity, uptake and accumulation. Sci. Total Environ. 408, 3053–3061.

Ma, C.X., White, J.C., Dhankher, O.P., Xing, B., 2015. Metal-based nanotoxicity and detoxification pathways in higher plants. Environ. Sci. Technol. 49 (12), 7109–7122.

Majumdar, S., Peralta-Videa, J.R., Castillo-Michel, H., Hong, J., Rico, C.M., Gardea-Torresdey, J.L., 2012. Applications of synchrotron μ-XRF to study the distribution of biologically important elements in different environmental matrices: a review. Anal. Chim. Acta 28, 1–16.

Majumder, S., Neogi, S., 2016. Antimicrobial activity of copper oxide nanoparticles coated on cotton fabric and synthesized by one-pot method. Adv. Sci. Eng. Med. 8, 102–111.

Maniprasad, P., Young, M., Santra, S., 2015. Mixed-valence core-shell copper loaded silica nanoparticle – a powerful antimicrobial composite material for agricultural crop protection. In: World Congress on New Technologies, Barcelona, Spain, pp. 1–8.

Marschner, H., 1995. Mineral Nutrition of Higher Plants. Academic Press, London, p. 889.

Miralles, P., Church, T.L., Harris, A.T., 2012. Toxicity, uptake, and translocation of engineered nanomaterials in vascular plants. Environ. Sci. Technol. 46, 9224–9239.

Moon, Y.S., Park, E.S., Kim, T.O., Lee, H.S., Lee, S.E., 2014. SELDI-TOF MS-based discovery of a biomarker in *Cucumis sativus* seeds exposed to CuO nanoparticles. Environ. Toxicol. Pharmacol. 38 (3), 922–931.

Mukherjee, A., Peralta-Videa, J.R., Gardea-Torresdey, J.G., White, J.C., 2016. Effects and uptake of nanoparticles in plants. In: Xing, B., Vecitis, C.D., Senesi, N. (Eds.), Engineered Nanoparticles and the Environment: Biophysicochemical Processes and Toxicity. John Wiley and Sons Inc, USA.

Musante, C., White, J.C., 2012. Toxicity of silver and copper to *Cucurbita pepo*: differential effects of nano and bulk-size particles. Environ. Toxicol. 279, 510–517.

Nair, P.M.G., Chung, I.M., 2014a. A mechanistic study on the toxic effect of copper oxide nanoparticles in soybean (*Glycine max* L.) root development and lignification of root cells. Biol. Trace Elem. Res. 162 (1–3), 342–352.

Nair, P.M.G., Chung, I.M., 2014b. Impact of copper oxide nanoparticles exposure on *Arabidopsis thaliana* growth, root system development, root lignification, and molecular level changes. Environ. Sci. Pollut. Res. 21 (22), 12709–12722.

Nair, P.M.G., Chung, I.M., 2015. Study on the correlation between copper oxide nanoparticles induced growth suppression and enhanced lignification in Indian mustard (*Brassica juncea* L.). Ecotoxicol. Environ. Saf. 113, 302–313.

Navarro, E., Baun, A., Behra, R., Hartmann, N., Filser, J., Miao, A.J., Quigg, A., Santschi, P., Sigg, L., 2008. Environmental behavior and ecotoxicity of engineered nanoparticles to algae, plants and fungi. Ecotoxicology (London, England) 17, 372–386.

Nekrasova, G.F., Ushakova, O.S., Ermakov, A.E., Uimin, M.A., Byzov, I.V., 2011. Effects of copper (II) ions and copper oxide nanoparticles on *Elodea densa* Planch. Russ. J. Ecol. 42 (6), 458–463.

Ogunkunle, C.O., Bornmann, R., Wagner, R., Fatoba, P.O., Frahm, R., Luetzenchirchen-Hecht, D., 2016. Biotransformation evidence of copper nanoparticles in cowpea (*Vigna unguiculata*) by XANES. In: 12th DELTA User Meeting and Annual Report 2016, Dortmund, Germany.

Ogunkunle, C.O., Folarin, O., Olorunmaiye, K.S., Fatoba, P.O., 2017. Bioaccumulation of copper and tissue partitioning of selected mineral elements in German round pea (*Kleine rheinlanderin*) under the influence of copper nanoparticles. Ann. Food Sci. Technol. 18 (4), 654–660.

Ogunkunle, C.O., Jimoh, M.A., Asogwa, N.T., Viswanathan, K., Vishwakarma, V., Fatoba, P.O., 2018. Effects of manufactured nano-copper on copper uptake, bioaccumulation and enzyme activities in cowpea grown on soil substrate. Ecotoxicol. Environ. Saf. 155, 86–93.

Ogunkunle, C.O., Bornmann, B., Wagner, R., Fatoba, P.O., Frahm, R., Luezenkirchen-Hecht, D., 2019. Copper uptake, tissue partitioning and biotransformation evidence by XANES in cowpea (*Vigna unguiculata L*) grown in soil amended with nano-sized copper particles. Environ. Nanotechnol. Monit. Manag. 12. https://doi.org/10.1016/j.enmm.2019.100231. Elsevier. Available online at.

Ogunkunle, C.O., Oyedeji, S., Okoro, H.K., Adimula, V., 2021. Interaction of nanoparticles with soil. In: Amrane, A., Mohan, D., Nguyen, T.A., Assad, A.A., Yasin, G. (Eds.), Nanomaterials for Soil Remediation. Elsevier, The Netherlands, pp. 101–132, https://doi.org/10.1016/B978-0-12-822891-3.00006-2 (Chapter 6).

OJEC, 1998. On the Quality of Water Intended for Human Consumption. Off. J. Eur. Communities L-330 (5 December 1998).

Pelegrino, M.T., Kohatsu, M.Y., Seabra, A.B., Monteiro, L.R., Gomes, D.G., Oliveira, H.C., Rolim, W.R., de Jesus, T.A., Batista, B.L., Lange, C.N., 2020. Effects of copper oxide nanoparticles on growth of lettuce (*Lactuca sativa* L.) seedlings and possible implications of nitric oxide in their antioxidative defense. Environ. Monit. Assess. 192, 232. https://doi.org/10.1007/s10661-020-8188-3.

Peng, C., Duan, D., Xu, C., Chen, Y., Sun, L., Zhang, H., Yuan, X., Zheng, L., Yang, Y., Yang, J., Zhen, X., Chen, Y., Shi, J., 2015. Translocation and biotransformation of CuO nanoparticles in rice (*Oryza sativa* L.) plants. Environ. Pollut. 197, 99–107.

Peng, C., Xu, C., Liu, Q., Sun, L., Luo, Y., Shi, J., 2017. Fate and transformation of CuO nanoparticles in the soil-rice system during the life cycle of rice plants. Environ. Sci. Technol. 51, 4907–4917.

Petrova, A., Plaksenkova, I., Kokina, I., Jermaļonoka, M., 2021. Effect of Fe_3O_4 and CuO nanoparticles on morphology, genotoxicity, and miRNA expression on different barley (*Hordeum vulgare* L.) genotypes. Sci. World J. 2021. https://doi.org/10.1155/2021/6644689.

Pramanik, A., Datta, A.K., Das, D., Kumbhakar, D.V., Ghosh, B., Mandal, A., Gupta, S., Saha, A., Sengupta, S., 2018a. Assessment of nanotoxicity (cadmium sulphide and copper oxide) using cytogenetical parameters in *Coriandrum sativum* L. (Apiaceae). Cytol. Genet. 52 (4), 299–304.

Pramanik, A., Datta, A.K., Das, D., Kumbhakar, D.V., Ghosh, B., Mandal, A., Gupta, S., Saha, A., Sengupta, S., 2018b. Assessment of mutagenic potentiality of chemically synthesized cadmium sulphide and copper oxide nanoparticles in *Coriandrum sativum* L. (Apiaceae). Cytol. Genet. 53 (4), 299–308.

Rai, M., Ingle, A.P., Pandit, R., Paralikar, P., Shende, S., Gupta, I., Biswas, J.K., da Silva, S.S., 2018. Copper and copper nanoparticles: role in management of insect-pests and pathogenic microbes. Nanotechnol. Rev. 7 (4), 303–315.

Rajput, V.D., Minkina, T.M., Behal, A., Sushkova, S.N., Mandzhieva, S., Singh, R., et al., 2018. Effects of zinc oxide nanoparticles on soil, plants, animals and soil organisms: a review. Environ. Nanotechnol. Monit. Manag. 9, 76–84.

Rajput, V., Minkina, T., Ahmed, B., Sushkova, S., Singh, R., Soldatov, M., Laratte, B., Fedorenko, A., Mandzhieva, S., Blicharska, E., Musarrat, J., Saquib, Q., Flieger, J., Gorovtsov, A., 2019. Interaction of copper-based nanoparticles to soil, terrestrial, and aquatic systems: critical review of the state of the science and future perspectives. Rev. Environ. Contam. Toxicol. https://doi.org/10.1007/398_2019_34.

Ranjan, A., Rajput, V.D., Minkina, T., Bauer, T., Chauhan, A., Jindal, T., 2021. Nanoparticles induced stress and toxicity in plants. Environ. Nanotechnol. Monit. Manage. 15. https://doi.org/10.1016/j.enmm.2021.100457.

Raven, J.A., Evans, M.C., Korb, R.E., 1999. The role of trace metals in photosynthetic electron transport in O_2—evolving organisms. Photosynth. Res. 60, 111–150.

Rawat, S., Pullagurala, V.L.R., Hernandez-Molina, M., Sun, Y., Niu, G., Hernandez-Viezcas, J.A., et al., 2018. Impacts of copper oxide nanoparticles on bell pepper (*Capsicum annum* L.) plants: a full life cycle study. Environ. Sci. Nano 5, 83–95.

Rawat, S., Cota-Ruiz, K., Dou, H., Pullagurala, V.L.R., Zuverza-Mena, N., White, J.C., Niu, G., Sharma, N., Hernandez-Viezcas, J.A., Peralta-Videa, J.R., Gardea-Torresdey, J.L., 2021. Soil-weathered CuO nanoparticles compromise foliar health and pigment production in spinach (*Spinacia oleracea*). Environ. Sci. Technol. https://doi.org/10.1021/acs.est.0c06548.

Rico, C.M., Majumdar, S., Duarte-Gardea, M., Peralta-Videa, J.R., Gardea-Torresdey, J.L., 2011. Interaction of nanoparticles with edible plants and their possible implications in the food chain. Agric. Food Chem. 59 (8), 3485–3498.

Rico, C.M., Peralta-Videa, J.R., Gardea-Torresdey, J.L., 2015. Chemistry, biochemistry of nanoparticles, and their role in antioxidant defense system in plants. In: Nanotechnology and Plant Sciences. Springer International Publishing, pp. 1–17.

Ruttkay-Nedecky, B., Krystofova, O., Nejdl, L., Adam, V., 2017. Nanoparticles based on essential metals and their phytotoxicity. J. Nanobiotechnol. 15, 33. https://doi.org/10.1186/s12951-017-0268-3.

Servin, A.D., De la Torre-Roche, R., Castillo-Michel, H., Pagano, L., Hawthorne, J., Musante, C., Pignatello, J., Uchimiya, M., White, J.C., 2017. Exposure of agricultural crops to nanoparticle CeO_2 in biochar-amended soil. Plant Physiol. Biochem. 110, 147–157.

Sharifi, S., Behzadi, S., Laurent, S., Laird Forrest, M., Stroeve, P., 2012. Toxicity of nanomaterials. Chem. Soc. Rev. 41, 2323–2343.

Sharma, P., Jha, A.B., Dubey, R.S., Pessarakli, M., 2012. Reactive oxygen species, oxidative damage, and antioxidative defense mechanism in plants under stressful conditions. J. Bot. 692, 1–27.

Shaw, A.K., Hossain, Z., 2013. Impact of nano-CuO stress on rice (*Oryza sativa* L.) seedlings. Chemosphere 93 (6), 906–915.

Shi, J.Y., Abid, A.D., Kennedy, I.M., Hristova, K.R., Silk, W.K., 2011. To duckweeds (*Landoltia punctata*), nanoparticulate copper oxide is more inhibitory than the soluble copper in the bulk solution. Environ. Pollut. 159 (5), 1277–1282.

Shi, J.Y., Peng, C., Yang, Y.Q., Yang, J.J., Zhang, H., Yuan, X.F., Chen, Y.X., Hu, T., 2014. Phytotoxicity and accumulation of copper oxide nanoparticles to the Cu-tolerant plant *Elsholtzia splendens*. Nanotoxicology 8 (2), 179–188.

Shi, J., Ye, J., Fang, H., Zhang, S., Xu, C., 2018. Effects of copper oxide nanoparticles on paddy soil properties and components. Nanomaterials 2018 (8), 839. https://doi.org/10.3390/nano8100839.

Siddiqui, M.H., Al-Whaibi, M.H., Mohammad, F. (Eds.), 2015. Nanotechnology and Plant Sciences: Nanoparticles and Their Impact on Plants. Springer.

Singh, D., Kumar, A., 2018. Investigating long-term effect of nanoparticles on growth of *Raphanus sativus* plants: a trans-generational study. Ecotoxicology 27, 23–31.

Solymosi, K., Bertrand, M., 2012. Soil metals, chloroplasts, and secure crop production: a review. Agron. Sustain. Dev. 32, 245–272.

Srivastava, A.K., Dwivedi, K.N., 2018. Formulation and characterization of copper nanoparticles using *Nerium odorum* Soland leaf extract and its antimicrobial activity. Int. J. Drug Dev. Res. 10 (3), 29–34.

Stampoulis, D., Sinha, S.K., White, J.C., 2009. Assay-dependent phytotoxicity of nanoparticles to plants. Environ. Sci. Technol. 43, 9473–9479.

Tamilvanan, A., Balamurugan, K., Ponappa, K., Madhan Kumar, B., 2014. Copper nanoparticles: synthetic strategies, properties and multifunctional application. Int. J. Nanosci. 13 (2), 1430001.

Tang, Y., He, R., Zhao, J., Nie, G., Xu, L., Xing, B., 2016. Oxidative stress-induced toxicity of CuO nanoparticles and related toxicogenomic responses in *Arabidopsis* thaliana. Environ. Pollut. 212, 605–614.

Tripathi, D.K., Gaur, S., Singh, S., Singh, S., Pandey, R., Singh, V.P., Sharm, N.C., Prasad, S.M., Dubey, N.K., Chauhan, D.K., 2016. An overview on manufactured nanoparticles in plants: uptake, translocation, accumulation and phytotoxicity. Plant Physiol. Biochem. https://doi.org/10.1016/j.plaphy.2016.07.030.

Trujillo-Reyes, J., Majumdar, S., Botez, C.E., Peralta-Videa, J.R., Gardea-Torresdey, J.L., 2014. Exposure studies of core-shell Fe/Fe_3O_4 and Cu/CuO NPs to lettuce (*Lactuca sativa*) plants: are they a potential physiological and nutritional hazard? J. Hazard. Mater. 267, 255–263.

Wang, Z.Y., Xie, X.Y., Zhao, J., Liu, X.Y., Feng, W.Q., White, J.C., Xing, B.S., 2012. Xylem- and phloem-based transport of CuO nanoparticles in maize (*Zea mays* L.). Environ. Sci. Technol. 46 (8), 4434–4441.

Wang, Z., von dem Bussche, A., Kabadi, P.K., Kane, A.B., Hurt, R.H., 2013. Biological and environmental transformations of copper-based nanomaterials. ACS Nano 7, 8715–8727.

Wang, P., Lombi, E., Zhao, F.J., Kopittke, P.M., 2016a. Nanotechnology: a new opportunity in plant sciences. Trends Plant Sci. 21, 699–712.

Wang, Z., Xu, L., Zhao, J., Wang, X., White, J.C., Xing, B., 2016b. CuO nanoparticle interaction with *Arabidopsis thaliana*: toxicity, parent-progeny transfer, and gene expression. Environ. Sci. Technol. 50 (11), 6008–6016.

Wang, Y., Deng, C., Rawat, S., Cota-Ruiz, K., Medina-Velo, I., Gardea-Torresdey, J.L., 2021. Evaluation of the effects of nanomaterials on rice (*Oryza sativa* L.) responses: underlining the benefits of nanotechnology for agricultural applications. ACS Agric. Sci. Technol. 1 (2), 44–54.

Xiong, T., Dumat, C., Dappe, V., Vezin, H., Schreck, E., Shahid, M., Pierart, A., Sobanska, S., 2017. Copper oxide nanoparticle foliar uptake, phytotoxicity, and consequences for sustainable urban agriculture. Environ. Sci. Technol. 51, 5242–5251.

Xiong, T., Zhang, S., Kang, Z., Zhang, T., Li, S., 2021a. Dose-dependent physiological and transcriptomic responses of lettuce (*Lactuca sativa* L.) to copper oxide nanoparticles—insights into the phytotoxicity mechanisms. Int. J. Mol. Sci. 22, 3688. https://doi.org/10.3390/ijms22073688.

Xiong, T., Zhang, T., Xian, Y., Kang, Z., Zhang, S., Dumat, C., Shahid, M., Li, S., 2021b. Foliar uptake, biotransformation, and impact of CuO nanoparticles in *Lactuca sativa* L. var. ramosa Hort. Environ. Geochem. Health. https://doi.org/10.1007/s10653-020-00734-9 (0123456789.,-volV 0123458697).

Yang, Z., Chen, J., Dou, R.Z., Gao, X., Mao, C.B., Wang, L., 2015. Assessment of the phytotoxicity of metal oxide nanoparticles on two crop plants, maize (*Zea mays* L.) and rice (*Oryza sativa* L.). Int. J. Environ. Res. Public Health 12 (12), 15100–15109.

Yang, Z., Xiao, Y., Jiao, T., Zhang, Y., Chen, J., Gao, Y., 2020. Effects of copper oxide nanoparticles on the growth of rice (*Oryza sativa* L.) seedlings and the relevant physiological responses. Int. J. Environ. Res. Public Health 17, 1260. https://doi.org/10.3390/ijerph17041260.

Yruela, I., 2005. Copper in plants. Braz. J. Plant Physiol. 17, 145–156.

Yusefi-Tanha, E., Fallah, S., Rostamnejadi, A., Pokhrel, L.R., 2020. Particle size and concentration dependent toxicity of copper oxide nanoparticles (CuONPs) on seed yield and antioxidant defense system in soil grown soybean (*Glycine max* cv. Kowsar). Sci. Total Environ. https://doi.org/10.1016/j.scitotenv.2020.136994.

Zhao, L., Peng, B., Hernandez-Viezcas, J.A., Rico, C., Sun, Y., Peralta-Videa, J.R., Tang, X., Niu, G., Jin, L., Varela-Ramirez, A., Jian-ying, Z., Gardea-Torresdey, J.L., 2012. Stress response and tolerance of *Zea mays* to CeO_2 nanoparticles: cross talk among H_2O_2, heat shock protein, and lipid peroxidation. ACS Nano 6, 9615–9622.

Zhao, L.J., Huang, Y.X., Hu, J., Zhou, H.J., Adeleye, A.S., Keller, A.A., 2016a. H-1 NMR and GC-MS based metabolomics reveal defense and detoxification mechanism of cucumber plant under nano-Cu stress. Environ. Sci. Technol. 50, 2000–2010.

Zhao, L., Huang, Y., Zhou, H., Adeleye, A.S., Wang, H., Ortiz, C., Mazer, S.J., Keller, A.A., 2016b. GC-TOFMS based metabolomics and ICP-MS based metallomics of cucumber (*Cucumis sativus*) fruits reveal alteration of metabolites profile and biological pathway disruption induced by nano copper. Environ. Sci. Nano 3, 1114–1123.

Zia, M., Zafar, H., Gul, F.Z., Abbasi, B.H., Rizvi, Z.F., Mannan, A., 2021. Synergistic influence of CuO nanoparticles and spectral lights transforms biomass, antioxidative response, and antioxidants in *Brassica nigra*. Plant Cell Tissue Organ Cult. 145, 261–274. https://doi.org/10.1007/s11240-020-02006-x.

Zuverza-Mena, N., Medina-Velo, I.A., Barrios, A.C., Tan, W., Peralta-Videa, J.R., Gardea-Torresdey, J.L., 2015. Copper nanoparticles/compounds impact agronomic and physiological parameters in cilantro (*Coriandrum sativum*). Environ Sci Process Impacts 17 (10), 1783–1793.

CHAPTER

Nanostructured materials based on copper/carbon as a plant growth stimulant

15

Shagufta Afreen[a], Rishabh Anand Omar[b], Neetu Talreja[c], Divya Chauhan[d], R.V. Mangalaraja[c], and Mohammad Ashfaq[c,e]

[a]*CAS Key Laboratory of Bio-Based Materials, Qingdao Institute of Bioenergy and Bioprocess Technology, Chinese Academy of Sciences, Qingdao, PR China,*
[b]*Center for Environmental Science and Engineering, Indian Institute of Technology Kanpur, Kanpur, India,*
[c]*Advanced Ceramics and Nanotechnology Laboratory, Department of Materials Engineering, Faculty of Engineering, University of Concepción, Concepción, Chile,*
[d]*Department of Chemical and Biomedical Engineering, University of South Florida, Tampa, FL, United States,*
[e]*School of Life Science, BS Abdur Rahman Institute of Science and Technology, Chennai, India*

1 Introduction

Technological advancements of nanostructured materials have played a foremost role in the development of numerous areas such as energy, catalysts, semiconductors, cosmetics, drug delivery, nanomedicine, sensors, and agriculture. Usually, nanoparticles (NPs) exist within the atmosphere from natural resources like dust storms, forest fires, and volcanoes. Carbon-based nanostructured materials (CNM) such as fullerene (C_{60}), carbon nanotubes (CNTs), carbon nanofibers (CNFs), graphite, etc. as well as metal- and metal oxide-based nanomaterials such as CuO, TiO_2, CeO_2, Fe_3O_4, and ZnO are extensively used as fertilizers, micronutrient delivery systems, or carriers for agrochemicals or growth stimulators. Moreover, these nanostructured materials protect against various diseases. A plant's development and growth are dependent upon water, oxygen, minerals, sunlight, and other nutrients that might be regulated by phytohormones. Interestingly, nanostructured materials might improve a plant's water content, minerals, and nutrients, thereby upregulating the phytohormones and subsequently growth of the plants (Buzea et al., 2007; Ma et al., 2015; Servin et al., 2015; Zaytseva and Neumann, 2016; Chauhan et al., 2020; Afreen et al., 2020; Mohammad Ashfaq et al., 2019; Omar et al., 2019a,b; Ashfaq and Khan, 2017).

Recently, nanostructured materials-based insecticides, fungicides, and nanofertilizers have been investigated for use in organic fertilizers, genetic modification, plant disease control, and improving the growth of plants. Usually, these nanostructured materials might enhance the germination rate, protect against biotic and abiotic

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stress, and improve nutrient efficiency, thereby improving the yield of crops (de la Rosa et al., 2017; Raliya et al., 2016; Ibrahim et al., 2019; Farooq et al., 2021; Rajput et al., 2020; Ali et al., 2021; Zhao et al., 2020). Cu and CNM continuously gain the interest of researchers, especially in agricultural applications. The Cu NPs have strong antibacterial and antifungal activity, thereby protecting against various plant diseases. Numerous studies suggest that Cu NPs show positive effects on plants at a lower concentration, yet exhibit phytotoxicity at a higher concentration due to accumulation at the root surface, as Cu NPs have a strong positive charge. The positive charge of the NPs and the negative charge of the plants lead to a strong electrostatic attraction that leads to accumulation of NPs within the plants. Extensive use of these metals-based NPs might lead to environmental health effects (Hong et al., 2015; Keller et al., 2017; Tolaymat et al., 2015; Usman et al., 2020). In this context, CNMs have the potential to resolve such issues associated with metal NPs. The CNMs such as CNTs and CNFs easily penetrate within the seed coat and translocate from root to shoot to leaves through plasmodesmata, symplastic, and apoplastic pathways (Ashfaq et al., 2017a; Lin et al., 2009b). The Cu and CNMs might enhance the quality of several crops such as peanuts, soybeans, mung beans, corn, broccoli, lettuce, tomatoes, potatoes, and mustard because of improved translocation ability (Dubey and Mailapalli, 2016; Shojaei et al., 2019; Prasad et al., 2017). The CNMs like CNTs, CNFs, graphene, and fullerene have the potential ability to be easily functionalized with a different surface group, which might be beneficial for the development and growth of the plants. The CNFs and CNTs act as carriers for various agrochemicals, fertilizers, or micronutrients that augment plant growth. Moreover, insignificant toxicity of CNFs was observed in comparison with that of other CNMs, including CNTs (Ashfaq et al., 2013; Sasidharan et al., 2021). The CNFs have a highly negative-charged surface that makes it a potential candidate for agrochemicals, fertilizers, or micronutrient carriers within the plants due to its graphitic nature. Moreover, CNM has both positive and negative effects on the growth of plants, which might vary with different materials and different species. The adverse effects of the CNMs on plants include reduced germination rate and suppressed the plant growth due to the accumulation on the root surface (Husen and Siddiqi, 2014; Mukherjee et al., 2016; Colman et al., 2013). Several plant species such as soybean, maize, ryegrass, barley, and wheat show a toxic response that reduces germination of the seed, expression of the gene, and length of shoot against the exposure of CNM and metal oxide-based NPs like CuO and ZnO (Dimkpa et al., 2012, 2015; Ghosh et al., 2015; El-Temsah and Joner, 2012; Colman et al., 2013; Abd El-Azeim et al., 2020). This chapter mainly summarizes research of Cu and CNM in the yield of crops. Moreover, uptake, translocation, and organic effect of the nanostructured materials are discussed to enhance knowledge of nanostructured materials and their uses in the sustainable development of plant growth stimulators.

2 Natural plant growth regulator/phytohormones

The development and growth of plants depend on various factors like water, sunlight, oxygen, minerals, and other nutrients. These factors stimulate or regulate the

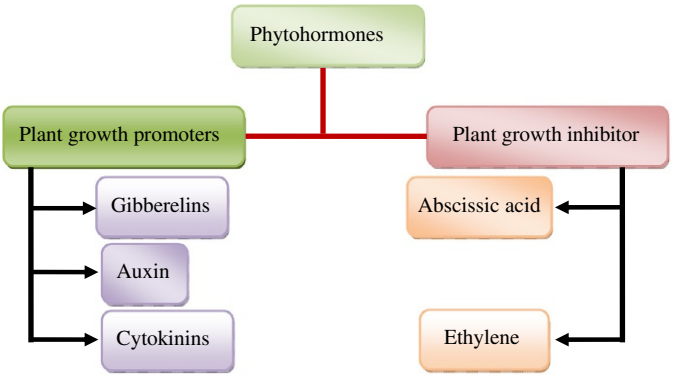

FIG. 1

Schematic representation of the phytohormones.

development of plants' natural compounds and external conditions, known as phytohormones or plant hormones. The phytohormones are active and natural factors for plant metabolism that may control physiological action and mediate responses during the plant's growth (Ashfaq and Khan, 2017; Santner et al., 2009; Kamiya, 2010; Blázquez et al., 2020). Usually, phytohormones are characterized into two groups. (1) Plant growth regulators include gibberellins that stimulate cell division and cell elongation, improve seed germination, and inhibit dormancy; auxins promote apical dominance and abscission of the leaves; and cytokinins promote cell division. (2) Plant growth inhibitors include abscisic acid that helps in the development of seed and maturations, and ethylene is a multifunctional phytohormone that regulates senescence and growth of the plants. Fig. 1 is a schematic representation of the phytohormones. Such compounds are extremely small in concentrations that trigger the development and growth of the plants. These phytohormones are sprayed on the soil around the plants. However, the effects are shirt-lived and therefore these phytohormones must be reapplied to achieve the desired effects. In this context, nanostructured materials might be suitable alternatives to resolve such issues. Nanomaterials depend on the properties of soil (composition, penetration, porosity, and heterogenicity) and properties of nanostructured materials (like the shape, size, and agglomeration ability) (Cano et al., 2016).

3 Effect of NPs on plants

NPs have an effect that depends on their dimension, shape, solubility, chemical composition, surface structure, and accumulation level (Mustafa et al., 2011). On the other hand, NP effects may depend on the plant's species, growing conditions, substratum form, temperature, light intensity, concentration of NPs used, application method (foliar or soil), and dosage. As a result of their adsorption properties, they affect the bioavailability and toxicity of organic contaminants in the soil along with the microbial community of the soil's rhizosphere (Khodakovskaya et al., 2013;

Shrestha et al., 2013; Yang et al., 2006; Gohari et al., 2020). The potential effects of NPs on the plant's well-being and the environment must be thoroughly evaluated before they are widely commercialized. In soil, NPs can accumulate as time passes due to their fragile migration capacity if they reach the soil by agricultural use, depression of the atmosphere, rain erosion, surface flooding, or other pathways. Numerous studies show that the soil NPs are more concentrated in soil than water or air, and soils may become the primary source of environmental NPs (Gottschalk et al., 2009). Stampoulis et al. and Wang et al. both reported that CuO NPs didn't affect zucchini or corn sprouting but stifled the elongation of their roots. On the contrary, a few studies have shown that NPs can benefit plants too (Stampoulis et al., 2009; Wang et al., 2012b). Several studies have shown that the TiO_2 NPs facilitated photosynthesis and nitrogen metabolism, which enhanced spinach growth if adequately delivered (Hong et al., 2005; Zheng et al., 2005; Yang et al., 2006). In 2016, Li et al. observed that carbon dots (CD) played a promising role in promoting mung bean growth at 0–1.0 mg/mL concentration. Studies have shown that CDs tend to improve mung bean's nutrient assimilation (Li et al., 2016). Burlaka et al. considered CNMs to be the main transmission agents during plant transgenic methods due to their unique chemical structure (Burlaka et al., 2015). There was also a study showing that the germination and prolongation of the zucchini root (Stampoulis et al., 2009) for the seed species was not affected by multiwalled carbon nanotubes (MWCNTs). ZnO NPs at 400 and 800 mg/kg both for the root growth were not affected by biomass (Zhao et al., 2013). No significant adverse physiological effects of corn exposed to ZnO NPs were reported (Zhang et al., 2015). Therefore, the generation, transport, deposition, and interaction of such particles must be understood to improve their consumption. The resulting studies indicated that NPs influence plants positively, negatively, and neutrally. Some of the more positive effects include stimulating seed germination, enhancing plant growth, higher biomass in the plant, influencing flowers/fruits/seeds, improving starch and gluten content with higher chlorophyll content, and rapid photosynthesis (Linglan et al., 2008). Such variations in the current research results may suggest that their organic effects depend on size, composition, surface structure, solubility, shape, and aggregation level of NPs. Comparing the results of the studies is complicated due to the many factors involved.

4 NPs uptake, translocation, and biological effect in plant system

Nanoagriculture uses nanotechnology to increase crop, fuel, and other plant yields. Also, NPs accumulate in plants, but there is a lack of clarification and study on the process of accumulation and the NPs pathway movement. In these experiments, the cell surface, chemical structure, and porosity of the walls were evaluated for their ability to serve NPs on the cell walls (Carpita et al., 1979). The result estimated that the membrane borders cannot be penetrated by particles with a diameter greater than the pores of the cell wall. Nevertheless, several literature studies have shown that

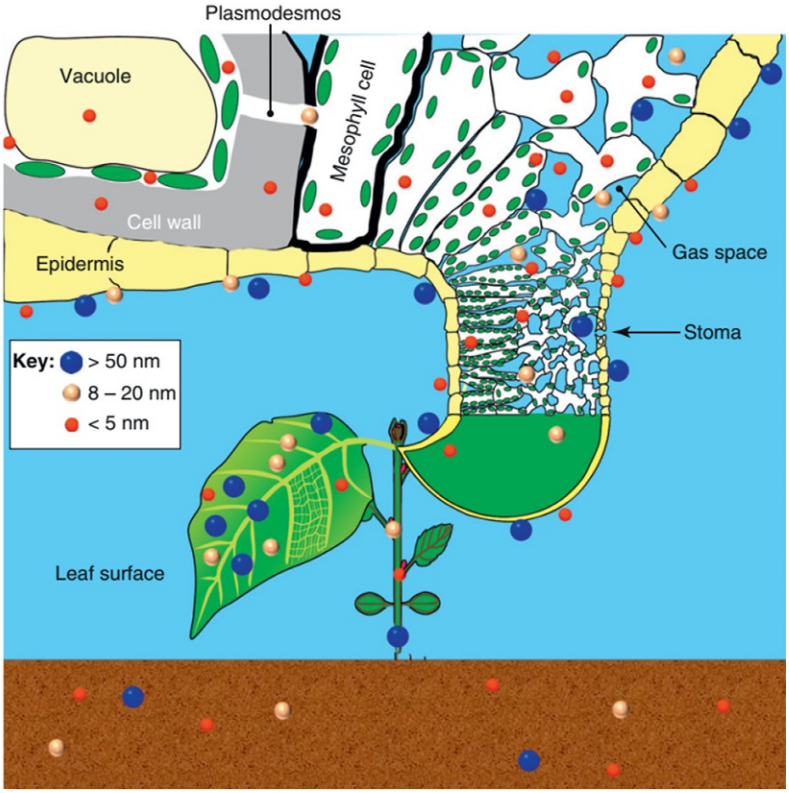

FIG. 2

Translocation of NPs based on size within the plants.

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NPs are found inside the plant organism. The NPs on the plant surfaces are thought to be adsorbed (Dietz and Herth, 2011; Lv et al., 2019) (Fig. 2).

NPs can also enter the plant via the stomata. In any case, NPs should be stored on the external periclinal walls of the epidermal cells, and the behavior of the plants should be characterized by those NPs, with their dimensions greater than that of the pore of the cell wall. The accumulation of NPs in pumpkin roots (Zhu et al., 2008) has also been recognized for soybeans, tomatoes, cucumbers, corn, alfalfa, rice, and beans (Gui et al., 2015; López-Moreno et al., 2010; Peng et al., 2015). Interestingly, the reciprocal connection between NP's size and cell wall size is a problem that arises from these experiments, as it's been reported that the NPs might be collected in plant bodies, even if size exceeds the limit for pores of the cell wall. Capillary rods interact simplistically with and translocate the transport of absorbed carbon-based material, so nanomaterial absorption can be measured (Rico et al., 2011). Therefore, xylem

participates successfully in nanomaterial transport and translocation. Nanomaterial uptake usually includes active transport, which is mediated individually by a vascular bundle, i.e., by root to root, xylem, and phloem (Etxeberria et al., 2009). The dimensions and diameters of CNTs affect the CNTs' use; when CNTs are small, they cannot penetrate or effectively take root. This may lead to cells spreading or spilling, and, if too bulky, the cells can stay outside the plant (Li et al., 2005, 2001). The hydrophilicity of CNTs increases with its interaction with other CNTs (C70) (Zhang et al., 2017). One organic particle in isothiocyanate and fluoresces increases single-walled carbon nanotube (SWCNT) assimilation, which enhances if the length is less than 500 nm (Samaj et al., 2004). Effectively generated carbon nanomaterials can be exchanged at another level. For the foliar application of nanomaterials, NPs are absorbed either by stomatal pathways or cuticles, and the measurement of efficiently absorbed NPs by stomates increases up to 40 nm (Buick et al., 1993; Eichert and Goldbach, 2008).

5 NPs phytotoxicity and permissible limit

Phytohormones, widely used in agriculture, are a key player in growth and development, but their desertion may adversely affect human health and well-being. Several studies reported plants having phytohormones, in the presence of several types of CNTs in a soil environment, increases the endogenous concentration of phytohormones. Some of these CNTs include indole-3 acetic acid, which is essentially able to take place under specific process of physiology including cell lengthening and division, a protective mechanism under biotic and abiotic drive by the expression of several genes; steroidal hormones like brassinolide that regulate plant growth and formative, processing, and resistance to biotic and abiotic stresses, including cold stress and pathogenic disease (Haubrick et al., 2006; Vriet et al., 2013); gibberellins, which regulate growth and affect various formative processes, such as prolonging stems, seed germination and dormancy, blooming, extension of the leaf, sex expression, leaf and fruit senescence, and enzyme induction (Rodrigues et al., 2012; Iqbal and Ashraf, 2013); and cytokinins, which include isopentenyl adenine that regulates various vital metabolic reactions of plants (Ma, 2008). Subsequently, NPs have a very attractive function and effect on plant growth, metabolism, and yield. The regulatory mechanisms of certain essential plant hormones, i.e., the gene transcription involved in the biosynthesis and hormones signaling can be affected by the introduction of NPs. The NPs control the repressive or gene responses, i.e., genes used in the biosynthesis of abscisic acid or components of ethylene signaling (Kaveh et al., 2013; Syu et al., 2014).

Nanomaterials depend on both the properties of the soil (size of a particle, heterogeneity, composition, penetration, and porosity) and the property of the NPs (shape, structure, and agglomeration). An investigation into the response of six crop species – barley, corn, rice, soybean, switchgrass, tomato, and tobacco cell cultures – to single-walled carbon nanohorn (SWCNH) exposure showed that these types of nanomaterials

accelerate the germination of certain crops and enhance the growth of various corn, tomato, rice, and soybean organs (Lahiani et al., 2015; Talreja and Kumar, 2018). The charge on CNTs also affects the soil surface, as CNTs display negatively loaded as an outlet, while positive loading CNTs are kept within cells (Lu et al., 2014). CNTs stimulate soil mineralization at lower concentrations, which increases soil fertility. The large use of nanotubes on agricultural soil primarily increases food production. The existence in the soil of many nanomaterials such as CNT improves and enhances endogenous plant phytohormone levels (Rui et al., 2016). Subsequently, NPs have a very attractive function and effect on plant growth, metabolism, and yield. The regulatory mechanisms of certain essential plant hormones, i.e., the gene transcription involved in the biosynthesis and hormones signaling can be affected by the introduction of NPs. NPs control the repressive or gene responses, thereby genes used in the biosynthesis of abscisic acid or components of ethylene signaling (Kaveh et al., 2013; Syu et al., 2014). Nanomaterials have played a significant role in plant growth but may also affect others adversely (Nadiminti et al., 2013; Lombi et al., 2012). In such examples, the dosage of nanostructured compounds, their composition, physical properties, and the structures used by the cell membranes and cell walls were analyzed in individual mediums. Many significant properties might be related to both positive and negative effects of NPs, as well as the important basic NPs mechanism for tropical transport (Nevius et al., 2012) (Fig. 3).

6 Effect of Cu-based nanostructured material used as a growth stimulator

The Cu NPs have unique properties that connect to the smaller and high specific surface area giving them physical resistance, chemical reactivity, electrical conductivity, magnetism, and optical effects (Hong et al., 2015). Cu NPs have a stimulatory effect at low concentration but with a high concentration give an inhibitory effect. Low dosages (5–20 mg/plant) of Cu NPs produce metabolic effects by aggregating Cu, producing reactive oxygen species (ROS) and causing cellular metabolism disturbance (Keller et al., 2017). It is a fundamental factor that trace elements with unique organic roles are found in limited amounts in all living beings, including plants, animals, or microorganisms. The plants involved in lignin synthesis are due to the Cu activating certain enzymes important in several enzyme systems. It is also required in photosynthesis, responsible for the breathing of plants, and allows plant carbohydrates and proteins to metabolize. Furthermore, the aroma and color of the flowers are improved.

The Cu-based compounds have been reported to be one of the first fungicides used to manage plant infection (Johnson, 1935). It had been reported that fungicide activity was also checked if finely isolated metal copper was suspended. The various metal components have been promoted and extensively used to control microorganism-induced plant diseases (Saddler, 2007). Still, even sustainable agriculture depends on copper to influence certain diseases. The significance of Cu

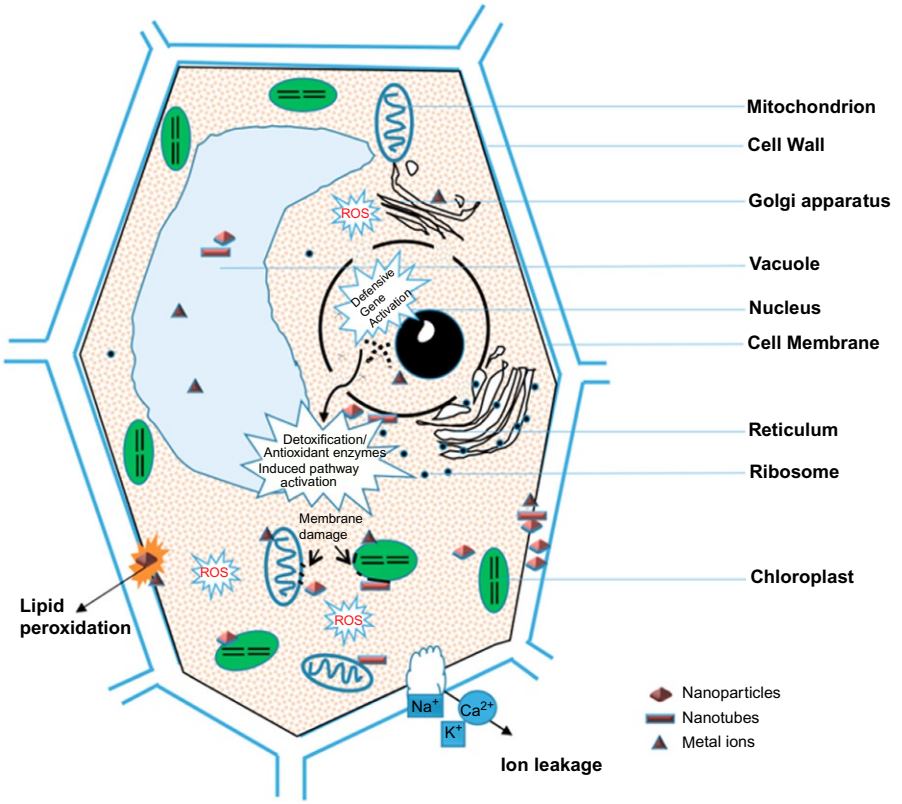

FIG. 3

Schematic illustration of a cell and the effect of NP exposure.

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NPs is primarily focused on pathogens of human and food industries (Yoon et al., 2007; Raffi et al., 2010). However, those beneficial microbes on plant pathogens of agricultural importance are rare. Cu NPs toxicity and bioavailability on Mung bean (*Phaseolus radiates*) and wheat (*Triticum aestivum*) plants were investigated. The researchers used homogeneous NPs exposure to plant agar testing as a growth substratum (Lee et al., 2008; Munzuroglu and Geckil, 2002). Both plant growth rates were impaired, and due to the exposure of NPs on plant seedlings, the growths of the studied organisms were inversely related to the concentration of NPs exposure. The wheat crop displayed a higher accumulation of Cu NPs in its roots because of its morphological origin, therefore the level of bioaccumulation increased with the rise of Cu NPs concentration and particle agglomeration. The concentration of Cu NPs in growth media was increased, and the bioavailability of Cu NPs to the test plants was

estimated by estimating the bioaccumulation factor. Nevertheless, the germination of lettuce seeds exhibited an improvement in the shoot-to-root ratio compared to the control plant in the presence of Cu NPs. The direct effects of Cu NPs visualized from infected plants on crop production, root-to-shoot length, biomass accumulation, and germination in plant and food crops are evident (Lombardi and Sebastiani, 2005). The application of Cu NPs produced higher quality tomato plants for the human diet because of the aggregation of bioactive compounds. The superlative treatment is 250 mg/L Cu NPs based on the results obtained in vitamin C and total phenols. However, it is not recommended to apply 500 mg/L Cu NPs, as it caused negative effects on the content of bioactive compounds or, in some cases, did not affect them at all (Niederberger, 2007; Franke et al., 2006; Kolmakov and Moskovits, 2004). Size-dependent properties such as fluorescence, degrading photocatalysis, or biotechnological applications in soil regeneration, sensor growth, and agrochemicals were presented in metal/metal oxide-NPs. It exhibited size-dependent properties such as fluorescence, photocatalytic degradation, or magnetism, which have biotechnological applications in soil remediation, sensor growth, and agrochemicals (Kolmakov and Moskovits, 2004; Franke et al., 2006).

In general, the effects of metal or metal oxide NPs on plants are predicted to be substantially dependent on chemical properties and colloidal features including sediments, soil or sludge, and organic content for plants. Metal NPs play an essential part in plant growth under low concentration conditions at the plant's tolerance limit. If plants consume excess metals, there are adverse consequences including reduced growth and cell division irregularities. In this case, excess metal NPs that act as a cofactor of enzymes are involved in the formation of intermediate metabolites. The response of plants to metal NPs often varies with the nature of the metal, plant type, and growth stages. There was no systematic research on the various biological components and risks of NPs in the agro-ecosystem, including plants, plant pathogens, and beneficial microbes.

7 Effect of CNM used as a growth stimulator

Nanotechnology has created a very diverse role in different scientific disciplines, although its application in agriculture is of great importance in a range of fields. Because of its unique features and diverse applications in different fields of science and technology, nanotechnology gained significant attention and has been rapidly expanded recently. The different forms of nanomaterials and their application have been further developed, and among them, there has been extensive study of CNMs including graphite, diamond, fullerene, graphene, CNTs, and CNFs. The large development of CNMs has resulted in their possible release into living systems, either deliberately in discharges or inadvertently in spillages, and there is greater risk for adverse environmental effects. Studies have shown that the nanomaterial is either beneficial or detrimental to crops depending on their size, shape, level of concentration, chemical composition, solubility, etc. Therefore, these CNMs might be used in various end

applications like environmental remediation, sensors, antibacterial agents, drug delivery, medicine, wound healing, energy, and agriculture (Ashfaq et al., 2014, 2016, 2017a,b, 2019; Singh et al., 2013; Tripathi et al., 2016; Kumar et al., 2018, 2011; Bhadauriya et al., 2018; Irsad et al., 2020; Talreja et al., 2020, 2014; Kumar and Talreja, 2019; Khare et al., 2013; Saraswat et al., 2012). The CNMs most frequently studied for these purposes include fullerene C_{60}, CNTs, and CNFs. As CNM has a propensity to accumulate, it is considered extremely hydrophobic, and it could be expected to settle in a living system. Thus, to assist the flow of organic substances into the cytoplasm, only low surface friction of CNTs is required. Some edible plants can absorb CNMs with specific absorption and accumulation mechanisms.

7.1 Effect of fullerene (C_{60}) on plants

Carbon allotropes are widely used as conductive materials, such as fullerene, that can facilitate the removal of biological contaminants, for use in optical devices and various drugs, and can also act as a carrier for drug delivery systems (Upadhyayula et al., 2009; Saeedi et al., 2019). These nanomaterials have a strong antioxidant ability that maintains superoxide radicals at basal levels and reduces oxidative stress (Dugan et al., 2001; Shweta et al., 2016). The presence of fullerene in the form of black aggregates is reported to be more abundant in seeds and roots compared to rice seeds, leaves, and stalks. However, in mature plants, a more vigorous translocation from the roots to the plant's higher portion is observed. Thus, fullerene aggregates were present mostly in or near the vascular system of stem and leaves, leaving the roots devoid of fullerene (Santos et al., 2013). The aggregation of fullerene in the leaves indicates that nutrients and water are transferred through xylene. It reveals that the individual NPs of fullerenes enters plant roots through osmotic strain, capillaries, and pores via intercellular plasmodesmata or sympathy routes in the cell walls. The fullerene is the only particle with a smaller diameter than the cell wall's pores, which may be why it easily passes through the plasma membrane (Santos et al., 2013).

7.2 Effect of CNTs on plants

CNTs have a considerably significant property owing to its outstanding physical, electronic, electrical, and thermal properties for the environmental sources of production, reuse, degradation, and transportation. CNTs are commonly used in plant sciences (phyto- nanotechnology), resulting in changes in traditional plant production processes, chemical detoxification (pesticides and fertilizers), enhanced disease resistance, and serving as plant growth regulators. CNTs are tightly packed catalytic particles in vertical films, and each particle participates in the formation and aggregation of nanotubes leading to vertical growth. CNTs transmit essential chemical compounds to the cell at the cellular level by breaching the cell wall, which can be a matter of concern. The cell wall and membrane penetration are achieved through the use of SWCNTs impregnated with cellulose in tobacco cells (Liu et al., 2009) and transported intracellularly by cellulose-induced nanoholes (Serag et al., 2012). Fig. 4 shows the microscopic images of BY2 cells exposed to SWCNTs.

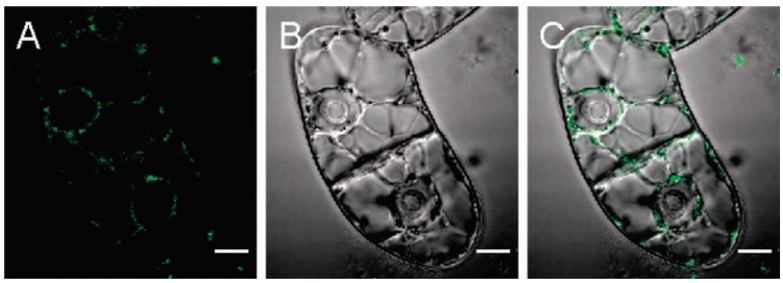

FIG. 4

Microscopic images of BY2 cells exposed to SWCNTs.

The image was taken with permission from Liu, Q., Chen, B., Wang, Q., Shi, X., Xiao, Z., Lin, J., Fang, X. 2009. Carbon nanotubes as molecular transporters for walled plant cells. Nano Lett., 9(3), 1007–1010. Copyright © 2009, American Chemical Society.

Its penetration into the plant system is inversely proportional to its size, which is a significant factor in increasing the growth and seed production of the plant. In comparison, MWCNTs actively increase seed germination, shown by germinating tomato seeds, by penetrating the seed's coat and increasing the growth of mustard (Mondal et al., 2011) and tomato seeds (Khodakovskaya et al., 2009; Villagarcia et al., 2012). Tripathi et al. found similar effects on grain plants with water-soluble MWCNT, as they increased their water intake, which is regarded as a stimulant to growth (Tripathi and Sarkar, 2015). CNTs are completely involved in increasing the growth and development of aquaporin genes and proteins in tobacco cells and, by enhancing its reproduction genes, can also enhance a plant's reproductive health (Khodakovskaya et al., 2012). It is reported that growing CNTs translocated to the functional site, such as fruits, leaves, and roots, which may require a close association with the seedling cells of tomatoes. The overall expression of the seeds, leaves, and roots of the plants was substantially improved. CNTs are phytotoxic in plant cells, leading to accumulation and induced dose-based cell death (De La Torre-Roche et al., 2013). Electrolyte leakage and swelling of the cell surface are signs of cell death. Therefore, it might enhance the root production of (*Cucumis sativus*), onion (*Allium cepa*), and nanotubes formed on the root of both functionalized and nonfunctionalized CNTs, but none of them reached the roots.

The SWCNT has a diameter of approximately 1–2 nm and a length of about 0.1 μm (Ren et al., 2007). Various studies have shown that surface modification of CNM increases the dispersion and stability of CNM surfaces in the water column (Parise et al., 2013; Yan et al., 2013; Cui et al., 2019; Hao et al., 2012). Contrarily, after 84 h of treatment, there is no uptake of SWCNTs and its available sources in the cucumber seedling. The SWCNTs were found to be bound to the exterior surface of primary and secondary roots in the form of a nanotube layer (Lou et al., 2011). Theoretically, the SWCNTs are too wide to reach the cell wall. Nevertheless, evidence of plasma membrane endocytosis formation in an *Arabidopsis thaliana* leaf cell indicates the presence of CNTs, and further research with other edible plants

has high significance (Lin et al., 2009a). Thus, researchers are now examining the cell suspension of Nicotiana tobacco. Bright yellow indicates that the water-soluble single-wall nanotube, ≤ 500 nm long, penetrates endocytosis in the intact cell wall membrane (Khodakovskaya et al., 2012).

The MWCNTs have a diameter between 1 mm and 20 nm. Seeds and roots are used to develop tomato seedlings through the formation of new pores and water sources (Chekin et al., 2012). Previously, the epidermal and roots of the seedlings eventually reach the epidermal and root hair-cell walls, thereby MWCNTs are displayed on the root surface (Smirnova et al., 2012). Also, certain studies indicate that MWCNTs penetrate tomato seeds and increase the germination of seeds by increasing water consumption (Wang et al., 2012a). The MWCNTs improve seed germination in 20 days by up to 90%, compared to 71% of the control sample, as well as the biomass of the plant (Tan and Fugetsu, 2007). Several nanotubes were present in the vascular system in seeds treated with MWCNTs and none in the tissues. No negative effects on seed germination and root elongation were observed in the zucchini species (Stampoulis et al., 2009).

7.3 Effect of graphene

Graphene is an allotropic carbon with two-dimensional crystalline dimensions that can be described as a single atomic graphite layer. This is due to graphene accumulation using H_2O_2 visualization, along with visible signs of necrotic damage and electrolyte leakage, indicating an oxidation stress mechanism (Al-Ghamdi et al., 2014; Mogharabi et al., 2014). It defined the accumulation of graphene as leading to cell death, indicated by leakage of electrolytes from cells. Therefore, graphene treatment significantly improved the root surface of the cabbage, and an excess of graphene may induce swelling on *Origanum vulgare* (Al-Ghamdi et al., 2014). This causes cell death and aggregation depending on dosage. Because of the aggregation process, graphene is known to induce phytotoxic effects in plant cells (Sasidharan et al., 2011). Therefore, the toxic effects of graphene on terrestrial plant species, such as tomatoes, cabbage, and red spinach, are unexpected. The same pattern of growth was reported in tomatoes, cabbage, and red spinach using graphene nanomaterial (Begum et al., 2011). At higher graphene concentrations (1000 mg/L), red spinach and cabbage root hair growth decreased as opposed to control plants. Extended exposure with time at varying concentrations is used to assess possible risks and assessment of graphene toxicity levels for terrestrial plant organisms (Anjum et al., 2013). Table 1 summarizes CNM, metals, and metal oxides-based nanostructured materials effect on the growth of several plants.

7.4 CNFs

CNFs are a relatively newer nanomaterial and very similar to CNTs. Moreover, CNFs hold metal NPs either to the tip or middle of the fibers. CNFs have unique characteristics such as high electronic conductivity, high surface area, easy functionalization,

Table 1 CNM, metals, and metal oxides-based nanostructured material's effect in several plant growth factors at the level of concentrations in different species of plant.

S. no.	Plant	Nanomaterials	Concentration	Effects on plants	References
1.	Wheat	o-MWCNT	0, 80, and 160 mg/L	Improved root length.	Wang et al. (2012a)
2.	Rice	CNTs	–	Improved water content and germination levels for seeds.	Nair et al. (2012)
3.	Barley and soybean	MWCNT	50, 100, and 200 mg/L	The seed germination increases by 50% (barley and soybean) and by 90% (corn). Enhances root length by 26% (soybean); shoot length and leaf length enhancement up to 40% (corn).	Lahiani et al. (2015)
4.	Bitter melon	Fullerols(C_{60})$(OH)_{20}$	0.943, 4.72, 9.43, 10.88, and 47.2 mg/L	Improved biomass and quality of medicinal plants.	Kole et al. (2013)
5.	Oat	MWCNT	70, 80, 90 µg/mL	Stimulating seed germination and growth of seedlings; enhances root hair and root, vascular tissue rates, chlorophyll quality, stomatological conductivity, relative water status, and photosynthetic efficiency.	Joshi et al. (2018)
6.	*Spinacia oleracea*	CuO	200 mg/kg	Improved photosynthesis and processing of biomass.	Wang et al. (2019)
7.	Castor plant	MWCNTs	50 and 100 µg/mL	The seed germination improves by 96.7%, seedling strength index 8 was 400, with fresh and dry weights improving.	Fathi et al. (2017)
8.	Rice	Graphene, GO, graphing ribbon	5, 50, 100, 200 mg/L	Improve seed germination at a lower level but delayed with the higher concentration.	Liu et al. (2015)
9.	*Solanum Lycopersicum*	CuO	150–340 µg/mL	Phytophthora infestations effectively controlled from late-black illness	Giannousi et al. (2013)

Continued

Table 1 CNM, metals, and metal oxides-based nanostructured material's effect in several plant growth factors at the level of concentrations in different species of plant—cont'd

S. no.	Plant	Nanomaterials	Concentration	Effects on plants	References
10.	Tomato	MWCNTs	10, 20, 40 mg/L	Increasing seed humidity and speed of germination.	Khodakovskaya et al. (2009)
11.	*Prunus domestica* fruits	ZnO, CuO, and Ag NPs	100 and 1000 μg/mL	The symptoms of grey mold caused by B. Cinereals and diseases of soil have been eliminated.	Malandrakis et al. (2019)
12.	Tomato, Onion, Turnip, Radish	CNTs	10, 20 and 40 mg/L	Enhanced the seed germination of tomato and onion.	Haghighi and Teixeira da Silva (2014)
13.	Wheat	Carbon nano-dots	150 mg/L	Increase the root growth (10×)	Tripathi and Sarkar (2015)
14.	Mustard	Pristine, oxidized MWCNT	2.3–46.0 mg/L	Improved the seed germination and increased the growth of root and shoot.	Mondal et al. (2011)
15.	Arabidopsis rice	SWCNTs	5–250 mg/L	Increased cell aggregation, condensation of chromate, deposition of the plasma membrane, accumulation of H_2O_2.	Shen et al. (2010)

and insignificant toxicity among all CNM, including CNTs, and are extensively used in various end applications including agriculture (Ashfaq et al., 2013, 2017a; Kumar et al., 2018). The CNFs easily translocate within the plants through root to shoot to leaf. Moreover, CNFs have graphitic content and are therefore highly negatively charged. The highly negatively charged CNFs easily translocate within the negatively charged plant cell wall due to electrostatic repulsion. Usually, the translocation ability of NPs or CNFs depends on two factors: (1) The size of CNFs is around 20–300 nm, so they easily translocate within plants, and (2) the surface charge of CNFs are highly negatively charged so they easily translocate with the negative plant cell wall. These two beneficial factors of CNFs make them a suitable candidate as carriers for the delivery of NPs, agrochemicals, fertilizers, or micronutrients. However, nanosized CNFs might be difficult to apply in the field. In this context, a similar group developed Cu–Zn CNF-incorporated, PVA starch-based composite for the delivery of micronutrients. The data suggested that the prepared Cu-Zn-CNF polymer composite efficiently delivered micronutrients within the plants, which enhanced water uptake, high germination rate, high chlorophyll content, and high protein content, therefore improving the crop yield (Kumar et al., 2018).

In general, CNMs have extraordinary characteristics like high surface area, easy functionalization, high conductivity, and insignificant toxicity, making them a suitable candidate for various end applications including agriculture.

8 Conclusion and future prospective

CNMs are increasing root and shoot growth in various stages, boosting productivity, and even encouraging cell elongation and growing crop yield. For agriculture, horticulture, and the bioenergy sector, CNM has a stimulating role to play in water absorption, germination, photosynthesis, biomass, crop yield, and disease protection. However, their increasing application in recent years has raised concerns concerning the likely biological and environmental risks, optimization, and safety assessments. The ecotoxicity results of CNM are insufficient compared to application-oriented science, and encounters with plant species and materials, growth media, and analytical technologies are not sufficient. Since CNMs exhibit certain unique and responsive properties, the ecological system is likely to be affected by the individual plants or microbial species. Similarly, metal NPs tend to be of concern to the climate and human well-being. The effects of CNMs on the optimal concentration through hormesis and stress protection systems are positive, while higher concentrations either produce no effects or adverse effects. CNM variability may not only be due to CNM concentration but also the fact that it has a heterogeneous effect on size, structure, chemical composition, and surface area of different plant species. Recently, usage has also emerged as a new technical method for the synthesis of various NPs (including bacteria, algae, and vascular plants) to regulate the shape, structure, calculation, and monodispersal of metal NPs. Researchers are now evaluating its relationship with living organisms through the physicochemical properties of metal NPs. Thus,

nanotechnology technologies include sustainable farming activities that are cost-effective, standard methods of research, and assessment indexes of nanomaterial toxicity that are relatively straightforward today. Morphological, anatomic, physiological, and biochemical indices cannot be analyzed in detail to indicate plant toxicity to NPs. The physical and chemical characteristics of NPs are specific, and further analysis and scientific study are still required. Safety and risk assessment standards shall be established, including exposure routes, safe exposure doses, etc. The purpose of this chapter is to provide scientific knowledge for the use of NPs.

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References

Abd El-Azeim, M.M., Sherif, M.A., Hussien, M.S., Tantawy, I.A.A., Bashandy, S.O., 2020. Impacts of nano- and non-nanofertilizers on potato quality and productivity. Acta Ecol. Sin. 40 (5), 388–397.

Afreen, S., Talreja, N., Chauhan, D., Ashfaq, M., 2020. Chapter 15—Polymer/metal/carbon-based hybrid materials for the detection of heavy metal ions. In: Abd-Elsalam, K.A. (Ed.), Multifunctional Hybrid Nanomaterials for Sustainable Agri-Food and Ecosystems. Elsevier.

Al-Ghamdi, A.A., Gupta, R.K., Kahol, P.K., Wageh, S., Al-Turki, Y.A., El Shirbeeny, W., Yakuphanoglu, F., 2014. Improved solar efficiency by introducing graphene oxide in purple cabbage dye sensitized TiO2 based solar cell. Solid State Commun. 183, 56–59.

Ali, S., Mehmood, A., Khan, N., 2021. Uptake, translocation, and consequences of nanomaterials on plant growth and stress adaptation. J. Nanomater. 2021, 6677616.

Anjum, N.A., Singh, N., Singh, M.K., Shah, Z.A., Duarte, A.C., Pereira, E., Ahmad, I., 2013. Single-bilayer graphene oxide sheet tolerance and glutathione redox system significance assessment in faba bean (*Vicia faba* L.). J. Nanopart. Res. 15 (7), 1–12. 1770.

Ashfaq, M., Singh, S., Sharma, A., Verma, N., 2013. Cytotoxic evaluation of the hierarchical web of carbon micronanofibers. Ind. Eng. Chem. Res. 52 (12), 4672–4682.

Ashfaq, M., Khan, S., 2017. Role of phytohormones in improving the yield of oilseed crops. In: P. Ahmad, (Ed.), Oilseed Crops. Wiley.

Ashfaq, M., Khan, S., Verma, N., 2014. Synthesis of PVA-CAP-based biomaterial in situ dispersed with Cu nanoparticles and carbon micro-nanofibers for antibiotic drug delivery applications. Biochem. Eng. J. 90, 79–89.

Ashfaq, M., Verma, N., Khan, S., 2016. Copper/zinc bimetal nanoparticles-dispersed carbon nanofibers: a novel potential antibiotic material. Mater. Sci. Eng. C 59, 938–947.

Ashfaq, M., Verma, N., Khan, S., 2017a. Carbon nanofibers as a micronutrient carrier in plants: efficient translocation and controlled release of Cu nanoparticles. Environ. Sci. Nano 4 (1), 138–148.

Ashfaq, M., Verma, N., Khan, S., 2017b. Highly effective Cu/Zn-carbon micro/nanofiber-polymer nanocomposite-based wound dressing biomaterial against the P. aeruginosa multi- and extensively drug-resistant strains. Mater. Sci. Eng. C 77, 630–641.

Ashfaq, M., Talreja, N., Chuahan, D., Srituravanich, W., 2019. Carbon nanostructure-based materials: a novel tool for detection of Alzheimer's disease. In: Ashraf, G.M., Alexiou, A. (Eds.), Biological, Diagnostic and Therapeutic Advances in Alzheimer's Disease: Non-Pharmacological Therapies for Alzheimer's Disease. Springer Singapore, Singapore.

Begum, P., Ikhtiari, R., Fugetsu, B., 2011. Graphene phytotoxicity in the seedling stage of cabbage, tomato, red spinach, and lettuce. Carbon 49 (12), 3907–3919.

Bhadauriya, P., Mamtani, H., Ashfaq, M., Raghav, A., Teotia, A.K., Kumar, A., Verma, N., 2018. Synthesis of yeast-immobilized and copper nanoparticle-dispersed carbon nanofiber-based diabetic wound dressing material: simultaneous control of glucose and bacterial infections. ACS Appl. Bio Mater. 1 (2), 246–258.

Blázquez, M.A., Nelson, D.C., Weijers, D., 2020. Evolution of plant hormone response pathways. Annu. Rev. Plant Biol. 71 (1), 327–353.

Buick, R.D., Buchan, G.D., Field, R.J., 1993. The role of surface tension of spreading droplets in absorption of a herbicide formulation via leaf stomata. Pestic. Sci. 38 (2–3), 227–235.

Burlaka, O.M., Pirko, Y.V., Yemets, A.I., Blume, Y.B., 2015. Plant genetic transformation using carbon nanotubes for DNA delivery. Cytol. Genet. 49 (6), 349–357.

Buzea, C., Pacheco, I.I., Robbie, K., 2007. Nanomaterials and nanoparticles: sources and toxicity. Biointerphases 2 (4), 2815690.

Cano, A.M., Kohl, K., Deleon, S., Payton, P., Irin, F., Saed, M., Shah, S.A., Green, M.J., Cañas-Carrell, J.E., 2016. Determination of uptake, accumulation, and stress effects in corn (*Zea mays* L.) grown in single-wall carbon nanotube contaminated soil. Chemosphere 152, 117–122.

Carpita, N., Sabularse, D., Montezinos, D., Delmer, D.P., 1979. Determination of the pore size of cell walls of living plant cells. Science 205 (4411), 1144.

Chauhan, D., Afreen, S., Talreja, N., Ashfaq, M., 2020. Chapter 8—Multifunctional copper polymer-based nanocomposite for environmental and agricultural applications. In: Abd-Elsalam, K.A. (Ed.), Multifunctional Hybrid Nanomaterials for Sustainable Agri-Food and Ecosystems. Elsevier.

Chekin, F., Bagheri, S., Arof, A.K., Hamid, S.B.A., 2012. Preparation and characterization of Ni(II)/polyacrylonitrile and carbon nanotube composite modified electrode and application for carbohydrates electrocatalytic oxidation. J. Solid State Electrochem. 16 (10), 3245–3251.

Colman, B.P., Arnaout, C.L., Anciaux, S., Gunsch, C.K., Hochella Jr., M.F., Kim, B., Lowry, G.V., McGill, B.M., Reinsch, B.C., Richardson, C.J., Unrine, J.M., Wright, J.P., Yin, L., Bernhardt, E.S., 2013. Low concentrations of silver nanoparticles in biosolids cause adverse ecosystem responses under realistic field scenario. PLoS One 8 (2), e57189.

Cui, D., Ruan, H., Zhang, X., Hu, S., Huang, P., Song, H., Wang, K., Ruan, J., 2019. Effects of single walled carbon nanotubes on Arabidopsis mesophyll cells. ECS Trans. 41 (40), 43–48.

de la Rosa, G., García-Castañeda, C., Vázquez-Núñez, E., Alonso-Castro, Á.J., Basurto-Islas, G., Mendoza, Á., Cruz-Jiménez, G., Molina, C., 2017. Physiological and biochemical response of plants to engineered NMs: implications on future design. Plant Physiol. Biochem. 110, 226–235.

De La Torre-Roche, R., Hawthorne, J., Deng, Y., Xing, B., Cai, W., Newman, L.A., Wang, Q., Ma, X., Hamdi, H., White, J.C., 2013. Multiwalled carbon nanotubes and C60 fullerenes differentially impact the accumulation of weathered pesticides in four agricultural plants. Environ. Sci. Technol. 47 (21), 12539–12547.

Dietz, K.-J., Herth, S., 2011. Plant nanotoxicology. Trends Plant Sci. 16 (11), 582–589.

Dimkpa, C.O., McLean, J.E., Latta, D.E., Manangón, E., Britt, D.W., Johnson, W.P., Boyanov, M.I., Anderson, A.J., 2012. CuO and ZnO nanoparticles: phytotoxicity, metal speciation, and induction of oxidative stress in sand-grown wheat. J. Nanopart. Res. 14 (9), 1125.

Dimkpa, C.O., Hansen, T., Stewart, J., McLean, J.E., Britt, D.W., Anderson, A.J., 2015. ZnO nanoparticles and root colonization by a beneficial pseudomonad influence essential metal responses in bean (*Phaseolus vulgaris*). Nanotoxicology 9 (3), 271–278.

Dubey, A., Mailapalli, D.R., 2016. Nanofertilisers, nanopesticides, nanosensors of pest and nanotoxicity in agriculture. In: Lichtfouse, E. (Ed.), Sustainable Agriculture Reviews. Vol. 19. Springer International Publishing, Cham.

Dugan, L.L., Lovett, E.G., Quick, K.L., Lotharius, J., Lin, T.T., O'Malley, K.L., 2001. Fullerene-based antioxidants and neurodegenerative disorders. Parkinsonism Relat. Disord. 7 (3), 243–246.

Eichert, T., Goldbach, H.E., 2008. Equivalent pore radii of hydrophilic foliar uptake routes in stomatous and astomatous leaf surfaces—further evidence for a stomatal pathway. Physiol. Plant. 132 (4), 491–502.

El-Temsah, Y.S., Joner, E.J., 2012. Impact of Fe and Ag nanoparticles on seed germination and differences in bioavailability during exposure in aqueous suspension and soil. Environ. Toxicol. 27 (1), 42–49.

Etxeberria, E., Gonzalez, P., Pozueta, J., 2009. Evidence for two endocytic transport pathways in plant cells. Plant Sci. 177 (4), 341–348.

Farooq, T., Adeel, M., He, Z., Umar, M., Shakoor, N., da Silva, W., Elmer, W., White, J.C., Rui, Y., 2021. Nanotechnology and plant viruses: an emerging disease management approach for resistant pathogens. ACS Nano. https://doi.org/10.1021/acsnano.0c10910.

Fathi, Z., Nejad, R.-A.K., Mahmoodzadeh, H., Satari, T.N., 2017. Investigating of a wide range of concentrations of multi-walled carbon nanotubes on germination and growth of castor seeds (*Ricinus communis* L.). J. Plant Protect. Res. 57 (3), 228–236.

Franke, M.E., Koplin, T.J., Simon, U., 2006. Metal and metal oxide nanoparticles in chemiresistors: does the nanoscale matter? Small 2 (1), 36–50.

Ghosh, M., Bhadra, S., Adegoke, A., Bandyopadhyay, M., Mukherjee, A., 2015. MWCNT uptake in *Allium cepa* root cells induces cytotoxic and genotoxic responses and results in DNA hyper-methylation. Mutat. Res. 774, 49–58.

Giannousi, K., Avramidis, I., Dendrinou-Samara, C., 2013. Synthesis, characterization and evaluation of copper based nanoparticles as agrochemicals against *Phytophthora infestans*. RSC Adv. 3 (44), 21743–21752.

Gohari, G., Mohammadi, A., Akbari, A., Panahirad, S., Dadpour, M.R., Fotopoulos, V., Kimura, S., 2020. Titanium dioxide nanoparticles (TiO2 NPs) promote growth and ameliorate salinity stress effects on essential oil profile and biochemical attributes of *Dracocephalum moldavica*. Sci. Rep. 10 (1), 912.

Gottschalk, F., Sonderer, T., Scholz, R.W., Nowack, B., 2009. Modeled environmental concentrations of engineered nanomaterials (TiO2, ZnO, Ag, CNT, fullerenes) for different regions. Environ. Sci. Technol. 43 (24), 9216–9222.

Gui, X., Deng, Y., Rui, Y., Gao, B., Luo, W., Chen, S., Van Nhan, L., Li, X., Liu, S., Han, Y., Liu, L., Xing, B., 2015. Response difference of transgenic and conventional rice (*Oryza sativa*) to nanoparticles (γFe2O3). Environ. Sci. Pollut. Res. 22 (22), 17716–17723.

Haghighi, M., Teixeira da Silva, J.A., 2014. The effect of carbon nanotubes on the seed germination and seedling growth of four vegetable species. J. Crop Sci. Biotechnol. 17 (4), 201–208.

Hao, Y., Yang, X., Shi, Y., Xing, J., Marowitch, J., Chen, J., Chen, J., 2012. FITC delivery into plant cells using magnetic single-walled carbon nanotubes. J. Nanosci. Nanotechnol. 12 (8), 6287–6293.

Haubrick, L.L., Torsethaugen, G., Assmann, S.M., 2006. Effect of brassinolide, alone and in concert with abscisic acid, on control of stomatal aperture and potassium currents of *Vicia faba* guard cell protoplasts. Physiol. Plant. 128 (1), 134–143.

Hong, F., Zhou, J., Liu, C., Yang, F., Wu, C., Zheng, L., Yang, P., 2005. Effect of nano-TiO2 on photochemical reaction of chloroplasts of spinach. Biol. Trace Elem. Res. 105 (1), 269–279.

Hong, J., Rico, C.M., Zhao, L., Adeleye, A.S., Keller, A.A., Peralta-Videa, J.R., Gardea-Torresdey, J.L., 2015. Toxic effects of copper-based nanoparticles or compounds to lettuce (*Lactuca sativa*) and alfalfa (*Medicago sativa*). Environ. Sci.: Processes Impacts 17 (1), 177–185.

Husen, A., Siddiqi, K.S., 2014. Carbon and fullerene nanomaterials in plant system. J. Nanobiotechnol. 12 (1), 16.

Ibrahim, A.S., Fahmy, A.H., Ahmed, S.S., 2019. Copper nanoparticles elevate regeneration capacity of (*Ocimum basilicum* L.) plant via somatic embryogenesis. Plant Cell Tiss. Org. Cult. 136 (1), 41–50.

Iqbal, M., Ashraf, M., 2013. Gibberellic acid mediated induction of salt tolerance in wheat plants: growth, ionic partitioning, photosynthesis, yield and hormonal homeostasis. Environ. Exp. Bot. 86, 76–85.

Irsad, I., Talreja, N., Chauhan, D., Rodríguez, C.A., Mera, A.C., Ashfaq, M., 2020. Nanocarriers: an emerging tool for micronutrient delivery in plants. In: Aftab, T., Hakeem, K.R. (Eds.), Plant Micronutrients: Deficiency and Toxicity Management. Springer International Publishing, Cham.

Johnson, G.F., 1935. The early history of copper fungicides. Agric. Hist. 9 (2), 67–79.

Joshi, A., Kaur, S., Singh, P., Dharamvir, K., Nayyar, H., Verma, G., 2018. Tracking multi-walled carbon nanotubes inside oat (*Avena sativa* L.) plants and assessing their effect on growth, yield, and mammalian (human) cell viability. Appl. Nanosci. 8 (6), 1399–1414.

Kamiya, Y., 2010. Plant hormones: versatile regulators of plant growth and development. Annu. Rev. Plant Biol. 61 (1).

Kaveh, R., Li, Y.-S., Ranjbar, S., Tehrani, R., Brueck, C.L., Van Aken, B., 2013. Changes in *Arabidopsis thaliana* gene expression in response to silver nanoparticles and silver ions. Environ. Sci. Technol. 47 (18), 10637–10644.

Keller, A.A., Adeleye, A.S., Conway, J.R., Garner, K.L., Zhao, L., Cherr, G.N., Hong, J., Gardea-Torresdey, J.L., Godwin, H.A., Hanna, S., Ji, Z., Kaweeteerawat, C., Lin, S., Lenihan, H.S., Miller, R.J., Nel, A.E., Peralta-Videa, J.R., Walker, S.L., Taylor, A.A., Torres-Duarte, C., Zink, J.I., Zuverza-Mena, N., 2017. Comparative environmental fate and toxicity of copper nanomaterials. NanoImpact 7, 28–40.

Khare, P., Talreja, N., Deva, D., Sharma, A., Verma, N., 2013. Carbon nanofibers containing metal-doped porous carbon beads for environmental remediation applications. Chem. Eng. J. 229, 72–81.

Khodakovskaya, M., Dervishi, E., Mahmood, M., Xu, Y., Li, Z., Watanabe, F., Biris, A.S., 2009. Carbon nanotubes are able to penetrate plant seed coat and dramatically affect seed germination and plant growth. ACS Nano 3 (10), 3221–3227.

Khodakovskaya, M.V., de Silva, K., Biris, A.S., Dervishi, E., Villagarcia, H., 2012. Carbon nanotubes induce growth enhancement of tobacco cells. ACS Nano 6 (3), 2128–2135.

Khodakovskaya, M.V., Kim, B.-S., Kim, J.N., Alimohammadi, M., Dervishi, E., Mustafa, T., Cernigla, C.E., 2013. Carbon nanotubes as plant growth regulators: effects on tomato growth, reproductive system, and soil microbial community. Small 9 (1), 115–123.

Kole, C., Kole, P., Randunu, K.M., Choudhary, P., Podila, R., Ke, P.C., Rao, A.M., Marcus, R.K., 2013. Nanobiotechnology can boost crop production and quality: first evidence from increased plant biomass, fruit yield and phytomedicine content in bitter melon (*Momordica charantia*). BMC Biotechnol. 13 (37), 1472–6750.

Kolmakov, A., Moskovits, M., 2004. Chemical sensing and catalysis by one-dimensional metal-oxide nanostructures. Annu. Rev. Mat. Res. 34 (1), 151–180.

Kumar, D., Talreja, N., 2019. Nickel nanoparticles-doped rhodamine grafted carbon nanofibers as colorimetric probe: naked eye detection and highly sensitive measurement of aqueous Cr3+ and Pb2+. Korean J. Chem. Eng. 36 (1), 126–135.

Kumar, V., Talreja, N., Deva, D., Sankararamakrishnan, N., Sharma, A., Verma, N., 2011. Development of bi-metal doped micro- and nano multi-functional polymeric adsorbents for the removal of fluoride and arsenic(V) from wastewater. Desalination 282, 27–38.

Kumar, R., Ashfaq, M., Verma, N., 2018. Synthesis of novel PVA–starch formulation-supported cu–Zn nanoparticle carrying carbon nanofibers as a nanofertilizer: controlled release of micronutrients. J. Mater. Sci. 53 (10), 7150–7164.

Lahiani, M.H., Chen, J., Irin, F., Puretzky, A.A., Green, M.J., Khodakovskaya, M.V., 2015. Interaction of carbon nanohorns with plants: uptake and biological effects. Carbon 81, 607–619.

Lee, W.M., An, Y.J., Yoon, H., Kweon, H.S., 2008. Toxicity and bioavailability of copper nanoparticles to the terrestrial plants mung bean (*Phaseolus radiatus*) and wheat (*Triticum aestivum*): plant agar test for water-insoluble nanoparticles. Environ. Toxicol. Chem. 27 (9), 1915–1921.

Li, Y., Kim, W., Zhang, Y., Rolandi, M., Wang, D., Dai, H., 2001. Growth of single-walled carbon nanotubes from discrete catalytic nanoparticles of various sizes. J. Phys. Chem. B 105 (46), 11424–11431.

Li, H.J., Lu, W.G., Li, J.J., Bai, X.D., Gu, C.Z., 2005. Multichannel ballistic transport in multiwall carbon nanotubes. Phys. Rev. Lett. 95 (8), 15.

Li, W., Zheng, Y., Zhang, H., Liu, Z., Su, W., Chen, S., Liu, Y., Zhuang, J., Lei, B., 2016. Phytotoxicity, uptake, and translocation of fluorescent carbon dots in mung bean plants. ACS Appl. Mater. Interfaces 8 (31), 19939–19945.

Lin, C., Fugetsu, B., Su, Y., Watari, F., 2009a. Studies on toxicity of multi-walled carbon nanotubes on Arabidopsis T87 suspension cells. J. Hazard. Mater. 170 (2), 578–583.

Lin, S., Reppert, J., Hu, Q., Hudson, J.S., Reid, M.L., Ratnikova, T.A., Rao, A.M., Luo, H., Ke, P.C., 2009b. Uptake, translocation, and transmission of carbon nanomaterials in rice plants. Small 5 (10), 1128–1132.

Linglan, M., Chao, L., Chunxiang, Q., Sitao, Y., Jie, L., Fengqing, G., Fashui, H., 2008. Rubisco activase mRNA expression in spinach: modulation by nanoanatase treatment. Biol. Trace Elem. Res. 122 (2), 168–178.

Liu, Q., Chen, B., Wang, Q., Shi, X., Xiao, Z., Lin, J., Fang, X., 2009. Carbon nanotubes as molecular transporters for walled plant cells. Nano Lett. 9 (3), 1007–1010.

Liu, S., Wei, H., Li, Z., Li, S., Yan, H., He, Y., Tian, Z., 2015. Effects of graphene on germination and seedling morphology in rice. J. Nanosci. Nanotechnol. 15 (4), 2695–2701.

Lombardi, L., Sebastiani, L., 2005. Copper toxicity in *Prunus cerasifera*: growth and antioxidant enzymes responses of in vitro grown plants. Plant Sci. 168 (3), 797–802.

Lombi, E., Nowack, B., Baun, A., McGrath, S.P., 2012. Evidence for effects of manufactured nanomaterials on crops is inconclusive. Proc. Natl. Acad. Sci. 109 (49), E3336.
López-Moreno, M.L., de la Rosa, G., Hernández-Viezcas, J.A., Peralta-Videa, J.R., Gardea-Torresdey, J.L., 2010. X-ray absorption spectroscopy (XAS) corroboration of the uptake and storage of CeO2 nanoparticles and assessment of their differential toxicity in four edible plant species. J. Agric. Food Chem. 58 (6), 3689–3693.
Lou, J.C., Jung, M.J., Yang, H.W., Han, J.Y., Huang, W.H., 2011. Removal of dissolved organic matter (DOM) from raw water by single-walled carbon nanotubes (SWCNTs). J. Environ. Sci. Health A 46 (12), 1357–1365.
Lu, Y., Yang, K., Lin, D., 2014. Transport of surfactant-facilitated multiwalled carbon nanotube suspensions in columns packed with sized soil particles. Environ. Pollut. 192, 36–43.
Lv, J., Christie, P., Zhang, S., 2019. Uptake, translocation, and transformation of metal-based nanoparticles in plants: recent advances and methodological challenges. Environ. Sci. Nano 6 (1), 41–59.
Ma, Q.H., 2008. Genetic engineering of cytokinins and their application to agriculture. Crit. Rev. Biotechnol. 28 (3), 213–232.
Ma, C., White, J.C., Dhankher, O.P., Xing, B., 2015. Metal-based nanotoxicity and detoxification pathways in higher plants. Environ. Sci. Technol. 49 (12), 7109–7122.
Malandrakis, A.A., Kavroulakis, N., Chrysikopoulos, C.V., 2019. Use of copper, silver and zinc nanoparticles against foliar and soil-borne plant pathogens. Sci. Total Environ. 670, 292–299.
Mogharabi, M., Abdollahi, M., Faramarzi, M.A., 2014. Safety concerns to application of graphene compounds in pharmacy and medicine. DARU J. Pharm. Sci. 22 (1), 23.
Mohammad Ashfaq, N.T., Chuahan, D., Srituravanich, W., 2019. Polymeric Nanocomposite-Based Agriculture Delivery System: Emerging Technology for Agriculture. IntechOpen.
Mondal, A., Basu, R., Das, S., Nandy, P., 2011. Beneficial role of carbon nanotubes on mustard plant growth: an agricultural prospect. J. Nanopart. Res. 13 (10), 4519–4528.
Mukherjee, A., Majumdar, S., Servin, A.D., Pagano, L., Dhankher, O.P., White, J.C., 2016. Carbon nanomaterials in agriculture: a critical review. Front. Plant Sci. 7 (172), 1–16.
Munzuroglu, O., Geckil, H., 2002. Effects of metals on seed germination, root elongation, and coleoptile and hypocotyl growth in *Triticum aestivum* and *Cucumis sativus*. Arch. Environ. Contam. Toxicol. 43 (2), 203–213.
Mustafa, S., Khan, H.M., Shukla, I., Shujatullah, F., Shahid, M., Ashfaq, M., Azam, A., 2011. Effect of ZnO nanoparticles on ESBL producing *Escherichia coli* & Klebsiella spp. East. J. Med. 16 (4), 253–257.
Nadiminti, P.P., Dong, Y.D., Sayer, C., Hay, P., Rookes, J.E., Boyd, B.J., Cahill, D.M., 2013. Nanostructured liquid crystalline particles as an alternative delivery vehicle for plant agrochemicals. ACS Appl. Mater. Interfaces 5 (5), 1818–1826.
Nair, R., Mohamed, M.S., Gao, W., Maekawa, T., Yoshida, Y., Ajayan, P.M., Kumar, D.S., 2012. Effect of carbon nanomaterials on the germination and growth of rice plants. J. Nanosci. Nanotechnol. 12 (3), 2212–2220.
Nevius, B.A., Chen, Y.P., Ferry, J.L., Decho, A.W., 2012. Surface-functionalization effects on uptake of fluorescent polystyrene nanoparticles by model biofilms. Ecotoxicology 21 (8), 2205–2213.
Niederberger, M., 2007. Nonaqueous sol–gel routes to metal oxide nanoparticles. Acc. Chem. Res. 40 (9), 793–800.

Omar, R.A., Afreen, S., Talreja, N., Chauhan, D., Ashfaq, M., 2019a. Impact of nanomaterials in plant systems. In: Prasad, R. (Ed.), Plant Nanobionics: Volume 1, Advances in the Understanding of Nanomaterials Research and Applications. Springer International Publishing, Cham.

Omar, R.A., Afreen, S., Talreja, N., Chauhan, D., Ashfaq, M., Srituravanich, W., 2019b. Impact of nanomaterials on the microbial system. In: Prasad, R. (Ed.), Microbial Nanobionics: Volume 1, State-of-the-Art. Springer International Publishing, Cham.

Parise, A., Thakor, H., Zhang, X., 2013. Activity inhibition on municipal activated sludge by single-walled carbon nanotubes. J. Nanopart. Res. 16 (1), 2159.

Peng, J., Xu, W., Teoh, C.L., Han, S., Kim, B., Samanta, A., Er, J.C., Wang, L., Yuan, L., Liu, X., Chang, Y.-T., 2015. High-efficiency in vitro and in vivo detection of Zn2+ by dye-assembled upconversion nanoparticles. J. Am. Chem. Soc. 137 (6), 2336–2342.

Prasad, R., Bhattacharyya, A., Nguyen, Q.D., 2017. Nanotechnology in sustainable agriculture: recent developments, challenges, and perspectives. Front. Microbiol. 8, 1014.

Raffi, M., Mehrwan, S., Bhatti, T.M., Akhter, J.I., Hameed, A., Yawar, W., ul Hasan, M.M., 2010. Investigations into the antibacterial behavior of copper nanoparticles against *Escherichia coli*. Ann. Microbiol. 60 (1), 75–80.

Rajput, V., Minkina, T., Mazarji, M., Shende, S., Sushkova, S., Mandzhieva, S., Burachevskaya, M., Chaplygin, V., Singh, A., Jatav, H., 2020. Accumulation of nanoparticles in the soil-plant systems and their effects on human health. Ann. Agric. Sci. 65 (2), 137–143.

Raliya, R., Franke, C., Chavalmane, S., Nair, R., Reed, N., Biswas, P., 2016. Quantitative understanding of nanoparticle uptake in watermelon plants. Front. Plant Sci. 7, 1288.

Ren, D., Guo, Z., Du, F., Zheng, J., Chen, Y., 2007. A nanohybrid material of SWNTs covalently functionalized with porphyrin for light harvesting antenna: synthesis and photophysical properties. J. Nanosci. Nanotechnol. 7 (4–5), 1539–1545.

Rico, C.M., Majumdar, S., Duarte-Gardea, M., Peralta-Videa, J.R., Gardea-Torresdey, J.L., 2011. Interaction of nanoparticles with edible plants and their possible implications in the food chain. J. Agric. Food Chem. 59 (8), 3485–3498.

Rodrigues, C., de Vandenberghe, L.P.S., de Oliveira, J., Soccol, C.R., 2012. New perspectives of gibberellic acid production: a review. Crit. Rev. Biotechnol. 32 (3), 263–273.

Rui, M., Ma, C., Hao, Y., Guo, J., Rui, Y., Tang, X., Zhao, Q., Fan, X., Zhang, Z., Hou, T., Zhu, S., 2016. Iron oxide nanoparticles as a potential iron fertilizer for peanut (*Arachis hypogaea*). Front. Plant Sci. 7. https://doi.org/10.3389/fpls.2016.00815. Available: http://europepmc.org/abstract/MED/27375665, https://europepmc.org/articles/PMC4899443, https://europepmc.org/articles/PMC4899443?pdf=render [Accessed 2016].

Saddler, G., 2007. Phytobacteriology: principles and practice—by J.D. Janse. Plant Pathol. 56 (1), 198.

Saeedi, M., Eslamifar, M., Khezri, K., Dizaj, S.M., 2019. Applications of nanotechnology in drug delivery to the central nervous system. Biomed. Pharmacother. 111, 666–675.

Samaj, J., Baluska, F., Voigt, B., Schlicht, M., Volkmann, D., Menzel, D., 2004. Endocytosis, actin cytoskeleton, and signaling. Plant Physiol. 135 (3), 1150–1161.

Santner, A., Calderon-Villalobos, L.I.A., Estelle, M., 2009. Plant hormones are versatile chemical regulators of plant growth. Nat. Chem. Biol. 5 (5), 301–307.

Santos, S.M.A., Dinis, A.M., Rodrigues, D.M.F., Peixoto, F., Videira, R.A., Jurado, A.S., 2013. Studies on the toxicity of an aqueous suspension of C60 nanoparticles using a bacterium (*gen. Bacillus*) and an aquatic plant (*Lemna gibba*) as in vitro model systems. Aquat. Toxicol. 142–143, 347–354.

Saraswat, R., Talreja, N., Deva, D., Sankararamakrishnan, N., Sharma, A., Verma, N., 2012. Development of novel in situ nickel-doped, phenolic resin-based micro–nano-activated carbon adsorbents for the removal of vitamin B-12. Chem. Eng. J. 197, 250–260.

Sasidharan, A., Panchakarla, L.S., Chandran, P., Menon, D., Nair, S., Rao, C.N.R., Koyakutty, M., 2011. Differential nano-bio interactions and toxicity effects of pristine versus functionalized graphene. Nanoscale 3 (6), 2461–2464.

Sasidharan, V., Sachan, D., Chauhan, D., Talreja, N., Ashfaq, M., 2021. Three-dimensional (3D) polymer—metal–carbon framework for efficient removal of chemical and biological contaminants. Sci. Rep. 11 (1), 7708.

Serag, M.F., Kaji, N., Tokeshi, M., Baba, Y., 2012. Introducing carbon nanotubes into living walled plant cells through cellulase-induced nanoholes. RSC Adv. 2 (2), 398–400.

Servin, A., Elmer, W., Mukherjee, A., De la Torre-Roche, R., Hamdi, H., White, J.C., Bindraban, P., Dimkpa, C., 2015. A review of the use of engineered nanomaterials to suppress plant disease and enhance crop yield. J. Nanopart. Res. 17 (2), 92.

Shen, C.X., Zhang, Q.F., Li, J., Bi, F.C., Yao, N., 2010. Induction of programmed cell death in Arabidopsis and rice by single-wall carbon nanotubes. Am. J. Bot. 97 (10), 1602–1609.

Shojaei, T.R., Salleh, M.A.M., Tabatabaei, M., Mobli, H., Aghbashlo, M., Rashid, S.A., Tan, T., 2019. Chapter 11—Applications of nanotechnology and carbon nanoparticles in agriculture. In: Rashid, S.A., Raja Othman, R.N.I., Hussein, M.Z. (Eds.), Synthesis, Technology and Applications of Carbon Nanomaterials. Elsevier.

Shrestha, B., Acosta-Martinez, V., Cox, S.B., Green, M.J., Li, S., Cañas-Carrell, J.E., 2013. An evaluation of the impact of multiwalled carbon nanotubes on soil microbial community structure and functioning. J. Hazard. Mater. 261, 188–197.

Shweta, Tripathi, D.K., Singh, S., Singh, S., Dubey, N.K., Chauhan, D.K., 2016. Impact of nanoparticles on photosynthesis: challenges and opportunities. Mater. Focus 5 (5), 405–411.

Singh, S., Ashfaq, M., Singh, R.K., Joshi, H.C., Srivastava, A., Sharma, A., Verma, N., 2013. Preparation of surfactant-mediated silver and copper nanoparticles dispersed in hierarchical carbon micro-nanofibers for antibacterial applications. N. Biotechnol. 30 (6), 656–665.

Smirnova, E., Gusev, A., Zaytseva, O., Sheina, O., Tkachev, A., Kuznetsova, E., Lazareva, E., Onishchenko, G., Feofanov, A., Kirpichnikov, M., 2012. Uptake and accumulation of multiwalled carbon nanotubes change the morphometric and biochemical characteristics of *Onobrychis arenaria* seedlings. Front. Chem. Sci. Eng. 6 (2), 132–138.

Stampoulis, D., Sinha, S.K., White, J.C., 2009. Assay-dependent phytotoxicity of nanoparticles to plants. Environ. Sci. Technol. 43 (24), 9473–9479.

Syu, Y.Y., Hung, J.H., Chen, J.C., Chuang, H.W., 2014. Impacts of size and shape of silver nanoparticles on Arabidopsis plant growth and gene expression. Plant Physiol. Biochem. 83, 57–64.

Talreja, N., Kumar, D., 2018. Engineered Nanoparticles' Toxicity: Environmental Aspects T2—Nanotechnology in Environmental Science T3. Wiley Online Books, pp. 737–758.

Talreja, N., Kumar, D., Verma, N., 2014. Removal of hexavalent chromium from water using Fe-grown carbon nanofibers containing porous carbon microbeads. J. Water Process Eng. 3, 34–45.

Talreja, N., Jung, S., Yen, L.T.H., Kim, T., 2020. Phenol-formaldehyde-resin-based activated carbons with controlled pore size distribution for high-performance supercapacitors. Chem. Eng. J. 379, 122332.

Tan, X.-M., Fugetsu, B., 2007. Multi-walled carbon nanotubes interact with cultured rice cells: evidence of a self-defense response. J. Biomed. Nanotechnol. 3 (3), 285–288.

Tolaymat, T., El Badawy, A., Sequeira, R., Genaidy, A., 2015. A system-of-systems approach as a broad and integrated paradigm for sustainable engineered nanomaterials. Sci. Total Environ. 511, 595–607.

Tripathi, S., Sarkar, S., 2015. Influence of water soluble carbon dots on the growth of wheat plant. Appl. Nanosci. 5 (5), 609–616.

Tripathi, K.M., Tyagi, A., Ashfaq, M., Gupta, R.K., 2016. Temperature dependent, shape variant synthesis of photoluminescent and biocompatible carbon nanostructures from almond husk for applications in dye removal. RSC Adv. 6 (35), 29545–29553.

Upadhyayula, V.K., Deng, S., Mitchell, M.C., Smith, G.B., 2009. Application of carbon nanotube technology for removal of contaminants in drinking water: a review. Sci. Total Environ. 408 (1), 1–13.

Usman, M., Farooq, M., Wakeel, A., Nawaz, A., Cheema, S.A., Rehman, H.u., Ashraf, I., Sanaullah, M., 2020. Nanotechnology in agriculture: current status, challenges and future opportunities. Sci. Total Environ. 721, 137778.

Villagarcia, H., Dervishi, E., de Silva, K., Biris, A.S., Khodakovskaya, M.V., 2012. Surface chemistry of carbon nanotubes impacts the growth and expression of water channel protein in tomato plants. Small 8 (15), 2328–2334.

Vriet, C., Russinova, E., Reuzeau, C., 2013. From squalene to brassinolide: the steroid metabolic and signaling pathways across the plant kingdom. Mol. Plant 6 (6), 1738–1757.

Wang, X., Han, H., Liu, X., Gu, X., Chen, K., Lu, D., 2012a. Multi-walled carbon nanotubes can enhance root elongation of wheat (*Triticum aestivum*) plants. J. Nanopart. Res. 14 (6), 841.

Wang, Z., Xie, X., Zhao, J., Liu, X., Feng, W., White, J.C., Xing, B., 2012b. Xylem- and phloem-based transport of CuO nanoparticles in maize (*Zea mays* L.). Environ. Sci. Technol. 46 (8), 4434–4441.

Wang, Y., Lin, Y., Xu, Y., Yin, Y., Guo, H., Du, W., 2019. Divergence in response of lettuce (var. ramosa Hort.) to copper oxide nanoparticles/microparticles as potential agricultural fertilizer. Environ. Pollut. Bioavail. 31 (1), 80–84.

Yan, S., Zhao, L., Li, H., Zhang, Q., Tan, J., Huang, M., He, S., Li, L., 2013. Single-walled carbon nanotubes selectively influence maize root tissue development accompanied by the change in the related gene expression. J. Hazard. Mater. 247, 110–118.

Yang, F., Hong, F., You, W., Liu, C., Gao, F., Wu, C., Yang, P., 2006. Influence of nano-anatase TiO2 on the nitrogen metabolism of growing spinach. Biol. Trace Elem. Res. 110 (2), 179–190.

Yoon, K.-Y., Hoon Byeon, J., Park, J.-H., Hwang, J., 2007. Susceptibility constants of *Escherichia coli* and *Bacillus subtilis* to silver and copper nanoparticles. Sci. Total Environ. 373 (2–3), 572–575.

Zaytseva, O., Neumann, G., 2016. Carbon nanomaterials: production, impact on plant development, agricultural and environmental applications. Chem. Biol. Technol. Agric. 3 (1), 17.

Zhang, R., Zhang, H., Tu, C., Hu, X., Li, L., Luo, Y., Christie, P., 2015. Phytotoxicity of ZnO nanoparticles and the released Zn(II) ion to corn (*Zea mays* L.) and cucumber (*Cucumis sativus* L.) during germination. Environ. Sci. Pollut. Res. Int. 22 (14), 11109–11117.

Zhang, H., Chen, W., Shen, X., Zhang, M., Yang, Y., White, J.C., Tao, S., Wang, X., 2017. Influence of multi-walled carbon nanotubes and fullerenes on the bioaccumulation and elimination kinetics of phenanthrene in geophagous earthworms (*Metaphire guillelmi)*. Environ. Sci. Nano 4 (9), 1887–1899.

Zhao, L., Sun, Y., Hernandez-Viezcas, J.A., Servin, A.D., Hong, J., Niu, G., Peralta-Videa, J.R., Duarte-Gardea, M., Gardea-Torresdey, J.L., 2013. Influence of CeO2 and ZnO nanoparticles on cucumber physiological markers and bioaccumulation of Ce and Zn: a life cycle study. J. Agric. Food Chem. 61 (49), 11945–11951.

Zhao, L., Lu, L., Wang, A., Zhang, H., Huang, M., Wu, H., Xing, B., Wang, Z., Ji, R., 2020. Nano-biotechnology in agriculture: use of nanomaterials to promote plant growth and stress tolerance. J. Agric. Food Chem. 68 (7), 1935–1947.

Zheng, L., Hong, F., Lu, S., Liu, C., 2005. Effect of nano-TiO2 on strength of naturally aged seeds and growth of spinach. Biol. Trace Elem. Res. 104 (1), 83–91.

Zhu, H., Han, J., Xiao, J.Q., Jin, Y., 2008. Uptake, translocation, and accumulation of manufactured iron oxide nanoparticles by pumpkin plants. J. Environ. Monit. 10 (6), 713–717.

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CHAPTER

16 Applications of copper nanoparticles in plant protection and pollution sensing: Toward promoting sustainable agriculture

Mansi Bakshi and Arun Kumar

Department of Civil Engineering, Indian Institute of Technology Delhi, New Delhi, India

1 Introduction

Nanotechnology is one of the most significant and emerging technologies of the present world. The last two decades have witnessed tremendous growth in nanotechnology and its potential application field has been extending from industrial to day-to-day usage materials. It deals with the manipulation of material properties at the atomic, molecular, and macromolecular scales. These materials which are generated after these manipulations are termed nanomaterials or more specifically engineered nanomaterials (ENMs). Further, these nanomaterials are made of nanoparticles (NPs) or more specifically engineered nanoparticles (ENPs). Nanoparticles are defined as particles having at least one dimension between 1 and 100 nm (US EPA). NPs include both metallic particles like silver, gold, titanium, cerium, zinc, copper, and nonmetallic like carbon nanotubes and fullerenes. The properties exhibited by these NPs are completely different from those possessed by their bulk forms. Because of their nanoscale properties, nanoparticles find potential uses and applications in various domains such as industrial, domestic, environmental, and agriculture. Thus, nano-based materials and structures are rapidly evolving, with their real-world applications projected to bring ground-breaking changes.

One of the most significant contributions of nanotechnology is anticipated to be in the field of agriculture. The agriculture sector faces the great challenge of not only feeding more people but also combating other threats in the form of land degradation, climate change, depleting water resources, pesticide and fertilizer accumulation, and surface runoff (Freibauer et al., 2011; FAO/WHO, 2010, 2013; Parisi et al., 2015). Nanotechnology-based innovations can be seen as viable solutions in enhancing agricultural production while simultaneously minimizing the environmental impact of the agriculture sector. Technological innovations in the field of agriculture can be viewed as one of the most important contributions that nanotechnology could make

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for achieving the sustainable development goals of zero hunger, conservation of water and land resources, and promoting sustainable agricultural practices (Ghormade et al., 2011; Chen and Yada, 2011; Diallo et al., 2013; de Oliveira et al., 2014).

Worldwide, around 2 million metric tons of pesticides are used to control pests and pathogens, roughly 90% of which are lost to the air, soil, or water bodies during or after applications (Stephenson et al., 2001; Ghormade et al., 2011). This also leads to their high residual concentration and accumulation in environmental compartments of soil and water, leading to serious consequences for their physical properties as well as micro- and macrofauna. Further, reckless, and nontargeted usage of pesticides increases resistance to pests and pathogens. Nanomaterials exhibit several useful properties needed for nanopesticides formulations. These include stiffness, permeability, thermal stability, solubility, crystallinity, and biodegradability (Bouwmeester et al., 2009; Khot et al., 2012). Nanomaterials-based pesticides or more specifically nanopesticides include either small engineered structures exhibiting pesticidal properties or small particles of active pesticidal ingredients (Bouwmeester et al., 2009; Ghormade et al., 2011; de Oliveira et al., 2014; Campos et al., 2019). These nanopesticides are then delivered to the plants through various techniques, such as nanoemulsions, nanoencapsulation, or as nanocontainers or nanocages (Bouwmeester et al., 2009; Khot et al., 2012; Nuruzzaman et al., 2019). The case of large-scale fertilizer application is similar to that of pesticides, most of which are lost as runoff, and thereby remain unavailable to plants. Similarly, excessive and indiscriminate fertilizer usage leads to their accumulation in terrestrial and aquatic ecosystems (Tilman et al., 2002; Heffer and Prud'homme, 2016). Nanotechnology exhibits the potential for developing slow-release fertilizers that release specific nutrient solution required by an individual crop according to its need.

NP-based agrochemical formulations have shown the promising potential of controlled and efficient delivery of pesticides and fertilizers. This is aimed toward a slow and sufficient amount of agrochemicals for obtaining the fullest biological efficacy while minimizing the environmental impacts (Tsuji, 2001; Wilson et al., 2008). Compared to their conventional forms, these NP-based agrochemical formulations exhibit higher surface area, surface tension, solubility, mobility, and lower toxicity (Sasson et al., 2007; Adisa et al., 2019). Their high surface tension holds the plant material more strongly while smaller particle size induces systemic activity (Yan et al., 2005; Siddiqui et al., 2015; Rasool et al., 2019). These nanoformulations can also be used for the controlled release of important micronutrients like manganese, copper, iron, zinc, boron, chlorine, and molybdenum. This, in turn, could lead to optimal plant growth while also preventing unnecessary wastage and higher intake by plants. Furthermore, these micronutrients could also be provided to the plants through foliar applications by using nanoformulations in crop sprays (Ghormade et al., 2011; Kah et al., 2019).

In the agriculture sector, Cu-NPs have gained wide attention due to their multiple applications. Copper (Cu) being an essential micronutrient for crop growth, the use of Cu-NPs containing for improvement of crop yield and plant protection is being increasingly considered. Further, Cu-NPs containing agrochemicals such as pesticides

and fungicides are being widely considered as an alternative to their conventional forms. Also, the well-established antimicrobial activity of conventional copper (Cu), which intensifies at the nanoscale is being investigated for developing nanopesticides that can be used in less quantity while providing maximum action against pests and pathogens. Cu-NPs can thus serve a great role in protecting crops against pests and diseases due to their known multifaceted action against several microbes.

This book chapter aims to review the applications of copper nanoparticles (Cu-NPs) with respect to crop protection and pollution sensing. Firstly, the chapter explores their use in agrochemicals like fungicides and pesticides for controlling plant diseases focusing on their mode of action on plant pathogens. Further, we review their role and application in nanosensors for the detection of pesticides and other pollutants. Lastly, we explore how the use of nano-based innovations can improve agricultural productivity in a sustainable manner to ensure higher food production, thereby contributing toward food security.

2 Copper nanoparticles: Applications for promoting sustainable agriculture

Copper (Cu) is a widely distributed and highly essential micronutrient that plays a vital role in the functioning of major plant physiological processes, such as photosynthesis, enzymatic processes, carbohydrates, cell wall, and protein metabolism, and mitochondrial respiration needed by plants for their growth, development, and functioning (Krämer and Clemens, 2005; Kabata-Pendias, 2010; DalCorso et al., 2014; Gabal et al., 2018). It exhibits a key role in chlorophyll formation by affecting electron transportation in photosystem I (PSI) (Yruela, 2009). It is also involved in the activation of the lignin synthesis enzyme and escalating color formation in flowers and vegetables. It is required in combating oxidative stress and cellular task such as cell wall synthesis (Hänsch and Mendel, 2009). Both Cu deficiency and excessive Cu concentration can alter the process of photosynthesis, chloroplast structure, and thylakoid membrane composition. High levels of Cu in the growing medium can burn root tips thereby restricting root growth, reducing plant biomass, reduce branching and inducing chlorosis, and eventually declining plant growth (Zhao et al., 2010; Rehman et al., 2019). It can cause inhibition of photosystem II (PSII) which is more sensitive to Cu toxicity than photosystem I (PSI). Often, due to high levels of Cu competing with elements such as iron (Fe), molybdenum (Mo), or zinc (Zn), the plant may exhibit deficiency symptoms of these nutrients. Furthermore, its excess presence in plants can induce oxidative stress leading to antioxidant responses by the plant (Quartacci et al., 2001).

At the nanoscale also, copper has been gaining wide popularity due to its diverse characteristics and multipurpose applications. Copper nanoparticles (Cu-NPs), copper oxide nanoparticles (CuO-NPs), and other copper-based nanomaterials are increasingly being used in nanoformulations and agro-chemicals for efficient delivery and controlled release of pesticides and fertilizers (Keller et al., 2017).

Their antimicrobial activity as antifungal and antibacterial agents is utilized for preventing plant diseases while also promoting plant growth. Their use in nanosensors for the detection of pesticides and, toxins, and other chemical pollutants is an efficient way to prevent environmental pollution from persistent chemicals in soil. The various applications Cu-NPs for enhancing agricultural productivity include nanotechnology-enabled delivery of chemicals and nutraceuticals, applications in food production and packaging; water and wastewater treatment, bio-sensing systems for environmental monitoring, detection of persistent pesticides, and use in soil remediation. This book chapter explores the application of antimicrobial and pesticide properties of Cu-NPs for plant protection and pathogen control. It also discusses their role in pollution management through use in nanosensors (Fig. 1).

2.1 Antimicrobial activity of copper nanoparticles: Role in plant protection

Every year several tons of food crops are destroyed by plant disease-causing bacteria and fungus, causing huge economic losses to agriculture (Pham et al., 2019). Copper nanoparticles (Cu-NPs) have attracted a great deal of attention in the field of plant protection due to their broad-spectrum antimicrobial activity. Exhibiting great affinity toward surface carboxyl group, Cu-NPs can strongly bind to microbial cell walls, release Cu ions, and induce membrane leakage (Ingle et al., 2014). They are also responsible for the generation of reactive oxygen species (ROS), disruption of cellular metabolic pathways, oxidative stress development, loss of enzymatic activity, protein dysfunction, alteration of membrane integrity, and cell death (Mekahlia and Bouzid, 2009; Raffi et al., 2010; Lemire et al., 2013; Wang et al., 2017; Arjunan et al., 2017).

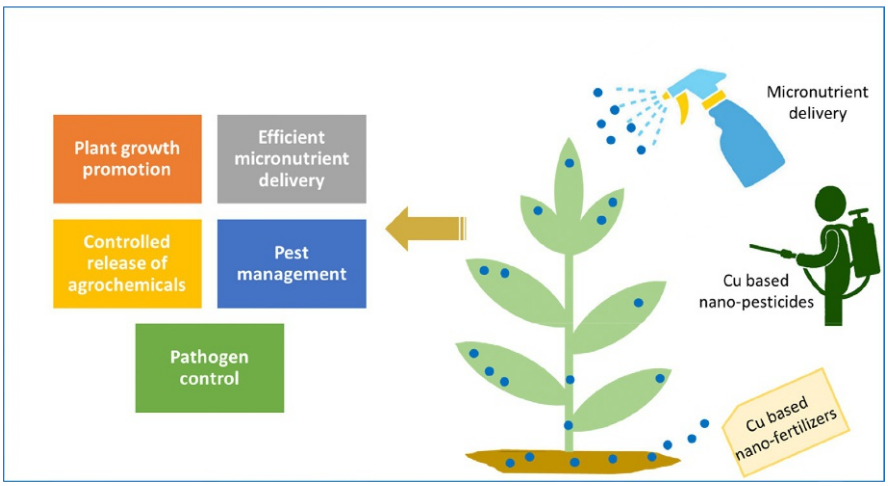

FIG. 1

Applications of copper nanoparticles for sustainable agriculture.

Since earlier days, copper (Cu) has been used in agriculture as a Bordeaux mixture, a well-known fungicide composed of copper sulfate and calcium hydroxide ($CuSO_4 \cdot 5H_2O + Ca(OH)_2$) (Vogelweith and Thiéry, 2018). However, Cu-NPs exhibit the great advantage of their small size compared to their conventional forms used in agriculture. The small size of Cu-NPs facilitates their easy absorption by the plants and easy penetration in cell membranes, even at low doses of application (Radad et al., 2012; Ameh and Sayes, 2019; Rajput et al., 2020). Additionally, the low cost of Cu-NPs makes them a more cost-effective and popular choice compared to other equally efficient but far expensive nanoparticles, such as gold (Au-NPs) and silver (Ag-NPs) (Ingle et al., 2014; Rai et al., 2018).

In bacteria, their antimicrobial activity is proposedly associated with damage to the bacterial cell wall and membrane leakage. Attack of oxy radicals on the outer membrane of the cell or on RNA, DNA, or lipids can ultimately lead to bacterial cell death. Cu-NPs adhesion on the bacterial cell surface depends on the surface roughness and electrostatic interactions along with other factors, such as chemical composition, and hydrophobicity (Tiwari et al., 2016). Due to their single peptidoglycan layer, Gram-negative bacteria are more sensitive to the activity of Cu-NPs compared to Gram-positive strains (Rajeshkumar et al., 2019). In fungi, Cu-NPs are reported to cause changes in the morphology, structure, and function of fungal mycelium. Furthermore, in cells of fungi, Cu-NPs can induce oxidative stress, cause cell membrane damage, impact the process of DNA replication and protein synthesis, and cause cell death (Pariona et al., 2019; Mali et al., 2020).

Several research groups have synthesized Cu-NPs through different methods and investigated their mode of action against bacteria and fungi-causing diseases in plant (Table 1). Cu-NPs have been synthesized by either chemical methods or green synthesis methods (Ingle et al., 2014; Shende et al., 2015; Viet et al., 2016; Pariona et al., 2019; Mali et al., 2020). A green synthesis method involves the use of one or more plant part extract, such as extract of leaf, fruit, or flower for synthesizing Cu-NPs. Chemical methods involve the use of stabilizers, reducing agents, dispersants, and capping agents for synthesizing cost-effective and inexpensive Cu-NPs. The green synthesis route is usually considered safer, eco-friendly, and cost-effective than the chemical route as it is free of toxic chemicals and does not create toxic residual issues.

Javadhesari et al. (2019) synthesized CuO-NPs through a mechanochemical method using two different Cu-containing precursors, namely, $CuSO_4 \cdot 5H_2O$ and $CuCl_2 \cdot 2H_2O$. Their antibacterial activity was tested against *Escherichia coli* and *Staphylococcus aureus*. Cu-NPs synthesized through this method showed a growth reduction of ≈ 99.8% in both bacteria. The synthesized CuO-NPs had a more antibacterial effect against *Staphylococcus aureus* rather than against *Escherichia coli*. The group reported higher inhibitory properties of CuO-NPs against bacteria when prepared by this method compared to other chemical methods. Saharan et al. (2013) prepared Cu-chitosan nanoparticles by ionic gelation method involving ionic crosslinking between chitosan and tripolyphosphate (TPP). Their antifungal activity was tested against three fungi *Alternaria alternata*, *Macrophomina phaseolina*, and

Table 1 Copper nanoparticle synthesized through green and chemical methods and their antimicrobial activity.

NP type	Targeted pathogen	Pathogen species	Synthesis method	Process of synthesis	Remarks	References
Cu-NPs	Bacteria and fungi	*E. coli*, *P. acne*, *K. pneumoniae*, *S. typhi*, *P. aeruginosa*; *F. oxysporum* , *F. graminearum*, *F. culmorum*	Green synthesis	Fruit juice extract of *Citrus medica* Linn.	Cu-NPs demonstrated significant inhibitory activity; cost-effective, nontoxic, and eco-friendly method	Shende et al. (2015)
CuO-NPs	Bacteria	*E. coli*, *S. aureus*	Green synthesis	Leaf extract of *Cedrus deodara*	Simple, facile, and eco-friendly method; CuO-NPs exhibited maximum zone of inhibition compared to available drugs	Ramzan et al. (2021)
Cu-NPs	Bacteria	*E. coli*, *Streptococcus* sp., *Rhizobium* sp., *Klebsiella* sp.	Green synthesis	Leaf extract of *Cissus arnotiana*	Gram-negative strains were more sensitive to Cu-NPs activity than Gram-positive strains	Rajeshkumar et al. (2019)
Cu-NPs	Bacteria and fungi	*E. coli*, *Streptococcus* sp., *Klebsiella* sp., *Rhizobacterium*; *Aspergillus flavus*, *A. fumigates*, *F. oxysporum*	Green synthesis	Seed extract of *Persea americana*	Nontoxic, cost-effective; displayed effective antibacterial and antifungal activity	Rajeshkumar and Rinitha (2018)
Cu-NPs	Bacteria	*Enterococcus faecalis*, *Proteus mirabilis*, *Klebsiella pneumonia*, *Staphylococcus aureus*	Green synthesis	Flower extract of *Azadirachta indica*	Cu-NPs exhibited excellent antimicrobial activity with maximum activity against *Proteus mirabilis*; simple, cost-effective, and reproducible method	Gopalakrishnan and Muniraj (2021)
Cu-NPs	Fungi	*F. oxysporum*	Green synthesis	Leaf extract of *Celastrus paniculatus*	Inhibition in mycelial growth of the fungus was concentration-dependent	Mali et al. (2020)

Cu-NPs	Fungi	*F. solani*, *Neofusicoccum* sp., *F. oxysporum*	Green synthesis	Ascorbic acid as reducing agent and sodium citrate as a dispersant and protecting agent	High antifungal efficacy against the three species; cell walls damage and hyphae destruction; adequate particle size and the coating used in the synthesis process greatly contributed to the antifungal activity	Pariona et al. (2019)
Cu-NPs	Fungi	*Fusarium oxysporum*	Green synthesis	Ascorbic acid as reducing agent and sodium citrate as a dispersant and protecting agent	Cu-NPs effectively reduced wilt disease caused by *Fusarium*; Promoted growth of tomato plants and increased chlorophyll content	Lopez-Lima et al. (2021)
Cu-NPs	Fungi	*F. oxysporum*, *Phytophthora capsici*	Green chemical reduction method	Ascorbic acid as both reducing agent and antioxidant agent and polyvinylpyrrolidone (PVP) as a stabilizer	Growth inhibition increased with increasing Cu-NPs concentration. Stronger antifungal activity for *P. capsici* compared to *F. oxysporum*	Pham et al. (2019)
Cu-NPs	Fungi	*Fusarium* sp.	Chemical reduction method	Cetyltrimethylammonium bromide (CTAB) as a reductive agent	Concentration-dependent increase in inhibition efficiency of Cu-NPs	Viet et al. (2016)
Cu-chitosan NPs	Fungi	*Alternaria alternata*, *Macrophomina phaseolina*, *Rhizoctonia solani*	Ionic gelation method	Ionic cross-linking between chitosan and tripolyphosphate (TPP)	Maximum inhibition rate for spore germination of *A. alternata*. Inhibition of mycelial growth in *M. phaseolina*	Saharan et al. (2013)
CuO-NPs	Bacteria	*E. coli*, *S. aureus*	Mechanochemical method	Two different Cu containing precursors along with NaOH and NaCl as a diluent phase	NPs had least tendency for agglomeration; the ultrasmall size of the synthesized NPs reduced bacterial growth by ≈ 99.8%; *S. aureus* was more susceptible to their antibacterial activity	Javadhesari et al. (2019)

Rhizoctonia solani. Maximum activity was observed in *A. alternata* whose growth was inhibited by these Cu-chitosan nanoparticles by 89.5% and spore germination rate by 87.4%. They also inhibited the mycelial growth of *M. phaseolina* by 87.6% at the highest concentration.

Pham et al. (2019) prepared Cu-NPs through a method involving green chemical reduction. They used ascorbic acid (ABA) as both reducing as well as an antioxidant agent and using polyvinylpyrrolidone (PVP) as a stabilizer. Their antifungal activity was tested against two plant pathogenic fungi, i.e., *F. oxysporum* and *P. capsici*. Cu-NPs at the smallest particle size of 53 nm exhibited the highest antifungal activities compared with other size samples. Further, the antifungal activity was found to be stronger against *P. capsici* as compared to *F. oxysporum.* The growth inhibition was highest at increasing concentration and decreasing particle size of Cu-NPs. Cu-NPs were synthesized for a short reactive time by chemical reduction method using cetyltrimethylammonium bromide (CTAB) as a reducing agent (Viet et al., 2016). Their antifungal activity was tested against *Fusarium* sp. isolated from tomato and dragon fruit plants. Cu-NPs prevented the formation of fungal colonies and inhibited the fungal growth by 93.98% at a concentration of 450 ppm. The diameter of the fungal colony did not increase and this inhibition was concentration dependent.

Pariona et al. (2019) prepared Cu-NPs-based fungicide through the green synthesis route and investigated its antifungal activity against *Fusarium solani*, *Neofusicoccum* sp., and *Fusarium oxysporum*. They observed morphological changes in the mycelium of the fungi such as alterations in color, form, texture, and density induced by Cu-NPs. Dissolved copper ions from Cu-NPs induced reactive oxygen species (ROS) and oxidized the major cell wall components of the fungus, such as glucan and chitin, leading to disintegration of the cell wall. However, Cu-NPs impact varied in all the three fungal species with *Neofusicoccum* sp. exhibiting the highest level of tolerance to their activity. Similarly, all three species exhibited different levels of cell wall damage and oxidative stress-induced damage. This was due to the varying compositions of fungal cell walls in all three fungal species leading to different responses and different oxidative stress mechanisms for each fungus species. Cu-NPs were prepared from the extract of *Cedrus deodara*, a plant well-known for its antibacterial activity due to the presence of alkaloids. The Cu-NPs showed inhibitory activity against *E. coli* and *S. aureus* with maximum inhibition against *E. coli* at a concentration of 150 mg/mL (Ramzan et al., 2021). This approach was facile, nontoxic, low-cost, and very safe.

Rajeshkumar and Rinitha (2018) synthesized Cu-NPs through an eco-friendly green route by using seed extract of *Persea americana* (avocado). They tested its antibacterial activity against *E. coli*, *Streptococcus* sp., *Klebsiella* sp., and *Rhizobacterium* and antifungal activity against *Aspergillus flavus*, *Aspergillus fumigates*, and *Fusarium oxysporum*. The maximum zone of inhibition was obtained in Gram-positive bacteria *Streptococcus* while the lowest zone of inhibition was observed in *Rhizobacterium*. In another study, Rajeshkumar et al. (2019) synthesized Cu-NPs using the medicinal plant *Cissus arnotiana* and evaluated their antibacterial activity against two Gram-negative bacteria *E. coli*, and *Klebsiella* sp. and two

Gram-positive bacteria *Streptococcus* sp., and *Rhizobium* sp. The highest Cu-NPs activity was observed for Gram-negative strains chiefly *E. coli*. This was attributed to the thin peptidoglycan layer found in Gram-negative bacteria which was particularly sensitive to the electrostatic interactions occurring between the bacterial cell wall and Cu-NPs surfaces. Gopalakrishnan and Muniraj (2021) synthesized Cu-NPs using the flower broth obtained from *Azadirachta indica* (neem). The Cu-NPs exhibited excellent antimicrobial activity against *Enterococcus faecalis*, *Proteus mirabilis*, *Klebsiella pneumonia*, and *Staphylococcus aureus*, with maximum activity reported against *Proteus mirabilis*.

Cu-NPs were synthesized using fruit juice of *Citrus medica* (citron) and their antimicrobial activity was tested against five species of bacteria namely *Escherichia coli*, *Propionibacterium acne*, *Klebsiella pneumoniae*, *Salmonella typhi*, and *Pseudomonas aeruginosa* and three plant pathogenic fungi *Fusarium oxysporum*, *F. graminearum*, and *F. culmorum* (Shende et al., 2015). In bacteria, *E. coli* was highly susceptible to the antimicrobial activity of Cu-NPs while in fungi *F. culmorum* was found to be most sensitive. The antibacterial sensitivity followed the order *E. coli* > *K. pneumoniae* > *P. aeruginosa* > *P. acnes* > *S. typhi*. Among the fungi, the sensitivity order was *F. culmorum* > *F. oxysporum* > *F. graminearum*. Mali et al. (2020) synthesized Cu-NPs following the green route and using the ayurvedic medicinal plant *Celastrus paniculatus*. Their antifungal activity was tested against phytopathogenic fungi *Fusarium oxysporum.* The fungi exhibited mycelial growth inhibition in a concentration-dependent manner.

The effectiveness of green synthesized Cu-NPs for the treatment wilt causing fungus *Fusarium oxysporum* f.sp. *lycopersici* (FOL) was studied by Lopez-Lima et al. (2021). Simultaneously, the group also investigated their plant growth-promoting role in tomato plants. Cu-NPs reduced the growth of the fungus by inducing changes in mycelium such as shrinking and surface roughness, development of tumor-like vesicles, and deformation of hyphae. Cu-NP treatment significantly reduced the incidence of the wilt disease by 68% and severity by 66.5%. Further, Cu-NPs treatment increased the tomato plant's growth, significantly improving their chlorophyll content index (CCI) from 19.3% to 28.6% in a concentration-dependent manner. This is because, through nanoformulations, Cu-NPs effectively delivered copper as a micronutrient to the plants leading to its growth, while in the case of commercial fungicide containing copper hydroxide, higher and uncontrolled uptake of copper ions occurs hindering the healthy development of plants. This study suggested that copper nanoparticles can serve as fungicides as well as plant growth promoters, especially in soils facing copper deficiency.

2.2 Copper-based nanosensors for pollutant detection

Sensors incorporated with nanomaterials are called nanosensors. These nanosensors have found several applications in the food processing unit and in the field of environmental monitoring. Nanosensors are currently used in food manufacturing industries for the detection of pathogens, toxins, and chemicals in food, to stop the

spreading in supply chains. Detection and removal of contaminated samples at the early and initial stages could help prevent foodborne illness and also help prevent wide-scale food spoilage. In the agriculture sector, they are useful for real-time detection of pollutants, such as pesticides and their residues, chemicals, and various inorganic pollutants contributing toward an overall increased agricultural productivity by preventing damage. Prevention of this damage and loss can increase food and agricultural production, ultimately contributing to food security.

Even though conventional methods of pollutant detection and sensing, such as gas chromatography (GC), and high-performance liquid chromatography (HPLC) exhibit great efficiency for pollutant detection they employ slow, expensive, manual, and often time-consuming methods. Further, they are unsuited for on-site detection or field analysis of samples. On the other hand, nanosensors offer higher sensitivity, great selectivity, quick responses, lower detection limits, and small sizes (Liu et al., 2008; Ghormade et al., 2011) Thus, nanosensors can be used as a rapid diagnostic tool for the detection of pollutants, toxins, and harmful chemicals in soil, water, and agriculture products (Fig. 2). Table 2 compiles a list of Cu-NPs-based nanosensors for the detection of pesticides and other environmental pollutants.

Fabrication with Cu-NPs is especially useful in sensors employing enzymes, such as acetylcholinesterase (AChE)-based biosensors. This is because in these biosensors instability and poor conductivity of enzyme molecules lead to their poor performance. But the use of nanomaterials greatly improves their conductivity, sensitivity, stability, and performance (Songa and Okonkwo, 2016; Kaushal et al., 2020; Kannan and Guo, 2020; Bharti et al., 2021).

Bao et al. (2019) developed acetylcholinesterase (AChE)-based electrochemical biosensor for the detection of Malathion, an organophosphate pesticide (OP). They constructed it by immobilizing AChE and chitosan on three-dimensional graphene-copper oxide nanoflowers nanocomposites (3DG-CuO-NFs). The network-like structure of the 3DG-CuO-NFs nanocomposites increased the effective specific surface area and provided a favorable microenvironment for AChE loading leading to an overall excellent performance toward Malathion sensitivity. The sensor exhibited

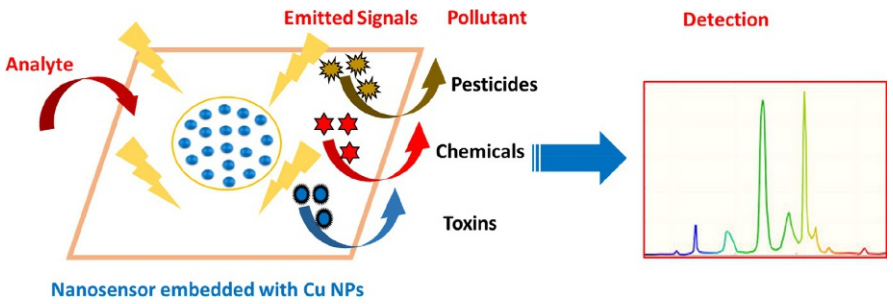

FIG. 2

Use of copper nanoparticles (Cu-NPs) in sensors for detection of chemicals, toxins, and pollutants.

Table 2 Copper nanoparticle-based sensors for detection of various pollutants.

NP type	Synthesis method	Targeted pollutant	Pollutant type	Remarks	References
Amino acid-synthesized CuO nanostructures	Low-temperature hydrothermal growth method	Malathion	Organophosphate pesticide	Detecting extremely low concentration of malathion, field-level applicability	Soomro et al. (2016)
Copper nanoparticles embedded in chitosan (Cu-NPs-CH)	In situ formation of nanoparticles into CH polymeric matrices	Nitroaniline	Nitrophenols	Simultaneous detection and reduction of 4-nitroaniline	Bakhsh et al. (2019)
CuO nanostructures grown over indium tin oxide (ITO) based electrode	Low-temperature hydrothermal route using pimelic acid as a growth template	Chlorpyrifos, fenthion, and methyl parathion	Organophosphorus pesticides	High sensitivity to organophosphorus pesticides and signal reproducibility, successful recoveries	Tunesi et al. (2018)
CuO-NPs-based sensing platform	CuO-NPs drop-casted onto the SPCE (screen printed counterelectrodes)	Catechol, phenol and 4-dichlorophenol; 3-(3,4-dichlorophenyl)-1,1-dimethylurea (DCMU)	Phenolic compounds and pesticide	Different detection mode for each type of pollutant, high reproducibility, and sensitivity, detection of phenolic compounds below the threshold values	Pino et al. (2016)
Acetylcholinesterase-based three-dimensional graphene-copper oxide nanoflowers nanocomposites (AChE-CS/3DG-CuO-NFs/GCE)	AChE and chitosan immobilized on 3DG-CuO NFs nanocomposites	Malathion	Organophosphate pesticides	3DG-CuO NFs nanocomposites increased the effective specific surface area leading to improved performance, good selectivity, ideal stability, satisfactory recoveries	Bao et al. (2019)
CuO nanoparticles biosynthesized by fruit extract of *Fortunella japonica*	Fruit extract of *Fortunella japonica* was used as a reducing and stabilizing agent	4-Nitrophenol	Phenolic compound	Good reproducibility and high selectivity, catalytic reduction of 4-nitrophenol (4-NP) to 4-aminophenol (4-AP)	Singh et al. (2017)

Continued

Table 2 Copper nanoparticle-based sensors for detection of various pollutants—cont'd

NP type	Synthesis method	Targeted pollutant	Pollutant type	Remarks	References
As-prepared CuO nanostructures	CuO nanocrystals with the leaf-like, dumbbell-like, and flower-like nanostructures formed through different additives introduction	4-Nitrophenol	Phenolic compound	CuO nanostructures with different morphologies presented different catalytic activities	Khan et al. (2019)
CuO nanostructures with leaf-like, dumbbell-like, and flower-like shapes	Shape controlled synthesis through a simple reflux method.	4-Nitrophenol	Phenolic compound	Correlation between properties and shapes of nanomaterials. CuO nanostructures with different morphologies presented different catalytic activities. The catalytic activity gradually decreased from leaf-like > flower-like > dumbbell-like, attributed to surface area reductions and active site number	Che et al. (2015)
Copper nanoparticles decorated nanoporous polyaniline-zeolite (Cu-NPs-PANI-nano-ZSM-5) nanocomposite	Dispersed PANI-nano-ZSM-5 was added to colloidal Cu-NPs solution	Hydrazine and phenylhydrazine	Inorganic environmental pollutant	The sensor exhibited remarkably high activity and sensitivity when compared to individual constituents	Kaur et al. (2016)

a large linear range, high sensitivity, great reproducibility, and stability toward Malathion. These results indicate that the proposed sensor could also be used for the on-site detection of organophosphorus pesticides. Bakhsh et al. (2019) designed an electrochemical sensor by coating copper nanoparticles embedded chitosan (Cu-NPs-CH) on a glassy carbon electrode. This sensor was used for simultaneous tracing and complete reduction of 4-nitroaniline (4-NA). These results suggest that Cu-NPs embedded CH exhibits good catalytic activity for 4-NA reduction compared to those using cobalt nanoparticles (Co-NPs) and silver nanoparticles (Ag-NPs). The developed Cu-NPs-based nanosensor exhibited high catalytic performance as well as ease of separation. The reduction process for 4-NA and 4-NP was completed within a short time showing its promising potential for the detection and removal of nitroaromatic pollutants.

Che et al. (2015) synthesized CuO nanostructures with various shapes and sizes such as leaf-like, dumbbell-like, and flower-like structures through the use of different additives. Their activity was tested for the reduction of 4-nitrophenol. The catalytic activity followed the order gradually leaf-like > flower-like > dumbbell-like structures. This was attributed to the shape and surface area of the structures and the activity site number on the surface of CuO-NPs.

An electrochemical sensor constituting copper nanoparticles decorated polyaniline-nanocrystalline zeolite organic-inorganic hybrid material (Cu-NPs-PANI-Nano-ZSM-5) was synthesized by Kaur et al. (2016). It was used for the detection of environmental pollutants hydrazine (HZ) and phenylhydrazine (PhZ). The sensor exhibited high electrocatalytic activity, stability, sensitivity, and selectivity. The silanol groups present in Nano-ZSM-5 and the –NH group present in polyaniline interacted with the amine group of both HZ and PhZ due to hydrogen bonding. The sensor was employed for the detection of these pollutants in real samples from contaminated water bodies. The sensor was found to be reliable and sensitive with a recovery value in the range of 99%–101%.

Tunesi et al. (2018) developed an electrode-based sensor by growing CuO nanostructures in situ over an indium tin oxide (ITO) substrate. It was used for the detection of three organophosphorus pesticides chlorpyrifos, fenthion, and methyl parathion in real vegetable samples of cabbage and spinach. The sensor exhibited good inhibition signal sensitivity and repeatability. Maximum signal inhibition was achieved in the case of chlorpyrifos followed by fenthion and methyl parathion. The developed sensor was successful in detecting chlorpyrifos, fenthion, and methyl parathion even at a very low concentration range.

Copper nanostructures were synthesized by Soomro et al. (2016) using a hydrothermal growth method that utilized amino acids such as glycine, serine, threonine, and histidine. These green amino acids were used as bio-compatible templates. While all the as-synthesized sensors were sensitive toward Malathion, the glycine-based nanostructures, in particular, exhibited the greatest sensitivity. The developed sensor demonstrated high reproducibility, stability, and strong antiinterference capability in the presence of co-existing pesticides such as lindane, carbendazim, and trichlorfon. The developed sensor showed sensitivity toward

Malathion detection even at a very low concentration of the pesticides, thereby making its field applicability highly feasible.

Pino et al. (2016) developed a copper oxide nanoparticles (CuO-NPs)-based sensing system for the detection of three phenolic compounds namely catechol, phenol, 4-chlorophenol, and pesticide 1-dimethylurea (DCMU). The sensing platform showed great sensitivity toward phenolic compounds with the highest sensitivity toward catechol and lowest toward phenol. The difference in sensitivity was due to different affinities of these phenolic compounds toward forming complexes with the CuO NPs. The sensor exhibited high reproducibility and sensitivity and great analytical performance making it a promising device for environmental monitoring. Khan et al. (2019) synthesized Cu-NPs loaded chitosan-graphene oxide (GO) nanocomposite fibers (CH + GO) that were prepared for the detection and catalytic reduction of 4-nitrophenol (4-NP). The developed Cu@CH + GO nanosensor was stable, reusable with high sensitivity, and great catalytic reduction capability for 4-NP in water samples.

In another study, Singh et al. (2017) developed an electrochemical sensing system by synthesizing CuO-NPs from fruit extract of *Fortunella japonica*. These biosynthesized CuO-NPs were then dropped cast on the screen-printed electrode (SPE) and used for sensing, detection, and remediation of 4-nitro phenol (4-NP). The synthesis of CuO-NPs is achieved using fruit extract of plant *Fortunella japonica* as a reducing and stabilizing agent. CuO-NPs showed good reproducibility, high selectivity with great catalytic activity, and successfully degraded 4-NP to 4-aminophenol (4-AP) in the presence of NaBH4. The results are very promising for 4-NP determination in real samples. The small size of the SPE/CuONPs sensor can support the fabrication of a miniaturized device that can be easily used in fields or on-site for the environmental monitoring and remediation of 4-NP.

3 Nano-based technology for achieving sustainable agriculture: The way forward

The world population is rapidly rising and estimated to reach ~ 9.6 billion (between 8.3 and 10.9 billion) by 2050 which would require an approximate 70% increase in food production (Prosekov and Ivanova, 2018; Tilman et al., 2011). The agriculture sector faces the great challenge of feeding the burgeoning human pollution by producing more food with lesser input costs, on an already shrinking and degrading land. Further, in the current agricultural scenario, most of the food production systems are unsustainable and compromise the ability of the Earth to produce food in the future. Today's food production systems are highly unsustainable and compromise the Earth's capacity to produce food in the future. This paradox makes the global food production scenario in the present as well as in the future highly critical, thus, making future global food security even more uncertain. The agricultural sector faces the global challenges of climate change, urbanization while causing environmental issues such as runoff and accumulation of heavy metals, pesticides, and fertilizers in

the environmental compartments. According to the reports by experts of the Standing Committee on Agricultural Research (SCAR), food production is exceeding or very close to exceeding environmental limits (Mathijs, 2012). Land-use change and subsequent land degradation, and the dependence on fossil fuels, contribute to about one-fourth of greenhouse gas emissions. The agricultural sector along with fisheries is considered as the major driver of biodiversity loss. Reckless use of persistent pesticides and heavy metals in fertilizers has seriously contaminated groundwater and soil at various places posing great social, economic, environmental, and health risks to humans and other species. Soil, being an indispensable medium for food production, is a great resource that has been severely contaminated, primarily due to unsustainable agricultural activities. Restoration of this contaminated soil is a major sustainable development goal set by the United Nations development program for 2030. Therefore, the challenge that lies before us is that how we can feed the burgeoning human population through food production with lesser input costs and on an already shrinking and degrading land, sustainably without harming the environment. Thus, the need of the hour is that we provide such a solution to this great challenge that not only fulfills the food demand of the ever-growing human population but also minimizes the hazards posed by processes involved in food production and agriculture.

Therefore, we need viable solutions to meet these challenges and make the agriculture sector more sustainable. This includes the sustainable transformation of agriculture to

(i) increase food production,
(ii) minimize the ecological footprints of the agriculture sector,
(iii) prevent reckless use of agrochemicals,
(iv) prevent misuse of water resources,
(v) minimizing hazards in the form of chemical pollutants, and their residues,
(vi) reduce emissions and runoffs from agricultural fields,
(vii) reduce agricultural wastage, and
(viii) prevent land and soil degradation due to agricultural activities.

For making agroecosystems more sustainable, we need scientific tools along with social and economic reforms. Therefore, further advance and innovative technologies are needed to deal with the situation. Technologies can enhance food production in agriculture and at the same time remediate the pollution caused by such production practices. Therefore, these technologies should be economical, sustainable, and efficient. A review of land management and increased agricultural productivity in the 21st century mentions the characteristics of truly sustainable technology as (i) uses of one or more renewable resources, (ii) does not break down due to evolutionary change, (iii) possesses a broad spectrum of applicability, and (iv) affordable in the context of the local economy and crop value (Crute, 2003).

Nanotechnology has great potential in various sectors where it can serve to cost-effectively optimize production processes, increase efficiency, and maximize productivity, thereby contributing to an overall sustainable economic growth (Chen and Yada, 2011). Novel tools are being designed which can operate at the nanoscale to

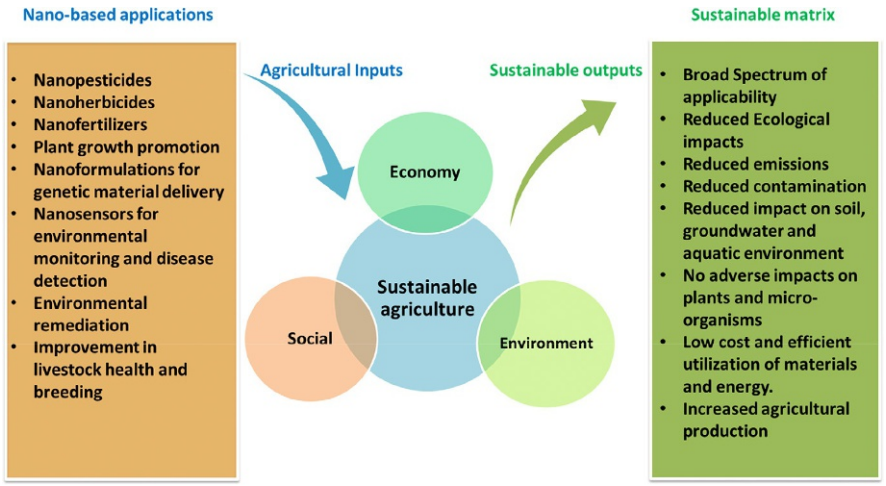

FIG. 3

Agricultural inputs of nano-based innovations and their sustainable outcomes.

boost the growth of the agriculture sector. Apart from advances discussed above the other applications of nano-based innovations in agriculture include an increase in crop productivity, improvement in health and breeding of livestock, conversion of agricultural and animal wastes to useful energy, and other valuable byproducts. Thus, nano-based innovations can help achieve the biggest challenge of making agricultural production more sustainable (Fig. 3).

Nanotechnology could redefine the entire notion of sustainable agriculture and provide various economic, environmental, and social benefits. However, nanotechnology presents an interesting dichotomy in terms of environmental health and safety. While some believe that nanotechnology can play a significant role in advancing sustainable development by making agricultural processes more sustainable, others believe that it may expose the environment to new and not fully understood nanoparticle toxicity and that too, on a large scale. At the same time, a rising number of publications on the toxic aspects of nanoparticles indicate the risks and uncertainties associated with the use of nanomaterials. To avoid any health and environmental risks arising out of it, detailed life cycle assessment (LCA), geno-toxicological and eco-toxicological studies are very essential to ensure the safety of these nanomaterials and the threats arising from their field utilization. Furthermore, serious and immediate attention needs to be given to designing risks associated with the framework, policies, and decision-making laws.

4 Conclusion

The last two decades have witnessed tremendous growth in nanotechnology and its potential application field has been extending from industrial to day-to-day usage materials. Copper nanoparticles (Cu-NPs), in particular, have been gaining wide

attention due to their cost-effectiveness, well-known antimicrobial activities, and essential micronutrient status. This book chapter explored the rising usage and application potential of Cu-NPs for agricultural purposes. It discussed their usage in agrochemicals like nanopesticides for controlling plant diseases and their mode of action on plant pathogens responsible for causing them. Further, it discussed their usage in nanosensors for sensitive detection of organic and inorganic pollutants in the soil such as chemicals, toxins, and pesticides. From the perspective of sustainable agriculture, Cu-NPs multifunctionality shows the promising potential to positively impact the agricultural sector by offering plant protection, plant growth promotion, crop nutrition, agricultural runoff reduction, and management of plant diseases to prevent food wastage. Finally, the effective utilization of nanotechnology-based innovations can play a crucial role in making the agricultural sector more sustainable.

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References

Adisa, I.O., Pullagurala, V.L.R., Peralta-Videa, J.R., Dimkpa, C.O., Elmer, W.H., Gardea-Torresdey, J.L., White, J.C., 2019. Recent advances in nano-enabled fertilizers and pesticides: a critical review of mechanisms of action. Environ. Sci. Nano 6 (7), 2002–2030.

Ameh, T., Sayes, C.M., 2019. The potential exposure and hazards of copper nanoparticles: a review. Environ. Toxicol. Pharmacol. 71, 103220.

Arjunan, N., Singaravelu, C.M., Kulanthaivel, J., Kandasamy, J., 2017. A potential photocatalytic, antimicrobial and anticancer activity of chitosan-copper nanocomposite. Int. J. Biol. Macromol. 104, 1774–1782. 11th APCCS-2016-Chemistry, Environmental, Biotechnology and Biomedical Aspects of Chitin and Chitosan.

Bakhsh, E.M., Ali, F., Khan, S.B., Marwani, H.M., Danish, E.Y., Asiri, A.M., 2019. Copper nanoparticles embedded chitosan for efficient detection and reduction of nitroaniline. Int. J. Biol. Macromol. 131, 666–675.

Bao, J., Huang, T., Wang, Z., Yang, H., Geng, X., Xu, G., Samalo, M., Sakinati, M., Huo, D., Hou, C., 2019. 3D graphene/copper oxide nano-flowers based acetylcholinesterase biosensor for sensitive detection of organophosphate pesticides. Sens. Actuators B 279, 95–101.

Bharti, A., Kumar, V., Singh, M., Bhatt, G.D., 2021. Role of nanosensors in agriculture sciences. Int. J. Agric. Biosci. 1 (1), 1–3.

Bouwmeester, H., Dekkers, S., Noordam, M.Y., Hagens, W.I., Bulder, A.S., De Heer, C., Ten Voorde, S.E., Wijnhoven, S.W., Marvin, H.J., Sips, A.J., 2009. Review of health safety aspects of nanotechnologies in food production. Regul. Toxicol. Pharmacol. 53 (1), 52–62.

Campos, E.V., Proença, P.L., Oliveira, J.L., Bakshi, M., Abhilash, P.C., Fraceto, L.F., 2019. Use of botanical insecticides for sustainable agriculture: future perspectives. Ecol. Indic. 105, 483–495.

Che, W., Ni, Y., Zhang, Y., Ma, Y., 2015. Morphology-controllable synthesis of CuO nanostructures and their catalytic activity for the reduction of 4-nitrophenol. J. Phys. Chem. Solid 77, 1–7.

Chen, H., Yada, R., 2011. Nanotechnologies in agriculture: new tools for sustainable development. Trends Food Sci. Technol. 22 (11), 585–594.

Crute, I.R., 2003. Increased crop productivity from renewable inputs—a scientific challenge for the 21st century. In: BCPC International Congress Crop Science and Technology. Proceedings of an International Congress held at the SECC, Glasgow, Scotland, UK, 10–12 November 2003. BCPC, Alton, UK, pp. 3–14.

DalCorso, G., Manara, A., Piasentin, S., Furini, A., 2014. Nutrient metal elements in plants. Metallomics 6 (10), 1770–1788.

de Oliveira, J.L., Campos, E.V.R., Bakshi, M., Abhilash, P.C., Fraceto, L.F., 2014. Application of nanotechnology for the encapsulation of botanical insecticides for sustainable agriculture: prospects and promises. Biotechnol. Adv. 32 (8), 1550–1561.

Diallo, M.S., Fromer, N.A., Jhon, M.S., 2013. Nanotechnology for sustainable development: retrospective and outlook. In: Nanotechnology for Sustainable Development. Springer, Cham, pp. 1–16.

FAO/WHO, 2010. FAO/WHO Expert Meeting on the Application of Nanotechnologies in the Food and Agriculture Sectors. Potential Food Safety Implications. Meeting Report. FAO and WHO, Rome.

FAO/WHO, 2013. State of the Art on the Initiatives and Activities Relevant to Risk Assessment and Risk Management of Nanotechnologies in the Food and Agriculture Sectors. Meeting Report. FAO and WHO, Rome.

Freibauer, A., Mathijs, E., Brunori, G., Damianova, Z., Faroult, E., Girona, J., O′Brien, L., Treyer, S., 2011. Sustainable food consumption and production in a resource-constrained world summary findings of the EU SCAR third foresight exercise. EuroChoices 10 (2), 38–43.

Gabal, E., Ramadan, M.M., Alghuthaymi, M.A., Abd-Elsalam, K.A., 2018. Copper nanostructures applications in plant protection. In: Nanobiotechnology Applications in Plant Protection. Springer, Cham, pp. 63–86.

Ghormade, V., Deshpande, M.V., Paknikar, K.M., 2011. Perspectives for nano-biotechnology enabled protection and nutrition of plants. Biotechnol. Adv. 29 (6), 792–803.

Gopalakrishnan, V., Muniraj, S., 2021. Neem flower extract assisted green synthesis of copper nanoparticles–optimisation, characterisation and anti-bacterial study. Mater. Today 36, 832–836.

Hänsch, R., Mendel, R.R., 2009. Physiological functions of mineral micronutrients (Cu, Zn, Mn, Fe, Ni, Mo, B, Cl). Curr. Opin. Plant Biol. 12 (3), 259–266.

Heffer, P., Prud'homme, M., 2016. Fertilizer outlook 2016–2020. In: 84th IFA Annual Conference, Moscow, Russia, pp. 1–5.

Ingle, A.P., Duran, N., Rai, M., 2014. Bioactivity, mechanism of action, and cytotoxicity of copper-based nanoparticles: a review. Appl. Microbiol. Biotechnol. 98 (3), 1001–1009.

Javadhesari, S.M., Alipour, S., Mohammadnejad, S., Akbarpour, M.R., 2019. Antibacterial activity of ultra-small copper oxide (II) nanoparticles synthesized by mechanochemical processing against *S. aureus* and *E. coli*. Mater. Sci. Eng. C 105, 110011.

Kabata-Pendias, A., 2010. Trace Elements in Soils and Plants. CRC Press.

Kah, M., Tufenkji, N., White, J.C., 2019. Nano-enabled strategies to enhance crop nutrition and protection. Nat. Nanotechnol. 14 (6), 532–540.

Kannan, P., Guo, L., 2020. Nanosensors for food safety. In: Nanosensors for Smart Cities. Elsevier, pp. 339–354.

Kaur, B., Srivastava, R., Satpati, B., 2016. Copper nanoparticles decorated polyaniline–zeolite nanocomposite for the nanomolar simultaneous detection of hydrazine and phenylhydrazine. Cat. Sci. Technol. 6 (4), 1134–1145.

Kaushal, S., Nanda, S.S., Samal, S., Yi, D.K., 2020. Strategies for the development of metallic-nanoparticle-based label-free biosensors and their biomedical applications. ChemBioChem 21 (5), 576–600.

Keller, A.A., Adeleye, A.S., Conway, J.R., Garner, K.L., Zhao, L., Cherr, G.N., Hong, J., Gardea-Torresdey, J.L., Godwin, H.A., Hanna, S., Ji, Z., 2017. Comparative environmental fate and toxicity of copper nanomaterials. NanoImpact 7, 28–40.

Khan, S.B., Ali, F., Akhtar, K., 2019. Chitosan nanocomposite fibers supported copper nanoparticles based perceptive sensor and active catalyst for nitrophenol in real water. Carbohydr. Polym. 207, 650–662.

Khot, L.R., Sankaran, S., Maja, J.M., Ehsani, R., Schuster, E.W., 2012. Applications of nanomaterials in agricultural production and crop protection: a review. Crop Prot. 35, 64–70.

Krämer, U., Clemens, S., 2005. Functions and homeostasis of zinc, copper, and nickel in plants. In: Molecular Biology of Metal Homeostasis and Detoxification. Springer, Berlin, Heidelberg, pp. 215–271.

Lemire, J.A., Harrison, J.J., Turner, R.J., 2013. Antimicrobial activity of metals: mechanisms, molecular targets and applications. Nat. Rev. Microbiol. 11, 371–384.

Liu, S., Yuan, L., Yue, X., Zheng, Z., Tang, Z., 2008. Recent advances in nanosensors for organophosphate pesticide detection. Adv. Powder Technol. 19 (5), 419–441.

Lopez-Lima, D., Mtz-Enriquez, A.I., Carrión, G., Basurto-Cereceda, S., Pariona, N., 2021. The bifunctional role of copper nanoparticles in tomato: effective treatment for *Fusarium* wilt and plant growth promoter. Sci. Hortic. 277, 109810.

Mali, S.C., Dhaka, A., Githala, C.K., Trivedi, R., 2020. Green synthesis of copper nanoparticles using *Celastrus paniculatus* Willd. leaf extract and their photocatalytic and antifungal properties. Biotechnol. Rep. 27, e00518.

Mathijs, E., 2012. Sustainable food consumption and production in a resource-constrained world. In: The Futures of Agriculture. Brief No. 1—English. Global Forum on Agricultural Research (GFAR), Rome.

Mekahlia, S., Bouzid, B., 2009. Chitosan-copper (II) complex as antibacterial agent: synthesis, characterization and coordinating bond-activity correlation study. Phys. Procedia 2, 1045–1053.

Nuruzzaman, M., Liu, Y., Rahman, M.M., Dharmarajan, R., Duan, L., Uddin, A.F.M.J., Naidu, R., 2019. Nanobiopesticides: composition and preparation methods. In: Nano-Biopesticides Today and Future Perspectives. Academic Press, pp. 69–131.

Pariona, N., Mtz-Enriquez, A.I., Sánchez-Rangel, D., Carrión, G., Paraguay-Delgado, F., Rosas-Saito, G., 2019. Green-synthesized copper nanoparticles as a potential antifungal against plant pathogens. RSC Adv. 9 (33), 18835–18843.

Parisi, C., Vigani, M., Rodríguez-Cerezo, E., 2015. Agricultural nanotechnologies: what are the current possibilities? Nano Today 10 (2), 124–127.

Pham, N.D., Duong, M.M., Le, M.V., Hoang, H.A., 2019. Preparation and characterization of antifungal colloidal copper nanoparticles and their antifungal activity against *Fusarium oxysporum* and *Phytophthora capsici*. C. R. Chim. 22 (11–12), 786–793.

Pino, F., Mayorga-Martinez, C.C., Merkoçi, A., 2016. High-performance sensor based on copper oxide nanoparticles for dual detection of phenolic compounds and a pesticide. Electrochem. Commun. 71, 33–37.

Prosekov, A.Y., Ivanova, S.A., 2018. Food security: the challenge of the present. Geoforum 91, 73–77.

Quartacci, M.F., Cosi, E., Navari-Izzo, F., 2001. Lipids and NADPH-dependent superoxide production in plasma membrane vesicles from roots of wheat grown under copper deficiency or excess. J. Exp. Bot. 52, 77–84.

Radad, K., Al-Shraim, M., Moldzio, R., Rausch, W.D., 2012. Recent advances in benefits and hazards of engineered nanoparticles. Environ. Toxicol. Pharmacol. 34 (3), 661–672.

Raffi, M., Mehrwan, S., Bhatti, T.M., Akhter, J.I., Hameed, A., Yawar, W., ul Hasan, M.M., 2010. Investigations into the antibacterial behavior of copper nanoparticles against *Escherichia coli*. Ann. Microbiol. 60, 5–80.

Rai, M., Ingle, A.P., Pandit, R., Paralikar, P., Shende, S., Gupta, I., Biswas, J.K., da Silva, S.S., 2018. Copper and copper nanoparticles: role in management of insect-pests and pathogenic microbes. Nanotechnol. Rev. 7 (4), 303–315.

Rajeshkumar, S., Rinitha, G., 2018. Nanostructural characterization of antimicrobial and antioxidant copper nanoparticles synthesized using novel *Persea americana* seeds. OpenNano 3, 18–27.

Rajeshkumar, S., Menon, S., Kumar, S.V., Tambuwala, M.M., Bakshi, H.A., Mehta, M., Satija, S., Gupta, G., Chellappan, D.K., Thangavelu, L., Dua, K., 2019. Antibacterial and antioxidant potential of biosynthesized copper nanoparticles mediated through *Cissus arnotiana* plant extract. J. Photochem. Photobiol. B 197, 111531.

Rajput, V., Minkina, T., Sushkova, S., Behal, A., Maksimov, A., Blicharska, E., Ghazaryan, K., Movsesyan, H., Barsova, N., 2020. ZnO and CuO nanoparticles: a threat to soil organisms, plants, and human health. Environ. Geochem. Health 42 (1), 147–158.

Ramzan, M., Obodo, R.M., Mukhtar, S., Ilyas, S.Z., Aziz, F., Thovhogi, N., 2021. Green synthesis of copper oxide nanoparticles using *Cedrus deodara* aqueous extract for antibacterial activity. Mater. Today 36, 576–581.

Rasool, A., Shah, W.H., Tahir, I., Rehman, R.U., 2019. Application of nanoparticles in crop production and protection. In: Plant Nanobionics. Springer, Cham, pp. 235–253.

Rehman, M., Liu, L., Bashir, S., Saleem, M.H., Chen, C., Peng, D., Siddique, K.H., 2019. Influence of rice straw biochar on growth, antioxidant capacity and copper uptake in ramie (*Boehmeria nivea* L.) grown as forage in aged copper-contaminated soil. Plant Physiol. Biochem. 138, 121–129.

Saharan, V., Mehrotra, A., Khatik, R., Rawal, P., Sharma, S.S., Pal, A., 2013. Synthesis of chitosan based nanoparticles and their in vitro evaluation against phytopathogenic fungi. Int. J. Biol. Macromol. 62, 677–683.

Sasson, Y., Levy-Ruso, G., Toledano, O., Ishaaya, I., 2007. Nanosuspensions: emerging novel agrochemical formulations. In: Insecticides Design Using Advanced Technologies. Springer, Berlin, Heidelberg, pp. 1–39.

Shende, S., Ingle, A.P., Gade, A., Rai, M., 2015. Green synthesis of copper nanoparticles by *Citrus medica* Linn.(Idilimbu) juice and its antimicrobial activity. World J. Microbiol. Biotechnol. 31 (6), 865–873.

Siddiqui, M.H., Al-Whaibi, M.H., Mohammad, F., 2015. Nanotechnology and Plant Sciences. Springer International Publishing, Switzerland, https://doi.org/10.1007/978-3-319-14502-0.

Singh, S., Kumar, N., Kumar, M., Agarwal, A., Mizaikoff, B., 2017. Electrochemical sensing and remediation of 4-nitrophenol using bio-synthesized copper oxide nanoparticles. Chem. Eng. J. 313, 283–292.

Songa, E.A., Okonkwo, J.O., 2016. Recent approaches to improving selectivity and sensitivity of enzyme-based biosensors for organophosphorus pesticides: a review. Talanta 155, 289–304.

Soomro, R.A., Hallam, K.R., Ibupoto, Z.H., Tahira, A., Sherazi, S.T.H., Memon, S.S., Willander, M., 2016. Amino acid assisted growth of CuO nanostructures and their potential application in electrochemical sensing of organophosphate pesticide. Electrochim. Acta 190, 972–979.

Stephenson, G.R., Coats, J.R., Yamamoto, H., 2001. Pesticide use and world food production: risks and benefits. In: Expert Committee on Weeds Comité d'experts en malherbologie. Proceedings of the 2000 National Meeting, pp. 9–15.

Tilman, D.J.D.P.M., Knops, J., Wedin, D., Reich, P., 2002. Plant diversity and composition: effects on productivity and nutrient dynamics of experimental grasslands. In: Biodiversity and Ecosystem Functioning: Synthesis and Perspectives. Oxford University Press, Oxford, UK, pp. 21–35.

Tilman, D., Balzer, C., Hill, J., Befort, B.L., 2011. Global food demand and the sustainable intensification of agriculture. Proc. Natl. Acad. Sci. U. S. A. 108 (50), 20260–20264. https://doi.org/10.1073/pnas.1116437108.

Tiwari, M., Jain, P., Hariharapura, R.C., Narayanan, K., Bhat, U., Udupa, N., Rao, J.V., 2016. Biosynthesis of copper nanoparticles using copper-resistant *Bacillus cereus*, a soil isolate. Process Biochem. 51 (10), 1348–1356.

Tsuji, K., 2001. Microencapsulation of pesticides and their improved handling safety. J. Microencapsul. 18 (2), 137–147.

Tunesi, M.M., Kalwar, N., Abbas, M.W., Karakus, S., Soomro, R.A., Kilislioglu, A., Abro, M.I., Hallam, K.R., 2018. Functionalised CuO nanostructures for the detection of organophosphorus pesticides: a non-enzymatic inhibition approach coupled with nano-scale electrode engineering to improve electrode sensitivity. Sens. Actuators B 260, 480–489.

Viet, P.V., Nguyen, H.T., Cao, T.M., Hieu, L.V., 2016. Fusarium antifungal activities of copper nanoparticles synthesized by a chemical reduction method. J. Nanomater. 2016.

Vogelweith, F., Thiéry, D., 2018. An assessment of the non-target effects of copper on the leaf arthropod community in a vineyard. Biol. Control 127, 94–100.

Wang, L., Hu, C., Shao, L., 2017. The antimicrobial activity of nanoparticles: present situation and prospects for the future. Int. J. Nanomedicine 12, 1227.

Wilson, M.A., Tran, N.H., Milev, A.S., Kannangara, G.K., Volk, H., Lu, G.M., 2008. Nanomaterials in soils. Geoderma 146 (1–2), 291–302.

Yan, J., Huang, K., Wang, Y., Liu, S., 2005. Study on anti-pollution nano-preparation of dimethomorph and its performance. Chin. Sci. Bull. 50 (2), 108–112.

Yruela, I., 2009. Copper in plants: acquisition, transport and interactions. Funct. Plant Biol. 36 (5), 409–430.

Zhao, G., Zhang, H., Fan, Q., Ren, X., Li, J., Chen, Y., Wang, X., 2010. Sorption of copper (II) onto super-adsorbent of bentonite–polyacrylamide composites. J. Hazard. Mater. 173, 661–668.

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PART

Antimicrobials

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CHAPTER

17 Biosynthesis and antibacterial activity of Cu and CuO nanoparticles against pathogenic microorganisms

R. Britto Hurtado[a,b], Y. Delgado-Beleño[a,c], C.E. Martinez-Nuñez[a,c], M. Cortez-Valadez[d], and M. Flores-Acosta[a]

[a]*Department of Physics Research, University of Sonora, Hermosillo, Sonora, Mexico*

[b]*State University of Sonora, Hermosillo, Sonora, Mexico,*

[c]*Optical and Laser Spectroscopy Group, Popular University of Cesar, Valledupar, Colombia,*

[d]*CONACYT—Department of Physics Research, University of Sonora, Hermosillo, Sonora, Mexico*

1 Introduction

The applications of nanomaterials have increased in different fields of technology and industry. Metallic and semiconductor nanoparticles have been implemented with important nanotechnological advances in food, textiles, agriculture, sensors, and construction materials among others (dos Santos et al., 2020; Salem and Fouda, 2021; Panpatte et al., 2016; Priyadarshini and Pradhan, 2017; Mohajerani et al., 2019). The mechanical, optical, chemical, magnetic, and electronic properties of nanoparticles enable the development of better and new products, which have been very attractive to both scientists and companies. Currently, many articles with incorporated nanoparticles are used with specific functions. Nowadays, several products with incorporated nanoparticles with antiviral, antibacterial, and regenerative properties are available for consumer use (Fröhlich and Roblegg, 2012). The empirical and accidental way in which Chinese and Egyptian artisans used gold colloids to color crystals and ceramics is now a thing of the past. On the other hand, the current use of products that contain nanoparticles must be safe for the environment and humans, since the nanoparticles present in food are destined to be ingested. Also, nanoparticles in paints, cosmetics, pesticides, and food packaging ingredients can be accidentally ingested and enter the gastrointestinal tract, so consideration should be given to appropriate concentrations and frequency of application. It is known that the synthesis of nanoparticles and the manufacture of nanotechnological products are related to procedures that involve toxic and costly substances. Therefore, new alternative and environmentally friendly methodologies have emerged to reduce costs and pollution, to generate safer production processes for people and the environment. These alternative methods of synthesizing nanomaterials use extracts from plants,

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fungi, algae, microorganisms, and organic molecules. Thus, by using nanoparticles synthesized with a green synthesis approach, toxicity is minimized and biocompatible materials are obtained. Nanoparticles synthesized by green methods have been reported, including metallic, polymeric, semiconductor nanoparticles, alloys, and carbon allotropes (De Silva et al., 2017; Iravani, 2011; Makarov et al., 2014; Parveen et al., 2016).

In the case of copper nanoparticles, they are widely used in catalysis, solar energy, medicine, and as antibacterial agents (Flemming and Trevors, 1989; Gawande et al., 2016; Ren et al., 2009). For example, there are recent reports of copper nanoparticles (CuNPs) and copper oxide nanoparticles (CuONPs) with promising antimicrobial properties. CuNPs with a size of ~ 5 nm were studied against *Escherichia coli*, *Staphylococcus aureus*, and *Candida albicans* (Bogdanović et al., 2014). Therefore, copper nanoparticles are used in agriculture, pharmaceuticals, biomedicine, and health against pathogenic microorganisms. Pathogens are infectious agents (viruses, bacteria, fungi, protozoa, etc.) capable of causing an infectious disease in a host (plant, animal, or human). Kanhed et al. reported the synthesis of copper nanoparticles with sizes between 3 and 10 nm using chemical reduction method and showed that CuNPs exhibit good antifungal activity against phytopathogenic fungi: *Phoma destructiva*, *Curvularia lunata*, *Alternaria alternata*, and *Fusarium oxysporum* (Kanhed et al., 2014). The use of chitosan-coupled copper nanoparticles (Ch-CuNPs) was recently reported against the phytopathogens *Rhizoctonia solani* and *Pythium aphanidermatum*, which cause buffering disease, inhibiting mycelial growth up to 98% (Vanti et al., 2020). Also, the use of copper nanoparticles was reported as a new simple, cost-effective, selective strategy for label-free fluorescence detection of drugs in clinical diagnostics (Wang et al., 2015) and CuNPs that could be used as coating agents in surgical devices and medical implants to control infections of the pathogen *Pseudomonas aeruginosa*, frequently associated with nosocomial infections (LewisOscar et al., 2015). Similarly, the inhibitory effect of CuONPs against Gram-positive and Gram-negative bacteria was reported, analyzing the size of the nanoparticles and their relationship with the antimicrobial activity (Azam et al., 2012). Mahapatra et al. reported CuO nanoparticles with a particle size of 80–160 nm with good antibacterial activity against *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, *Salmonella paratyphi*, and *Shigella* strains (Mahapatra et al., 2008). The biosynthesis of CuO nanoparticles using the fungus *Penicillium chrysogenum* was also reported, CuONPs exhibited antibacterial activity against *Ralstonia solanacearum* and *Erwinia amylovora*. Therefore, CuONPs are an important alternative in the agricultural area to curb the proliferation of plant pathogenic fungi and bacteria (El-Batal et al., 2020). Ahmad et al. reported biosynthesis of copper oxide nanoparticles using neem (*Azadirachta indica* A.) leaf extract. They have shown that *A. indica* extract and its fractions combined with CuONP prove to be less toxic to seeds, offering a promising route for the development of copper-based green fungicides that can help to combat modern synthetic fungicide problems (Ahmad et al., 2020). Metallic nanoparticles such as silver, platinum, and gold are also used in similar applications, but Cu is interesting because it is an abundant material in nature, low cost, and

resistant to corrosion and oxidation. Copper is a metal considered nontoxic for the environment, plays an important role in the photosynthesis process of plants, occurs naturally in all waters and soils, and acts as a fungicide and bactericide product. Also, it is known as a trace element that contributes to maintaining healthy blood vessels, bones, and the immune system. Therefore, the development of copper-based nanotechnological products using biosynthesis is currently important to improve the quality of food, devices, and important applications against pathogenic microorganisms.

2 Biosynthesis of Cu and CuO nanoparticles

The biosynthesis of nanoparticles can be defined as the use of biological entities or substances extracted from them to obtain nanostructured materials. The term "bio" refers to living organisms and "synthesis" is used to describe the method or technique used to obtain a new material. In general, nanomaterial synthesis processes are classified into two groups: *top-down* and *bottom-up* approaches (Fig. 1). Nanoparticle synthesis methods that use the *top-down* approach are related to physical processes and consist of subjecting the bulk material to pulverization until obtaining smaller and smaller sizes with dimensions of 10^{-9} m.

High-energy mechanical milling and laser ablation are two characteristic examples of these physical procedures. In the first case, the material is subjected to

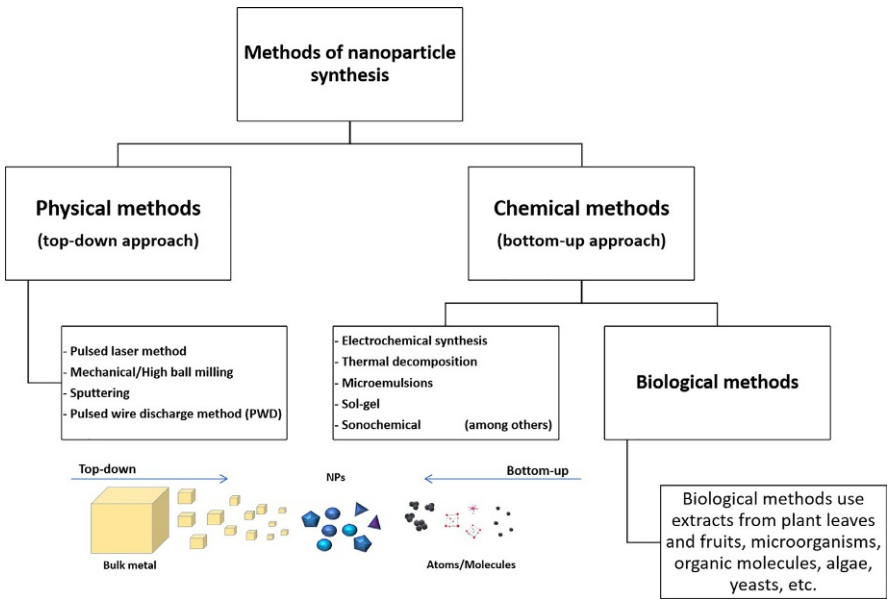

FIG. 1

Bottom-up and the top-down approaches in the synthesis of nanomaterials.

grinding using planetary ball mills, the sample is placed in a cylindrical container with grinding balls. Then, the container acts as a planetary system rotating in an orbit around its center, generating shattering collisions between the grinding balls. Finally, due to the centrifugal acceleration force and other acting forces generated with the Coriolis acceleration the sample is pulverized. The mechanochemical activation of crystalline solids tends to produce textural and structural changes, which can be of great interest in the development of new materials (Boldyrev, 1993). Containers and balls are constructed of materials with high resistance to abrasion, including agate, silicon nitride, tungsten carbide, hardened chrome steel, and stainless steel. Cu nanoparticles and some copper nanocomposites have been synthesized using high-energy ball milling. Barai et al. synthesized nanocrystalline copper crystals with sizes between 30 and 40 nm by high-energy milling (Barai et al., 2012). Also, studies on grain size variation of Cu nanopowders subjected to ball milling and antibacterial activity of copper oxide nanoparticles prepared by mechanical milling were reported (Amal et al., 2019; Lasio et al., 2018). This method could have some disadvantages, for example, the nonavailability of equipment in the laboratory. Another disadvantage is that the sample could be contaminated due to the natural abrasion of the balls with time, so the final sample could contain residues of nanoparticles from the material of the balls. Also, the total control of the nanoparticle sizes to be synthesized is not guaranteed. In the second case, laser ablation is the process of removing material from a surface by the incidence of a laser beam, using a continuous or pulsed flow of radiation. Usually, liquids are used to obtain stable nanoparticle suspensions from bulk material, such as metal, alloy, or ceramic (Kim et al., 2017; Mafuné et al., 2000; Semaltianos, 2010). The laser ablation method has been used extensively to obtain Cu and CuO nanoparticles. Goncharova et al. recently used a pulsed laser in liquid to control the chemical and morphological evolution of copper nanoparticles (Goncharova et al., 2019). Aghdam et al. reported that ablation time and laser fluence, affect the composition, morphology, and optical properties of copper oxide nanoparticles using a nanosecond pulsed Ce:Nd: YAG laser and pure Cu in water (Dizajghorbani Aghdam et al., 2019). Likewise, CuO nanoparticles were synthesized using a pulsed Nd: YAG laser and copper granules immersed in deionized water with antibacterial properties against *Escherichia coli* and *Staphylococcus aureus* bacteria using a liquid medium method (Khashan et al., 2016). Although the laser ablation technique is relatively simple and follows a clean process as it does not generate large residues or impurities in the sample, the acquisition of the equipment is considered expensive. To have a continuous or pulsed high power Nd: YAG laser, as well as its maintenance, requires considerable investment and energy costs. Therefore, alternative synthesis methods that are economically feasible and use naturally occurring components have been used such as biological or green synthesis methods.

In contrast to top-down methods, bottom-up approaches for the synthesis of nanomaterials are related to chemical processes and have a greater impact on materials science. Experimental advances have made it possible to control the physical properties of nanostructures more efficiently such as size, shape, and morphology. Chemical methods make it easier to obtain bimetallic nanostructures of different

shapes and nanocomposites. Bottom-up consists of bonding matter atom by atom (condensation of atoms or molecular entities in a gas phase or solution) to build agglomerates that form larger systems up to nanometric sizes. The chemical processes of nanoparticles follow a reduction-oxidation reaction, i.e., to initiate the nanostructure formation stage, to obtain this, it is necessary to have a solution with precursor ions and a reducing agent that supplies electrons from its chemical structure to neutralize the ions present in the medium, followed by the controlled aggregation of these atoms. Some reducing agents of synthetic origin are sodium borohydride, sodium citrate, hydrazine, among others (Duan et al., 2015). Also, to prevent agglomeration and nanoparticles of large size, a capping agent is required in the synthesis process. For example, some of the most used capping agents are povidone or PVP, chitosan, sodium dodecyl sulfate (SDS), sodium polyacrylate, etc. (Javed et al., 2020). The capping agent can be a surfactant compound, a polymer, a quaternary salt, or some other organic molecule and is an important element to preserve the colloidal dispersion in the synthesis of nanoparticles to prevent the formation of agglomerates. The use of a capping agent causes a repulsive force that counteracts the Van der Waals forces in the medium, according to the study of Roucoux et al. the stabilization process in colloidal systems can be by electrostatic, steric, or electrosteric stabilization (Roucoux et al., 2002). In the former, the presence of ions around the particles generates an electrostatic repulsion. In steric stabilization, the molecules used in the redox reaction or the aggregation of the stabilizing agent are adsorbed on the surface of the particles generating an osmotic repulsion. Electrosteric stabilization could be defined as a combination of the two previous ones. Some chemical synthesis methods frequently used to obtain metallic, semiconductor, and nanocomposite nanoparticles are sonochemical synthesis, chemical vapor deposition (CVD), sol-gel, molecular self-assembly, and molecular beam epitaxy (MBE) (Kumar et al., 2018). For example, Cu nanoparticles were obtained by reduction of a copper salt by sodium citrate and myristic acid (Khanna et al., 2007). Wu and Chen reported the synthesis of CuNPs by reduction of cupric chloride with hydrazine in the aqueous solution of CTAB (cetyl trimethyl ammonium bromide) (Wu and Chen, 2004). Likewise, the synthesis of Cu_2O nanoparticles by the sol-gel technique using sodium hydroxide (NaOH), and CuO nanoparticles by chemical vapor deposition (Shi et al., 2017; Kayani et al., 2015) were reported.

Chemical synthesis methods are efficient for obtaining different Cu nanostructures. However, chemical methods use substances that are toxic to the environment and humans. The use of toxic compounds constrains their applications in medicine, food, and biocompatible products. Therefore, with biosynthesis methods, it is possible to use compounds of biological origin, such as plant extracts, algae, fungi, and organic molecules with reducing and capping properties that decrease the effects of toxicity and help to develop versatile, reliable, biocompatible, and low-cost nanoparticles and devices (Fig. 2). Organic compounds are extracted from plants, fruits, and vegetables that replace chemical reagents in the oxidation-reduction process for nanoparticle formation (Duan et al., 2015). Among the compounds with reducing and stabilizing properties are phenols such as gallic acid, as well as saccharides,

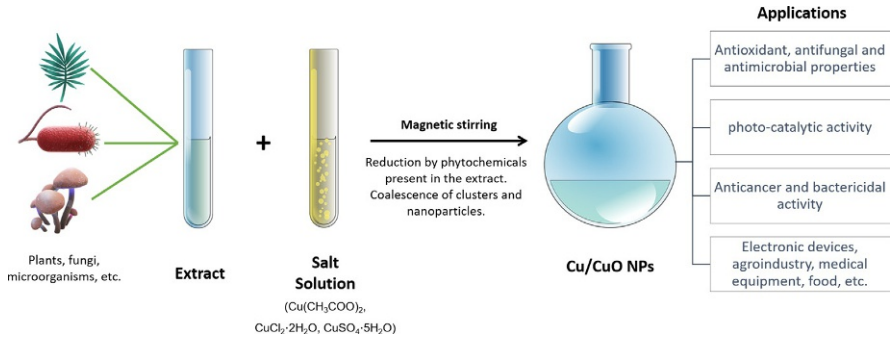

FIG. 2

Schematic representation of the ecological synthesis of Cu and CuO nanoparticles.

amino acids, and other organic acids with antioxidant properties. A recent study reported the synthesis of CuNPs using *Syzygium aromaticum* bud extract indicating through Fourier transform infrared spectroscopy (FT-IR) analysis that tannins, flavonoids, alkaloids, and carotenoids are abundant in the bud extract contributing to the formation of the nanoparticles (Rajesh et al., 2018). Also, the synthesis of CuNPs with excellent antioxidant and antimicrobial activity against a wide range of skin burn pathogens was reported using polysaccharides and the fungus *Pleurotus ostreatus* as a reducing and preservative medium (El-Batal et al., 2018). Additionally, the synthesis of CuNPs using *Aspergillus niger* strain STA9 was reported as an environmentally friendly, cost-effective method with anticancer activity against human hepatocellular carcinoma cell lines (Huh-7). Also, with antidiabetic properties with inhibition of *alpha-glucosidase* and antibacterial effects against *Escherichia coli*, *Staphylococcus aureus*, *Klebsiella pneumoniae*, *Micrococcus luteus*, and *Bacillus subtilis* (Noor et al., 2020). Mahmoud et al. reported the synthesis of CuNPs using *Plantago asiatica* leaf extract and demonstrated through FT-IR analysis that the adsorption of phytochemicals (polysaccharides and ascorbic acid) are essentials for the stability of nanoparticles (Nasrollahzadeh et al., 2017). The aqueous extract of *Calotropis procera* L. was used as a low-cost and eco-friendly method for the rapid biosynthesis of copper nanoparticles with a mean size of 15 ± 1.7 nm and evaluated for their cytotoxicity in HeLa, A549, and BHK21 tumor cells with an MTT dye conversion assay with excellent biocompatibility (Harne et al., 2012). Also, *Thymus vulgaris* L. leaf extract was used as a mild, renewable, nontoxic reducing agent and as an effective stabilizer to obtain CuNPs without the addition of a surfactant (Issaabadi et al., 2017). Recently, the use for the first time of *Curcuma longa* extract for the synthesis of CuNPs with sizes from 5 to 25 nm with good antibacterial activity against Gram-positive and Gram-negative bacteria was reported (Jayarambabu et al., 2020). Suarez-Cerda et al. synthesized CuNPs using ascorbic acid as a reducing agent and different cyclodextrins as capping agents, presenting an alternative biosynthesis with organic molecules and compounds (Suárez-Cerda et al., 2017). Ascorbic acid (vitamin C) is commonly used as a reducing and protective agent.

Vitamin C is a water-soluble nutrient found in a wide variety of foods and plants, making it an excellent nontoxic, inexpensive, and environmentally friendly material for the synthesis of nanoparticles. Xiong et al. synthesized highly stable dispersion of copper particles with an average particle size of less than 2 nm using L-ascorbic acid as both a reducing and capping agent precursor in an aqueous medium (Xiong et al., 2011). Similarly, a rapid, economical, energy-efficient, and nontoxic waste-free green synthesis method of Ag and Cu nanoparticles was reported using ascorbic acid as a reducing agent in chitosan solutions (Zain et al., 2014). Spherical copper nanoparticles with an average diameter of 90 nm were reported using ascorbic acid as reductant and the cationic surfactant cetyl trimethyl ammonium bromide (CTAB) as capping agent (Biçer and Şişman, 2010).

On the other hand, the use of copper oxide nanoparticles in various applications such as antimicrobial agents, agricultural fertilizer, and photocatalyst, among others, stands out (Ahamed et al., 2014; Chang et al., 2011; Tran and Nguyen, 2014). We reported the synthesis of CuONPs using *Cissus quadrangularis* plant extract with a diameter of 30 ± 2 nm and showed that the obtained CuNPs exhibit better antifungal performance against two fungal strains (*Aspergillus niger* and *Aspergillus flavus*) as compared to the standard commercially available fungicide Carbendazim (Devipriya and Roopan, 2017). Starch extracted from *Solanum tuberosum* (potato) was used as a green synthesis method to obtain CuONPs with efficient antimicrobial properties against *Bacillus cereus* 9634, *Shigella sonnei*, *Staphylococcus epidermidis* 1435, *Enterococcus* 1237, *Pseudomonas aeruginosa* PAO1 27853, and *Escherichia coli* 25922 and anticancer activity against MCF-7 cell line (Alishah et al., 2017). *Aloe vera* leaf extract was used for green synthesis of CuO nanoparticles as a nontoxic method and tested against three bacterial fish pathogens *Aeromonas hydrophila*, *Pseudomonas fluorescens*, and *Flavobacterium branchiophilum* (Kumar et al., 2015). Recently, the utilization of plant extract of *Gloriosa superba* L. in the efficient synthesis of spherical CuO nanoparticles with sizes of 5–10 nm with significant antibacterial activity against pathogenic bacterial strains, namely Gram-negative *Klebsiella aerogenes*, *Pseudomonas desmolyticum* and *Escherichia coli*, Gram-positive bacteria *Staphylococcus aureus* was reported (Naika et al., 2015). In this case, it was suggested that the ions released from the nanoparticles adhere to the negatively charged bacterial cell wall to break it, disrupting biochemical processes leading to protein denaturation and cell death.

Recently, NPs obtained using algae and fungi have gained high consideration as a less toxic, cost-effective, and environmentally friendly method with antibacterial, antioxidant, free radical scavenging, anticancer, and biocompatibility properties (AlNadhari et al., 2021). Marine algae are an important source of antioxidant compounds, with wide applications in the prevention and treatment of various diseases, as well as in food preservation. For example, the synthesis of silver and copper nanoparticles using the algae extract *Botryococcus braunii* with antimicrobial activity against two Gram-negative bacterial strains *Pseudomonas aeruginosa* (MTCC 441) and *Escherichia coli* (MTCC 442) was reported, two Gram-positive bacterial strains *Klebsiella pneumoniae* (MTCC 109) and *Staphylococcus aureus* (MTCC 96),

and a fungal strain *Fusarium oxysporum* (MTCC 2087) (Arya et al., 2018). Likewise, *Bifurcaria bifurcata* algae extract was used as an environmentally friendly method to obtain copper oxide nanoparticles with sizes between 5 and 45 nm, without requiring any chemical reagent or surfactant and with good antibacterial activity against two different strains of bacteria *Enterobacter aerogenes* (Gram-negative) and *Staphylococcus aureus* (Gram-positive) (Abboud et al., 2014). The fungus *Stereum hirsutum* was used in the biosynthesis of 5–20 nm spherical copper/copper oxide nanoparticles in different pH conditions and the presence of protein bound to copper and copper oxide nanoparticles was analyzed using FT-IR. They concluded that the release of extracellular protein by *S. hirsutum* is responsible for the formation and stabilization of nanoparticles biosynthesized in an aqueous medium (Cuevas et al., 2015). Copper oxide nanoparticles with a diameter of 3.6 nm synthesized with algal extract showed antimicrobial activity against *Escherichia coli* bacteria and were used for drinking water disinfection (Bhattacharya et al., 2019). One study reported antimicrobial and anticancer activities in vitro of CuONPs biologically synthesized using brown alga against cell line (MCF-7) and the bacteria *Pseudomonas aeruginosa* and *Aspergillus niger* (Ramaswamy et al., 2016). Araya-Castro et al. reported a green synthesis method to obtain CuONPs using protein fractions separated from an aqueous extract of the brown algae *Macrocystis pyrifera* and verified through FTIR measurements that functional groups of proteins are essential in the reduction and stabilization of nanoparticles (Araya-Castro et al., 2021). Table 1 shows a list of Cu and CuO nanoparticles obtained by biosynthesis processes. The organic agent used

Table 1 Copper and copper oxide nanoparticles synthesized using biosynthesis methods.

Nanoparticle	Bio-agent used	Size/ morphology	Applications	References
Cu	*Crocus sativus* L. leaf aqueous extract	27.5 nm/ spherical	Peripheral nervous system treatment	Zhang et al. (2020)
	Falcaria vulgaris leaf extract	20–25 nm/ spherical	Cytotoxicity, antioxidant, antifungal, antibacterial, and cutaneous wound healing activities	Zangeneh et al. (2019)
	Cissus arnotiana plant extract	60–90 nm/ spherical	Antibacterial and antioxidant activities	Rajeshkumar et al. (2019)
	Celastrus paniculatus leaves extract	2–10 nm/ spherical	Photocatalytic and antifungal properties	Mali et al. (2020)

Table 1 Copper and copper oxide nanoparticles synthesized using biosynthesis methods—cont'd

Nanoparticle	Bio-agent used	Size/ morphology	Applications	References
	Fruit extract of *Piper retrofractum* Vahl	2–10 nm/ spherical	Antibacterial activity	Amaliyah et al. (2020)
	Aspergillus versicolor	23–82 nm/ spherical	Application in controlling of rotting plant pathogens	Ammar et al. (2019)
	P. granatum seeds extract (biological molecules)	40–80 nm/ semispherical	Photocatalytic activity	Nazar et al. (2018)
	Broccoli green extract	~ 4.8 nm/ spherical	Antioxidant, sensing, and catalytic activity	Prasad et al. (2016)
	Terminalia arjuna bark extract	~ 23 nm/ spherical	Antimicrobial activity	Yallappa et al. (2013)
	Zingiber officinale and *Allium sativum*-derived extracts	Different sizes/ spherical	Anticancer and bactericidal activity	Yaqub et al. (2020)
	Hagenia abyssinica (*Brace*) *JF. Gmel*. leaf extract	34.76 nm/ spherical	Antimicrobial properties	Murthy et al. (2020)
	Aqueous extracts of bilberry (*Vaccinium myrtillus* L.)	2–10 nm, together with larger aggregates	Antimicrobial activity	Benassai et al. (2021)
	Citron juice (*Citrus medica* Linn)	10–60 nm/ spherical	Antimicrobial activity	Shende et al. (2015)
	Eryngium caucasicum aqueous extracts	< 40 nm/ spherical	Antioxidant and antimicrobial properties	Hasheminya and Dehghannya (2020)
	Cissus vitiginea	5–20 nm/ spherical	Antioxidant and antimicrobial activity	Wu et al. (2020)
	Extract of *Jatropha curcas* leaves	10 ± 1 and 12 ± 1 nm/ spherical	Photocatalytic activity	Ghosh et al. (2020)
	Alchornea laxiflora leaf extract	3.29 ± 0.57 nm/spherical	Catalytic application	Olajire et al. (2018)

Continued

Table 1 Copper and copper oxide nanoparticles synthesized using biosynthesis methods—cont'd

Nanoparticle	Bio-agent used	Size/ morphology	Applications	References
	Glucose	200 ± 50/ spherical	–	Upadhyay and Kumar (2017)
	Pectin and ascorbic acid	Average diameters of 61.9 ± 19.4 and 40.9 ± 13.6 nm	Antimicrobial activities	Li et al. (2020)
	Agaricus bisporus aqueous extract	~ 10 nm/ agglomerated morphology	Antibacterial activity	Sriramulu et al. (2020)
	Lemon juice (without peal)	50 nm/ spherical	Catalytic activity	Raiza et al. (2019)
	Soybeans (l)	5.67 nm/ quasispherical	Antibacterial activity	Dealba-Montero et al. (2017)
	Citrus limon fruits extract	28 nm/ spherical	Antibacterial activity	Amer and Awwad (2021)
	Magnolia kobus leaf extract	37 nm/ spherical	Antibacterial activity	Lee et al. (2013)
CuO	*Gum karaya*	2–10 nm/ spherical	Antibacterial application	Padil and Černík (2013)
	Momordica charantia	61.48 ± 2 nm/ nanorods	Antimicrobial activity (potential applications in the field of nanomedicine)	Qamar et al. (2020)
	Orange, lemon, and tangerine peel extracts	48–76 nm/ spherical	Antimicrobial properties on various micro-organisms that are resistant to antibiotics	Tshireletso et al. (2021)
	Extract of herbal tea (*Stachys lavandulifolia*) flowers	15–25 nm/ spherical	Catalytic activity	Veisi et al. (2021)
	Anthemis nobilis flowers extract	29–61 nm/ rectangular	Catalytic activity	Nasrollahza-deh et al. (2015b)
	Gundelia tournefortii extract	30–50 nm/ spherical	Catalytic activity	Nasrollahza-deh et al. (2015a)
	Sinapic acid	> 200 nm/ spherical	Antiangiogenic therapy for breast cancer	Raj Preeth et al. (2019)

Table 1 Copper and copper oxide nanoparticles synthesized using biosynthesis methods—cont'd

Nanoparticle	Bio-agent used	Size/ morphology	Applications	References
	Ficus religiosa leaf extract	~ 577 nm/ spherical	Anticancer activity	Sankar et al. (2014)
	Olea europaea leaf extract	20–50 nm/ spherical	Anticancer agents	Sulaiman et al. (2018)
	Leaf extract of *Cymbopogon citratus* (CLE)	11.4–14.5 nm/ spherical	Antibacterial and antibiofilm agents	Cherian et al. (2020)
	Laurus nobilis leaf extract	90 and 250 nm/ spherical	Antioxidant and antibacterial activity	Bulut Kocabas et al. (2021)
	Adiantum lunulatum plant extract	5 ± 1.5 nm/ spherical	Antioxidant activity	Sarkar et al. (2020)
	Catha edulis leaves extract	Different sizes/ spherical	Antibacterial Activity	Andualem et al. (2020)
	Black bean extract	~ 26.6 nm/ spherical	Anticancer activity	Nagajyothi et al. (2017)
	Gloriosa superba L. extract	5–10 nm/ spherical	Antibacterial activity	Naika et al. (2015)
	Aloe barbadensis Miller extract	15 and 30 nm/ spherical	–	Gunalan et al. (2012)
	Ruellia tuberosa aqueous extract	~ 83.23 nm/ nanorods	Antibacterial activity	Vasantharaj et al. (2019)
	Cordia sebestena flower aqueous extract	20 and 35 nm/ spherical	Antibacterial activity against selected pathogenic bacterial organisms	Prakash et al. (2018)
	Leaves of *Ormocarpum cochinchinense*	Agglomerated clusters	Anticancer activity	Gnanavel et al. (2017)
	Annona muricata leaf extract	30–40 nm/ semispherical	Photocatalytic activity	Kayalvizhi et al. (2020)
	Citrofortunella microcarpa leaves extract	54–68 nm/ spherical	Photocatalytic activity	Rafique et al. (2020)
	The fruit and leaf extracts of *Tamarindus indica* L.	5–10 nm/ spherical	Photocatalytic and antibacterial activity	Zaman et al. (2020)
	Moringa oleifera leaves extract	6 and 61 nm/ spherical	Water treatment	Galan et al. (2018)
	Ailanthus altissima leaf aqueous extract	20 nm/ spherical shapes.	Antibacterial activity	Awwad and Amer (2020)

is shown extracts from different parts of plants (flower, fruits, leaves, etc.), organic molecules, fungi, and vegetables. It is important to highlight that in these biosynthesis processes the organic agents reported act as reducing and capping agents for the nanomaterials, without the need to use another chemical component for synthesis. Most of the nanoparticles mentioned in Table 1 have sizes smaller than 100 nm and have important applications in catalysis, treatment of tumor diseases, and antifungal and antibacterial agents.

In general, the functional groups present in the extracts used in nanoparticle biosynthesis processes are identified by FT-IR. This technique studies the interaction of infrared radiation with the sample in which the molecules absorb the frequencies that are characteristic of their structure, reflecting vibrations of the groups of atoms. It is a spectroscopy technique widely used for the characterization of different compounds in organic synthesis, polymer science, food analysis, among other areas (Mukhopadhyay, 2003). For example, among the bands that are commonly identified correspond to the carboxyl group, with C=O stretching bands at 1700 cm^{-1} and –COOH at 3500 cm^{-1}. Sharma et al. reported the synthesis of CuO nanoparticles with *Calotropis gigantea* leaf extract identifying by FT-IR analysis absorption peaks at 1591 and 3432 cm^{-1} due to bending and stretching vibrations of adsorbed water and surface hydroxyl groups (Sharma et al., 2015). Also, different types of biological molecules within *P. granatum* seed extract were reported as reducing agents during the formation of CuNPs nanoparticles and then as stabilizing and capping agents to protect nanoparticles from degradation in the air (Nazar et al., 2018). They used the FT-IR technique to identify the functional groups in *P. granatum* seed extract and found a broad peak at 3229 cm^{-1} corresponding to the OH group characteristic of polyphenolic compounds, another peak at 2900 cm^{-1} from C–H stretching, and peaks at 1573 cm^{-1}, 1600 cm^{-1} and 1073 cm^{-1} due to aromatic compounds in phenols and C–O stretching of alcohols and carboxylic groups. In a similar report, large-scale synthesis of Cu nanoparticles using nontoxic and inexpensive materials like curd, milk, and herbal extracts such as tamarind and lemon juice as capping agents was reported. By FT-IR analysis they determined that the C=O, O–H, C–O stretching frequencies are due to the presence of carboxylic acids present on the surface of copper nanoparticles (Sastry et al., 2013).

3 Antibacterial activity of Cu and CuO nanoparticles

Due to their high surface area-to-volume ratio and crystallographic structure, the nanoparticles have different optical, magnetic, electrical, catalytic, and biological properties from their bulk counterparts (Martinez-Nuñez et al., 2018; Delgado-Beleño et al., 2018). The surface area of nanoparticles has been reported to be in the range 24–265.33 m^2/g, and this feature enhances their reactive side as a relevant property for catalytic reactivity. Dealba-Montero et al. reported that the antimicrobial activity of nanoparticles is most effective when the NPs have a very high surface area to volume ratio (Dealba-Montero et al., 2017; Din et al., 2017). Au and Ag metal nanoparticles (Castellano et al., 2007; Delgado-Beleño et al., 2018) are widely studied as

antimicrobial agents due to their favorable response to kill or slow down the growth of phytopathogens and multidrug-resistant bacteria (Taran et al., 2017). Recently, research on Cu and CuO nanoparticles and their applications as antibacterial agents have increased due to their bioavailability and low-cost production compared to other metal nanoparticles. On the other hand, CuNPs and CuO NPs have surface areas of 24–30 and 52.6 m^2/g with particle sizes between 20–45 nm and 2–6 nm, respectively. This feature provides a highly efficient surface for antibacterial activity (Ponce and Klabunde, 2005; Singh et al., 2019). Moreover, CuNPs and CuONPs synthesized by green methods have been reported to present lower toxicity in humans, animals, and plants (Tran et al., 2017; El-Refai et al., 2018). Consequently, nanoparticles obtained by ecological methods with antibacterial properties are prominent for applications in agriculture, animal husbandry, medicine, and the food industry. Recently, cotton fibers impregnated with CuNPs and CuONPs were shown to have favorable antibacterial properties (Xu et al., 2018; Vasantharaj et al., 2019). Mejía et al. reported the antibacterial activity of titanium-aluminum nitride coatings doped with silver and copper nanoparticles against two of the main pathogens associated with infections frequently found in hospital environments: *Staphylococcus aureus* and *Escherichia coli* (Mejía et al., 2019). Also, CuNPs and Cu/Ni NPs have been used in dental materials for their antibacterial properties on dental pathogens (Argueta-Figueroa et al., 2014). CuONPs have been applied in food packaging and the development of antibacterial masks (Hashmi et al., 2019; Peighambardoust et al., 2019). On the other hand, the influence of the size and morphology of CuNPs and CuONPs nanoparticles on the antibacterial response and the mechanisms behind their bacteriostatic action should be considered.

Majumdar et al. compared the antibacterial activity of CuNPs with sizes 18, 24, 28, and 33 nm against *Xanthomonas oryzae* pv. *oryzae*, which is a bacterium that causes a devastating disease in rice (Majumdar et al., 2019). The research showed that nanoparticles with a size of 28 nm presented a better antibacterial response. The research showed that for nanoparticles that are larger than 33 nm in size, the antibacterial activity decreases due to the agglomeration of the nanoparticles. Zakharova et al. showed that the bacteriostatic action of copper nanoparticles is most effective when the nanoparticle sizes go from 100 to 50 nm (Zakharova et al., 2015).

The shape-dependent antibacterial activity is not yet clear. The predominant shape in most literature reports on the synthesis of Cu and CuO nanoparticles are spherical geometries. However, it has been reported that plate-shaped CuO nanomaterials showed higher antibacterial activity compared to grain-shaped or needle-shaped CuO NPs (Ananth et al., 2015). Furthermore, Laha et al. reported that spherical-shaped CuO NPs showed higher antibacterial activity against Gram-positive bacteria, while sheet-shaped CuONPs showed higher responses against Gram-negative bacteria (Laha et al., 2014). Furthermore, the cytotoxicity of CuNPs and CuONPs is closely related to the concentration of copper salt used in the synthesis process and to the bacterial strains used for the assay. Table 2 shows reports on the minimum inhibitory concentration (MIC) and minimum bactericidal concentration (MBC) of Cu and CuO nanoparticles obtained at a molar concentration of 0.1, 0.005, and 0.3. CuNPs presented a bacteriostatic action with doses lower than 5 $\mu g\ mL^{-1}$ and CuO

Table 2 MIC and MBC of Cu and CuO nanoparticles of Gram-negative and Gram-positive bacteria.

Nanoparticles	Concentration of salt (M)	Bacteria	MIC (μg/mL)	MBC (μg/mL)	References
Cu	0.1	*S. aureus* (+)	3.2	4.3	Valodkar et al. (2012)
		E. coli (–)	1.6	2.1	
		Salmonella typhi (–)	3.6	4.9	
	0.1	*E. coli* (–)	7.5	3.0	Chatterjee et al. (2012)
CuO	0.3	*S. aureus* (+)	6.12	12.5	Yousefvand et al. (2021)
		E. coli (–)	3.12	6.25	
		P. aeruginosa (–)	12.5	25	
	0.005	*E. coli* (–)	16	18.5	Gopinath et al. (2016)
		P. aeruginosa (–)	17.5	19	
		S. aureus (+)	19.5	22.5	
		B. cereus (+)	21	24	

NPs a higher concentration of nanoparticles per mL. The action of nanomaterials on the bacterial cell wall is still under investigation.

Three mechanisms have been reported to explain the antibacterial action effect of Cu and CuO nanoparticles to inhibit and kill bacteria. The first and most suggested one consists of the generation of reactive oxygen species (ROS) such as superoxide anion (O_2^-), hydroxyl radicals (OH^-), and hydrogen peroxide (H_2O_2) from Cu and CuO NPs. Another theory suggests that the gradual release of ions from the nanoparticles causes a degradation of the antioxidant capacity of the bacteria, inactivating their metabolic function. Finally, the destruction of the bacterial cell wall due to the accumulation of NPs and penetration into the cytoplasmic/periplasmic region causes a structural change and subsequent death of the bacteria. Regarding the ROS generation mechanism from nanoparticles, Chatterjee et al. reported that CuNPs cause multiple toxic effects such as lipid peroxidation, protein oxidation, and DNA degradation inhibiting some important functions in *E. coli* bacteria and causing cell death (Chatterjee et al., 2014). Chatterjee compared the ROS level of untreated cells of *E. coli* with treated cells to concentrations of 3.0 μg mL^{-1} (MIC) and 7.5 μg mL^{-1} (MBC) of copper nanoparticles and found amounts of ROS 1.8 and 2.5 higher on treated cells. Besides, treated cells with copper salt present an insignificant ROS, suggesting that the high level of ROS in cells of *E. coli* are induced by the nanoparticles and not the copper ions. Additionally, lipid peroxidation by ROS occurs due to the removal of a hydrogen atom from the methylene group in a polyunsaturated fatty acid by superoxide anion and hydroxyl radicals,

leaving an unpaired electron on the carbon atom. Then, the carbon atom rearranges into a conjugated diene, which reacts with oxygen to form a peroxy radical (Janero, 1990). Concerning CuO nanoparticles, it has been reported to be accumulated in the cell membrane/wall causing morphological changes and membrane/wall damage, generating intracellular ROS, mainly superoxide anions. The membrane damage causes a massive loss of intracellular compounds like adenosine triphosphate (ATP) an important coenzyme that provides energy to drive many processes in bacteria, leading to oxidative stress and subsequent cellular death (Applerot et al., 2012). On the other hand, the accumulation of the NPs on the bacterial cell wall resulted in the formation of cavities/pits, subsequently, the nanoparticles penetrating the cytoplasm region causing the release of intracellular components such as small potassium ions, phosphate, DNA, and RNA molecules (Meghana et al., 2015). Also, the intracellular nanoparticles disrupt cell function thereby affecting proteins and DNA. Finally, the last mechanism of bacteriostatic action of Cu and CuO nanoparticles suggests that the release of ions from nanoparticles can combine with plasma membrane by the adhesion of the bacteria with copper ions. The ions attached to the cell wall and altering the permeability of the membrane, which causes leakage of intracellular ions and low molecular weight metabolites. Also, copper ions are released and absorbed into the cytoplasm leading to their destruction and degradation (Raffi et al., 2010). The adhesion of the NPs to the bacterial cell wall is due to the opposite electrical charges between the NPs and the bacteria. The overall charge of the bacterial cells is negative due to the excess of carboxyl groups present on the bacterial surface lipoproteins and the copper components release Cu^{2+} ions. A representative scheme of the different mechanisms of action of the cytotoxicity of Cu and CuO NPs is shown in Fig. 3. The antibacterial activity of CuNPs is probably due to more than one mechanism (Majumdar et al., 2019).

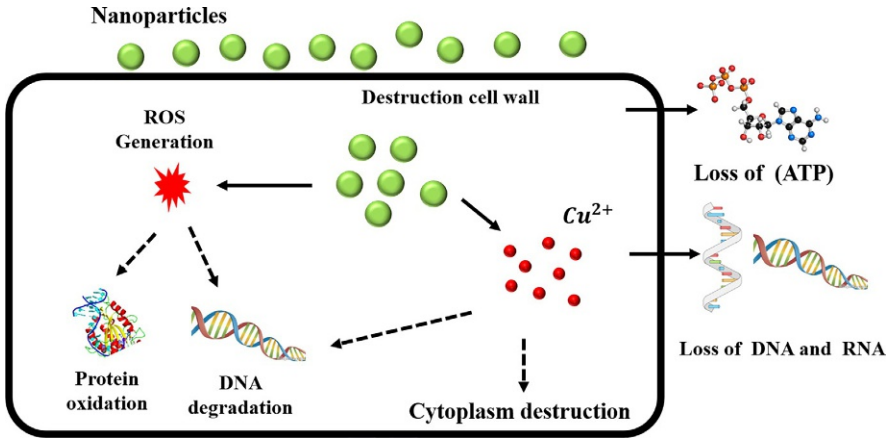

FIG. 3

Schematic diagram of the different mechanisms of cytotoxicity action of Cu and CuO nanoparticles.

4 Biological properties of Cu and CuO nanoparticles in food and plants

Copper is a chemical element commonly found in the earth surface, and underground, and almost every hydric source and could be present in different phases like dissolved, suspended, or sedimentary (Georgopoulos, 2011). Because of that, life on the planet has been evolved incorporating this essential element in several biological processes. Copper is known as a micronutrient, which means, a nutrient that is required in small concentrations, specifically less than 0.01% of the dry tissue weight. As a consequence, its presence is required for the proper growth of a great number of terrestrial and aquatic plants and the proper functioning of tissues and animal organs (Pinang, 1987; Rai et al., 2018). A significant amount of copper is present in chloroplasts, where it is found forming tight bonds with ligand parts of some amino acid functional groups constitutive of some plant proteins (Aguirre and Pilon, 2016). Besides, Cu ions play an important role in the process of synthesis of chlorophyll and other plant pigments. This means, copper is a preponderant element in the proper functioning of the photosynthesis process (Hewitt, 1979). Consequently, is relevant to determine the effects and consequences of the deficiency and excess of copper due to its role in plant metabolism. In this regard, copper deficiency can result in several diseases that could lead to poor growth and several problems to the suitable formation of seeds and fruits (Marschner, 2011; Rai et al., 2018).

Copper is a chemical nutrient essential in minimal concentrations (Wada, 2004; WHO Expert Committee on Trace Elements in Human Nutrition and World Health Organization, 1973). These nutrients play an essential role in maintaining the integrity of several physiological and metabolic processes involved in living tissues (Bhattacharya et al., 2016). Also, copper is present in almost every tissue of the human body and is vital to the proper functioning of a great number of metabolic enzymes and proteins. In the same way, is essential for the integrity of the tissue present in the skin, hair, and blood vessels. Similarly, to the epithelial and connective tissues throughout the body (Gropper and Smith, 2012; Harris, 2007). Besides, copper ions could act as an antioxidant, neutralizing oxygen radicals produced by aerobic metabolism, which can damage proteins, lipids, and DNA that may favor the development of several forms of cancer (Bhattacharya et al., 2016; Davis, 2003; Nelson et al., 1994). However, the health benefits of copper depend on an appropriate concentration in the organism. Consequently, the Cu deficiency could have a detrimental impact on the immune system as a result of its importance in some structural barriers such as the skin, mucus layers in the nasal passage, or the intestine (Bonham et al., 2002). On the other hand, the excess of Copper could be detrimental to the lifestyle of children and adults. Table 3, summarizes the function of Copper over some enzymes and the symptoms of its deficit and excess (Wada, 2004).

The Cu^{2+} oxidation state of copper is the most important and is easily bioavailable in water and soil (Georgopoulos, 2011; Levason and Spicer, 1987). Further, most copper ions in foods are found in a Cu^{2+} form usually bound to amino acids constituents of some food proteins but could be reduced simply to Cu^{1+} form due

Table 3 Functions of copper, symptoms of their deficiency, and excess states.

Trace element	Enzymes	Physiological functions	Symptoms of deficiency state	Symptoms of excess state
Copper	Ceruloplasmin Monoamine oxidase Cytochrome oxidase Ascorbic acid oxidase Dopamine β-hydroxylase Superoxide dismutase, etc.	Hemopoiesis Bone metabolism Connective tissue metabolism	Anemia Leukopenia Neutropenia Disturbed maturation of myeloleukocytes Bone changes (children): Reduced osseous age, irregular/spurring metaphysis, bone radiolucency, bone cortex thinning.	Nausea, vomiting, heartburn, diarrhea, jaundice, hemoglobinuria, hematuria, oliguria, anuria, hypotension, coma, melena

to the interaction with acidic environments like the gastric acid on the stomach, for instance. Later Cu^{1+} could be absorbed by the intestine and transported to different tissues and body organs, especially the liver and lung (Gropper and Smith, 2012). In particular, amino acids constituent of some proteins like albumin, which play an important role in human plasma, have a high affinity for copper ions, as consequence could be rapidly deposited in various organs like the liver (Gropper and Smith, 2012; Linder and Hazegh-Azam, 1996). The mechanism of copper interaction with organic and inorganic compounds constitutes the key to understand its biological properties. In this matter, a usual Cu interaction involves the catalysis by electron transfer of its accessible oxidation states (Cu^{1+} or Cu^{2+}) (Georgopoulos, 2011; Lund, 1986). The authors Clarkson and Hanson (Hanson, 1980) include copper in a nutrient group known as "prosthetic group," which means ions that could mediate as electron transfer and generally are attracted to the lone electron pair occurring especially with N, and S atoms (Hewitt, 1979). For instance, Cu ions usually tend to adopt a tetragonal geometry involving two bonds to N-histidine and S-methionine constitutive atoms of some ligand proteins (Marschner, 2011). Therefore, the sensing of the copper species, especially Cu^{2+} ions, has gathered great interest in chem-sensing and molecular imaging fields, due to the dynamics of ionic copper in several biological processes (Choi et al., 2009; Eckstein et al., 2019; Fan et al., 2012).

Zero-valent copper (Cu^0), like Cu nanoparticles (CuNPs), have different physical, chemical, and biological properties than ionic copper. These properties could vary according to their sizes, shapes, crystallinity, and aggregation, among other factors (Ameh and Sayes, 2019). Additionally, the CuNPs could have the ability to release

great numbers of ions under acid conditions. This reactivity with acid environments seems to be a common property in the different species of copper. As a result, this fact could lead to an increase in their reactivity against organic matter (Chen et al., 2006). In addition to the situation described before, the release of ions may be stimulated with a higher specific surface area, which indicates that ions concentration in acid environments may increase drastically over smaller and smaller sizes of CuNPs (Chen et al., 2006). Regarding, the proper use of this property might have a significant impact on specific applications in the food industry like bacterial and fungus growth control over crops and food conservation. Also, the toxic dose of CuNPs could be significantly lower than its ionic species in plants and animals (Ameh and Sayes, 2019). In this matter, considering a bit of context, around the world a meaningful portion of the crops is lost under the action of different diseases as a consequence of organisms and microorganisms like insects, bacteria, and fungus, among others (Rai et al., 2018). The development of alternatives to prevent these diseases avoiding the use of aggressive chemical agents that could be detrimental to the soil, hydric sources and human health is urgent and necessary for the next decades. Following the problem, Cu-based fungicide and bactericide like copper sulfate have been used to treat a diverse number of plant diseases and to promote its healthy growth (Borkow and Gabbay, 2005). The continuum advance and development of nanoscience and nanotechnology and its applications has brought a positive impact to different fields of human activities. In this sense, the nanotechnology application to agriculture has been used and is going to be used to preserve and improve food production over the next decades (Ismail et al., 2017; Mukhopadhyay, 2014; Shang et al., 2019; Singh Sekhon, 2014).In this matter, the preparation and implementation of different complexes, metallic surfaces, and nanostructured composites incorporating cupric ions have been used against various types of bacteria, fungus, and algae in applications of different fields. For instance, in medicine as medical treatments as pathogen growth control (Cady et al., 2011; Creaven et al., 2010; Santo et al., 2012; Srivastava, 2009). Besides, CuNPs with sizes inferior to 50 nm, have demonstrated to have a relevant antimicrobial activity comparable with commercial agrochemicals at low concentrations (Esteban-Tejeda et al., 2009; Online et al., 2013). Also, nanostructures of copper have proved to be more effective than another Cu-based inorganic compound controlling the growth of some types of bacteria (Rai et al., 2018).

Considering the negative effects on plants of the copper deficiency described in the previous section, the suitable soil treatment with CuNPs becomes an excellent way to improve the productivity of a great variety of crops. Fig. 4 summarizes some meaningful properties of CuNPs which constitutes the reason for its potential applications in different fields of science and industry. Therefore, it is easy to conclude that the use of CuNPs in agriculture is a powerful tool to prevent plant diseases and promote healthy plant growth and seed and fruit production without a second thought. However, caution needs to be taken according to the property CuNPs in acidic soils, where a higher concentration of cupric ions could be obtained. As a result, the environment might be affected negatively, and consequently, human health may be at risk (Du et al., 2018; Shah et al., 2016; Zuverza-Mena et al., 2015). Some reactions

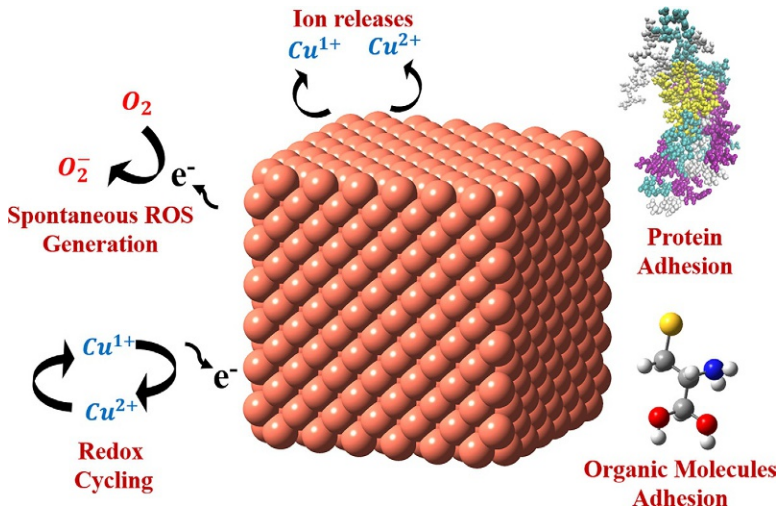

FIG. 4

Chemical and biochemical reactions of copper nanoparticles.

include oxidation of lipid or protein biomolecules, conjugation with proteins or organic molecules, dissolution into cupric ions, generation of reactive oxygen species (ROS), and REDOX cycling between Cu^{2+} and Cu^{1+} (Ameh and Sayes, 2019).

In the food industry, a lot of research has been made to develop techniques to contribute to the preservation of distinct alimentary products over the transportation process. Food processing and packaging, among others, are the keys to making raw food marketable with a long shelf life and nanotechnology has increased their effectiveness (Chellaram et al., 2014). In particular, the typical use of food packaging is maintaining the quality and safety over external physical, chemical, and biological agents preventing the interaction with the content. Although, the new active and intelligent food packaging techniques allow the interaction with food and the environment to delay oxidation, control the respiration rate, and control microbial growth, among other factors (Brody et al., 2008). In this sense, the bactericide properties of composites containing CuNPs have been studied to prepare an effective system to be used to obtain materials to be implemented as active food packaging to improve the preservation (Longano et al., 2012). Similarly, other studies report the use of films loaded with CuNPs to be used in food packaging due to their excellent antimicrobial activity and mechanical stability while reducing the water vapor permeability (dos Santos et al., 2020; Ebrahimiasl and Rajabpour, 2015). The research of the properties of metallic nanoparticles continues and their use in the food industry is vital to avoid the implementation of strong chemical agents or antibiotics to extend the shelf life of the food products.

Another copper species is the copper oxide (CuO) (Chang et al., 2011; Jadhav et al., 2011) or its less stable form di-copper oxide (Cu_2O) (Chen et al., 2005; Zhu et al., 2013). Especially the more stable species CuO with nanometric sizes manifest

interesting properties to be used in different fields of science and industry. The nanoparticles of CuO (CuONPs) have different physical, chemical, and biological properties than ionic copper, and properties similar to CuNPs. In particular, agricultural products such as fertilizers and pesticides incorporating CuONPs have been used to control some plant pathogen due to their ability to release ions under certain conditions (Ameh and Sayes, 2019). In another hand, it reported the concentration-dependency efficiency of CuONPs with a size less than 50 nm, enhances the seed germinations on some plant species like soybean and chickpea (Adhikari et al., 2012; Rai et al., 2018). Similarly, root and shoot biomass show meaningful increase under concentrations between 60 and 100 ppm. However, it could be toxic for concentrations over 2000 ppm (Adhikari et al., 2012; Rai et al., 2018). On another hand, metallic oxide nanoparticles manifest similar antimicrobial properties to metallic nanoparticles and have been studied in the control of foodborne pathogens to be implemented in food packaging techniques (Brody et al., 2008; Espitia et al., 2012). Besides, a metal oxide sensor has been implemented to evaluate the food quality due to the sensing of different parameters especially gases from rotten or spoiled food like fish and animal products (Galstyan et al., 2018). CuONPs have additional properties as antifungal agents and antioxidant capabilities similar to the CuNPs, among others, make them prominent to be implemented in food industry applications. For instance, food pathogens control in the active food packaging techniques and gas sensing for food quality control (Brody et al., 2008; Creaven et al., 2010; Das et al., 2013; Esteban-Tejeda et al., 2009; Meghana et al., 2015; Santo et al., 2012). In particular to the poultry industry, the efficacy of CuONPs again foodborne pathogens concerning *Salmonella* and *Campylobacter* has been investigated along with Ag and ZnO nanoparticles (Duffy et al., 2018). The study shows an excellent response again the bacteria *Campylobacter*, however, shows inefficiencies again *Salmonella* due to its Cu resistance mechanism, which could be involved in the CuONPs resistance (Duffy et al., 2018).

The biological properties of copper species are based on the suitable balance between essentiality and toxicity (Georgopoulos, 2011). The natural availability of copper species in the environment does not represent a special risk to the terrestrial and aquatic ecosystem. However, the engineered Cu nanoparticles prevenient to human activities could be detrimental to bacterial communities due to their affinity for soil surfaces and the impact could be higher as a consequence of the reactivity with acid soils (Shah et al., 2016). Besides, the ability of soil to remove organic pollutants could be compromised, resulting in secondary problems related to their accumulation. Additionally, some bacterial communities resistant to Cu may proliferate destroying the environmental balance (Shah et al., 2016). Respecting the human hazards of CuNPs, relatively larger particles can persist in lung tissues for long periods which can lead to oxidative stress and inflammatory response (Ameh and Sayes, 2019). Human activities develop in industrial facilities could expose human beings to high levels of copper species especially for the respiratory tract. Similarly, the gastrointestinal tract is also a potential route of entry of copper and under the reaction with gastric acid, increases the ionic levels on the body producing abnormal

functions in some organs like the liver (Ameh and Sayes, 2019). Other studies show that CuONPs can release Cu ions which generate reactive oxygen species producing damages to mitochondria and DNA of human lung cells (Hanagata et al., 2011). On another hand, some plant species studies, for instance, cilantro, reveal the negative effects over the seed germination and the biomass due to the exposure to nano and bulk of Cu and CuO. According to this study, exposure of cilantro to copper species at 80 mg kg^{-1} does not significantly affect Cu concentration in the root. However, the concentration in shoots could be significant and could reduce elongation by more than 11% (Zuverza-Mena et al., 2015). Comparative studies show the negative effects like the water content, biomass, nutritional quality, and genotoxicity over other plant species like oregano and cucumber (Du et al., 2018; Mosa et al., 2018).

The mining industry usually constitutes an important source of heavy metals that pollute hydric sources and consequently, terrestrial and aquatic biota might be in danger. Higher levels of metals as cobalt (Co), nickel (Ni), manganese (Mn), and of course copper (Cu) have been measured in tissues of some aquatic plant species, over the dose considered toxic to plants (Samecka-Cymerman and Kempers, 2004). Although these plants were able to survive in highly contaminated sites, do not indicate that the ecosystem is usually able to adapt to the toxic effects of the higher concentration of heavy metals as a consequence of human activity. Copper, in particular, has been identified as one of the most toxic metals to aquatic organisms and ecosystems (Solomon, 2009). Higher concentrations of Cu in aquatic ecosystems could be directly detrimental to some biological functions of some varieties of plants, fish, and shellfish (Costa et al., 2018; Solomon, 2009).

5 Future perspective: Biosynthesis and applications of Cu and CuO nanoparticles

The physical and chemical properties of nanomaterials are highly attractive to enhance and improve different fields of basic sciences and technology. Nanoparticles are applied in the design and manufacture of more efficient devices, in the generation of clean and renewable energies, and are being used as drug carriers for the treatment of diseases. They are also used in paints, cosmetics, and textiles with antiviral and antibacterial properties. The physical and chemical properties of nanoparticles can be massively applied in agribusiness. For example, in soil preparation, plant growth, distribution, and preparation of products and pest control against phytopathogenic microorganisms. However, the most efficient synthesis processes for nanomaterials that offer stable particles with size and shape control are expensive and often require sophisticated equipment. Moreover, the inclusion of chemicals in the synthesis processes can be toxic to the environment and humans, which limits the applications of nanomaterials in different areas. Therefore, the development of clean, biocompatible, nontoxic methods for the synthesis of nanoparticles is necessary. An alternative solution to counteract the high costs and toxicity in the production of nanomaterials has been advancing in recent years and increasingly shows great

advances in nanoparticle synthesis processes. These synthesis processes, called eco-friendly, allow the chemical reduction and stabilization of nanoparticles with the ability to control size and shape. The ecological methods use extracts from different plants, vegetable extracts, algae, molecules found in living beings with antioxidant properties that are used as ion reducing agents to form agglomerates of nanometric sizes. Ecological synthesis methods are highly attractive for their simplicity and reproducibility. These "green" chemistry approaches do not require sophisticated equipment or high costs, are environmentally friendly and we believe they can help in future challenges concerning environmental care, sustainable development, and promising applications in the clinical field, as well as in the cosmetics, textile, and food industries. Much research is still needed to determine how toxic nanoparticles can be and the reactions they can have in the environment and when interacting with cells, blood, or the brain. Although there are no reported cases of diseases caused by the use of commercialized products containing nanoparticles. However, it is important to take due precautions, especially with food products or products that in any way come into contact with people's skin. Questions about the safety of nanoparticles are bound to arise, and these questions help us to come up with solutions. In food, nanoparticles show prominent applications, from seeding, preservation, and distribution. Products developed through nanotechnologies are expected to increase significantly. Therefore, the production of biosynthesized nanomaterials will be important for cost and environmental impact. With the progress of new research on the toxicity of biosynthesized nanomaterials, the interaction with safe nanoparticles could increase considerably. It is very probable that, soon, the ceilings of our homes, construction materials, paints, plants, pesticides, personal care products, our clothes and the food we consume will contain or have been processed with nanomaterials. Nanotechnological advances based on the green synthesis of nanomaterials will most probably generate production processes for nanomaterials that are safer for people, fauna, flora, and the environment.

It is very important to consider that, with the increase in nanotechnological applications, the production of nanoparticles that are economically accessible, efficient, and that have the resources available for their production will be required. In this sense, several nanomaterials are currently being synthesized and applied, such as metallic nanoparticles (silver, gold, platinum, copper) and their oxides, carbon-derived nanomaterials (graphene, carbon quantum dots, carbon nanotubes), semiconductor nanoparticles, nanoalloys, etc. We consider that, for practical purposes and industrial applications, among metallic materials, copper is a potentially exploitable element for nanotechnological applications. It is an inexpensive metal, with an accessible price, attractive properties, and applications. Copper is a noble metal, has high electrical conductivity, ductility, low oxidation states, and is a recyclable metal that does not degrade or lose its chemical or physical properties, and is an abundant material in nature. Copper has been used to innovate in renewable energy, energy efficiency, energy management, and transportation systems.

Copper has bactericidal properties, is found in many foods, and is vital for optimal health of the human body (considering the levels tolerated by the organism.

Excess copper can damage cells in the liver, kidneys, and brain, causing Wilson's disease). The antimicrobial properties of copper have been applied since ancient times in the manufacture of containers and as a water decontaminant and it is expected that, with nanotechnological advances, copper and copper oxide nanoparticles will play a greater role in sensor applications that can identify phytopathogenic bacteria and identify changes in food quality, antimicrobial agents, fungicides in agriculture, food packaging, among others. Fungi and phytopathogenic bacteria considerably affect the growth of plants, fruits, and during the distribution of foodstuffs, generating large economic losses. These losses could be minimized with the use of nanomaterials, wasted food will be essential to feed the ever-growing world population and decrease the prices of products since losses ultimately determine the final price given to consumers. Also, pathogens are harmful to health and can be transmitted through food ingestion. On the other hand, overuse of synthetic pesticides can cause soil damage that prevents it from functioning as a vital ecosystem that sustains plants, animals, and humans. CuNPs and CuONPs synthesized by environmentally friendly methods can be used as a new antibacterial and antifungal agent in agriculture to control plant and food pathogenic microorganisms. Researchers have found that copper ions detach from the surfaces of the nanoparticles and penetrate the cells causing damage to the cytoplasmic membrane causing oxidative stress, which produces alterations and damage to the enzymes, thus achieving the elimination of the pathogen. In this way, it is expected that copper nanoparticles and their oxides obtained by green synthesis will be applied to the soil and replace the excessive use of synthetic chemicals to achieve higher crop yields and improve postharvest treatments until they are marketed. The study of copper-based nanomaterials and their interaction with organic and inorganic matter will help for better application in different fields of science and industry in the coming decades. Nowadays, the food industry is facing serious challenges in different aspects from crop production risk or conservation during the transportation process, for instance. Climate change is also an important factor that aggravates the efforts to overcome these challenges. Efforts to develop methods and processes to be more efficient to fight the action of food pathogens against plants and agricultural products avoiding strong agrochemical products will characterize the nanomaterial research. Concerning this matter, the research in properties and application of the different copper species may be relevant to contribute to overcoming the difficulties describe before. Similarly, the negative impacts of the indiscriminate use of nanoparticles are going to be the motive of research as well. Engineered nanoparticles have proved to be dangerous to destroy the fragile equilibria between species in the ecosystem, especially microorganisms. In consequence, the future perspectives of the research are obtained knowledge to contribute to the advance of science and industry. Also, the optimization of techniques that implement nanomaterials to solve relevant problems we afront nowadays along with the preservation of the environment. The availability of large and important copper deposits, the abundant availability of natural resources to obtain nanoparticles using "green" methods, and the nanotechnological developments applied in different areas of science and industry, give us good reasons to consider that copper nanomaterials will be an element of vital importance for society in the future.

6 Conclusion

Copper and copper oxide nanoparticles have generated a great deal of interest in recent years for their different applications in science and industry due to their physicochemical properties. Physical and chemical methods are usually used for the synthesis of nanomaterials, but recently ecological methods for the synthesis of copper nanoparticles are emerging as an eco-friendly synthesis method. Biosynthesis of nanoparticles represents a low-cost and low-toxicity alternative method for obtaining biocompatible nanoparticles that can be applied against fungi and plant pathogenic bacteria in plants and food. CuNPs and CuONPs are effective inhibiting the growth of Gram-positive and Gram-negative bacteria. Copper nanoparticles obtained by biological methods have shown some promising results, and interesting applications and developments are expected in this field. The use of products that can be used in real life is still in the preliminary stages. Therefore, it is important to carry out further research on the toxic effects of nanotechnological products that interact with humans and the environment. Additionally, it is necessary to have control over the concentrations of nanomaterials recommended for use in agriculture.

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References

Abboud, Y., Saffaj, T., Chagraoui, A., El Bouari, A., Brouzi, K., Tanane, O., Ihssane, B., 2014. Biosynthesis, characterization and antimicrobial activity of copper oxide nanoparticles (CONPs) produced using brown alga extract (*Bifurcaria bifurcata*). Appl. Nanosci. 4, 571–576.

Adhikari, T., Kundu, S., Biswas, A.K., Kundu, S., Tarafdar, J.C., Rao, A.S., 2012. Effect of copper oxide nano particle on seed germination of selected crops. J. Agric. Sci. Technol. 2, 815–823.

Aguirre, G., Pilon, M., 2016. Copper delivery to chloroplast proteins and its regulation. Front. Plant Sci. 6, 1–10.

Ahamed, M., Alhadlaq, H.A., Khan, M.A.M., Karuppiah, P., Al-Dhabi, N.A., 2014. Synthesis, characterization, and antimicrobial activity of copper oxide nanoparticles. J. Nanomater, 1–4. ID 637858.

Ahmad, H., Venugopal, K., Bhat, A.H., Kavitha, K., Ramanan, A., Rajagopal, K., Srinivasan, R., Manikandan, E., 2020. Enhanced biosynthesis synthesis of copper oxide nanoparticles (CuO-NPs) for their antifungal activity toxicity against major phyto-pathogens of apple orchards. Pharm. Res. 37, 1–12.

Alishah, H., Pourseyedi, S., Ebrahimipour, S.Y., Mahani, S.E., Rafiei, N., 2017. Green synthesis of starch-mediated CuO nanoparticles: preparation, characterization, antimicrobial activities and in vitro MTT assay against MCF-7 cell line. Rend. Lincei 28, 65–71.

AlNadhari, S., Al-Enazi, N.M., Alshehrei, F., Ameen, F., 2021. A review on biogenic synthesis of metal nanoparticles using marine algae and its applications. Environ. Res. 194, 110672.

Amal, M.I., Wibowo, J.T., Nuraini, L., Senopati, G., Hasbi, M.Y., Priyotomo, G., 2019. Antibacterial activity of copper oxide nanoparticles prepared by mechanical milling. IOP Conf. Ser.: Mater. Sci. Eng. 578, 012039. Institute of Physics Publishing.

Amaliyah, S., Pangesti, D.P., Masruri, M., Sabarudin, A., Sumitro, S.B., 2020. Green synthesis and characterization of copper nanoparticles using *Piper retrofractum* Vahl extract as bioreductor and capping agent. Heliyon 6, e04636.

Ameh, T., Sayes, C.M., 2019. The potential exposure and hazards of copper nanoparticles: a review. Environ. Toxicol. Pharmacol. 71, 103220.

Amer, M.W., Awwad, A.M., 2021. Green synthesis of copper nanoparticles by *Citrus limon* fruits extract, characterization and antibacterial activity. Chem. Int. 7, 1–8.

Ammar, H.A., Rabie, G.H., Mohamed, E., 2019. Novel fabrication of gelatin-encapsulated copper nanoparticles using aspergillus versicolor and their application in controlling of rotting plant pathogens. Bioprocess Biosyst. Eng. 42, 1947–1961.

Ananth, A., Dharaneedharan, S., Heo, M.S., Mok, Y.S., 2015. Copper oxide nanomaterials: synthesis, characterization and structure-specific antibacterial performance. Chem. Eng. J. 262, 179–188.

Andualem, W.W., Sabir, F.K., Mohammed, E.T., Belay, H.H., Gonfa, B.A., 2020. Synthesis of copper oxide nanoparticles using plant leaf extract of *Catha edulis* and its antibacterial activity. J. Nanotechnol, 1–10. ID 2932434.

Applerot, G., Lellouche, J., Lipovsky, A., Nitzan, Y., Lubart, R., Gedanken, A., Banin, E., 2012. Understanding the antibacterial mechanism of CuO nanoparticles: revealing the route of induced oxidative stress. Small 8, 3326–3337.

Araya-Castro, K., Chao, T.C., Durán-Vinet, B., Cisternas, C., Ciudad, G., Rubilar, O., 2021. Green synthesis of copper oxide nanoparticles using protein fractions from an aqueous extract of brown algae *Macrocystis pyrifera*. Processes 9, 78.

Argueta-Figueroa, L., Morales-Luckie, R.A., Scougall-Vilchis, R.J., Olea-Mejía, O.F., 2014. Synthesis, characterization and antibacterial activity of copper, nickel and bimetallic Cu-Ni nanoparticles for potential use in dental materials. Prog. Nat. Sci. Mater. Int. 24, 321–328.

Arya, A., Gupta, K., Chundawat, T.S., Vaya, D., 2018. Biogenic synthesis of copper and silver nanoparticles using green alga *Botryococcus braunii* and its antimicrobial activity. Bioinorg. Chem. Appl., 1–9. ID 7879403.

Awwad, A.M., Amer, A.W., 2020. Biosynthesis of copper oxide nanoparticles using *Ailanthus altissima* leaf extract and antibacterial activity. Chem. Int. 6, 210–217.

Azam, A., Ahmed, A.S., Oves, M., Khan, M.S., Memic, A., 2012. Size-dependent antimicrobial properties of CuO nanoparticles against Gram-positive and -negative bacterial strains. Int. J. Nanomedicine 7, 3527.

Barai, K., Tiwary, C.S., Chattopadhyay, P.P., Chattopadhyay, K., 2012. Synthesis of free standing nanocrystalline Cu by ball milling at cryogenic temperature. Mater. Sci. Eng. A 558, 52–58.

Benassai, E., Del Bubba, M., Ancillotti, C., Colzi, I., Gonnelli, C., Calisi, N., Salvatici, M.C., Casalone, E., Ristori, S., 2021. Green and cost-effective synthesis of copper nanoparticles by extracts of non-edible and waste plant materials from Vaccinium species: characterization and antimicrobial activity. Mater. Sci. Eng. C 119, 111453.

Bhattacharya, P.T., Misra, S.R., Hussain, M., 2016. Nutritional aspects of essential trace elements in oral health and disease: an extensive review. Scientifica (Cairo) 2016, 1–12. ID 5464373.

Bhattacharya, P., Swarnakar, S., Ghosh, S., Majumdar, S., Banerjee, S., 2019. Disinfection of drinking water via algae mediated green synthesized copper oxide nanoparticles and its toxicity evaluation. J. Environ. Chem. Eng. 7, 102867.

Biçer, M., Şişman, I., 2010. Controlled synthesis of copper nano/microstructures using ascorbic acid in aqueous CTAB solution. Powder Technol. 198, 279–284.

Bogdanović, U., Lazić, V., Vodnik, V., Budimir, M., Marković, Z., Dimitrijević, S., 2014. Copper nanoparticles with high antimicrobial activity. Mater. Lett. 128, 75–78.

Boldyrev, V.V., 1993. Mechanochemistry and mechanical activation of solids. Solid State Ion. 537, 63–65.

Bonham, M., O'Connor, J.M., Hannigan, B.M., Strain, J.J., 2002. The immune system as a physiological indicator of marginal copper status? Br. J. Nutr. 87, 393–403.

Borkow, G., Gabbay, J., 2005. Copper as a biocidal tool. Curr. Med. Chem. 12, 2163–2175.

Brody, A.L., Bugusu, B., Han, J.H., Sand, C.K., McHugh, T.H., 2008. Innovative food packaging solutions. J. Food Sci. 73, 107–116.

Bulut Kocabas, B., Attar, A., Peksel, A., Altikatoglu Yapaoz, M., 2021. Phytosynthesis of CuONPs via *Laurus nobilis*: determination of antioxidant content, antibacterial activity, and dye decolorization potential. Biotechnol. Appl. Biochem. 68, 889–895.

Cady, N.C., Behnke, J.L., Strickland, A.D., 2011. Copper-based nanostructured coatings on natural cellulose: nanocomposites exhibiting rapid and efficient inhibition of a multi-drug resistant wound pathogen, *A. baumannii*, and mammalian cell biocompatibility in vitro. Adv. Funct. Mater. 21, 2506–2514.

Castellano, J.J., Shafii, S.M., Ko, F., Donate, G., Wright, T.E., Mannari, R.J., Payne, W.G., Smith, D.J., Robson, M.C., 2007. Comparative evaluation of silver-containing antimicrobial dressings and drugs. Int. Wound J. 4, 114–122.

Chang, M.H., Liu, H.S., Tai, C.Y., 2011. Preparation of copper oxide nanoparticles and its application in nanofluid. Powder Technol. 207, 378–386.

Chatterjee, A.K., Sarkar, R.K., Chattopadhyay, A.P., Aich, P., Chakraborty, R., Basu, T., 2012. A simple robust method for synthesis of metallic copper nanoparticles of high antibacterial potency against *E. coli*. Nanotechnology 23, 085103.

Chatterjee, A.K., Chakraborty, R., Basu, T., 2014. Mechanism of antibacterial activity of copper nanoparticles. Nanotechnology 25, 135101.

Chellaram, C., Murugaboopathi, G., John, A.A., Sivakumar, R., Ganesan, S., Krithika, S., Priya, G., 2014. Significance of nanotechnology in food industry. APCBEE Proc. 8, 109–113.

Chen, C.H., Yamaguchi, T., Sugawara, K.I., Koga, K., 2005. Role of stress in the self-limiting oxidation of copper nanoparticles. J. Phys. Chem. B 109, 20669–20672.

Chen, Z., Meng, H., Xing, G., Chen, C., Zhao, Y., Jia, G., Wang, T., Yuan, H., Ye, C., Zhao, F., Chai, Z., Zhu, C., Fang, X., Ma, B., Wan, L., 2006. Acute toxicological effects of copper nanoparticles in vivo. Toxicol. Lett. 163, 109–120.

Cherian, T., Ali, K., Saquib, Q., Faisal, M., Wahab, R., Musarrat, J., 2020. *Cymbopogon citratus* functionalized green synthesis of CuO-nanoparticles: novel prospects as antibacterial and antibiofilm agents. Biomol. Ther. 10, 169.

Choi, M.G., Cha, S., Lee, H., Jeon, H.L., Chang, S.K., 2009. Sulfide-selective chemosignaling by a Cu^{2+} complex of dipicolylamine appended fluorescein. Chem. Commun. 47, 7390–7392.

Costa, M.B., Tavares, F.V., Martinez, C.B., Colares, I.G., de Martins, C.M.G., 2018. Accumulation and effects of copper on aquatic macrophytes *Potamogeton pectinatus* L.: potential application to environmental monitoring and phytoremediation. Ecotoxicol. Environ. Saf. 155, 117–124.

Creaven, B.S., Duff, B., Egan, D.A., Kavanagh, K., Rosair, G., Thangella, V.R., Walsh, M., 2010. Anticancer and antifungal activity of copper(II) complexes of quinolin-2(1H)-one-derived Schiff bases. Inorg. Chim. Acta 363, 4048–4058.

Cuevas, R., Durán, N., Diez, M.C., Tortella, G.R., Rubilar, O., 2015. Extracellular biosynthesis of copper and copper oxide nanoparticles by *Stereum hirsutum*, a native white-rot fungus from Chilean forests. J. Nanomater., 1–7. ID 789089.

Das, D., Nath, B.C., Phukon, P., Dolui, S.K., 2013. Synthesis and evaluation of antioxidant and antibacterial behavior of CuO nanoparticles. Colloids Surf. B Biointerfaces 101, 430–433.

Davis, C.D., 2003. Low dietary copper increases fecal free radical production, fecal water alkaline phosphatase activity and cytotoxicity in healthy men. J. Nutr. 133, 522–527.

De Silva, K.K.H., Huang, H.H., Joshi, R.K., Yoshimura, M., 2017. Chemical reduction of graphene oxide using green reductants. Carbon 119, 190–199.

Dealba-Montero, I., Guajardo-Pacheco, J., Morales-Sánchez, E., Araujo-Martínez, R., Loredo-Becerra, G.M., Martínez-Castañón, G.A., Ruiz, F., Jasso, M.E.C., 2017. Antimicrobial properties of copper nanoparticles and amino acid chelated copper nanoparticles produced by using a soya extract. Bioinorg. Chem. Appl. 2017, 15–17.

Delgado-Beleño, Y., Martinez-Nuñez, C.E., Cortez-Valadez, M., Flores-López, N.S., Flores-Acosta, M., 2018. Optical properties of silver, silver sulfide and silver selenide nanoparticles and antibacterial applications. Mater. Res. Bull. 99, 385–392.

Devipriya, D., Roopan, S.M., 2017. *Cissus quadrangularis* mediated ecofriendly synthesis of copper oxide nanoparticles and its antifungal studies against *Aspergillus niger*, *Aspergillus flavus*. Mater. Sci. Eng. C 80, 38–44.

Din, M.I., Arshad, F., Hussain, Z., Mukhtar, M., 2017. Green adeptness in the synthesis and stabilization of copper nanoparticles: catalytic, antibacterial, cytotoxicity, and antioxidant activities. Nanoscale Res. Lett. 12, 638.

Dizajghorbani Aghdam, H., Azadi, H., Esmaeilzadeh, M., Moemen Bellah, S., Malekfar, R., 2019. Ablation time and laser fluence impacts on the composition, morphology and optical properties of copper oxide nanoparticles. Opt. Mater. 91, 433–438.

dos Santos, C.A., Ingle, A.P., Rai, M., 2020. The emerging role of metallic nanoparticles in food. Appl. Microbiol. Biotechnol. 104, 2373–2383.

Du, W., Tan, W., Yin, Y., Ji, R., Peralta-Videa, J.R., Guo, H., Gardea-Torresdey, J.L., 2018. Differential effects of copper nanoparticles/microparticles in agronomic and physiological parameters of oregano (*Origanum vulgare*). Sci. Total Environ. 618, 306–312.

Duan, H., Wang, D., Li, Y., 2015. Green chemistry for nanoparticle synthesis. Chem. Soc. Rev. 44, 5778–5792.

Duffy, L.L., Osmond-McLeod, M.J., Judy, J., King, T., 2018. Investigation into the antibacterial activity of silver, zinc oxide and copper oxide nanoparticles against poultry-relevant isolates of *Salmonella* and *Campylobacter*. Food Control 92, 293–300.

Ebrahimiasl, S., Rajabpour, A., 2015. Synthesis and characterization of novel bactericidal cu/HPMC BNCs using chemical reduction method for food packaging. J. Food Sci. Technol. 52, 5982–5988.

Eckstein, C., Law, C.S., Lim, S.Y., Kaur, S., Kumeria, T., Ferré-Borrull, J., Abell, A.D., Marsal, L.F., Santos, A., 2019. Nanoporous photonic crystals with tailored surface chemistry for ionic copper sensing. J. Mater. Chem. C 7, 12278–12289.

El-Batal, A.I., Al-Hazmi, N.E., Mosallam, F.M., El-Sayyad, G.S., 2018. Biogenic synthesis of copper nanoparticles by natural polysaccharides and *Pleurotus ostreatus* fermented fenugreek using gamma rays with antioxidant and antimicrobial potential towards some wound pathogens. Microb. Pathog. 118, 159–169.

El-Batal, A.I., El-Sayyad, G.S., Mosallam, F.M., Fathy, R.M., 2020. *Penicillium chrysogenum*-mediated mycogenic synthesis of copper oxide nanoparticles using gamma rays for in vitro antimicrobial activity against some plant pathogens. J. Clust. Sci. 31, 79–90.

El-Refai, A.A., Ghoniem, G.A., El-Khateeb, A.Y., Hassaan, M.M., 2018. Eco-friendly synthesis of metal nanoparticles using ginger and garlic extracts as biocompatible novel antioxidant and antimicrobial agents. J. Nanostruct. Chem. 8, 71–81.

Espitia, P.J.P., de Soares, N.F.F., dos Coimbra, J.S.R., de Andrade, N.J., Cruz, R.S., Medeiros, E.A.A., 2012. Zinc oxide nanoparticles: synthesis, antimicrobial activity and food packaging applications. Food Bioprocess Technol. 5, 1447–1464.

Esteban-Tejeda, L., Malpartida, F., Esteban-Cubillo, A., Pecharromn, C., Moya, J.S., 2009. Antibacterial and antifungal activity of a soda-lime glass containing copper nanoparticles. Nanotechnology 20, 505701.

Fan, J., Liu, X., Hu, M., Zhu, H., Song, F., Peng, X., 2012. Development of an oxidative dehydrogenation-based fluorescent probe for Cu^{2+} and its biological imaging in living cells. Anal. Chim. Acta 735, 107–113.

Flemming, C.A., Trevors, J.T., 1989. Copper toxicity and chemistry in the environment: a review. Water Air Soil Pollut. 44, 143–158.

Fröhlich, E., Roblegg, E., 2012. Models for oral uptake of nanoparticles in consumer products. Toxicology 291, 10–17.

Galan, C.R., Silva, M.F., Mantovani, D., Bergamasco, R., Vieira, M.F., 2018. Green synthesis of copper oxide nanoparticles impregnated on activated carbon using *Moringa oleifera* leaves extract for the removal of nitrates from water. Can. J. Chem. Eng. 96, 2378–2386.

Galstyan, V., Bhandari, M.P., Sberveglieri, V., Sberveglieri, G., Comini, E., 2018. Metal oxide nanostructures in food applications: quality control and packaging. Chem. Aust. 6, 1–21.

Gawande, M.B., Goswami, A., Felpin, F.X., Asefa, T., Huang, X., Silva, R., Zou, X., Zboril, R., Varma, R.S., 2016. Cu and Cu-based nanoparticles: synthesis and applications in catalysis. Chem. Rev. 116, 3722–3811.

Georgopoulos, P.G., 2011. Environmental copper: its dynamics and human. J. Toxicol. Environ. Health 4, 37–41.

Ghosh, M.K., Sahu, S., Gupta, I., Ghorai, T.K., 2020. Green synthesis of copper nanoparticles from an extract of *Jatropha curcas* leaves: characterization, optical properties, CT-DNA binding and photocatalytic activity. RSC Adv. 10, 22027–22035.

Gnanavel, V., Palanichamy, V., Roopan, S.M., 2017. Biosynthesis and characterization of copper oxide nanoparticles and its anticancer activity on human colon cancer cell lines (HCT-116). J. Photochem. Photobiol. B Biol. 171, 133–138.

Goncharova, D.A., Kharlamova, T.S., Lapin, I.N., Svetlichnyi, V.A., 2019. Chemical and morphological evolution of copper nanoparticles obtained by pulsed laser ablation in liquid. J. Phys. Chem. C 123, 21731–21742.

Gopinath, V., Priyadarshini, S., Al-Maleki, A.R., Alagiri, M., Yahya, R., Saravanan, S., Vadivelu, J., 2016. In vitro toxicity, apoptosis and antimicrobial effects of phyto-mediated copper oxide nanoparticles. RSC Adv. 6, 110986–110995.

Gropper, S.S., Smith, J.L., 2012. Advanced Nutrition and Human Metabolism. Cengage Learning.

Gunalan, S., Sivaraj, R., Venckatesh, R., 2012. *Aloe barbadensis* Miller mediated green synthesis of mono-disperse copper oxide nanoparticles: optical properties. Spectrochim. Acta A Mol. Biomol. Spectrosc. 97, 1140–1144.

Hanagata, N., Zhuang, F., Connolly, S., Li, J., Ogawa, N., Xu, M., 2011. Molecular responses of human lung epithelial cells to the toxicity of copper oxide nanoparticles inferred from whole genome expression analysis. ACS Nano 5, 9326–9338.

Hanson, J.B., 1980. The mineral nutrition of higher plants. Annu. Rev. 31, 239–298.

Harne, S., Sharma, A., Dhaygude, M., Joglekar, S., Kodam, K., Hudlikar, M., 2012. Novel route for rapid biosynthesis of copper nanoparticles using aqueous extract of *Calotropis procera* L. latex and their cytotoxicity on tumor cells. Colloids Surf. B Biointerfaces 95, 284–288.

Harris, E.D., 2007. Copper homeostasis: the role of cellular transporters. Nutr. Rev. 59, 281–285.

Hasheminya, S.M., Dehghannya, J., 2020. Green synthesis and characterization of copper nanoparticles using *Eryngium caucasicum* Trautv aqueous extracts and its antioxidant and antimicrobial properties. Part. Sci. Technol. 9, 284–288.

Hashmi, M., Ullah, S., Kim, I.S., 2019. Copper oxide (CuO) loaded polyacrylonitrile (PAN) nanofiber membranes for antimicrobial breath mask applications. Curr. Res. Biotechnol. 1, 1–10.

Hewitt, E.J., 1979. Principles of plant nutrition. Nature 278, 101.

Iravani, S., 2011. Green synthesis of metal nanoparticles using plants. Green Chem. 13, 2638–2650.

Ismail, M., Prasad, R., Ibrahim, A.I.M., Ahmed, A.I.S., 2017. Modern Prospects of Nanotechnology in Plant Pathology. Springer, Singapore, pp. 305–317.

Issaabadi, Z., Nasrollahzadeh, M., Sajadi, S.M., 2017. Green synthesis of the copper nanoparticles supported on bentonite and investigation of its catalytic activity. J. Clean. Prod. 142, 3584–3591.

Jadhav, S., Gaikwad, S., Nimse, M., Rajbhoj, A., 2011. Copper oxide nanoparticles: synthesis, characterization and their antibacterial activity. J. Clust. Sci. 22, 121–129.

Janero, D.R., 1990. Malondialdehyde and thiobarbituric acid-reactivity as diagnostic indices of lipid peroxidation and peroxidative tissue injury. Free Radic. Biol. Med. 9, 515–540.

Javed, R., Zia, M., Naz, S., Aisida, S.O., Ain, N.U., Ao, Q., 2020. Role of capping agents in the application of nanoparticles in biomedicine and environmental remediation: recent trends and future prospects. J. Nanobiotechnol. 18, 1–15.

Jayarambabu, N., Akshaykranth, A., Venkatappa Rao, T., Venkateswara Rao, K., Rakesh Kumar, R., 2020. Green synthesis of Cu nanoparticles using *Curcuma longa* extract and their application in antimicrobial activity. Mater. Lett. 259, 126813.

Kanhed, P., Birla, S., Gaikwad, S., Gade, A., Seabra, A.B., Rubilar, O., Duran, N., Rai, M., 2014. In vitro antifungal efficacy of copper nanoparticles against selected crop pathogenic fungi. Mater. Lett. 115, 13–17.

Kayalvizhi, S., Sengottaiyan, A., Selvankumar, T., Senthilkumar, B., Sudhakar, C., Selvam, K., 2020. Eco-friendly cost-effective approach for synthesis of copper oxide nanoparticles for enhanced photocatalytic performance. Optik 202, 163507.

Kayani, Z.N., Umer, M., Riaz, S., Naseem, S., 2015. Characterization of copper oxide nanoparticles fabricated by the sol–gel method. J. Electron. Mater. 44, 3704–3709.

Khanna, P.K., Gaikwad, S., Adhyapak, P.V., Singh, N., Marimuthu, R., 2007. Synthesis and characterization of copper nanoparticles. Mater. Lett. 61, 4711–4714.

Khashan, K.S., Sulaiman, G.M., Abdulameer, F.A., 2016. Synthesis and antibacterial activity of CuO nanoparticles suspension induced by laser ablation in liquid. Arab. J. Sci. Eng. 41, 301–310.

Kim, M., Osone, S., Kim, T., Higashi, H., Seto, T., 2017. Synthesis of nanoparticles by laser ablation: a review. KONA Powder Part. J., 2017009.

Kumar, P.P.N.V., Shameem, U., Kollu, P., Kalyani, R.L., Pammi, S.V.N., 2015. Green synthesis of copper oxide nanoparticles using *Aloe vera* leaf extract and its antibacterial activity against fish bacterial pathogens. Bionanoscience 5, 135–139.

Kumar, S., Bhushan, P., Bhattacharya, S., 2018. Fabrication of nanostructures with bottom-up approach and their utility in diagnostics, therapeutics, and others. In: Environmental, Chemical and Medical Sensors. Springer, Singapore, pp. 167–198.

Laha, D., Pramanik, A., Laskar, A., Jana, M., Pramanik, P., Karmakar, P., 2014. Shape-dependent bactericidal activity of copper oxide nanoparticle mediated by DNA and membrane damage. Mater. Res. Bull. 59, 185–191.

Lasio, B., Pia, G., Garroni, S., Orrù, R., Takacs, L., Delogu, F., 2018. Non-monotonic variation of the grain size in Cu nanopowders subjected to ball milling. Mater. Lett. 212, 171–173.

Lee, H.J., Song, J.Y., Kim, B.S., 2013. Biological synthesis of copper nanoparticles using *Magnolia kobus* leaf extract and their antibacterial activity. J. Chem. Technol. Biotechnol. 88, 1971–1977.

Levason, W., Spicer, M.D., 1987. The chemistry of copper and silver in their higher oxidation states. Coord. Chem. Rev. 76, 45–120.

LewisOscar, F., MubarakAli, D., Nithya, C., Priyanka, R., Gopinath, V., Alharbi, N.S., Thajuddin, N., 2015. One pot synthesis and anti-biofilm potential of copper nanoparticles (CuNPs) against clinical strains of *Pseudomonas aeruginosa*. Biofouling 31, 379–391.

Li, P.J., Liang, J.Y., Su, D.L., Huang, Y., Pan, J.J., Peng, M.F., Li, G.Y., Shan, Y., 2020. Green and efficient biosynthesis of pectin-based copper nanoparticles and their antimicrobial activities. Bioprocess Biosyst. Eng. 43, 2017–2026.

Linder, M.C., Hazegh-Azam, M., 1996. Copper biochemistry and molecular biology. Am. J. Clin. Nutr. 63, 797S–811S.

Longano, D., Ditaranto, N., Cioffi, N., Di Niso, F., Sibillano, T., Ancona, A., Conte, A., Del Nobile, M.A., Sabbatini, L., Torsi, L., 2012. Analytical characterization of laser-generated copper nanoparticles for antibacterial composite food packaging. Anal. Bioanal. Chem. 403, 1179–1186.

Lund, H., 1986. Catalysis by electron transfer reagents in organic electrochemistry. J. Mol. Catal. 38, 203–226.

Mafuné, F., Kohno, J.Y., Takeda, Y., Kondow, T., Sawabe, H., 2000. Formation and size control of silver nanoparticles by laser ablation in aqueous solution. J. Phys. Chem. B 104 (39), 9111–9117.

Mahapatra, O., Bhagat, M., Gopalakrishnan, C., Arunachalam, K.D., 2008. Ultrafine dispersed CuO nanoparticles and their antibacterial activity. J. Exp. Nanosci. 3, 185–193.

Majumdar, T.D., Singh, M., Thapa, M., Dutta, M., Mukherjee, A., Ghosh, C.K., 2019. Size-dependent antibacterial activity of copper nanoparticles against *Xanthomonas oryzae* pv. *oryzae*—a synthetic and mechanistic approach. Colloids Interface Sci. Commun. 32, 100190.

Makarov, V.V., Love, A.J., Sinitsyna, O.V., Makarova, S.S., Yaminsky, I.V., Taliansky, M.E., Kalinina, N.O., 2014. "Green" nanotechnologies: synthesis of metal nanoparticles using plants. Acta Nat. 6, 20.

Mali, S.C., Dhaka, A., Githala, C.K., Trivedi, R., 2020. Green synthesis of copper nanoparticles using *Celastrus paniculatus* Willd. leaf extract and their photocatalytic and antifungal properties. Biotechnol. Rep. 27, e00518.

Marschner, H., 2011. Mineral Nutrition of Higher Plants. Academic Press.

Martinez-Nuñez, C.E., Delgado-Beleño, Y., Cortez-Valadez, M., Flores-López, N.S., Flores-Acosta, M., Castillón-Barraza, F.F., 2018. Non-resonant enhancement mechanism in SERS effect due to copper oxide quantum dots stabilized in synthetic zeolite F9-NaX. Mater. Chem. Phys. 211, 150–159.

Meghana, S., Kabra, P., Chakraborty, S., Padmavathy, N., 2015. Understanding the pathway of antibacterial activity of copper oxide nanoparticles. RSC Adv. 5, 12293–12299.

Mejía, H.D., Echavarría, A.M., Bejarano, G., 2019. Influence of Ag-Cu nanoparticles on the microstructural and bactericidal properties of TiAlN(Ag,Cu) coatings for medical applications deposited by Direct Current (DC) magnetron sputtering. Thin Solid Films 687, 137460.

Mohajerani, A., Burnett, L., Smith, J.V., Kurmus, H., Milas, J., Arulrajah, A., Horpibulsuk, S., Kadir, A.A., 2019. Nanoparticles in construction materials and other applications, and implications of nanoparticle use. Materials (Basel) 12, 3052.

Mosa, K.A., El-Naggar, M., Ramamoorthy, K., Alawadhi, H., Elnaggar, A., Wartanian, S., Ibrahim, E., Hani, H., 2018. Copper nanoparticles induced genotoxicty, oxidative stress, and changes in superoxide dismutase (SOD) gene expression in cucumber (*Cucumis sativus*) plants. Front. Plant Sci. 9, 1–13.

Mukhopadhyay, S., 2003. FTIR spectroscopy—principles and applications. J. Text. Assoc. 64, 187–191.

Mukhopadhyay, S.S., 2014. Nanotechnology in agriculture: prospects and constraints. Nanotechnol. Sci. Appl. 7, 63–71.

Murthy, H.C.A., Desalegn, T., Kassa, M., Abebe, B., Assefa, T., 2020. Synthesis of green copper nanoparticles using medicinal plant *Hagenia abyssinica* (Brace) JF. Gmel. Leaf extract: antimicrobial properties. Gmel. Leaf extract: antimicrobial properties. J. Nanomater., 1–12. ID 3924081.

Nagajyothi, P.C., Muthuraman, P., Sreekanth, T.V.M., Kim, D.H., Shim, J., 2017. Green synthesis: in-vitro anticancer activity of copper oxide nanoparticles against human cervical carcinoma cells. Arab. J. Chem. 10, 215–225.

Naika, H.R., Lingaraju, K., Manjunath, K., Kumar, D., Nagaraju, G., Suresh, D., Nagabhushana, H., 2015. Green synthesis of CuO nanoparticles using *Gloriosa superba* L. extract and their antibacterial activity. J. Taibah Univ. Sci. 9, 7–12.

Nasrollahzadeh, M., Maham, M., Mohammad Sajadi, S., 2015a. Green synthesis of CuO nanoparticles by aqueous extract of *Gundelia tournefortii* and evaluation of their catalytic activity for the synthesis of N-monosubstituted ureas and reduction of 4-nitrophenol. J. Colloid Interface Sci. 455, 245–253.

Nasrollahzadeh, M., Mohammad Sajadi, S., Rostami-Vartooni, A., 2015b. Green synthesis of CuO nanoparticles by aqueous extract of *Anthemis nobilis* flowers and their catalytic activity for the A3 coupling reaction. J. Colloid Interface Sci. 459, 183–188.

Nasrollahzadeh, M., Momeni, S.S., Sajadi, S.M., 2017. Green synthesis of copper nanoparticles using *Plantago asiatica* leaf extract and their application for the cyanation of aldehydes using $K_4Fe(CN)_6$. J. Colloid Interface Sci. 506, 471–477.

Nazar, N., Bibi, I., Kamal, S., Iqbal, M., Nouren, S., Jilani, K., Umair, M., Ata, S., 2018. Cu nanoparticles synthesis using biological molecule of *P. granatum* seeds extract as reducing and capping agent: growth mechanism and photo-catalytic activity. Int. J. Biol. Macromol. 106, 1203–1210.

Nelson, R.L., Davis, F.G., Sutter, E., Sobin, L.H., Kikendall, J.W., Bowen, P., 1994. Body iron stores and risk of colonic neoplasia. J. Natl. Cancer Inst. 86, 455–460.

Noor, S., Shah, Z., Javed, A., Ali, A., Hussain, S.B., Zafar, S., Ali, H., Muhammad, S.A., 2020. A fungal based synthesis method for copper nanoparticles with the determination of anti-cancer, antidiabetic and antibacterial activities. J. Microbiol. Methods 174, 105966.

Olajire, A.A., Ifediora, N.F., Bello, M.D., Benson, N.U., 2018. Green synthesis of copper nanoparticles using *Alchornea laxiflora* leaf extract and their catalytic application for oxidative desulphurization of model oil. Iran. J. Sci. Technol. Trans. A Sci. 42, 1935–1946.

Online, V.A., Giannousi, K., Avramidis, I., 2013. Synthesis, characterization and evaluation of copper based nanoparticles as agrochemicals against *Phytophthora infestans*. RCS Adv. 3, 21743–21752.

Padil, V.V.T., Černík, M., 2013. Green synthesis of copper oxide nanoparticles using gum karaya as a biotemplate and their antibacterial application. Int. J. Nanomedicine 8, 889.

Panpatte, D.G., Jhala, Y.G., Shelat, H.N., Vyas, R.V., 2016. Nanoparticles: the next generation technology for sustainable agriculture. In: Microbial Inoculants in Sustainable Agricultural Productivity: Vol. 2: Functional Applications, Springer, New Delhi, pp. 289–300.

Parveen, K., Banse, V., Ledwani, L., 2016. Green synthesis of nanoparticles: their advantages and disadvantages. AIP Conf. Proc. 1724, 020048.

Peighambardoust, S.J., Peighambardoust, S.H., Mohammadzadeh Pournasir, N., Pakdel, P., 2019. Properties of active starch-based films incorporating a combination of Ag, ZnO and CuO nanoparticles for potential use in food packaging applications. Food Packag. Shelf Life 22, 100420.

Pinang, P., 1987. Ecotoxicity of copper to aquatic biota a review. Environ. Res. 282, 274–282.

Ponce, A.A., Klabunde, K.J., 2005. Chemical and catalytic activity of copper nanoparticles prepared via metal vapor synthesis. J. Mol. Catal. A Chem. 225, 1–6.

Prakash, S., Elavarasan, N., Venkatesan, A., Subashini, K., Sowndharya, M., Sujatha, V., 2018. Green synthesis of copper oxide nanoparticles and its effective applications in Biginelli reaction, BTB photodegradation and antibacterial activity. Adv. Powder Technol. 29, 3315–3326.

Prasad, P.R., Kanchi, S., Naidoo, E.B., 2016. In-vitro evaluation of copper nanoparticles cytotoxicity on prostate cancer cell lines and their antioxidant, sensing and catalytic activity: one-pot green approach. J. Photochem. Photobiol. B Biol. 161, 375–382.

Priyadarshini, E., Pradhan, N., 2017. Gold nanoparticles as efficient sensors in colorimetric detection of toxic metal ions: a review. Sens. Actuators B 238, 888–902.

Qamar, H., Rehman, S., Chauhan, D.K., Tiwari, A.K., Upmanyu, V., 2020. Green synthesis, characterization and antimicrobial activity of copper oxide nanomaterial derived from *Momordica charantia*. Int. J. Nanomedicine 15, 2541.

Raffi, M., Mehrwan, S., Bhatti, T.M., Akhter, J.I., Hameed, A., Yawar, W., Ul Hasan, M.M., 2010. Investigations into the antibacterial behavior of copper nanoparticles against *Escherichia coli*. Ann. Microbiol. 60, 75–80.

Rafique, M., Shafiq, F., Ali Gillani, S.S., Shakil, M., Tahir, M.B., Sadaf, I., 2020. Eco-friendly green and biosynthesis of copper oxide nanoparticles using *Citrofortunella microcarpa* leaves extract for efficient photocatalytic degradation of Rhodamin B dye form textile wastewater. Optik 208, 164053.

Rai, M., Ingle, A.P., Pandit, R., Paralikar, P., Shende, S., Gupta, I., Biswas, J.K., Da Silva, S.S., 2018. Copper and copper nanoparticles: role in management of insect-pests and pathogenic microbes. Nanotechnol. Rev. 7, 303–315.

Raiza, A.J., Pandian, K., Kumar, R.G., 2019. Biosynthesis of copper nanoparticles supported on zeolite Y and its application in catalytic C-N cross coupling reactions between amines and aryl halides. ChemistrySelect 4, 1964–1970.

Raj Preeth, D., Shairam, M., Suganya, N., Hootan, R., Kartik, R., Pierre, K., Suvro, C., Rajalakshmi, S., 2019. Green synthesis of copper oxide nanoparticles using sinapic acid: an underpinning step towards antiangiogenic therapy for breast cancer. J. Biol. Inorg. Chem. 24, 633–645.

Rajesh, K.M., Ajitha, B., Reddy, Y.A.K., Suneetha, Y., Reddy, P.S., 2018. Assisted green synthesis of copper nanoparticles using *Syzygium aromaticum* bud extract: physical, optical and antimicrobial properties. Optik 154, 593–600.

Rajeshkumar, S., Menon, S., Venkat Kumar, S., Tambuwala, M.M., Bakshi, H.A., Mehta, M., Satija, S., Gupta, G., Chellappan, D.K., Thangavelu, L., Dua, K., 2019. Antibacterial and antioxidant potential of biosynthesized copper nanoparticles mediated through *Cissus arnotiana* plant extract. J. Photochem. Photobiol. B Biol. 197, 111531.

Ramaswamy, S.V.P., Narendhran, S., Sivaraj, R., 2016. Potentiating effect of ecofriendly synthesis of copper oxide nanoparticles using brown alga: antimicrobial and anticancer activities. Bull. Mater. Sci. 39, 361–364.

Ren, G., Hu, D., Cheng, E.W.C., Vargas-Reus, M.A., Reip, P., Allaker, R.P., 2009. Characterisation of copper oxide nanoparticles for antimicrobial applications. Int. J. Antimicrob. Agents 33, 587–590.

Roucoux, A., Schulz, J., Patin, H., 2002. Reduced transition metal colloids: a novel family of reusable catalysts? Chem. Rev. 102, 3757–3778.

Salem, S.S., Fouda, A., 2021. Green synthesis of metallic nanoparticles and their prospective biotechnological applications: an overview. Biol. Trace Elem. Res., 1–27.

Samecka-Cymerman, A., Kempers, A.J., 2004. Toxic metals in aquatic plants surviving in surface water polluted by copper mining industry. Ecotoxicol. Environ. Saf. 59, 64–69.

Sankar, R., Maheswari, R., Karthik, S., Shivashangari, K.S., Ravikumar, V., 2014. Anticancer activity of *Ficus religiosa* engineered copper oxide nanoparticles. Mater. Sci. Eng. C 44, 234–239.

Santo, C.E., Quaranta, D., Grass, G., 2012. Antimicrobial metallic copper surfaces kill *Staphylococcus haemolyticus* via membrane damage. Microbiology 1, 46–52.

Sarkar, J., Chakraborty, N., Chatterjee, A., Bhattacharjee, A., Dasgupta, D., Acharya, K., 2020. Green synthesized copper oxide nanoparticles ameliorate defence and antioxidant enzymes in *Lens culinaris*. Nanomaterials 10, 312.

Sastry, A.B.S., Karthik Aamanchi, R.B., Sree Rama Linga Prasad, C., Murty, B.S., 2013. Large-scale green synthesis of Cu nanoparticles. Environ. Chem. Lett. 11, 183–187.

Semaltianos, N.G., 2010. Nanoparticles by laser ablation. Crit. Rev. Solid State Mater. Sci. 35, 105–124.

Shah, V., Luxton, T.P., Walker, V.K., Brumfield, T., Yost, J., Shah, S., Wilkinson, J.E., Kambhampati, M., 2016. Fate and impact of zero-valent copper nanoparticles on geographically-distinct soils. Sci. Total Environ. 573, 661–670.

Shang, Y., Hasan, K., Ahammed, G.J., Li, M., Yin, H., 2019. Applications of nanotechnology in plant growth and crop protection: a review. Molecules 24, 2558.

Sharma, J.K., Akhtar, M.S., Ameen, S., Srivastava, P., Singh, G., 2015. Green synthesis of CuO nanoparticles with leaf extract of *Calotropis gigantea* and its dye-sensitized solar cells applications. J. Alloys Compd. 632, 321–325.

Shende, S., Ingle, A.P., Gade, A., Rai, M., 2015. Green synthesis of copper nanoparticles by *Citrus medica* Linn. (Idilimbu) juice and its antimicrobial activity. World J. Microbiol. Biotechnol. 31, 865–873.

Shi, G., Liu, J., Chen, B., Bao, Y., Xu, J., 2017. Phase-controlled growth of cubic phase CuO nanoparticles by chemical vapor deposition. Phys. Status Solidi Appl. Mater. Sci. 214, 1700041.

Singh Sekhon, B., 2014. Nanotechnology in agri-food production: an overview. Nanotechnol. Sci. Appl. 7, 31.

Singh, J., Kumar, V., Kim, K.H., Rawat, M., 2019. Biogenic synthesis of copper oxide nanoparticles using plant extract and its prodigious potential for photocatalytic degradation of dyes. Environ. Res. 177, 108569.

Solomon, F., 2009. Impacts of copper on aquatic ecosystems and human health. Environ. Commun. 15, 25–29.

Sriramulu, M., Shanmugam, S., Ponnusamy, V.K., 2020. *Agaricus bisporus* mediated biosynthesis of copper nanoparticles and its biological effects: an in-vitro study. Colloids Interface Sci. Commun. 35, 100254.

Srivastava, A., 2009. Antiviral activity of copper complexes of isoniazid against RNA tumor viruses. Resonance 14, 754–760.

Suárez-Cerda, J., Espinoza-Gómez, H., Alonso-Núñez, G., Rivero, I.A., Gochi-Ponce, Y., Flores-López, L.Z., 2017. A green synthesis of copper nanoparticles using native cyclodextrins as stabilizing agents. J. Saudi Chem. Soc. 21, 341–348.

Sulaiman, G.M., Tawfeeq, A.T., Jaaffer, M.D., 2018. Biogenic synthesis of copper oxide nanoparticles using *Olea europaea* leaf extract and evaluation of their toxicity activities: an in vivo and in vitro study. Biotechnol. Prog. 34, 218–230.

Taran, M., Rad, M., Alavi, M., 2017. Antibacterial activity of copper oxide (CuO) nanoparticles biosynthesized by bacillus sp. FU4: optimization of experiment design. Pharm. Sci. 23, 198–206.

Tran, T.H., Nguyen, V.T., 2014. Copper oxide nanomaterials prepared by solution methods, some properties, and potential applications: a brief review. Int. Sch. Res. Notices, 1–14. ID 856592.

Tran, C.D., Makuvaza, J., Munson, E., Bennett, B., 2017. Biocompatible copper oxide nanoparticle composites from cellulose and chitosan: facile synthesis, unique structure, and antimicrobial activity. ACS Appl. Mater. Interfaces 9, 42503–42515.

Tshireletso, P., Ateba, C.N., Fayemi, O.E., 2021. Spectroscopic and antibacterial properties of CuONPs from orange, lemon and tangerine peel extracts: potential for combating bacterial resistance. Molecules 26, 586.

Upadhyay, L.S.B., Kumar, N., 2017. Green synthesis of copper nanoparticle using glucose and polyvinylpyrrolidone (PVP). Inorg. Nano-Metal Chem. 47, 1436–1440.

Valodkar, M., Rathore, P.S., Jadeja, R.N., Thounaojam, M., Devkar, R.V., Thakore, S., 2012. Cytotoxicity evaluation and antimicrobial studies of starch capped water soluble copper nanoparticles. J. Hazard. Mater. 201–202, 244–249.

Vanti, G.L., Masaphy, S., Kurjogi, M., Chakrasali, S., Nargund, V.B., 2020. Synthesis and application of chitosan-copper nanoparticles on damping off causing plant pathogenic fungi. Int. J. Biol. Macromol. 156, 1387–1395.

Vasantharaj, S., Sathiyavimal, S., Saravanan, M., Senthilkumar, P., Gnanasekaran, K., Shanmugavel, M., Manikandan, E., Pugazhendhi, A., 2019. Synthesis of ecofriendly copper oxide nanoparticles for fabrication over textile fabrics: characterization of antibacterial activity and dye degradation potential. J. Photochem. Photobiol. B Biol. 191, 143–149.

Veisi, H., Karmakar, B., Tamoradi, T., Hemmati, S., Hekmati, M., Hamelian, M., 2021. Biosynthesis of CuO nanoparticles using aqueous extract of herbal tea (*Stachys lavandulifolia*) flowers and evaluation of its catalytic activity. Sci. Rep. 11, 1–13.

Wada, O., 2004. What are trace elements?—their deficiency and excess states. Jpn. Med. Assoc. J. 47, 351.

Wang, H.B., Zhang, H.D., Chen, Y., Ou, L.J., Liu, Y.M., 2015. Poly(thymine)-templated fluorescent copper nanoparticles for label-free detection of N-acetylcysteine in pharmaceutical samples. Anal. Methods 7, 6372–6377.

WHO Expert Committee on Trace Elements in Human Nutrition, World Health Organization, 1973. Trace Elements in Human Nutrition. World Health Organ. Tech. Rep. Ser. 532.

Wu, S.H., Chen, D.H., 2004. Synthesis of high-concentration Cu nanoparticles in aqueous CTAB solutions. J. Colloid Interface Sci. 273, 165–169.

Wu, S., Rajeshkumar, S., Madasamy, M., Mahendran, V., 2020. Green synthesis of copper nanoparticles using *Cissus vitiginea* and its antioxidant and antibacterial activity against urinary tract infection pathogens. Artif. Cells Nanomed. Biotechnol. 48, 1153–1158.

Xiong, J., Wang, Y., Xue, Q., Wu, X., 2011. Synthesis of highly stable dispersions of nanosized copper particles using L-ascorbic acid. Green Chem. 13, 900–904.

Xu, Q., Ke, X., Ge, N., Shen, L., Zhang, Y., Fu, F., Liu, X., 2018. Preparation of copper nanoparticles coated cotton fabrics with durable antibacterial properties. Fibers Polym. 19, 1004–1013.

Yallappa, S., Manjanna, J., Sindhe, M.A., Satyanarayan, N.D., Pramod, S.N., Nagaraja, K., 2013. Microwave assisted rapid synthesis and biological evaluation of stable copper nanoparticles using *T. arjuna* bark extract. Spectrochim. Acta A Mol. Biomol. Spectrosc. 110, 108–115.

Yaqub, A., Malkani, N., Shabbir, A., Ditta, S.A., Tanvir, F., Ali, S., Naz, M., Kazmi, S.A.R., Ullah, R., 2020. Novel biosynthesis of copper nanoparticles using *Zingiber* and *Allium* sp. with synergic effect of doxycycline for anticancer and bactericidal activity. Curr. Microbiol. 77, 2287–2299.

Yousefvand, P., Mohammadi, E., Zhuang, Y., Bloukh, S.H., Edis, Z., Gamasaee, N.A., Cai, Y., 2021. Biothermodynamic, antiproliferative and antimicrobial properties of synthesized copper oxide nanoparticles. J. Mol. Liq. 324, 114693.

Zain, N.M., Stapley, A.G.F., Shama, G., 2014. Green synthesis of silver and copper nanoparticles using ascorbic acid and chitosan for antimicrobial applications. Carbohydr. Polym. 112, 195–202.

Zakharova, O.V., Godymchuk, A.Y., Gusev, A.A., Gulchenko, S.I., Vasyukova, I.A., Kuznetsov, D.V., 2015. Considerable variation of antibacterial activity of Cu nanoparticles suspensions depending on the storage time, dispersive medium, and particle sizes. Biomed. Res. Int. 2015, 1–11. ID 412530.

Zaman, M.B., Poolla, R., Singh, P., Gudipati, T., 2020. Biogenic synthesis of CuO nanoparticles using *Tamarindus indica* L. and a study of their photocatalytic and antibacterial activity. Environ. Nanotechnol. Monit. Manag. 14, 100346.

Zangeneh, M.M., Ghaneialvar, H., Akbaribazm, M., Ghanimatdan, M., Abbasi, N., Goorani, S., Pirabbasi, E., Zangeneh, A., 2019. Novel synthesis of *Falcaria vulgaris* leaf extract conjugated copper nanoparticles with potent cytotoxicity, antioxidant, antifungal, antibacterial, and cutaneous wound healing activities under in vitro and in vivo condition. J. Photochem. Photobiol. B Biol. 197, 111556.

Zhang, P., Cui, J., Mansooridara, S., Kalantari, A.S., Zangeneh, A., Zangeneh, M.M., Sadeghian, N., Taslimi, P., Bayat, R., Şen, F., 2020. Suppressor capacity of copper nanoparticles biosynthesized using *Crocus sativus* L. leaf aqueous extract on methadone-induced cell death in adrenal phaeochromocytoma (PC12) cell line. Sci. Rep. 10.

Zhu, H., Du, M., Yu, D., Wang, Y., Wang, L., Zou, M., Zhang, M., Fu, Y., 2013. A new strategy for the surface-free-energy-distribution induced selective growth and controlled formation of Cu_2O-Au hierarchical heterostructures with a series of morphological evolutions. J. Mater. Chem. A 1, 919–929.

Zuverza-Mena, N., Medina-Velo, I.A., Barrios, A.C., Tan, W., Peralta-Videa, J.R., Gardea-Torresdey, J.L., 2015. Copper nanoparticles/compounds impact agronomic and physiological parameters in cilantro (*Coriandrum sativum*). Environ Sci Process Impacts 17, 1783–1793.

CHAPTER

18 Antimicrobial activity of copper nanomaterials: Current status and future perspectives

V. Bhuvaneshwari[a], Nirmal Kumar Ramasamy[b], S. Idhaya Kumar[c], S. Kalaivani[c], D. Vaidehi[c], and D. Karthik Kumar[d]

[a]*Department of Biotechnology, Sri Shakthi Institute of Engineering and Technology, Coimbatore, Tamil Nadu, India*

[b]*Department of Biotechnology, PSGR Krishnammal College for Women, Coimbatore, Tamil Nadu, India*

[c]*Department of Biotechnology, Kongunadu Arts and Science College, Coimbatore, Tamil Nadu, India*

[d]*Viyen Biotech LLP, Coimbatore, Tamil Nadu, India*

1 Introduction

The modern world has adapted to travel with modern technology and inventions but yet there is self-sufficiency due to various problems which are still untreated. A new field called nanotechnology has emerged for solving problems in a scientific and eco-friendly approach. Nanotechnology is an eco-friendly, sustainable, and cheap tool, due to its potential use of nanomaterials, such as nanosensors, nanocarriers, nanochips, nanotechnology-based nanopesticides, nanofertilizers, nanopackaging, and nanotechnology-based genetic engineering offers a great scope for improving non-toxic agricultural food and preserving the safety of the environment (Madanayake et al., 2021). Nanotechnology has provided innovative and useful frontiers to the agriculture sector by contributing practical applications in regular practices and ways in agriculture. There is a high possibility that nanotechnology have an important impact on sustainable agriculture and crop growth (Singh et al., 2021). Food production can be increased by protecting the crop from biotic and abiotic stress through developing drought and insect-pest-resistant crop varieties (Jia et al., 2012). Also, through improved fertilizers, the nutrition required for plant growth can be supplied. But there are certain limitations that excessive use of chemical fertilizers may pose a threat to the fertility status of the soil. But nanofertilizers carry and supply nutrients to the plant system for an extended period, without environmental hazard. The sustainable growth of agriculture can greatly be accelerated by this technique. Copper oxide is an inorganic compound and inhibits the microbial growth of various pathogens which

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can be used as a nontoxic antimicrobial agent. Copper functions in regulating plant growth and development, including seed production (Sommer, 1931). In-plant copper plays a major role in chlorophyll synthesis, electron transport chains, photosynthesis, oxidative stress protection as well as the metabolism of protein, carbohydrate, and cell wall. About 70% of total copper plays a major role in the synthesis of chloroplasts (Kanhed et al., 2014; Kasana et al., 2016). Copper involves in several enzyme systems that regulate the rate of many biochemical reactions in the plant. It also activates enzymes involved in lignin synthesis and is also required in the process of photosynthesis. Copper sulfate and copper oxide made fertilizers are used for the production of copper nanoparticles (CuNPs) to increase sustainable agriculture (Da Costa and Sharma, 2016; Qureshi et al., 2018; Van Ha et al., 2020). CuNPs have better antibacterial, antifungal, and insecticidal potential than CuONPs. CuNPs/CuONPs may be used for sustainable food and agriculture industries (Worrall et al., 2018; Rehman et al., 2019). Even at a lower concentration, novel formulations such as CuNP-based nano pesticides and nanofertilizer are reported by Shang et al. (2019). But at higher concentrations, copper is toxic to plants and affects plant growth as well as impairment of cellular processes. So maintaining soil health by application of nutrients in an adequate amount is an effective way for its growth, yield, and balanced nutrition.

2 Application of nanoparticles for sustainable agriculture

Existing problems in agriculture-related crop production and protection are high. In the production aspect, excess application of chemical-related fertilizers imposes a threat in affecting the soil fertility and soil microbes which are capable of fixing nitrogen and solubilizing phosphates. Similarly, the pesticides and herbicides used for crop protection are making human life more critical. Reports claim the presence of pesticide residues in agriculturally based food products (Anzene et al., 2014). Nanotechnology is one of the most fascinating and advancing sciences and possesses the potential to revolutionize many disciplines of science, technology, medicine, and agriculture. NPs act as a vehicle to absorb, encapsulate, entrap, or link active molecules for developing effective agricultural formulations to promote sustainable agriculture (Ditta et al., 2015; El-Saadony et al., 2020). The application of NPs in agriculture is currently being explored in nanobarcoding, nanosensors, plant hormone delivery, controlled release of agrochemicals, transfer of target genes, water management, and seed germination (Chibber et al., 2013). Metal NPs, mainly copper, exhibit an outstanding inhibitory effect on Gram-positive and Gram-negative bacteria, and therefore metal NPs such as CuNP synthesized using green technology used to control pests and pathogenic microbes. The antibacterial activity of CuONPs/CuNPs might be due to the free radicals production on the NPs surface leading to the damage of lipids in bacterial cell membrane resulting in leakage and breakdown of the bacterial cell membrane (Rafique et al., 2017; Bhuvaneshwari et al., 2018; Rai et al., 2018). CuNPs can be used to increase solubility, thus reducing toxicity (Ivask et al., 2010; Peng et al., 2015). There different methods used for the synthesis of CuONPs/CuNPs include chemical, physical, and biological methods. Among them,

CuONP synthesized using biological method have shown better antibacterial activity (Zuverza-Mena et al., 2015; Vaidehi et al., 2018; Logpriya et al., 2018).

3 Metabolism of copper in plants

Endocytosis is the main pathway for the infusion of CuNPs in the plant cell. Copper ions in an adequate concentration will stimulate the growth of the plant and act as a microelement (Miralles et al., 2012; Farajzadeh Memari Tabrizi et al., 2009). Nanofertilizers can be used as an alternative to traditional fertilizers to increase efficient nutrients use for sustainable agriculture (Singh, 2017). For healthy growth and development of plant, Cu from the soil should be absorbed and transported throughout the plant, disseminated, and compartmentalized within different tissues and cautiously regulated within different cells and organelles. Copper can remobilize in plants from one place to other through xylem from roots to leaves and CuONPs will act on the leaf surface and translocate both to other leaf parts and roots through the phloem (Peng et al., 2015; Cao et al., 2020) and is illustrated in Fig. 1.

Cu deficiency causes a decrease in the formation of plastocyanin a major element in photosynthesis and also causes disintegration of the thylakoid membrane in the chloroplast. The extreme condition may also cause chlorosis and necrosis. Plants having copper deficiency will express a change in the series of gene expression and causes morphological changes in root and leaf architecture (Yruela, 2005).

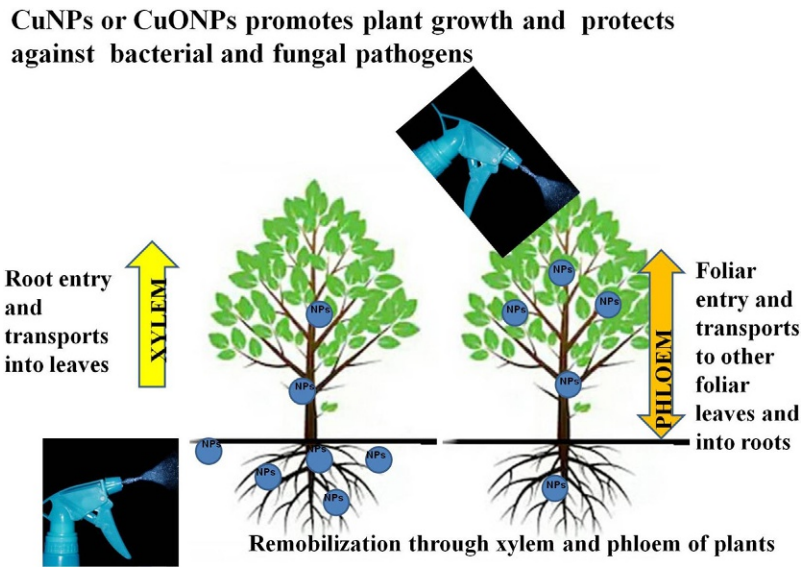

FIG. 1

Foliar and root application of CuNPs or CuONPs leading to remobilization and its plant protection against bacterial and fungal pathogens.

4 Biosynthesis of CuNPs

4.1 Biosynthetic method of nanoparticle preparation

Biosynthesis of NPs aims at utilizing waste or renewable materials with minimum use of energy and risk. The three main requirements of biosynthesis of NPs are choice of eco-friendly nontoxic solvent (preferably water), reducing and stabilizing agents such as plant extract, microbes, metabolites, and enzymes, and biocompounds (Raveendran et al., 2003). The synthetic processes need to be performed close to neutral pH, at ambient temperature and pressure, thus biological systems act as the most appropriate factory for attaining such conditions. The synthesis of CuNPs/CuONPs by using biomaterials has recently attracted considerable attention because it is a simple, one-step process, nontoxic, eco-friendly and energy-efficient nature, and biodegradable, avoids the use of chemical reducing agents and stabilizers, and is cost-effective. More recently, the utilization of plant extracts or their phytocompounds for the synthesis of metal NPs has attracted the attention of numerous investigators (Castillo-Henríquez et al., 2020).

4.2 Green synthesis of nanomaterials

Recently, the biosynthetic method utilizing plant extracts has drawn attention as a simple and viable alternative to physical and chemical methods. Furthermore, this method can be a simple and eco-friendly synthetic route with wide application as metal oxide NPs (Castillo-Henríquez et al., 2020). Copper acetate, copper chloride, copper sulfate, and copper nitrate are used to synthesize CuNPs from various groups of plants. The synthesis was carried out by heating 1.0 mM copper sulfate aqueous extract at 1:1 ratio with leaf broth. The temperature and the concentration of leaf broth and $CuSO_4 \cdot 5H_2O$ affect the synthesis rate and particle size of the prepared CuNPs. The CuNP solution obtained was purified by repeated centrifugation followed by the redispersion of the pellet in the deionized water. The size of synthesized CuNPs ranges from 110 to 280 nm. The covalent reduction of Cu^{2+} ions from copper salts to CuNPs without agglomeration may be due to the presence of phenolics, polyphenolics, and other metabolites in the leaf extracts. Due to the presence of carbonyl and hydroxyl groups in phenolic and polyphenolic compounds, they can chelate and bind to metal ions, which enhance the interaction with proteins and membranes. Thus these phytoconstituents are believed to function as both reducing and capping agents in the stabilization of prepared CuNPs (Chung et al., 2017). The reduction of copper ions to give CuNPs may be due to the presence of phenolic compounds in the root extract of *Rheum palmatum* L. (Bordbar et al., 2017). Phenolics and polyphenolic compounds such as flavonoids have antioxidant potential and can directly scavenge the reactive oxygen species (ROS) by donating hydrogen and electrons. CuNP synthesized using *Cuminum cyminum* seed extract demonstrated antibacterial activity against *Bacillus* sp., *Pseudomonas* sp., *Staphylococcus* sp., *Escherichia coli* and possessed prominent fungicidal activity against *Penicillium* sp., *Aspergillus niger*, *Aspergillus flavus*, and *Rhizopus* spp. (Rajesh et al., 2018). CuNP synthesized using *Citrus medica* Linn. (Idilimbu) juice showed higher antibacterial activity against *Escherichia coli* than *Propionibacterium acnes*, *Pseudomonas aeruginosa*, *Klebsiella pneumoniae*, and *Salmonella typhi* and

have antifungal activity against plant pathogenic fungi *Fusarium culmorum* (Shende et al., 2015). Harne et al. (2012) reported novel and rapid synthesis of CuNPs using an aqueous extract of *Calotropis procera* L. latex which showed antioxidant activities. Previously CuONPs were synthesized from various plant extracts such as *Acalypha indica*, *Gloriosa superba*, *Citrus limon*, *Citrus medica*, *Fragaria ananassa*, *Psidium guajava*, *Vitis vinifera*, *Phyllanthus amarus*, *Terminalia arjuna*, *Calotropis gigantean*, *Euphorbia tirucalli*, *Malva sylvestris*, *Solanum lycopersicum*, *Cinnamomum champora*, *Cassia alata*, *Azadirachta indica*, *Tamarindus indica*, *Saraca indica*, *Carica papaya*, Catha edulis, *Punica granatum*, *Syzygium alternifolium*, *Ziziphus spina-christi*, *Capparis spinosa*, and their antioxidant and antimicrobial activities were also reported (Angrasan and Subbaiya, 2014; Duman et al., 2016; Prasad et al., 2017; Yulizar et al., 2018; Vaidehi et al., 2018; Kumar et al., 2020; Andualem et al., 2020). Revathi and Thambidurai (2019) reported CuO incorporated CS-neem seed and its antioxidant and antibacterial potential. Logpriya et al. (2018) and Bharathi et al. (2019) produced CuONPs by using ascorbic acid, rutin, respectively, as reducing agents in the presence of chitosan. Chitosan led to the higher stability of CuNPs and avoided agglomeration. The authors defined the synthesis of copper nanoparticles as fast, inexpensive, environmentally friendly, and high energy efficient. In addition, the concentration of chitosan was positively correlated to copper nanoparticle size.

4.3 Microbial synthesis

Microbial synthesis of metal NPs using bacteria, fungi, and algae can provide inorganic materials either intracellularly or extracellularly. Microbial synthesis of metal NPs can be used as an eco-friendly method of nanofactories (Li et al., 2011). The microbial production of CuNPs using bacteria, fungi, and algae is comparatively considered as a novel and ecofriendly approach. Different strategies used for the synthesis of metallic NPs employed by using extracellular secretion from a microorganism or utilizing living and dead biomass of microorganisms (Bhattacharya and Gupta, 2005). The occurrence of the wide variation in the production of metallic NPs by living cells may be due to the involvement of organelles and compounds which are responsible for the production of NPs with different shapes and sizes. The reason may be due to the difference in the mechanisms involved in the bioreduction of metal ions (Singh, 2015).

4.3.1 Bacteria

In general, the production of metallic NPs by bacteria takes advantage of shorter generation times (18 min) than yeast (100 min) and *Chlorella vulgaris* (microalgae) which take 3.35 days. Consequently, metabolites with a greater capacity of chemically reducing metal ions are synthesized during the stationary phase leading to the production of metallic NPs (de Andrade et al., 2017). The metallic nanoparticle production is the result of a general microbial detoxification mechanism by converting soluble metals to insoluble nanosized structures (Abboud et al., 2014). A wide range of bacteria can reduce metal ions (metallic nanoparticle production) by their compounds such as proteins, polysaccharides, and periplasmic proteins (Singh et al., 2010; Lee et al., 2013; Singh, 2015). From the midgut of *Stibara* species, a Gram-negative bacterium *Serratia* was isolated and used to produce polydispersed CuNPs using 5 mM copper

sulfate showed 10–30 nm (Saif Hasan et al., 2008). From soil, *Pseudomonas stutzeri* was isolated for the synthesis of CuNPs by using 1 mM copper sulfate, and 8–15 nm spherical NPs were produced (Varshney et al., 2010). For instance, Singh et al. (2010) described the production of NPs from *Escherichia coli* proteins and acted on their stabilization. Saif Hasan et al. (2008) reported the bacterial synthesis of CuNPs and CuONPs. Varshney et al. (2010) reported nonpathogenic bacteria *Pseudomonas stutzeri*-mediated synthesis of CuNPs which is easy, fast, and cost-effective. The metabolites from *Pseudomonas stutzeri* may contain many biocompounds which can able to reduce metal ions by producing CuNPs besides stabilizing them.

4.3.2 Fungi

Honary et al. (2012) reported the production of CuNPs using the extracellular metabolites of three species of *Penicillium*: *Penicillium aurantiogriseum*, *Penicillium citrinum*, and *Penicillium waksmanii.* The authors reported a direct correlation among pH (5–9), the concentration of copper (1, 3, and 5 mM of $CuSO_4$), polydispersity index and particle size, lowest concentration of $CuSO_4$, and lowest pH led to the production of smallest (diameter) CuNPs. The biosynthesis of extracellular production of CuONPs using wide range of fungi such as *Penicillium aurantiogriseum*, *Penicillium citrinum*, *Penicillium waksmanii*, *Trichoderma* sp., etc. was already reported (Honary et al., 2012; de Andrade et al., 2017; Saravanakumar et al., 2019; Consolo et al., 2020). There is no proof that a specific type of protein, or carbohydrate, or lipid or any other molecule is responsible for the production of metallic NPs (Singh, 2015). In general, proteins appear to be essential to the synthesis of CuNPs, in which the amide groups account for the stability of the capping agents around CuNPs (Shobha et al., 2014). The biosynthesis of CuNPs and CuONPs using extracellular extract of *Stereum hirsutum*, a native white-rot fungus may contain secreted enzymes leading to the production and stability of metallic NPs (Cuevas et al., 2015). The oxidative stress is often associated with a high concentration of Cu (Jomova and Valko, 2011). Cell membrane plays a major role instead of cytoplasm and the effect of pH on the production of metallic NPs by *Hypocrea lixii*. At an acid pH (2–4), the membrane of microorganisms is positively charged leading to a subsequent reduction of metal biosorption (Salvadori et al., 2013). Alternatively, at pH 5, the cell membrane of microorganisms is negatively charged, favoring the biosorption of copper. Ahmad et al. (2007) produced $CuAlO_2$ (bimetallic nanomaterial) by *Humicola* sp., by exploiting the unique valence controlled nanosynthesis.

4.3.3 Algae

Abboud et al. (2014) were the first to report the bioproduction of CuONPs which are spherical in shape with the size of 5–45 nm from algae (*Bifurcaria bifurcata*). Saran et al. (2017) reported the biosynthesis of CuONPs using cell-free extract of the cyanobacteria *Spirulina platensis* and its antibacterial activity.

5 Plant disease control and management

Crops are exposed to various kinds of stress such as abiotic stresses and biotic stress factors (Harne et al., 2012). Conventional herbicides, fungicides, and pesticides are

commonly used to protect crops. Conventional pesticides have a high chemical composition, and we need to use them at a higher dosage to give higher efficiency (Angrasan and Subbaiya, 2014). This also causes damage to the crop and the soil, and thus the fertility of the soil is depleted. NPs are specific and more efficient as a carrier; due to the nanoscale structure, they have high permeability specificity stiffness crystallite thermal stability and solubility (Shukla et al., 2019). CuNPs have been synthesized in varied sizes from 5 to 295 nm using latex from plants, leaf extracts, and microbes. Biosynthesized CuNPs show better antibacterial and antifungal activity inhibiting the growth of plant pathogens. CuNPs at lower concentrations induce the germination and growth of plants, whereas, at higher concentrations, they retarded the plant growth (Kasana et al., 2017). Exploring CuNPs is the beginning of disease management, further studies have to be done for utilizing them to protect the plants from different pathogens. The antibacterial study revealed the fact that CuNPs exhibited superiority over CuONPs with has a wide range of applications such as heat transfer systems, antimicrobials, sensors, and catalysts. Previously, copper and its compound are used as microbicides and molluscicides. Murthy et al. (2018) reviewed the green synthesis of CuNPs and CuONPs by using various plant extracts as reported by global researchers.

6 Antibacterial potential of copper-based nanoparticles

The metal NPs such as Ag, Cu, etc. are found to have antimicrobial activity due to their minute size and large surface volume ratio for interacting closely with microbial membranes. It was clear that CuONPs have shown superior antibacterial activity against *Bacillus subtilis* subsp. *spizizenii*, indicating Gram-positive bacteria are more sensitive to CuONPs than Gram-negative bacteria (Abboud et al., 2014). The difference in the sensitivity of CuONPs to Gram-positive and Gram-negative bacteria populations could be due to the variation in the physiology, metabolism, or cell structure, and degree of contact of organisms with NPs. For instance, the higher sensitivity among Gram-positive bacteria *Bacillus subtilis* subsp. *spizizenii* to the CuONPs has been featured to the more amount of amines and carboxyl groups on their cell surface and greater affinity of copper toward these groups. Nanocopper suppressed the growth of *Xanthomonas axonopodis* pv. *punicae* and the water-soaked lesions (bacterial blight disease) induced in pomegranate. Copper oxide NPs (CuONPs) synthesized with a spherical shape and size less than 17 nm showed antibacterial activity against *Chryseobacterium indoltheticum*, *Brevibacillus laterosporus*, and *Pantoea ananatis* strains. Fan et al. (2021) reported the potential use of Cu-based nanocomposites for the efficient management of bacterial spot-on pepper. Table 1 consolidates the antibacterial potential of copper-based nanomaterials against bacterial phytopathogens. The toxic effect of CuONPs is evidenced by damage to the cell membrane, cell membrane degradation cavity and hole formation, blebs, cellular collapse, and finally lysis of cells. This damage may be due to the interaction of the ions, the oxide-reduction reactions, and the generation of ROS (Concha-Guerrero et al., 2014). Fig. 2 illustrates the damage caused to bacterial cells due to the action of copper-based nanomaterials.

Table 1 Antibacterial activity of copper nanoparticles against plant bacterial pathogen.

Nanomaterial	Antibacterial activity against plant bacterial pathogen	Reference
Copper nanoform	*Xanthomonas axonopodis* pv. *punicae*	Mondal and Mani (2012)
CuNPs	*Brevibacillus laterosporus, Chryseobacterium indoltheticum, Pantoea ananatis*	Concha-Guerrero et al. (2014)
CuNPs	*Pseudomonas syringae*	Banik and Luque (2017)
CuONPs-streptomycin	*Clavibacter michiganensis* subsp. *sepedonicus, Ralstonia solanacearum, Dickeya solani*	El-Batal et al. (2019)
CuNPs	*X. axonopodis* pv. *punicae*, *Pantoea* sp., *Serratia nematodiphila*, *Bacillus* sp.	Chikte et al. (2019)
CuONPs	*Ralstonia solanacearum*	Chen et al. (2019)
Copper-zinc hybrid NPs	Copper-Tolerant *X. perforans*	Carvalho et al. (2019)
CuNPs	*Agrobacterium tumefaciens*, *D. dadantii*, *Erwinia amylovora*, *Pectobacterium carotovorum*, *Pseudomonas corrugata*, *Pseudomonas savastanoi* pv. *savastanoi*	Varympopi et al. (2020)
Cu_2O NPs	*Bacillus subtilis, Staphylococcus aureus, Pseudomonas aeruginosa*	Bezza et al. (2020)
CuNPs	*Escherichia coli, Pseudomonas aeruginosa, Staphylococcus aureus,* and *Bacillus subtilis*	Murthy et al. (2020)
CuNPs	*Escherichia coli* and *Staphylococcus aureus*	Benassai et al. (2020)
CuNPs	*Escherichia coli, Klebsiella pneumoniae, Staphylococcus aureus,* and *Enterococcus faecalis*	Das et al. (2020)
CuNPs	*X. axonopodis* pv. *citri*	Nargund et al. (2021)
Cu nanocomposite	*X. euvesicatoria*	Fan et al. (2021)

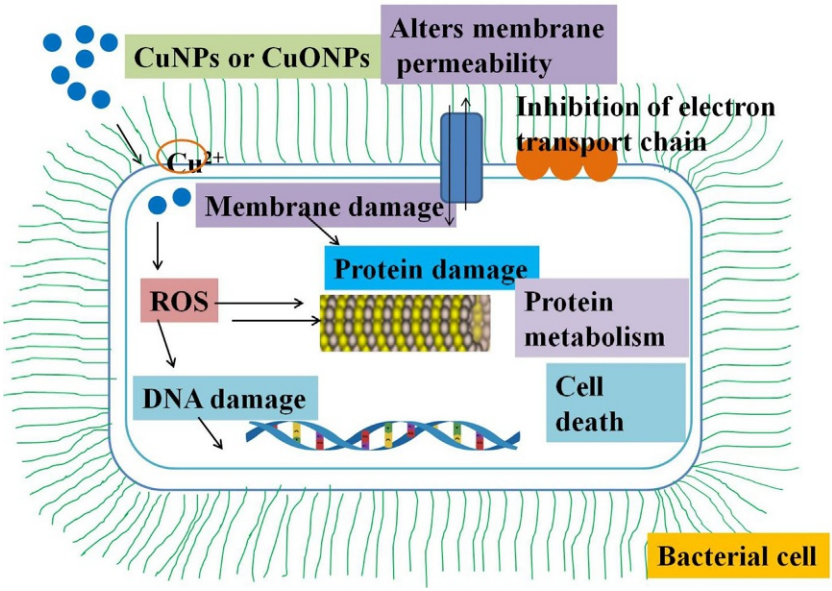

FIG. 2

Schematic representation of the bacterial cell damage by the CuNPs or CuONPs.

7 Antifungal activity of copper-based nanoparticles

Numerous studies have reported the antimicrobial activity of Cu-NPs against several fungi such as *Fusarium* sp., *Colletotrichum* sp., *Aspergillus niger*, *Poria hypolateritia* Berk. ex Cooke, *Penicillium* sp. as shown in Table 2. Red root-rot disease caused by *Poria hypolateritia* Berk. ex Cooke affects the entire root system of tea plants leading to economical loss due to the sudden death of bushes. Soil application of CuNPs (at different dosages) showed a significant decrease in red root-rot disease incidence (Ponmurugan et al., 2016). Green and blue molds, caused by the fungal pathogens *Penicillium italicum* and *Penicillium digitatum*, respectively, are the most important disease of Citrus fruits causing commercial damage. CuNPs show better antifungal activity against the pathogenic *Penicillium* sp. than the CuONPs (Chalandar et al., 2017). Antifungal activity of CuNPs has been found against different fungal species such as *Aspergillus niger*, *Alternaria solani*, *Alternaria alternata*, *Fusarium* sp., *Rhizoctonia solani*, and *Phoma destructiva* (Nemati et al., 2015; Aleksandrowicz-Trzcińska et al., 2018; Pandey et al., 2018). Microscopic observation revealed that CuNPs. Ag/CuNPs caused a damage effects on fungal hyphae and conidia of *Alternaria alternata* and *Botrytis cinerea*, which are plant pathogens (Ouda, 2014). Foliar application of CuNPs in a tomato

Table 2 Antifungal activity of copper nanoparticles against plant fungal pathogen.

Nanomaterial	Antifungal activity against plant fungal pathogen	Reference
Cu_2O, CuO, and Cu/Cu_2O·NPs	*Phytophthora infestans*	Giannousi et al. (2013)
Copper (CuNPs and Ag/copper Ag/CuNPs)	*Alternaria alternata* and *Botrytis cinerea*	Ouda (2014)
CuNPs	*Curvularia lunata* MTCC 2030, *Alternaria alternata* MTCC6572, *Fusarium oxysporum* MTCC1755 and *Phoma destructive* DBT66	Kanhed et al. (2014)
Cu-chitosan NPs	*Alternaria solani* and *Fusarium oxysporum*	Saharan et al. (2015)
CuNPs synthesized using *Citrus medica*	*Fusarium culmorum, Fusarium oxysporum,* and *Fusarium graminearum*	Shende et al. (2015)
CuNPs	*Fusarium* expansum, *Alternaria* solani, and *Alternaria* alternate	Nemati et al. (2015)
CuNPs	*Fusarium equiseti, Fusarium oxysporum,* and *Fusarium culmorum*	Bramhanwade et al. (2016)
CuNPs	*Fusarium* sp.	Viet et al. (2016)
Eichhornia-mediated CuONPs	*Fusarium culmorum* and *Aspergillus niger*	Vanathi et al. (2016)
CuNPs	*Botyritis cinerea*	Hao et al. (2017)
CuNPs	*Alternaria alternate,* Phytophthora cinnamomi	Banik and Luque (2017)
CuNPs	*Alternaria alternate*	Al-Dhabaan et al. (2017)
Chitosan, zinc oxide, and copper nanocomposites	*Botyritis cinerea*	Al-Dhabaan et al. (2017)
CuNPs, CuONPs	*Penicillium italicum* and *Penicillium digitatum*	Chalandar et al. (2017)
CuNPs	*Rhizoctonia solani (2 strains), Fusarium oxysporum, Fusarium redolens along with Fistulina hepatica, Grifola frondosa, Meripilus giganteus*	Aleksandrowicz-Trzcińska et al. (2018)
CuNPs	*Alternaria solani*	Quiterio-Gutiérrez et al. (2019)
CuNPs	*Sclerotinia sclerotioum*	Abdel-Halim and El-Ghanam (2019)
Cu NPs	*Verticillium dahliae, Colletotrichum gloeosporioides, Fusarium oxysporum* f.sp., *Radicis lycopersici*, and *Fusarium solani*	Malandrakis et al. (2019)

Table 2 Antifungal activity of copper nanoparticles against plant fungal pathogen—cont'd

Nanomaterial	Antifungal activity against plant fungal pathogen	Reference
CuNPs	*Fusarium oxysporum* and *Phytophthora capsici*	Pham et al. (2019)
CuNPs	*Fusarium oxysporum*	Mali et al. (2020)
Chitosan-silver-copper nanocomposite	*Candida albicans*	Ashrafi et al. (2020)
CuNPs, CuONPs	*Colletotrichum gloeoesporioides*	Oussou-Azo et al. (2020)
CuNPs,	*Saccharomyces cerevisiae* and *Candida albicans*	Benassai et al. (2020)
CuNPs	*Aspergillus niger, Aspergillus flavus, Candida albicans,* and *Candida glabrata*	Das et al. (2020)
CuONPs	*Candida albicans, Aspergillus flavus, Microsporum canis, Candida glabrata*	Rabiee et al. (2020)
CuNPs, CuONPs	*Colletotrichum gloeoesporioides*	Oussou-Azo et al. (2020)

crop decreased the disease severity infested by *Alternaria solani* and generated beneficial changes by increasing the enzymatic and nonenzymatic antioxidant compounds (Quiterio-Gutiérrez et al., 2019). CuNPs significantly suppressed *Botrytis cinerea* symptoms in vivo. CuNPs are more fungi toxic to spores of *Colletotrichum gloeosporioides, Fusarium oxysporum* f.sp. *radicis-lycopersici*, *Verticillium dahliae*, *Fusarium solani* than the hyphae exhibiting good potentials as nanofungicides (Malandrakis et al., 2019). As an alternative control measure for fungal disease, biologically synthesized copper nanofungicide plays an important role with very high surface area, increasing the diffusion in the rhizosphere and reduces the dependency on bulk copper fungicide available in the market.

8 Antimicrobial mechanisms of copper-based nanoparticles

It has been proposed that the enhanced antimicrobial activity of Cu-NPs compared to copper salts may be due to their crystallographic surface structure and high surface volume ratio. Green synthesized CuONPs showed potential inhibition against both Gram-negative and Gram-positive bacterial pathogens. CuNPs interact and disturb the microbial cell wall components due to the presence of carboxyl group,

leading to damage of membrane which lowers the electrochemical potential, loss in membrane integrity, disruption of cell permeability, and release of integral components (Raffi et al., 2010). It also targets the DNA, interferes with protein metabolism, and causes cell damage leading to microbial cell death (Rai et al., 2018). It has momentous antibacterial action and there is a greater affinity of copper ions due to the presence of more amines and carboxyl groups on their cell surface. Because of the larger surface area of the NPs, it could be strongly attached and adsorbed onto the surface of the microbial cells illustrating the efficient antibacterial and antifungal properties. CuONPs also disrupt the biochemical processes of the bacterial cells, denaturing functional biomolecules (Kim et al., 2000; Wei et al., 2010). Similarly, Ruparelia et al. (2008) and Raffi et al. (2010) demonstrated that Cu ions discharged from the CuNPs/CuONPs may interact on the surface of a pathogenic cell, and may bind to the DNA molecules by disordering the helical structure due to cross-linking between the nucleic acid strands and distort the protein structures and disrupt the biochemical processes. Simultaneously, the discharged copper ions attached to their outer surfaces might be moved inside the microbial cells causing protein denaturation and disruption of the cell membrane leading to cell apoptosis (Palza, 2015). Cu^{2+} may be the exciting force behind the antimicrobial properties of Cu nanocomposites (Delgado et al., 2011). NPs stimulate the production of ROS causing oxidative damage to the microbial cells. The nonspecific mode of action of Cu^{2+} or CuNPs/CuONPs against microbial cells makes them good antimicrobial agents with least chance of microbial resistance development. Cu-chitosan NPs enhanced enzyme activities involved in plant defense by chitosan participants in ROS scavenging system (Saharan et al., 2015). CuNPs nearly have the same mode of action for Cu-chitosan nanocomposites such as the production of ROS and membrane disruption (Ingle et al., 2014). Due to the surface charge and increased surface area-to-volume ratio of CuNPs and CuONPs, damage the enzymes, and by the production of ROS they cause DNA fragmentation, mitochondrial-dependent caspase-mediated apoptosis, disrupt the membrane permeability leading to the disruption of cell integrity, especially the vegetative parts. The strong adherence of NPs to the cell surface could induce detrimental changes, such as physical cutting, water channel blocking, increase in membrane permeability, and even the penetration of NPs into fungus cells, which could result in the death of the cell (Wang et al., 2014) (Fig. 3). Alternatively, the existence of NPs could induce ROS accumulation via impairing the ROS-scavenging system of fungi (Liu et al., 2016). Another mechanism of NP toxicity to fungi was the dissolution of copper ions from copper-based NPs (Zarzuela et al., 2017). CuO is slowly oxidized into cupric ion, which is then released in the biological system to produce lethal hydroxyl free radicals in the immediate vicinity of the lipid membrane. These free radicals generate oxidative deterioration of lipids, which form cell membrane (Howlett and Avery, 1997) that causes an outflow of K^+ ions and other substances from the cell (Lippert et al., 2003), ultimately leading to the disturbance of major biochemical reactions that occur inside the cells.

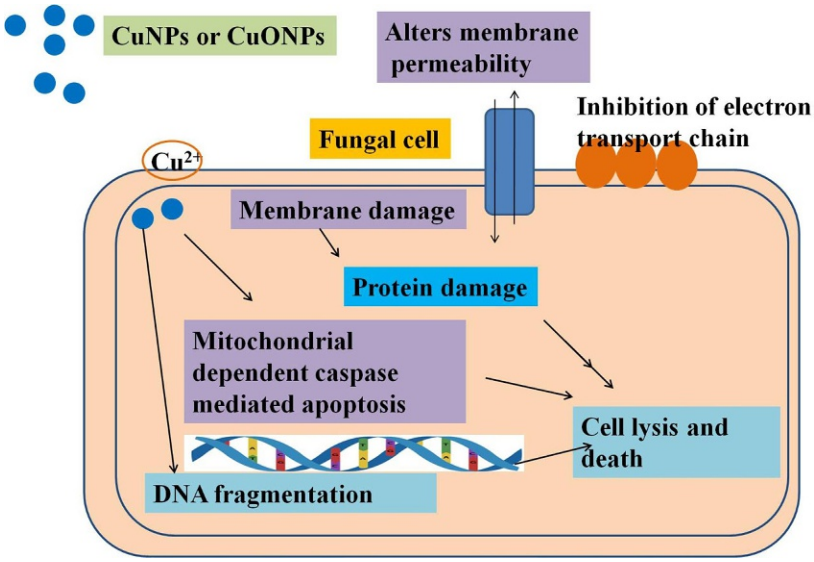

FIG. 3

Schematic representation of the fungal cell damage by the CuNPs or CuONPs.

9 Nanosensors for plant pathogen detection

Plant infections caused due to the communal attack of plant pathogens resulting in achievable yield and economic loss on other cash crops compared with food cash crops (Pan et al., 2010; Thind, 2012). Due to the increase in world population day by day, the main task is how to fulfill the growing requirement of the population with an eco-friendly approach using less input expense and limited land. The CuNPs-modified gold electrode is able to sense the fungal pathogen *Sclerotinia sclerotiorum* infection in oilseed rape (Wang et al., 2010). CuONPs and nanostructural layer biosensors are able to sense *Aspergillus niger* fungi (Etefagh et al., 2013).

10 Impacts of nanofertilizer in agriculture

Due to the limited availability of food sources and resources, global food security faces many threatening (van Dijk and Meijerink, 2014). Generally, crop productivity and the fertility of the soil can be enriched by conventional fertilizer (Giannousi et al., 2013). The fertility of the soil is determined by the micro and macronutrients in soil, mostly magnesium, potassium, phosphate, ammonium as major nutrients for the crop. Copper is a macronutrient that constitutes about 70% of the chloroplast. Conventional fertilizer contains nitrogen 30%–40%, phosphorus 18%–20%, and potassium 35%–40% (Heffer and Prud'homme, 2012). Using this fertilizer, it may

produce a lot of residues, which will be deposit in the soil mixed with the river, thus causing the depletion of the drinking water (Jiang et al., 2006). Nanofertilizers are synthesized in a specific manner that regulates the release of nutrients depending on the crop requirement. Nanomodulated fertilizer will increase crop productivity and reduce fertilizer exposure to the soil at a drastic level (Kale and Gawade, 2016). Balancing the fertilizer management, irrigation, and use of quality seed increase crop productivity up to 35%–40% (Manjaiah et al., 2019).

The application of CuNPs increased the shelf life of tomato fruits and thus stored for a longer time without spoilage. The foliar treatment of CuNPs induces the production of better quality tomato fruits with increased bioactive compounds such as lycopene, vitamin C, total phenols, and flavonoids and increased antioxidant potential for the human diet. It also increased the activity of the antioxidant enzymes such as catalase and superoxide dismutase to eliminate the formation of ROS (López-Vargas et al., 2018). The toxicity of CuNPs has been reported widely in various plant species but at the same time, many positive reports are also available. Some researchers reported the hazardous effect of NPs on germination, accumulation, and growth (Rajput et al., 2018). The environmental fate of CuONPs needs to be determined carefully and used as a criterion for sustainable applications in agriculture. CuONPs increase the growth of soybean at 100 ppm and chickpea seedlings at 60 ppm. Above this concentration, their growth was inhibited by CuONPs may be due to the accumulation and uptake of nano-CuO particles by the roots dependent on the exposure concentrations (Adhikari et al., 2012).

11 Conclusion and future perspectives

Copper plays a main function in the metabolic, structural, and physiological role of a macromolecule. From the above studies, we conclude that the CuNPs at the adequate level show greater value in agriculture in various ways. CuNPs are more useful as a fertilizer, herbicide, pesticide, and fungicide. Thus the copper provides the great effect of sustainable agriculture without damaging soil fertility. CuNPs have better antimicrobial and antifungal effects than CuONPs. They can also be used for packing food to delaying the growth of germs and fungi. Metallic nanomaterial has wide antimicrobial activity against bacteria, fungi, and viruses that are active. It has been identified to be a cheap eco-microbicide for agriculture with effective nanometallic bactericide and fungicide potential (Fig. 4).

Cu-based nanoformulation was successfully developed and assessed for its utility for disease control at the field level. Effective control of pathogen was achieved at doses that were eightfold lower than the conventional copper-based antimicrobial agents. The use of nanoformulations thus avoids the excessive usage of Cu and consequent environmental hazards (Chikte et al., 2019). Singh et al. (2021) reported the recent advancement in nanochemical applications for sustainable agricultural practices. Several recent researchers reported the potential of nanotechnology in improving the agriculture sector by enhancing the efficiency of plant growth and providing eco-friendly solutions to agricultural problems and thus enhance food productivity and security. Khan et al. (2021) also reported the use of nanotechnology as an alternative for the eco-friendly

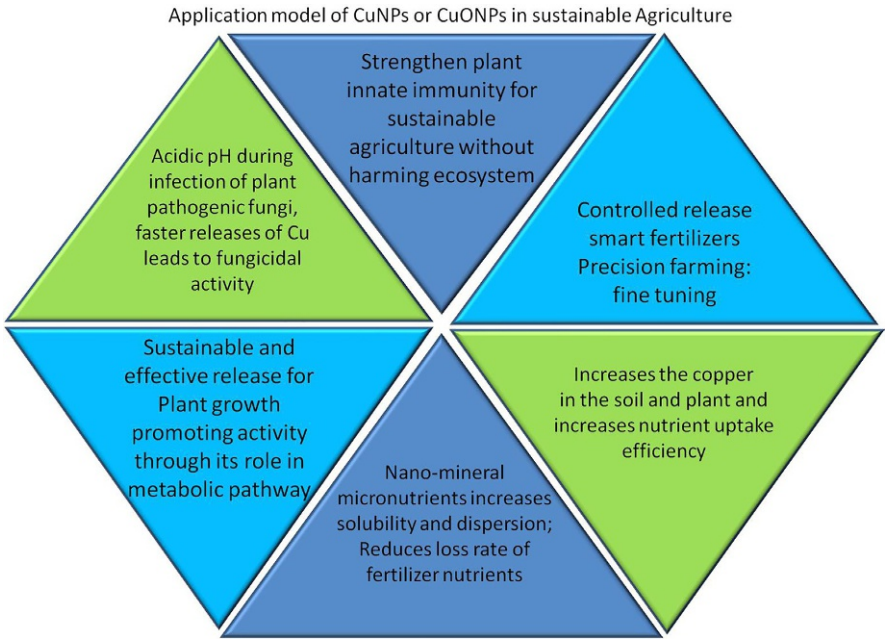

FIG. 4

Illustrated the application of CuNPs and CuONPs for sustainable agriculture.

and sustainable management of pests and phytopathogens on crops with improved plant growth. Bahrulolum et al. (2021) also reported the latest innovations in the production of metal nanoparticles using green synthesis and microorganisms. The application of these biosynthesized NPs in various agricultural sectors to achieve food security, improve crop production, and reduce the use of chemical pesticides. In this frame, we had proposed the mechanism of damage caused to phytopathogens by these metal nanoparticles are presented. This gives an insight into recent advancements in nanotechnology-based agrochemicals that have revolutionized the agriculture sector. Further, the implementation barriers related to the nanomaterial use in agriculture, their commercialization potential, nanomaterial safety, exposure levels, and toxicological repercussions to the environment and human health and the need for policy regulations to assess possible nano-agricultural risks are yet to be analyzed before field applications.

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References

Abboud, Y., Saffaj, T., Chagraoui, A., El Bouari, A., Brouzi, K., Tanane, O., Ihssane, B., 2014. Biosynthesis, characterization and antimicrobial activity of copper oxide nanoparticles (CONPs) produced using brown alga extract (*Bifurcaria bifurcata*). Appl. Nanosci. 4 (5), 571–576.

Abdel-Halim, K.Y., El-Ghanam, A.A., 2019. Antifungal potent of some metallic nanoparticles against *Sclerotinia sclerotiorum* on common bean plants: an emphasis for biochemical alterations and metal accumulation. Acad. J. Life Sci. 5 (11), 93–106.

Adhikari, T., Kundu, S., Biswas, A.K., Tarafdar, J.C., Rao, A.S., 2012. Effect of copper oxide nanoparticle on seed germination of selected crops. J. Agric. Sci. Technol. A 2 (6A), 815.

Ahmad, A., Jagadale, T., Dhas, V., Khan, S., Patil, S., Pasricha, R., Ravi, V., Ogale, S., 2007. Fungus-based synthesis of chemically difficult-to-synthesize multifunctional nanoparticles of $CuAlO_2$. Adv. Mater. 19 (20), 3295–3299.

Al-Dhabaan, F.A., Shoala, T., Ali, A.A., Alaa, M., Abd-Elsalam, K., 2017. Chemically-produced copper, zinc nanoparticles and chitosan–bimetallic nanocomposites and their antifungal activity against three phytopathogenic fungi. Int. J. Agric. Technol. 13 (5), 753–769.

Aleksandrowicz-Trzcińska, M., Szaniawski, A., Olchowik, J., Drozdowski, S., 2018. Effects of copper and silver nanoparticles on growth of selected species of pathogenic and wood-decay fungi in vitro. For. Chron. 94 (2), 109–116.

Andualem, W.W., Sabir, F.K., Mohammed, E.T., Belay, H.H., Gonfa, B.A., 2020. Synthesis of copper oxide nanoparticles using plant leaf extract of *Catha edulis* and its antibacterial activity. J. Nanosci. https://doi.org/10.1155/2020/2932434, 2932434.

Angrasan, J.K.V.M., Subbaiya, R., 2014. Biosynthesis of copper nanoparticles by *Vitis vinifera* leaf aqueous extract and its antibacterial activity. Int. J. Curr. Microbiol. App. Sci. 3 (9), 768–774.

Anzene, J.S., Tyohemba, R.L., Ahile, U.J., Emezi, K.S.A., 2014. Organochlorine pesticide residues analysis of postharvest cereal grains in Nasarawa State, Nigeria. Int. J. Agron. Agric. Res. 5 (5), 59–64.

Ashrafi, M., Bayat, M., Mortazavi, P., Hashemi, S.J., Meimandipour, A., 2020. Antimicrobial effect of chitosan–silver–copper nanocomposite on *Candida albicans*. J. Nanostruct. Chem. 10 (1), 87–95.

Bahrulolum, H., Nooraei, S., Javanshir, N., Tarrahimofrad, H., Mirbagheri, V.S., Easton, A.J., Ahmadian, G., 2021. Green synthesis of metal nanoparticles using microorganisms and their application in the agrifood sector. J. Nanobiotechnol. 19 (1), 1–26.

Banik, S., Luque, A.P., 2017. In vitro effects of copper nanoparticles on plant pathogens, beneficial microbes and crop plants. Span. J. Agric. Res. 15 (2), 23.

Benassai, E., Del Bubba, M., Ancillotti, C., Colzi, I., Gonnelli, C., Calisi, N., Salvatici, M.C., Casalone, E., Ristori, S., 2020. Green and cost-effective synthesis of copper nanoparticles by extracts of non-edible and waste plant materials from *Vaccinium* species: characterization and antimicrobial activity. Mater. Sci. Eng. C 119, 111453.

Bezza, F.A., Tichapondwa, S.M., Chirwa, E.M., 2020. Fabrication of monodispersed copper oxide nanoparticles with potential application as antimicrobial agents. Sci. Rep. 10 (1), 1–18.

Bharathi, D., Ranjithkumar, R., Chandarshekar, B., Bhuvaneshwari, V., 2019. Bio-inspired synthesis of chitosan/copper oxide nanocomposite using rutin and their anti-proliferative activity in human lung cancer cells. Int. J. Biol. Macromol. 141, 476–483.

Bhattacharya, D., Gupta, R.K., 2005. Nanotechnology and potential of microorganisms. Crit. Rev. Biotechnol. 25 (4), 199–204.
Bhuvaneshwari, V., Vaidehi, D., Logpriya, S., 2018. Green synthesis of copper oxide nanoparticles for biological applications. Microbiol. Curr. Res. 2 (1).
Bordbar, M., Sharifi-Zarchi, Z., Khodadadi, B., 2017. Green synthesis of copper oxide nanoparticles/clinoptilolite using *Rheum palmatum* L. root extract: high catalytic activity for reduction of 4-nitro phenol, rhodamine B, and methylene blue. J. Sol-Gel Sci. Technol. 81 (3), 724–733.
Bramhanwade, K., Shende, S., Bonde, S., Gade, A., Rai, M., 2016. Fungicidal activity of Cu nanoparticles against *Fusarium* causing crop diseases. Environ. Chem. Lett. 14 (2), 229–235.
Cao, Y., Ma, C., Chen, H., Zhang, J., White, J.C., Chen, G., Xing, B., 2020. Xylem-based long-distance transport and phloem remobilization of copper in *Salix integra* Thunb. J. Hazard. Mater, 122428.
Carvalho, R., Duman, K., Jones, J.B., Paret, M.L., 2019. Bactericidal activity of copper-zinc hybrid nanoparticles on copper-tolerant *Xanthomonas perforans*. Sci. Rep. 9 (1), 1–9.
Castillo-Henríquez, L., Alfaro-Aguilar, K., Ugalde-Álvarez, J., Vega-Fernández, L., Montes de Oca-Vásquez, G., Vega-Baudrit, J.R., 2020. Green synthesis of gold and silver nanoparticles from plant extracts and their possible applications as antimicrobial agents in the agricultural area. Nanomaterials (Basel) 10 (9), 1763.
Chalandar, H.E., Ghorbani, H.R., Attar, H., Alavi, S.A., 2017. Antifungal effect of copper and copper oxide nanoparticles against *Penicillium* on orange fruit. Biosci. Biotechnol. Res. Asia 14 (1), 279–284.
Chen, J., Mao, S., Xu, Z., Ding, W., 2019. Various antibacterial mechanisms of biosynthesized copper oxide nanoparticles against soilborne *Ralstonia solanacearum*. RSC Adv. 9 (7), 3788–3799.
Chibber, S., Ansari, S.A., Satar, R., 2013. New vision to CuO, ZnO, and TiO_2 nanoparticles: their outcome and effects. J. Nanopart. Res. 15 (4), 1492.
Chikte, R.G., Paknikar, K.M., Rajwade, J.M., Sharma, J., 2019. Nanomaterials for the control of bacterial blight disease in pomegranate: quo vadis? Appl. Microbiol. Biotechnol. 103 (11), 4605–4621.
Chung, I.M., Abdul Rahuman, A., Marimuthu, S., Vishnu Kirthi, A., Anbarasan, K., Padmini, P., Rajakumar, G., 2017. Green synthesis of copper nanoparticles using *Eclipta prostrata* leaves extract and their antioxidant and cytotoxic activities. Exp. Ther. Med. 14 (1), 18–24.
Concha-Guerrero, S.I., Brito, E.M.S., Piñón-Castillo, H.A., Tarango-Rivero, S.H., Caretta, C.A., Luna-Velasco, A., Duran, R., Orrantia-Borunda, E., 2014. Effect of CuO nanoparticles over isolated bacterial strains from agricultural soil. J. Nanomater. 2014.
Consolo, V.F., Torres-Nicolini, A., Alvarez, V.A., 2020. Mycosynthetized Ag, CuO and ZnO nanoparticles from a promising *Trichoderma harzianum* strain and their antifungal potential against important phytopathogens. Sci. Rep. 10 (1), 1–9.
Cuevas, R., Durán, N., Diez, M.C., Tortella, G.R., Rubilar, O., 2015. Extracellular biosynthesis of copper and copper oxide nanoparticles by *Stereum hirsutum*, a native white-rot fungus from chilean forests. J. Nanomater. 2015.
Da Costa, M.V.J., Sharma, P.K., 2016. Effect of copper oxide nanoparticles on growth, morphology, photosynthesis, and antioxidant response in *Oryza sativa*. Photosynthetica 54 (1), 110–119.

Das, P.E., Abu-Yousef, I.A., Majdalawieh, A.F., Narasimhan, S., Poltronieri, P., 2020. Green synthesis of encapsulated copper nanoparticles using a hydroalcoholic extract of *Moringa oleifera* leaves and assessment of their antioxidant and antimicrobial activities. Molecules 25 (3), 555.

de Andrade, C.J., De Andrade, L.M., Mendes, M.A., Do, C.A.O., 2017. An overview on the production of microbial copper nanoparticles by bacteria, fungi and algae. Glob. J. Eng. Res. 17 (1).

Delgado, K., Quijada, R., Palma, R., Palza, H., 2011. Polypropylene with embedded copper metal or copper oxide nanoparticles as a novel plastic antimicrobial agent. Lett. Appl. Microbiol. 53 (1), 50–54.

Ditta, A., Arshad, M., Ibrahim, M., 2015. Nanoparticles in sustainable agricultural crop production: applications and perspectives. In: Nanotech. Plant Sci. Springer, Cham, pp. 55–75.

Duman, F., Ocsoy, I., Kup, F.O., 2016. Chamomile flower extract-directed CuO nanoparticle formation for its antioxidant and DNA cleavage properties. Mater. Sci. Eng. C 60, 333–338.

El-Batal, A.I., Balabel, N.M., Attia, M.S., El-Sayyad, G.S., 2019. Antibacterial and antibiofilm potential of mono-dispersed stable copper oxide nanoparticles-streptomycin nanodrug: implications for some potato plant bacterial pathogen treatment. J. Clust. Sci., 1–20.

El-Saadony, M.T., El-Hack, A., Mohamed, E., Taha, A.E., Fouda, M.M., Ajarem, J.S., Maodaa, S.N., Allam, A.A., Elshaer, N., 2020. Ecofriendly synthesis and insecticidal application of copper nanoparticles against the storage pest *Tribolium castaneum*. Nanomaterials 10 (3), 587.

Etefagh, R., Azhir, E., Shahtahmasebi, N., 2013. Synthesis of CuO nanoparticles and fabrication of nanostructural layer biosensors for detecting *Aspergillus niger* fungi. Sci. Iran. 20 (3), 1055–1058.

Fan, Q., Liao, Y.Y., Kunwar, S., Da Silva, S., Young, M., Santra, S., Minsavage, G.V., Freeman, J.H., Jones, J.B., Paret, M.L., 2021. Antibacterial effect of copper composites against *Xanthomonas euvesicatoria*. Crop Prot. 139, 105366.

Farajzadeh Memari Tabrizi, E., Yarnia, M., Khorshidi, M.B., Ahmadzadeh, V., 2009. Effects of micronutrients and their application method on yield, crop growth rate (CGR) and net assimilation rate (NAR) of corn cv. Jeta. Jeta. Int. J. Food Agric. Environ. 7 (2), 611–615.

Giannousi, K., Avramidis, I., Dendrinou-Samara, C., 2013. Synthesis, characterization and evaluation of copper based nanoparticles as agrochemicals against *Phytophthora infestans*. RSC Adv. 3 (44), 21743–21752.

Hao, Y., Cao, X., Ma, C., Zhang, Z., Zhao, N., Ali, A., Hou, T., Xiang, Z., Zhuang, J., Wu, S., Xing, B., 2017. Potential applications and antifungal activities of engineered nanomaterials against gray mold disease agent *Botrytis cinerea* on rose petals. Front. Plant Sci. 8, 1332.

Harne, S., Sharma, A., Dhaygude, M., Joglekar, S., Kodam, K., Hudlikar, M., 2012. Novel route for rapid biosynthesis of copper nanoparticles using aqueous extract of *Calotropis procera* L. latex and their cytotoxicity on tumor cells. Colloids Surf. B. Biointerfaces 95, 284–288.

Heffer, P., Prud'homme, M., 2012. Fertilizer outlook 2012-2016. In: IFA. 80th IFA Annual Conference, Doha, Qatar.

Honary, S., Barabadi, H., Gharaei-Fathabad, E., Naghibi, F., 2012. Green synthesis of copper oxide nanoparticles using *Penicillium aurantiogriseum, Penicillium citrinum* and *Penicillium waksmanii*. Dig. J. Nanomater. Biostruct. 7 (3), 999–1005.

Howlett, N.G., Avery, S.V., 1997. Induction of lipid peroxidation during heavy metal stress in *Saccharomyces cerevisiae* and influence of plasma membrane fatty acid unsaturation. Appl. Environ. Microbiol. 63 (8), 2971–2976.

Ingle, A.P., Duran, N., Rai, M., 2014. Bioactivity, mechanism of action, and cytotoxicity of copper-based nanoparticles: a review. Appl. Microbiol. Biotechnol. 98 (3), 1001–1009.

Ivask, A., Bondarenko, O., Jepihhina, N., Kahru, A., 2010. Profiling of the reactive oxygen species-related ecotoxicity of CuO, ZnO, TiO_2, silver and fullerene nanoparticles using a set of recombinant luminescent *Escherichia coli* strains: differentiating the impact of particles and solubilised metals. Anal. Bioanal. Chem. 398 (2), 701–716.

Jia, B., Mei, Y., Cheng, L., Zhou, J., Zhang, L., 2012. Preparation of copper nanoparticles coated cellulose films with antibacterial properties through one-step reduction. ACS Appl. Mater. Interfaces 4 (6), 2897–2902.

Jiang, J., Cai, D.Q., Yu, Z.L., Wu, Y.J., 2006. Loss-Control Fertilizer Made by Active Clay, Flocculant and Sorbent. Chinese Patent Specification ZL200610040631, p. 1.

Jomova, K., Valko, M., 2011. Advances in metal-induced oxidative stress and human disease. Toxicology 283 (2-3), 65–87.

Kale, A.P., Gawade, S.N., 2016. Studies on nanoparticle induced nutrient use efficiency of fertilizer and crop productivity. Green Chem. Tech. Lett. 2, 88–92.

Kanhed, P., Birla, S., Gaikwad, S., Gade, A., Seabra, A.B., Rubilar, O., Duran, N., Rai, M., 2014. In vitro antifungal efficacy of copper nanoparticles against selected crop pathogenic fungi. Mater. Lett. 115, 13–17.

Kasana, R.C., Panwar, N.R., Kaul, R.K., Kumar, P., 2016. Copper nanoparticles in agriculture: biological synthesis and antimicrobial activity. In: Nanosci. Food Agri. vol. 3. Springer, Cham, pp. 129–143.

Kasana, R.C., Panwar, N.R., Kaul, R.K., Kumar, P., 2017. Biosynthesis and effects of copper nanoparticles on plants. Environ. Chem. Lett. 15 (2), 233–240.

Khan, M., Khan, A.U., Hasan, M.A., Yadav, K.K., Pinto, M., Malik, N., Yadav, V.K., Khan, A.H., Islam, S., Sharma, G.K., 2021. Agro-nanotechnology as an emerging field: a novel sustainable approach for improving plant growth by reducing biotic stress. Appl. Sci. 11 (5), 2282.

Kim, J.H., Cho, H., Ryu, S.E., Choi, M.U., 2000. Effects of metal ions on the activity of protein tyrosine phosphatase VHR: highly potent and reversible oxidative inactivation by Cu^{2+} ion. Arch. Biochem. Biophys. 382 (1), 72–80.

Kumar, H., Bhardwaj, K., Dhanjal, D.S., Nepovimova, E., Şen, F., Regassa, H., Singh, R., Verma, R., Kumar, V., Kumar, D., Bhatia, S.K., 2020. Fruit extract mediated green synthesis of metallic nanoparticles: a new avenue in pomology applications. Int. J. Mol. Sci. 21 (22), 8458.

Lee, H.J., Song, J.Y., Kim, B.S., 2013. Biological synthesis of copper nanoparticles using Magnolia kobus leaf extract and their antibacterial activity. J. Chem. Technol. Biotechnol. 88 (11), 1971–1977.

Li, X., Xu, H., Chen, Z.S., Chen, G., 2011. Biosynthesis of nanoparticles by microorganisms and their applications. J. Nanomater. 2011.

Lippert, H., Brinkmeyer, R., Mülhaupt, T., Iken, K., 2003. Antimicrobial activity in sub-Arctic marine invertebrates. Polar Biol. 26 (9), 591–600.

Liu, Z., Zhang, M., Han, X., Xu, H., Zhang, B., Yu, Q., Li, M., 2016. TiO2 nanoparticles cause cell damage independent of apoptosis and autophagy by impairing the ROS-scavenging system in *Pichia pastoris*. Chem. Biol. Interact. 252, 9–18.

Logpriya, S., Bhuvaneshwari, V., Vaidehi, D., SenthilKumar, R.P., Malar, R.N., Sheetal, B.P., Amsaveni, R., Kalaiselvi, M., 2018. Preparation and characterization of ascorbic acid-mediated chitosan–copper oxide nanocomposite for anti-microbial, sporicidal and biofilm-inhibitory activity. J. Nanostruct. Chem. 8 (3), 301–309.

López-Vargas, E.R., Ortega-Ortíz, H., Cadenas-Pliego, G., de Alba Romenus, K., Cabrera De La Fuente, M., Benavides-Mendoza, A., Juárez-Maldonado, A., 2018. Foliar application of copper nanoparticles increases the fruit quality and the content of bioactive compounds in tomatoes. Appl. Sci. 8 (7), 1020.

Madanayake, N.H., Hossain, A., Adassooriya, N.M., 2021. Nanobiotechnology for agricultural sustainability, and food and environmental safety. Qual. Assur. Saf. Crops Food 13 (1), 20–36.

Malandrakis, A.A., Kavroulakis, N., Chrysikopoulos, C.V., 2019. Use of copper, silver and zinc nanoparticles against foliar and soil-borne plant pathogens. Sci. Total Environ. 670, 292–299.

Mali, S.C., Dhaka, A., Githala, C.K., Trivedi, R., 2020. Green synthesis of copper nanoparticles using *Celastrus paniculatus* Willd. leaf extract and their photocatalytic and antifungal properties. Biotech. Rep. 27, e00518.

Manjaiah, K.M., Mukhopadhyay, R., Paul, R., Datta, S.C., Kumararaja, P., Sarkar, B., 2019. Clay minerals and zeolites for environmentally sustainable agriculture. In: Modified Clay and Zeolite Nanocomposite Materials. Elsevier, pp. 309–329.

Miralles, P., Church, T.L., Harris, A.T., 2012. Toxicity, uptake, and translocation of engineered nanomaterials in vascular plants. Environ. Sci. Technol. 46 (17), 9224–9239.

Mondal, K.K., Mani, C., 2012. Investigation of the antibacterial properties of nanocopper against Xanthomonas axonopodis pv. punicae, the incitant of pomegranate bacterial blight. Ann. Microbiol. 62 (2), 889–893.

Murthy, H.A., Abebe, B., Prakash, C.H., Shantaveerayya, K., 2018. A review on green synthesis of Cu and CuO nanomaterials for multifunctional applications. Mater. Sci. Res. India 15 (3), 279–295.

Murthy, H.C., Desalegn, T., Kassa, M., Abebe, B., Assefa, T., 2020. Synthesis of green copper nanoparticles using medicinal plant *Hagenia abyssinica* (Brace) JF. Gmel. leaf extract: antimicrobial properties. J. Nanomater. 2020.

Nargund, V.B., Vinay, J.U., Basavesha, K.N., Chikkanna, S., Jahagirdar, S., Patil, R.R., 2021. Green nanotechnology and its application in plant disease management. In: Emerging Trends Plant Pathol. Springer, Singapore, pp. 591–609.

Nemati, A., Shadpour, S., Khalafbeygi, H., Ashraf, S., Barkhi, M., Soudi, M.R., 2015. Efficiency of hydrothermal synthesis of nano/microsized copper and study on in vitro antifungal activity. Mater. Manuf. Process. 30 (1), 63–69.

Ouda, S.M., 2014. Antifungal activity of silver and copper nanoparticles on two plant pathogens, *Alternaria alternata* and *Botrytis cinerea*. Res. J. Microbiol. 9 (1), 34.

Oussou-Azo, A.F., Nakama, T., Nakamura, M., Futagami, T., Vestergaard, M.D.C.M., 2020. Antifungal potential of nanostructured crystalline copper and its oxide forms. Nanomaterials (Basel) 10 (5), 1003.

Palza, H., 2015. Antimicrobial polymers with metal nanoparticles. Int. J. Mol. Sci. 16 (1), 2099–2116.

Pan, L., Qiu, H., Dou, C., Li, Y., Pu, L., Xu, J., Shi, Y., 2010. Conducting polymer nanostructures: template synthesis and applications in energy storage. Int. J. Mol. Sci. 11 (7), 2636–2657.

Pandey, S., Giri, K., Kumar, R., Mishra, G., Rishi, R.R., 2018. Nanopesticides: opportunities in crop protection and associated environmental risks. Proc. Natl. Acad. Sci. India B—Biol. Sci. 88 (4), 1287–1308.

Peng, C., Duan, D., Xu, C., Chen, Y., Sun, L., Zhang, H., Yuan, X., Zheng, L., Yang, Y., Yang, J., Zhen, X., 2015. Translocation and biotransformation of CuO nanoparticles in rice (*Oryza sativa* L.) plants. Environ. Pollut. 197, 99–107.

Pham, N.D., Duong, M.M., Le, M.V., Hoang, H.A., 2019. Preparation and characterization of antifungal colloidal copper nanoparticles and their antifungal activity against *Fusarium oxysporum* and *Phytophthora capsici*. C. R. Chim. 22 (11–12), 786–793.

Ponmurugan, P., Manjukarunambika, K., Elango, V., Gnanamangai, B.M., 2016. Antifungal activity of biosynthesised copper nanoparticles evaluated against red root-rot disease in tea plants. J. Exp. Nanosci. 11 (13), 1019–1031.

Prasad, K.S., Patra, A., Shruthi, G., Chandan, S., 2017. Aqueous extract of *Saraca indica* leaves in the synthesis of copper oxide nanoparticles: finding a way towards going green. J. Nanosci. 2017.

Quiterio-Gutiérrez, T., Ortega-Ortiz, H., Cadenas-Pliego, G., Hernández-Fuentes, A.D., Sandoval-Rangel, A., Benavides-Mendoza, A., Cabrera-de la Fuente, M., Juárez-Maldonado, A., 2019. The application of selenium and copper nanoparticles modifies the biochemical responses of tomato plants under stress by *Alternaria solani*. Int. J. Mol. *Sci.* 20 (8), 1950.

Qureshi, A., Singh, D.K., Dwivedi, S., 2018. Nano-fertilizers: a novel way for enhancing nutrient use efficiency and crop productivity. Int. J. Curr. Microbiol. App. Sci. 7 (2), 3325–3335.

Rabiee, N., Bagherzadeh, M., Kiani, M., Ghadiri, A.M., Etessamifar, F., Jaberizadeh, A.H., Shakeri, A., 2020. Biosynthesis of copper oxide nanoparticles with potential biomedical applications. Int. J. Nanomedicine 15, 3983–3999.

Raffi, M., Mehrwan, S., Bhatti, T.M., Akhter, J.I., Hameed, A., Yawar, W., Ul Hasan, M.M., 2010. Investigations into the antibacterial behavior of copper nanoparticles against Escherichia coli. Ann. Microbiol. 60 (1), 75–80.

Rafique, M., Shaikh, A.J., Rasheed, R., Tahir, M.B., Bakhat, H.F., Rafique, M.S., Rabbani, F., 2017. A review on synthesis, characterization and applications of copper nanoparticles using green method. Nano 12 (04), 1750043.

Rai, M., Ingle, A.P., Pandit, R., Paralikar, P., Shende, S., Gupta, I., Biswas, J.K., da Silva, S.S., 2018. Copper and copper nanoparticles: role in management of insect-pests and pathogenic microbes. Nanotechnol. Rev. 7 (4), 303–315.

Rajesh, K.M., Ajitha, B., Reddy, Y.A.K., Suneetha, Y., Reddy, P.S., Ahn, C.W., 2018. A facile bio-synthesis of copper nanoparticles using *Cuminum cyminum* seed extract: antimicrobial studies. Adv. Nat. Sci. Nanosci. Nanotechnol. 9 (3), 035005.

Rajput, V.D., Minkina, T., Suskova, S., Mandzhieva, S., Tsitsuashvili, V., Chapligin, V., Fedorenko, A., 2018. Effects of copper nanoparticles (CuO NPs) on crop plants: a mini review. BioNanoScience 8 (1), 36–42.

Raveendran, P., Fu, J., Wallen, S.L., 2003. Completely "green" synthesis and stabilization of metal nanoparticles. J. Am. Chem. Sci 125 (46), 13940–13941.

Rehman, M., Liu, L., Wang, Q., Saleem, M.H., Bashir, S., Ullah, S., Peng, D., 2019. Copper environmental toxicology, recent advances, and future outlook: a review. Environ. Sci. Pollut. Res., 1–14.

Revathi, T., Thambidurai, S., 2019. Cytotoxic, antioxidant and antibacterial activities of copper oxide incorporated chitosan-neem seed biocomposites. Int. J. Biol. Macromol. 139, 867–878.

Ruparelia, J.P., Chatterjee, A.K., Duttagupta, S.P., Mukherji, S., 2008. Strain specificity in antimicrobial activity of silver and copper nanoparticles. Acta Biomater. 4 (3), 707–716.

Saharan, V., Sharma, G., Yadav, M., Choudhary, M.K., Sharma, S.S., Pal, A., Raliya, R., Biswas, P., 2015. Synthesis and in vitro antifungal efficacy of Cu–chitosan nanoparticles against pathogenic fungi of tomato. Int. J. Biol. Macromol. 75, 346–353.

Saif Hasan, S., Singh, S., Parikh, R.Y., Dharne, M.S., Patole, M.S., Prasad, B.L.V., Shouche, Y.S., 2008. Bacterial synthesis of copper/copper oxide nanoparticles. J. Nanosci. Nanotechnol. 8 (6), 3191–3196.

Salvadori, M.R., Lepre, L.F., Ando, R.A., do Nascimento, C.A.O., Corrêa, B., 2013. Biosynthesis and uptake of copper nanoparticles by dead biomass of *Hypocrea lixii* isolated from the metal mine in the Brazilian Amazon region. PLoS One 8 (11), e80519.

Saran, S., Sharma, G., Kumar, M., Ali, M.I., 2017. Biosynthesis of copper oxide nanoparticles using cyanobacteria *Spirulina platensis* and its antibacterial activity. Int. J. Pharm. Sci. Res. 8, 3887–3892.

Saravanakumar, K., Shanmugam, S., Varukattu, N.B., MubarakAli, D., Kathiresan, K., Wang, M.H., 2019. Biosynthesis and characterization of copper oxide nanoparticles from indigenous fungi and its effect of photothermolysis on human lung carcinoma. J. Photochem. Photobiol. B Biol. 190, 103–109.

Shang, Y., Hasan, M., Ahammed, G.J., Li, M., Yin, H., Zhou, J., 2019. Applications of nanotechnology in plant growth and crop protection: a review. Molecules 24 (14), 2558.

Shende, S., Ingle, A.P., Gade, A., Rai, M., 2015. Green synthesis of copper nanoparticles by *Citrus medica* Linn. (Idilimbu) juice and its antimicrobial activity. World J. Microbiol. Biotechnol. 31 (6), 865–873.

Shobha, G., Moses, V., Ananda, S., 2014. Biological synthesis of copper nanoparticles and its impact. Int. J. Pharm. Sci. Invent. 3 (8), 6–28.

Shukla, P., Chaurasia, P., Younis, K., Qadri, O.S., Faridi, S.A., Srivastava, G., 2019. Nanotechnology in sustainable agriculture: studies from seed priming to post-harvest management. Nanotechnol. Environ. Eng. 4 (1), 11.

Singh, O.V. (Ed.), 2015. Bio-Nanoparticles: Biosynthesis and Sustainable Biotechnological Implications. John Wiley & Sons.

Singh, M.D., 2017. Nano-fertilizers is a new way to increase nutrients use efficiency in crop production. Int. J. Agric. Sci. ISSN 0975-3710.

Singh, V.A., Patil, R., Anand, A., Milani, P., Gade, W.N., 2010. Biological synthesis of copper oxide nano particles using *Escherichia coli*. Curr. Nanosci. 6 (4), 365–369.

Singh, H., Sharma, A., Bhardwaj, S.K., Arya, S.K., Bhardwaj, N., Khatri, M., 2021. Recent advances in the applications of nano-agrochemicals for sustainable agricultural development. Environ. Sci. Process Impacts 23 (2), 213–239.

Sommer, A.L., 1931. Copper as an essential for plant growth. Plant Physiol. 6 (2), 339.

Thind, T.S., 2012. Phytopathogenic procaryotes and plant diseases. Plant Dis. Res. 27 (1), 125.

Vaidehi, D., Bhuvaneshwari, V., Bharathi, D., Sheetal, B.P., 2018. Antibacterial and photocatalytic activity of copper oxide nanoparticles synthesized using *Solanum lycopersicum* leaf extract. Mater. Res. Express 5 (8), 085403.

van Dijk, M., Meijerink, G.W., 2014. A review of food security scenario studies: gaps and ways forward. In: The Food Puzzle: Pathways to Securing Food for All. Wageningen UR, pp. 30–32.

Van Ha, C., Van Nguyen, D., Nguyen, H.M., Le, N.T., Nguyen, K.H., Le, H.M., Nguyen, A.T., Dinh, N.T.T., Hoang, S.A., 2020. Copper nanoparticle application enhances plant growth and grain yield in maize under drought stress conditions. bioRxiv.

Vanathi, P., Rajiv, P., Sivaraj, R., 2016. Synthesis and characterization of *Eichhornia*-mediated copper oxide nanoparticles and assessing their antifungal activity against plant pathogens. Bull. Mater. Sci. 39 (5), 1165–1170.

Varshney, R., Bhadauria, S., Gaur, M.S., Pasricha, R., 2010. Characterization of copper nanoparticles synthesized by a novel microbiological method. JOM 62 (12), 102–104.

Varympopi, A., Dimopoulou, A., Theologidis, I., Karamanidou, T., Kaldeli Kerou, A., Vlachou, A., Karfaridis, D., Papafotis, D., Hatzinikolaou, D.G., Tsouknidas, A., Skandalis, N., 2020. Bactericides based on copper nanoparticles restrain growth of important plant pathogens. Pathogens 9, 1024.

Viet, P.V., Nguyen, H.T., Cao, T.M., Hieu, L.V., 2016. *Fusarium* antifungal activities of copper nanoparticles synthesized by a chemical reduction method. J. Nanomater. 2016.

Wang, Z., Wei, F., Liu, S.Y., Xu, Q., Huang, J.Y., Dong, X.Y., Yu, J.H., Yang, Q., Zhao, Y.D., Chen, H., 2010. Electrocatalytic oxidation of phytohormone salicylic acid at copper nanoparticles-modified gold electrode and its detection in oilseed rape infected with fungal pathogen *Sclerotinia sclerotiorum*. Talanta 80 (3), 1277–1281.

Wang, X., Liu, X., Chen, J., Han, H., Yuan, Z., 2014. Evaluation and mechanism of antifungal effects of carbon nanomaterials in controlling plant fungal pathogen. Carbon 68, 798–806.

Wei, Y., Chen, S., Kowalczyk, B., Huda, S., Gray, T.P., Grzybowski, B.A., 2010. Synthesis of stable, low-dispersity copper nanoparticles and nanorods and their antifungal and catalytic properties. J. Phys. Chem. C 114 (37), 15612–15616.

Worrall, E.A., Hamid, A., Mody, K.T., Mitter, N., Pappu, H.R., 2018. Nanotechnology for plant disease management. Agronomy 8 (12), 285.

Yruela, I, 2005. Copper in plants. Braz. J. Plant Physiol. 17, 145–156.

Yulizar, Y., Latifah, I., Bakri, R., Apriandanu, D.O.B., 2018. Plants extract mediated synthesis of copper (II) oxide nanoparticles using *Oldenlandia corymbosa* L. leaf. AIP Conf. Proc. vol. 2023 (1), 020097. AIP Publishing LLC.

Zarzuela, R., Carbú, M., Gil, M.A., Cantoral, J.M., Mosquera, M.J., 2017. CuO/SiO_2 nanocomposites: a multifunctional coating for application on building stone. Mater. Des. 114, 364–372.

Zuverza-Mena, N., Medina-Velo, I.A., Barrios, A.C., Tan, W., Peralta-Videa, J.R., Gardea-Torresdey, J.L., 2015. Copper nanoparticles/compounds impact agronomic and physiological parameters in cilantro (*Coriandrum sativum*). Environ. Sci. Process Impacts 17 (10), 1783–1793.

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CHAPTER

19 Copper-based nanostructures: Antimicrobial properties against agri-food pathogens

J.M. Rajwade, R.C. Chikte, N. Singh, and K.M. Paknikar
Nanobioscience Group, Agharkar Research Institute, Pune, India

1 Introduction

Copper (Cu) is an indispensable element since prehistoric times and its demand is projected to increase in the years to come (Solomon et al., 2014; Gawande et al., 2016; Rötzer and Schmidt, 2020). It was the first metal extracted and used by humans. Traditionally, copper was used as a coinage metal along with gold and silver. Pieces of evidence from archaeology indicate the importance and utility of copper since 8000–5000 BC. Procedures for copper mining, extraction, purification, etc., were being continuously developed and vessels of copper were used by the royal families during ceremonies. It has excellent electrical conductivity and heat transfer properties and hence it has been extensively used in electrical equipment, industrial heat transfer machinery, construction, optics, and electronics. Copper exists in four oxidation states (0, + 1, + 2, + 3) and hence it is widely used as a catalyst in organic transformations, electrocatalysis, and photocatalysis (Gawande et al., 2016). Copper is an essential micronutrient in plants and humans since it has an important role in several cellular processes such as electron transport, nitrite, and nitric oxide reduction, oxygen binding activation and reduction, etc. (Solomon et al., 2014).

Early civilizations used copper vessels for cooking food and storing drinking water (Rusjan, 2012; Vincent et al., 2018; Arendsen et al., 2019). Medicinal usage of copper in the form of *Tamra bhasma* was reported in ancient Ayurveda scripts. Later, the "oligodynamic effect" of copper was documented (Kraemer, 1905). Compounds of silver, copper, mercury, tellurium, magnesium, arsenic oxides, etc., were used as antimicrobials until the discovery of antibiotics by Sir Alexander Fleming in 1920 (Lemire et al., 2013). The indiscriminate use of antibiotics has led to the burgeoning issue of resistance in microorganisms and proving to be an era of a renaissance for metal-based antimicrobials. In 2008, the EPA officially recognized copper and its alloys as the first effective metallic antimicrobial agent (http://www.epa.gov/pesticides/factsheets/copper-alloy-products.htm).

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Pathogenic microorganisms remain to be a continuous threat to mankind as they are big contributors to economic losses in agriculture and processed food (Miao et al., 2019). Crop losses due to bacterial, fungal, and viral diseases have been well documented (Agrios, 1995; Elmer and White, 2018). In the 1880s, a paste containing copper sulfate and lime was applied by farmers in Bordeaux, France, to control downy mildew in grapes and it continues to be used in organic farming even today (Rusjan, 2012; Lamichhane et al., 2018). Resistance to antimicrobials is reported in the case of phytopathogens also making traditional antibiotics ineffective. Since the dawn of "Nanotechnology" in the past two decades, newer forms of both, rare and precious, as well as abundant and inexpensive metals are being synthesized and explored by mankind (Gawande et al., 2016) and copper is no exception. Nanomaterials contain particles with dimensions in the nanometer size range (1–100 nm) and these often exhibit physicochemical, mechanical, electromagnetic properties that are different from the same material in its bulk form. Copper metal, as well as copper oxide nanoparticles, have been synthesized and assessed for their potential antimicrobial effects. The present chapter focuses on antimicrobial activities of copper-based nanomaterials specifically against agri-food pathogens.

2 Methods for the synthesis of copper nanoparticles

Copper is extremely reactive and its salts can undergo both oxidation as well as reduction reactions. It is because of this chemical property, metallic copper, copper oxide, and copper-alloy nanomaterials have been prepared involving physical, chemical, and biological processes. Fig. 1 gives an overview of all the processes reported to date for the synthesis of Cu nanostructures. While physical and chemical processes have been widely practiced to obtain copper nanoparticles on a large scale and a subject of extensive reviews (Camacho-Flores et al., 2015; Gawande et al., 2016; Khan et al., 2016; Din and Rehan, 2017; Powar et al., 2019); biological synthesis routes have also received the attention of researchers. The latter are described as eco-friendly processes in which copper-based nanoparticles can be produced using molecules of plant, animal, or microbial origin. The use of nontoxic renewable chemicals, reaction conditions such as ambient temperature and neutral pH are the fundamental principles of "green chemistry" (Ray et al., 2015). Parameters during synthesis (viz., pH, the ratio of reactants, mixing, temperature, reaction time, etc.) are optimized for obtaining monodisperse and stable nanoparticles (Singh et al., 2016). Nayantara and Pawan (2018) reviewed the advantages of the biological synthesis of nanoparticles in comparison to physical and chemical methods. It was observed that the nanoparticles produced using extracts obtained from medicinal plants were pharmacologically active (Singh et al., 2016).

Some examples of biosynthesized copper nanoparticles are enlisted in Table 1.

A survey of the literature shows that the applications of copper nanoparticles are increasing in the agro and food sector (Fig. 2). The central idea is to reduce the chemical inputs, detecting diseases early so that yield/productivity is unaffected

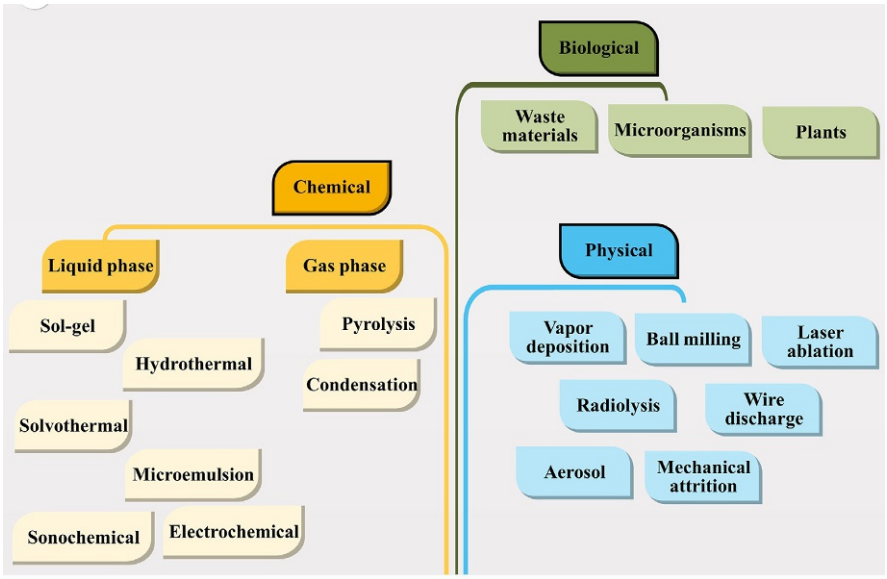

FIG. 1

Summary of the various methods used for the synthesis of Cu nanostructures.

Table 1 Biosynthesis of copper nanostructures.

Species	Nanoparticles characteristics (size nm, shape)	References
Bacteria		
Pseudomonas stutzeri	8–15	Varshney et al. (2010)
Pseudomonas fluorescens	49 Spherical, hexagonal	Shantkriti and Rani (2014)
Pseudomonas fluorescens ATCC 17397	15.6–34.2	Gomaa et al. (2019)
Morganella morganii	3–10	Ramanathan et al. (2013)
Serratia (copper/copper oxide nanoparticle)	10–30	Hasan et al. (2008)
Bacillus cereus	11–33	Tiwari et al. (2016)
Streptomyces capillispiralis Ca-1	3.6–59 Spherical	Hassan et al. (2018)
Streptomyces griseus	5–50	Ponmurugan et al. (2016)

Continued

Table 1 Biosynthesis of copper nanostructures—cont'd

Species	Nanoparticles characteristics (size nm, shape)	References
Fungi		
Penicillium aurantiogriseum, *Penicillium citrinum*, and *Penicillium waksmanii*	90–295	Honary et al. (2012)
Penicillium chrysogenum filtrate	9.70	El-Batal et al. (2019)
Stereum hirsutum	5–20 Spherical	Cuevas et al. (2015)
Plants		
Magnolia leaf extract	40–100	Lee et al. (2013)
Syzygium aromaticum (clove)	5–40	Subhankari and Nayak (2013)
Syzygium aromaticum bud extract	15–20	Rajesh et al. (2018a)
Zingiber officinale, *Piper nigrum*, and *Piper longum*	15–30	Shah et al. (2019)
Zingiber officinale	10	Chitra et al. (2015)
Camellia sinensis plant powder	100–200	Ibrahim et al. (2020)
Hawthorn berries extract	200	Długosz et al. (2020)
Gum arabic	19–35	Chawla et al. (2020)
Citrus medica Linn.	10–60	Shende et al. (2015)
Capparis zeylanica	50–100 Cubical	Saranyaadevi et al. (2014)
Azadirachta indica	48 Cubical	Nagar and Devra (2018)
Ziziphus spina-christi	8–15 Cubic	Khani et al. (2018)
Phyllanthus embilica	15–30	Caroling et al. (2015)
Eugenol (4-allyl-2-methoxyphenol) extracted from *O. sanctum* leaves	250 Flower-like	Siddiqui et al. (2020)
Tinospora cordifolia (Giloy)	63.3–143	Sharma et al. (2019)
Aloe vera leaf extract	20	Kumar et al. (2015)
Ananas comosus L. (pineapple)	30–50	Mercy Ranjitham et al. (2015)
Punica granatum	15–20	Kaur et al. (2016)
Cuminum cyminum (Cumin)	18–25	Rajesh et al. (2018b)
Mandarin (*Citrus reticulata*)	10–40	Trang et al. (2018)
Falcaria vulgaris	20–25	Zangeneh et al. (2019)
Persea Americana (Avocado)	42–90	Rajeshkumar and Rinitha (2018)
Cardiospermum halicacabum	30–40	Punniyakotti et al. (2020)
Walnut leaf extract	80	Asemani and Anarjan (2019)

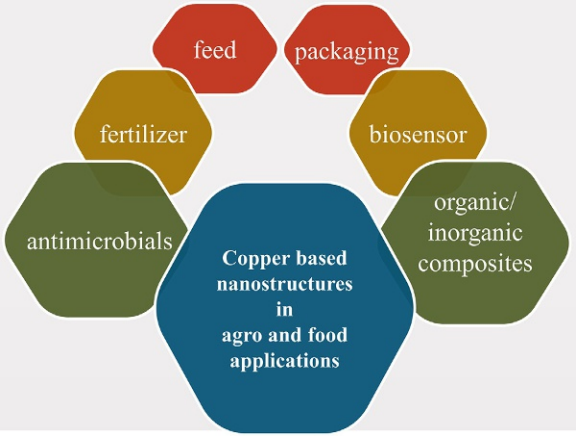

FIG. 2

Possibilities for applications of copper nanostructures in agro and food industry.

or even enhanced. Thus, nanotechnology is being considered mainly for achieving sustainable agriculture (Elmer and White, 2018). The reports on antimicrobial activity of nanoparticles and organic/inorganic composites against phytopathogens, along with copper-based fertilizers, biosensors, feed supplements, and packaging will be the focus of the following sections.

3 CuNPs applications in agriculture

As stated in the earlier section, the use of copper in agriculture for controlling plant pathogens is documented for almost 13 decades. Copper is abundantly available and hence a relatively inexpensive material for agro-based applications. The broad-spectrum antimicrobial characteristics of nanoscale copper were proved along with silver against model microorganisms such as *Escherichia coli*, *Staphylococcus aureus*, and *Candida* sp. (Cioffi et al., 2005; Ruparelia et al., 2008). Specifically, after methods for green synthesis of copper nanoparticles (CuNPs) were explored, efforts to prove the effectivity of copper nanostructures on bacterial and fungal plant pathogens were undertaken. Following is a brief account of this research.

Commercially available "Nanocopper" was evaluated against *Xanthomonas campestris* pv. *phaseoli* (Mondal and Mani, 2009) and *Xanthomonas oryzae* pv. *oryzae* (Mondal et al., 2010). At a concentration of 0.2 mg/L, "nanocopper" was proved to be effective against *Xanthomonas axonopodis* pv. *punicae* (Mondal and Mani, 2012). A novel formulation containing copper nanoparticles stabilized by three biopolymers, viz., gelatin, chitosan, and gum arabic were prepared and assessed against *Xanthomonas axonopodis* pv. *punicae* under in vitro, and under field conditions. The bioactivity of the formulation was obtained at eightfold lower doses in comparison to

conventional copper oxychloride (Chikte et al., 2019). CuNPs produced using extracts of *Ocimum sanctum* leaf were found to exert an antibacterial effect on *Xanthomonas axonopodis* pv. *punicae* at a concentration of 0.01 mg/mL (Shende et al., 2016). *Ralstonia solanacearum*, the causal agent of bacterial wilt was inhibited by cuprous oxide nanoparticles (CuONPs) under laboratory and greenhouse conditions (Chen et al., 2019). The antibacterial and antibiofilm potential of CuO-streptomycin composite was evaluated in vitro against pathogenic bacteria-causing brown, ring, soft rot, and blackleg diseases in potatoes. Biofilms of *Clavibacter michiganensis* subsp. *sepedonicus*, *Ralstonia solanacearum*, and *Dickeya solani* were inhibited. According to the authors, CuO-streptomycin acted synergistically (El-Batal et al., 2019). Copper nanoparticle drug conjugates had extraordinary physicochemical and functional attributes and were described to be effective against both viruses and bacteria (Gatadi et al., 2021). Inorganic nanomaterials are effective against the surface and airborne viruses and can be used for antiviral coating applications (Shah and Huseien, 2020). CuNP synthesized by the chemical reduction method were inhibitory to *Phoma destructiva*, *Curvularia lunata*, *Alternaria alternata*, and *Fusarium oxysporum* at concentrations (Kanhed et al., 2014). Bramhanwade et al. (2016) proved that CuNPs prepared by the cetyl trimethyl ammonium bromide method exhibited antifungal activity against *Fusarium equiseti*, *F. oxysporum*, *F. culmorum*. Several phytopathogens (*Rhizoctonia solani*, *Alternaria carthami*, *Rhizopus stolonifer*, *Aspergillus niger*, *Fusarium oxysporum* f.sp. udum, *Colletotrichum gloeosporioides*, *Colletotrichum lindemuthianum*, and *Drechslera sorghicola*, *Fusarium oxysporum* f.sp. *carthami*, *Fusarium oxysporum* f.sp. ciceri, *Macrophomina phaseolina*, *Rhizoctonia bataticola*, and *Rhizopus stolonifer*) were also inhibited by CuNPs albeit to a varying extent and effective concentrations were in the range 0.01–0.06 mg/L (Shende et al., 2016).

A field study was performed to assess the role of CuNPs in controlling infection by the fungal pathogen *Sclerotium rolfsii* in tomatoes. The particles (synthesized using *Citrus sinensis* juice) caused a reduction of lesions on the stem without noticeable phytotoxicity. Plants recovered after the infection showed increased biomass characteristics (Kale et al., 2017). CuNPs produced using aqueous plant extract of *Moringa oleifera* Lam. showed antimicrobial activity against *Streptomyces griseus* and *Aspergillus niger* (Saran et al., 2017). Hassan et al. (2018) reported the synthesis of copper nanoparticles using biomass of the endophytic actinomycete *Streptomyces capillispiralis* Ca-1, which was isolated from a healthy medicinal plant (*Convolvulus arvensis*) (L.). The particles were found to be applicable for control of phytopathogens, infectious microorganisms, insects and pests. Several composites containing Cu or CuO nanoparticles have been prepared and their antibacterial applications are evaluated. Monodisperse copper nanoparticles (2–5 nm) embedded into submicron-sized particles of sepiolite ($Mg_8Si_{12}O_{30}(OH)_4(H_2O)_4{\cdot}8H_2O$), were observed to possess strong bactericidal activity against *Staphylococcus aureus* and *Escherichia coli* (Esteban-Cubillo et al., 2006). These Cu/sepiolite nanoparticles exhibited microbicidal activities similar to triclosan. In a separate study, copper nanoparticles were adsorbed onto mullite in the synthesis of a ceramic with antibacterial activity. Mullite per se had a positive effect on antimicrobial characteristics (Bagchi et al., 2012).

The antifungal activity of CuNPs and chitosan-ZnO-Cu nanocomposites against three phytopathogenic fungi (*A. alternata*, *R. solani*, and *B. cinerea*) varied with species tested. Overall, in strawberry seedlings application of nanoparticles decreased the incidence of the pathogen as well as the number of rotten strawberry fruits (Al-Dhabaan et al., 2017). According to Mohamed et al. (2018), the Cu-chitosan nano composition acted dually; the vascular wilt disease (caused by *Fusarium oxysporum*) was effectively controlled in the date palm while eliciting an immune response. Synthesis of copper-chitosan nanoparticles with antifungal properties against phytopathogens was reported by Koul et al. (2019). According to the authors, a strong bond formation was observed between the N of chitosan and Cu. The formulation could be applied as a spray once a week to achieve fungicidal effects in crop plants.

Ouda (2014) reported the antifungal activity of copper (CuNPs and silver/copper, Ag/CuNPs) nanoparticles against two plant pathogenic fungi, viz., *Alternaria alternata* and *Botrytis cinerea*. The hyphal growth was affected due to the nanoparticles. Cu/Zn hybrid nanoparticles were studied for their antibacterial activity against copper-tolerant and copper-sensitive strains of *Xanthomonas perforans*, *X. euvesicatoria*, *X. vesicatoria*, and *X. gardneri*, the causative agents of bacterial spot disease of tomatoes. The hybrid nanoparticles showed better efficiency in the management of bacterial spot disease as compared to micron-sized copper as indicated by the reduced disease severity. The xanthomonadin pigment synthesis in *X. perforans* was affected by treatment with Cu/Zn hybrid nanoparticles. Furthermore, the particles were nonphytotoxic to tomato plants (Carvalho et al., 2019). A recent study reported the synthesis of a nanocomposite of copper oxide and functionalized graphene-like carbon, with an average thickness of 7–11 nm. The leaf extract of *Adhatoda vasica* was used as a reducing and capping agent. The nanocomposites showed significant antibacterial activity against the pathogenic Gram-positive and Gram-negative bacterial strains (viz., *Escherichia coli*, *Pseudomonas aeruginosa*, *Klebsiella pneumoniae*, and *Staphylococcus aureus*). Antifungal activity against *Aspergillus niger* and *Candida albicans* was observed (Bhavyasree and Xavier, 2020).

CuNP synthesized and stabilized using various sugars (viz., dextrose, dextrin, and β-cyclodextrin) were reported to exhibit antifungal activity against the rice pathogen. The characteristics of CuNPs were attributed to the amphiphilic nature of the sugar molecules. (Ray et al., 2015). In a comprehensive study, Banik and Perez-de-Luque (2017) studied the effects of copper nanoparticles on plant pathogens, beneficial microbes, and crop plants in vitro. Copper nanoparticles acted synergistically with copper oxychloride causing inhibition of the oomycete *Phytophthora cinnamomi*. CuNPs promoted the growth of several plant pathogenic fungi, viz., *Botrytis fabae*, *Fusarium oxysporum* f.sp. *ciceris*, *F. oxysporum* f.sp. *melonis*, *Alternaria alternata*, and *P. syringae*, and sporulation of *T. harzianum* at low concentrations which would not be beneficial for agricultural applications. They were not significantly biocidal against *Rhizobium* spp. and *Trichoderma harzianum*. However, in presence of CuNPs, the rate of seed germination in wheat was higher.

Extensive studies on in vitro growth of fungal pathogens causing damping-off and wood decay, viz., *Rhizoctonia solani* (2 strains), *Fusarium oxysporum*, *F. redolens*,

and *Phytophthora cactorum*, *Fistulina hepatica*, *Grifola frondosa*, *Meripilus giganteus* and *Sparassis crispa* in the presence of copper nanoparticles (CuNPs) were carried out (Aleksandrowicz-Trzcińska et al., 2018). Although genus and species-dependent differences in CuNP toxicity was observed, it was proposed that nanomaterials could be used possibly for protecting nursery seedlings and safeguarding trees and wood. The authors have suggested that the user needs to be aware of the fact that certain fungi could be insensitive to a particular type of nanoparticles. Ponmurugan et al. (2016) report on the antimicrobial effects of nanocopper in *P. hypolateritia*, which is a causative agent of red root-rot disease in tea plants. The fungicidal activity was observed at a dose of 2.5 mg/L which was higher as compared to the conventional carbendazim treatment. Nanocopper application, however, had beneficial effects on the leaf yield and improved soil macronutrients. Small alterations in the microbial population were observed in nanocopper-treated plants which were regarded as "trivial."

According to another study on the antifungal activity of CuNPs against *F. oxysporum*, isolated from the infected date palm it was observed that, large size (345.1 nm), polygonal copper nanoparticles were better in comparison to spherical particles of size 278.1 nm when used at an equal concentration (Mohamed et al., 2018). In a study by Vera-Reyes et al. (2019) several metal oxide nanoparticles were evaluated for their antibacterial and antifungal effects. The minimum effective doses were 700–1000 mg/L depending on the type of nanoparticles. The activity was determined against *Fusarium oxysporum* (causing root rot), *Alternaria solani* (causing blight disease), and the bacterial pathogens *Clavibacter michiganensis* and *Pseudomonas syringae*. The antifungal activity of CuO was better than its antibacterial activity. In a study carried out under nursery conditions, copper nanoparticles did not affect the growth parameters of English oak (*Quercus robur* L.) and the extent of powdery mildew infection on leaves. However, CuNPs caused spontaneous ectomycorrhizal colonization of English oak (*Quercus robur* L.) seedlings growing in containers and *Sphaerosporella brunnea*, *Thelephora terrestris*, *Paxillus involutus*, and *Laccaria proxima* were detected after foliar application of nanoparticles (Olchowik et al., 2017).

The sensitivity of seven fungal species (viz., *A. alternata*, *B. cinerea*, *M. fructicola*, *C. gloeosporioides*, *F. solani*, *F. oxysporum* f.sp. *radicis lycopersici*, and *V. dahliae*) against metal-based antimicrobial nanoparticles was evaluated (Malandrakis et al., 2020). The mycelial growth of all fungal pathogens was adversely affected due to CuNPs in comparison to a reference protective fungicide containing $Cu(OH)_2$. Except for *B. cinerea*, *A. alternata*, and *M. fructicola*, Cu-NPs showed more toxicity than $CuSO_4$. The study compared the effects of the nanomaterials and respective bulk materials on fungal hyphae and spores and hence it is important. Malandrakis et al. (2020) recently reported that CuNPs were effective in controlling both the resistant and sensitive strains of *Botrytis cinerea*. The CuNPs inhibited the benzimidazoles, thiophanate methyl, carbendazim, as well as QoI pyraclostrobin-resistant phenotypes in in vitro screening procedures. Synergistic effects were documented along with nanoparticles specific effects in comparison to $Cu(OH)_2$ which is used

conventionally. ATP metabolism was implicated in the mode of action of CuNPs because of their synergistic effects with fluazinam which is an inhibitor of oxidative phosphorylation. Furthermore, the study demonstrated that the fungicidal action of CuNPs was due to the released copper ions. Due to synergism with conventional fungicides, the researchers suggest the use of nanomaterials as a sustainable strategy for combating disease resistance. Siddiqi and Husen (2016) have documented the use of fungi in the biosynthesis of metal nanoparticles. The chemistry of nanoparticles formation using enzymes and other biomolecules is explained with possible applications of these nanoparticles as inhibitors of pathogenic fungi. CuNPs were found to be effective against several Gram-negative plant pathogens, *Agrobacterium tumefaciens*, *Dickeya dadantii*, *Erwinia amylovora*, *Pectobacterium carotovorum*, and *Pseudomonas savastanoi* pv. *savastanoi*, but not effective against *Pseudomonas corrugata* and *Xanthomonas campestris* pv. *campestris*. For comparison, Kocide (copper hydroxide) and Nordox (copper oxide) were evaluated and the overall activity of nanocopper was higher than the commercial formulations (Varympopi et al., 2020). Copper nanoparticles have also been reported as plant growth stimulators. Zhao et al. (2020) and Singh et al. (2020) have reviewed extensively the applications of nanobiotechnology in agriculture. To facilitate the use of nanotechnology in sustainable agriculture the authors propose the designing of new/better-suited nanomaterials than the existing materials. Specific nanoparticles that stimulate plant growth, as well as the abiotic and biotic interactions with plants, may be required. To exemplify, under greenhouse conditions, CuO NPs applied as root irrigation, reduced disease incidence, and disease index in tobacco (Chen et al., 2019). In an interesting study on the wheat—*Pseudocercosporella herpotrichoides* pathosystem, Belava et al. (2017) proved that seed treatment with CuNPs affected the response of the plant to the pathogen. During the initial stages of the pathological process, no phytotoxic effects were observed. In another study, the effects of nanoparticles on seed germination traits and seed pathogen infection rate in forage sorghum (*Sorghum bicolor*) and cowpea (*Vigna unguiculata*) were evaluated and it was observed that ZnO, CuO entered the seed via pores in the seed coat. Nanoparticles enhanced germination and strongly influenced seed germination traits (Maity et al., 2018). Nagaonkar et al. (2015) observed mito-accelerating effect on root meristematic cells in *Allium cepa* plants after the application of CuNPs. Increased fruit quality (firmness) in tomatoes and the content of bioactive compounds (vitamin C, lycopene, and the ABTS antioxidant capacity) were reported by López-Vargas et al. (2018). The studies by Ma et al. (2019) prove the potential of nanoscale platforms, viz., $Cu_3(PO_4)_2{\cdot}3H_2O$ nanosheets, and CuONPs to deliver critical micronutrients at early stages of plant development. The foliar-applied nanomaterials not only delivered the micronutrient more effectively but also suppressed *Fusarium oxysporum* f.sp. *lycopersici* infection in tomatoes. A time-dependent modulation of pathogenesis-related genes viz., transcriptional activator [PTI5], polyphenol oxidase [PPO], and plant resistance protein 1A1 [PRP1A1] was observed in nanomaterials treated plants. This response was rapid after treatment with nanosheets and a little late in the case of CuONPs. Such studies at the transcriptome level can provide insights to optimize the use of

nanomaterials in precision agriculture. The essential metal-based nanoparticles (copper/iron NPs) were proved to be extremely effective against *Meloidogyne incognita* and *Meloidogyne javanica*, the root-knot nematodes (Gkanatsiou et al., 2019). The activity was superior in comparison to fosthiazate, the commercial nematicide. The components of the nanoparticles served as essential micronutrients in plants as evidenced by the increase in the fresh weight of biomass of treated tomato plants. Such unique studies highlight the pesticidal potential of CuNPs.

A recent study by Cumplido-Nájera et al. (2019) reported the synergistic effect of copper nanoparticles and potassium silicate in reducing the severity of infection due to *Clavibacter michiganensis* in the tomato plants. The application altered the levels of various antioxidant enzymes, reduced glutathione, and the total phenol content of leaves. All these increased the tolerance of the plants to *C. michiganensis*, an economically important pathogen of tomatoes. In another study, a nanoencapsulated formulation of thyme and dill essential oils with copper NPs was prepared with the aim of research in nanotechnology for postharvest applications such as prevention of fungal diseases and maintaining food freshness and quality (Weisany et al., 2019). Evaluation of this formulation against *Colletotrichum nymphaeae* indicated enhanced activity due to the presence of copper nanoparticles. Conidial germination was inhibited and treatment resulted in deformations in hyphal morphology and reduced mycelial growth. According to the authors, these represent a new strategy for plant disease management. CuNP synthesized using the mint leaf extracts inhibited *Colletotrichum capsici*, the pathogen causing fruit rot in chillies. The activity was observed at a reduced dosage in comparison to commercial fungicides (Iliger et al., 2021).

The literature on biosynthesized metal nanoparticles exhibiting antimicrobial activities against plant pathogens as well as their role as plant nutrients is recently documented (Nayantara and Pawan, 2018). Yadav et al. (2018) have reviewed the nanoparticles synthesized using fungi and/or their metabolites. These "myconanoparticles" are now being studied in various agricultural applications. Particularly copper nanoparticles have proved to inhibit the growth of fungal hyphae and conidial germination. Several myconanoparticles can be used in biosensor applications and the authors hope for the commercialization of myconanoparticles for successful plant disease management. In the review by Elmer and White (2018), several types of nanoparticles/nanomaterials have been suitably designed/tailored for applications in biosensing, as delivery vehicles for agrichemicals and genetic materials, and as agents that inhibit or control the growth of plant pathogens. Specifically, the literature reports suggest that the use of CuNPs in agriculture is an ecologically feasible and effective strategy for the management of a variety of bacterial and fungal phytopathogens (Rajwade et al., 2020). Recently Cartwright et al. (2020) have highlighted the importance of surface functionalization (coatings) on the uptake and mobilization of nanoparticles intended for use in agriculture. According to the authors, pretuning is essential for achieving cost-effective nanomaterials that would not agglomerate and produce desirable effects.

Treatment of wastes generated is a very important aspect. To this end, in a novel application, Cu_2O nanoparticles were evaluated in the disinfection of secondary effluents and removal of pathogenic microorganisms. Cu_2O nanoparticles supported onto natural clinoptilolite displayed antibacterial activity against *Escherichia coli* and *Staphylococcus aureus* in pure culture. Protozoa (viz., *Paramecium caudatum*, and *Euplotes affinis*) were also killed (Hrenovic et al., 2012). This demonstrates the use of supported Cu_2O in tertiary wastewater treatment. Copper-doped nanophotocatalysts (TiO_2 nanoparticles) were prepared and shown to be effective antimicrobials against *E. coli* and *S. aureus*. Visible light photocatalysis could thus find application in wastewater treatment (Yadav et al., 2014).

4 CuNPs applications in food packaging

Spoilage in raw and processed foods caused due to physical and chemical agents, and microbiological contaminants during storage and transportation has always been a cause of concern all over the world. Similar to pests and pathogen attacks on crops, damage to food is associated with huge economic losses with implications on food security. Food safety is a topic of extremely high concern in the food industry. Food packaging is a very important aspect that ensures food safety. To this end, materials containing nanoparticles with antimicrobial properties are emerging as new antimicrobial packagings. Although antimicrobial activities of nanoparticles are well known, several researchers report successful binding with cationic polymers, small ligands, and biomolecules onto their surfaces for further improvement in bioactivity (Bahramia et al., 2020). A recent review by Tian et al. (2021) highlights the application of inorganic nanomaterials in the control of foodborne pathogens that pose a great threat to food safety. Nanomaterials can be included to prolong the shelf life of foods (Hoseinnejad et al., 2018). Bio-nanocomposites and nanoencapsulated systems have been successfully employed to achieve active packaging systems that inhibit or even kill the microorganisms implicated in the spoilage of food (Al-Tayyar et al., 2020; Chawla et al., 2021). The utility of chitosan and its nanocomposites for food packaging and food preservation applications has been a subject of a recent review (Kumar et al., 2020). The authors suggest that incorporation of nanomaterials as coating or treatments led to shelf-life extension of dairy products, fresh produce, animal products, and bread.

Reduced graphene oxide-copper hybrid (rGO-Cu) systems displaying diverse morphologies were prepared via a facile approach. rGO-Cu system exhibited time-dependent killing of *E. coli* and *B. subtilis*. Treatment of cells with such hybrids containing Cu caused degradation of the cell wall, ROS generation, alteration in protein content, and induced lipid peroxidation leading to a cytotoxic response (Maiti et al., 2019). An antimicrobial packaging film (APF) composed of cellulose nanowhiskers, CNW (0.5%)-sodium alginate, SA (3%), and CuO NPs (5 mM) was reported by Saravanakumar et al. (2020). The CNW was added for maintaining barrier properties,

SA was the plasticizer, and CuO nanoparticles were incorporated for antimicrobial properties. The film showed promising antibacterial activity against *S. aureus*, *E. coli*, *Salmonella* sp., *C. albicans*, and *Trichoderma* spp., as well as antioxidant activity in terms of DPPH and ABTS scavenging. Thus the film proves to be an active food packaging system (FPS) for its utility in the food industry, overcoming the limitations in conventional food packaging.

Akhavan and Ghaderi (2010) evaluated the antimicrobial activity of Cu and CuO nanoparticles embedded in silica thin films prepared by the sol-gel method. Although both exhibited antibacterial characteristics, Cu-embedded films were better than CuO-embedded films by a factor of ~ 2.1. However, when both the films were evaluated for antimicrobial activity under photocatalytic conditions, because of the thin oxide layer on the surface, CuO embedded films were better. In another study, Jia et al. (2012) reported the preparation of Cu-modified regenerated cellulose films. The cellulose-cuprammonium solution was reduced by aq. $NaBH_4$ to form Cu^0 from Cu^{2+}. The films exhibited efficient antibacterial activity against *Staphylococcus aureus* and *Escherichia coli*. Bionanocomposite films comprising bimetallic Ag-Cu nanoparticles and fish skin gelatin were prepared and studied for their thermal, mechanical, rheological, structural, and antibacterial properties (Arfat et al., 2017). The composite films were not only superior in all the above aspects but also exhibited improved UV-barrier properties. The authors suggest the utility of such materials as active food packaging materials for protection against microorganisms causing food spoilage. In a study, CuO NPs were incorporated in alginate-based impression materials (Ginjupalli et al., 2018). The authors reported no alteration in the physicochemical properties of the gel and concluded that CuO NPs incorporated in alginate materials can be considered as materials with disinfectant properties. A nanocopper/polypropylene packaging material was developed and was found suitable for maintaining product quality. The films exhibited antioxidant and antimicrobial properties which could extend the shelf life of packaged food (Shi et al., 2021). CuS NPs were embedded in carrageenan to form a film and antibacterial activity against *Escherichia coli* (99.2% inhibition) and *Staphylococcus aureus* (99.9% inhibition) was reported. Upon near-infrared irradiation, the antibacterial activity in the food sample was enhanced, and films were reported to be transparent, with enhanced mechanical properties and thermal stability (Li et al., 2020). Natural polymers, specifically those of microbial origin have been recently reviewed for application as delivery systems (Sampathkumar et al., 2020). The major applications of these polymers in food fortification and food preservation along with nano-delivery systems for use in agriculture were presented. The authors indicate the importance of assessing the "safety" of nanomaterials as well as addressing the issues of public perception on the use of nanomaterials (Sampathkumar et al., 2020; Adisa et al., 2019; Lang et al., 2021). Recently, Bilal et al. (2021) and Videira-Quintela et al. (2021) have reviewed the potential uses of polysaccharides-based bionanostructures as "smart" and "active" packaging materials ideally suited for food applications. These could be fortified with antimicrobial nanomaterials and other materials to achieve desirable characteristics.

CuNPs were proved to be effective in the control of stored grain pest, *Tribolium castaneum* (El-Saadony et al., 2020). The nanoparticles were synthesized using cell-free culture extract of the copper-resistant bacterium *Pseudomonas fluorescens* MAL2 representing an eco-friendly process. *Salmonella* and *Campylobacter* represent pathogenic bacteria that are important in the poultry industry. Duffy et al. (2018) carried out in vitro studies on the effect of antimicrobial nanoparticles on these bacterial genera. The poultry pathogenic strains of both the genera were inhibited by CuO nanoparticles. Overall bacterial growth was dependent on the concentration of nanoparticles, but strain-level differences were also observed. More detailed studies on nanomaterials designed to increase the shelf life of animal feed are warranted and such materials will be beneficial for the poultry industry, meat industry, etc.

5 Mechanisms underlying the antimicrobial activity of copper nanoparticles

According to a recent review on the mechanism of action of antimicrobial nanoparticles, the authors state that the antibacterial mechanisms are poorly understood (Wang et al., 2017). Induction of oxidative stress, metal ion release, and nonoxidative mechanisms are the accepted modes and thus, antimicrobial nanomaterials exhibit multilevel actions. To counteract these different modes, a microbe will have to undergo several mutations in its genes simultaneously. The occurrence of such multiple simultaneous gene mutations in a single cell is very improbable. From the point of view of developing resistance to a particular nanomaterial, this is difficult (Lemire et al., 2013; Wang et al., 2017; Tian et al., 2021). Slavin et al. (2017) suggest that exposure to nanoparticles is effective and bacteria cannot escape the antimicrobial effects because several pathways are activated by NPs. Bezza et al. (2020) reported the bactericidal activity of lipopeptide biosurfactant stabilized Cu_2O NPs and inhibitory effects were attributed to the generation of ROS (Fig. 3).

It is reported that both size and shape affect the antimicrobial properties of copper nanoparticles (Ruparelia et al., 2008; Hajipour et al., 2012; Shahzadi et al., 2018). A dose-dependent antimicrobial effect is observed when nanoparticles have physical interactions with bacterial cells; nano-rough surfaces increase point-of-contact with bacterial cells leading to physical cell destruction (Seil and Webster, 2012). In the study by Yoon et al. (2007), the reduced viability of bacteria in the presence of copper nanoparticles was attributed to protein inactivation via thiol interactions. According to the studies by Chakrapani et al. (2014), Kruk et al. (2015), and Aziz et al. (2015) the metallic nanoparticles due to electrostatic interactions get adsorbed onto the bacterial cell wall. The particles further form "pits" which lead to loss of cell membrane integrity leading to leakage of cytoplasmic fluids. Apart from these, the particles damage the respiratory enzymes and generate ROS (Kruk et al., 2015). Intracellular binding to phosphorus and sulfur moieties present in the DNA and RNA has adverse effects on replication ultimately leading to cell death (Roy et al., 2016). In a recent study, copper was proved to act synergistically with TiO_2 and antibacterial activity

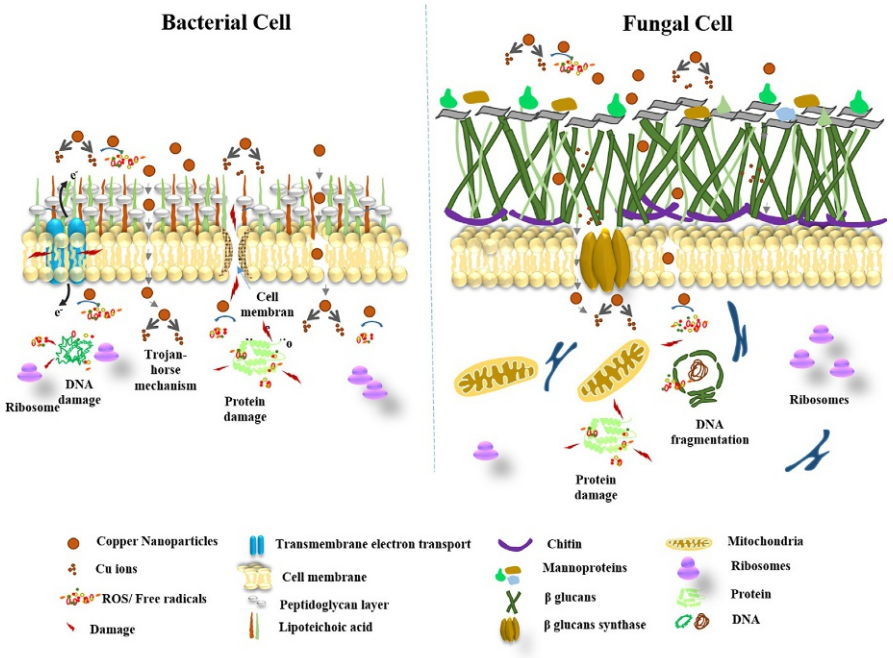

FIG. 3

Interactions of microbes with copper nanostructures: mechanisms explained.

was mediated through the generation of ROS in the dark. This activity was attributed to Cu and the particles caused cell shrinkage and release of cytoplasmic contents because of the disruption of the cell wall and cell membrane (Chen et al., 2014). Copper is extremely sensitive to air, and the oxide phases are thermodynamically more stable (Jeong et al., 2008). The formation of oxides on the surface of the nanoparticles is inevitable. During the bactericidal action of CuONPs, several researchers agree on a combination of mechanisms that operate. These mechanisms include mechanical damage, penetration of nanoparticles into the cell, ROS generation by attached particles, and the formation of copper ions from the surface of the nanoparticles. This multipronged antibacterial action will make it difficult for bacteria to develop a resistance against CuONPs (Pandey et al., 2012; Applerot et al., 2012). Specifically in the case of spores of *Bacillus anthracis*, the biowarfare agent, Pandey et al. (2014) describe a "germinate and kill" strategy with CuO nanorods, because spores have unique cell wall components as well as specific proteins that bind the DNA making them resistant to most of the sporicidal agents. The various oxidation states of copper contribute to the reactivity and antimicrobial activity. The findings of Meghana et al. (2015) add strong supporting evidence to the contact killing mechanism of CuO and Cu_2O. Both types of particles were reported to damage the cell membrane. The Cu_2O particles formed copper(I)-peptide complex while

CuO caused the generation of ROS. Further, the cuprous state was involved in protein binding, and specifically, Fumarase A was inactivated by Cu_2O (Meghana et al., 2015). In the case of *Ralstonia solanacearum*, CuONPs caused nanomechanical damage to cells and were adsorbed on multiple sites. The CuONPs prevented biofilm formation, reducing swarming motility, and disturbing ATP production. Genes involved in pathogenicity and motility were downregulated upon interaction with CuONPs (Chen et al., 2019). A recent study by Thakur et al. (2020) states that membrane damage occurs due to spherical CuO nanoparticles causing cell lysis in *Bacillus subtilis*, *Klebsiella pneumoniae*, and *Staphylococcus aureus*. Further, it was reported that gum arabic capped copper nanoparticles which were obtained by reduction with L-ascorbic acid were nontoxic to Caco-2 cells and exhibited antimicrobial activity against *Salmonella typhimurium* (Chawla et al., 2020). While some proposed mechanisms relate to the physical structure of the nanoparticles (i.e., the membrane-damaging abrasiveness of the nanoparticle), others relate to the enhanced release of antibacterial metal ions from nanoparticle surfaces. The specific surface area of a dose of nanoparticles increases as the particle size decreases, allowing for greater material interaction with the surrounding environment (Seil and Webster, 2012). Copper inherently exhibits antibacterial activity. In an attempt to distinguish between the specific effects of nanoparticles and effects due to ions released by nanoparticles, bathocuproine was added as a copper-ion-specific chelator (Ruparelia et al., 2008). Interestingly, in this study, Gram-positive bacteria were more susceptible than Gram-negative bacteria. The antibacterial activity of CuNPs was attributed to the Cu^{2+} ions arising from the surface of the nanoparticles which interacted with DNA causing degradation (Chatterjee et al., 2014). The group studied the interactions of pUC19 DNA with CuNPs in vitro. In presence of *E. coli* cells, nanoparticles caused lipid peroxidation, generation of ROS, protein oxidation, and DNA degradation. Recently, studies on the mechanism of action of copper nanoparticles and copper ions were performed on *Pseudomonas aeruginosa* biofilms (Singh et al., 2019). Distinct nanoparticles-specific and ions-specific effects were observed during the transcriptome analysis. *Pseudomonas aeruginosa* harbors a copper transporter in the membrane which confers copper resistance via efflux mechanisms. Under the influence of NPs as well as ionic copper, the genes responsible for copper transport were upregulated, however, nanoparticles showed effects on various cellular processes and damaged cells to a greater extent as compared to ionic copper. This study supports the use of copper nanoparticles in medical settings. Detailed investigations on the antimicrobial activity of soluble vs nanoparticulate forms of copper were reported by Bastos et al. (2020). Copper toxicity was attributed to intracellular copper loading and not to contact the association with the membrane in *E. coli*. Intracellular loading would occur in the case of soluble copper. Thiosalicylic acid stabilized CuNPs interacted with the cell division proteins like FtsZ and FtsI, destabilizing them. Thus CuNPs inhibited bacterial cell division (Ganesh Kumar et al., 2020). Overall, the bactericidal effect of nanoparticles is dependent on the size, shape, surface characteristics, and concentration of nanoparticles, the media used, and the initial concentration of microorganisms. Particularly in the case of agricultural applications the mode of

delivery, role of epiphytic microflora, interactions with soil organic matter, other agrochemicals, etc., assume importance. Similarly, when particles are used as packaging materials, the nature of the composite, concentration of particles, the food matrix, etc., would undoubtedly affect the antimicrobial characteristics. A detailed study on pluronic acid-based micelles with covalently clustered copper nanoparticles on surface and containing chlorine dioxide was carried out by Li et al. (2018). These micelles were described to be multifunctional entities that exhibited "release-killing," "contact-killing," and "antiadhesion" properties. Mirhosseini and Bafghi (2019) reported synergistic effects of CuO and MgO nanoparticles against *E. coli* and *S. aureus* and antibacterial effects were attributed to the damage to cell membrane. According to the authors, a combination of nanoparticles could be effectively used to control pathogens in the food industry. The work of Pariona et al. (2019) proves the potential fungicidal activity of CuNPs (obtained using green synthesis) against *Fusarium solani*, *Neofusicoccum* sp., and *Fusarium oxysporum*. CuNPs caused alterations in the morphology of the mycelium, cell membrane damage, and generation of oxidative damage was also observed. Generally, nanoforms showed better toxicity to spores, suppressed symptoms, and inhibited disease development (Malandrakis et al., 2019). In a recent review, all different routes for the synthesis of metal and metal oxide nanoparticles used as new generation antimicrobials were documented (Correa et al., 2020; Sánchez-López et al., 2020). Key topics such as methods for evaluating antimicrobial activity as well as the mechanisms underlying were also discussed.

6 Emerging concerns about the toxicity of copper nanostructures in plants and animals

Nanotechnology is recognized as a key enabling technology for the 21st century (Sekhon, 2014; Elmer and White, 2018) with contributions in several areas ranging from space sciences to energy sector, novel materials for several industrial applications, agricultural production, etc. Particularly, in areas such as crop production, food processing, and additives, novel and functional foods, nanomaterials are introduced intentionally (Thiruvengadam et al., 2018; Hoseinnejad et al., 2018). Thus during production, transport, and usage, there is an intentional or nonintentional release of nanomaterials in the environment. Nanomaterials applied for crop protection have an immediate environmental risk associated with humans as well as for nontarget plant species, animals, insects, and the soil ecosystem by and large. Thus studies that evaluate the risks of nanomaterials are extremely necessary to address the concerns on the introduction of new, anthropogenic materials to the environment. According to Lang et al. (2021), a critical analysis of the nanoparticles applied in the food supply chain is very essential.

Considering the possible increase in the environmental concentration of nanomaterials, Rastogi et al. (2017) surveyed the impact of metal and metal oxide nanoparticles on plants. Parameters such as size, the concentration of nanoparticles, and methodology of exposure to nanoparticles affect plants and oxidative burst causes

toxicity. In another study, copper nanoparticles synthesized using microwave energy and stabilized with leaf extract of *Prosopis cineraria* was proved to have broad-spectrum antibacterial activity but were reported to be cytotoxic to MCF-7 cells (Jinu et al., 2017). When copper nanoparticles-mullite composite was studied, it displayed negligible cytotoxicity in human cancer cell lines (Bagchi et al., 2012). Recently, Ude et al. (2019) assessed the toxicity of CuO nanomaterials in a physiologically relevant in vitro cell culture system. Intestinal microfold (M) cell (Caco-2/Raji B) and mucus-secreting (Caco-2/HT29-MTX) coculture systems were developed to understand the effect of nano CuO on barrier integrity, viability, and interleukin (IL)-8 secretion. The results indicate that the Caco-2/Raji B coculture model was more sensitive to CuO. The coculture models were less sensitive as compared to the monoculture Caco-2 in vitro model. Thus, more in vitro models are required to understand the effects of ingested nanomaterials. In the case of pluronic acid-based micelles with covalently clustered copper nanoparticles, Li et al. (2018) reported synergism between the copper nanoparticles and chlorine dioxide and safety with blood samples, lung function tests were established in histopathological studies.

A recent review of the literature (Coelho et al., 2020; Singh et al., 2020) suggests that the use of copper-based microbicidal agents cause severe damage to the agroecosystems thereby adversely affecting human health. Measures such as lowering the copper application rates, exploring nonchemical alternatives to control pathogens and pests, implementing effective cultural practices need to be adopted in organic agriculture. Appropriate policies on the use of copper in agriculture have to be formulated jointly by the researchers, farmers, and regulatory agencies which could be implemented both at the local and national level (EUR-Lex, 2015; Keulemans et al., 2019; Lamichhane et al., 2018).

7 Concluding remarks

The increase in pest and pathogen attacks along with decreasing soil quality and climate change is the foremost hindering factor in achieving and sustaining food security. Not only crop production but processed food also requires the interventions of "Nanotechnology," the newer technology, as a possible solution to address the needs of the growing population. The use of nanomaterials in agriculture will be a delivery platform for various agrochemicals. Particularly copper and its oxides are popular antimicrobials and are already being assessed against bacterial and fungal plant pathogens. This work is reviewed in this chapter. The effects of copper, as well as copper oxide nanoparticles, are observed at multiple levels in bacteria and fungi and hence nanoparticles can be looked at as potent inhibitors against phytopathogens. The inclusion of copper-based nanomaterials as antimicrobial agents is promising and nanoparticles demonstrated improvement in characteristics of the packaging materials. In European countries regulations on the use of these "newer" materials are formulated and other nations would soon have their rules and implement them. This is warranted considering the risks posed due to the usage of nanomaterials.

References

Adisa, I.O., Pullagurala, V.L.R., Peralta-Videa, J.R., Dimkpa, C.O., Elmer, W.H., Gardea-Torresdey, J.L., White, J.C., 2019. Recent advances in nano-enabled fertilizers and pesticides: a critical review of mechanisms of action. Environ. Sci. Nano 6, 2002–2030.

Agrios, G.N., 1995. Plant Pathology Development and Current Trends. Academic Press, Elsevier.

Akhavan, O., Ghaderi, E., 2010. Cu and CuO nanoparticles immobilized by silica thin films as antibacterial materials and photocatalysts. Surf. Coat. Technol. 205, 219–223.

Al-Dhabaan, F.A., Shoala, T., Ali, A.A.M., Abd-Elsalam, K., 2017. Chemically-produced copper, zinc nanoparticles and chitosan-bimetallic nanocomposites and their antifungal activity against three phytopathogenic fungi. Int. J. Agric. Technol. 13, 753–769.

Aleksandrowicz-Trzcińska, M., Szaniawski, A., Olchowik, J., Drozdowski, S., 2018. Effects of copper and silver nanoparticles on growth of selected species of pathogenic and wood-decay fungi in vitro. For. Chron. 94, 109–116.

Al-Tayyar, N.A., Youssef, A.M., Al-Hindi, R.R., 2020. Antimicrobial packaging efficiency of ZnO-SiO_2 nanocomposites infused into PVA/CS film for enhancing the shelf life of food products. Food Packag. Shelf Life 25, 100523.

Applerot, G., Lellouche, J., Lipovsky, A., Nitzan, Y., Lubart, R., Gedanken, A., Banin, E., 2012. Understanding the antibacterial mechanism of CuO nanoparticles: revealing the route of induced oxidative stress. Small 8, 3326–3337.

Arendsen, L.P., Thakar, R., Sultan, A.H., 2019. The use of copper as an antimicrobial agent in health care, including obstetrics and gynecology. Clin. Microbiol. Rev. 32, e00125-18.

Arfat, Y.A., Ahmed, J., Hiremath, N., Auras, R., Joseph, A., 2017. Thermo-mechanical, rheological, structural and antimicrobial properties of bionanocomposite films based on fish skin gelatin and silver-copper nanoparticles. Food Hydrocoll. 62, 191–202.

Asemani, M., Anarjan, N., 2019. Green synthesis of copper oxide nanoparticles using *Juglans regia* leaf extract and assessment of their physico-chemical and biological properties. Green Processes Synth. 8, 557–567.

Aziz, N., Faraz, M., Pandey, R., Shakir, M., Fatma, T., Varma, A., Barman, I., Prasad, R., 2015. Facile algae-derived route to biogenic silver nanoparticles: synthesis, antibacterial, and photocatalytic properties. Langmuir 31, 11605–11612.

Bagchi, B., Dey, S., Bhandary, S., Das, S., Bhattacharya, A., Basu, R., Nandy, P., 2012. Antimicrobial efficacy and biocompatibility study of copper nanoparticle adsorbed mullite aggregates. Mater. Sci. Eng. C 32, 1897–1905.

Bahramia, A., Delshadib, R., Jafari, S.M., 2020. Active delivery of antimicrobial nanoparticles into microbial cells through surface functionalization strategies. Trends Food Sci. Technol. 99, 217–228.

Banik, S., Perez-de-Luque, A., 2017. In vitro effects of copper nanoparticles on plant pathogens, beneficial microbes and crop plants. Span. J. Agric. Res. 15, 23.

Bastos, C.A.P., Faria, N., Wills, J., Malmberg, P., Nathalie, S., Rees, P., Powell, J.J., 2020. Copper nanoparticles have negligible direct antibacterial impact. NanoImpact 17, 100192.

Belava, V.N., Panyuta, O.O., Yakovleva, G.M., Pysmenna, Y.M., Volkogon, M.V., 2017. The effect of silver and copper nanoparticles on the wheat—*Pseudocercosporella herpotrichoides* Pathosystem. Nanoscale Res. Lett. 12, 250.

Bezza, F.A., Tichapondwa, S.M., Chirwa, E.M.N., 2020. Fabrication of monodispersed copper oxide nanoparticles with potential application as antimicrobial agents. Sci. Rep. 10, 16680.

Bhavyasree, P.G., Xavier, T.S., 2020. Green synthesis of copper oxide/carbon nanocomposites using the leaf extract of *Adhatoda vasica* Nees, their characterization and antimicrobial activity. Heliyon 6, e03323.

Bilal, M., Gul, I., Basharat, A., Qamar, S.A., 2021. Polysaccharides-based bio-nanostructures and their potential food applications. Int. J. Biol. Macromol. 176, 540–557.
Bramhanwade, K., Shende, S., Bonde, S., Gade, A., Rai, M., 2016. Fungicidal activity of Cu nanoparticles against *Fusarium* causing crop diseases. Environ. Chem. Lett. 14, 229–235.
Camacho-Flores, B.A., Martínez-Álvarez, O., Arenas-Arrocena, M.C., Garcia-Contreras, R., Argueta-Figueroa, L., De La Fuente-Hernández, J., Acosta-Torres, L.S., 2015. Copper: synthesis techniques in nanoscale and powerful application as an antimicrobial agent. J. Nanomater., 1–10.
Caroling, G., Vinodhini, E., Ranjitham, A.M., Shanthi, P., 2015. Biosynthesis of copper nanoparticles using aqueous *Phyllanthus embilica* (Gooseberry) extract-characterisation and study of antimicrobial effects. Int. J. Nanomater. Chem. 1, 53–63.
Cartwright, A., Jackson, K., Morgan, C., Anderson, A., Britt, D.W., 2020. A review of metal and metal-oxide nanoparticle coating technologies to inhibit agglomeration and increase bioactivity for agricultural applications. Agronomy 10, 1018.
Carvalho, R., Duman, K., Jones, J.B., Paret, M.L., 2019. Bactericidal activity of copper-zinc hybrid nanoparticles on copper-tolerant *Xanthomonas perforans*. Sci. Rep. 9, 1–9.
Chakrapani, V., Ahmed, K.B.A., Kumar, V.V., Ganapathy, V., Anthony, S.P., Anbazhagan, V., 2014. A facile route to synthesize casein capped copper nanoparticles: an effective antibacterial agent and selective colorimetric sensor for mercury and tryptophan. RSC Adv. 4, 33215–33221.
Chatterjee, A.K., Chakraborty, R., Basu, T., 2014. Mechanism of antibacterial activity of copper nanoparticles. Nanotechnology 25, 135101.
Chawla, P., Kumar, N., Bains, A., Dhull, S.B., Kumar, M., Kaushik, R., Punia, S., 2020. Gum arabic capped copper nanoparticles: synthesis, characterization, and applications. Int. J. Biol. Macromol. 146, 232–242.
Chawla, R., Sivakumar, S., Kaur, H., 2021. Antimicrobial edible films in food packaging: current scenario and recent nanotechnological advancements-a review. Carbohydr. Polym. Technol. Appl. 2, 100024.
Chen, S., Guo, Y., Zhong, H., Chen, S., Li, J., Ge, Z., Tang, J., 2014. Synergistic antibacterial mechanism and coating application of copper/titanium dioxide nanoparticles. Chem. Eng. J. 256, 238–246.
Chen, J., Mao, S., Xu, Z., Ding, W., 2019. Various antibacterial mechanisms of biosynthesized copper oxide nanoparticles against soilborne *Ralstonia solanacearum*. RSC Adv. 9, 3788–3799.
Chikte, R.G., Paknikar, K.M., Rajwade, J.M., Sharma, J., 2019. Nanomaterials for the control of bacterial blight disease in pomegranate: quo vadis? Appl. Microbiol. Biotechnol. 103, 4605–4621.
Chitra, K., Manikandan, A., Moortheswaran, S., Reena, K., Antony, S.A., 2015. *Zingiber officinale* extracted green synthesis of copper nanoparticles: structural, morphological and antibacterial studies. Adv. Sci. Eng. Med. 7, 710–716.
Cioffi, N., Torsi, L., Ditaranto, N., Tantillo, G., Ghibelli, L., Sabbatini, L., Bleve-Zacheo, T., D'Alessio, M., Zambonin, P.G., Traversa, E., 2005. Copper nanoparticle/polymer composites with antifungal and bacteriostatic properties. Chem. Mater. 17, 5255–5262.
Coelho, F.C., Squitti, R., Ventriglia, M., Cerchiaro, G., Daher, J.P., Rocha, J.G., Rongioletti, M.C., Moonen, A.C., 2020. Agricultural use of copper and its link to Alzheimer's disease. Biomol. Ther. 10, 897.
Correa, M.G., Martínez, F.B., Vidal, C.P., Streitt, C., Escrig, J., de Dicastillo, C.L., 2020. Antimicrobial metal-based nanoparticles: a review on their synthesis, types and antimicrobial action. Beilstein J. Nanotechnol. 11, 1450–1469.

Cuevas, R., Durán, N., Diez, M.C., Tortella, G.R., Rubilar, O., 2015. Extracellular biosynthesis of copper and copper oxide nanoparticles by *Stereum hirsutum*, a native white-rot fungus from Chilean forests. J. Nanomater. Article ID 789089, 7 pages.

Cumplido-Nájera, C.F., González-Morales, S., Ortega-Ortíz, H., Cadenas-Pliego, G., Benavides-Mendoza, A., Juárez-Maldonado, A., 2019. The application of copper nanoparticles and potassium silicate stimulate the tolerance to *Clavibacter michiganensis* in tomato plants. Sci. Hortic. 245, 82–89.

Din, M.I., Rehan, R., 2017. Synthesis, characterization, and applications of copper nanoparticles. Anal. Lett. 50, 50–62.

Długosz, O., Chwastowski, J., Banach, M., 2020. Hawthorn berries extract for the green synthesis of copper and silver nanoparticles. Chem. Pap. 74, 239–252.

Duffy, L.L., Osmond-McLeod, M.J., Judy, J., King, T., 2018. Investigation into the antibacterial activity of silver, zinc oxide and copper oxide nanoparticles against poultry-relevant isolates of *Salmonella* and *Campylobacter*. Food Control 92, 293–300.

El-Batal, A.I., Balabel, N.M., Attia, M.S., El-Sayyad, G.S., 2019. Antibacterial and antibiofilm potential of mono-dispersed stable copper oxide nanoparticles-streptomycin nanodrug: implications for some potato plant bacterial pathogen treatment. J. Clust. Sci., 1–20.

Elmer, W., White, J.C., 2018. The future of nanotechnology in plant pathology. Annu. Rev. Phytopathol. 56, 111–133.

El-Saadony, M.T., Abd El-Hack, M.E., Taha, A.E., Fouda, M.M.G., Ajarem, J.S., Maodaa, S.N., Allam, A.A., Elshaer, N., 2020. Ecofriendly synthesis and insecticidal application of copper nanoparticles against the storage pest *Tribolium castaneum*. Nanomaterials 10, 587.

Esteban-Cubillo, A., Pecharromán, C., Aguilar, E., Santarén, J., Moya, J.S., 2006. Antibacterial activity of copper monodispersed nanoparticles into sepiolite. J. Mater. Sci. 41, 5208–5212.

EUR-Lex, 2015. Commission Implementing Regulation (EU) 2015/232 of 13 February 2015. Available from: https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32015R0232&from=EN. (Accessed 24 April 2020).

Ganesh Kumar, N., Pandey, S.D., Mallick, S., Ghosh, S.K., Pramanik, P., Ghosh, A.S., 2020. Thiol stabilized copper nanoparticles exert antimicrobial properties by preventing cell division in *Escherichia coli*. Indian J. Biochem. Biophys. 57, 151–157.

Gatadi, S., Madhavi, Y.V., Nanduri, S., 2021. Nanoparticle drug conjugates treating microbial and viral infections: a review. J. Mol. Struct. 1228, 129750.

Gawande, M.B., Goswami, A., Felpin, F.X., Asefa, T., Huang, X., Silva, R., Zou, X., Zboril, R., Varma, R.S., 2016. Cu and Cu-based nanoparticles: synthesis and applications in catalysis. Chem. Rev. 116, 3722–3811.

Ginjupalli, K., Alla, R., Shaw, T., Tellapragada, C., Gupta, L.K., Upadhya, P.N., 2018. Comparative evaluation of efficacy of zinc oxide and copper oxide nanoparticles as antimicrobial additives in alginate impression materials. Mater. Today 5, 16258–16266.

Gkanatsiou, C., Ntalli, N., Menkissoglu-Spiroudi, U., Dendrinou-Samara, C., 2019. Essential metal-based nanoparticles (copper/iron NPs) as potent nematicidal agents against *Meloidogyne* spp. J. Nanotechnol. Res. 1, 044–058.

Gomaa, E.Z., Housseiny, M.M., Omran, A.A.A.K., 2019. Fungicidal efficiency of silver and copper nanoparticles produced by *Pseudomonas fluorescens* ATCC 17397 against four *Aspergillus* species: a molecular study. J. Clust. Sci. 30, 181–196.

Hajipour, M.J., Fromm, K.M., Ashkarran, A.A., de Aberasturi, D.J., de Larramendi, I.R., Rojo, T., Serpooshan, V., Parak, W.J., Mahmoudi, M., 2012. Antibacterial properties of nanoparticles. Trends Biotechnol. 30, 499–511.

Hasan, S.S., Singh, S., Parikh, R.Y., Dharne, M.S., Patole, M.S., Prasad, B.L., Shouche, Y.S., 2008. Bacterial synthesis of copper/copper oxide nanoparticles. J. Nanosci. Nanotechnol. 8 (6), 3191–3196.

Hassan, S.E.D., Salem, S.S., Fouda, A., Awad, M.A., El-Gamal, M.S., Abdo, A.M., 2018. New approach for antimicrobial activity and bio-control of various pathogens by biosynthesized copper nanoparticles using endophytic actinomycetes. J. Radiat. Res. Appl. Sci. 11, 262–270.

Honary, S., Barabadi, H., Gharaei-Fathabad, E., Naghibi, F., 2012. Green synthesis of copper oxide nanoparticles using *Penicillium aurantiogriseum*, *Penicillium citrinum* and *Penicillium waksmanii*. Dig. J. Nanomater. Biostruct. 7, 999–1005.

Hoseinnejad, M., Jafari, S.M., Katouzian, I., 2018. Inorganic and metal nanoparticles and their antimicrobial activity in food packaging applications. Crit. Rev. Microbiol. 44, 161–181.

Hrenovic, J., Milenkovic, J., Daneu, N., Kepcija, R.M., Rajic, N., 2012. Antimicrobial activity of metal oxide nanoparticles supported onto natural clinoptilolite. Chemosphere 88, 1103–1107.

Ibrahim, S., Jakaria, N.Z., Rozali, S., Ghazali, N.N.N., Ab Karim, Sabri, M.F.M., 2020. Biosynthesis of copper oxide nanoparticles using *Camellia sinensis* plant powder. In: Advances in Material Sciences and Engineering. Springer, Singapore, pp. 233–238.

Iliger, K.S., Sofi, T.A., Bhat, N.A., Ahanger, F.A., Chandra Sekhar, J., Elhendi, A.Z., Al-Huqail, A.A., Khan, F., 2021. Copper nanoparticles: green synthesis and managing fruit rot disease of chilli caused by *Colletotrichum capsica*. Saudi J. Biol. Sci. 28, 1477–1486.

Jeong, S., Woo, K., Kim, D., Lim, S., Kim, J.S., Shin, H., Xia, Y., Moon, J., 2008. Controlling the thickness of the surface oxide layer on Cu nanoparticles for the fabrication of conductive structures by ink-jet printing. Adv. Funct. Mater. 18, 679–686.

Jia, B., Mei, Y., Cheng, L., Zhou, J., Zhang, L., 2012. Preparation of copper nanoparticles coated cellulose films with antibacterial properties through one-step reduction. ACS Appl. Mater. Interfaces 4, 2897–2902.

Jinu, U., Gomathi, M., Saiqa, I., Geetha, N., Benelli, G., Venkatachalam, P., 2017. Green engineered biomolecule-capped silver and copper nanohybrids using *Prosopis cineraria* leaf extract: enhanced antibacterial activity against microbial pathogens of public health relevance and cytotoxicity on human breast cancer cells (MCF-7). Microb. Pathog. 105, 86–95.

Kale, R.A., Shende, S.S., Deshmukh, A.M., Waghmare, D.H., 2017. Green synthesis of copper nanoparticles by *Citrus sinensis* and evaluation of its role in management of stem rot of tomato. Trends Biosci. 10, 4708–4715.

Kanhed, P., Birla, S., Gaikwad, S., Gade, A., Seabra, A.B., Rubilar, O., Duran, N., Rai, M., 2014. In vitro antifungal efficacy of copper nanoparticles against selected crop pathogenic fungi. Mater. Lett. 115, 13–17.

Kaur, P., Thakur, R., Chaudhury, A., 2016. Biogenesis of copper nanoparticles using peel extract of *Punica granatum* and their antimicrobial activity against opportunistic pathogens. Green Chem. Lett. Rev. 9, 33–38.

Keulemans, W., Bylemans, D., de Coninck, B., 2019. Farming Without Plant Protection Products: Can We Grow Without Using Herbicides, Fungicides and Insecticides? European Parliament. http://www.europarl.europa.eu/cmsdata/185760/EPRS_IDA(2019)634416_EN.pdf.

Khan, A., Rashid, A., Younas, R., Chong, R., 2016. A chemical reduction approach to the synthesis of copper nanoparticles. Int. Nano Lett. 6, 21–26.

Khani, R., Roostaei, B., Bagherzade, G., Moudi, M., 2018. Green synthesis of copper nanoparticles by fruit extract of *Ziziphus spina-christi* (L.) Willd.: application for adsorption of triphenylmethane dye and antibacterial assay. J. Mol. Liq. 255, 541–549.

Koul, A., Mathur, A., Hattewar, J., 2019. Copper-chitosan fused nanoparticles as A best possible remedy against fungal phyto-pathogens. Acta Sci. Agric. 4, 69–72.

Kraemer, H., 1905. The oligodynamic action of copper foil on certain intestinal organisms. Proc. Am. Philos. Soc. 179, 51–65.

Kruk, T., Szczepanowicz, K., Stefańska, J., Socha, R.P., Warszyński, P., 2015. Synthesis and antimicrobial activity of monodisperse copper nanoparticles. Colloids Surf. B Biointerfaces 128, 17–22.

Kumar, P.V., Shameem, U., Kollu, P., Kalyani, R.L., Pammi, S.V.N., 2015. Green synthesis of copper oxide nanoparticles using *Aloe vera* leaf extract and its antibacterial activity against fish bacterial pathogens. BioNanoScience 5, 135–139.

Kumar, S., Mukherjee, A., Dutta, J., 2020. Chitosan based nanocomposite films and coatings: emerging antimicrobial food packaging alternatives. Trends Food Sci. Technol. 97, 196–209.

Lamichhane, J.R., Osdaghi, E., Behlau, F., Köhl, J., Jones, J.B., Aubertot, J.N., 2018. Thirteen decades of antimicrobial copper compounds applied in agriculture. A review. Agron. Sustain. Dev. 38, 28.

Lang, C., Mission, E.G., Fuaad, A.A.H.A., Shaalan, M., 2021. Nanoparticle tools to improve and advance precision practices in the agrifoods sector towards sustainability-a review. J. Clean. Prod., 126063.

Lee, H.-J., Song, J.Y., Kim, B.S., 2013. Biological synthesis of copper nanoparticles using *Magnolia kobus* leaf extract and their antibacterial activity. J. Chem. Technol. Biotechnol. 88, 1971–1977.

Lemire, J.A., Harrison, J.J., Turner, R.J., 2013. Antimicrobial activity of metals: mechanisms, molecular targets and applications. Nat. Rev. Microbiol. 11, 371–384.

Li, Y., Pi, Q.-m., You, H.-h., Li, J.-q., Wang, P.-c., Yange, X., Wu, Y., 2018. A smart multifunctional coating based on antipathogen micelles tethered with copper nanoparticles via a biosynthesis method using L-vitamin C. RSC Adv. 8, 18272.

Li, F., Liu, Y., Cao, Y., Zhang, Y., Zhe, T., Guo, Z., Sun, X., Wang, Q., Wang, L., 2020. Copper sulfide nanoparticle-carrageenan films for packaging application. Food Hydrocoll. 109, 106094.

López-Vargas, E.R., Ortega-Ortíz, H., Cadenas-Pliego, G., de Alba Romenus, K., Cabrera de la Fuente, M., Benavides-Mendoza, A., Juárez-Maldonado, A., 2018. Foliar application of copper nanoparticles increases the fruit quality and the content of bioactive compounds in tomatoes. Appl. Sci. 8, 1020.

Ma, C., Borgatta, J., De La Torre-Roche, R., Zuverza-Mena, N., White, J.C., Hamers, R.J., Elmer, W.H., 2019. Time-dependent transcriptional response of tomato (*Solanum lycopersicum* L.) to Cu nanoparticle exposure upon infection with *Fusarium oxysporum* f. sp. *lycopersici*. ACS Sustain. Chem. Eng. 7, 10064–10074.

Maiti, M., Sarkar, M., Maiti, S., Liu, D., 2019. Efficacy of shape-monitored reduced graphene oxide–copper nanohybrids: anti-bacterial attributes for food safety and dye degradation studies. New J. Chem. 43, 662–674.

Maity, A., Natarajan, N., Pastor, M., Vijay, D., Gupta, C.K., Wasnik, V.K., 2018. Nanoparticles influence seed germination traits and seed pathogen infection rate in forage sorghum (*Sorghum bicolour*) and cowpea (*Vigna unguiculata*). NISCAIR-CSIR, India 56, 363–372.

Malandrakis, A.A., Kavroulakis, N., Chrysikopoulos, C.V., 2019. Use of copper, silver and zinc nanoparticles against foliar and soil-borne plant pathogens. Sci. Total Environ. 670, 292–299.

Malandrakis, A.A., Kavroulakis, N., Chrysikopoulos, C.V., 2020. Synergy between Cu-NPs and fungicides against *Botrytis cinerea*. Sci. Total Environ. 703, 135557.
Meghana, S., Kabra, P., Chakraborty, S., Padmavathy, N., 2015. Understanding the pathway of antibacterial activity of copper oxide nanoparticles. RSC Adv. 5, 12293–12299.
Mercy Ranjitham, A., Selva Ranjani, G., Caroling, G., 2015. Biosynthesis, characterization, antimicrobial activity of copper nanoparticles using fresh aqueous *Ananas comosus* L. (Pineapple) extract. Int. J. PharmTech. Res. 8, 750–769.
Miao, H., Teng, Z., Wang, C., Chong, H., Wang, G., 2019. Recent progress in two-dimensional antimicrobial nanomaterials. Chem. A Eur. J. 25, 929–944.
Mirhosseini, M., Bafghi, A.K., 2019. The combined effect of copper oxide and magnesium oxide nanoparticles against some water and food borne bacteria. Iran. J. Med. Microbiol. 13, 233–250.
Mohamed, E.A., Gaber, M.H., Elsharabasy, S.F., 2018. Evaluating the in vivo efficacy of copper-chitosan nanocomposition for treating vascular wilt disease in date palm. Int. J. Environ. Agric. Biotechnol. 3, 239085.
Mondal, K.K., Mani, C., 2009. Suppression of common bacterial blight in mung bean by phylloplane resident *Pseudomonas fluorescens* strain MBPF-01 alone and in combination with nanocopper. Indian Phytopathol. 62, 445–448.
Mondal, K.K., Mani, C., 2012. Investigation of the antibacterial properties of nanocopper against *Xanthomonas axonopodis* pv. *punicae*, the incitant of pomegranate bacterial blight. Ann. Microbiol. 62, 889–893.
Mondal, K.K., Bhar, L.M., Mani, C., 2010. Combined efficacy of *Pseudomonas fluorescens* strain MBPF-01 and nanocopper against bacterial leaf blight in rice. Indian Phytopathol. 63, 266–268.
Nagaonkar, D., Shende, S., Rai, M., 2015. Biosynthesis of copper nanoparticles and its effect on actively dividing cells of mitosis in *Allium cepa*. Biotechnol. Prog. 31, 557–565.
Nagar, N., Devra, V., 2018. Green synthesis and characterization of copper nanoparticles using *Azadirachta indica* leaves. Mater. Chem. Phys. 213, 44–51.
Nayantara, Pawan, K., 2018. Biosynthesis of nanoparticles using eco-friendly factories and their role in plant pathogenicity: a review. J. Biotechnol. Res. Innov. 2, 63–73.
Olchowik, J., Bzdyk, R.M., Studnicki, M., Bederska-Błaszczyk, M., Urban, A., Aleksandrowicz-Trzcińska, M., 2017. The effect of silver and copper nanoparticles on the condition of English oak (*Quercus robur* L.) seedlings in a container nursery experiment. Forests 8, 310.
Ouda, S.M., 2014. Antifungal activity of silver and copper nanoparticles on two plant pathogens, *Alternaria alternata* and *Botrytis cinerea*. Res. J. Microbiol. 9, 34.
Pandey, P., Merwyn, S., Agarwal, G.S., Tripathi, B.K., Pant, S.C., 2012. Electrochemical synthesis of multi-armed CuO nanoparticles and their remarkable bactericidal potential against waterborne bacteria. J. Nanopart. Res. 14, 709–721.
Pandey, P., Packiyaraj, M.S., Nigam, H., Agarwal, G.S., Singh, B., Patra, M.K., 2014. Antimicrobial properties of CuO nanorods and multi-armed nanoparticles against *B. anthracis* vegetative cells and endospores. Beilstein J. Nanotechnol. 5, 789–800.
Pariona, N., Mtz-Enriquez, A.I., Sánchez-Rangel, D., Carrión, G., Paraguay-Delgado, F., Rosas-Saito, G., 2019. Green-synthesized copper nanoparticles as a potential antifungal against plant pathogens. RSC Adv. 9, 18835–18843.
Ponmurugan, P., Manjukarunambika, K., Elango, V., Gnanamangai, B.M., 2016. Antifungal activity of biosynthesised copper nanoparticles evaluated against red root-rot disease in tea plants. J. Exp. Nanosci. 11, 1019–1031.

Powar, N.S., Patel, V.J., Pagare, P.K., Pandav, R.S., 2019. Cu nanoparticle: synthesis, characterization and application. Chem. Methodol. 3, 457–480.

Punniyakotti, P., Panneerselvam, P., Perumal, D., Aruliah, R., Angaiah, S., 2020. Anti-bacterial and anti-biofilm properties of green synthesized copper nanoparticles from *Cardiospermum halicacabum* leaf extract. Bioprocess Biosyst. Eng., 1–9.

Rajesh, K., Ajitha, B., Reddy, Y., Suneetha, Y., Reddy, P.S., 2018. Assisted green synthesis of copper nanoparticles using *Syzygium aromaticum* bud extract: physical, optical and antimicrobial properties. Optik 154, 593–600.

Rajesh, K.M., Ajitha, B., Reddy, Y.A.K., Suneetha, Y., Reddy, P.S., Ahn, C.W., 2018b. A facile bio-synthesis of copper nanoparticles using *Cuminum cyminum* seed extract: antimicrobial studies. Adv. Nat. Sci. Nanosci. Nanotechnol. 9, 035005.

Rajeshkumar, S., Rinitha, G., 2018. Nanostructural characterization of antimicrobial and antioxidant copper nanoparticles synthesized using novel *Persea americana* seeds. OpenNano 3, 18–27.

Rajwade, J.M., Chikte, R.G., Paknikar, K.M., 2020. Nanomaterials: new weapons in a crusade against phytopathogens. Appl. Microbiol. Biotechnol. 104, 1437–1461.

Ramanathan, R., Field, M.R., O'Mullane, A.P., Smooker, P.M., Bhargava, S.K., Bansal, V., 2013. Aqueous phase synthesis of copper nanoparticles: a link between heavy metal resistance and nanoparticle synthesis ability in bacterial systems. Nanoscale 5 (6), 2300–2306.

Rastogi, A., Zivcak, M., Sytar, O., Kalaji, H.M., He, X., Mbarki, S., Brestic, M., 2017. Impact of metal and metal oxide nanoparticles on plant: a critical review. Front. Chem. 5, 1–16.

Ray, D., Pramanik, S., Mandal, R.P., Chaudhuri, S., De, S., 2015. Sugar-mediated 'green' synthesis of copper nanoparticles with high antifungal activity. Mater. Res. Express 2, 105002.

Rötzer, N., Schmidt, M., 2020. Historical, current, and future energy demand from global copper production and its impact on climate change. Resources 9, 44.

Roy, K., Sarkar, C.K., Ghosh, C.K., 2016. Antibacterial mechanism of biogenic copper nanoparticles synthesized using *Heliconia psittacorum* leaf extract. Nanotechnol. Rev. 5, 529–536.

Ruparelia, J.P., Chatterjee, A.K., Duttagupta, S.P., Mukherji, S., 2008. Strain specificity in antimicrobial activity of silver and copper nanoparticles. Acta Biomater. 4, 707–716.

Rusjan, D., 2012. Copper in horticulture. In: Fungicides for Plant and Animal Diseases. IntechOpen, pp. 257–278.

Sampathkumar, K., Tan, K.X., Loo, S.C.J., 2020. Developing nano-delivery systems for agriculture and food applications with nature-derived polymers. iScience 23, 101055.

Sánchez-López, E., Gomes, D., Esteruelas, G., Bonilla, L., Lopez-Machado, A.L., Galindo, R., Cano, A., Espina, M., Ettcheto, M., Camins, A., Silva, A.M., Durazzo, A., Santini, A., Garcia, M.L., Souto, E.B., 2020. Metal-based nanoparticles as antimicrobial agents: an overview. Nanomaterials 10, 292.

Saran, M., Vyas, S., Mathur, M., Bagaria, A., 2017. Green synthesis and characterisation of CuNPs: insights into their potential bioactivity. IET Nanobiotechnol. 12, 357–364.

Saranyaadevi, K., Subha, V., Ravindran, R.E., Renganathan, S., 2014. Synthesis and characterization of copper nanoparticle using *Capparis zeylanica* leaf extract. Int. J. ChemTech Res. 6, 4533–4541.

Saravanakumar, K., Sathiyaseelan, A., Mariadoss, A.V.A., Xiaowen, H., Wang, M.H., 2020. Physical and bioactivities of biopolymeric films incorporated with cellulose, sodium alginate and copper oxide nanoparticles for food packaging application. Int. J. Biol. Macromol. 153, 207–214.

Seil, J.T., Webster, T.J., 2012. Antimicrobial applications of nanotechnology: methods and literature. Int. J. Nanomedicine 7, 2767–2781.
Sekhon, B.S., 2014. Nanotechnology in agri-food production: an overview. Nanotechnol. Sci. Appl. 7, 31.
Shah, K.W., Huseien, G.F., 2020. Inorganic nanomaterials for fighting surface and airborne pathogens and viruses. Nano Express 1, 032003.
Shah, R., Pathan, A., Vaghela, H., Ameta, S.C., Parmar, K., 2019. Green synthesis and characterization of copper nanoparticles using mixture (*Zingiber officinale, Piper nigrum* and *Piper longum*) extract and its antimicrobial activity. Chem. Sci. Trans. 8 (1), 63–69.
Shahzadi, S., Zafar, N., Sharif, R., 2018. Antibacterial activity of metallic nanoparticles. In: Bacterial Pathogenesis and Antibacterial Control. IntechOpen, London, pp. 51–71.
Shantkriti, S., Rani, P., 2014. Biological synthesis of copper nanoparticles using *Pseudomonas fluorescens*. Int. J. Curr. Microbiol. App. Sci. 3, 374–383.
Sharma, P., Pant, S., Dave, V., Tak, K., Sadhu, V., Reddy, K.R., 2019. Green synthesis and characterization of copper nanoparticles by *Tinospora cordifolia* to produce nature-friendly copper nano-coated fabric and their antimicrobial evaluation. J. Microbiol. Methods 160, 107–116.
Shende, S., Ingle, A.P., Gade, A., Rai, M., 2015. Green synthesis of copper nanoparticles by *Citrus medica Linn*. (Idilimbu) juice and its antimicrobial activity. World J. Microbiol. Biotechnol. 31, 865–873.
Shende, S., Gaikwad, N., Bansod, S., 2016. Synthesis and evaluation of antimicrobial potential of copper nanoparticle against agriculturally important phytopathogens. Synthesis 1, 41–47.
Shi, Y.-J., Wrona, M., Hu, C.-Y., Nerín, C., 2021. Copper release from nano-copper/polypropylene composite films to food and the forms of copper in food simulants. Innov. Food Sci. Emerg. Technol. 67, 102581.
Siddiqi, K.S., Husen, A., 2016. Fabrication of metal nanoparticles from fungi and metal salts: scope and application. Nanoscale Res. Lett. 11, 1–15.
Siddiqui, H., Qureshi, M.S., Haque, F.Z., 2020. Biosynthesis of flower-shaped CuO nanostructures and their photocatalytic and antibacterial activities. Nano-Micro Lett. 12, 29.
Singh, P., Kim, Y.J., Zhang, D., Yang, D.C., 2016. Biological synthesis of nanoparticles from plants and microorganisms. Trends Biotechnol. 34, 588–599.
Singh, N., Paknikar, K.M., Rajwade, J., 2019. RNA-sequencing reveals a multitude of effects of silver nanoparticles on *Pseudomonas aeruginosa* biofilms. Environ. Sci. Nano 6, 1812–1828.
Singh, R.P., Handa, R., Manchanda, G., 2020. Nanoparticles in sustainable agriculture: an emerging opportunity. J. Control. Release 329, 1234–1248.
Slavin, Y.N., Asnis, J., Häfeli, U.O., Bach, H., 2017. Metal nanoparticles: understanding the mechanisms behind antibacterial activity. J. Nanobiotechnol. 15, 1–20.
Solomon, E.I., Heppner, D.E., Johnston, E.M., Ginsbach, J.W., Cirera, J., Qayyum, M., Kieber-Emmons, M.T., Kjaergaard, C.H., Hadt, R.G., Tian, L., 2014. Copper active sites in biology. Chem. Rev. 114, 3659–3853.
Subhankari, I., Nayak, P.L., 2013. Synthesis of copper nanoparticles using *Syzygium aromaticum* (cloves) aqueous extract by using green chemistry. World J. Nanosci. Technol. 2, 14–17.
Thakur, S., Shandilya, M., Thakur, S., Sharma, D.K., 2020. Growth mechanism and characterization of CuO nanostructure as a potent antimicrobial agent. Surf. Interfaces 20, 100551.

Thiruvengadam, M., Rajakumar, G., Chung, I.M., 2018. Nanotechnology: current uses and future applications in the food industry. 3 Biotech 8 (1), 74.

Tian, Y., Cai, R., Yue, T., Gao, Z., Yuan, Y., Wang, Z., 2021. Application of nanostructures as antimicrobials in the control of foodborne pathogen. Crit. Rev. Food Sci. Nutr., 1–18.

Tiwari, M., Jain, P., Hariharapura, R.C., Narayanan, K., Bhat, U., Udupa, N., Venkata Rao, J., 2016. Biosynthesis of copper nanoparticles using copper-resistant *Bacillus cereus*, a soil isolate. Process Biochem. 51, 1348–1356.

Trang, N.T.H., Dung, P.D., Van, P.T.H., Thang, P.Q., 2018. Green synthesis of copper nanoparticles using Mandarin (*Citrus reticulata*) peel extract and antifungal study. Asian J. Biotechnol. Bioresour. Technol., 1–9.

Ude, V.C., Brown, D.M., Stone, V., Johnston, H.J., 2019. Using 3D gastrointestinal tract in vitro models with microfold cells and mucus secreting ability to assess the hazard of copper oxide nanomaterials. J. Nanobiotechnol. 17, 1–20.

Varshney, R., Bhadauria, S., Gaur, M.S., Pasricha, R., 2010. Characterization of copper nanoparticles synthesized by a novel microbiological method. J. Mater. 62, 102–104.

Varympopi, A., Dimopoulou, A., Theologidis, I., Karamanidou, T., Kerou, A.K., Vlachou, A., Karfaridis, D., Papafotis, D., Hatzinikolaou, D., Tsouknidas, A., Skandalis, N., 2020. Bactericides based on copper nanoparticles restrain growth of important plant pathogens. Pathogens 9, 1024.

Vera-Reyes, I., Esparza-Arredondo, I.J.E., Lira-Saldivar, R.H., Granados-Echegoyen, C.A., Alvarez-Roman, R., Vásquez-López, A., De los Santos-Villarreal, G., Díaz-Barriga Castro, E., 2019. In vitro antimicrobial effect of metallic nanoparticles on phytopathogenic strains of crop plants. J. Phytopathol. 167, 461–469.

Videira-Quintela, D., Martin, O., Montalvo, G., 2021. Recent advances in polymer-metallic composites for food packaging applications. Trends Food Sci. Technol. 109, 230–244.

Vincent, M., Duval, R.E., Hartemann, P., Engels-Deutsch, M., 2018. Contact killing and antimicrobial properties of copper. J. Appl. Microbiol. 124, 1032–1046.

Wang, L., Hu, C., Shao, L., 2017. The antimicrobial activity of nanoparticles: present situation and prospects for the future. Int. J. Nanomedicine 12, 1227.

Weisany, W., Samadi, S., Amini, J., Hossaini, S., Yousefi, S., Maggi, F., 2019. Enhancement of the antifungal activity of thyme and dill essential oils against *Colletotrichum nymphaeae* by nano-encapsulation with copper NPs. Ind. Crop Prod. 132, 213–225.

Yadav, H.M., Otari, S.V., Koli, V.B., Mali, S.S., Hong, C.K., Pawar, S.H., Delekar, S.D., 2014. Preparation and characterization of copper-doped anatase TiO_2 nanoparticles with visible light photocatalytic antibacterial activity. J. Photochem. Photobiol. A Chem. 280, 32–38.

Yadav, R.N., Chitara, M.K., Zaidi, N.W., Khan, A.I., Singh, U.S., Singh, H.B., 2018. Novel facets and challenges in the management of phytopathogens using myconanoparticles. Int. J. Curr. Microbiol. App. Sci. 7, 3296–3308.

Yoon, K.Y., Byeon, J.H., Park, J.H., Hwang, J., 2007. Susceptibility constants of *Escherichia coli* and *Bacillus subtilis* to silver and copper nanoparticles. Sci. Total Environ. 373, 572–575.

Zangeneh, M.M., Ghaneialvar, H., Akbaribazm, M., Ghanimatdan, M., Abbasi, N., Goorani, S., Pirabbasi, E., Zangeneh, A., 2019. Novel synthesis of *Falcaria vulgaris* leaf extract conjugated copper nanoparticles with potent cytotoxicity, antioxidant, antifungal, antibacterial, and cutaneous wound healing activities under in vitro and in vivo condition. J. Photochem. Photobiol. B 197, 111556.

Zhao, L., Lu, L., Wang, A., Zhang, H., Huang, M., Wu, H., Xing, B., Wang, Z., Ji, R., 2020. Nano-biotechnology in agriculture: use of nanomaterials to promote plant growth and stress tolerance. J. Agric. Food Chem. 68, 1935–1947.

Further reading

Adhikari, T., Sarkar, D., Mashayekhi, H., Xing, B., 2016. Growth and enzymatic activity of maize (*Zea mays* L.) plant: solution culture test for copper dioxide nano particles. J. Plant Nutr. 39, 99–115.

Alswat, A.A., Ahmad, M.B., Saleh, T.A., 2017. Preparation and characterization of zeolite\ zinc oxide-copper oxide nanocomposite: antibacterial activities. Colloid Interface Sci. Commun. 16, 19–24.

Bagchi, B., Kar, S., Dey, S.K., Bhandary, S., Roy, D., Mukhopadhyay, T.K., Das, S., Nandy, P., 2013. In situ synthesis and antibacterial activity of copper nanoparticle loaded natural montmorillonite clay based on contact inhibition and ion release. Colloids Surf. B. Biointerfaces 108, 358–365.

Calvano, C.D., Picca, R.A., Bonerba, E., Tantillo, G., Cioffi, N., Palmisano, F., 2016. MALDI-TOF mass spectrometry analysis of proteins and lipids in *Escherichia coli* exposed to copper ions and nanoparticles. J. Mass Spectrom. 51, 828–840.

El-Batal, A.I., El-Sayyad, G.S., Mosallam, F.M., Fathy, R.M., 2020. *Penicillium chrysogenum*-mediated mycogenic synthesis of copper oxide nanoparticles using gamma rays for in vitro antimicrobial activity against some plant pathogens. J. Clust. Sci. 31, 79–90.

Hafeez, A., Razzaq, A., Mahmood, T., Jhanzab, H.M., 2015. Potential of copper nanoparticles to increase growth and yield of wheat. J. Nanosci. Adv. Technol. 1, 6–11.

Hemmati, F., Bahrami, A., Esfanjani, A.F., Hosseini, H., McClements, D.J., Williams, L., 2021. Electrospun antimicrobial materials: advanced packaging materials for food applications. Trends Food Sci. Technol. 111, 520–533.

Kaur, P., 2018. Biosynthesis of nanoparticles using eco-friendly factories and their role in plant pathogenicity: a review. Biotechnol. Res. Innov. 2, 63–73.

Mahdi, Z.M., Ghaneialvar, H., Akbaribazm, M., Ghanimatdan, M., Abbasi, N., Goorani, S., Pirabbasi, E., Zangeneh, A., 2019. Novel synthesis of *Falcaria vulgaris* leaf extract conjugated copper nanoparticles with potent cytotoxicity, antioxidant, antifungal, antibacterial, and cutaneous wound healing activities under in vitro and in vivo condition. J. Photochem. Photobiol. B Biol. 197, 111556.

Mohamed, E.A., 2018. Non-dependency of in vitro fungicidal efficiency of copper nanoparticles against *fusarium oxysporum* upon particle size. J. Plant Pathol. Microbiol. 9, 432.

Nabila, M.I., Kannabiran, K., 2018. Biosynthesis, characterization and antibacterial activity of copper oxide nanoparticles (CuO NPs) from actinomycetes. Biocatal. Agric. Biotechnol. 15, 56–62.

Sanchez-Sanhueza, G., Fuentes-Rodriguez, D., Bello-Toledo, H., 2016. Copper nanoparticles as potential antimicrobial agent in disinfecting root canals. A systematic review. Int. J. Odontostomat. 10, 547–554.

Shah, V., Belozerova, I., 2009. Influence of metal nanoparticles on the soil microbial community and germination of lettuce seeds. Water Air Soil Pollut. 197, 143–148.

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PART

Veterinary applications

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CHAPTER

Copper nanoparticles: Synthesis, characterization, and its veterinary applications

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Atef A. Hassan, Rasha M.H. Sayed-ElAhl, Ahmed M.A. El-Hamaky, Mogda K. Mansour, and Noha H. Oraby

Animal Health Research Institute (AHRI), Agriculture Research Center (ARC), Giza, Egypt

1 Introduction

Worldwide, animal production is of significant importance to human health and the food supply. Those issues that affect animal production are urgently given much attention. The last 100 years have shown progressive advancements in nanotechnology that help in the production of new useful strategies for health (Bai et al., 2018). Significant uses in biomedicine have been undertaken for the diagnosis of infections, cancer detection and therapy, the release of drugs to targeted sites, and others (Li et al., 2013; De Silva et al., 2015; Hemmati et al., 2020). Metal nanomaterials have significant properties that are better than bulk metals and hence have potentiated a wide range of applications in biomedicine. Nowadays, nanosized particles of minerals range from 1 to 100 nm and have shown beneficial application in animal health (Sri Sindhura et al., 2014; Peters et al., 2016; Salem and Fouda, 2021). The continuous awareness of the use of commercial antibiotics has resulted in recognizing the rise of antimicrobial resistance, which initiated a critical need and search for new agents. The nanostructures of CuNPs have significant properties such as thermoconductivity, fluid viscosity, and low price of synthesis that contributes to their use in biomedicine (Hsiao et al., 2006; Huang et al., 2008; Tamilvanan et al., 2014; Boyles et al., 2016). Hence, several studies evaluated different methods in the synthesis of CuNPs such as vacuum vapor deposition (Liu and Bando, 2003), microwave irradiation methods (Zhao et al., 2004), chemical reduction (Yang and Zhu, 2003), and laser ablation (Yeh et al., 1999). Moreover, several nanocomposites (NCPs) of metals such as nanoshells and quantum dots have been used in biomedical application as sensors, drug delivery, diagnosis, antimicrobial agents, and MRI imaging (Hassan et al., 2019, 2020; Hill and Li, 2017). Additionally, other tools like microfluidics, nanomaterial, and bioanalytical nanosensors have been recently used as in the detection of infection and its therapy

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(Meena et al., 2018; Hassan et al., 2020). The use of CuNPs in veterinary applications, animal health, and production have shown great efficiency (Hemmati et al., 2020). Therefore, the present review was undertaken to highlight the benefits of CuNP use in different fields of animal health including their antimicrobial potentials against several animal pathogens. The CuNP mechanisms of action, toxicity, and other uses are fully discussed in this chapter.

2 Synthesis methods of copper nanoparticles

There are several methods for the synthesis of CuNPs, i.e., chemical (Ramyadevi et al., 2012), physical (Blosi et al., 2011), and biological (Harne et al., 2012; Lee et al., 2013) (Fig. 1).

2.1 Physical and chemical methods

The most common physical methods to synthesize nanoparticles are laser ablation, aerosol techniques, and radiolysis. While they require high-cost equipment and high energy in the application, they are not typically used for large-scale

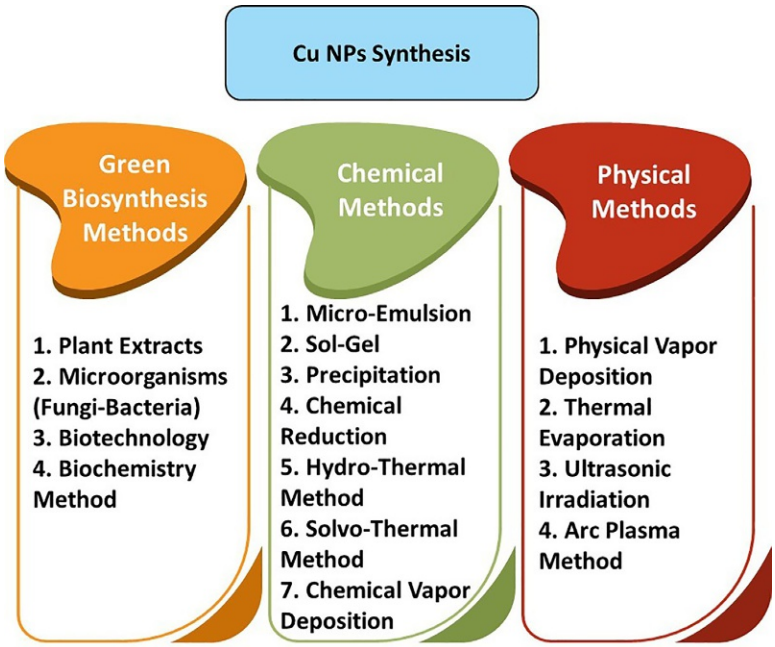

FIG. 1

Methods of synthesis of copper nanoparticles.

production (Thakkar et al., 2010). The chemical methods of CuNPs synthesis include the microemulsion technique and microwave irradiation (El-Nour et al., 2010; Galletti et al., 2013; Mandal and De, 2015; Sudha et al., 2021). These methods are of environmental concern and health hazard of workers due to the use of large concentrations of chemicals and the high cost of its application.

2.2 Green biosynthesis of CuNPs

There are safe and environmentally friendly methods available for large-scale production.

2.2.1 Plant synthesis of copper nanoparticles

The use of medicinal plants is cost-effective and has yielded nonhazardous products (Khaldari et al., 2021). The green synthesis of CuNPs by plant extracts such as Terminalia Arjuna bark (Yallappa et al., 2013), Magnolia leaf extract (Lee et al., 2011; Gopinath et al., 2014), and curcumin extract (Jayarambabu et al., 2020) was undertaken. Mohamed (2020) synthesized Cu/Cu_2O NPs by the chemical reduction method using the extract of seedless dates. Murthy et al. (2018) used *Hagenia Abyssinica* leaf extract in CuNPs synthesis, which showed antibacterial activity against *E. coli*, *Pseudomonas aeruginosa*, *Staphylococcus aureus*, and *Bacillus subtilis*. Moreover, Khani et al. (2018), Thakur et al. (2018), Ahmed et al. (2019), and Amer and Awwad (2021) detected the ability of medicinal plants in green synthesis of CuNPs as *Azadirachta indica* leaf, *Ziziphus spinachristi* (L.), *Asparagus adscendens* Roxb, and *Citrus limon* fruits extract, respectively. The biosynthesized CuNPs showed significant antimicrobial potentials against fungal and bacterial pathogens. These methods were simple, of a low price, and safely used (Asamoah et al., 2020).

2.2.2 Microbial synthesis of CuNPs

The microbial synthesis of copper nanoparticles had been reported using bacteria such as *Pseudomonas stutzeri* that produced spherical nanoparticles (Ramanathan et al., 2011; Omran, 2020). Some studies biosynthesized copper nanoparticles using fungi (*Aspergillus* species and *Penicillium vaksmanii*) (Pavani et al., 2013) and *Streptomyces* sp. (Bukhari et al., 2021). They found that the prepared CuNPs have high antimicrobial potential against pathogens like *E. coli*, *Candida albicans*, and *Salmonella typhimurium*.

2.2.3 Characterization of copper nanoparticles

There are several instruments used in the identification of nanomaterials such as UV-spectrophotometers, scanning electron microscopy (SEM), transmission electron microscopy (TEM), and X-ray methods (Fig. 2) (Rajendran et al., 2013; Sasaki et al., 2016; Kayalvizhi et al., 2020; Sudha et al., 2021).

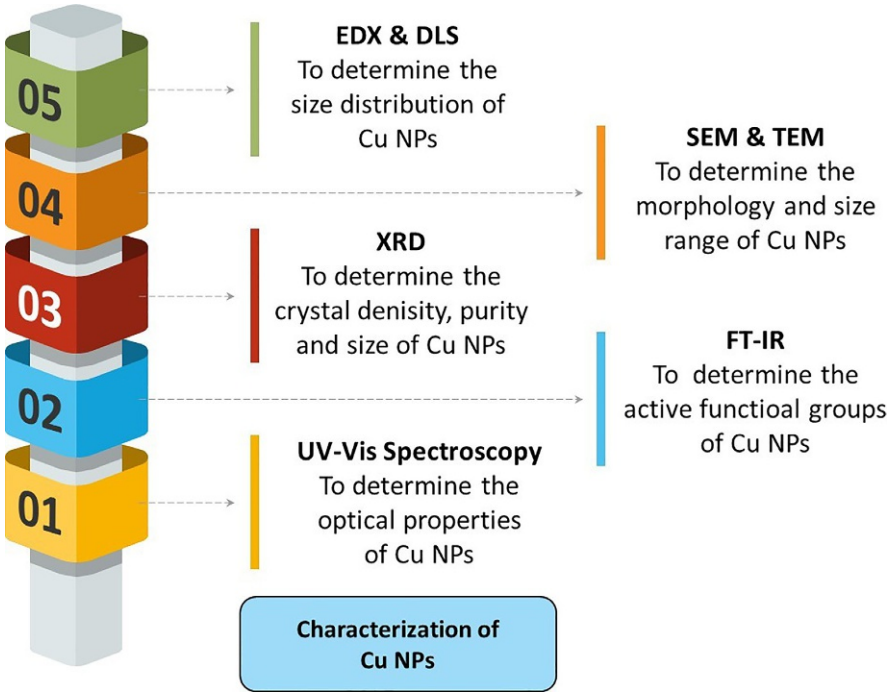

FIG. 2

Methods of characterization of copper nanoparticles.

3 Applications of copper nanoparticles and nanocomposites (NCPs) in veterinary medicine

Over the past decades, there have been a variety of nanomaterial applications used in biomedicine including metal nanoparticles, carbon nanoparticles, nanoshells, quantum dots, nanoemulsion, chitosan nanoparticles, silica nanoparticles, and nanosensors as well as nanotechnology applications in food (Zhang et al., 2016; Kayalvizhi et al., 2020). Some metal nanoparticles such as CuNPs are employed as antimicrobial agents and in biosensing, bioimaging, and tumor treatment (Mishra et al., 2009; Hassan et al., 2019, 2020; Amer and Awwad, 2021). These advancements resulted in the synthesis of efficient nanoproduct tools that benefits domestic animal health (Fig. 3).

3.1 Antimicrobial activity of CuNPs for control of animal diseases

CuNPs exhibit activities as strong antimicrobial agents that enable their use in drug transfer to target diseased tissues and for the treatment of infectious diseases (Ashfaq et al., 2019).

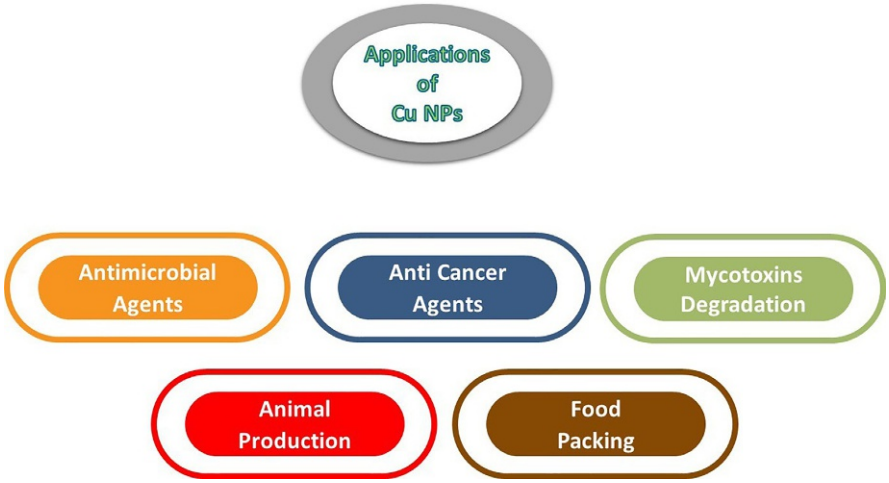

FIG. 3

Applications of copper nanoparticles.

3.1.1 Antibacterial activity of CuNPs

The smaller particle size of nanomaterial tends to enhance its antibacterial properties, and there are a larger number of atoms on the surface available to interact with bacterial cells (Gong et al., 2007; Marambio-Jones and Hoek, 2010; Camacho-Flores et al., 2015; Hemmati et al., 2020). The nanosized metals have significantly higher activities than bulk metals (Stankic et al., 2016). Their antibacterial properties initiate applications in various fields such as medical instruments, water treatment, and food processing (Yoon et al., 2007; Veerapandian et al., 2012). Santo et al. (2012) and Asamoah et al. (2020) reported antimicrobial activities for the treatment of several infectious pathogens. Longano et al. (2012) described that NCP fabrication of CuNPs by laser suppressed the growth of *Pseudomonas* spp. that proliferates in processed food. Similarly, Bajpai et al. (2012), Rubilar et al. (2013), and Shende et al. (2015) detected that CuNPs loaded in cotton fabric observed significant antibacterial activity and inhibited the growth of *M. luteus*, *S. aureus*, *E. coli*, *Kl. pneumonia*, and *Ps. Aeruginosa*, and the inhibitory zone was 26 mm. Also Zain et al. (2014) indicated that the bimetallic Ag/Cu nanoparticles gained antimicrobial potential against *B. subtilis* and *E. coli*, and the inhibitory concentration was 0.054 and 0.076 mg/L, respectively. Similarly, CuNP causes inhibition of bacterial cells *E. coli* and *S. aureus* (DeAlba-Montero et al., 2017) and Gram-positive and Gram-negative bacteria (Xu et al., 2009; Amer and Awwad, 2021; Alzahrani and Ahmed, 2016). Moreover, they have antimicrobial potential against *S. aureus*, *B. subtilis*, and *E. coli* (Shobha et al., 2014), as well as *Micrococcus luteus*, *Klebsiella pneumonia*, and *Pseudomonas aeruginosa* (Ramyadevi et al., 2012). The activity of *E. coli* and *B. subtilis* bacteria were suppressed by increasing CuNPs levels (Yoon et al., 2007; Lee et al., 2013;

Bukhari et al., 2021). They found that the prepared CuNPs have high antimicrobial potentials against pathogens like *E. coli*, *Candida albicans*, and *Salmonella*.

Ancona et al. (2014) and Arjunan et al. (2017) detected the antimicrobial and antitumor activities of Cu/Chitosan NCP. Similar activities were observed by the NCP of CuNPs/zeolite (Palza et al., 2018), while the conjugation of polycaprolactone with CuO potentiated the growth inhibition of microbial activities (Muñoz-Escobar et al., 2019). Prokhorov et al. (2019) found the growth inhibition of Cu/chitosan NCP against *St. aureus*, and this activity was because the NPs changed the electron transfer in bacterial cells, which leads to destruction, damage, and finally cell death. Moreover, Kalińska et al. (2019) synthesized silver-copper nanoparticles (AgCuNPs) that has antibacterial activity against causes of mastitis. Whereas Al-Hakkani (2020) green-synthesized CuNPs and used it to inhibit the growth of several types of Gram-negative bacteria.

3.1.2 Antifungal activity of CuNPs in control of animal fungal diseases

CuNPs inhibit the fungal growth activity of *A. flavus* and *A. niger*, *P. chrysogenum*, *Alternaria alternata*, and *Fusarium solani* (Ghasemian et al., 2012; Abd-Elsalam et al., 2019). Mixtures of CuNPs with acrylic paints have antifungal activity against *Stachybotrys chartarum*, which was lower than the minimal inhibitory concentration (MIC) of carneic acid alone (Wei et al., 2010). Ramyadevi et al. (2012) illustrated the antifungal potential of CuNPs against *A. flavus*, *A. niger*, and *C. albicans*, and the inhibitory zone was 23 mm. Also, CuNP potentiated its action for the *Candida* species recovered from animal mastitis (Kruk et al., 2015). The treatment with 250 mg/mL of CuNPs inhibited the fungal growth of *A. niger*, *F. solani*, and *A. solani* (Essa and Khallaf, 2016). Moreover, copper with chitosan nanogels exhibited a powerful fungicidal activity against *F. graminearum* and others (Brunel et al., 2013). Santos et al. (2013) investigated the combination of CuNPs with traditional antifungals, and this increased their antifungal activity by 1.6-fold (Amphotericin B, Clotrimazole, Nystatin, Fluconazole, and Ciprofloxacin). Another study detected the antifungal activity of CuNPs against the growth of several *Fusarium* and *Penicillium digitatum* species, and MIC were 40 and 60 mg/mL, respectively (Viet et al., 2016; Bouson et al., 2017; Youssef et al., 2017). Kasana et al. (2016) and Vanathi et al. (2016) green-biosynthesized CuNPs and detected their potential in growth inhibition of pathogenic fungi such as *Fusarium* sp., *Aspergillus* sp., and *Penicillium* species. Recently, hybrid nanomaterials were employed for several biomedical uses. This hybrid caused beneficial changes in nanomaterials such as Cu-loaded CS nanogels, which have strong synergistic antifungal activities against *Fusarium* sp. (Brunel et al., 2013) and other fungi such as *A. flavus* (Kaur et al., 2015; Abd-Elsalam et al., 2020). Monda et al. (2020), Saharan et al. (2013), and Tantubay et al. (2015) found that 0.1% of CS-CuNPs have significant antifungal potential against *A. alternata* and *R. solani*, while it is was found that the hybrid of CuNPs with hyperbranched polyester polyols have fungicide action against members of *Aspergillus* sp. (Medvedeva et al., 2017). However, the CuO/ZnO functional NCPs synthesized by coprecipitation was able to inhibit the fungal growth of *A. flavus* and *Trichoderma* sp. better than pure CuO

or ZnO (Phiwdang et al., 2013). Hence, there is huge interest in the use of NCPs of metals as polymers in different biomedical applications (Katerine et al., 2018; Singh et al., 2017; Hassan et al., 2021a,b). The NCP of AgNPs and CuNPs resulted in significant fungicidal activities higher than both agents alone (Cioffi et al., 2005). CS-Cu and CS-Zn NCPs have antifungal activity for *A. alternata* and *A. flavus* and are used as novel antimicrobial agents (Kaur et al., 2015; Saharan et al., 2015). Furthermore, numerous CuNPs and their hybrids have significant potential against fungal and bacterial animal diseases such as *S. cerevisiae*, *E. coli*, and *S. aureus* (Arjunan et al., 2017; Rubina et al., 2017). Al-Dhabaan et al. (2017) reported that the hybrid of chitosan, zinc oxide, and copper (CS Zn-Cu NCs) have the potential to inhibit the growth of fungal infection causes such as *A. alternata* and *Botrytis cinerea*. The hybrid of CuNPs with chitosan (Cu-CMC) suppressed the growth of *E. coli* and *C. tropicalis* strains (Tantubay et al., 2015; Zhang et al., 2020), while the hybrid of Cu/Ag-CNT/chitosan showed significant antimicrobial potential that inhibited the growth of *S. aureus* and *A. flavus* within 10 min of exposure and did not have any toxic effects (Morsi et al., 2017; Solairaj et al., 2017). Safaei et al. (2019) found that the hybrid nanomaterial of CuO alginate has antifungal activities for *A. niger*. Moreover, Gaballah et al. (2019) detected the antifungal activity of aminothiazole (ester)-functionalized PVC against *C. albicans* and *A. flavus*, and this was enhanced by the incorporation of AgNPs or CuNPs. The conductive Cu-core/Ag-subshell/polyaniline (PANI)-shell NCPs showed effective antifungal activity against *A. flavus* (Mohsen et al., 2018), whereas the NCPs of $CuFe_2O_4$ doped with Ag have more inhibition of fungal growth observed than undoped $CuFe_2O_4$ against *C. albicans*, *A. flavus*, and *A. niger* (Thakare et al., 2018). Cheong et al. (2020) studied the antifungal potential of graphene oxides in combination with CuNPs at a ratio of 30:70 (GO:CuNPs and GO-PEG:CuNPs) against *Candida albicans*, and their MIC_{50} were between 185 and 225 μg/mL. Other studies reported that CuNPs can inhibit microbial growth and tumor cells (Al-Hakkani, 2020; Oussou-Azo et al., 2020). Recently, Kumar et al. (2020a) and Hassan et al. (2021a,b) investigated the antifungal effects of Cu-CS NCPs against mycotoxigenic fungi and mycotoxins produced in animal and poultry feeds. The results supported the potential CuNPs components to be embedded or incorporated into biomedical dressings, instruments, and/or other medical devices to combat animal fungal infections in the future. It is suggested that the toxicity of NCPs against fungal cells is due to suppression of protein synthesis and destruction of cells (Alghuthaymi et al., 2020).

3.2 Detection and degradation of mycotoxins

To now, the detection methods of mycotoxins required prolonged incubation, organic solvents for mycotoxin extraction, and extensive dilution of the test samples, which are the main limitations of ELISA microplate assays. The attachment of antibodies against mycotoxins on the surface of magnetic particles increased their stability, making it possible to quantify AFB1 at a limit of 20 mg/mL in only 20 min (Urusov et al., 2014). On the other hand, there are few reports in the application

of CuNPs in the elimination of mycotoxins. The applications include removal of fungal pollutions, detoxification of mycotoxins, and influence of the carcinogenic effects of mycotoxins (Horky et al., 2018; Hassan et al., 2021a,b). Shamsudeen and Shrivastava (2013) detected that Cu proteinate, compared to $CuSO_4$, has a high potential to eliminate the toxicity of aflatoxicosis in broiler chickens and promote their products, while Asghar et al. (2018) found that iron nanoparticles have a significantly higher ability to detoxify AFB1 than CuNPs and AgNPs. Recently, Fadl et al. (2020) illustrated that copper nanoparticles have adsorbent potentials against mycotoxins and degraded the adverse changes of ochratoxicosis in fish when added to fish feed at a concentration of 0.5 g/kg. Also, hybrid NCPs based on organic polymeric and inorganic matrices as effective antiaflatoxigenic strains were explored (Jampílek and Kráĺová, 2020). Moreover, Cu-CS NCP hydrogels have the potential of growth inhibition against aflatoxigenic *A. flavus* and hence prevention of AFs production (Abd-Elsalam et al., 2020). Currently, Hassan et al. (2021a,b) investigated Cu-CS NCPs ability against mycotoxigenic fungi and mycotoxins production in chickens. The obtained results showed significant improvements in the health status of chickens after supplementation of aflatoxicated feeds with Cu-CS NCPs. Therefore, the efficacy of CuNPs in detoxification of mycotoxicosis in animal needs further advanced research work.

3.3 Anticancer activity of CuNPs

In the last decade, the anticancer potential, delivery of anticancer drugs, and degradation of DNA by CuNPs were evaluated by Jose et al. (2011). Valodkar et al. (2011a,b) detected that CuNPs was an effective anticancer agent against respiratory and alimentary tract system tumors in human, pig, and mouse embryonic fibroblast cells. Saranya and Ali (2017) found that CuNPs initiated significant toxic effects for mammary gland tumors in woman at a dose of 200 and 250 μg/mL, which reduced the activity of cancer cells to 20% and 50%, respectively. But Harne et al. (2012), Vaid et al. (2020), and Sharma et al. (2020) showed excellent anticancer activity of CuNPs at a low dose against HeLa, A549, and BHK21 cells (120 μg/mL). In a recent study, the CuNPs showed anticancer activities for intestinal, liver, and mammary gland tumors, and the inhibitory levels were 11.21, 19.88, and 12.21 μg/mL, respectively (Hassanien et al., 2018). Chakraborty and Basu (2017) illustrated the antitumor potentials of CuNPs against skin melanoma, lung cancer, and rat glioblastoma; MIC50 dose was 1.71, 1.81, and 1.88 μg/mL, respectively. The hybrid CuNPs with albumin protein showed high toxicity against breast cancer cells and caused its apoptosis and final death (Azizi et al., 2017; Vaid et al., 2020), while Laha et al. (2015) detected that the conversion of CuNPs to folate can be passively absorbed by the tumor cell of lymphoma in mice and decrease its toxicity and tumor size. Other studies on breast cancer by Jeronsia et al. (2016) and Siddiqui et al. (2013) resulted that CuONPs caused a decrease in proliferation rate and reduction the tumor cell viability, while Nagajyothi et al. (2016) and Sankar et al. (2014) detected their antitumor activities toward cervical and lung cell tumors that resulted in penetration,

destruction, and final death of tumor cells. Pandey et al. (2016), Yugandhar et al. (2017), and Thamer and Barakat (2019) illustrated that CuNPs initiated oxidative stress and toxicity in lung tumor cells and mammary gland tumors. Moreover, Al-Hakkani (2020) and Sharma et al. (2020) showed the antimicrobial and antitumor activities of CuONPs. Currently, Hassan et al. (2021b) detected the anticancer activity of CS-Cu NCPs against hepatic carcinoma in aflatoxicated chickens at a dose of 2 mg/kg of feed. The illustrated forgoing results need further investigation soon for the successful use of CuNPs as anticancer agents for some human and animal cancers (Fig. 4).

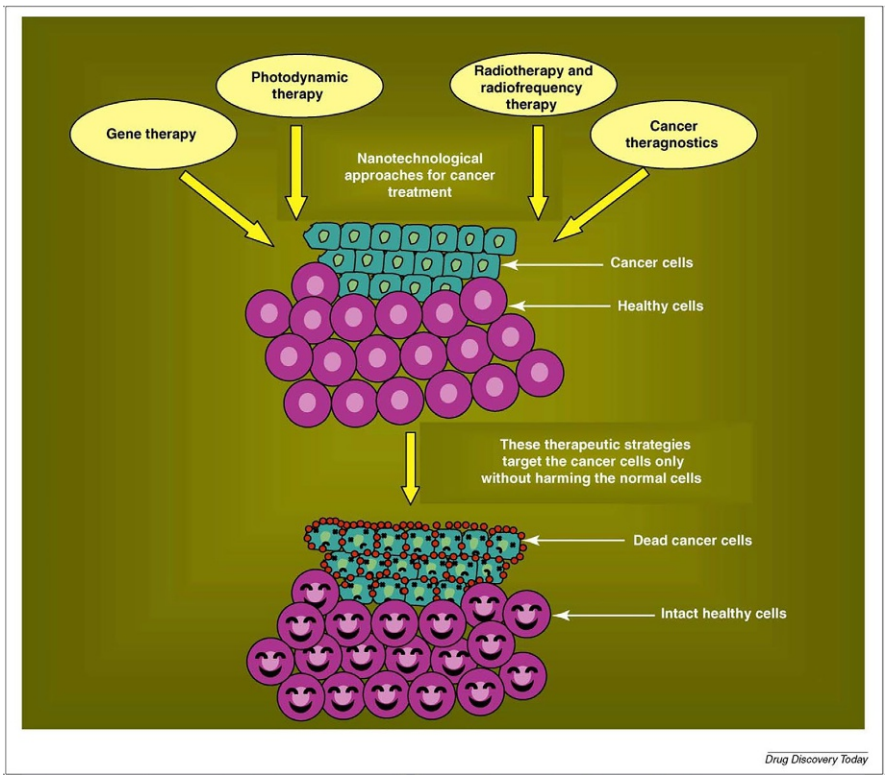

FIG. 4

Anticancer activity of CuNPs. Different approaches of nanotechnology such as gene therapy, photodynamic therapy, radiotherapy, radiofrequency therapy, and cancer theragnostic are being applied for the treatment of cancer. These advanced technologies help target cancer cells only without affecting normal cells. Ultimately, this leads to death of the cancer cells while the normal healthy cells survive.

Copyright from: Misra, R., Acharya, S., Sahoo, S.K., 2010. Cancer nanotechnology: application of nanotechnology in cancer therapy. Drug Discov. Today 15 (19/20), 824–850.

3.4 Animal production, growth promoters, nutrition, and immune status

The supplementations of animal feed with CuNPs have significant use for their health and production. The nanosized particle range elevates the metabolic activity of food in animals (Mahler et al., 2012). The use of CuNPs in animal feed is to stimulate the growth performance of the animals (Zhao et al., 2007; Hill and Li, 2017; Shen et al., 2020; Song et al., 2020) and high absorption and availability of feed nutrients in the intestinal tract (Scott et al., 2018), while Gonzales-Eguia et al. (2009) demonstrated that elevated feed efficiency, immune status, and body weight gain in the piglet. Mroczek-Sosnowska et al. (2014, 2015a,b, 2017) administered nano-$CuSO_4$ colloid (50 ppm) and $CuSO_4$-colloid (950 ppm) in ovo injection at the stage of developing chicken embryo and found that it does not pose a threat of extensive accumulating of this element in organs and muscles of birds at the age at slaughter. As a result, meat and internal organs do not pose a threat to consumers' health. Moreover, the CuNPs supplementation in fish and poultry feed is used to elevate the growth performance of animals (Civardi et al., 2015; Mroczek-Sosnowska et al., 2015a; Joshua et al., 2016; Al-Bairuty et al., 2016; El-Kassas et al., 2018). Additionally, CuNP improved the metabolic activities and growth performance in pigs and sheep (Gonzales-Eguia et al., 2009; Song et al., 2020), respectively. Moreover, CuNPs supplementation in animal diets elevated superoxide dismutase (SOD) that induced the antioxidant actions in animals (Lien, 2009; Refaie et al., 2015; Shen et al., 2020; Hassan et al., 2021b). Furthermore, the parental administration CuNPs in chickens resulted in a significant elevation of their health status (Miroshnikov et al., 2015). Similarly, the addition of CuNPs in rabbits fed at different concentrations raised their productivity and health (Refaie et al., 2015). Also, the cholesterol levels after adding CuNPs to a poultry diet were decreased as reported by Payvastegan et al. (2013), and a reduction in blood urea also due to increased metabolic rates (Yang et al., 2009; Scott et al., 2016). Moreover, the NCPs of CuNPs with chitosan and silica nanoparticles improved the health status, growth performance, and immune status of chickens (Wang et al., 2011; Zheng et al., 2013; Minglei et al., 2013). However, added Cu nanoparticles to poultry feed that resulted in increased absorption nutrients and hence elevated their growth performance. Also, adding CuNP to a fish diet was investigated by El Basuini et al. (2016, 2017), who reported that the feed supplementation with CuNPs resulted in high feed efficiency, protein retention, immune response, reduction of glucose level, and antioxidant defense system. Muralisankar et al. (2016) detected that the addition of CuNP to freshwater prawns feed (20 mg/kg) resulted in improved health status and growth performance. A significant reduction of glucose and lipid profile in rats was reported after administration of CuNPs (5 mg/kg) (Canli and Canli, 2017). Therefore, there are significant findings for beneficial health via supplementation of CuNPs in animal and poultry feed, which needs intensive laboratories study for future worldwide application (Salem and Fouda, 2021).

3.5 Food safety, protection, and packing

The worldwide outbreaks of food-borne pathogens revealed the significant importance of food preservation and the use of antimicrobials packaging. Nanotechnology has produced novel food packaging materials that have antimicrobial properties and novel sensors that formed acceptable colors and odors of food (Silvestre et al., 2011; Kaur et al., 2015). Food contamination with poisoning microbes such as *E. coli* O157:H7 was a cause of intestinal infections (Akbar and Anal, 2013), and hence prevention of their activities must be undertaken (Luning et al., 2008). Antimicrobial compounds in food packaging systems provide food safety and prolonged shelf life of the product (Bajpai et al., 2012) and protects against bacterial infection (Li et al., 2009). The traditional method of packing protects food from exposure to environmental pollution, while the recent active packing used antimicrobial agents to prevent microbial food spoilage (De-Azeredo, 2013). Moreover, inactive packaging, a direct interaction between the food, and nanomaterials lead to microbial inactivation and final death (Soares et al., 2009; De Silva et al., 2015; Zhang et al., 2020). Jafarizadeh et al. (2019) found that active packaging enhances food safety and prolonged shelf life. Another study investigated intelligent actions applied in food packaging such as sensing, detecting, tracking, recording, and communicating (Yam et al., 2005; Yalcin and Otles, 2008; Kumar et al., 2020b). Interestingly, NCP materials have several advantages over conventional food packaging materials owing to their superior polymeric properties and nanomaterials (Longano et al., 2012; Kaur et al., 2015; Hoffmann et al., 2019).

3.6 Other benefits of copper nanoparticles

Recently, CuNPs were used for heat transfer systems (Eastman et al., 2001), cytotoxicity "anticancer" activity (Chakraborty and Basu, 2017; Salem and Fouda, 2021), antimicrobial activity (Esteban-Cubillo et al., 2006), antifungal activity (Ranjitham et al., 2015; Jayandran et al., 2015), superstrong materials (Guduru et al., 2007), sensors (Kang et al., 2007), catalysts (Nasrollahzadeh and Sajadi, 2015; Sinha and Ahmaruzzaman, 2015), and antioxidant activity (Subbaiya and Selvam, 2015; Kalpana et al., 2016). Moreover, they were used in solar cells (Lee et al., 2009) and lasers (Stouwdam and Janssen, 2008; Ustinov et al., 2000), as dye degradation catalysts (Niharika and Vijay, 2018), and as antifever mosquito agent for *Aedes aegypti* species (Selvan et al., 2018).

4 Mechanism of CuNPs antimicrobial activity

The mechanism of antimicrobial action is suggested due to the affinity between CuNPs and microbial cells, which results in microbial cell injury caused by hydrogen peroxide liberation penetrating microbial cells, the destruction of cytoplasmic contents, interacting and leading to final cell death (Azam et al., 2012). The CuNPs

have greater antimicrobial activity than the bulk $CuSO_4$ due to their accumulation inside the cell cytoplasm, and they could be used instead of existing antibiotics (Azam et al., 2012; Mandal and De, 2015). There are several mechanisms of antimicrobial activity of NPs including contact of NPs and penetration of the cell walls, destroying microbial cells generating reactive oxygen species (ROS) release of ions (mainly Cu ions), and causing oxidative stress (Applerot et al., 2012; Rudramurthy et al., 2016). The release of metallic ions resulted in depolarization of cell membranes, lipid peroxidation, protein oxidation, and DNA damage (Chatterjee et al., 2014; Huang et al., 2020). Rubilar et al. (2013) illustrated that Cu_2ONPs adhere to the cell surface, causing damage to the cell membrane, increasing their permeability, and decreasing the activity of an organism in the Cu_2O solution. Based on oxidative stress, Diaz-Visurrage et al. (2011) and Chang et al. (2012) found that NPs may enter the microbial cells via endocytosis. Thus, the antimicrobial potential of CuNPs is related to induction of ROS (Chang et al., 2012; Hassan et al., 2021b) and the ions released by the nanostructures (Ballo et al., 2016). Also, CuNP has antimicrobial potential without causing cytotoxicity (Rajasekaran and Santra, 2015) and prevents the loss of nutrients in the intestine (Højberg et al., 2005). These activities of CuNP are affected by conditions of synthesis such as temperature, aeration, pH, and concentration (Pramanik et al., 2012). Oussou-Azo et al. (2020) showed that nanoforms of copper had significant antifungal activities, with CuNPs offering the most sustainable efficacy and being more effective than its oxidative form (CuO-NPs) (Fig. 5).

5 Mechanism of CuNPs cytotoxicity

Nowadays, there are many challenges related to the potentially toxic effects of nanomaterials. The cytotoxic effects of NPs on cells resulting from destructive changes causes a loss of cell activities. The cytotoxicity of NPs has been detected against bovine mastitis (Jagielski et al., 2018), larvae development, and animal organs (Ostaszewska et al., 2016, 2017). CuNPs can penetrate cells and pass throughout the blood supply to tissues (Moghimi and Hunter, 2001; Gatoo et al., 2014) and lymph vesicles (Manolova et al., 2008). The toxic effects for HepG2 cells increased (3.0%–54.5%) as the doses increased (1–500 μg/mL) (Chung et al., 2017). When the small size of NPs enters the cell cytoplasm, it is well phagocytosed in macrophages leading to the destruction of NPs (Chono et al., 2006). Larger size NPs over 100 nm cannot be phagocytosed, which causes inflammatory and immune response, resulting in damage and destruction of cells (Song et al., 2014; Sadiq et al., 2015; Hedberg et al., 2016), whereas the inhalation of CuNPs caused the initiation of several immunomodulation effects and inflammatory responses in mice (Kim et al., 2011; Zhang et al., 2012; Wang et al., 2017). Moreover, CuNP injected in ovo chicken embryos do no cause immune-stimulatory changes (Scott et al., 2016). Hua et al. (2014) and Wang et al. (2015) reported that, in fish, IL-6 and tumor factors were elevated as the dose of CuNPs increased. In addition, CuNPs induced apoptosis in the intestinal cells through the mitochondrial pathway in *Epinephelus coioides* (Wang et al., 2017). However, the LD50 of CuNPs in mice was

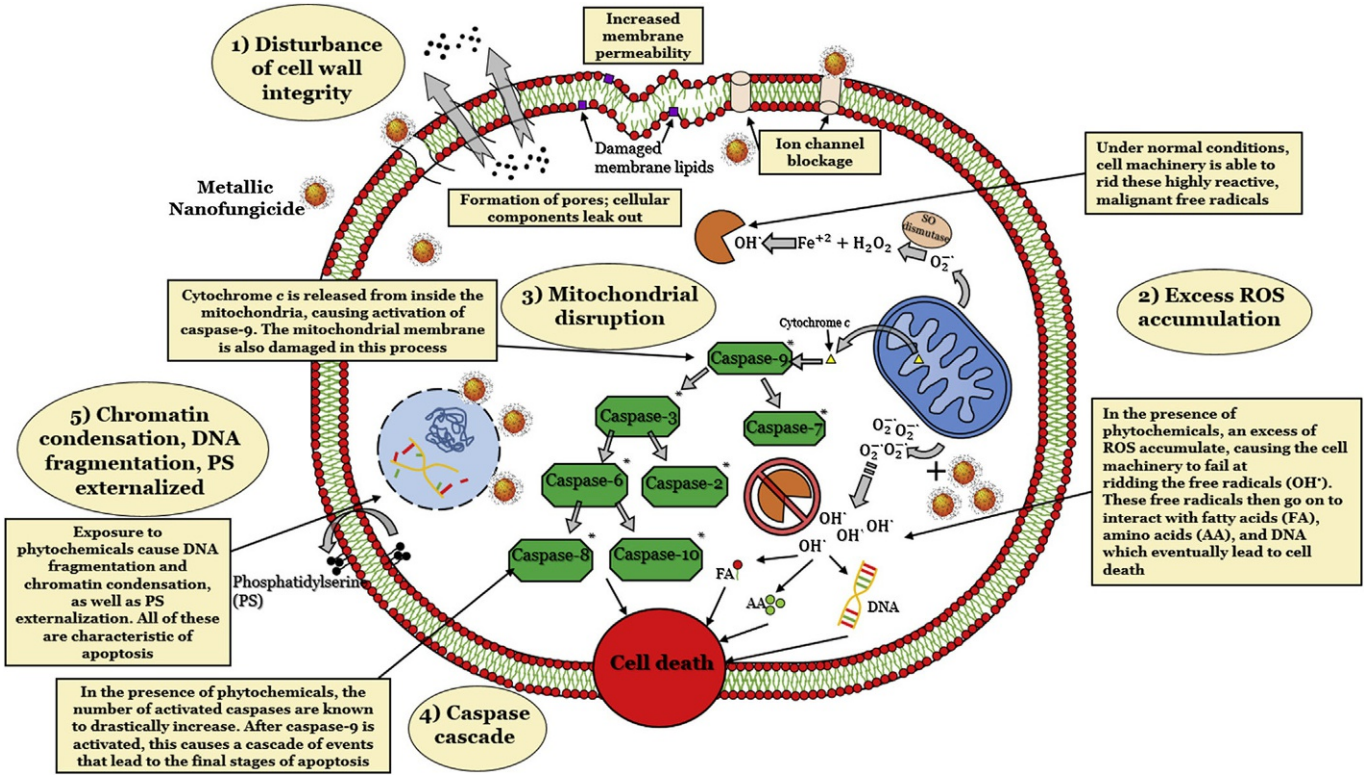

FIG. 5

Modes of antimicrobial activity of CuNPs facilitated by (1) disturbance of cell wall/membrane integrity, (2) generation of ROS, (3) mitochondrial disruption, (4) caspase cascade, and (5) chromatin condensation leading to apoptosis.

Copyright from: Mohamed, E.A., 2020. Green synthesis of copper & copper oxide nanoparticles using the extract of seedless dates. Heliyon 6, e03123. https://doi.org/10.1016/j.heliyon.

413 mg/kg, which resulted in a significant alteration in the function of internal organs such as liver and kidney (Sarkar et al., 2011). Adamcakova-Dodd et al. (2015) detected that the inhalation of copper nanoparticles caused pulmonary inflammation in dams and strong immunomodulatory effects in offspring. On the other hand, the composites of CuNPs in the polymer matrices (hydrogel or polypropylene) showed variable cytotoxicity; hydrogel requires concentrations higher than 0.5% of CuNP (Palza et al., 2017). They added that polypropylene caused negative effects even at higher concentrations (20% of CuNPs). Hejazy et al. (2018) found that nanosized copper yielded several hepatic and respiratory changes in rats (necrotic lesions) (Cholewińska et al., 2018; Tang et al., 2019). Furthermore, CuNPs can result in injuries to the kidney, liver, and spleen of mice, and their apoptosis can cause embryonic damage of red worms (Zhang et al., 2018).

Moreover, the junction of CuNPs can occurred in polymer form at low doses to avoid cell toxicity (Hassan et al., 2020). Although, data related to harmful effects of CuNPs is not sufficient, special attention is required for the known toxicity risk of CuNPs before biomedical applications are applied. Hence, nanotechnology has huge significant progressive advancement in the applications of biotechnology and biomedicine as they increase the safety of health and production, and hence elevation of national income (Fig. 6).

6 Conclusion and future prospective

In the last decades, nanotechnology has enabled the production of new beneficial nanosized materials. Metals NPs, particularly CuNPs, have contributed to the creation

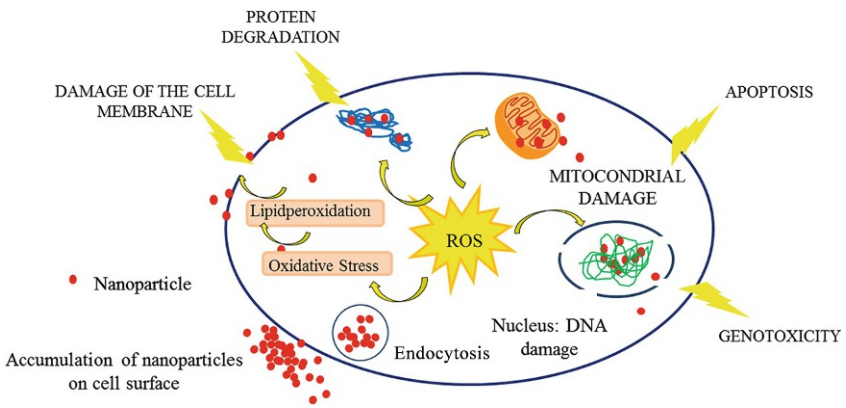

FIG. 6

Schematic mechanism of cytotoxic activity of nanoparticles (NPs).

Copyright from: Romero, C.M., Alvarez, A., Martínez, M.A., Chaves, S., 2018. Fungal nanotechnology: a new approach toward efficient biotechnology application. In: Prasad R., Kumar V., Kumar M., Wang S. (Eds.), Fungal Nanobionics: Principles and Applications. Springer, Singapore.

of significant antimicrobial agents, mycotoxins degradation, anticancer agents and therapy, and drug delivery. Other uses include the diagnosis of diseases, food and feed supplements, and preservation and packing of food. Several studies found that the green biosynthesis of CuNPs is a chemical pollution-free, eco-friendly, and environmentally benign approach in comparison to other methods of synthesis. There is a correlation between Cu-based nanostructure, electrical and chemical properties, and their microbial toxicity. The supplementation of animal feed with CuNPs have significant use for their health and production, while it has a significant effect on antimicrobial food packaging and preservation against food-borne pathogens. The actions of CuNPs include disrupted cell membranes, changes in cytoplasmic contents, destruction of the organelle, and cell damage. Meanwhile, the production of ROS as a result of NP stress over cells end by cell necrosis and hence help in tumors therapy. Data related to harmful effects of CuNPs is not sufficient, and special attention is required for the known toxicity risk of CuNPs before applying in human and animal sciences. Soon, there will be progressive advances in nanobiomedical science and availability of its application in improving human and animal health.

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References

Abd-Elsalam, K.A., Al-Dhabaan, F.A., Alghuthaymi, M., Njobeh, P.B., Almoammar, H., 2019. Nanobiofungicides: present concept and future perspectives in fungal control. Nano-Biopesticides Today and Future Perspectives. Elsevier, pp. 315–351.

Abd-Elsalam, K.A., Alghuthaymi, M.A., Shami, A., Rubina, M.S., Abramchuk, S.S., Shtykova, E.V., Vasil'kov, A.Y., 2020. Copper-chitosan nanocomposite hydrogels against aflatoxigenic *Aspergillus flavus* from dairy cattle feed. J. Fungi 6, 112.

Adamcakova-Dodd, A., Monick, M.M., Powers, L.S., 2015. Effects of prenatal inhalation exposure to copper nanoparticles on murine dams and offspring. Part. Fibre Toxicol. 12, 30.

Ahmed, S., Saifullah, M., Ahmad, B., Swami, L., Ikram, S., 2019. Green synthesis of silver nanoparticles using *Azadirachta indica* aqueous leaf extract. J. Radiat. Res. Appl. Sci. 9 (1), 1–7.

Akbar, A., Anal, K.A., 2013. Zinc oxide nanoparticles loaded active packaging, a challenge study against *Salmonella typhimurium* and *Staphylococcus aureus* in ready-to-eat poultry meat. Food Cont. 38, 88–95.

Al-Bairuty, G.A., Boyle, D., Henry, T.B., Handy, R.D.M., 2016. Sublethal effects of copper sulphate compared to copper nanoparticles in rainbow trout (*Oncorhynchus mykiss*) at low pH: physiology and metal accumulation. Aquat. Toxicol. 174, 188–198.

Al-Dhabaan, F.A., Shoala, T., Ali, A.A.M., Alaa, M., Abd-Elsalam, K., 2017. Chemically-produced copper, zinc nanoparticles and chitosan–bimetallic nanocomposites and their antifungal activity against three phytopathogenic fungi. Int. J. Agric. Technol. 13 (5), 753–769.

Alghuthaymi, M.A., Abd-Elsalam, K.A., Shami, A., Said-Galive, E., Shtykova, E.V., Naumkin, A.V., 2020. Silver/chitosan nanocomposites: preparation and characterization and their fungicidal activity against dairy cattle toxicosis *Penicillium expansum*. J. Fungi 6, 51.

Al-Hakkani, M.F., 2020. Biogenic copper nanoparticles and their applications: review. SN Appl. Sci. 2, 505.

Alzahrani, E., Ahmed, R.A., 2016. Synthesis of copper nanoparticles with various sizes and shapes: application as a superior non-enzymatic sensor and antibacterial agent. Int. J. Electrochem. Sci. 11, 4712–4723.

Amer, M.W., Awwad, A.M., 2021. Green synthesis of copper nanoparticles by *Citrus limon* fruits extract, characterization and antibacterial activity. Chem. Int. 7 (1), 1–8. https://doi.org/10.5281/zenodo.4017993.

Ancona, A., Sportelli, M.C., Trapani, A., Picca, R.A., Palazzo, C., Bonerba, E., Mezzapesa, F.P., Tantillo, G., Trapani, G., Cioffi, N., 2014. Synthesis and characterization of hybrid copper–chitosan nano–antimicrobials by femtosecond laser–ablation in liquids. Mater. Lett. 136, 397–400.

Applerot, G., Lellouche, J., Lipovsky, A., Nitzan, Y., Lubart, R., Gedanken, A., Banin, E., 2012. Understanding the antibacterial mechanism of CuO nanoparticles: revealing the route of induced oxidative stress. Small 8, 3326–3337.

Arjunan, N., Singaravelu, C.M., Kulanthaivel, J., Kandasamy, J., 2017. A potential photocatalytic, antimicrobial and anticancer activity of chitosan-copper nanocomposite. Int. J. Biol. Macromol. 104, 1774–1782.

Asamoah, R., Yaya, A., Mensah, B., Nbalayim, P., Apalangya, V., Bensah, Y., Damoah, L., Agyei-Tuffour, B., Dodoo-Arhin, D., Annan, E., 2020. Synthesis and characterization of zinc and copper oxide nanoparticles and their antibacteria activity. Materials 7, 100099. https://doi.org/10.1016/j.rinma.100099.

Asghar, M.A., Zahir, E., Shahid, S.M., Khan, M.N., Asghar, M.A., Iqbal, J., Walker, G., 2018. Iron, copper and silver nanoparticles: green synthesis using green and black tea leaves extracts and evaluation of antibacterial, antifungal and aflatoxin B1 adsorption activity. LWT: Food Sci. Technol., 90–98e107.

Ashfaq, M., Talreja, N., Chuahan, D., Srituravanich, W., 2019. Polymeric nanocomposite-based agriculture delivery system: emerging technology for agriculture. In: Genetic Engineering. IntechOpen.

Azam, A., Ahmed, A.S., Oves, M., Khan, M.S., Habib, S.S., Memic, A., 2012. Antimicrobial activity of metal oxide nanoparticles against Gram-positive and Gram-negative bacteria: a comparative study. Int. J. Nanomedicine 7, 6003–6009.

Azizi, M., Ghourchian, H., Yazdian, F., Dashtestani, F., Alizadeh Zeinabad, H., 2017. Cytotoxic effect of albumin coated copper nano-particle on human breast cancer cells of MDA-MB 231. PLoS One 12, e0188639.

Bai, D.P., Lin, X.Y., Huang, Y.F., Zhang, X.F., 2018. Theranostics aspects of various nanoparticles in veterinary medicine. Int. J. Mol. Sci. 19, 3299–3331.

Bajpai, S.K., Bajpai, M., Sharma, L., 2012. Copper nanoparticles loaded alginate-impregnated cotton fabric with antibacterial properties. J. Appl. Polym. Sci. 126, E318–E325.

Ballo, M.K.S., Rtimi, S., Pulgarin, C., Hopf, N., Berthet, A., Kiwi, J., Moreillon, P., Entenza, J.M., Bizzini, A., 2016. *In vitro* and *in vivo* effectiveness of an innovative silver-copper nanoparticle coating of catheters to prevent methicillin-resistant Staphylococcus aureus infection. Antimicrob. Agents Chemother. 60, 5349–5356.

Blosi, M., Albonetti, S., Dondi, M., Martelli, C., Baldi, G., 2011. Microwave-assisted polyol synthesis of Cu nanoparticles. J. Nanopart. Res. 13, 127–138.

Bouson, S., Krittayavathananon, A., Phattharasupakun, N., Siwayaprahm, P., Sawangphruk, M., 2017. Antifungal activity of water-stable copper-containing metal-organic frameworks. R. Soc. Open Sci. 4 (10), 170654.

Boyles, M.S.P., Ranninger, C., Reischl, R., Rurik, M., Tessadri, R., Kohlbacher, O., Duschl, A., Huber, C.G., 2016. Copper oxide nanoparticle toxicity profiling using untargeted metabolomics. Part. Fibre Toxicol. 13, 49.

Brunel, F., El Gueddari, N.E., Moerschbacher, B.M., 2013. Complexation of copper (II) with chitosan nanogels: toward control of microbial growth. Carbohydr. Polym. 92 (2), 1348–1356.

Bukhari, S.I., Hamed, M.M., Al-Agamy, M.H., Gazwi, H.S.S., Radwan, H.H., Youssif, A.M., 2021. Biosynthesis of copper oxide nanoparticles using *Streptomyces* MHM38 and its biological applications. J. Nanomater. 2021, 6693302. 16 pages https://doi.org/10.1155/2021/6693302.

Camacho-Flores, B.A., Martínez-Álvarez, O., Arenas-Arrocena, M.C., Garcia-Contreras, R., Argueta-Figueroa, L., de la Fuente-ernández, J., Acosta-Torres, L.S., 2015. Copper: synthesis techniques in nanoscale and powerful application as an antimicrobial agent. J. Nanomater., 1–10.

Canli, E.G., Canli, M., 2017. Effects of aluminum, copper, and titanium nanoparticles on some blood parameters in Wistar rats. Turk. J. Zool. 41, 259–266.

Chakraborty, R., Basu, T., 2017. Metallic copper nanoparticles induce apoptosis in a human skin melanoma A-375 cell line. Nanotechnology 28, 105101.

Chang, Y.N., Zhang, M., Xia, L., Zhang, J., Xing, G., 2012. The toxic effects and mechanisms of CuO and ZnO nanoparticles. Materials 5, 2850–2871.

Chatterjee, A.K., Chakraborty, R., Basu, T., 2014. Mechanism of antibacterial activity of copper nanoparticles. Nanotechnology 25, 135101.

Cheong, Y.K., Arce, M.P., Benito, A., Chen, D., Crisóstomo, N.L., Kerai, L., Rodríguez, V., Valverde, J.L., Vadalia, M., Cerpa-Naranjo, A., Ren, G., 2020. Synergistic antifungal study of PEGylated graphene oxides and copper nanoparticles against *Candida albicans*. Nanomaterials 10 (819), 1–19.

Cholewińska, E., Ognik, K., Fotschki, B., Zduńczyk, Z., Juśkiewicz, J., 2018. Comparison of the effect of dietary copper nanoparticles and one copper (II) salt on the copper biodistribution and gastrointestinal and hepatic morphology and function in a rat model. PLoS One 13 (5), e0197083.

Chono, S., Tanino, T., Seki, T., Morimoto, K., 2006. Influence of particle size on drug delivery to rat alveolar macrophages following pulmonary administration of ciprofloxacin incorporated into liposomes. J. Drug Target. 14, 557–566.

Chung, I., Abdul Rahuman, A., Marimuthu, S., Vishnu Kirthi, A., Anbarasan, K., Padmini, P., Rajakumar, G., 2017. Green synthesis of copper nanoparticles using *Eclipta prostrata* leaves extract and their antioxidant and cytotoxic activities. Exp. Ther. Med. 14, 18–24.

Cioffi, N., Torsi, L., Ditaranto, N., Tantillo, G., Ghibelli, L., Sabbatini, L., Bleve-Zacheo, T., D'Alessio, M., Zambonin, P.G., Traversa, E., 2005. Copper nanoparticle/polymer composites with antifungal and bacteriostatic properties. Chem. Mater. 17 (21), 5255–5262.

Civardi, C., Schubert, M., Fey, A., Wick, P., Schwarze, F.W., 2015. Micronized comparative effects of nano, mineral and organic selenium on growth performance, immunity responses and total antioxidant activity in broiler chickens. Int. J. Biol. Pharm. Allied Sci. 4, 583–595.

De Silva, R.T., Pasbakhsh, P., Lee, S.M., Kit, A.Y., 2015. ZnO deposited/ encapsulated halloysite–poly (lactic acid) nanocomposites for high-performance packaging films with improved mechanical and antimicrobial properties. Appl. Clay Sci. 111, 10–20.

DeAlba-Montero, I., Guajardo-Pacheco, J., Morales-Sánchez, E., Araujo-Martínez, R., Loredo-Becerra, G.M., Martínez-Castañón, G.A., Ruiz, F., Compeán Jasso, M.E., 2017. Antimicrobial properties of copper nanoparticles and amino acid chelated copper nanoparticles produced by using a soya extract. Bioinorg. Chem. Appl. 2017. https://doi.org/10.1155/2017/1064918, 1064918.

De-Azeredo, H.M, 2013. Antimicrobial nanostructures in food packaging. Trends Food Sci. Technol. 30 (1), 56–69.

Diaz-Visurrage, J., Gutierrez, C., Plessing, C., Garcia, A., 2011. Metal Nanostructures as Antimicrobial Agents. vol. 257 Formatex, Badajoz, Spain, pp. 210–218.

Eastman, J.A., Choi, S., Li, S., Yu, W., Thompson, L., 2001. Anomalously increased effective thermal conductivities of ethylene glycol-based nanofluids containing copper nanoparticles. Appl. Phys. Lett. 78, 718–720.

El Basuini, M.F., El-Hais, A.M., Dawood, M.A.O., Abou-Zeid, A.E., EL-Damrawy, S.Z., Khalafalla, M.M.E., Dossou, S., 2016. Effect of different levels of dietary copper nanoparticles and copper sulphate on growth performance, blood biochemical profiles, antioxidant status and immune response of red sea bream (*Pagrus major*). Aquaculture 455, 32–40.

El Basuini, M.F., El-Hais, A.M., Dawood, M.A.O., Abou-Zeid, A.E.-S., EL-Damrawy, S.Z., Khalafalla, M.M.E.-S., Koshio, S., Ishikawa, M., Dossou, S., 2017. Effects of dietary copper nanoparticles and vitamin C supplementations on growth performance, immune response and stress resistance of red sea bream. *Pagrus major*. Aquac. Nutr., 1–12.

El-Kassas, S., Abdo, S.E., El-Naggar, K., Abdo, W., Kirrella, A.A., Nashar, T.O., 2018. Ameliorative effect of dietary supplementation of copper oxide nanoparticles on inflammatory and immune responses in commercial broiler under normal and heat-stress housing conditions. J. Therm. Biol. 78, 235–246.

El-Nour, K.M.A., Eftaiha, A.A., Al-Warthan, A., Ammar, R.A., 2010. Synthesis and applications of silver nanoparticles. Arab. J. Chem. 3 (3), 135–140.

Essa, A.M.M., Khallaf, M.K., 2016. Antimicrobial potential of consolidation polymers loaded with biological copper nanoparticles. BMC Microbiol. 16, 144.

Esteban-Cubillo, A., Pecharromán, C., Aguilar, E., Santarén, J., Moya, J.S., 2006. Antibacterial activity of copper monodispersed nano-particles into sepiolite. J. Mater. Sci. 41, 5208–5212.

Fadl, S.E., El-Shenawy, A.M., Gad, D.M., El Diasty, E.M., El-Sheshtawy, H.S., Abdo, W.S., 2020. Trial for reduction of Ochratoxin A residues in fish feed by using nanoparticles of hydrated sodium aluminum silicates (NPsHSCAS) and copper oxide. Toxicon 184, 1–9.

Gaballah, S.T., Khalil, A.M., Rabie, S.T., 2019. Thiazole derivatives-functionalized polyvinyl chloride nanocomposites with photostability and antimicrobial properties. J. Vinyl Addit. Technol. 25 (1), E137–E146.

Galletti, A.M.R., Antonetti, C., Marracci, M., Piccinelli, F., Tellini, B., 2013. Novel microwave-synthesis of Cu nanoparticles in the absence of any stabilizing agent and their antibacterial and antistatic applications. Appl. Surf. Sci. 280, 610–618.

Gatoo, M.A., Naseem, S., Arfat, M.Y., Mahmood Dar, A., Qasim, K., Zubair, S., 2014. Physicochemical properties of nanomaterials: implication in associated toxic manifestations. Biomed. Res. Int., 1–8.

Ghasemian, E., Naghoni, A., Tabaraie, B., Tabaraie, T., 2012. In vitro susceptibility of filamentous fungi to copper nanoparticles assessed by rapid XTT colorimetry and agar dilution method. J. Mycol. Med. 22, 322–328.

Gong, P., Li, H., He, X., Wang, K., Hu, J., Zhang, S., Yang, X., 2007. Preparation and antibacterial activity of Fe_3O_4@Ag nanoparticles. Nanotechnology 18 (28), 1000–1010.

Gonzales-Eguia, A., Fu, C., Lu, F., Lien, T., 2009. Effects of nanocopper on copper availability and nutrients digestibility, growth performance and serum traits of piglets. Livest. Sci. 126, 122–129.

Gopinath, M., Subbaiya, R., Selvam, M.M., Suresh, D., 2014. Synthesis of copper nanoparticles from *Nerium oleander* leaf aqueous extract and its antibacterial activity. Int. J. Curr. Microbiol. App. Sci. 3 (9), 814–818.

Guduru, R.K., Murty, K.L., Youssef, K.M., Scattergood, R.O., Koch, C.C., 2007. Mechanical behavior of nanocrystalline copper. Mater. Sci. Eng. A 463, 14–21.

Harne, S., Sharma, A., Dhaygude, M., Joglekar, S., Kodam, K., Hudlikar, M., 2012. Novel route for rapid biosynthesis of copper nanoparticles using aqueous extract of *Calotropis procera* L. Latex and their cytotoxicity on tumor cells. Colloids Surf. B: Biointerfaces 95, 284–288.

Hassan, A.A., Sayed El-Ahl, R.H., Oraby, N.H., El Hamaky, A.M.A., 2019. Metal nanoparticles for management of mycotoxigenic fungi and mycotoxicosis diseases of animals and poultry. In: Nanomycotoxicology. Elsevier Academic Press, pp. 251–263 (Chapter 11).

Hassan, A.A., Mansour, M.K., El Hamaky, A.M., Sayed El-Ahl, R.M., Oraby, N.H., 2020. Multifunctional hybrid nanomaterials for sustainable agrifood and ecosystems. In: Nanomaterials and Nanocomposite Application in Veterinary Medicine. Elsevier Academic Press, pp. 251–263.

Hassan, A.A., Mansour, M.K., El Hamaky, A.M., Sayed El-Ahl, R.M., Oraby, N.H., 2021a. Effect of hybrid nanomaterial of copper-chitosan against aflatoxigenic fungi in animal and poultry feeds. (in press).

Hassan, A.A., Mansour, M.K., Sayed El Ahl, R.M., Oraby, N.H., 2021b. Availability of use copper-chitosan Nanocomposite in control the carcinogenic effects induced by aflatoxin B_1 and ochratoxin A in chickens. (in press).

Hassanien, R., Husein, D.Z., Al-Hakkani, M.F., 2018. Biosynthesis of copper nanoparticles using aqueous *Tilia* extract: antimicrobial and anticancer activities. Heliyon 4, e01077.

Hedberg, J., Karlsson, H.L., Hedberg, Y., Blomberg, E., Odnevall, W.I., 2016. The importance of extracellular speciation and corrosion of copper nanoparticles on lung cell membrane integrity. Colloids Surf. B Biointerfaces 141, 291–300.

Hejazy, M., Koohi, M.K., Bassiri Mohamad Pour, A., Najafi, D., 2018. Toxicity of manufactured copper nanoparticles—a review. Nanomed. Res. J. 3 (1), 1–9.

Hemmati, S., Ahmeda, A., Salehabadi, Y., Zangeneh, A., Zangeneh, M.M., 2020. Synthesis, characterization, and evaluation of cytotoxicity, antioxidant, antifungal, antibacterial, and cutaneous wound healing effects of copper nanoparticles using the aqueous extract of strawberry fruit and L-ascorbic acid. Polyhedron 04 (180). https://doi.org/10.1016/j.poly.2020.114425, 114425.

Hill, E.K., Li, J., 2017. Review: current and future prospects for nanotechnology in animal production. J. Anim. Sci. Biotechnol., 2–13.

Hoffmann, T., Amaral Peters, D., Angioletti, B., Bertoli, S., Peres Vieira, L., Ratto Reiter, M.G., Krebs De Souza, C., 2019. Potentials nanocomposites in food packaging. Chem. Eng. Trans. 75, 253–258. https://doi.org/10.3303/CET1975043.

Højberg, O., Canibe, N., Poulsen, H.D., Hedemann, M.S., Jensen, B.B., 2005. Influence of dietary zinc oxide and copper sulfate on the gastrointestinal ecosystem in newly weaned piglets. Appl. Environ. Microbiol. 71 (5), 2267–2277.

Horky, P., Skalickova, S., Baholet, D., Skladanka, J., 2018. Nanoparticles as a solution for eliminating the risk of mycotoxins. Nanomaterials 8, 727.

Hsiao, M.T., Chen, S.F., Shieh, D.B., Yeh, C.S., 2006. One-pot synthesis of hollow Au_3Cu_1 spherical-like and biomineral botallackite $Cu_2(OH)_3C_1$ flower-like architectures exhibiting antimicrobial activity. J. Phys. Chem. B 110, 205–210.

Hua, J., Vijver, M.G., Ahmad, F., Richardson, M.K., Peijnenburg, W.J., 2014. Toxicity of different-sized copper nano- and submicron particles and their shed copper ions to zebrafish embryos. Environ. Toxicol. Chem. 33, 1774–1782.

Huang, Z., Cui, F., Kang, H., Chen, J., Zhang, X., Xia, C., 2008. Highly dispersed silica-supported copper nanoparticles prepared by precipitation – gel method: a simple but efficient and stable catalyst for glycerol hydrogenolysis. Chem. Mater. 20, 5090–5099.

Huang, W., Yan, M., Duan, H., Bi, Y., Cheng, X., Yu, H., 2020. Synergistic antifungal activity of green synthesized silver nanoparticles and epoxiconazole against *Setosphaeria turcica*. J. Nanomater., 9535432. 7 pages.

Jafarizadeh, H., Sayyar, Z., Anarjan, N., Berenjian, A., 2019. Nanobiotechnology in food packaging. In: Nanobiotechnology in Food; Concepts, Application and Perspectives, pp. 69–79, https://doi.org/10.1007/978-3-030-05846-3-50.

Jagielski, T., Bakuła, Z., Pleń, M., Kamiński, M., Nowakowska, J., Bielecki, J., Wolska, K., Grudniak, A.M., 2018. The activity of silver nanoparticles against microalgae of the *Prototheca* genus. Nanomedicine 13, 1025–1036.

Jampílek, J., Králová, K., 2020. Nanocomposites: synergistic nanotools for management of mycotoxigenic fungi. In: Nanomycotoxicology. Academic Press, Amsterdam, Netherlands, pp. 349–383.

Jayandran, M., Haneefa, M.M., Balasubramanian, V., 2015. Green synthesis of copper nanoparticles using natural reducer and stabilizer and an evaluation of antimicrobial activity. J. Chem. Pharm. Res. 7, 251–259.

Jayarambabu, N., Akshaykranth, A., Venkatappa Rao, T., Venkateswara Rao, K., Rakesh Kumar, R., 2020. Green synthesis of Cu nanoparticles using *Curcuma longa* extract and their application in antimicrobial activity. Mater. Lett. 259, 126813.

Jeronsia, J.E., Raj, D.V., Joseph, L.A., Rubini, K., Das, S.J., 2016. In vitro antibacterial and anticancer activity of copper oxide nanostructures in human breast cancer Michigan Cancer Foundation-7 cells. J. Med. Sci. 36 (4), 145.

Jose, G.P., Santra, S., Mandal, S.K., Sengupta, T.K., 2011. Singlet oxygen-mediated DNA degradation by copper nanoparticles: potential towards cytotoxic effect on cancer cells. J. Nanobiotechnol. 9, 9.

Joshua, P.P., Valli, C., Balakrishnan, V., 2016. Effect of in ovo supplementation of nano forms of zinc, copper, and selenium on post-hatch performance of broiler chicken. Vet. World 9, 287–294.

Kalińska, A., Jaworski, S., Wierzbicki, M., Gołe˛biewski, M., 2019. Silver and copper nanoparticles—an alternative in future mastitis treatment and prevention. Int. J. Mol. Sci. 20, 1672.

Kalpana, V., Chakraborthy, P., Palanichamy, V., Rajeswari, V.D., 2016. Synthesis and characterization of copper nanoparticles using *Tridax procumbens* and its application in degradation of Bismarck brown. Int. J. ChemTech Res. 10, 17.

Kang, S., Pinault, M., Pfefferle, L.D., Elimelech, M., 2007. Single-walled carbon nanotubes exhibit strong antimicrobial activity. Langmuir 23 (17), 8670–8673.

Kasana, R.C., Panwar, N.R., Kaul, R.K., Kumar, P., 2016. Copper nanoparticles in agriculture: biological synthesis and antimicrobial activity. In: Ranjan, S., Dasgupta, N., Lichtfouse, E. (Eds.), Nanoscience in Food and Agriculture 3. Springer, Cham, pp. 129–143.

Katerine, I., Arreche, A.R., Sambeth, E.J., Bellotti, N., Vega-Baudrit, J.R., Redondo-Gomez, C., Vazquez, P.G., 2018. Antifungal activity of cotton fabrics finished modified silica- silver- carbon-based hybrid nanoparticles. Text. Res. J., 0040517518755792.

Kaur, P., Thakur, R., Barnela, M., Chopra, M., Manuja, A., Chaudhury, A., 2015. Synthesis, characterization and *in vitro* evaluation of cytotoxicity and antimicrobial activity of chitosan-metal nanocomposites. J. Chem. Technol. Biotechnol. 90 (5), 867–873.

Kayalvizhi, S., Sengottaiyan, A., Selvankumar, T., Senthilkumar, B., Sudhakar, C., Selvam, K., 2020. Eco-friendly cost-effective approach for synthesis of copper oxide nanoparticles for enhanced photocatalytic performance. Optik (Stuttg) 202, 163507.

Khaldari, I., Naghavi, M.R., Motamedi, E., 2021. Synthesis of green and pure copper oxide nanoparticles using two plant resources via solidstate route and their phytotoxicity assessment. RSC Adv. 2021 (11), 3346.

Khani, R., Roostaei, B., Bagherzade, G., Moudi, M., 2018. Green synthesis of copper nanoparticles by fruit extract of *Ziziphus spinachristi* (L.) Willd. Application for adsorption of triphenylmethane dye and antibacterial assay. J. Mol. Liq. 255, 541–549.

Kim, J.S., Adamcakova-Dodd, A., O'Shaughnessy, P.T., Grassian, V.H., Thorne, P.S., 2011. Effects of copper nanoparticle exposure on host defense in a murine pulmonary infection model. Part. Fibre Toxicol. 8, 29.

Kruk, T., Szczepanowicz, K., Stefanska, J., Socha, R.P., Warszyński, P., 2015. Synthesis and antimicrobial activity of monodisperse copper nanoparticles. Colloids Surf. B Biointerfaces 128, 17–22.

Kumar, A., Singh, P.P., Prakash, B., 2020a. Unravelling the antifungal and anti-aflatoxin B1 mechanism of chitosan nanocomposite incorporated with *Foeniculum vulgare* essential oil. Carbohydr. Polym. 236, 116050.

Kumar, S., Mukherjee, A., Dutta, J., 2020b. Chitosan based nanocomposite films and coatings: emerging antimicrobial food packaging alternatives. Trends Food Sci. Technol. 97, 196–209.

Laha, D., Pramanik, A., Chattopadhyay, S., Dash, S.K., Roy, S., Pramanik, P., Karmakar, P., 2015. Folic acid modified copper oxide nanoparticles for targeted delivery in *in vitro* and *in vivo* systems. RSC Adv. 5, 68169.

Lee, W., Kang, S.H., Kim, J.Y., Kolekar, G.B., Sung, Y.E., Han, S.H., 2009. TiO_2 nanotubes with a ZnO thin energy barrier for improved current efficiency of CdSe quantum-dot-sensitized solar cells. Nanotechnology 20, 335706.

Lee, H., Lee, G., Jang, N., Yun, J., Song, J., Kim, B., 2011. Biological synthesis of copper nanoparticles using plant extract. Nanotechology 1 (1), 371–374.

Lee, H.J., Song, J.Y., Kim, B.S., 2013. Biological synthesis of copper nano-particles using *Magnolia kobus* leaf extract and their antibacterial activity. J. Chem. Technol. Biotechnol. 88 (11), 1971–1977.

Li, X., Xing, Y., Jiang, Y., Ding, Y., Li, W., 2009. Antimicrobial activities of ZnO powder-coated PVC film to inactivate food pathogens. Int. J. Food Sci. Technol. 44, 2161–2168.

Li, X.D., Gao, J.Y., Yang, Y., 2013. Nanomaterials in the application of tumor vaccines: advantages and disadvantages. Onco Targets. Ther. 6, 629–634.

Lien, T.F., 2009. Nanosize of copper sulfate and effects on growth, copper availability, and excretion of pigs. Int. J. Livest. Res. 1, 30–36.

Liu, Z., Bando, Y., 2003. A novel method for preparing copper nanorods and nanowires. Adv. Mater. 15, 303–305.

Longano, D., Ditaranto, N., Cioffi, N., Di Niso, F., Sibillano, T., Ancona, A., Conte, A., Del Nobile, M.A., Sabbatini, L., Torsi, L., 2012. Analytical characterization of laser-generated copper nanoparticles for antibacterial composite food packaging. Anal. Bioanal. Chem. 403, 1179–1186.

Luning, P.A., Bango, L., Kussaga, J., Rovira, J., Marcelis, W.J., 2008. Comprehensive analysis and differentiated assessment of food safety control systems: a diagnostic instrument. Trends Food Sci. Technol. 19, 522–534.

Mahler, G.J., Esch, M.B., Tako, E., Southard, T.L., Archer, S.D., Glahn, R.P., Shuler, M.L., 2012. Oral exposure to polystyrene nanoparticles affects iron absorption. Nat. Nanotechnol. 7, 264–271.

Mandal, S., De, S., 2015. Catalytic and fluorescence studies with copper nanoparticles synthesized in polysorbates of varying hydrophobicity. Colloids Surf. 467, 233–250.

Manolova, V., Flace, A., Bauer, M., Schwarz, K., Saudan, P., Bachmann, M.F., 2008. Nanoparticles target distinct dendritic cell populations according to their size. Eur. J. Immunol. 38, 1404–1413.

Marambio-Jones, C., Hoek, E.M.V., 2010. A review of the antibacterial effects of silver nanomaterials and potential implications for human health and the environment. J. Nanopart. Res. 12, 1531–1551.

Medvedeva, O.I., Kambulova, S.S., Ulakhovich, N.A., Vorobev, V.V., Evtyugin, V.G., Khaldeeva, E.V., Kutyreva, M.P., 2017. Formation of copper nanoparticles with hyperbranched polyesterpolyols as a template. Russ. J. Gen. Chem. 87 (9), 1985–1994.

Meena, N.S., Sahni, Y.P., Thakur, D., Singh, R.P., 2018. Applications of nanotechnology in veterinary therapeutics. J. Entomol. Zool. Stud. 6 (2), 167–175.

Minglei, S., Zheng, L., Xiaoye, G., Xiu'an, Z., 2013. Copper silicate nano-particles: effects of intestinal microflora, nitrogen metabolism and ammonia emission from excreta of yellow-feathered broilers. Nutr. Feed Sci. Technol. 25, 1843–1850.

Miroshnikov, S.A., Yausheva, E.V., Sizova, E.A., Miroshnikova, E.P., Levahin, V.I., 2015. Comparative assessment of effect of copper nano- and microparticles in chicken. Orient. J. Chem. 31 (4), 2327–2336.

Mishra, B., Patel, B.B., Tiwari, S., 2009. Colloidal nanocarriers: a review on formulation technology, types and applications toward targeted drug delivery. Nanomedicine 6, 9–24.

Moghimi, S.M., Hunter, A.C., 2001. Capture of stealth nanoparticles by the body's defences. Crit. Rev. Ther. Drug Carrier Syst. 18, 527–550.

Mohamed, E.A., 2020. Green synthesis of copper & copper oxide nanoparticles using the extract of seedless dates. Heliyon 6, e03123.

Mohsen, R.M., Morsi, S.M.M., Abu-Ayana, Y.M., Ghoneim, A.M., 2018. Synthesis of conductive Cu-core/Ag-subshell/polyaniline-shell nanocomposites and their antimicrobial activity. Egypt. J. Chem. 61 (5), 939–952.

Monda, E., Masanga, J., Alakonya, A., 2020. Variation in occurrence and aflatoxigenicity of *Aspergillus flavus* from two climatically varied regions in Kenya. Toxins 12, 34.

Morsi, R.E., Alsabagh, A.M., Nasr, S.A., Zaki, M.M., 2017. Multifunctional nanocomposites of chitosan, silver nanoparticles, copper nanoparticles and carbon nanotubes for water treatment: antimicrobial characteristics. Int. J. Biol. Macromol. 97, 264–269.

Mroczek-Sosnowska, N., Sawosz, E., Vadalasetty, K.P., Łukasiewicz, M., Niemiec, J., Wierzbicki, M., Chwalibog, A., 2015a. Nanoparticles of copper stimulate angiogenesis at systemic and molecular level. Int. J. Mol. Sci. 16 (3), 4838–4849.

Mroczek-Sosnowska, N., Łukasiewicz, M., Adamek, D., Kamaszewski, M., Niemiec, J., Wnuk-Gnich, A., Scott, A., Chwalibog, A., Sawosz, E., 2017. Effect of copper nanoparticles administered in ovo on the activity of proliferating cells and on the resistance of femoral bones in broiler chickens. Arch. Anim. Nutr. 71 (4), 327–332.

Mroczek-Sosnowska, N., Łukasiewicz, M., Wnuk, A., Sawosz, E., Niemiec, J., 2014. Effect of copper nanoparticles and copper sulfate administered *in ovo* on copper content in breast muscle, liver and spleen of broiler chickens. Ann. Warsaw Univ. Life Sci. SGGW Anim. Sci. 53, 135–142.

Mroczek-Sosnowska, N., Łukasiewicz, M., Wnuk, A., Sawosz, E., Niemiec, J., Skot, A., Jaworski, S., Chwalibog, A., 2015b. *In ovo* administration of copper nanoparticles and copper sulfate positively influences chicken performance: effect of Cu on chicken performance. J. Sci. Food Agric. 96, 3058–3062.

Muñoz-Escobar, A., Ruíz-Baltazar, Á.D.J., Reyes-López, S.Y., 2019. Novel route of synthesis of PCL-CuONPs composites with antimicrobial properties. Dose-Response 17 (3), 1–11.

Muralisankar, T., Saravana Bhavan, P., Radhakrishnan, S., Seenivasan, C., Srinivasan, V., 2016. The effect of copper nanoparticles supplementation on freshwater prawn *Macrobrachium rosenbergii* postlarvae. J. Trace Elem. Med. Biol. 34, 39–49.

Murthy, H.C.A., Abebe, B., Zeleke, T.D., 2018. Material science research India a review on green synthesis and applications of Cu and CuO nanoparticles. Mater. Sci. Res. India 15, 2018.

Nagajyothi, P.C., Muthuraman, P., Sreekanth, T.V.M., Kim, D.H., Jaesool, S., 2016. Green synthesis: *in vitro* anti-cancer activity of copper oxide nanoparticles against human cervical carcinoma cells. Arab. J. Chem. 10, 215–225.

Nasrollahzadeh, M., Sajadi, S.M., 2015. Green synthesis of copper nanoparticles using *Ginkgo biloba* L. leaf extract and their catalytic activity for the Huisgen [3 + 2] cycloaddition of azides and alkynes at room temperature. J. Colloid Interface Sci. 457, 141–147.

Niharika, N., Vijay, D., 2018. Synthesis of copper nanoparticles and their catalytic activity in oxidation of threonine. Res. J. Recent Sci. 7 (3), 14–21.

Omran, B.A., 2020. Prokaryotic microbial synthesis of nanomaterials (the world of unseen). In: Nanobiotechnology: A Multidisciplinary Field of Science. Springer, pp. 37–79.

Ostaszewska, T., Chojnacki, M., Kamaszewski, M., Sawosz-Chwalibóg, E., 2016. Histopathological effects of silver and copper nanoparticles on the epidermis, gills, and liver of Siberian sturgeon. Environ. Sci. Pollut. Res. 23, 1621–1633.

Ostaszewska, T., Śliwiński, J., Kamaszewski, M., Sysa, P., Chojnacki, M., 2017. Cytotoxicity of silver and copper nanoparticles on rainbow trout (*Oncorhynchus mykiss*) hepatocytes. Environ. Sci. Pollut. Res. 25, 908–915.

Oussou-Azo, A.F., Nakama, T., Nakamura, M., Futagami, T., Catherine, M., Vestergaard, M., 2020. Antifungal potential of nanostructured crystalline copper and its oxide forms. Nanomaterials 10, 1003.

Palza, H., Galarce, N., Bejarano, J., Beltran, M., Caviedes, P., 2017. Effect of copper nanoparticles on the cell viability of polymer composites. Int. J. Polym. Mater. Polym. Biomater. 66, 462–468.

Palza, H., Nuñez, M., Bastías, R., Delgado, K., 2018. In situ antimicrobial behavior of materials with copper-based additives in a hospital environment. Int. J. Antimicrob. Agents 51 (6), 912–917.

Pandey, N., Dhiman, S., Srivastava, T., Majumder, S., 2016. Transition metal oxide nanoparticles are effective in inhibiting lung cancer cell survival in the hypoxic tumor microenvironment. Chem. Biol. Interact. 254, 221–230.

Pavani, K.V., Srujana, N., Preethi, G., Swati, T., 2013. Synthesis of copper nanoparticles by *Aspergillus* species. Lett. Appl. NanoBioSci. 2 (2), 110–113.

Payvastegan, S., Farhoomand, P., Delfani, N., 2013. Growth performance, organ weights and, blood parameters of broilers fed diets containing graded levels of dietary canola meal and supplemental copper. J. Poult. Sci. 50, 354–363.

Peters, R.J.B., Bouwmeester, H., Gottardo, S., Amenta, V., Arena, M., Brandhoff, P., Marvin, H.J.P., Mech, A., Moniz, F.B., Pesudo, L.Q., Rauscher, H., Schoonjans, R., Undas, A.K., Vettori, M.V., Weigel, S., Aschberger, K., 2016. Nanomaterials for products and application in agriculture, feed and food. Trends Food Sci. Technol. 54, 155–164.

Phiwdang, K., Phensaijai, M., Pecharapa, W., 2013. Study of antifungal activities of CuO/ZnO nanocomposites synthesized by co-precipitation method. Adv. Mat. Sci. Technol. 802, 89–93.

Pramanik, A., Laha, D., Bhattacharya, D., Pramanik, P., Karmakar, P., 2012. A novel study of antibacterial activity of copper iodide nanoparticle mediated by DNA and membrane damage. Colloids Surf. B Biointerfaces 96, 50–55.

Prokhorov, E., España-Sánchez, B.L., Luna-Barcenas, G., Padilla-Vaca, F., Cruz-Soto, M.E., Vázquez-Lepe, M.O., Kovalenko, Y., Elizalde-Peña, E.A., 2019. Chitosan/copper nanocomposites: correlation between electrical and antibacterial properties. Colloids Surf. B Biointerfaces 180, 186–192.

Rajasekaran, P., Santra, S., 2015. Hydrothermally treated chitosan hydrogel loaded with copper and zinc particles as a potential micronutrient-based antimicrobial feed additive. Front. Vet. Sci. 2, 62.

Rajendran, D., Thulasi, A., Jash, S., Selvaraju, S., Rao, S.B., 2013. Synthesis and application of nano minerals in livestock industry. In: Sampath, K.T., Ghosh, J., Bhatta, R. (Eds.), Animal Nutrition and Reproductive Physiology (Recent Concepts). Satish Ser. Publ. House, Delhi, pp. 517–530.

Ramanathan, R., Bhargavan, S.K., Bansal, V., 2011. Biological synthesis of copper/copper oxide nanoparticles. In: *Chemeca*: Engineering a Better World. Sydney Hilton Hotel, NSW, Australia, pp. 18–21. http://www.conference.net.au.

Ramyadevi, J., Jeyasubramanian, K., Marikani, A., Rajakumar, G., Rahuman, A.A., 2012. Synthesis and antimicrobial activity of copper nanoparticles. Mater. Lett. 71, 114–116.

Ranjitham, A.M., Ranjani, G.S., Caroling, G., 2015. Biosynthesis, characterization, antimicrobial activity of copper nanoparticles using fresh aqueous *Ananas comosus* L. (pineapple) extract. Int. J. Pharm. Technol. Res. 8, 750–769.

Refaie, A.M., Ghazal, M.N., Easa, F.M., Barakat, S.A., Ge, Y., Wh, E., 2015. Nano-copper as a new growth promoter in the diet of growing New Zealand white rabbits. Egypt. J. Rabbit Sci. 25, 39–57.

Rubilar, O., Rai, M., Tortella, G., Cristina, M., Amedea, D., Seabra, B., Durán, N., 2013. Review: biogenic nanoparticles: copper, copper oxides, copper sulphides, complex copper nanostructures and their applications. Biotechnol. Lett. 35, 1365–1375.

Rubina, M.S., Vasil'kov, A.Y., Naumkin, A.V., Shtykova, E.V., Abramchuk, S.S., Alghuthaymi, M.A., Abd-Elsalam, K.A., 2017. Synthesis and characterization of chitosan-copper nanocomposites and their fungicidal activity against two sclerotia–forming plant pathogenic fungi. J. Nanostruct. Chem. 7 (3), 249–258.

Rudramurthy, G., Swamy, M., Sinniah, U., Ghasemzadeh, A., 2016. Nanoparticles: alternatives against drug-resistant pathogenic microbes. Molecules 21, 836.

Sadiq, R., Khan, Q.M., Mobeen, A., Hashmat, A.J., 2015. In vitro toxicological assessment of iron oxide, aluminium oxide and copper nanoparticles in prokaryotic and eukaryotic cell types. Drug Chem. Toxicol. 38, 152–161.

Safaei, M., Taran, M., Imani, M.M., 2019. Preparation, structural characterization, thermal properties and antifungal activity of alginate-CuO bionanocomposite. Mater. Sci. Eng. C 101, 323–329.

Saharan, V., Mehrotra, A., Khatik, R., Rawal, P., Sharma, S.S., Pa, A., 2013. Synthesis of chitosan-based nanoparticles and their *in vitro* evaluation against phytopathogenic fungi. Int. J. Biol. Macromol. 62, 677–683.

Saharan, V., Sharma, G., Yadav, M., Choudhary, M.K., Sharma, S.S., Pal, A., Raliya, R., Biswas, P., 2015. Synthesis and *in vitro* antifungal efficacy of Cu-chitosan nanoparticles against pathogenic fungi of tomato. Int. J. Biol. Macromol. 75, 346–353.

Salem, S.S., Fouda, A., 2021. Green synthesis of metallic nanoparticles and their prospective biotechnological applications: an overview. Biol. Trace Elem. Res. 199, 344–370.
Sankar, R., Maheswari, R., Karthik, S., Shivashangari, K.S., Ravikumar, V., 2014. Anticancer activity of *Ficus religiosa* engineered copper oxide nanoparticles. Mater. Sci. Eng. C 44, 234–239.
Santo, C.E., Quaranta, D., Grass, G., 2012. Antimicrobial metallic copper surfaces kill *Staphylococcus haemolyticus* via membrane damage. Microbiol. Open 1 (1), 46–52.
Santos, K.K.A., Matias, E.F.F., Tintino, S.R., Souza, C.E.S., Braga, M.F.B.M., Guedes, G.M.M., Costa, J.G.M., Menezes, I.R.A., Coutinho, H.D.M., 2013. Enhancement of the antifungal activity of antimicrobial drugs *by Eugenia uniflora* L. J. Med. Food 16 (7), 669–671.
Saranya, R., Ali, M.M., 2017. Synthesis of colloidal copper nano-particles and its cytotoxicity effect on MCF-7 breast cancer cell lines. J. Chem. Pharm. Sci. 974, 1–5.
Sarkar, A., Das, J., Manna, P., 2011. Nano copper induces oxidative stress and apoptosis in kidney via both extrinsic and intrinsic pathways. Toxicology 18, 208–217.
Sasaki, M., Suyama, T., Tanaka, T., Yokoyama, S., 2016. Primordial black hole scenario for the gravitational-wave event GW150914. Phys. Rev. Lett. 117 (6), 061101.
Scott, A., Vadalasetty, K.P., Sawosz, E., Łukasiewicz, M., Vadalasetty, R.K.P., Jaworski, S., Chwalibog, A., 2016. Effect of copper nanoparticles and copper sulphate on metabolic rate and development of broiler embryos. Anim. Feed Sci. Technol. 220, 151–158.
Scott, A., Vadalasetty, K.P., Chwalibog, A., Sawosz, E., 2018. Review copper nanoparticles as an alternative feed additive in poultry diet: a review. Nanotechnol. Rev. 7 (1), 69–93.
Selvan, S.M., Anand, K.V., Govindaraju, K., Tamilselvan, S., Kumar, V.G., Subramanian, K., Sevathapandian Kannan, M., Raja, K., 2018. Green synthesis of copper oxide nanoparticles and mosquito larvicidal activity against dengue, zika and chikungunya causing vector *Aedes aegypti*. IET Nanobiotechnol. 12, 1042–1046.
Shamsudeen, P., Shrivastava, H.P., 2013. Biointeraction of chelated and inorganic copper with aflatoxin on growth performance of broiler chicken. Int. J. Vet. Sci. 2, 106–110.
Sharma, M., Sharma, A., Majumder, S., 2020. Synthesis, microbial susceptibility and anti-cancerous properties of copper oxide nanoparticles-review. Nano Express 1 (2020). https://doi.org/10.1088/2632-959X/ab9241, 012003.
Shen, X., Song, C., Wu, T., 2020. Effects of nano-copper on antioxidant function in copper-deprived Guizhou black goats. Biol. Trace Elem. Res. https://doi.org/10.1007/s12011-020-02342-1.
Shende, S., Ingle, A.P., Gade, A., Rai, M., 2015. Green synthesis of copper nanoparticles by *Citrus medica* Linn. (Idilimbu) juice and its antimicrobial activity. J. Microbiol. Biotechnol. 31, 865–873.
Shobha, G., Moses, V., Anand, S., 2014. Biological synthesis of copper nanoparticles and its impact. Int. J. Pharm. Sci. Invent. 3, 6–28.
Siddiqui, M.A., Alhadlaq, H.A., Ahmad, J., Al-Khedhiary, A.A., Musarrat, J., Ahamed, M., 2013. Copper oxide induced mitochondria-mediated apoptosis in human hepatocarcinoma cells. PLoS One 8, e69534.
Silvestre, C., Duraccio, D., Cimmino, S., 2011. Food packaging based on polymer nanomaterials. Prog. Polym. Sci. 36, 1766–1782.
Singh, T., Shukla, S., Kumar, P., Wahla, V., Bajpai, V.K., 2017. Application of nanotechnology in food science: perception and overview. Front. Microbiol. 8, 1–7.
Sinha, T., Ahmaruzzaman, M., 2015. Biogenic synthesis of Cu nanoparticles and its degradation behavior for methyl red. Mater. Lett. 159, 168–171.

Soares, N., Silva, C.A.S., Santiago-Silva, P., Espitia, P.J.P., Goncalves, M.P.J.C., Lopez, M.J.G., Miltz, J., Cerqueira, M.A., Vicente, A.A., Teixeira, J., 2009. In: dos Reis Coimbra, J.A.T.J.S. (Ed.), Engineering Aspects of Milk and Dairy Products: Active and Intelligent Packaging for Milk and Milk Products. CRC Press, pp. 155–174, https://doi.org/10.1201/9781420090390-c8.

Solairaj, D., Rameshthangam, P., Muthukumaran, P., Wilson, J., 2017. Studies on electrochemical glucose sensing, antimicrobial activity and cytotoxicity of fabricated copper nanoparticle immobilized chitin nanostructure. Int. J. Biol. Macromol. 101, 668–679.

Song, L., Connolly, M., Fernández-Cruz, M.L., Vijver, M.G., Fernández, M., Conde, E., de Snoo, G.R., Peijnenburg, W.J., Navas, J.M., 2014. Species-specific toxicity of copper nanoparticles among mammalian and piscine cell lines. Nanotoxicology 8, 383–393.

Song, C., Gan, S., Shen, X., 2020. Effects of nano-copper poisoning on immune and antioxidant function in the Wumeng semi-fine wool sheep. Biol. Trace Elem. Res. https://doi.org/10.1007/s12011-020-02085-z.

Sri Sindhura, K., Prasad, T.N.V.K.V., Panner Selvam, P., Hussain, O.M., 2014. Synthesis, characterization and evaluation of effect of phytogenic zinc nanoparticles on soil exo-enzymes. Appl. Nanosci. 4, 819–827.

Stankic, S., Suman, S., Haque, F., Vidic, J., 2016. Pure and multi-metal oxide nanoparticles: synthesis, antibacterial and cytotoxic properties. J. Nanobiotechol. 14, 73. https://doi.org/10.1186/s12951-016-0225-6.

Stouwdam, J.W., Janssen, R.A., 2008. Red, green, and blue quantum dot LEDs with solution-processable ZnO nanocrystal electron injection layers. J. Mater. Chem. 18, 1889.

Subbaiya, R., Selvam, M.M., 2015. Green synthesis of copper nanoparticles from *Hibicus rosasinensis* and their antimicrobial, antioxidant activities. J. Chem. Pharm. Res. 6, 1183–1190.

Sudha, V., Murugadoss, G., Thangamuthu, R., 2021. Structural and morphological tuning of Cu-based metal oxide nanoparticles by a facile chemical method and highly electrochemical sensing of sulphite. Sci. Rep. 11, 3413. https://doi.org/10.1038/s41598-021-82741.

Tamilvanan, A., Balamurugan, K., Ponappa, K., Madhan, K.B., 2014. Copper nanoparticles: synthetic strategies, properties and multifunctional application. Int. J. Nanosci. 13, 1430001.

Tang, H., Xu, M., Luo, J., Zhao, L., Ye, G., Shi, F., Cheng, L.V., Chen, H., Wang, Y., Li, Y., 2019. Liver toxicity assessments in rats following sub-chronic oral exposure to copper nanoparticles. Environ. Sci. Eur. 31, 30.

Tantubay, S., Mukhopadhyay, S.K., Kalita, H., Konar, S., Dey, S., Pathak, A., Pramanik, P., 2015. Carboxymethylated chitosan-stabilized copper nanoparticles: a promise to contribute a potent antifungal and antibacterial agent, J. Nanoparticle Res. 17 (6), 243.

Thakare, P.S., Padole, P.R., Bodade, A.B., Chaudhari, G.N., 2018. Microstructural and antifungal properties of silver substituted copper ferrite nanopowder synthesized by sol-gel method, indo am. J. Pharm. Sci. 5 (1), 52–63.

Thakkar, K.N., Mhatre, S.S., Parikh, R.Y., 2010. Biological synthesis of metallic nanoparticles. Nanomed. Nanotechnol. Biol. Med. 6 (2), 257–262.

Thakur, S., Sharma, S., Thakur, S., Rai, R., 2018. Green synthesis of copper nanoparticles using *Asparagus adscendens* Roxb. root and leaf extract and their antimicrobial activities. Int. J. Curr. Microbiol. App. Sci. 7 (4), 683–694.

Thamer, A., Barakat, N.T., 2019. Cytotoxic activity of green synthesis copper oxide nanoparticles using *Cordia myxa* L. aqueous extract on some breast cancer cell lines. J. Phys. Conf. Ser. 1294, 062104.

Urusov, A.E., Petrakova, A.V., Vozniak, M.V., Zherdev, A.V., Dzantiev, B.B., 2014. Rapid immunoenzyme assay of aflatoxin B1 using magnetic nanoparticles. Sensors 13, 21843–21857.

Ustinov, V., Zhukov, A., Kovsh, A., Mikhrin, S., Maleev, N., Volovik, B., Musikhin, Y.G., Shernyakov, Y.M., Kondat'eva, E.Y., Maximov, M., 2000. Long-wavelength quantum dot lasers on GaAs substrates. Nanotechology 11, 397.

Vaid, P., Raizada, P., Saini, A.K., Saini, R.V., 2020. Biogenic silver, gold and copper nanoparticles—a sustainable green chemistry approach for cancer therapy. Sustain. Chem. Pharm. 16. https://doi.org/10.1016/j.scp.2020.100247, 100247.

Valodkar, M., Nagar, P.S., Jadeja, R.N., Thounaojam, M.C., Devkar, R.V., Thakore, S., 2011a. Euphorbiaceae latex induced green synthesis of non-cytotoxic metallic nanoparticle solutions: a rational approach to antimicrobial applications. Colloids Surf. A Physicochem. Eng. Asp. 384, 337–344.

Valodkar, M., Modi, S., Pal, A., Thakore, S., 2011b. Synthesis and antibacterial activity of Cu, Ag and Cu–Ag alloy nanoparticles: a green approach. Mater. Res. Bull. 46, 384–389.

Vanathi, P., Rajiv, P., Sivaraj, R., 2016. Synthesis and characterization of *Eichhornia*-mediated copper oxide nanoparticles and assessing their antifungal activity against plant pathogens. Bull. Mater. Sci. 39 (5), 1165–1170.

Veerapandian, M., Sadhasivam, S., Choi, J., Yun, K., 2012. Glucosamine functionalized copper nanoparticles: preparation, characterization and enhancement of anti-bacterial activity by ultraviolet irradiation. Chem. Eng. J. 209, 558–567.

Viet, P.M., Nguyen, H.T., Cao, T.M., Hieu, L.V., 2016. *Fusarium* antifungal activities of copper nanoparticles synthesized by a chemical reduction method. J. Nanomater., 1957612.

Wang, S., Lawson, R., Ray, P.C., Yu, H., 2011. Toxic effects of gold nanoparticles on *Salmonella typhimurium* bacteria. Toxicol. Ind. Health 27, 547–554.

Wang, L.S., Wang, C.Y., Yang, C.H., Hsieh, C.L., Chen, S.Y., Shen, C.Y., Wang, J.J., Huang, K.S., 2015. Synthesis and antifungal effect of silver nanoparticles-chitosan composite particles. Int. J. Nanomedicine 10, 2685–2696.

Wang, T., Long, X., Chen, X., Liu, Y., Liu, Z., Han, S., Yan, S., 2017. Integrated transcriptome, proteome and physiology analysis of *Epinephelus coioides* after exposure to copper nanoparticles or copper sulfate. Nanotoxicology 11, 236–246.

Wei, Y., Chen, S., Kowalczyk, B., Huda, S., Gray, T.P., Grzybowski, B.A., 2010. Synthesis of stable, low-dispersity copper nanoparticles and nanorods and their antifungal and catalytic properties. J. Phys. Chem. C 114, 15612–15616.

Xu, T., Yu, X., Perlik, A.J., Tobin, W.F., Zweig, J.A., Tennant, K., Jones, T., Zuo, Y., 2009. Rapid formation and selective stabilization of synapses for enduring motor memories. Nature 462, 915–919.

Yalcin, B., Otles, S., 2008. Intelligent Food Packaging. 1734-459X. http://www.logforum.net/vol4/issue4/no3.

Yallappa, S., Manjanna, J., Sindhe, M.A., Satyanarayan, N.D., Pramod, S.N., Nagaraja, K., 2013. Microwave-assisted rapid synthesis and biological evaluation of stable copper nanoparticles using *T. Arjuna* bark extract. Spectrochim. Acta A 110, 108–115.

Yam, K.L., Takhistov, P.T., Miltz, J., 2005. Intelligent packaging: concepts and applications. J. Food Sci. 70 (1), R1–R10.

Yang, M., Zhu, J.J., 2003. Spherical hollow assembly composed of Cu_2O nanoparticles. J. Cryst. Growth 256, 134–138.

Yang, Y.X., Guo, J., Yoon, S.Y., Jin, Z., Choi, J.Y., Piao, X.S., Kim, B.W., Ohh, S.J., Wang, M.H., Chae, B.J., 2009. Early energy and protein reduction: effects on growth, blood profiles and expression of genes related to protein and fat metabolism in broilers. Br. Poultry Sci. 50, 218–227.

Yeh, M.S., Yang, Y.S., Lee, Y.P., Lee, H.F., Yeh, Y.H., Yeh, C.S., 1999. Formation and characteristics of Cu colloids from CuO powder by laser irradiation in 2-propanol. J. Phys. Chem. B 103, 6851–6857.

Yoon, K., Byeon, J.H., Park, J., Hwang, J., 2007. Susceptibility constants of *Escherichia coli* and *Bacillus subtilis* to silver and copper nanoparticles. Sci. Total Environ. 373, 572–575.

Youssef, K., Hashim, A.F., Rubina, R.S., Alghuthaymi, M.A., Abd-Elsalam, K.A., 2017. Fungicidal efficacy of chemically produced copper nanoparticles against *Penicilium digitatum* and *Fusarium solani* on citrus fruit. Philipp. Agric. Sci. 100, 69e78.

Yugandhar, P., Vasavi, T., Devi, P.U.M., Savithramma, N., 2017. Bioinspired green synthesis of copper oxide nanoparticles from *Syzygium alternifolium* (Wt.) Walp: characterization and evaluation of its synergistic antimicrobial and anticancer activity. Appl. Nanosci. 7, 417–427.

Zain, N.M., Stapley, A., Shama, G., 2014. Green synthesis of silver and copper nanoparticles using ascorbic acid and chitosan for antimicrobial applications. Carbohydr. Polym. 112, 195–202.

Zhang, L., Bai, R., Liu, Y., Meng, L., Li, B., Wang, L., Xu, L., Le Guyader, L., Chen, C., 2012. The dose-dependent toxicological effects and potential perturbation on the neurotransmitter secretion in brain following intranasal instillation of copper nanoparticles. Nanotoxicology 6, 562–575.

Zhang, X.F., Liu, Z.G., Shen, W., Gurunathan, S., 2016. Silver nanoparticles: synthesis, characterization, properties, applications, and therapeutic approaches. Int. J. Mol. Sci. 17, 1534.

Zhang, C.H., Wang, Y., Sun, Q.Q., Xia, L.L., Hu, J.J., Cheng, K., Wang, X., Fu, X.X., GU H., 2018. Copper nanoparticles show obvious *in vitro* and *in vivo* reproductive toxicity via ERK mediated signaling pathway in female mice. Int. J. Biol. Sci. 14 (13), 1834–1844.

Zhang, D., Liu, H.M., Shu, X., Feng, Y.P., Dong, P., Xie, X., Shi, Q., 2020. Nanocopper-loaded black phosphorus nanocomposites for efficient synergistic antibacterial application. J. Hazard. Mater. 393, 122317.

Zhao, J., Harper, A.F., Estienne, M.J., Webb, K.E., McElroy, A.P., Denbow, D.M., Zhao, Y., Zhu, J.J., Hong, J.M., Bian, N., Chen, H.Y., 2004. Microwave-induced polyol-process synthesis of copper and copper oxide nanocrystals with controllable morphology. Eur. J. Inorg. Chem. 20, 4072–4080.

Zhao, J., Harper, A.F., Estienne, M.J., Webb, K.E., McElroy, A.P., Denbow, D.M., 2007. Growth performance and intestinal morphology responses in early-weaned pigs to supplementation of antibiotic-free diets with an organic copper complex and spray-dried plasma protein in sanitary and nonsanitary environments. J. Anim. Sci. 85, 1302–1310.

Zheng, S.M., Guo, L.X., Zhan, X., 2013. Copper silicate nanoparticles: effects of intestinal microflora, nitrogen metabolism and ammonia emission from excreta of yellow-feathered broilers. Chin. J. Anim. Nutr. 8, 1837–1844.

CHAPTER

Safety considerations of copper nanoparticles as food and feed additives 21

Semih Otles[a] **and Buket Yalcin Sahyar**[b]

[a]*Engineering Faculty, Food Engineering Department, Ege University, Izmir, Turkey,*
[b]*Işık Tarım Ürünleri San.ve Tic. A.S., R&D Center, Izmir, Turkey*

1 Introduction

Firstly, the definition of nanotechnology as a term is explained in detail. The word form of nanotechnology is derived from the Latin nanus, which means dwarf, while numerous definitions exist on the technical definition of nanotechnology. One of them is The National Nanotechnology Initiative (Arlington, USA) definition, which expresses nanotechnology as the understanding and control of matter at dimensions between 1 and 100 nm, where unique phenomena enable novel applications. Other explanations are also more or less related to this basic definition, such as a field of technology and science, which is generally interested in tiny particles that are smaller than 100 nm (Senturk et al., 2013; Ötleş and Şahyar Yalçın, 2016), and also another explanation can be given as the science of manufacturing materials that have at least one-dimension below 100 nm (Otles and Sahyar Yalcin, 2017; Otles and Sahyar Yalcin, 2018). After comprehensive definitions of nanotechnology, another term is needed to be defined. This term is called nanoparticles, which can be defined as tiny (100 nm or less), three-dimensional shaped molecules that can easily boost surface area and have unique characteristics when compared with its macro form (Otles and Sahyar Yalcin, 2017). Various types of nanoparticles consist of different capacities that transfer numerous elements and acknowledge types of environmental situations. During the process of nanoparticles, the characteristics, properties, and production style are also changed (European Commission, 2009; Bunglavan et al., 2014; Trujillo et al., 2016).

Nanotechnology presents an essential position in the area of agriculture, food, and feed industry. It plays a vital function in those industries in the development of innovative and novel applications. The most widespread applications can be classified as food additives/supplements (nanonutraceuticals), nanoencapsulated agrochemicals (such as nanopesticides, fertilizers), active/intelligent packaging, and antimicrobials/biocides (Aschberger et al., 2015; Servin and White, 2016). In detail, nanotechnology for feed industry can be classified under these main topics: modification of natural ingredients, enhancing the nutritional quality of food and feed,

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modification of packaging product, increasing bioavailability of nutrients, and developing biosensors (Food Safety Authority of Ireland, 2008; Thulasi et al., 2013). As indicated by EFSA many applications of nanotechnology related to the food and feed industry exist in the market (Peters et al., 2014; Eleftheriadou et al., 2017). With respect to nanoparticles for the food and feed industry, the size of the nanoparticle as feed additives should not be more than 100 nm. Thus they could easily penetrate the stomach wall and into body cells faster than macroparticles. According to some researches, nanoadditives can easily be integrated into natural components. However, the improvement of a convenient delivery system remains a consideration because of the limited bioavailability of these types of molecules. This limitation caused by the epithelial barriers of the gastrointestinal tract and gastrointestinal degradation of these molecules by digestive enzymes is the main suspect. On the other hand, the studies at nanolevel offer opportunities for enhancing the functionality of food and feed molecules to the advantage of product quality (Bunglavan et al., 2014).

Currently, the expectation from nanotechnology applications is toward contributing many advantages to the food industry, desiring to boost quality and preservation. Therefore, food safety and quality assurance are becoming more significant day by day. There are numerous challenges and new consumption trends, which should be addressed by taking into consideration the whole stage of the supply chain for the food industry to maintain better public health. However, numerous researches suggest that exposure to specific engineered nanomaterials (ENMs) may contribute to health problems. For that reason, there is a requirement for additional examinations to show the biological and biochemical results of nanomaterials as food additive for consumption. Actual methods for microbial control and food safety assurance are not efficient enough for nanolevels, while nanotechnology is becoming a promptly broadening field for the food and feed industry. There are some current nano-related approaches on the market or at a development stage such as antimicrobial food-contact surfaces and packaging, nanosensors for rapid pathogen/contaminant detection, and nanodelivered biocidal methods, which denote enormous capability for the food industry. On the contrary, there are lots of studies which summarize toxicity profiles of used ENMs such as metal oxide nanoparticles, directly related to the promising food safety indications and health risks associated with the consumption of nanofood. It was shown that numerous health complexities associated with human exposure to the given ENMs are directly related to gut health that influences the control of fundamental toxicity. However, the toxicological studies, hazard analysis of ENMs, and exposure levels are still in the earliest phase of the studies (Martirosyan and Schneider, 2014; Eleftheriadou et al., 2017).

On the other hand, the recent application of nanotechnology in the feed industry is mainly focused on the animal feeding system. Nanotechnology in the animal feeding system is generally found in the form of nanomaterials. It is stated as an essential area that is used to increase the absorption of trace minerals by reducing the antagonistic effect among the bivalent cations. This technology is declared as a novel technology, which could be used in livestock nutrition for efficient uptake of nutrients for better use of feed additives. Although the application of nanotechnology represents

enormous benefits to improve the production efficiency of livestock, researches are still not enough to have a common perspective on them. Health and environmental effects of nanoparticles are still a concern (Gopi et al., 2017).

Safety considerations of copper nanoparticles as food and feed additives are discussed in this chapter. Before the safety considerations, the chapter starts with the definition of nanoparticles, especially copper nanoparticles, by using recent studies. Then, the focus is on the usability of these nanoparticles in the food and feed industry as an additive. Finally, safety considerations on the usage of copper nanoparticles as a food and feed additive are considered by taking into account regulations, authorities' perspectives, and scientific studies on toxicity.

2 Nanoparticles

Firstly the definition of the nanoparticle can be given basically as particles with a dimension between 1 and 100 nm. Nanomaterials could be characterized in several groups (organic and inorganic nanoparticles, emulsions, and nanoclays) (Figs. 1 and 2) depending on the chemical aspects of nanoparticles. Organic nanoparticles can be used to boost the number of nutrient feed systems to alter feed functionality. These nanoparticles can also be used as nanocapsules, which have been constructed to encapsulate nutrients that are carried through the gastrointestinal tract into the bloodstream. As a result, the encapsulation system has enhanced bioavailability without altering the appearance and taste of feed. Organic nanomaterials like proteins, fat, sugar molecules and nutraceuticals can be used in the food and feed in the form of encapsulation systems (liposomes, micelles, for delivery of food, and feed molecules) and packaging-related agents (identification markers, biosensors, antimicrobials, and shelf-life extenders). Inorganic nanoparticles can be defined as molecules constructed at the nanolevel, which are already confirmed to be used as additives

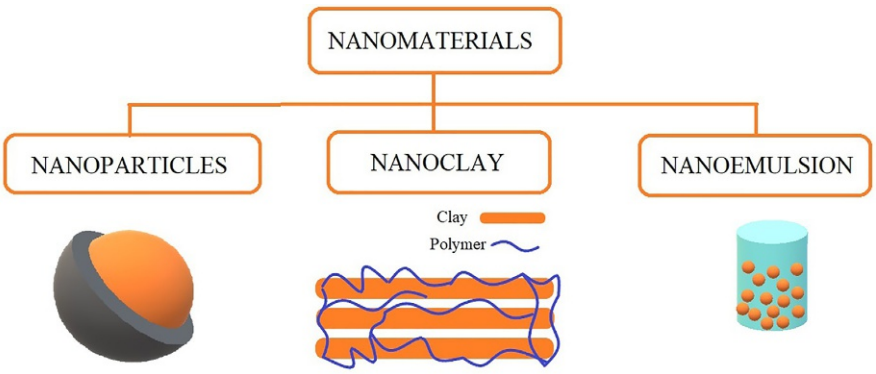

FIG. 1

Classification of nanomaterials.

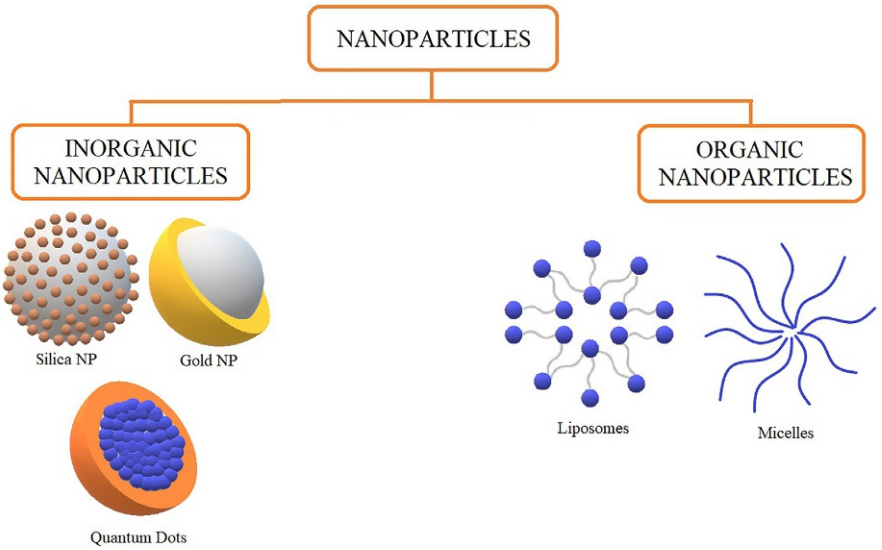

FIG. 2

Classification of nanoparticles.

in the feed (Bunglavan et al., 2014; Gopi et al., 2017). Secondly, metal nanoparticles are widely applied in food and feed industries. The main particles inside this group can be classified as nano titanium dioxide, nanosilver, and nanocopper. Metal nanoparticles can be defined as a nanoscale, pure metal particles (Table 1) or metal compounds (the chlorides, phosphates, oxides, sulfides, hydroxides and/or fluorides form of pure nanoparticles), which can be incorporated with conventional or new procedures (chemical and photochemical reactions, solution, thermal decomposition, electrochemical, and sonication) (Rajput, 2015; Sutradhar et al., 2014). However, most of these procedures have inevitable disadvantages such as use of hazardous chemicals, high energy requirements, boosted environmental toxicity, and high-cost impact (Senthilkumar and Sivakumar, 2014; Nakhjavani et al., 2017) (Table 1).

Recently, green synthesis, which can be defined as the preparation of nanoparticles from plant sources (especially from plant extracts as reducing agents), is gaining importance. Green synthesis has numerous advantages over classical and physical methods. The plant extracts, which are used in this process, consist of polyphenols, proteins, sugars, and terpenoids. These materials can be called phytochemicals, which act as a reducing agent during the synthesis process. These reducing agents are generally minerals. While in animal nutrition, nanotechnology mainly found an application area in the preparation of nanominerals, especially trace minerals with low bioavailability. Additionally, nanominerals lessen intestinal mineral antagonism by reducing excretion and environmental pollution. As a result, this process is eco-friendly, cost-effective, and does not need high energy, temperature pressure, or toxic chemical as reagents (Gopi et al., 2017; Asghar et al., 2018).

Table 1 Metal nanoparticles.

NP	Application	Benefit	Reference
N-Au	– Antimicrobial packaging		Silvestre et al. (2011) Azeredo et al. (2013)
N-Zn	– Antimicrobial packaging – Feeding supplement for fish	– Improve final weight and biochemical composition	Baltic and Boskovic (2017) Onuegbu et al. (2018)
N-Ag	– Antimicrobial packaging – Water purification – Antimicrobial packaging – Feed storage	– Higher bioavailability	Bunglavan et al. (2014) Al-Beitawi et al. (2017)
N-Ti	– Antimicrobial packaging – FC for packaging as a UV barrier	– The bacterial cell surface reaction – Cell contents damage (DNA, lipids, and protein) – High surface area	Azeredo et al. (2013) Bunglavan et al. (2014) Al-Beitawi et al. (2017)
N-Cu	– Antimicrobial packaging – Improvements in growth performance of piglet		Gonzales-Eguia et al. (2009)
N-Mg	– Antimicrobial packaging		Silvestre et al. (2011) Azeredo et al. (2013)
N-Si	– Antimicrobial packaging – Feed packaging		Baltic and Boskovic (2017) Bunglavan et al. (2014) Al-Beitawi et al. (2017)
N-Pt	– Biosensor construction		Wang et al. (2007) Echiegu (2017)
O-N-NC	– Biosensors for FP – Shelf-life extender and antimicrobial	– Increase bioavailability – Stabilize and deliver active components	FSAI (2008) Gopi et al. (2017)
N-Se	– Supplement for feed industry	– Decrease ruminal pH and ammonia concentration of sheep	Shi et al. (2011)

Abbreviations: *NP: nanoparticle, UV: ultraviolet, FC: feed colorant, N-Au: nanogold, N-ZnO: nanozinc oxide, N-Ag: nanosilver, N-Ti: nanotitanium, N-Cu: nanocopper, N-Mg: nanomagnesium, N-Si: nanosilicon, N-Pt: nanoplatinum, O-N-NC: organic nanoparticles as nanocapsule, N-Se: nanoselenium.*

2.1 Copper nanoparticles

Copper nanoparticles (Cu-NPs) are metal-based nanoparticles, which denote catalytic activity in organic transformation, and are profoundly conductive and inexpensive while comparing with silver and gold nanoparticles. These nanoparticles can be

maintained by surface attachment of the acrylic functionality and can be copolymerized with other acrylic monomers. Hence, these nanoparticles become an essential component of the polymer chain. These types of engineered copper nanoparticles show antimicrobial activity when compared with conventional copper-based biocides. These nanoparticles can be used as antibacterial coatings and paints in household components and food storage apparatus (Anyaogu et al., 2008). They can also be incorporated into application areas in the food contact polymers to boost barrier and mechanical attributes and used for the inhibition of plastic photodegradation. These metal nanoparticles or complex nanomaterial structures are efficient antimicrobials (colloids, oxides, and salts, complexes such as copper oxide zeolites form). These forms can be incorporated into the food industry for food preservation and inhibition of surface contamination. Additionally, copper-based nanoparticles can also be used as an efficient humidity sensor (Llorens et al., 2012), while their extraordinary performance still exists as antimicrobial and antibacterial agents (Majzlik et al., 2010, 2011). These nanoparticles have found numerous practical application areas. One of these application areas is polymeric beads, which are prepared mainly from activated carbon aerogels, carbon granules, and silica beads. Copper nanoparticles used in these beads play significant roles such as acting as an antibacterial agent, enhancing the porosity, and maintaining oxidative capacity (Khare et al., 2014; Chudobova et al., 2015; Powara et al., 2019).

Copper nanoparticles are inexpensive and highly abundant in nature, therefore the applications of these nanoparticles into the food and feed industry have increased. However, there are still some challenges about copper nanoparticles synthesis, especially the transformation from copper nanoparticles into copper oxide in the presence of air. This challenge can be overcome by testing different methods for nanoparticle production, such as wet chemical, microemulsion, micro-oven assisted, thermal decomposition, and green and biological models. There is no one convenient method for the production of copper nanoparticles. This explanation is also the same for other nanoparticles production. All nanoparticles should be produced according to the properties of application areas. The wet chemical model is the convenient one for some application areas, whereas green synthesis can be the only option for other application areas. However, many types of research have been endorsing that green or biological methods are better alternatives than the chemical and physical synthesis of nanoparticles thanks to the eco-friendly and nontoxic properties of these methods. Living organisms such as plants, fungi, and bacteria are used for the synthesis of nanoparticles, instead of hazardous chemical materials in these methods (Powara et al., 2019).

Numerous research studies are working on copper nanoparticles. Here are some examples. A copper nanoparticle was prepared by the chemical reduction technique by applying L-ascorbic acid as a declining and covering agent. The results showed promises and the application of ascorbic acid makes the method a nontoxic, cost-effective, and environmentally friendly (Umer et al., 2014). Copper nanoparticles are combined by using the solution reduction method, favorably. This method was declared as ecological and biodegradable, low-priced, and the most suitable while comparing with

the conventional methods (Chandra et al., 2014). The chemical reduction method was also used in another study to synthesize starch-protected zero-valent copper (Cu) nanoparticles. The results showed that the method is suitable for large-scale synthesis (Khan et al., 2016). In another development method, seed-mediated copper nanoparticles are used to fabricate a chemical sensor on the interlocked electrodes by applying a composite film. The results showed that the formulation of oxidation-free copper nanoparticles has been done successfully (Ankireddy et al., 2017).

3 Nanoparticles as food and feed additives

After a detailed definition of nanoparticles, some examples of the application of nanoparticles as food and feed additives are given. Firstly, an example of the application of nanoparticle is animal feeding additives, which can be mainly used for the administration of medication, nutrients, probiotics, supplements, and other substances. Recent studies have focused on nanotrace minerals as livestock additives, which are anticipated to denote the benefit of better bioavailability, minor dose rate, and uniform interaction with other components to fulfil the requirement of minerals of livestock. Additionally, thanks to these nanotrace minerals for their low dose usage, which gives them a chance to be a substitute for antibiotics as growth promoters, eradicate antibiotic residues in animal products, decline the contamination of the environment, and produce pollution-free animal products. Nanoparticles are not only used as a feed ingredient but can also be incorporated into the protein capsules/micelles or other natural feed ingredients (Hett, 2004; Taylor et al., 2004; Stanley and Dorris, 2000; Schmidt, 2009; Gopi et al., 2017). Secondly, nanoparticles as feed additives can provide direct transportation of molecules to targeted organs, and also systems preventing rapid degradability and can present health benefits. Silver nanoparticles can be defined as the most prevalent nanoparticle examined for the application in chicken feed used to enhance the microbiota of chickens. On the contrary, there are other studies, which have shown the high toxicity potential of silver nanoparticles in birds (Gangadoo et al., 2016). Some examples of metal-based nanoparticles as food and feed additives are given in Table 2.

Table 2 Metal-based nanoparticles as food and feed additives.

NP	Application	Benefit	Reference
N-Au	– Feed	-Prolong and improve digestive enzyme activity	Adegbeye et al. (2019)
N-Zn	– Feed	-Improve feed digestibility -Improve volatile fatty acids production -Prevent periodontal disease in horses -Enhance the growth and health of the fish (fingerlings of Labeo rohita)	Adegbeye et al. (2019) Thangapandiyan and Monika (2020)

Continued

Table 2 Metal-based nanoparticles as food and feed additives—cont'd

NP	Application	Benefit	Reference
N-Ag	– Feed – Food	– Prolong and improve digestive enzyme activity – Strong antimicrobial activity against gram ("+" and "−") microbes – Prevent periodontal disease in horses. – Potentially against the gastrointestinal parasites – Reduce coliform in ileal content of weaned piglets – Reduce the *C. perfringens*/ Cl*. histolyticum* pathogen group concentration – Antimicrobial against Escherichia coli and Bacillus subtilis. – The Ag-NPs (the extract of *Syzygium cumini* leaves) showed excellent antimicrobial activities against methicillin- and vancomycin-resistance *Staphylococcus aureus* bacterial strains and *Aspergillus flavus* and *A. parasiticus* fungal species – The aflatoxins (AFs) production was also significantly inhibited by using the Ag-NPs (the extract of Syzygium cumini leaves) – Antimicrobial activity against *Salmonella* and *Campylobacter*	Asghar et al. (2020) Adegbeye et al. (2019) Fondevila et al. (2009) Singh (2016) Yoon et al. (2007) Duffy et al. (2018a, 2018b)
N-Cu	– Feed – Food	– Strong antimicrobial activity against gram + and gram − microbes – Improve microbial growth – Against *Escherichia coli* and *Bacillus subtilis* – *Staphylococcus aureus, Escherichia coli,* and *Listeria* monocytogenes – A dose-dependent cytotoxic effect on K562 cells – Hydroxyapatite NPs, used modified with Cu^{2+} were shown to be potential supports for immobilization of the xylanase enzyme – Antimicrobial activity against *Salmonella* and *Campylobacter* – Significantly enhance the health and production of the farm animals	Mehdizadeh et al. (2020) Adegbeye et al. (2019) Yoon et al. (2007) Coutinho et al. (2020) Duffy et al. (2018a, 2018b) Yusof et al. (2019)
N-Mg	– Feed	– Strong antimicrobial activity against gram + and gram − microbes	Adegbeye et al. (2019)
–		– Prevent periodontal disease in horses	Adegbeye et al. (2019)
N-Se	– Feed	– To improve feed digestibility and volatile fatty acids production	Adegbeye et al. (2019)

Abbreviations*: NP: nanoparticle, N-Au: nanogold, N-ZnO: nanozinc oxide, N-Ag: nanosilver, N-Cu: nanocopper, N-Mg: nanomagnesium, N-Ca: nanocalcium, N-Se: nanoselenium.*

Additionally, nanoemulsion technology is an example of nanoparticles used for both food/feed additives. Microencapsulated products can be developed with this technology, which allows the ordered release of bioactive substances in the gastrointestinal tract. Nanoemulsions found a wide range of application areas from ready to drink products to powdered formulations strengthened with functional elements. When emulsions turn into nano form from the microphase, the physical properties, phase separation stability, and behavior are significantly changed. Thanks to the small particle size of nanoemulsions, they found an application area in low-fat products. Another example of additives for both food and feed applications is starch-based nanoparticles acting as colloids in aqueous solution and could found extensive application areas (Dziechciarek et al., 1998; Bunglavan et al., 2014). Another application area of nanoparticles in the agrifood/feed sector is vitamins and precursors. Nanoformulated carotenoids are an excellent example of this area, which is insoluble in water in the macro phase. Additionally, nanocarotenoids could be combined with cold water, and so their bioavailability is increased (Thulasi et al., 2013).

Alternatively, gelatin biopolymer nanoparticles have been taken into consideration with their available active group sites. The active groups of these nanoparticles easily attach to the target particles and act as a drug/nutraceutical delivery system to enhance the therapeutic effects and also used to decline the side effects of formulated drugs. These natural, biodegradable nanoparticles are biocompatible polymer, nontoxic, feasible, low-cost, and are used in parental formulations. In research, fish skin gelatin is provided from warm water species, which can be a substitute for pig and cow gelatin (Akbar et al., 2017).

A study was aimed to account for an eco-friendly synthesis of different NPs which is included in Cu-NPs using green tea and black tea leaves extracts. This production method of NPs is a simple, reliable, green, inexpensive, and economical biological procedure that could promote the industrial production of metal NPs without using any harmful reducing, capping, and dispersing agent. The results suggest that the synthesized NPs could be effectively utilized as an alternative antibacterial/antifungal agent against diseases caused by multiple drug-resistant pathogens. Additionally, these metal NPs may be utilized as possible aflatoxins adsorbent in human food and animal feed such as rice, wheat, maize, red chilies, and poultry feed. Lastly, the synthesized metal nanoparticles could be used as an effective fungicide in the agricultural field (Asghar et al., 2018).

A study is aimed to assess the in vitro activity of silver (Ag), zinc oxide (ZnO), and copper oxide (CuO) NPs against *Salmonella* and *Campylobacter* isolated from poultry. The minimum inhibitory concentration for all *Campylobacter* strains was in the order of $Au \geq CuO \geq ZnO$ nanoparticles. Ag NPs were the most effective against *Salmonella*. The growth kinetics of the Salmonella strains were also assessed during exposure to NPs in liquid media. Growth was dependent on NP concentration with some differences noted between strains. While these specific size nanoparticles are effective against pure cultures of bacteria the antimicrobial effectiveness of the nanoparticles should be further examined under industrial conditions. The antimicrobial effect against key pathogens of concern to the poultry industry denotes that there are opportunities for the poultry industry to benefit from nanoscience. Knowledge

of the effectiveness of NPs against these key pathogens should be incorporated into the development of future targeted applications such as crates, conveyor belts, or packaging. Nanoenabled control strategies devised in vitro are considered effective and safe in the real-world industry setting. Continuing research and development into nanoenabled control strategies will undoubtedly provide opportunities for the poultry industry to benefit from nanoscience (Duffy et al., 2018a, 2018b).

Recently a study compared the effects of different doses of waterborne Cu-NPs and CuO on blood and liver of selected groups of *Cyprinus (C) Carpio*. Significant changes were found in all assessed blood parameters of fish in response to increasing doses from 0 to 1.5 mg of Cu-NPs or CuO. Also, increased levels of lipid peroxide and reduced glutathione were observed in the livers of C. Carpio in Cu-NPs or CuO-treated groups. Significant histological alterations were induced by exposure of Cu-NPs or CuO in the liver of C. Carpio including focal necrosis, cloudy swelling of hepatocytes, degenerative hepatocytes, vacuolization, pyknotic nuclei, damaged central vein, nuclear hypertrophy, dilated sinusoid, vacuolated degeneration, congestion, and complete degeneration in a dose-dependent manner. The alterations in blood and liver specimens were also observed in the Cu-NP-treated fish when compared with the CuO-treated fish. It is shown that the Cu-NPs were more toxic than the CuO as shown by the hemato- and hepatotoxicity in C. Carpio of this study (Noureen et al., 2018).

In a study, Cu-NPs and CuO-NPs were used to extract *Lactobacillus*, *Enterococcus*, and *Enterobacterium* from the intestines of broilers. Additionally, strains of Bacillus subtilis 10,641 and *Bifidobacterium* were involved in probiotic strains. The data obtained in the course of the study testify to the insignificant biotoxicity of copper nanoparticles concerning representatives of the genera *Lactobacillus* and *Bifidobacterium*, with the most sensitive bacteria being the genus *Lactobacillus*. The insignificant biotoxicity of copper nanoparticles about representatives of the genera *Lactobacillus* and *Bifidobacterium* were studied. The Bioaccumulating ability of microorganisms of the studied metals was also examined. It was declared that the use of nanoparticles as a component of the fodder additive in small concentrations does not adversely affect not only the probiotic strains, but also the main representatives of the normoflora (*Lactobacillus*, *Enterococcus*, and *Enterobacterium*) of the poultry. The positive effect of the copper nanoparticles is directly related to the low level of dissociation of nanoparticles since biologically active ions will be released much more slowly, thereby creating a prolonged effect of exposure (Sizentsov et al., 2018).

Finally, the advantages of nanoparticles as food and feed additives can be summarized as improving functionality and bioavailability of nutrients, benefit on product quality and nutritional content, acting as a nutrient delivery system to transmit selected molecules directly to the selected places while there is still open points, dilemmas, and concerns on abnormal metabolism, toxicity, and environmental effects of these nanoparticles (Dziechciarek et al., 1998; Bunglavan et al., 2014; Singh, 2016). While there are numerous examples of nanoparticles as food and feed additives, silver and copper nanoparticles are gaining more importance and have a wide application area. Their most significant characteristic is the antimicrobial activity against bacteria. Next, the focus is on copper nanoparticles as an additive or supplement for the food and feed industry.

4 Copper nanoparticles as food and feed additives

Copper is a vital trace mineral involved in many physiological functions of the body. Copper nanoparticles have shown good potential to use as drugs for the cure of osteoporosis, antibacterial agents, additives in cattle and poultry, and the intrauterine contraceptive device (Liu et al., 2004; Hejazy et al., 2018). Copper oxide nanoparticles, which are accumulated on the surface of cotton fabrics using ultrasound irradiation, are shown as antibacterial activities against Escherichia coli (Gram-negative) and Staphylococcus aureus (Gram-positive) cultures (Perelshtein et al., 2009). Copper nanoparticles can also be used as a supplement in piglets, which shows critical enhancement in the growth performance of piglets while comparing with the macro size of copper particles. Additionally, enhancement of the digestibility of crude fat and energy in pigs could easily be seen (Eguia et al., 2009; Bunglavan et al., 2014; Singh, 2016). Copper nanoparticles, which are formulated with a low melting point soda-lime glass powder, have acquired high antibacterial and antifungal activities. This formulated nanoparticle is obtained by using a basic and trustworthy bottom-up route. This nanoparticle has shown great biocide activity, and so it can be called as a powerful green inorganic biocide agent with low toxicity for humans permitting its application in wide-ranging biocide applications (Esteban-Tejeda et al., 2009). Copper nanoparticles are also more bioavailable due to their small size and high surface to volume ratio (Sharif et al., 2020).

Additionally, copper nanoparticles (Cu-NP) have recently been reported as a bright alternative to antibacterial reagents and a growth promoter according to many studies. Cu-NP has also presented numerous effects on animal performance, counting on the shape, size, dose, and species (Scott et al., 2018). There are also numerous studies focused on the eco-friendly synthesis of metal-based nanoparticles. One of them is used as green and black tea extracts by using iron (Fe), copper (Cu), and silver (Ag) nanoparticles, and all these nanoparticles have shown significant antibacterial and antifungal activities and have also declined the aflatoxins production. As a result, they can be used as an antibacterial/antifungal agent and also can be used as aflatoxins adsorbent in food and feed like rice, wheat, maize, red chilies, and poultry feed (Asghar et al., 2018). Another example of the eco-friendly synthesis of a copper nanoparticle is using a type of plant leaf extract. This extract performs both as a reducing and as a capping agent. These formulated copper nanoparticles change their color after the addition of the extract into the copper sulfate solution. The formulated nanoparticles show antimicrobial activity against both Gram-positive and Gram-negative pathogens (Saranyaadevi et al., 2014).

In a study, biosynthesis of Cu-NPs using Indian traditional medicine, *Panchagavya* is used which is eco-friendly, simple, cost-effective, and nontoxic. The antioxidant and cytotoxicity activity of the NPs was also studied. The Cu-NPs biosynthesized using *Panchagavya* extract demonstrated a significant effect on brine shrimp lethality assay and could be used to study the toxicity of nanostructures. The advantage of this method is self-sufficiency and rapid results. These data are expected to facilitate pharmacological and nanotoxicological research (Arumugam et al., 2019).

There is a study that shows that copper products in an aqueous environment primarily causes a reduction of spermatozoa velocity (VCL). It revealed that contamination of the aqueous environment with copper mainly caused a reduction in male gamete velocity, which may impair reproduction. Various copper products have different effects on motility duration, which can also affect fertilization. Cu ion exerts more harmful effects on the spermatozoa motility of sea trout than copper nanoparticles. It has been suggested that nanotoxicity for copper nanoparticles is necessary to examine continuously the effect of different characteristics of nanoparticles, such as aggregation, shape, size, shape, structure, surface properties, coated agents, pH, water hardness, and aqueous solubility of NPs and changes in nanoproducts after prolonged water exposure on gametes, fertilization, and the developmental stages of organisms (Kowalska-Góralska et al., 2019).

Antibacterial, antioxidant, and anticancer effects of Cu-NPs fixed on cellulosic walnut shell material were investigated. The antibacterial properties of Cu-NPs were studied on three strains of bacteria: Staphylococcus aureus, Escherichia coli, and *Listeria monocytogenes*. The antimicrobial properties of Cu-NPs affect both Gram-positive and Gram-negative bacteria. The antioxidant properties of Cu-NPs increased with increase in the concentration. Additionally, Cu-NPs appeared to have a dose-dependent cytotoxic effect on K562 cells. These types of NPs found application areas in many pharmaceutical and food industries (Mehdizadeh et al., 2020).

In a study, a facile, ecological, and economical green method is described for the fabrication of Cu-NPs from the extract of Syzygiumcumini leaves. The Cu-NPs were crystalline, spherical, and in size ranging from 28 to 35 nm. The findings suggest that the green synthesis of metal NPs is simple, sustainable, nontoxic, economical, and energy-effective as compared to the other conventional approaches (Asghar et al., 2020).

Hydroxyapatite (HA) NPs are shown as promising materials for enzyme immobilization since they provide a high specific surface area for enzyme loading and can also be modified with metal ions (HA-Me^{2+}) to enable interaction with proteins. HA NPs, used pure or modified with metal ions (Cu^{2+} and Ni^{2+}), were shown to be potential supports for the immobilization of the xylanase enzyme. A simple, fast, and efficient immobilization protocol was developed using experimental design, generating derivatives by coordination interactions between metal ions on the support surface, and electron donor groups on the enzyme surface. The affinity constant values obtained from adsorption isotherms indicated that xylanase denoted a higher affinity for the HA-Cu^{2+} support compared to other combinations. This fact became even more evident in the recycling experiments, in which the derivative of HA-Cu^{2+} denoted the best results, resulting in a promising derivative for applications of industrial interest, such as in the biofuel, pharmaceutical, pulp, and food & beverage sectors (Coutinho et al., 2020).

A study was performed to determine the effect of Cu and CuO nanoparticles on the formation of a barley crop. The effect of presowing treatment of spring barley seeds by nanoparticles of Cu and CuO on the growth and development of plants, yield, and their nutritional value was studied. The use of Cu-NPs contributed to an

increase in grain yield by 17.3% compared with the control, while there was no decrease in nutritional value: metabolic energy, feed units, digested protein. Based on the research results, it is preferable to use Cu-NPs in comparison with CuO-NPs to obtain a higher barley yield (Seregina et al., 2020).

Cu-NPs significantly decreased fetal body weight, body length, and liver weights. Cu-NPs increased the liver concentration of Cu, and decreased protein levels and Fe in fetuses. Cu-NPs also increased oxidative stress and inflammation in the fetus after pregnant rats were exposed to high doses of Cu-NPs. Oral exposure to Cu-NPs during pregnancy increased Cu concentrations in the fetus, which not only affected fetal development but also significantly induced oxidative stress and inflammatory responses in fetal liver. Taken together, these findings are valuable to evaluate fetal risk assessment after oral exposure of Cu-NPs during pregnancy (Luo et al., 2020).

Cu-NP has also a positive effect on all behavioral patterns more than other groups which significantly reflect on the weight of the body, gaining of weight, and the intake of food in the Cu-NP-treated group of birds. The findings in a study stated that when the drinking water of broilers was supplemented with Cu-NP, there might be an improvement in the immunity, behavior, and productive performance more efficiently than $CuSO_4$ (El-kazaz and Hafez, 2020).

A study aimed to evaluate the influence of Cu-NPs on the growth, immunity, and oxidation resistance of common carp. Five groups of fish were fed diets with Cu-NPs at 0, 0.5, 1, 2, and 4 mg/kg for 8 weeks. The results suggested that Cu-NPs in diets increased the growth performance and reduced FCR with the linear and quadratic model. Also, common carp fed Cu-NPs showed increased carcass protein, lipid, and ash contents in a dose-dependent manner. The Cu accumulation in the carcass, liver, muscle, and gills increased by Cu-NPs and showed the maximum at 4 mg Cu-NPs/kg. Based on regression analysis, the requirement of dietary Cu-NPs for common carp was estimated to be 2.19–2.91 mg/kg diet (Dawood et al., 2020).

A study was aimed at studying the efficiency of a nanoscale alloy of copper (Cu) and zinc (Zn) to be used as a mineral additive for feeding broiler chickens, compared to inorganic and organic forms of these elements. There were three treatment groups with 24 chickens in each. Replacing the inorganic form of mineral supplements with the nanosized alloy resulted in a positive productive effect, with a tendency to increasing the content of serum protein. The nanoscale form of metals improved the activity of aminotransferases. As a result, nanoscale forms of Cu and Zn have a cumulative effect and may become an alternative to inorganic and organic forms of these elements in poultry nutrition (Sizova et al., 2020).

A study was performed to investigate the dose-dependent effects of copper oxide nanoparticles on the growth performance, immune status, oxidant/antioxidant capacity, DNA status, and histological structures of most edible parts of broiler chickens (muscle, heart, liver, spleen, and kidneys). Results of the study denoted that dose-dependent increases in malondialdehyde levels, copper contents, DNA fragmentation percent, and microscopic scoring in different examined organs of CuO-NPs-receiving groups associated with a remarkable reduction in weight gain, food conversion ratio, catalase activity, and antibody titer of both New Castle and Avian

Influenza viruses. It was concluded that CuO-NPs are considered cytotoxic and the study does not recommend adding CuO-NPs to poultry feed (Morsy et al., 2021).

Benefits and concerns for copper-based nanoparticles as food and feed additives from recent studies are presented in Table 3.

Table 3 Benefits and concerns for copper-based nanoparticles as food and feed additives from recent studies.

Application	Benefit	Concern	Reference
Feed additive for broiler chickens	– Lower feed conversion rate and mortality – Higher percentage of breast and leg muscles in the carcass	– NI	Mroczek Sosnowska et al. (2016)
Feed additive for red sea bream	– Enhanced growth and health – Significant effect on growth performance, feed efficiency and whole-body protein and lipid compositions – Enhanced immune response and resistance to low-salinity stress	– NI	El Basuini et al. (2017)
Feed additive	– Antibacterial reagent – Growth promoter – Immune modulatory	– Dose and duration optimization – Bioavailability need confirmation	Scott et al. (2018)
chitosan gel beads-based Cu-NP as a cattle feed additive	– Enhance cattle nutrition and productivity	– NI	Duffy et al. (2018a, 2018b)
Feed additive for poultry	– In small concentrations does not adversely affect the probiotic strains, especially (*Lactobacillus*, *Enterococcus*, and *Enterobacterium*) – Positive effect of Cu-NP being directly related with low level of dissociation	– Excessive supply into the environment has a negative effect on the growth of populations of the microorganisms	Sizentsov et al. (2018)

Table 3 Benefits and concerns for copper-based nanoparticles as food and feed additives from recent studies—cont'd

Application	Benefit	Concern	Reference
Subchronic oral exposure in rats	– NI	– Caused strong hepatic toxicity by inducing oxidative stress and inflammation	Tang et al. (2019)
Panchagavya-mediated copper nanoparticles as a feed additive into brine shrimp	– Ecofriendly, simple, cost effective, and nontoxic	– NI	Arumugam et al. (2019)
Feed additive into drinking water of broilers	– Improvement in the immunity, behavior, and productive performance	– NI	El-kazaz and Hafez (2020)

Abbreviations: *NI: not included in the study.*

As a result, the advantages of copper nanoparticles as food and feed additives can be summarized as acting as an antimicrobial agent (specifically effective against Gram-positive and Gram-negative bacteria, yeast, and also plant pathogenic fungi), uniform coating and distribution ability, enhance nutrition, and productivity. However, there are still concerns exist about dose-related studies, effects on inflammation and oxidative stress, and hepatic toxicity topics (Cioffi et al., 2004; Usman et al., 2013; Özer et al., 2014). Additionally, the antimicrobial activity of copper nanoparticles has been reported from their agglomeration and rapidly oxidation ability (Ghoshal et al., 2012; Bergin and Witzmann, 2013; Ghoshal et al., 2013; Azlin-Hasim et al., 2015; Hannon et al., 2016). Lastly, it can be concluded that a higher number of unknown side effects for the consumption of nanoparticles inhibit human-related studies and studies on food additives.

5 Safety considerations of copper nanoparticles

There are numerous dilemmas about the safety considerations of nanotechnology application in the food and feed industry. These considerations have addressed the uncertainties and the lack of toxicological data. There is still no reliable proof that could be declared that whether nanomaterials are either safer or more dangerous than their macro styles for the food and feed sector. The main classifications of engineered nanomaterials safety considerations are as follows. Firstly, engineered nanomaterials can be taken into considerations, which have many useful applications in food and food contact materials. According to legislations, those applications may depend upon a safety assessment because of the significant and unpredictable bioavailability

changes from the macro form into the nano form. Therefore, size is a fundamental feature in the bioavailability of nanomaterials. On the other hand, the physicochemical properties of the nanomaterial surface affect stability, agglomeration, interactions with mucus, various interaction mechanisms, absorption, and excretion. According to some studies, there are some key parameters (salt concentration, pH, and biochemical) in the luminal fluid matrix to determine the integrity, aggregation, and surface properties of nanoparticles. Additionally, physical forces, digestive enzymes, and microbes could also have influences. There should be more research to overcome the lack of knowledge on the kinetics and absorption of the full spectrum of food and food-related nanomaterials. Physicochemical aspects of nanomaterials with the gastrointestinal ecosystem should also be clearly explained to gain proper risk assessment. Validation and verification studies between laboratories could allow the achievements of sustainable methods (Bellmann et al., 2015; Lefebvre et al., 2015). Secondly, the knowledge of the engineered nanomaterials' effect on the gastrointestinal tract is limited. According to some research, it was declared that there was a connection between high levels of dietary nanoparticle uptake and Crohn's disease and ulcerative colitis. It has been stated that the accumulation of insoluble nanoparticles in humans could be accountable for the degradation of gastrointestinal functioning (Lomer et al., 2002; Martirosyan and Schneider, 2014). Thirdly, nanoparticles' biological conditions can be taken into considerations. Nanoparticles could interact with proteins, lipids, sugars, or other biomolecules, according to their biological conditions. This interaction can affect the surface structure of the nanoparticles and their aggregation behavior of biomolecules. According to some researches, these biomolecules are accountable for the primary interaction with living systems, which give a chance to identify the nanoparticles as biological materials (Lynch et al., 2007; Bunglavan et al., 2014). Lastly, engineered nanomaterials have particular physicochemical features and high reactivity because they easily affect basic cellular processes (proliferation, metabolism, and death). Additionally, they could also cause some toxic endpoints, which is the outcome in the dysfunction of these fundamental processes. Recently, the potential adverse health effects of engineered nanomaterials have been shown in several in vitro studies. These adverse effects can be described as inducing oxidative stress, releasing toxic ions, disrupting electron/ion cell membrane transport activity, and causing oxidative damage and lipid peroxidation. Thus, these effects can cause adverse effects on the respiratory, cardiovascular, and nervous systems (Landsiedel et al., 2012). Finally, the interference of reactive oxygen species (ROS) generation has been shown as the most significant pathogenic pathway linking engineered nanomaterials exposure to tissue damage (Donaldson et al., 2009), while cytotoxicity, genotoxicity, stimulation of an inflammatory and/or immune response have shown as other common toxicity endpoints (Chen et al., 2007; Martirosyan and Schneider, 2014).

After the identification of nanomaterials safety considerations, the safety considerations of metal-based nanoparticles are as follows. Even though the advantages are affiliated with the antimicrobial activity of metal-based nanoparticles, like enhanced food safety and shelf life, some considerations comprehend with the migration of

the nanoparticles from nanocoated food packaging into the food system and also their potential human toxicity once consumed (Hannon et al., 2016). These concerns directly come from the uncertain toxicity and migration mechanism of nanoparticles because of the nanolevel forms. Some of the specific safety considerations for metal-based nanoparticles, specifically Cu nanoparticles, as an additive for the food and feed industry are as follows. Firstly, a study denoted human exposure to silver and copper migration from a nanosilver and nanocopper food contact material (FCM) surface coating used in the theoretical plan as fruit juice packaging. Migration levels were acquired to surpass the European Commission's regulatory limit for permitted substances of 0.01 mg/kg. Substantial data show that the increased size-dependent dissolution of Cu-NPs cause higher migration when compared to AgNPs. Even though the expectation is high migration between nanoparticle and food simulant, there was no meaningful difference exist between particle concentrations found in the food stimulant (Hannon et al., 2016). Researches should be focused on the potential solutions for reducing interaction levels of nanoparticles while improving attachments on food packaging. Secondly, migration for nanoparticles can be defined as a mass transfer process by which low molecular weight ingredients initially denoted in the package are released into the food or feed product directly or modified atmosphere of the packaged product. The principle of migration consists of two stages. The first stage of migration is driven by the nanomaterials, which encapsulate within the surface layers during the following release of nanomaterials that should pass through gaps between polymer molecules of packaging materials. The releasing process directly depends on the polymer properties of packaging materials. The ratio and speed of migration are directly depends on the physical and chemical features of food and polymer and also their interaction capability. The controlling parameters for migration can be classified as concentration, molecular weight, particle size, diffusivity, and solubility of the target nanoparticles in the polymer and also temperature, food composition, structure and viscosity of the polymer, mechanical stress, pH value, and contact time (Huang et al., 2011; Huang et al., 2015). Finally, normal levels of copper uptake into the human body is maintained in the homeostasis while overload copper uptake in vivo can cause toxicological activities. Copper NPs could lead to critical toxicological effects, and the kidney and liver are the target organs of copper NPs while comparing with macro form (Zietz et al., 2003; Bertinato and L'Abbé, 2004; Hejazy et al., 2018).

5.1 Toxicity

After the main definition of safety considerations for Cu-NPs, the details for the toxicity of Cu-NPs as metal oxide nanoparticles are determined. Despite extensive usage and possible biomedical applications of copper nanoparticles, their biosafety concerns and kinetics persist uncertainly. Firstly, the essential stages of risk assessment of nanoparticle toxicity should be declared. According to authority definition; hazard identification, hazard characterization, exposure assessment, and risk characterization are the essential stages of risk assessment. If the exposure assessment

is taken into consideration, the theory gave the estimation of the particle with high risk but of little exposure. This little exposure is an insignificant risk, compared with particles of limited risk and high exposure for a longer term. Therefore, it can be concluded that characterizing both the nature and exposure time of nanoparticles is important and essential for detailed information of toxicity. According to studies, there are concerns directly related to the application of nanoparticles, which pose an undeniable risk of boosted bioavailability, induced ROS in the inflammatory digestive diseases, variation in the nutrient bioavailability by disrupted effects on protein and enzyme stability, and possible effects on nanoparticle biocomplexes in the process of heating or storage (FSAI, 2008; Bellmann et al., 2015; Gopi et al., 2017).

Additionally, the ecotoxicological effects and pathological risks of nanomaterials to animals and humans are considered a big challenge, even if the possible application of nanomaterials into numerous fields is great (Colvin, 2003; Royal Society and Royal Academy of Engineering, 2004). In research on benthic organisms, it was shown that the risk of nanoparticles has been directly related to the concentrations in the environment of these particles and also the form of their existence (such as; dispersed, attached, and/or incorporated in aggregates) and finally their distribution in the pelagic vs. benthic fields (Newell et al., 2005; Ward and Kach, 2009).

There are several studies on Cu-NPs to identify the toxicity of copper-based nanoparticles. One of them is focused on Cu-NPs and Cu ions toxicity after a single oral dose. As a result of various tests, Cu-NPs have shown the highest dissolution only in gastric conditions when compared with Cu ions under different physiological medium. It has also been revealed that Cu-NPs have been endeavored plain toxicological effects at higher dose levels compared with Cu ions. Additionally, they have shown sex-dependent differences in mortality, biochemistry, and histopathology. The major organs, which are affected by Cu-NPs, are the liver, kidney, and spleen. The conclusion for this study is that kinetics and toxicity of Cu-NPs are most likely affected by the release of Cu dissociated from Cu-NPs (Lee et al., 2016). According to another study, copper NPs have been presented among the most toxic nanomaterials for mammals. While copper with the macro size is a fundamental trace element and its deficiency leads to different diseases in humans. According to a study, the toxicity of these nanoparticles depends on sex. It is also declared that the increase in the production of reactive nitrogen species (RNS) and ROS play an important role in copper-induced organic dysfunction (Hejazy et al., 2018). Additionally, Cu-NPs have also shown high toxicity effects on a broad range of bacteria and fungi thanks to their high surface area-to-volume ratio. These nanoparticles have a different mechanism to kill cells, such as DNA damage, blocking biochemical pathways, membrane disruption, and complex formation with proteins (Cioffi et al., 2005; Ruparelia et al., 2008; Ren et al., 2009). Notwithstanding, those nanoparticles are acknowledged with their high sensitivity of oxygen forming by producing copper oxide nanoparticles, so it is fundamental to figure out a production model that will protect and bind the particles from any kind of oxidation (Kaninnen et al., 2008). Other studies claim that highly ionic metal oxide nanoparticles could be beneficial antimicrobial agents in a particular way if they are prepared with higher surface areas and different

crystal morphologies than usual (Stoimenov et al., 2002; Bata-Vidács et al., 2013). Moreover, a recent study has provided data on the possible harmful effects on some species of fish and invertebrates. Two species of suspension-feeding bivalves (mussels, Mytilus edulis; oysters, Crassostrea virginica) have been examined in this study, and results denoted that the aggregation process significantly improves by the uptake of 100 nm particles. It has also been declared that nanoparticles had a longer gut retention time when compared with 10-μm polystyrene beads. The data have shown that higher toxicological effects have been denoted by a higher intake of nanoparticles (Ward and Kach, 2009).

A recent study was focused on the extensive use of CuO-NPs in various industries and their wide range of applications have led to their accumulation in different ecological niches of the environment. This excess exposure raises concern about its potential toxic effects on various organisms including humans. The single acute dose (2000 mg/kg) and multiple-dose subacute (30, 300, and 1000 mg/kg daily for 28 days) oral toxicity studies of CuO-NPs in female albino Wistar rats following OECD guidelines 420 and 407, respectively, were conducted to declare the hazardous potential of CuO-NPs. There are numerous tests from blood analysis to histopathology of the tissues that were carried out. It was found that the higher dose treatments of the acute and subacute study caused significant alterations in biochemical and antioxidant parameters of the liver, kidney, and brain tissues of the rat. It was inferred from the results that the toxicity observed in the liver, kidney, and brain of treated rats could be due to the increased generation of reactive oxygen species by CuO-NPs. Results of this study leads to an inference that an oxidative stress condition might have occurred in the treated rat tissues due to enhanced ROS generation. Hence, this study concludes that short- and long-term toxicity studies are necessary for any novel nanomaterials before becoming commercialized (Bugata et al., 2019).

A recent study investigated the potential fetal toxic effects of Cu-NPs. Cu-NPs were orally administered to pregnant Sprague-Dawley rats from gestation days (GDs) 3–18 at a dose of 60, 120, and 180 mg/kg/day. During the fetal examination, no toxicities were observed regarding general clinical signs. However, Cu-NPs significantly decreased fetal body weight, body length, and liver weights. Cu ions and Cu macroparticles (MPs) exhibited similar effects on fetal development. The toxic effects of Cu-NPs on fetal development were mainly manifested as a decrease in fetal body weight, body length, and liver weight, and Cu ions and Cu-MPs exhibited similar effects. Cu-NPs also significantly decreased the level of Fe and total protein in the fetus. Oxidative stress and inflammatory responses were observed in the fetal liver, significantly different from the influence of Cu ions and Cu-MPs. In summary, Cu-NPs have negative effects on fetal organs, fetal development, and the nutritional intake of the fetus. Besides, findings indicated that Cu ions could cause damage in Cu-NP-treated fetuses, and this part of the toxic effect may be caused by the release of Cu ions from the Cu-NPs (Luo et al., 2020).

Some recent examples of the toxicity effect of copper nanoparticles as food and feed additives are presented in Table 4.

Table 4 Some recent examples of the toxicity effect of copper nanoparticles used as food and feed additives.

Nanoparticle	Toxicity	Reference
Cu-NPs	– Toxic effect on bacteria and fungi	Cioffi et al. (2005) Ruparelia et al. (2008) Ren et al. (2009)
	– Higher intake of nanoparticles from fish species shows higher toxicological effect	Ward and Kach (2009)
	– Highest dissolution (84.5%) in gastric conditions – Major effected organs are liver, kidney, and spleen	Lee et al. (2016)
	– RNS and ROS plays an important role in organic dysfunction – Toxic for mammals – Toxicity depend on sex – An adverse impact on algae (effects on growth, pigmentation, and oxidative stress response) – Cu ion exerts more harmful effect on the spermatozoa motility of sea trout than copper nanoparticles – -Oral toxicity studies of CuO-NPs in female albino Wistar rats highly observed in the liver, kidney, and brain of treated rats, which could be due to the increased generation of reactive oxygen species by CuO-NPs. – -Cu-NPs significantly decreased fetal body weight, body length, and liver weights. – -Cu-NPs also increased oxidative stress and inflammation in the fetus after pregnant rats were exposed to high doses of Cu-NPs. – Cu-NPs significantly induced oxidative stress and inflammatory responses in fetal liver. – Cu-NPs are toxic to fish health as these induced several adverse effects, including changes in the liver antioxidant enzyme activities, oxidative stress, marked histological and hematological alterations in *C. carpio*.	Hejazy et al. (2018) Wan et al. (2018) Kowalska-Góralska et al. (2019) Bugata et al. (2019) Luo et al. (2020) Noureen et al. (2018)

5.2 Regulations

The details about regulations are as follows. Firstly, the EUON (European Union Observatory for Nanomaterials) is mentioned. The definition of food, novel food, nanomaterials as food additives, labeling food containing engineered nanomaterials, nanomaterials in plastic food contact materials, and nanomaterials in active and intelligent food contact materials are briefly given. The second regulation is Novel Foods Regulation (EC) No 2015/2283, which is directly related to the food that is developed by using nanotechnology, where the risk assessments still need further development and studies. The third regulation is Food Additives Regulation (EC) No 1333/2008, which is considered food and feed additives, but it has still no certain solution or guide for nanoadditives side effects, usage procedure, and classification and safety requirements.

Moreover, the Food Safety Authority of Ireland (FSAI) has presented a report in 2010 to give some information about nanotechnology and food. In this report, food additives declared that their safety assessment must be done by the European Food Safety Authority (EFSA), before being added to the list of permitted additives. This term can be considered as a general and recent comment for nanoadditives, which is a gate for the novel food classification, identification, and assessment.

According to FAO/WHO, the potential implications of nanotechnologies on human health are still not clearly understood and many countries have emphasized the need for early consideration of the food safety implications of these technologies.

The research and development studies still ongoing:

- FAO/WHO has presented a technical paper entitled "State of the art on the initiatives and activities relevant to risk assessment and risk management of nanotechnologies in the food and agriculture sectors" (FAO/WHO, 2013).
- FAO and WHO held an Expert Meeting on the "Application of nanotechnologies in the food and agriculture sectors: potential food safety implications" (FAO/WHO, 2010).

In 2010, the Organization for Economic Co-operation and Development (OECD) Working Party on Nanotechnology (WPN) established a program, the goal of which was to contribute an inventory, summary, and overview of regulatory approaches, legislative regimes, and government-sponsored regulatory science research and other research programs, institutions, and infrastructure in foods and medical products that contain the application of nanotechnology. According to the OECD report, numerous legislations already exist, which also include nanomaterials as food additives in many countries from Australia to the United States (OECD, 2013). However, the uncertainties and drawbacks remain and need to be solved with detailed scientific research and development, which has to finalize the studies to cover all considerations with reliable lab-scale studies.

FDA (US Food & Drug Administration) has published "Guidance for Industry: Assessing the Effects of Significant Manufacturing Process Changes, Including Emerging Technologies, on the Safety and Regulatory Status of Food Ingredients and Food Contact Substances, Including Food Ingredients that Are Color Additives (2014) and Guidance for Industry Use of Nanomaterials in Food for Animals (2015),"

which cannot be declared as obligation or regulation. They are called as a suggestion for the industry. In the guidance, the safety term for novel nanomaterial as animal food additives has been given with the definition. If the novel food additive is not classified under the 'Guidance for Industry (GFI) #221, Recommendations for Preparation and Submission of Animal Food Additive Petitions,' it should consist of the scientific data fundamental to indicate the safety of the nanomaterial animal food additive for humans and target animals under the conditions of expected application.

6 Conclusion

Despite incredible improvements in nanoparticle production, there are still several main challenges, need to be solved precisely. The conclusion can be done by mentioning the novel benefits and considerations of scientific studies and regulatory studies to highlight the considerations of copper nanoparticles as food and feed additives. The benefits can be declared as improving food safety and shelf life of the product, improving functionality and bioavailability of nutrients, benefit on product quality and nutritional content, acting as a nutrient delivery system to transmit selected molecules directly to the selected places for nanotechnology, acting as an antimicrobial agent (specifically effective against Gram-positive and Gram-negative bacteria, yeast, and also plant pathogenic fungi), uniform coating and distribution ability, enhance nutrition, and productivity for nanoparticles (especially for copper nanoparticles). On the other hand, the considerations can be declared as potential to cause health considerations of exposure to the nanoparticles, not efficient analytical methods exist for nanoscale measurements specifically for microbial control and food safety, the environmental effect of nanoparticles were not extensively identified, uncertainties and the lack of toxicological data still existed, unclearness of significant and unpredictable bioavailability changes from the macro form into the nano form and finally some evidence was found that dietary nanoparticles uptake is directly related with some chronic diseases.

References

Adegbeye, M.J., Elghandour, M.M.M.Y., Barbabosa-Pliego, A., Monroy, J.C., Mellado, M., Reddy, P.R.K., Salem, A.Z.M., 2019. Nanoparticles in equine nutrition: mechanism of action and application as feed additives. J. Equine Vet. Sci. 78, 29–37.

Akbar, I., Jaswir, I., Jamal, P., Octavianti, F., 2017. Fish gelatin nanoparticles and their food applications: a review. Int. Food Res. J. 24, 255–264.

Al-Beitawi, N.A., Shaker, M.M., El-Shuraydeh, K.N., Blaha, J., 2017. Effect of nanoclay minerals on growth performance, internal organs and blood biochemistry of broiler chickens compared to vaccines and antibiotics. J. Appl. Anim. Res. 45, 543–549.

Ankireddy, K., Druffel, T., Vunnam, S., Filipič, G., Dharmadasa, R., Amos, D.A., 2017. Seed mediated copper nanoparticle synthesis for fabricating oxidation free interdigitated electrodes using intense pulse light sintering for flexible printed chemical sensors. J. Mater. Chem. C, 1–18. https://doi.org/10.1039/C7TC03522E.

Anyaogu, K.C., Fedorov, A.V., Neckers, D.C., 2008. Synthesis, characterization, and antifouling potential of functionalized copper nanoparticles. Langmuir 24, 4340–4346.

Arumugam, D.G., Sivaji, S., Dhandapani, K.V., Nookala, S., Ranganathan, B., 2019. Panchagavya mediated copper nanoparticles synthesis, characterization andevaluating cytotoxicity in brine shrimp. Biocatal. Agric. Biotechnol. 19, 101132.

Aschberger, K., Gottardo, S., Amenta, V., Arena, M., Moniz, F.B., Bouwmeester, H., Brandhoff, P., Mech, A., Pesudo, L.Q., Rauscher, H., Schoonjans, R., Vettori, M.V., Peters, R., 2015. Nanomaterials in food-current and future applications and regulatory aspects. J. Phys. Conf. Ser. 617, 012032.

Asghar, M.A., Zahir, E., Shahid, S.M., Khan, M.N., Asghar, M.A., Iqbal, J., Walker, G., 2018. Iron, copper and silver nanoparticles: green synthesis using green and black tea leaves extracts and evaluation of antibacterial, antifungal and aflatoxin B1 adsorption activity. LWT-Food Sci. Technol. 90, 98–107.

Asghar, M.A., Zahir, E., Asghar, M.A., Iqbal, J., Rehman, A.A., 2020. Facile, one-pot biosynthesis and characterization of iron, copper and silver nanoparticles using Syzygium cumini leaf extract: as an effective antimicrobial and aflatoxin B1 adsorption agents. PLoS One 15 (7). https://doi.org/10.1371/journal.pone.0234964, e0234964.

Azeredo, B.P., Sadhu, J., Ma, J., Jacobs, K., Kim, J., Lee, K., Ferreira, P., 2013. Silicon nanowires with controlled sidewall profile and roughness fabricated by thin-film dewetting and metal-assisted chemical etching. Nanotechnology 24, 225–305.

Azlin-Hasim, S., Cruz-Romero, M.C., Ghoshal, T., Morris, M.A., Cummins, E., Kerry, J.P., 2015. Application of silver nanodots for potential use in antimicrobial packaging applications. Innov. Food Sci. Emerg. Technol. 27, 136–143.

Baltic, M.Z., Boskovic, M., 2017. Nanotechnology: meat safety revolution. In: Prasad, R., Kumar, V., Kumar, M. (Eds.), Nanotechnology Food and Environmental Paradigm. Springer Nature Singapore Pte. Ltd, pp. 46–64, https://doi.org/10.1007/978-981-10-4678-0_3.

Bata-Vidács, I., Adányi, N., Beczner, J., Farkas, J., Székács, A., 2013. In: Méndez-Vilas, A. (Ed.), Nanotechnology and Microbial Food Safety, Microbial Pathogens and Strategies for Combating Them: Science, Technology And Education. © FORMATEX, pp. 155–169.

Bellmann, S., Carlander, D., Fasano, A., Momcilovic, D., Scimeca, J.A., Waldman, W.J., Gombau, L., Tsytsikova, L., Canady, R., Pereira, D.I.A., Lefebvre, D.E., 2015. Mammalian gastrointestinal tract parameters modulating the integrity, surface properties, and absorption of food-relevant nanomaterials. WIREs Nanomed. Nanobiotechnol. https://doi.org/10.1002/wnan.1333.

Bergin, I.L., Witzmann, F.A., 2013. Nanoparticle toxicity by the gastrointestinal route: evidence and knowledge gaps. Int. J. Biomed. Nanosci. Nanotechnol. 3 (1–2), 1–44.

Bertinato, J., L'Abbé, M.R., 2004. Maintaining copper homeostasis: regulation of copper-trafficking proteins in response to copper deficiency or overload. J. Nutr. Biochem. 15 (6), 316–322.

Bugata, L.S.P., Venkata, P.P., Gundu, A.R., Fazlur, R.M., Reddy, U.A., Kumar, J.M., Mekala, V.R., Bojja, S., Mahboob, M., 2019. Acute and subacute oral toxicity of copper oxide nanoparticlesin female albino Wistar rats. J. Appl. Toxicol. 39 (5), 702–716.

Bunglavan, S.J., Garg, A.K., Dass, R.S., Shrivastava, S., 2014. Use of nanoparticles as feed additives to improve digestion and absorption in livestock. Int. J. Livestock Res. 2 (3), 36–47.

Chandra, S., Kumar, A., Tomar, P.K., 2014. Synthesis and characterization of copper nanoparticles by reducing agent. J. Saudi Chem. Soc. 18, 149–153.

Chen, Z., Meng, H., Xing, G., Chen, C., Zhao, Y., 2007. Toxicological and biological effects of nanomaterials. Int. J. Nanotechnol. 4, 179–196.

Chudobova, D., Cihalova, K., Kopel, P., Melichar, L., Ruttkay-Nedecky, B., Vaculovicova, M., Adam, V., Kizek, R., 2015. Complexes of metal-based nanoparticles with chitosan suppressing the risk of Staphylococcus aureus and Escherichia coli infections. In: Nanotechnology in Diagnosis, Treatment and Prophylaxis of Infectious Diseases, pp. 217–232, https://doi.org/10.1016/b978-0-12-801317-5.00013-x.

Cioffi, N., Torsi, L., Ditaranto, N., Sabbatini, L., Zambonin, P.G., Tantillo, G., Ghibelli, L., D'Alessio, M., Bleve-Zacheo, T., Traversa, E., 2004. Antifungal activity of polymer-based copper nanocomposite coatings. Appl. Phys. Lett. 85, 2417–2419.

Cioffi, N., Torsi, L., Ditaranto, N., Tantillo, G., Ghibelli, L., Sabbatini, L., Bleve-Zacheo, T., D'Alessio, M., Zambonin, P.G., Traversa, E., 2005. Copper nanoparticle/polymer composites with antifungal and bacteriostatic properties. Chem. Mater. 17, 5255–5262.

Colvin, V.L., 2003. The potential environmental impact of engineered nanomaterials. Nat. Biotechnol. 21, 1166–1170.

Coutinho, T.C., Tardioli, P.W., Farinas, C.S., 2020. Hydroxyapatite nanoparticles modified with metal ions for xylanase immobilization. Int. J. Biol. Macromol. 150, 344–353.

Dawood, M.A.O., Eweedah, N.M., Moustafa, E.M., El-Sharawy, M.E., Soliman, A.A., Amer, A.A., Atia, M.H., 2020. Copper nanoparticles mitigate the growth, immunity, and oxidation resistance in common carp (Cyprinus carpio). Biol. Trace Elem. Res. 198, 283–292.

Donaldson, K., Borm, P.J., Castranova, V., Gulumian, M., 2009. The limits of testing particle-mediated oxidative stress in vitro in predicting diverse pathologies; relevance for testing of nanoparticles. Part. Fibre Toxicol. 6. https://doi.org/10.1186/1743-8977-6-13.

Duffy, C., O'Riordan, D., O'Sullivan, M., Jacquier, J.-C., 2018a. In vitro evaluation of chitosan copper chelate gels as a multimicronutrient feed additive for cattle. J. Sci. Food Agric. 98 (11), 4177–4183.

Duffy, L.L., Osmond-McLeod, M.J., Judy, J., King, T., 2018b. Investigation into the antibacterial activity of silver, zinc oxide and copper oxide nanoparticles against poultry-relevant isolates of Salmonella and Campylobacter. Food Control. https://doi.org/10.1016/j.foodcont.2018.05.008.

Dziechciarek, Y., Van Schijndel, R.J.G., Gotlieb, K.F., Feil, H., Van Soest, J.J.G., 1998. Development of Starchbased Nanoparticles: Structure, Colloidal and Rheological Properties. Presented at Meeting of Dutch Society of Rheology, Oct. 22.Ed. Prentice Hall, Upper Saddle River, NJ, p. 784.

Echiegu, E.A., 2017. Nanotechnology applications in the food industry. In: Prasad, R., Kumar, V., Kumar, M. (Eds.), Nanotechnology Food and Environmental Paradigm. Springer Nature Singapore Pte Ltd, pp. 154–171, https://doi.org/10.1007/978-981-10-4678-0_9.

Eguia, A.G., Fu, C.M., Lu, F.Y., Lien, T.F., 2009. Effects of nanocopper on copper availability and nutrients digestibility, growth performance and serum traits of piglets. Livest. Sci. 126, 122–129.

El Basuini, M.F., El-Hais, A.M., Dawood, M.A.O., Abou-Zeid, A.E.-S., EL-Damrawy, S.Z., Khalafalla, M.M.E.-S., Koshio, S., Ishikawa, M., Dossou, S., 2017. Effects of dietary copper nanoparticles and vitamin C supplementations on growth performance, immune response and stress resistance of red sea bream, Pagrus major. Aquacult. Nutr. 23, 1329–1340.

Eleftheriadou, M., Pyrgiotakis, G., Demokritou, P., 2017. Nanotechnology to the rescue: using nano-enabled approaches in microbiological food safety and quality. Curr. Opin. Biotechnol. 44, 87–93.

El-kazaz, S.E., Hafez, M.H., 2020. Evaluation of copper nanoparticles and copper sulfate effect on immune status, behavior, and productive performance of broilers. J. Adv. Vet. Anim. Res. 7 (1), 16–25.

Esteban-Tejeda, L., Malpartida, F., Esteban-Cubillo, A., Pecharrom'an, J., Moya, J.S., 2009. Antibacterial and antifungal activity of a soda-lime glass containing copper nanoparticles. Nanotechnology 20 (505701), 1–6.

European Commission, 2009. Regulation (EC) no 1223/2009 of the European Parliament and the council of 30 November 2009 on cosmetic products. Off. J. Eur. Union 342, 59.

FAO/WHO, 2010. Expert Meeting on the Application of Nanotechnologies in the Food and Agriculture Sectors: Potential Food Safety Implications Meeting Report. FAOand WHO, Rome.

FAO/WHO, 2013. State of the Art on the Initiatives and Activities Relevant to Risk Assessment and Risk Management of Nanotechnologies in the Food and Agriculture Sectors. FAO/WHO technical paper, FAOand WHO, Rome.

Fondevila, M., Herrer, R., Casallas, M.C., Abecia, L., Ducha, J.J., 2009. Silver nanoparticlesas a potential antimicrobial additive for weaned pigs. Anim. Feed Sci. Technol. 150, 259–269.

Food Safety Authority of Ireland, 2008. The Relevance of Food Safety of Applications of Nanotechnology in the Food and Feed Industries. Court lower abbey street, Abbey, Dublin, p. 1. www.fsai.ie.

FSAI, 2008. Zoonotic Tuberculosis and Food Safety, first ed. Food Safety Authority of Ireland, Dublin, Ireland.

Gangadoo, S., Stanley, D., Hughes, R.J., Moore, R.J., Chapman, J., 2016. Nanoparticles in feed: Progress and prospects in poultry research. Trends Food Sci. Technol. 58, 115–126.

Ghoshal, T., Shaw, M.T., Bolger, C.T., Holmes, J.D., Morris, M.A., 2012. A general method for controlled nanopatterning of oxide dots: a microphase separated block copolymer platform. J. Mater. Chem. 22 (24), 12083–12089.

Ghoshal, T., Shaw, M.T., Bolger, C.T., Holmes, J.D., Morris, M.A., 2013. Size and space controlled hexagonal arrays of superparamagnetic iron oxide nanodots: magnetic studies and application. Sci. Rep. 3 (2772), 1–8.

Gopi, M., Pearlin, B., Kumar, R.D., Shanmathy, M., Prabakar, G., 2017. Role of nanoparticles in animal and poultry nutrition: modes of action and applications in formulating feed additives and food processing. Int. J. Pharm. 13 (7), 724–731.

Hannon, J.C., Kerry, J.P., Cruz-Romero, M., Azlin-Hasim, S., Morris, M., Cummins, E., 2016. Human exposure assessment of silver and copper migrating from an antimicrobial nanocoated packaging material into an acidic food simulant. Food Chem. Toxicol. https://doi.org/10.1016/j.fct.2016.07.004.

Hejazy, M., Koohi, M.K., Pour, A.B.M., Najaf, D., 2018. Toxicity of manufactured copper nanoparticles—a review. Nanomed Res J. 3 (1), 1–9.

Hett, A., 2004. Nanotechnology: Smart Matter, Many Unknowns. Swiss Reinsurance Co, Zurich, p. 55.

Huang, Y., Chen, S., Bing, X., Gao, C., Wang, T., Yuan, B., 2011. Nanosilver migrated into food-simulating solutions from commercially available food fresh containers. Packag. Technol. Sci. 24 (5), 291–297.

Huang, J.-Y., Li, X., Zhou, W., 2015. Safety assessment of nanocomposite for food packaging application. Trends Food Sci. Technol. https://doi.org/10.1016/j.tifs.2015.07.002.

Kaninnen, P., Johans, C., Merta, J., Kontturi, K., 2008. Influence of ligand structure on the stability and oxidation of copper nanoparticles. J. Colloid Interface Sci. 318, 88–95.

Khan, A., Rashid, A., Younas, R., Chong, R., 2016. A chemical reduction approach to the synthesis of copper nanoparticles. Int. Nano Lett. 6, 21–26. https://doi.org/10.1007/s40089-015-0163-6.

Khare, P., Sharma, A., Verma, N., 2014. Synthesis of phenolic precursor-based porous carbon beads in situ dispersed with copper-silver bimetal nanoparticles for antibacterial applications. J. Colloid Interface Sci. 418, 216–224.

Kowalska-Góralska, M., Dziewulska, K., Kulasza, M., 2019. Effect of copper nanoparticles and ions on spermatozoa motility of sea trout (Salmo trutta m. Trutta L.). Aquat. Toxicol. 211, 11–17.

Landsiedel, R., Fabian, E., Ma-Hock, L., van Ravenzwaay, B., Wohlleben, W., Wiench, K., Oesch, F., 2012. Toxico-/biokinetics of nanomaterials. Arch. Toxicol. 86, 1021–1060.

Lee, I.-C., Ko, J.-W., Park, S.-H., Lim, J.-O., Shin, I.-S., Moon, C., Kim, S.-H., Heo, J.-D., Kim, J.-C., 2016. Comparative toxicity and biodistribution of copper nanoparticles and cupric ions in rats. Int. J. Nanomedicine 11, 2883–2900.

Lefebvre, D.E., Venema, K., Gombau, L., Valerio Jr., L.G., Raju, J., Bondy, G.S., Bouwmeester, H., Singh, R.P., Clippinger, A.J., Collnot, E.M., Mehta, R., Stone, V., 2015. Utility of models of the gastrointestinal tract for assessment of the digestion and absorption of engineered nanomaterials released from food matrices. Nanotoxicology 9 (4), 523–542.

Liu, G., Li, X., Qin, B., Xing, D., Guo, Y., Fan, R., 2004. Investigation of the mending effect and mechanism of copper nano-particles on a tribologically stressed surface. Tribol. Lett. 17 (4), 961–966.

Llorens, A., Lloret, E., Picouet, P.A., Trbojevich, R., Fernandez, A., 2012. Metallic-based micro and nanocomposites in food contact materials and active food packaging. Trends Food Sci. Technol. 24, 19–29.

Lomer, M.C., Thompson, R.P., Powell, J.J., 2002. Fine and ultrafine particles of the diet: influence on the mucosal immune response and association with Crohn's disease. Proc. Nutr. Soc. 61, 123–130.

Luo, J., Hao, S., Zhao, L., Shi, F., Ye, G., He, C., Lin, J., Zhang, W., Liang, H., Wang, X., Guo, H., He, R., Tang, H., Li, Y., 2020. Oral exposure of pregnant rats to copper nanoparticles caused nutritionalimbalance and liver dysfunction in fetus. Ecotoxicol. Environ. Saf. 206, 111206.

Lynch, I., Cedervall, T., Lundqvist, M., Cabaleiro-Lago, C., Linse, S., Dawson, K.A., 2007. The nanoparticle protein complex as a biological entity; a complex fluids and surface science challenge for the 21st century. J. Colloid Interface Sci. 134-135, 167–174.

Majzlik, P., Strasky, A., Nemec, M., Trnkova, L., Havel, L., Zehnalek, J., Babula, P., Kizek, R., 2010. Remediation potential of bacteria for removing heavy metals from environment. Listy Cukrov. Reparske. 126, 414–415.

Majzlik, P., Strasky, A., Adam, V., Nemec, M., Trnkova, L., Zehnalek, J., Hubalek, J., Provaznik, I., Kizek, R., 2011. Influence of zinc (II) and copper (II) ions on Streptomyces bacteria revealed by electrochemistry. Int. J. Electrochem. Sci. 6, 2171–2191.

Martirosyan, A., Schneider, Y.-J., 2014. Engineered nanomaterials in food: implications for food safety and consumer health. Int. J. Environ. Res. Public Health 11, 5720–5750. https://doi.org/10.3390/ijerph110605720.

Mehdizadeh, T., Zamani, A., Froushani, S.M.A., 2020. Preparation of cu nanoparticles fixed on cellulosic walnut shell material and investigation of its antibacterial, antioxidant and anticancer effects. Heliyon 6, e03528.

Morsy, E.A., Hussien, A.M., Ibrahim, M.A., Farroh, K.Y., Hassanen, E.I., 2021. Cytotoxicity and genotoxicity of copper oxide nanoparticles in chickens. Biol. Trace Elem. Res. https://doi.org/10.1007/s12011-021-02595-4.

Mroczek Sosnowska, N., Łukasiewicz, M., Wnuk, A., Sawosz, E., Niemiec, J., Skot, A., Jaworski, S., Chwalibog, A., 2016. In ovo administration of copper nanoparticles and copper sulfate positively influences chicken performance. J. Sci. Food Agric. 96 (9), 3058–3062.

Nakhjavani, M., Nikkhah, V., Sarafraz, M.M., Shoja, S., Sarafraz, M., 2017. Green synthesis of silver nanoparticles using green tea leaves: experimental study on the morphological, rheological and antibacterial behaviour. Int. J. Heat Mass Transf., 1–9.

Newell, R.I.E., Fisher, T.R., Holyoke, R.R., Cornwell, J.C., 2005. Influence of eastern oysters on nitrogen and phosphorus regeneration in Chesapeake Bay, USA. In: Dame, R.F., Olenin, S. (Eds.), The Comparative Roles of Suspension-Feeders in Ecosystems. Springer, Dordrecht, The Netherlands, pp. 93–120.

Noureen, A., Jabeen, F., Tabish, T.A., Yaqub, S., Ali, M., Chaudhry, A.S., 2018. Assessment of copper nanoparticles (Cu-NPs) and copper (II) oxide (CuO) induced hemato- and hepatotoxicity in *Cyprinus carpio*. Nanotechnology, 1–25. https://doi.org/10.1088/1361-6528/aaaaa7.

OECD, 2013. Regulatory Frameworks for Nanotechnology in Foods and Medical Products: Summary Results of a Survey Activity, OECD Science, Technology and Industry Policy Papers, No. 4, OECD Pub. Paris., https://doi.org/10.1787/5k47w4vsb4s4-en.

Onuegbu, C.U., Aggarwal, A., Singh, N.B., 2018. ZnO nanoparticles as feed supplement on growth performance of cultured African catfish fingerlings. J. Sci. Ind. Res. 77, 213–218.

Ötleş, S., Şahyar Yalçın, B., 2016. In: Gurumezescu, A.M. (Ed.), Protein-based dietary supplements as nutraceuticals, nutraceuticals, nanotechnology. Agri-food industry, Elsevier Inc, pp. 761–781.

Otles, S., Sahyar Yalcin, B., 2017. Nanotechnology and shelf-life of animal foods. In: Prasad, R., Kumar, V., Kumar, M. (Eds.), Nanotechnology Food and Environmental Paradigm. Springer Nature Singapore Pte Ltd, pp. 35–43, https://doi.org/10.1007/978-981-10-4678-0_2.

Otles, S., Sahyar Yalcin, B., 2018. Nanotechnology application and emergence in agriculture. In: Singh, H.B., Fraceto, L.F., de Lima, R. (Eds.), Emerging Trends in Agri-nanotechnology. CAB International, pp. 204–213. J Fundam Appl Sci.

Özer, E.A., Özcan, M., Didin, M., 2014. Nanotechnology in food and agriculture industry. In: Malik, A., et al. (Eds.), Food Processing: Strategies for Quality Assessment, Food Eng. Series. Springer, https://doi.org/10.1007/978-1-4939-1378-7_19.

Perelshtein, I., Applerot, G., Perkas, N., Wehrschuetz-Sigl, E., Hasmann, A., Guebitz, G., Gedanken, A., 2009. CuO–cotton nanocomposite: formation, morphology, and antibacterial activity. Surf. Coat. Technol. 204, 54–57.

Peters, R., Brandhoff, P., Weigel, S., Marvin, H., Bouwmeester, H., Aschberger, K., Rauscher, H., Amenta, V., Arena, M., Botelho Moniz, F., Gottardo, S., Mech, A., 2014. Inventory of Nanotechnology Applications in the Agricultural, Feed and Food Sector. EFSA Supporting Publ, p. 11.

Powara, N.S., Patel, V.J., Pagare, P.K., Pandav, R.S., 2019. Cu nanoparticle: synthesis, characterization and application. Chem. Methodol. 3, 457–480.

Rajput, N., 2015. Methods of preparation of nanoparticles—a review. Int. J. Adv. Eng. Tech. 7 (4), 1806–1811.

Ren, G., Hu, D., Cheng, E.W.C., Vargas-Reus, M.A., Reip, P., Allaker, R.P., 2009. Characterization of copper oxide nanoparticles for antimicrobial applications. Int. J. Antimicrob. Agents 33, 587–590.

Royal Society and Royal Academy of Engineering, 2004. Nanoscience and Nanotechnologies: Opportunities and Uncertainties. Royal Society Policy Document 19/04. The Royal Society, London, p. 113.

Ruparelia, J., Chatterjee, A., Duttagupta, S., Mukherji, S., 2008. Strain specificity in antimicrobial activity of silver and copper nanoparticles. Acta Biomater. 4, 707–716.

Saranyaadevi, K., Subha, V., Ernest Ravindran, R.S., Renganathan, S., 2014. Synthesis and characterization of copper nanoparticle using *Capparis Zeylanica*leaf extract. Int. J. Chem. Tech. Res. 6 (10), 4533–4541.

Schmidt, C.W., 2009. Nanotechnology-related environment, health and safety research: examining the national strategy. Environ. Health Perspect. 117, 158–161.

Scott, A., Vadalasetty, K.P., Chwalibog, A., Sawosz, E., 2018. Copper nanoparticles as an alternative feed additive in poultry diet: a review. Nanotechnol. Rev. 7 (1), 69–93.

Senthilkumar, S.R., Sivakumar, T., 2014. Green tea (*Camellia sinensis*) mediated synthesis of zinc oxide (ZNO) nanoparticles and stu.dies on their antimicrobial activities. Int. J. Pharm. Pharm. Sci. 6 (6), 461–465.

Senturk, A., Yalcin, B., Otles, S., 2013. Nanotechnology as a food perspective. J. Nanomater. Molec. Nanotech. 2 (6), 1–8.

Seregina, T., Chernikova, O., Mazhaysky, Y., Ampleeva, L., 2020. Features of the influence of copper nanoparticles and copper oxide on the formation of barley crop. Agron. Res. 18 (1), 1010–1017.

Servin, A.D., White, J.C., 2016. Nanotechnology in agriculture: next steps for understanding engineered nanoparticle exposure and risk. NanoImpact 1, 9–12.

Sharif, M., Rahman, M.A., Ahmed, B., Abbas, R.Z., Hassan, F., 2020. Copper nanoparticles as growth promoter, antioxidant and anti-bacterial agents in poultry nutrition: prospects and future implications. Biol. Trace Elem. Res. https://doi.org/10.1007/s12011-020-02485-1.

Shi, L., Xun, W., Yue, W., Zhang, C., Ren, Y., Quiang, L., Wang, Q., Shi, L., 2011. Effect of elemental nano-selenium on feed digestibility, rumen fermentation and purine derivatives in sheep. Anim. Feed Sci. Technol. 163, 136–142.

Silvestre, C., Duraccio, D., Cimmino, S., 2011. Food packaging based on polymer nanomaterials. Prog. Polym. Sci. 36, 1766–1782.

Singh, P.K., 2016. Use of nano feed additives in livestock feeding. Int. J. Livest. Res. 6 (1), 1–14.

Sizentsov, A.N., Kvan, O.V., Miroshnikova, E.P., Gavrish, I.A., Serdaeva, V.A., Bykov, A.V., 2018. Assessment of biotoxicity of Cu nanoparticles with respect to probiotic strains of microorganisms and representatives of the normal flora of the intestine of broiler chickens. Environ. Sci. Pollut. Res. 25, 15765–15773. https://doi.org/10.1007/s11356-018-1761-4.

Sizova, E., Miroshnikov, S., Lebedev, S., Usha, B., Shabunin, S., 2020. Use of nanoscale metals in poultry diet as a mineral feed additive. Anim. Nutr. 6 (2), 185–191.

Stanley, S.L., Dorris, L.L., 2000. Glyconutrionals: implications in antimicrobial activity. GlycoSci. 1, 1–4.

Stoimenov, P.K., Klinger, R.L., Marchin, G.L., Klabunde, K.J., 2002. Metal oxide nanoparticles as bactericidal agents. Langmuir 17, 6679–6686.

Sutradhar, P., Saha, M., Maiti, D., 2014. Microwave synthesis of copper oxide nanoparticles using tea leaf and coffee powder extracts and its antibacterial activity. J Nanostructure Chem. 4 (1), 1–6.

Tang, H., Xu, M., Luo, J., Zhao, L., Ye, G., Shi, F., Lv, C., Chen, H., Wang, Y., Li, Y., 2019. Liver toxicity assessments in rats following sub-chronic oral exposure to copper nanoparticles. Environ. Sci. Eur. 31, 30. https://doi.org/10.1186/s12302-019-0214-0.

Taylor, S., Qu, L., Kitaygorodskiy, A., Teske, J., Latour, R.A., Sun, Y.P., 2004. Synthesis and characterization of peptide-functionalized polymeric nanoparticles. Biomacromolecules 5, 245–248.

Thangapandiyan, S., Monika, S., 2020. Green synthesized zinc oxide nanoparticles as feed additives to improve growth, biochemical, and hematological parameters in freshwater fish *Labeo rohita*. Biol. Trace Elem. Res. 195, 636–647. https://doi.org/10.1007/s12011-019-01873-6.

Thulasi, A., Rajendran, D., Jash, S., Selvaraju, S., Lyju Jose, V., Velusamy, S., Mathivanan, S., 2013. Nanobiotechnology in animal nutrition. In: Sampath, K.T., Ghosh, J. (Eds.), Animal Nutrition and Reproductive Physiology (Recent Concepts), 1st ed. Satish Serial Publishing House, pp. 499–516.

Trujillo, L.E., Ávalos, R., Granda, S., Guerra, L.S., País-Chanfrau, J.M., 2016. Nanotechnology applications for food and bioprocessing industries. Biol. Med. (Aligarh) 8, 289. https://doi.org/10.4172/0974-8369.1000289.

Umer, A., Naveed, S., Ramzan, N., Rafique, M.S., Imran, M., 2014. A green method for the synthesis of copper nanoparticles using L-ascorbic acid. Rev. Matér. 19 (3), 197–203.

Usman, M.S., Zowalaty, M.E.E., Shameli, K., Zainuddin, N., Salama, M., Ibrahim, N.A., 2013. Synthesis, characterization, and antimicrobial properties of copper nanoparticles. Int. J. Nanomedicine 8, 4467–4479.

Wan, J.-K., Chu, W.-L., Kok, Y.-Y., Cheong, K.-W., 2018. Assessing the toxicity of copper oxide nanoparticles and copper sulfate in a tropical Chlorella. J. Appl. Psychol. 30, 3153–3165.

Wang, B., Feng, W.W., Wang, M., Wang, T., Gu, Y., Zhu, M., Ouyang, H., Shi, J., Zhang, F., Zhao, Y., Chai, Z., Wang, H., Wang, J., 2007. A cute toxicological impact of nano- and submicro-scaled zinc oxide powder on healthy adult mice. J. Nanopart. Res. 10 (2), 263–276.

Ward, J.E., Kach, D.J., 2009. Marine aggregates facilitate ingestion of nanoparticles by suspension-feeding bivalves. Mar. Environ. Res. 68, 137–142.

Yoon, K.-Y., Byeon, J.H., Park, J.-H., Hwang, J., 2007. Susceptibility constants of Escherichia coli and Bacillus subtilis to silver and copper nanoparticles. Sci. Total Environ. 373, 572–575.

Yusof, H.M., Mohamad, R., Zaidan, U.H., Rahman, N.A., 2019. Microbial synthesis of zinc oxidenanoparticles and their potentialapplication as an antimicrobial agent and afeed supplement in animal industry: a review. J. Anim. Sci. Biotechnol. 10, 57. https://doi.org/10.1186/s40104-019-0368-z.

Zietz, B., Dieter, H., Lakomek, M., Schneider, H., Keslergaedtke, B., Dunkelberg, H., 2003. Epidemiological investigation on chronic copper toxicity to children exposed via the public drinking water supply. Sci. Total Environ. 302 (1–3), 127–144.

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PART

Agroecosystem applications

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CHAPTER

Cu-based nanomaterials for production of novel agrochemicals

22

Manviri Rani[a], Keshu[b], and Uma Shanker[b]

[a]*Malaviya National Institute of Technology, Jaipur, Rajasthan, India*

[b]*Dr B R Ambedkar National Institute of Technology, Jalandhar, Punjab, India*

1 Introduction

Agrochemicals are numerous chemical products widely utilized in agriculture to increase plant and animal crop production, for example, synthetic fertilizers, liming and acidifying agents, soil conditioners, pesticides, and herbicides, as well as chemicals utilized in the raising of livestock, such as antibiotics and hormones. Primarily, agrochemicals are connected to the different classes of pesticide chemicals including insecticides, herbicides, fungicides, and nematicides. Agrochemicals may have both an inorganic and organic chemical composition/structure. Hydrocarbons, having halogens, are extensively used as pesticides and herbicides, which include hexachlorocyclohexanes, dichlorodiphenyltrichloroethane, endosulfan isomers, ethylene dibromide, and CH_3Cl (Yeganeh et al., 2021). Agrochemicals may also damage the environment due to their inherent toxicity caused by lingering persistence and bioaccumulation/biomagnifications in the food chain, as well as accidental spills. Accumulation of halogenated pesticides and residual pesticides cause ecological and health problems such as rising neurological diseases and cancer among humans (Richter et al., 1992; Saunders et al., 2012; Kaushal et al., 2021). Excessive utilization of fertilizers results in natural water contaminated with a large concentration of nitrate, which is toxic for living creatures. Moreover, the discharge of fertilizers into lakes and rivers can enhance the growth of algae, which can badly affect the life cycle of fish and other aquatic life. Hence, the use of agrochemicals in many countries is regulated by the government, and special permission is required for purchase. Strict restrictions can result from misuse and improper storage, due to which several leakage accidents have taken place. During the utilization of these chemicals, appropriate storage and labeling systems, emergency cleanup apparatus, and clearance are frequently subjected to compulsory standardized regulations.

Besides the advantageous result in crop production, intensive agrotechnical practice results in the accumulation of poisonous chemicals in several ecosystems that then accumulates into plant tissue (Pajević et al., 2018). Hence, the main sink for pollutant accumulation is soil, by which a pollutant enters surface water or goes into

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the various parts of edible plants via leaching (Saxena et al., 2019). However, these persistent agrochemicals remain in the soil for a longer time due to intensive use. The accumulation of hazardous and toxic chemicals substances such as pesticides, heavy metals (Cr, Cd, Hg, As), dyes, phenols, and radionuclides into the environment is a concerning problem due to their possibly unfavorable influence on living organisms. The World Health Organization claims that approximately 3 million people are annually affected by poisonous pesticides either directly or indirectly (Nayak et al., 2018). Various types of molecules (lipid-soluble) such as herbicides and pesticides, which can remain in the body of biological organisms for a long time, can affect vital organs, resulting in severe health-related problems, as well as attacking and damaging the central nervous system (Rawtani et al., 2018; Tyagi et al., 2021).

Due to extensive use and toxic effects, coupled with the potential of bioaccumulation, the removal of these agrochemicals is mandated by low-cost and efficient advanced materials. Table 1 contains a list of various accidents that happened due to agrochemicals. Nanomaterials with high surface potential, particularly self-organization and interparticle aggregation, are now being applied in several fields including remediation techniques (Manav et al., 2018).

Nanotechnology utilizes nanoparticles in different ways (adsorption on surface, absorption of energy, reactions with chemical, photo-based catalysis, and filtration via pores) for removal of various pollutants present in our environment (Prasad et al., 2017). Different types of nanomaterials, such as carbon-based, inorganic, and polymeric, are used for environmental remediation. Unique surface chemistry can be generated on nanoparticles for target-specific agrochemicals such as functionalized or grafted with different types of functional groups (Prasad et al., 2017). Hence, it is proved that the arrival of nanomaterial-based technology may provide a path for sorting out various problems in the field of agriculture like cleanup of soil and aquatic bodies, as well as good fertilizer management.

Presently, various reports explain that diverse types of nanomaterials such as nanotechnology-based sensors, nanotubes, and nanocomposites can be widely utilized for identification, modification, and degradation of many pesticides (Rawtani et al., 2018; Rani et al., 2021). TiO_2 has a large band gap of ~ 3.4 eV and is one of the most explored semiconductors in advanced oxidation processes (AOPs) under an ultraviolet radiation source because of its suitable properties. To make AOPs cost-effective and eco-friendly, the development of sunlight or visible light-responsive semiconductors as photocatalysts are needed. Several semiconductors (SnO, iron oxides like Fe_2O_3 and Fe_3O_4, sulfides of Zn and Cd, ZrO_2, WO_3, and $SrTiO_3$) have been developed and investigated in place of titanium oxide and ZnO. Moreover, the main problems that arise with such semiconductors is their solubility in water and toxicity. Moreover, excessive use of these materials should be controlled via the use of alternative nanoparticles. Cu-based nanomaterials (CuO: band gap 1.2 eV) are being developed and used for several applications including treatment of organic pollutants. Khalaj et al. (2018) reviewed Cu-based nanomaterials for environmental decontamination by organic dyes and other inorganic contents, also discussing their technical and toxicological aspects. Cu is one of the most common metals found in

Table 1 Some important agrochemical-related accidents.

Pesticide	Place	Year	Causes	References
Parathion	Kerala, India	1958	Contaminated food due to leakage	Rani (2012)
	Bombay, India	1962	Inhalation in manufacturing plant	
HCH	Bombay, India	1963	Contaminated rice	
Endrin	Bombay, India	1964	Contaminated food	
DDT	Punjab, India	1965	Contaminated chutney	
Diazinon	Pune, India	1968	Contaminated food	
HCH	UP, India	1976	Mixed with wheat	
Endrin	Karnataka, India	1977	Contaminated crabs in rice field	
Aluminum phosphide	Rajasthan, India	1983	Contaminated food grain	
Methyl isocyanate	Bhopal, India	1984	Storage tank leakage	
Cartap hydrochloride	Tamil Nadu, India	1988	Factory workers	
Endosulfan	Kerala India	1997	Contamination due to aerial spray of endosulfan	
Phorate	Kerala, India	2001	Spray drift from banana field	
Endosulfan	MP, India	2002	Contaminated wheat flour	
2,3,7,8-Tetrachlorobenzo-10-dioxin (TCDD)	Seveso, Italy	1976	Air pollution due to poisonous gas of TCDD	De (2010)
Paraquat	Japan	1985	Mass poisoning	Nagami (2010)
Sarin		1995		
Pesticides	United States	1968–78	Contaminated food	Laseter (1979)

the form of oxides, hydroxides, etc. Cu-based chalcogenides containing metal atoms with relatively high earth-abundances are also in use because of their minimum toxicity compared with that of other heavy metal (Pb, Cd, and As)-based nanomaterials. They have versatile composition, structures, and stoichiometry and have many non-stoichiometric phases. Copper is a significant important material due to its peculiar chemical, electrical, optical, and thermal characteristics. The literature reports the narrow band gap of CuO and Cu_2O are good p-type semiconductors (Isherwood, 2017). These important characteristics of Cu-containing nanomaterials prompted their use in heterogeneous-based diverse catalytic processes such as the transformation of energy (Cu_2O: band energy of 2.0 eV) (Ke et al., 2014; Zhang et al., 2015), lithium-ion electrode systems, and biosensing in various claims related to biological systems (Etefagh et al., 2013; Razeeb et al., 2014). Copper-based nanoparticle application in the environmental field is quite an amazing category that presently attracts researchers. In this chapter, we reviewed the outcomes of nanomaterials in the extermination of agrochemicals present in the environment, especially with regard to Cu-based nanoparticles like copper oxide, copper hexacyanoferrate, CuS, and copper ternary disulfide. Types of agrochemicals have been quarantined including the classifications of pesticides. Different types of nanoparticles with Cu constituents have been introduced. Environmental health and safety aspects were also detailed while considering the toxicity of Cu-based nanoparticles on exposure both in vitro and in vivo on terrestrial organisms and humans. Because of environmental safety, a green process containing biogenic source like plants, enzymes, or biotemplates should be promoted for the synthesis of nanoparticles. Green-synthesized, copper-based nanomaterials' potential are also discussed. Moreover, green-synthesized particles are safe, biocompatible, and sustainable due to the higher efficiency of nanoparticles over nanomaterials synthesized from conventional or chemical processes. Various methods used for the synthesis of copper-based nanomaterials are presented in Fig. 1.

2 Environmental concerns of agrochemicals

Pollutants such as dyes, pesticides, polyaromatic hydrocarbons, phenols, etc. are causing major environmental concerns because of their toxicity (Kuroda et al., 1992). Among the agrochemicals that pose extreme threats to the environment are pesticides, agricultural chemicals, industry group formulates, NO_3^-, and biocide leftovers. The rapid growth in the worldwide population has led to intensive utilization of synthetic pesticides (15 kg ha^{-1}) based on stage and different categories of trees/crops (Ericksen, 2008). Only 10%–15% of pesticides reach their target once used on crops/plants; the rest remains unused and persists in the environment (Cahill et al., 2011). Nearly 220,000 deaths were reported by WHO due to the consumption of cheap and banned pesticide chemicals due to poverty. The availability of banned pesticides in the environment is due to their longer half-lives and illegal use. Kafilzadeh (2015) reported a high concentration of pesticides: 0.075 ppb (water), 8.750 ppb (sediment), and 4.446 ppb (fish) (Zhou et al., 2001).

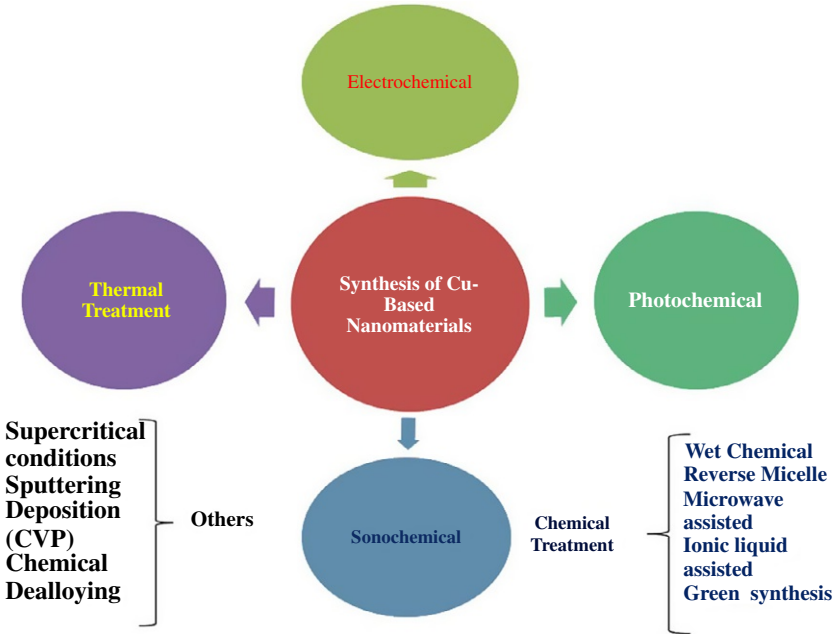

FIG. 1

Various methods used for synthesis of copper-based nanomaterials.

Moreover, the quantity of yearly used pesticides is nearly 1% for North America and 0.1% for the remaining countries (Gavrilescu, 2005). The residual pesticides remaining in farmed soils and runoff discharged to environmental bodies might cause negative effects on the environment and living creatures (Parrón et al., 2014; Van Toan et al., 2013). Presently, As (arsenic) contamination in groundwater is a serious health problem in Asia. In the Philippines, nitrate pollution in the groundwater in cropping of rice-based systems surpassed the limit of 10 mg L^{-1} for pure consumable water alone due to applications of fertilizers on a large amount of vegetables in the cropping structure (Bouman et al., 2002). In the Punjab state of India, the amount of nitrate increased by almost 2 mg L^{-1} between 1982 and 1988, while the use of nitrogen nourishment increased by approximately 60–190 kg ha^{-1}, mostly in rice-wheat cultivation (Singh et al., 1991). The negative effect on human health, mainly in children, may cause the blood disorder methemoglobinemia. The mean amount of biocide used regularly in rice crops changes from place to place globally depending on requirement (for example, 0.4 kg ha^{-1} in Tamil Nadu, India, and 3.8 kg ha^{-1} in China) (Bouman et al., 2002). A study from the Philippines revealed that the mean biocide amount in groundwater in the presence of irrigated-rice cropping was in range of 0.1 and 0.5 μg L^{-1}, which is a magnitude below biocide limits. Although, the observance of a temporary presence of high concentration (1.14–4.17 μg L^{-1}) cannot be avoided (Bouman et al., 2002). Farmers and their family members consuming

wastewater frequently suffer from health-related problems. Some traditional pesticides, for example, DDT insecticide has shown high persistence in biota for a longer time in contaminated groundwater, food, flora, and fauna. However, among various carcinogenic pesticides that have been banned, some new and modified pesticides still cause serious environmental problems.

Presently, awareness has increased among people related to the health risk arising due to pesticides and similar chemicals. Safe control and precaution are being considered when using those hazardous pesticide products.

3 Classification of pesticides

Most pesticides can be categorized as insecticides, herbicides, or fungicides. The list of majorly used pesticides and necessary compounds are arsenates, agricultural disinfectants, pesticides and arsenites, sheep dips, cattle dips, Bordeaux mixture, growth regulators, DDT, lindane, herbicides, fungicides, insecticides, agricultural and household poison, phytoactin, etc.

3.1 Herbicides

The largest used category of pesticides all over the worldwide is herbicides. Herbicides comprise 50% of the aggregate global usage of pesticide. Herbicides are mainly utilized in crops for the prevention of a large number of weeds and other undesirable plants.

3.2 Insecticides

This is the second major class of pesticides utilized in the biosphere such as organochlorines (DDT and chlordane), carbamates (carbaryl), organophosphates (parathion and diazinon), and pyrethroids (natural and synthetic). Nevertheless, the same assets by which those chemicals became popular resulted in their elimination from the marketplace due to very toxic properties. To reduce the toxic character of these compounds, a new modified series named pyrethroids were synthesized to displace them. The chemical compounds obtained from plants are called natural pyrethroids, which are present in the *Chrysanthemum*.

3.3 Fungicides

Fungicides are globally used for crop protection from different types of pathogenic fungi. The most applicable fungicides are halogenated compounds, organophosphates, dithiocarbamates, and carbamates.

3.4 Biological pesticides

A less-explored category of pesticides is biopesticides that are obtained from bioorganisms (plants, viruses or fungi, and bacteria). Biochemicals like plant growth

controllers, insect sexual attractants, and hormones are functionalized by mode of action. These biopesticides show very little risk to humans or the environment.

4 Photocatalysis

Water pollution has rapidly increased, thus the phenomenon of photocatalysis has gained massive popularity for the cleanup of a contaminated environment because of its eco-friendly and cost-effective advantages over other wastewater treatment procedures. Heterogeneous processes dominate over others due to the easy separating phenomenon of the catalyst from reaction vessel. Nanomaterial semiconductors, by appropriate band gaps, have been used for efficient production of electrons upon exposure to a light source (UV or visible) of a specific wavelength, which upon interaction with water molecules form reactive species and convert organic pollutants into nontoxic metabolites through photo-oxidation or photoreduction (Lavand and Malghe, 2015; Yasmina et al., 2014). Nanomaterials play a significant role in photocatalysis where they lead to hydrolysis or redox reactions, resulting in the removal of organic contaminants (Nazim et al., 2021). For an efficient catalyst suitable in AOPs, the nanomaterial should be easily obtainable, cost-effective, less toxic, chemically inert, and stable with photocatalytic potential.

Nanomaterials of various transition metal oxides and sulfides have been reported as outstanding photocatalysts with peculiar properties (morphology, smaller size, better adsorbing efficiency) and proven as a good emerging destructive technique. Due to the inherent destructive property, the phenomenon of mass transfer does not take place and the process can be done in the presence of ambient conditions by using the oxygen present in atmosphere as an oxidant. To enhance the degradation rate, the particle size of the catalyst must be modified via reducing. Moreover, doping or coupling with supplementary metal photocatalysts or with nitrogen is also supported. These modifications help in charge separation through the introduction of additional energy levels. The alteration of band energy of the photocatalyst caused efficient photo-oxidation or photoreduction.

Metal nanoparticles, nanocomposites, and biological nanocomposites have shown extreme applications in the area of industrial nanotechnology because of the modified mechanical, catalytic, optical, thermal stability, biocompatibility, and other unique properties. Design of those composites has been carried out by reinforcing nanofiller into metals (Co/Cr, Fe/MgO), ceramics (Al_2O_3/SiO_3, SiO_2/Ni), and polymers (polyester coupled with TiO_2) or biological polymers (Avérous and Pollet, 2012; Rhim et al., 2013).

Just like hydrolytic reactions in a water system (Meng et al., 2011), the most probable pathways of reactive sorbents (specific oxides of metal with excellent functionality) include nucleophile attacks on the organophosphorus pesticides resulting in the release of leaving groups through the transition state. These materials have more permeability, larger surface area ($> 100\ m^2\ g^{-1}$), and peculiar structure in the nano range with different crystal planes, and several edges, corners, and point defects

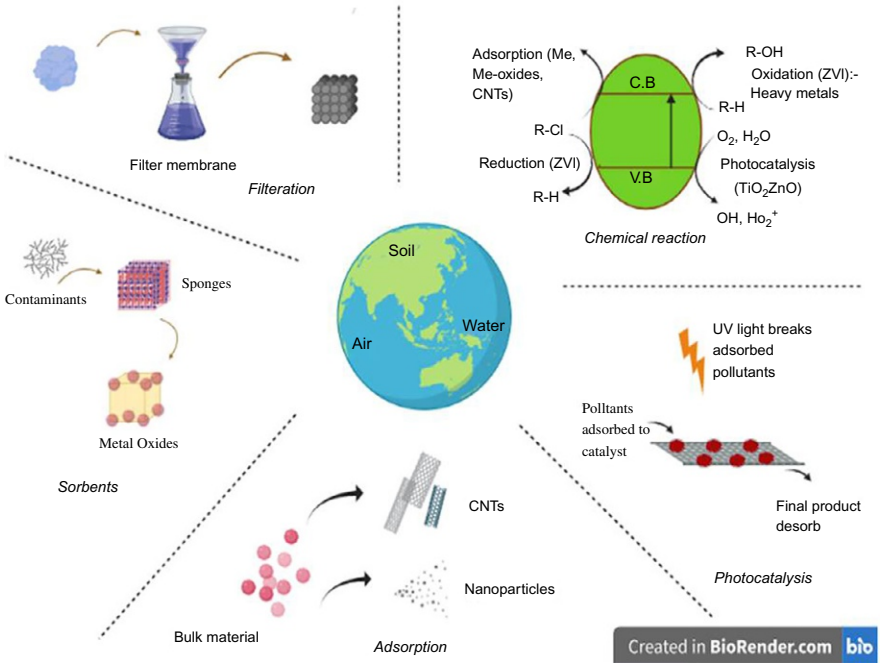

FIG. 2

Various environmental approaches used for removal of agrochemicals.

that play a role for active locations for quick reactive adsorption, as reported by Klabunde et al. (1996).

Copper-based ternary sulfide (CBTS) photocatalysts are a point of attention in environmental-related problems due to their higher light absorptivity coefficient, reusability (no loss of activity), and low toxicity. $CuInS_2$ as a photocatalyst has shown easy conversion of nitrate possibly into elemental nitrogen (conversion rate: 8.32 mg N/N) upon irradiation with visible light exposure (Molinari et al., 2020). For a detailed study, adsorption followed by a reduction pathway was given for the procedure, and it is important for the usage of sacrificial agents in the complete mineralization of nitrates. Fig. 2 represents various environmental approaches used for removal of agrochemicals.

5 Copper-based nanoparticles

5.1 CuO nanorods

Raul et al. (2014) investigated the simple chemically in situ soft fabrication of nanoscale copper (II) oxide. In brief, $CuCl_2$, sodium hydroxide, and capping solvent were mixed in a 2:1:1 ratio with 200 mL ethanol, and the mixture was refluxed for

15 h at 75°C. The dark brown precipitate, which was filtered, dried, and heated, was used for adsorption studies of Pb(II). Electron microscopy concluded the morphology of rhombohedral copper oxide was rod-like (~ diameter: 5 nm; length: 50 nm). For average surface area, BET study showed the 52.57 m^2 g^{-1} size of the nanorods.

5.2 Copper hexacyanoferrate-coupling ZnO nanocomposite

Synthesis of composites started first with a preparation of ZnO nanoparticles using the earlier-described process with a slight modification of employment of plant extract (Rani and Shanker, 2018).

In brief, a hydrous solution of $Zn(NO_3)_2$ (0.05 M, 100 mL) containing *A. indica* extract (2 mL) was continuously stirred (1 h, 50°C) followed by drop-wise addition of NaOH (0.01 M, 15–20 mL). Immediate precipitation of colorless $Zn(OH)_2$ was filtered and dried at 60°C for 4 h to get ZnO.

For fabrication of ZnO@CuHCF nanocomposite, a zinc oxide nanoparticle suspension in organic solvent was mixed into 100 mL of $Cu(NO_3)_2$ (0.1 M) aqueous solution containing 2 mL of leaf extracts. Later, $K_4[Fe(CN)_6]$ (0.1 M, 100 mL) along with 2 mL of *A. indica* was added drop-wise into the previously prepared mixture of salts that was magnetically stirred at normal parameters for 2 h. Precipitates formed in the reactions were washed many times with deionized water, filtered, and dried. Proper representation of the nanocomposite fabrication is shown in Fig. 3.

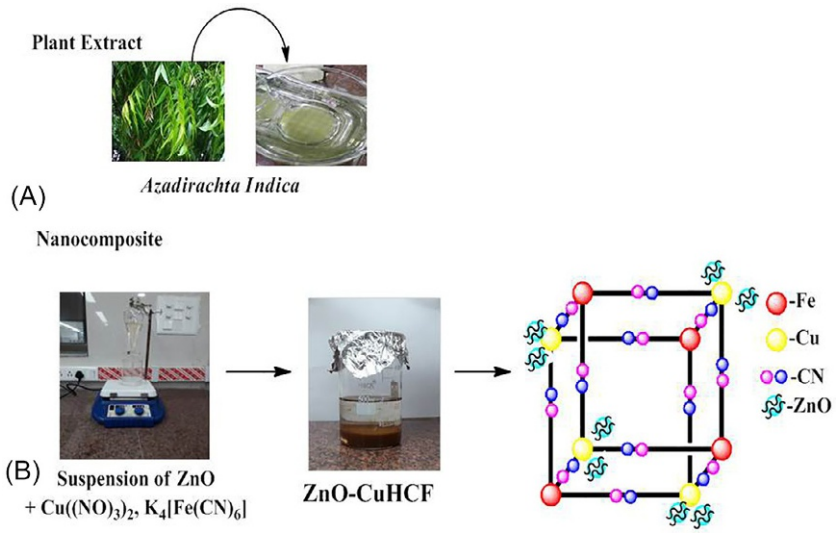

FIG. 3

Possible synthesis strategy for ZnO@CuHCF nanocomposite using *Azadirachta indica* as plant extract.

For comparison study, bare CuHCF nanoparticles were fabricated with potassium hexacyanoferrate solution (0.05 M, 100 mL) and mixed with copper nitrate solution (0.1 M, 100 mL) containing plant extract (2 mL). The reaction mixture was blended for 2 h at 50°C to obtain a precipitate that was filtered, washed, and dried at 60°C for 8 h.

5.3 Graphene/copper hexacyanoferrate nanocomposites

Ramos and Zarbin (2020) synthesized graphene/CuHCF nanocomposites by using graphene/CuO nanoparticle thin films as a precursor. Initially, dispersion of GO in water and $Cu(NO_3)_2$ nitrate solution in presence of $NaBH_4$ resulted in formation of graphene/Cu_2O/CuO film composite at the interface of H_2O/toluene liquid/liquid as shown in Fig. 4. The large transparency (94% of transmittance) and homogeneity property were offered by films. The structure of film is assumed to have homogeneous dispersion of Cu_2O and/or CuO (with diverse particle sizes and morphology) nanoparticles of over sheets of graphene.

Moreover, further deposition of films over glass substrates may be utilized for electrode purposes in cells using a solution of KCl/$[K_3Fe(CN)_6]$ in water, which acts as an electrolyte, and CuO nanoparticles acting as precursors for the electrochemical fabrication of CuHCF.

Copper oxide nanoparticles have gained significant attention recently because of their peculiar characteristics, low fabrication cost, and high stability. These nanomaterials have been applied in the area of photocatalysts, electrocatalysts, and supercapacitors. Cu is an inexpensive material as compared to noble metals such as Ag, Au, and Pt, and CuO nanoparticles are easy to fabricate via chemical methods, which is an easy and economical approach. CuO/C nanocomposites are very stimulating because of their multifunctionality in diverse applications such as electronics, electrodes, and catalytic roles.

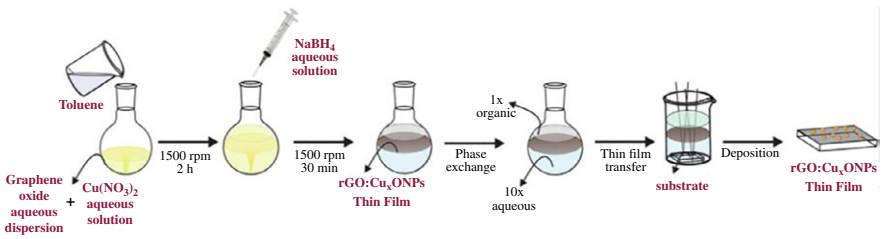

FIG. 4

Scheme for the preparation and deposition of rGO/CuxO NPs thin film.

5.4 Miscellaneous

Xu et al. (2019) studied the fabrication of active CuS nanophotocatalysts by using the dealloying technique. The synthesized nanophotocatalyst showed the excellent property of adsorption, large surface area, and less charge carrier recombination probability. Compositing chalcogenides of metal and GO upsurges use of light energy and enhanced charge parting along with the passage of reactants over the active places of catalyst, by which photocatalytic activity property can be enhanced.

Nanocomposites of GO/Cu-based ternary metal sulfide having rGO/CAS and rGO/$SnIn_4S_8$ were studied. However, there is more interest in Cu-based ternary metal sulfides due to their advanced characteristics (as mentioned earlier) and modified properties on composition with good supporting solids such as GO. The nanocomposite of RGO/Cu_2SnS_3 had a flower-like morphology, which was formed by employing a biomolecule-assisted solvothermal one-step technique (Vadivel et al., 2016). UV-vis diffuse reflectance spectra indicated that both pure Cu_2SnS_3 and GO/Cu_2SnS_3 nanocomposite revealed that the nanomaterial shows a higher absorption property in the presence of visible light than that of a native or single material. Factual was credited to high electronic communication between GO and Cu_2SnS_3. An investigation of the internal charge transmission phenomenon via photocurrent reports showed the higher current produced by the nanocomposite in comparison of Cu_2SnS_3. Moreover, the addition of GO to nanocomposites resulted in minimization of charge recombination possibility.

Liu et al. (2014) studied the photocatalytic potential of rGO/Cu_3SnS_4 composite fabricated using a one-step solvothermal method for the removal of rhodamine-B and phenolic colorants. The study of N_2 adsorption-desorption isotherms concluded that Cu_3SnS_4 and rGO/Cu_3SnS_4 composite were mesoporous materials having pore volumes of approximately 17 and 7 nm with an upper surface area of 60.5 $m^2\ g^{-1}$ compared with 19.4 $m^2\ g^{-1}$, respectively. Modified photocatalytic potential is credited to the synergy between the enhanced adsorption of pollutant, increased light absorption, and charge separation in the composite. Chen et al. (2021) used flower-type copper-phosphotriesterase (Cu-PTE) for the removal of organophosphorus pesticide. The modified nanocomposite shows better efficiency as compared to parent nanomaterials. The copper-zinc oxide (Cu-ZnO) nanoheterojunction was synthesized by using leaf extract of *Melia azedarach.* The biogenic agent acts as a reducing agent and prevents the agglomeration of nanoparticles. The Cu-ZnO was also used for the degradation of chlorpyriphos pesticide with solar irradiation. Approximately 91% of the pesticide degraded in 240 min at pH 6 (Pathania et al., 2021). The copper oxide/titanium dioxide/polyaniline (CuO/TiO_2/PANI) nanocomposite was utilized for the degradation of toxic and persistent chlorpyriphos pesticide from water. The synthesized nanocomposite efficiently removed 95% of chlorpyriphos within 90 min. The modified nanocomposite shows better efficiency as compared to CuO/TiO_2 and TiO_2/PANI under the same conditions (Nekooie et al., 2020). Table 2 summarizes detailed information about the use of copper-based nanomaterials used for the removal of various pesticides present in water.

Table 2 Performance of copper-based composite nanomaterial for treating pesticides in aqueous solution.

Material	Contaminants	Experimental conditions	Removal efficiency/ adsorption capacity	Time	References
$CuFe_3O_4$ (3 g L^{-1})	4-Nitrophenol (0.005 mol L^{-1})	0.1 mol L^{-1} $NaBH_4$, 2 mL H_2O_2, removal: 95% in 40 s			Feng et al. (2013)
$CuFe_2O_4$	Tetrabromobisphenol A	Dose: 0.1 g L^{-1}, C0: 10 ppm 0.2 mmol L^{-1}, permonosulfate	99% TOC removal: 57%	30 min	Ding et al. (2013)
CuO/ZnO	4-Nitrophenol	Dose: 1 g L^{-1} C0 = 30 mg L^{-1} Sunlight	99% 83% TOC removal	180 min	Qamar et al. (2015)
Copper	Endosulfan (1)	Completely annihilates in solution	Degradation		Mitra and Varshney (2013)
Ag/Cu NPs	Chlorpyriphos	Water, catalytic reduction			Rosbero and Camacho (2017)
CuO-chitosan (0.02 g)	Malathion (2)	99.9%, (k = 0.53 g mg^{-1} min^{-1})	Adsorption		Jaiswal et al. (2012)
CuO-MMT supported on chitosan, gum ghatti and poly lactic acid (0.5–3.0 g L^{-1})	Dichlorvos (20 – 100)	93.4%, 87.8%, and 63.3% removal, respectively	Adsorption		Sahithya et al. (2015)
CuO-MMT (0.5–3.0 g L^{-1})	Dichlorvos (20–100)	83.2%	Adsorption		Sahithya et al. (2015)
Cu-doped ZnO	Monocrotophos	pH 7; irradiation time 180 min; deg. 90%	Degradation		Hanh et al. (2019)
Copper-doped anatase/brookite TiO_2	Malathion (10,000 mg L^{-1})	pH 6; irradiation time 105 min; deg. 100%			Manga Raju et al. (2015)
Copper-phosphotriesterase	Organophosphorus pesticide	Catalytic efficiency increased 2.2-fold	Degradation		Chen et al. (2021)
Cu-ZnO	Chlorpyriphos pesticide	91%, pH 6	Degradation	240 min	Pathania et al. (2021)
Copper oxide/titanium dioxide/polyaniline (CuO/TiO_2/PANI)	Chlorpyriphos pesticide	95%	Degradation	90 min	Nekooie et al. (2020)

6 Degradation methodologies for agrochemicals

For the elimination of pesticides on large scale, still there is no proper technique available. Therefore, much research has continued onto the fabrication of effective, economical, cost-effective methods that could reach swift and large removal rates. This resulted in the use of various techniques for agrochemical elimination such as adsorption, coagulation, fluid extraction, bioremediation, aerobic degradation, electrochemical and biological oxidation, and solid phase extraction (Lagadec et al., 2000; Murthy, 2007; Rachna et al., 2020). For a decade, homogeneous and heterogeneous AOPs have been used. Nanotechnology based on semiconductors and nanofiltration membranes also have some advantages due to the unique properties of nanomaterials as well as their excitation in light, i.e., photocatalysis (Rachna et al., 2018, 2019; Rani et al., 2020).

Adsorption property has gained popularity because of its simple, resourceful, economical, and flexible outcomes. However, it is unresponsive to hazardous contaminants in wastewater management (Kyriakopoulos and Doulia, 2006). Some reviews have been published on the elimination of various types of pesticides from wastewater and river water by the use of diverse conservative adsorbents such as activated carbon, sawdust, plant materials, and carbonaceous compounds (Kyriakopoulos and Doulia, 2006; Ahmad et al., 2016). However, this method doesn't allow for a 100% elimination of insecticide, therefore additional chemicals are required to treat the pesticides' mineralization into smaller and safer metabolites. Extensive research in the modification and improvement of advanced methodologies to mineralize agrochemicals is still in a preliminary stage. This is possible due to the utilization of reactive nanomaterials like zerovalent nanocomposites or reactive sorbents. Nanomaterials include the formation of very effective and potential free radical molecules responsible for changing organic pollutants into inorganic salts, i.e., safer metabolites (Shanker et al., 2016; Rani et al., 2020). Heterogeneous types of photocatalysis works with the use of oxides of metals such as titanium oxides, zinc oxides, zirconium oxides, etc. and sulfides of metals such as zinc sulfide, and iron sulfide as semiconductor photocatalysts under UV/solar radiation (Wu et al., 2015).

Scattered information is also accessible in the literature on the utilization of copper by itself or braced with reduced graphene for the removal of the toxic pesticides lindane (Gupta et al., 2016) and endosulfan (Mitra and Varshney, 2013), respectively. Moreover, the nanocomposites of chitosan and chitosan-based helped to provide a higher elimination capacity toward toxic organophosphorus pest-killer chemicals (Dehaghi et al., 2014; Rani et al., 2020). Degradation of toxic dichlorvos with higher efficiency was achieved from nanobiocomposites of CuO-montmorillonite *gum ghatti* and CuO-montmorillonite-chitosan. The study also proved biological polymers had a significant role in the removal of pesticide via adsorption. Zinc oxide-zeolite and copper oxide-chitosan-based nanocomposites were found to be efficient for the removal of monocrotophos and malathion from wastewater through adsorption and photoactive behavior, respectively. The effect of synergism of bimetallic-oxides of cobalt and copper assisted $CuO\text{-}Co_3O_4@MnO_2$ in complete elimination

of phenolic pollutants (Sahithya et al., 2015; Jaiswal et al., 2012). Manga Raju et al. (2015) formed poly-3-thenoic acid coupled with titanium oxide nanocomposite that was further utilized for complete removal of toxic and persistent organophosphorus pesticide. A series of heterogeneous, polythenoic acid (P3TA)-sensitized, nanocomposite photocatalysts P3TA/Cu-TiO_2 were prepared by implying advanced sol-gel technique by using diverse percentages of weight (wt%) of P3TA to TiO_2 at room temperature. Thermogravimetric analysis (TGA), X-ray diffraction (XRD), X-ray photoelectron spectroscopy (XPS), Fourier transform infrared (FT-IR) spectroscopy, ultraviolet-visible diffuse reflectance spectroscopy (UV-vis DRS), Brunauer-Emmet-Teller (BET) surface area, field emission scanning electron microscopy (FESEM) with energy-dispersive X-ray spectroscopy (EDX), and high resolution transmission electron microscopy (HRTEM) analyses are the most popular techniques used for the characterization of copper-based nanomaterials. For the investigation of photocatalytic efficiency, organophosphorus pesticide (malathion) was degraded under visible light irradiation. The various characterization investigation results concluded that surface sensitization of P3TA and Cu-TiO_2 results in production of agglomerated multiparticle nanohybrids that showed good thermal stability when compared with pure TiO_2. The nanocomposite showed a broadband of absorption in the visible range, efficient adsorption properties, and increased photocatalytic potential supporting the narrow band gap, reduced size of particle, and enhanced surface area of titanium oxide nanoparticles. A surface study of the chemical composition results revealed that the presence of the constituent elements of both the P3TA and Cu-TiO_2 nanoparticles concluded with the presence of a strong interfacial interaction present in P3TA and Cu-TiO_2 proven by FT-IR studies. Experiments of photoluminescence and radical scavengers proved that OH radicals are the most important potential species and a reason for removal of malathion by oxidation mechanism. Results of diverse nanohybrid/malathion working parameters on the photocatalytic potential were analyzed, and a simple pathway was accordingly suggested.

Sahithya et al. (2015) carried out elimination of dichlorvos (OP insecticide) from an aqueous solution using biological polymer-improved montmorillonite MMT-copper oxide composites, i.e., MMT-CuO-polylactic acid (PLA), MMT-CuO-chitosan, and MMT-CuO-*gum ghatti* (Gg) with control (MMT-CuO). Optimization conditions of pH (3.0–12.0), initial DCV concentration (20–100 mg L^{-1}), contact time (1–12 h), temperature (20–50°C), and nanocomposite amount (0.5–3.0 g L^{-1}) were used during adsorption. Maximum elimination of DCV was reported as the following order: MMT-CuO-chitosan composite (93.4%) > MMT-CuO-Gg (87.8%) > MMT-CuO (83.2%) > MMT-CuO-PLA (63.3%). Equilibrium data supported Freundlich model with the maximum adsorption efficiency concluded to be a heterogeneous mode of DCV adsorption. Kinetics study revealed adsorption phenomenon followed pseudo-first-order kinetics with physisorption. Furthermore, thermodynamic parameters were also studied for the confirmation of spontaneity and endothermic behavior. For the confirmation of amines and alcohols, functional groups in DSV adsorption were investigated by FT-IR study. The study revealed that carbon atoms of DCV interacted with copper oxide and silicon atoms of MMT. This also confirms the involvement of

these atoms in adsorption phenomenon. Atomic force microscopic (AFM) study suggested that copper oxide nanoparticles were uniformly distributed on the surface of the MMT-CuO-chitosan nanocomposite, which further validates the efficacy of the nanocomposite for the complete elimination of pesticide from water.

Van et al. (2016) studied the effect of copper oxide nanoparticles on insecticidal activity and phytotoxicity in conventional and transgenic cotton. Copper oxide nanoparticles importantly inhibited the growth and development of both transgenic and conventional cotton. Copper oxide nanoparticles also minimized the uptake of nutrients, such as boron, molybdenum, manganese, magnesium, zinc, and iron. A lesser amount of copper oxide nanoparticles modified the expression of the Bt toxin protein of Bt-transgenic cotton. It was the first time the effect of nanoparticles on the expression of exogenous Bt gene of Bt transgenic crops was investigated.

Xie et al. (2011) studied the removal of lambda-cyhalothrin and cypermethrin present in water, mainly due to agricultural activity, as affected by humic acid (HA) and/or copper intermediates and degradation pathways. The effect of coexisting HAs or divalent copper ions on the photodegradation of pesticides lambda-cyhalothrin (l-CHT) and cypermethrin (CPM) in an aqueous solution was studied in the presence of the Xe lamp. The degradation efficiency of toxic pesticides l-CHT and CPM were improved due to $Cu_2þ$ or HA but restrained due to Cu2þ and HA. The first-order reaction kinetics were followed by intermediates formed during the photodegradation procedure. The intermediates l-CHT and CPM formed during photodegradation were identified by using GC-MS. The most probable possible photodegradation mechanism involved decarboxylation, dichlorination, ester bond cleavage, and phenyl group elimination.

Rafique et al. (2016) studied photodegradation of soil-incorporated chlorpyriphos in the presence of divalent copper and iron. The samples of soil spiked by chlorpyriphos and particular metal ions were exposed to UV-irradiation for a diverse time gap, then investigated using high-performance liquid chromatography technique. Both unsterile and disinfected control soil samples with a definite amount of pesticides and selected metals were incubated in the dark at room temperature aimed at same period gaps. The final conclusion from the investigations gives strong evidence of the first-order kinetics during photodegradation of chlorpyriphos. The dissipation half-life of chlorpyriphos reduced from 41 to 20 days in the presence of UV irradiation.

Dual roles were played by heavy metals in the elimination of pesticides present in the soil. The presence of a large amount of some pesticides in the soil may be reduced by using some metal ions such as iron that may improve the rate of degradation of pesticides as well as reduce their half-lives to an extent. The perseverance/degeneracy behavior of toxic and carcinogenic pesticides was also investigated in the presence of metals and bacterial growth populations that play valuable roles in the degradation of pesticides (Škrbić and Đurišić-Mladenović, 2010). Divalent copper ions can minimize the degeneracy of ethylene-thiourea formed by the decay of ethylene bis-dithiocarbamate fungicides. However, acceleration during the degradation process was observed by the presence of divalent copper ions. The presence of 20–50 mg L^{-1} of Mg, Zn, and Cu catalysts was also found to be responsible for

speeding the degradation of carbendazim and diuron (Škrbić et al., 2010). Investigations on the activity of aluminum iron-pillared clay and Fe-ZSM-5 catalysts for the elimination of water solution of imidacloprid in the presence of UV or visible light irradiation have been performed. Using photo-Fenton reaction and titanium oxide Degussa P25, comparison data was obtained (Guzsvány et al., 2012). Degradation mechanism of pesticides under sunlight by nanosized mixed metal oxides are illustrated in Fig. 5.

Liu et al. (2007) studied the photodegradation of the pesticides cypermethrin and cyhalothrin present in the soil by using copper metal. A serial quantity of the toxic pesticides was retrieved with a quantitative amount of copper ion in the soil that was then incubated for a fixed interval of time; the study of the extracts from the soil was performed by using gas chromatography (GC). The pyrethroids present in the water were degraded in the presence of UV light. The effect of Cu^{2+} on the degradation of the pesticides was measured with a half-life (0.5) of degradation. A negative relation between the degradation of the pyrethroid pesticides present in the soil and copper addition was observed. However, divalent copper ion could decrease

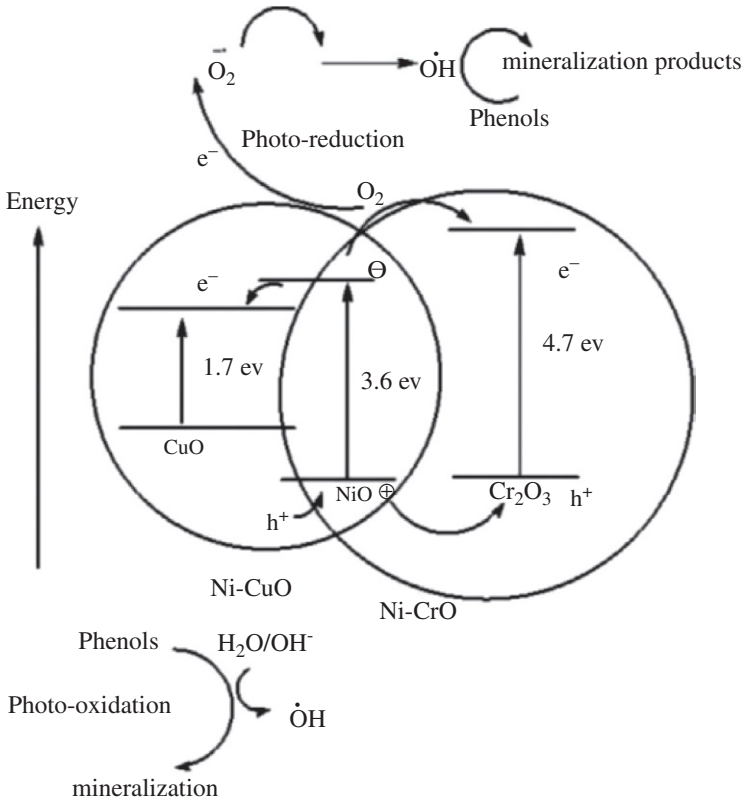

FIG. 5

Representation of degradation mechanism over nanosized mixed metal oxides.

the photodegradation of the pyrethroids present in the water. Because of the presence of copper ion in the soil, half-life of cyhalothrin increased from 8.1 to 10.9 days and in the case of cypermethrin increased from 8.1 to 10.9 days. As for the photodegradation process, half-life of cyhalothrin reduced from 173.3 to 115.5 min and for cypermethrin from 115.5 to 99.0 min. This data revealed that Cu affected the degradation of toxic persistent pesticides present in soil by using the potential activity of microorganisms. The difference in the efficiency for the removal of pyrethroid isomers was observed in soil. Cu could accelerate the removal of some of the main isomers. Raut et al. (2016) studied capacity of copper (Cu^0) nanoparticles in zero-valent (synthesized by chemical reduction method) and reducing agents for dechlorination of monochloroaromatics at room condition. Different contaminations such as chloropyridine (Cl-Py), chlorobenzene (Cl-B), chlorobiphenyl (Cl-BPh), and chlorotoluene (Cl-T) were degraded. Different factors like pH, amount of nanocatalyst, and reducing agent were used to understand the degradation of pesticides; moreover, the reusability of the catalyst was also examined. In the presence of zero-valent nanoparticles of copper and sodium borohydride, nearly complete dechlorination of all the chlorine-containing aromatic compounds occurred within a half-day. However, only 70% of dehalogenation was found with 5% acidified alcohol, and the mechanism of dechlorination revealed the importance of zero-valent copper nanoparticles. Comparison of kinetics data of chloroaromatics and chloroaliphatics showed a rate of dehalogenation reduced from 0.23 h^{-1} to 0.15 h^{-1} in the presence of nanosized copper oxide and sodium borohydride for (Cl-B) and Cl-BPh, respectively. Finally, identification of metabolites such as biphenyls, benzene, and other products was performed by chromatographic (GC-MS) and spectroscopic (NMR) techniques.

Tamuly et al. (2014) studied the reduction of nitroaromatics catalyzed by green-synthesized copper oxide. The X-ray diffraction technique confirmed the crystal structure of the synthesized nanomaterial. The interplanar spacing of CuO nanoparticles was found at 0.16 nm, while FE-SEM analysis revealed the flower-shaped surface morphology. Synthesized nanosized copper oxide showed excellent catalytic potential for the reduction procedure of nitrobenzene to amino compounds with a high yield > 74%–96%. Water was used as a green solvent during the complete reaction. The CuO nanocatalyst was found to be reusable many times, confirming its sustainability.

7 Utilization of green-synthesized Cu-based nanomaterials

Nanomaterials synthesized by using a green method are economical. Presently, many researchers worldwide are examining the fabrication of nanosized particles by using visible sunlight or surfactants extracted from plants, microorganisms, water, and sometimes a combination of more than one source. As a result, the fabrication of nanoparticles through an environmentally favored green path depends on different types of natural biogenic sources, which is inspiring us toward sustainable development. For reconstructing the polluted environment, nanoparticles were widely used

for the elimination of harmful pesticides in the presence of different sources of light. A limited number of studies reported the utilization of green-synthesized nanostructures in the eradication of agrochemicals from water. Shanker et al. (2016) reported a facile method to synthesize many oxides of transition metals (ZnO, CuO, Co_3O_4, NiO, and Cr_2O_3) under daylight. The same group have utilized such nanomaterials for the mineralization of various organic colorants from synthetic wastewater.

Rani and Shanker (2018) carried out the elimination of chlorpyriphos, thiamethoxam, and tebuconazole from spiked water using green-fabricated crystalline hexacyanoferrates of different metals such as Zn, Cu, Co, and Ni. Distorted nanocubes of CuHCF (~ 100 nm) fabricated using *Sapindus mukorossi* (raw ritha) were able to remove 85%–91% of targeted pesticides (50 mg L^{-1}) when treated with very little amount of the catalyst (15 mg) at 7 pH under sunlight. High efficiency of CuHCF has been found against pesticides, and it converted them to minor and safe byproducts such as pyridin-3-ol, 3-aminopropanoic acid, and (*Z*) but-2-enal, as revealed by mass spectrometric analysis. It was also concluded that Cu metal-based catalysts have been rarely explored for the treatment of agrochemicals. Further studies in this area must be explored.

Jassal et al. (2016a,b) fabricated nanoparticles of potassium copper hexacyanoferrate (KCuHCF) using plant extract of *Aegle marmelos* as a natural surfactant. This nanocatalyst eradicated organic colorants to more than 94.72% under optimized parameters: concentration of amine (1.0×10^{-4} M), catalytic amount (25 mg), and neutral pH. The same catalyst showed excellent degradation capacity in the elimination of aromatic amines found in wastewater (88% of *p*-anisidine, 72% of *p*-toluidine, 69% aniline and 64% of *p*-chloroaniline) (Rani and Shanker, 2017). Due to its high basic nature, maximum adsorption of *p*-anisidine was observed on the acidic surface of catalysts. Statistical study of data shows good agreement with various adsorption isotherm relations that concluded the monolayer adsorption of AAs over the surface of catalyst. GC-MS revealed the formation of small, safer metabolites such as but-2-enal, benzoquinone, malonaldehyde hydroquinone, and 4-oxobut- 2-enoic acid.

Green-synthesized copper oxide nanoparticles were also employed for the removal of dye (Sankar et al., 2014). Copper oxide-chitosan-based green nanocomposites (CuO-Fe_2O_3-CS) showed excellent efficiency in the removal of carcinogenic and persistent PAHs such as anthracene (93%) and phenanthrene (90%) within 12 h under daylight at neutral pH (Rani et al., 2020). Degradation followed first-order kinetics and Langmuir isotherm model (R^2: 0.99; *P*-value < .05). Smaller and relatively safer byproducts were identified by gas chromatographic and mass spectrometric analysis.

Rani and Shanker (2018) synthesized highly crystalline bimetallic oxide nanostructures of Ni-Cu oxide and Cu-Cr oxide of size 50 nm with morphology such as nanorods and nanoflowers using *Aegle marmelos* leaf extract. The nanostructures were found to be highly efficient in hazardous phenols from water under daylight. The optimized parameter's phenol amount was 1×10^{-4} M; catalytic dose: 15 mg; neutral pH. 3-Aminophenol degraded > 97% of phenol, 2,4-DNP into smaller products, which were finally mineralized. Rani and Shanker (2018) carried out removal of methylene blue (MB) dye from water using poly (methyl methacrylate)/copper oxide

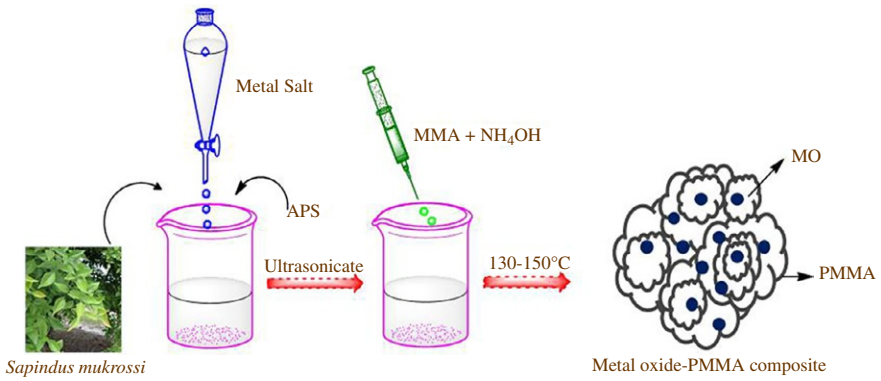

FIG. 6

Synthesis of CuO-polymethylmethacrylate self-assembled through a green method by using natural plant surfactant as *Sapindus mukorossi.*

green nanocomposites. Spherical and semicrystalline CuO-polymethylmethacrylate self-assembled through a green method using natural plant surfactant as *Sapindus mukorossi* (Fig. 6).

At optimized parameters (MB concentration: 2 mg L^{-1}; catalytic dose: 80 mg: pH 7), CuO-poly (methyl methacrylate) reported maximum elimination capacity (93%) than that of separate metal oxide. Smaller and safer products like (*Z*)-hexa-3,5-dien-1-ol, benzoquinone, and (*Z*)-buta-1,3-dien-1-ol were formed due to the degradation of MB.

8 Environmental, health, and safety aspects of Cu-based nanomaterials (toxicological studies)

The toxic aspects of nanomaterials in the environment should be studied before sending it to market for commercial applications. Nanomaterials can undergo possible leaching or being released upon use for industrial claims as well as eradication of contaminants from the environment. Excess of metals and nanoparticles are not accepted at any cost to the health and safety of organisms. Solutions to these problems look at controlled use and development of substituents to minimize the bioaccumulation of each metal framework. Some in vitro and in vivo studies related to both have been reported to understand the toxicity of Cu-based nanomaterials (Kamali et al., 2014).

Toxicity was found to be dependent on the nature of the organism and characteristics of nanomaterials and their exposure. CuO nanoparticles with a size of 34.38 ± 0.76 nm and surface area 29 m^2 g^{-1} were employed by Moschini et al. (2013) for cytotoxicity on alveolar epithelial cells belonging to human or mammalian cells. Toxicity of CuO uptake (by vesicle-assisted endocytosis and some unknown internalization tool) was credited to dissolve Cu^{2+} in the system and nature

of the CuO nanoparticles in addition to interaction with its surroundings. However, Piret et al. (2014) reported other mechanisms for CuO toxicity involving an elevation in the reactive oxygen species (ROS) production. Moreover, the upsurge of the Cu nanoparticles concentration (up to 100 ppm) can lead to a reduction in cell viability (Xu et al., 2012). According to Boyles et al. (2015), proinflammatory situations, oxidative stress, and programmed cell death are the main causes. Furthermore, characteristics of nanomaterials like nature, ionic state, surface oxidation, and hydrophobicity might be possible factors as seen from different types of toxicity generated from different types of carbon-coated and noncoated Cu nanoparticles (Minocha and Mumper, 2012).

Bulk particles of CuO NPs are safe, while Cu^{2+} (size > 80 nm) could highly hinder the growth of bacterial in the soil (Rousk et al., 2012). Despite these findings, Zhao et al. (2011) reported no major toxic effects of copper oxide nanoparticles and its counterpart. A majority of particles went toward juvenile carp (*Cyprinus carpio*), however, increasing the exposure time may significantly affect carp growth. Copper nanoparticles and copper oxide (10–100 nm) nanoparticles are the main reason behind decreasing the size, affecting content of nutrient and performance of enzyme in plants (Hong et al., 2015). A rise in a concentration of CuO NPs resulted from the enhancement in the copper quantity in the roots, which remarkably led to lignification of root cells and alteration in the development.

9 Conclusions, future scope, and recommendations

This chapter summarized the promising and unique physicochemical properties of Cu-based nanomaterials employed in the treatment of recalcitrant agrochemicals. Synthesis of different types like CuO, CuS, copper hexacyanoferrate, and copper ternary sulfides were presented along with applications and disposal while considering the characteristics of the nanomaterials, fabrication costs, and easy ability for recovery and reusability of Cu-based nanomaterials. Cost and the capability of fabricated materials involved precursors, apparatus used, and utilization of energy for the fabrication of the copper-based nanomaterials. Along with solvothermal or hydrothermal synthesis, the chemical reduction that led to precipitate the fabricated Cu-based nanomaterials is frequently used because of its relative simplicity and being economical and capable of facilitating the regulation and manipulation of the fabrication conditions to attain optimum properties for Cu-based nanomaterials (Khan et al., 2016).

Hence, this procedure would be mainly appropriate for the fabrication of nanoparticles on a large scale. Important characteristics, mainly morphology and crystalline structure, can help to identify the reactivity of the nanomaterials. Doping of narrow band gap Cu-based nanomaterials with an inorganic element makes them able to enhance their reactivity against targeted pollutants (Maragatha et al., 2017; Li et al., 2013a,b). Time, pH, temperature, catalyst dose, and pollutant

concentrations are some of the factors to control the efficiency of Cu-based nanomaterials. Modification in some characteristics such as crystallinity and stability of copper-based nanomaterials and leaching of Cu ions to the medium can be controlled. The same characteristics control their size-based toxic effect on the terrestrial and aquatic living beings. Alteration of nanoparticles by surface engineering, coupling, doping, or deposition with functional groups or incorporation of different metals enhanced the adsorption as well as semiconductor characteristics of copper-based nanomaterials. Various nanomaterials and modified nanomaterials were used as photocatalysts, adsorbents, heterogeneous redox, and photocatalysts or reactive sorbents for the removal of hazardous pesticides (Rani et al., 2021; Rani and Shanker, 2017; Jassal et al., 2016a,b).

The major outcomes of the chapter:

- Nanoparticles incorporated into biosorbents could be an eco-friendly solution.
- Improvement in efficacy or adsorption properties of commercial filters can be had via the use of nanoparticles.
- Nanomaterials having surfactants are also able to remove agrochemicals used in agriproducts and food materials.
- Mainly TiO_2, ZnO, and iron oxide nanoparticles have been used to eradicate agrochemical pollution in view of cheaper, commercially available, safer, and of high efficiency NPs.
- Nanocomposites comprised of bimetallic centers increases the photocatalytic efficiency of persistent agrochemicals and may be used as nanosensors for the identification of agrochemicals present in the environment.
- Nanophytoremediation proposed wide application in an environment for the removal of toxic agrochemicals from soils and aquatic bodies. The brief studies related to the effect of nanoparticles on agrochemical hyperaccumulation in both plants, i.e., land and water will be able to diminish the problem of environmental contamination of agrochemicals in an economical term.
- Organochlorines and organophosphates were rapidly eliminated by nanomaterials, but some pollutants have not yet been vastly studied such as carbamates and SU (future contaminants). Nanomaterial-mediated investigation on various traditional or upcoming pesticides is imperative to determine if there is a need to ban or restrict them.
- Cu-based materials were mainly used for dyes and were not much explored for agrochemical decontamination.
- Cu-based nanopesticides: Copper is essentially required by all living things for growth and development, carried from bacterial cells to the body to carry out fundamental biological functions (Yruela, 2009). The present uses of copper-based pesticides have increased the utilization of bulk and ionic forms into colloids (1–1000 nm) or nanopesticides, primarily because of the large range of peculiar physicochemical and biocidal characteristics of nanomaterials (NMs) (Civardi et al., 2015). Nanopesticides showed an enhanced 20%–30% capacity than their conventional techniques.

- AOP photocatalysis is a very excellent technique for purification of wastewater, which is a cost-effective and sustainable process compared to other pollutant water treatment techniques.
- CBTSs (semiconductor materials) and their composites (GO-supported Cu-based ternary sulfides) led to modification in photocatalytic potential in the degradation of pollutants and purification of wastewater. More exploration is still needed due to the vast activity of these materials for the removal of pharmaceuticals, toxic metals, emerging contaminants, and in water disinfection.

Finally, the chapter concluded and gives some suggestions related to utilization of green-fabricated nanoparticles synthesized in one step in the future (one-step synthetic procedure for the synthesis of surface modification) that would be economical and more efficient for photocatalysts. For sustainable developments, modification in biopolymer nanobiocomposites is the current need.

References

Ahmad, S., Ziya, A.B., Ashiq, M.N., Ibrahim, A.A., Shabbar, A., Naseeb, S., Muhammad, K., Muhammad, A., 2016. Improved magnetic and electrical properties of Cu doped FeNi invar alloys synthesized by chemical reduction technique. J. Magn. Magn. Mater. 419, 125–130.

Avérous, L., Pollet, E., 2012. Biodegradable polymers. In: Environmental Silicate Nano-Biocomposites. Springer, London, pp. 13–39.

Bouman, C.S., Oudemans-van Straaten, H.M., Tijssen, J.G., Zandstra, D.F., Kesecioglu, J., 2002. Effects of early high-volume continuous venovenous hemofiltration on survival and recovery of renal function in intensive care patients with acute renal failure: a prospective, randomized trial. Crit. Care Med. 30 (10), 2205–2211.

Boyles, M.S.P., et al., 2015. Copper oxide nanoparticle toxicity profiling using untargeted metabolomics. Part. Fibre Toxicol. 13 (1), 49.

Cahill, J.F., Lyons, D., Karst, J., 2011. Finding the "pitch" in ecological writing. Bull. Ecol. Soc. Am. 92 (2), 196–205.

Chen, J., Guo, Z., Xin, Y., et al., 2021. Preparation of efficient, stable and reusable copper-phosphotriesterase hybrid nanoflowers for biodegradation of organophosphorus pesticide. Enzyme Microb. Technol. 146, 109766.

Civardi, C., Schwarze, F.W., Wick, P., 2015. Micronized copper wood preservatives: an efficiency and potential health risk assessment for copper-based nanoparticles. Environ. Poll. 200, 126–132.

De, A.K., 2010. Environmental Chemistry, seventh ed. New Age International Publisher, New Delhi.

Dehaghi, S.M., Rahmanifar, B., Moradi, A.M., Azar, P.A., 2014. Removal of permethrin pesticide from water by chitosan–zinc oxide nanoparticles composite as an adsorbent. J. Saudi Chem. Soc. 18 (4), 348–355.

Ding, Y., Zhu, L., Wang, N., Tang, H., 2013. Sulfate radicals induced degradation of tetrabromobisphenol A with nanoscaled magnetic $CuFe_2O_4$ as a heterogeneous catalyst of peroxymonosulfate. Appl. Catal. B 129, 153–162.

Ericksen, P.J., 2008. Conceptualizing food systems for global environmental change research. Glob. Environ. Change 18 (1), 234–245.

Etefagh, R., Azhir, E., Shahtahmasebi, N., 2013. Synthesis of CuO nanoparticles and fabrication of nanostructural layer biosensors for detecting *Aspergillus niger* fungi. Sci. Iran. 20 (3), 1055–1058.

Feng, J., Su, L., Ma, Y., Ren, C., Guo, Q., Chen, X., 2013. $CuFe_2O_4$ magnetic nanoparticles: a simple and efficient catalyst for the reduction of nitrophenol. Chem. Eng. Sci. 221, 16–24.

Gavrilescu, M., 2005. Fate of pesticides in the environment and its bioremediation. Eng. Life Sci. 5 (6), 497–526.

Gupta, V.K., Chandra, R., Tyagi, I., Verma, M., 2016. Removal of hexavalent chromium ions using CuO nanoparticles for water purification applications. J. Colloid Interface Sci. 478, 54–62.

Guzsvány, V., Rajić, L., Jović, B., Orčić, D., Csanádi, J., Lazić, S., Abramović, B., 2012. Spectroscopic monitoring of photocatalytic degradation of the insecticide acetamiprid and its degradation product 6-chloronicotinic acid on TiO_2 catalyst. J. Environ. Sci. Health A 47 (12), 1919–1929.

Hanh, N.T., Le Minh Tri, N., Van Thuan, D., Thanh Tung, M.H., Pham, T.D., Minh, T.D., Trang, H.T., Binh, M.T., Nguyen, M.V., 2019. Monocrotophos pesticide effectively removed by novel visible light-driven Cu doped ZnO photocatalyst. J. Photochem. Photobiol. 382, 111923–111929.

Hong, J., Jie, H., Cyren, M.R., Lijuan, Z., Adeyemi, S.A., Arturo, A.K., Jose, R.P., Jorge, L.G., 2015. Toxic effects of copper-based nanoparticles or compounds to lettuce (*Lactuca sativa*) and alfalfa (*Medicago sativa*). Environ. Sci. Process. Impacts 17 (1), 177–185.

Isherwood, P.J.M., 2017. Copper zinc oxide: investigation into a p-type mixed metal oxide system. Vacuum 139, 173–177.

Jaiswal, M., Chauhan, D., Sankararamakrishnan, N., 2012. Copper chitosan nanocomposite: synthesis, characterization, and application in removal of organophosphorous pesticide from agricultural runoff. Environ. Sci. Pollut. Res. 19 (6), 2055–2062.

Jassal, V., Shanker, U., Gahlot, S., 2016. Green synthesis of some iron oxide nanoparticles and their interaction with 2-amino, 3-amino and 4-aminopyridines. Mater. Today. Proc. 3 (6), 1874–1882.

Jassal, V., Shanker, U., Kaith, B.S., 2016. Aegle marmelos mediated green synthesis of different nanostructured metal hexacyanoferrates: activity against photodegradation of harmful organic dyes. Scientifica 2016, 2715026.

Kafilzadeh, F., 2015. Distribution and sources of polycyclic aromatic hydrocarbons in water and sediments of the Soltan Abad River, Iran. Egypt. J. Aquat. Res. 41 (3), 227–231.

Kamali, A., Flanders, A.E., Brody, J., Hunter, J.V., Hasan, K.M., 2014. Tracing superior longitudinal fasciculus connectivity in the human brain using high resolution diffusion tensor tractography. Brain Struct. Funct. 219 (1), 269–281.

Kaushal, J., Khatri, M., Arya, S.K., 2021. A treatise on organophosphate pesticide pollution: current strategies and advancements in their environmental degradation and elimination. Ecotoxicol. Environ. Saf. 207, 111483.

Ke, F.S., Lauryn, J., Ling, H., Bo, Z., Jun-Tao, L., Xiao-Dong, Z., Shi-Gang, S., 2014. Negative electrode comprised of Fe_3O_4 nanoparticles and Cu nanowires for lithium-ion batteries. Solid State Ion. 262, 18–21.

Khalaj, M., Kamali, M., Khodaparast, Z., Jahanshahi, A., 2018. Copper-based nanomaterials for environmental decontamination – An overview on technical and toxicological aspects. Ecotoxicol. Environ. Saf. 148, 813–824.

Khan, A., Rashid, A., Younas, R., Chong, R., 2016. A chemical reduction approach to the synthesis of copper nanoparticles. Int. Nano Lett. 6 (1), 21–26.

Klabunde, K.J., Stark, J., Koper, O., Mohs, C., Park, D.G., Decker, S., Jiang, Y., Lagadic, I., Zhang, D., 1996. Nanocrystals as stoichiometric reagents with unique surface chemistry. J. Phys. Chem. 100 (30), 12142–12153.

Kuroda, K., Yamagachi, Y., Endo, G., 1992. Mitotic toxicity, sister chromatid exchange and rec assay of pesticides. Arch. Environ. Contam. Toxicol. 23, 13–18.

Kyriakopoulos, G., Doulia, D., 2006. Adsorption of pesticides on carbonaceous and polymeric materials from aqueous solutions: a review. Sep. Purif. Rev. 35 (3), 97–191.

Lagadec, A.J.M., Miller, D.J., Lilke, A.V., Hawthorne, S.B., 2000. Pilot-scale subcritical water remediation of polycyclic aromatic hydrocarbon-and pesticide-contaminated soil. Environ. Sci. Technol. 34 (8), 1542–1548.

Laseter, J.L., 1979. Approaches to monitoring organic environmental contaminants in food. In: Environmental Contamination of Food, pp. 187–194.

Lavand, A.B., Malghe, Y.S., 2015. Synthesis, characterization and visible light photocatalytic activity of nitrogen-doped zinc oxide nanospheres. J. Asian Ceram. Soc. 3 (3), 305–310.

Li, F., Chunyang, L., Qinpeng, S., Lijun, L., Ming, W., Manli, G., Yan, H., Zhou, N., Shouzhuo, Y., 2013a. Analysis of copper nanoparticles toxicity based on a stress-responsive bacterial biosensor array. Nanoscale 5 (2), 653–662.

Li, H., Zhang, S., Zhong, Q., 2013b. Effect of nitrogen doping on oxygen vacancies of titanium dioxide supported vanadium pentoxide for ammonia-SCR reaction at low temperature. J. Colloid Interface Sci. 402, 190–195.

Liu, T.-F., Sun, C., Ta, N., Hong, J., Yang, S.-G., Chen, C.-X., 2007. Effect of copper on the degradation of pesticides cypermethrin and cyhalothrin. J. Environ. Sci. 19, 1235–1238.

Liu, H., Chen, Z., Jin, Z., Su, Y., Wang, Y., 2014. A reduced graphene oxide supported Cu_3SnS_4 composite as an efficient visible-light photocatalyst. Dalton Trans. 43 (20), 7491–7498.

Manav, N., Dwivedi, V., Bhagi, A., 2018. Degradation of DDT, a pesticide by mixed metal oxides nanoparticles. Green Chemistry in Environmental Sustainability and Chemical Education. Springer.

Manga Raju, I., Siva Rao, T., Divya Laxmi, K.V., Chandra, R., Swathi Padmaja, J., Divya, G., Mantecca, P., et al., 2015. Toxicity evaluation of a new Zn-doped CuO nanocomposite with highly effective antibacterial properties. Toxicol. Sci. 146 (1), 16–30.

Maragatha, J., Rani, C., Rajendran, S., Karuppuchamy, S., 2017. Microwave synthesis of nitrogen doped Ti_4O_7 for photocatalytic applications. Phys. E Low-Dimens. Syst. Nanostruct. 93 (May), 78–82.

Meng, X., Geng, D., Liu, J., Li, R., Sun, X., 2011. Controllable synthesis of graphene-based titanium dioxide nanocomposites by atomic layer deposition. Nanotechnology 22 (16), 165602.

Minocha, S., Mumper, R.J., 2012. Effect of carbon coating on the physico-chemical properties and toxicity of copper and nickel nanoparticles. Small 8 (21), 3289–3299.

Mitra, D., Varshney, L., 2013. Remediation of pesticide endosulfan in solution by ionizing radiation, advanced oxidation process and copper nano particle interaction a comparative studies using GC-MS analysis. J. Environ. Sci. Toxic. Food Technol. 7 (2), 8–11.

Molinari, R., Lavorato, C., Argurio, P., 2020. Visible-light photocatalysts and their perspectives for building photocatalytic membrane reactors for various liquid phase chemical conversions. Catalysts 10 (11), 1334.

Moschini, E., Gualtieri, M., Colombo, M., Fascio, U., Camatini, M., Mantecca, P., 2013. The modality of cell-particle interactions drives the toxicity of nanosized CuO and TiO_2 in human alveolar epithelial cells. Toxicol. Lett. 222 (2), 102–116.

Murthy, S.K., 2007. Nanoparticles in modern medicine: state of the art and future challenges. Int. J. Nanomed. 2 (2), 129.

Nagami, H., 2010. Historical perspective of pesticide poisoning in Japan and measures taken by the Japanese Association of Rural Medicine. J. Rural Med. 5 (1), 129–133.
Nayak, S.K., Dash, B., Baliyarsingh, B., 2018. Microbial remediation of persistent agrochemicals by soil bacteria: an overview. In: Microbial Biotechnology. Springer.
Nazim, M., Khan, A.A.P., Asiri, A.M., Kim, J.H., 2021. Exploring rapid photocatalytic degradation of organic pollutants with porous CuO nanosheets: synthesis, dye removal, and kinetic studies at room temperature. ACS Omega 6 (4), 2601–2612.
Nekooie, R., Shamspur, T., Mostafavi, A., 2020. Novel CuO/TiO_2/PANI nanocomposite: preparation and photocatalytic investigation for chlorpyrifos degradation in water under visible light irradiation. J. Photochem. Photobiol. A Chem., 113038.
Pajević, S., Arsenov, D., Nikolić, N., Borišev, M., Orčić, D., Župunski, M., Mimica-Dukić, N., 2018. Heavy metal accumulation in vegetable species and health risk assessment in Serbia. Environ. Monit. Assess. 190 (8), 1–14.
Parrón, T., Requena, M., HernándezAlarcón, A.F.R., 2014. Environmental exposure to pesticides and cancer risk in multiple human organ systems. Toxic. Lett. 230 (2), 157–165.
Pathania, D., Sharma, A., Kumar, S., et al., 2021. Bio synthesized Cu-ZnO hetero nanostructure for catalytic degradation of organophosphate chlorpyrifos under solar illumination. Chemosphere 277, 130315.
Piret, J.P., Mejia, J., Lucas, S., Zouboulis, C.C., Saout, C., Toussaint, O., 2014. Sonicated and stirred copper oxide nanoparticles induce similar toxicity and pro-inflammatory response in N-hTERT keratinocytes and SZ95 sebocytes. J. Nanopart. Res. 16 (4).
Prasad, R., Bhattacharyya, A., Nguyen, Q.D., 2017. Nanotechnology in sustainable agriculture: recent developments, challenges, and perspectives. Front. Microbiol. 8, 1014.
Qamar, M.T., Aslam, M., Ismail, I.M., Salah, N., Hameed, A., 2015. Synthesis, characterization, and sunlight mediated photocatalytic activity of CuO coated ZnO for the removal of nitrophenols. ACS Appl. Mater. 7 (16), 8757–8769.
Rachna, Rani, M., Shanker, U., 2018. Enhanced photocatalytic degradation of chrysene by Fe_2O_3@ ZnHCF nanocubes. Chem. Eng. J. 348, 754–764.
Rachna, Rani, M., Shanker, U., 2019. Degradation of tricyclic polyaromatic hydrocarbons in water, soil and river sediment with a novel TiO_2 based heterogeneous nanocomposite. J. Environ. Manag. 248, 109340.
Rachna, Rani, M., Shanker, U., 2020. Sunlight assisted degradation of toxic phenols by zinc oxide doped prussian blue nanocomposite. J. Environ. Chem. Eng. 8 (4), 104040.
Rafique, N., Tariq, S.R., Ahad, K., Taj, T., 2016. Cu^{2+} and Fe^{2+} mediated photodegradation studies of soil-incorporated chlorpyrifos. Environ. Sci. Pollut. Res. 23, 4473–4480.
Ramos, M.K., Zarbin, A.J., 2020. Graphene/copper oxide nanoparticles thin films as precursor for graphene/copper hexacyanoferrate nanocomposites. Appl. Surf. Sci. 515, 146000.
Rani, M., 2012. Studies on Decay Profiles of Quinalphos and Thiram Pesticide (Ph.D. thesis). Indian Institute of Roorkee, Roorkee (Chapters 1 and 5).
Rani, M., Shanker, U., 2017. Removal of carcinogenic aromatic amines by metal hexacyanoferrates nanocubes synthesized via green process. J. Environ. Chem. Eng. 5, 5298–5311.
Rani, M., Shanker, U., 2018. Insight in to the degradation of bisphenol A by doped ZnO@ ZnHCF nanocubes: high photocatalytic performance. J. Colloid. Interf. Sci. 530, 16–28.
Rani, M., Rachna, Shanker, U., 2020. Metal oxide-chitosan based nanocomposites for efficient degradation of carcinogenic PAHs. J. Environ. Chem. Eng. 8, 103810.
Rani, M., Yadav, J., Keshu, Shanker, U., 2021. Green synthesis of sunlight responsive zinc oxide coupled cadmium sulfide nanostructures for efficient photodegradation of pesticides. J, Colloid. Interf. Sci. 601, 689–703.

Rani, M., Shanker, U., Yadav, J., Keshu, 2021. Degradation of pesticide residue by engineered nanomaterial. Sustain. Agric. Rev. 48, 259–310.

Raul, P.K., Senapati, S., Sahoo, A.K., Umlong, I.M., Devi, R.R., Thakur, A.J., Veer, V., 2014. CuO nanorods: a potential and efficient adsorbent in water purification. RSC Adv. 4 (76), 40580–40587.

Raut, S.S., Kamble, S.P., Kulkarni, P.S., 2016. Efficacy of zero-valent copper (Cu0) nanoparticles and reducing agents for dechlorination of mono chloroaromatics. Chemosphere 159, 359–366.

Rawtani, D., Khatri, N., Tyagi, S., Pandey, G., 2018. Nanotechnology-based recent approaches for sensing and remediation of pesticides. J. Environ. Manage. 206, 749–762.

Razeeb, K.M., et al., 2014. Antimicrobial properties of vertically aligned nano-tubular copper. Mater. Lett. 128, 60–63.

Rhim, J.W., Park, H.M., Ha, C.S., 2013. Bio-nanocomposites for food packaging applications. Prog. Poly. Sci. 38 (10–11), 1629–1652.

Richter, F.M., Rowley, D.B., DePaolo, D.J., 1992. Sr isotope evolution of seawater: the role of tectonics. ESPL 109 (1–2), 11–23.

Rosbero, T.M.S., Camacho, D.H., 2017. Green preparation and characterization of tentacle-like silver/copper nanoparticles for catalytic degradation of toxic chlorpyrifos in water. J. Environ. Chem. Eng. 5 (3), 2524–2532.

Rousk, J., Ackermann, K., Curling, S.F., Jones, D.L., 2012. Comparative toxicity of nanoparticulate CuO and ZnO to soil bacterial communities. PLoS One 7 (3).

Sahithya, K., Das, D., Das, N., 2015. Effective removal of dichlorvos from aqueous solution using biopolymer modified MMT–CuO composites: equilibrium, kinetic and thermodynamic studies. J. Mol. Liq. 211, 821–830.

Sankar, R., Manikandan, P., Malarvizhi, V., Fathima, T., Shivashangari, K.S., Ravikumar, V., 2014. Green synthesis of colloidal copper oxide nanoparticles using *Carica papaya* and its application in photocatalytic dye degradation. Spectrochim. Acta A Mol. Biomol. Spectrosc. 121 (75), 746–750.

Saunders, S.E., Bartz, J.C., Bartelt-Hunt, S.L., 2012. Soil-mediated prion transmission: is local soil-type a key determinant of prion disease incidence? Chemosphere 87 (7), 661–667.

Saxena, G., Purchase, D., Mulla, S.I., Saratale, G.D., Bharagava, R.N., 2019. Phytoremediation of heavy metal-contaminated sites: eco-environmental concerns, field studies, sustainability issues, and future prospects. Rev. Environ. Contam. Toxicol. 249, 71–131.

Shanker, U., Jassal, V., Rani, M., 2016. Catalytic removal of organic colorants from water using some transition metal oxide nanoparticles synthesized under sunlight. RSC Adv. 6 (97), 94989–94999.

Singh, Y., Khind, C.S., Singh, B., 1991. Efficient management of leguminous green manures in wetland rice. Adv. Agron. 45, 135–189.

Škrbić, B., Đurišić-Mladenović, N., 2010. Chemometric interpretation of heavy metal patterns in soils worldwide. Chemosphere 80 (11), 1360–1369.

Tamuly, C., Hazarika, M., Das, J., Bordoloi, M., Borah, D.J., Das, M.R., 2014. Bio-derived CuO nanoparticles for the photocatalytic treatment of dyes. Mater. Lett. 123, 202–205.

Tyagi, H., Chawla, H., Bhandari, H., Garg, S., 2021. Recent enhancements in visible light photocatalytic degradation of organochlorines pesticides: a review. Mater. Today. Proc. https://doi.org/10.1016/j.matpr.2020.12.1036.

Vadivel, S., Maruthamani, D., Paul, B., Dhar, S.S., Habibi-Yangjeh, A., Balachandran, S., Saravanakumar, B., Selvakumar, A., Selvam, K., 2016. Biomolecule-assisted solvothermal synthesis of Cu_3SnS_4 flowers/RGO nanocomposites and their visible-light-driven photocatalytic activities. RSC Adv. 6 (78), 74177–74185.

Van, N.L., Mac, C., Shang, J., Rui, Y., et al., 2016. Effects of CuO nanoparticles on insecticidal activity and phytotoxicity in conventional and transgenic cotton. Chemosphere 144, 661–670.

Van Toan, P., Sebesvari, Z., Bläsing, M., Rosendahl, I., Renaud, F.G., 2013. Pesticide management and their residues in sediments and surface and drinking water in the Mekong Delta, Vietnam. Sci. Total Environ. 452, 28–39.

Wu, W., Jiang, C., Roy, V.A., 2015. Recent progress in magnetic iron oxide–semiconductor composite nanomaterials as promising photocatalysts. Nanoscale 7 (1), 38–58.

Xie, J., Wang, P., Liu, J., Lv, X., Jiang, D., Sun, C., 2011. Photodegradation of lambda-cyhalothrin and cypermethrin in aqueous solution as affected by humic acid and/or copper: intermediates and degradation pathways. Environ. Toxicol. Chem. 30 (11), 2440–2448.

Xu, P., Xu, J., Liu, S., Ren, G., Yang, Z., 2012. In vitro toxicity of nanosized copper particles in PC12 cells induced by oxidative stress. J. Nanopart. Res. 14 (6).

Xu, C., Anusuyadevi, P.R., Aymonier, C., Luque, R., Marre, S., 2019. Nanostructured materials for photocatalysis. Chem. Soc. Rev. 48 (14), 3868–3902.

Yasmina, M., Mourad, K., Mohammed, S.H., Khaoula, C., 2014. Treatment heterogeneous photocatalysis; factors influencing the photocatalytic degradation by TiO_2. Energy Procedia 50, 559–566.

Yeganeh, M., Charkhloo, E., Sobhi, H.R., et al., 2021. Photocatalytic processes associated with degradation of pesticide in aqueous solutions: systematic review and meta-analysis. Chem. Eng. J. https://doi.org/10.1016/j.cej.2021.130081.

Yruela, I., 2009. Copper in plants: acquisition, transport and interactions. Funct. Plant Biol. 36, 409–430.

Zhang, G., Li, Z., Zheng, H., Fu, T., Ju, Y., Wang, Y., 2015. Environmental influence of the surface oxygenated groups of activated carbon on preparation of a nano Cu/AC catalyst and heterogeneous catalysis in the oxidative carbonylation of methanol. Appl. Catal. Environ. 179, 95–105.

Zhao, J., Wang, Z., Liu, X., Xie, X., Zhang, K., Xing, B., 2011. Distribution of CuO nanoparticles in juvenile carp (*Cyprinus carpio*) and their potential toxicity. J. Hazard. Mater. 197, 304–310.

Zhou, Y., Morais-Cabral, J.H., Kaufman, A, MacKinnon, R., 2001. Chemistry of ion coordination and hydration revealed by a K^+ channel–Fab complex at 2.0 Å resolution. Nature 414 (6859), 43–48.

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CHAPTER

Multifunctional copper-based nanocomposites in agroecosystem applications 23

Chandrasekaran Rajkuberan[a], Periakaruppan Rajiv[a], Manal Mostafa[b], and Kamel A. Abd-Elsalam[c]

[a]*Department of Biotechnology, Karpagam Academy of Higher Education, Coimbatore, India,*
[b]*Organic Egypt, Heliopolis University for Sustainable Development, Cairo, Egypt,*
[c]*Plant Pathology Research Institute, Agricultural Research Center (ARC), Giza, Egypt*

1 Introduction

Agriculture is the backbone of every country and plays a crucial role in the economy of the country. The intensive and extensive use of chemical-based fertilizers, insecticides, and micronutrients enhances plant growth, production, and protection (Shang et al., 2019). But in the present scenario, agriculture practices remain challenged due to toxicity, resistance, harmful effects, and low yields by the chemical-based methods (Shetty, 2004). In this junction, it is mandated to incorporate new hyphenated technology with the existing methods to improve crop production and protection. Although we have ample production of bio-based products such as insecticides, pesticides, and growth regulators, their practical application in crops remains a challenge in certain plants and species. The application of nano-size particles synthesized using bioresources is a indeed approach to overcome the problems in plant diseases.

Recent advancements made in science and technology have led to the development of nanotechnology. Particles in the range of 1–100 nm will have different optical and physical properties compared with the parent compound (Jeevanandam, 2018). Among the particles, metal/metal oxide, polymers, dendrimers, quantum dots, ceramics, carbon nanotubes are notably the preferred ones due to their unique optical, physical, and electronic properties. Nanoparticles have a broad range of applications in solar cells, lithium-ion batteries, electrocatalyst, dyeing industries, food industries, chemical industries, pharmaceutical sectors, antimicrobial, immunomodulant, anticancer, and diagnostic agents (Patil and Chandrasekaran, 2020). Moreover, nanoparticles can be easily conjugated with biomolecules, functional groups, proteins, DNA/RNA, organic/inorganic compounds for the desired applications (Khan et al., 2019a, b). These customized features in nanoparticles make them feasible to apply in all research and industrial sectors.

In agriculture, the role of metallic nanocomposite is momentously gaining attraction from researchers. Nanoparticles play a crucial role in environmental problems

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such as dye removal, detection of pollutants, heavy metals, water purification, and gas exchange (Sadegh et al., 2017). Likewise, in agriculture, metallic nanoparticles are involved in plant protection and production. Varieties of metallic nanoparticles (silver, gold, copper, zinc, iron oxide, graphene oxide, platinum, palladium, and cerium oxide) have been fabricated and usage has been exploited in various agricultural sectors and food packaging.

Notably, copper nanoparticles have gained significant interest due to their natural availability, simple synthesis, cost-effectiveness and wider applications in electrochemicals, solar cells, batteries, pharmaceuticals, drug delivery, antimicrobial agents and sensors (Gawande et al., 2016). Using copper nanoparticles in agriculture is an added advantage as copper is an essential vital element for plant growth and metabolism. Henceforth, the usage of copper and its composite materials in agriculture and the environmental problem are of primary concern. This chapter emphasizes the development of copper nanocomposite and its potential application in an agroecosystem.

2 Metallic nanoparticles

Nanoparticles differ in in size and shape. Nanoparticles can be zero-dimensional (nanodots), one-dimensional (graphene), two-dimensional (carbon nanotubes), and three-dimensional (gold nanoparticles) (Tiwari et al., 2012). Nanoparticles are of different size, shape, and structure. It will be spherical, cylindrical, hollow sphere, truncated, tubular, rod, spiral, flat, or irregular with the size ranging from 1 to 100 nm. Some nanoparticles are either amorphous or crystalline with single or multicrystal solids, either loose or agglomerated (Machado et al., 2015).

Nanoparticles are generally categorized into three groups: organic, inorganic, and carbon-based. Organic nanoparticles such as dendrimers, liposomes, micelles are biodegradable, nontoxic, and suitable for drug delivery. Carbon-based nanoparticles are completely based on carbon and can be classified as fullerenes, graphene, carbon nanotubes, and carbon nanofibers (Ealia and Saravanakumar, 2017). These kinds of nanomaterials are applicable in all research domains.

Inorganic nanomaterials are metallic nanoparticles synthesized from metals to nanometric sizes in the range of 0–100 nm. The metallic nanoparticles include silver, gold, copper, iron oxide, graphene oxide, platinum, palladium, and zinc. Metal oxide nanoparticles are nanoparticles synthesized from metals to modify the properties of metal-based nanoparticles (Sarkar et al., 2012). For instance, iron nanoparticles are readily oxidized into iron oxide nanoparticles in the presence of oxygen at room temperature. Metal oxide nanoparticles are aluminum oxide, iron oxide, copper oxide, zinc oxide, titanium oxide, and others. These metallic/metal oxide nanoparticles have multifunctional properties like unique optical-electronic properties, surface plasmon resonance, electrical, thermal conductivity, and other properties (Fedlheim and Foss, 2001). Henceforth, these kinds of metallic/metal oxide nanoparticles are getting overwhelming responses from different research fraternities and hold a strong niche in physical, chemical, and biological sectors.

The synthesis of metallic/metal oxide nanoparticles is a main concern for researchers and also an important factor for the successful usage of metallic nanoparticles from a commercial perspective. Conceivably, nanoparticles are synthesized by three methods: physical, chemical, and biological methods. But physical and chemical methods require high energy, usage of hazardous chemicals, and produce toxicity also. Later, in the biological method of synthesis, it employs bacteria, viruses, yeast, and fungi as reducing and stabilizing agents for the synthesis of metallic nanoparticles (Khandel et al., 2018). Though the synthesis method varies the metallic nanoparticles fabricated through any method, the synthesized metallic nanoparticles will exhibit stupendous activity in diversified applications.

2.1 Copper nanoparticles

Copper (Cu) is an important transition metal having novel physical and chemical properties. Moreover, Cu-based materials undergo a wide variety of chemical reactions via one- and two-electron pathways due to the Cu accessible oxidation states (Cu^0, Cu^I, CuII, and Cu^{III}). These notable features make Cu nanomaterials have a wide application in photocatalysis, electrocatalysis, and catalytic organic transformations.

The production of copper nanoparticles was achieved through three major routes: (i) physical, (ii) chemical, and (iii) biological methods as explained in Table 1.

Copper nanoparticle characteristics such as size, shape, and particle size distribution may vary depending on the method of synthesis. For instance, salts like cupric acetate (monohydrate) $(CH_3COO)_2Cu{\cdot}H_2O$), copper chloride dihydrate ($CuCl_2.2H_2O$)[20] and copper sulfate pentahydrate ($CuSO_4.5H_2O$), temperature, pH, and synthesis methods will determine the synthesis of copper nanoparticles characteristics. Synthesis of nanoparticles by physical methods produces nanoparticles quickly but requires high energy, pressure, and manpower.

Chemical-mediated synthesis of nanoparticles is a simple one-step procedure employing copper salts and reducing agent isopropyl alcohol with cetyl trimethyl ammonium bromide (CTAB), ascorbic acid, sodium borohydride, glucose, hydrazine, and polyol. Though chemical-mediated synthesis of copper nanoparticles can synthesize monodispersed nanoparticles, it involves the utilization of hazardous chemicals which restricts the applications in the medicinal sector. Recently, biogenic copper nanoparticles are a new module for generating copper nanoparticles encompassing biological resources like plants, microbes, and others. The so-called method produces polydispersed nanoparticles but it does not exert high toxicity to living beings and the environment.

Table 1 depicts the production of copper nanoparticles through different methods. These methods have pros and cons concerning the synthesis procedure, employing chemicals and others too; but eventually, the size and shape of copper nanoparticles are directly proportional to the reducing agent, temperature, energy, pressure, chemical, resources, and other features.

Table 1 provides the representative list of copper nanoparticles fabricated through physical, chemical and biological methods.

S.·No.	Name of the technique	Shape and Size	Reference
Physical methods			
1	Thermal Decomposition	Spherical, 4–18 nm.	Betancourt-Galindo et al. (2014)
2	Mechanical Ball	Spherical, 21 nm.	Yadav and Vasu (2016)
3	Laser Abrasion	Spherical, 5–16 nm	Sadrolhosseini et al. (2013)
4	Pulsed Wire Discharge		Suematsu et al. (2007)
5	Gas Evaporation	Spherical, 15–700 nm	Chepkasov et al. (2016)
Chemical methods			
6.	Chemical Reduction	Spherical, < 10 nm	Dang et al. (2011)
7.	Microemulsion Reduction		Qiu et al. (1999)
8.	Microemulsion Reduction		Kumar et al. (2013)
9.	Sonochemical	Spherical, 20–90 nm	Bhanjana et al. (2017)
Biological methods			
10.	Biological (*Hagenia abyssinica)*	Hexagonal, triangular, cylindrical, 34 nm	Murthy et al. (2020)
11.	Biological (*Celastrus paniculatus)*	Spherical, 2–10 nm	Mali et al. (2020)
12.	Biological (*Beta vulgaris*)	Spherical, 50 nm	Chandrasekaran et al. (2020)
13.	Biological (*Pseudomonas fluorescens* MAL2)	Spherical, 49 nm	Shantkriti and Rani (2014)
14.	Biological (*Trichoderma asperellum*)	Spherical, 10–190 nm.	Saravanakumar et al. (2019)

3 Nanocomposites

Nanocomposites are a combination of two different materials with improved properties; among the two different materials, one must be in the range of 0–100 nm (Okpala, 2013). Nanocomposites can be developed from materials like metals, polymers, and ceramics. The so-called nanocomposites have a combination or have markedly contrasting thermal, electrical, mechanical, optic, and catalytic properties from the

component materials. The nanocomposites can be categorized as zero-dimensional (core-shell), one-dimensional (nanowires and nanotubes), two-dimensional (lamellar), and three-dimensional (metal matrix composites) (Tiwari et al., 2012). Based on the structural insight, these nanocomposites can be grouped as nano-layered composites, nanofilamentary composites, and nano-particulate composites. These customized nanocomposites have emerged as materials of the 21st century having wide applications in all sectors of sciences.

The metal nanocomposite is a new generation of materials having metals/polymer/ceramics. These mixed composite materials perform a wide variety of functional roles in electrochemical cells, solar cells, sensors, environmental detection of pollutants, agriculture, and drug delivery. The metal nanocomposite is synthesized by two principles: (a) a top-down approach (b) a bottom-up approach. In the top-down approach, physical methods are employed, while in the bottom-up approach chemical methods are preferred. Among the chemical methods, coprecipitation, sol-gel, and the hydrothermal method are choices of interest because these methods produce uniformity in size and different forms of nanocomposite (nano-rods, nanowires, nanocubes) (Table 2).

The characterization of metallic nanocomposite is an integral part of nanotechnology. For characterization, UV–Vis spectroscopy, Fourier transform infra-red spectroscopy, transmission electron microscopy, scanning electron microscopy, X-ray diffraction, and thermal gravity analysis were performed. These characterization techniques will revive the size, shape, phase composition, and thermal stability. Sakib et al. (2019) synthesized the CuO/ZnO nanocomposite by a simple mechanochemical combustion method. The synthesized CuO/ZnO were exclusively characterized as illustrated in Fig. 1. In Fig. 2A, the XRD diffraction studies reveal that CuO/ZnO is in a wurtzite ZnO crystal structure and the composites are composed of

Table 2 Metallic nanocomposite materials produced by the aforementioned chemical methods.

S·No	Metal Nanocomposite	Size and Shape	References
1.	Mg-CuO	20 nm	Selvi et al. (2021)
2.	ZnO-CuO	3D Flower-like nano patches	Das and Srivastava (2017)
3.	ZnO-SnO_2	30 nm	Tarique (2019)
4.	MgO-Al_2O_3	4–30 nm	Subhan et al. (2017)
5.	ZnO-Fe_3O_4	40 nm	Manikandan et al. (2020)
6.	Ag-Activated Carbon	55 nm	Rodrigues et al. (2019)
7.	ZeoliteY-Fe_3O_4	< 100 nm	Kalhor and Zarnegar (2019)
8.	TiO_2-Graphene		Zhang et al. (2010)
9.	ZnO-kaolinite	14–48 nm	Kutláková et al. (2015)
10.	TiO_2-Clay	1.7–4.5 nm	Belessi et al. (2007)

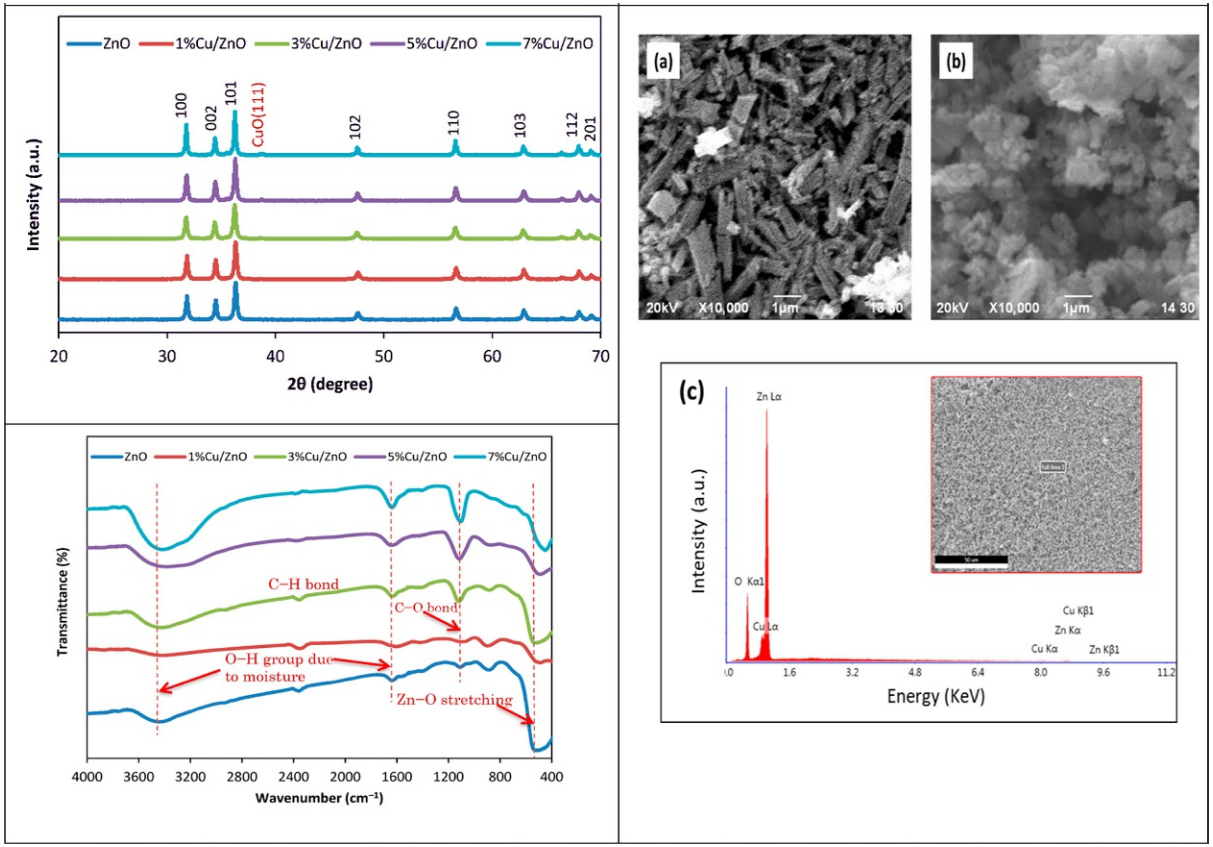

FIG. 1

(A) XRD of the CuO/ZnO nanocomposite, (B) SEM images of CuO/ZnO. (C) FTIR of the CuO/ZnO nanocomposite.

Images were obtained from Sakib, A.A.M., Masum, S.M., Hoinkis, J., Islam, R., Molla, M., Islam, A., 2019. Synthesis of CuO/ZnO nanocomposites and their application in photodegradation of toxic textile dye. J. Composit. Sci., 33, 91. This is an open-access article distributed under the Creative Commons Attribution License with permission from MDPI.

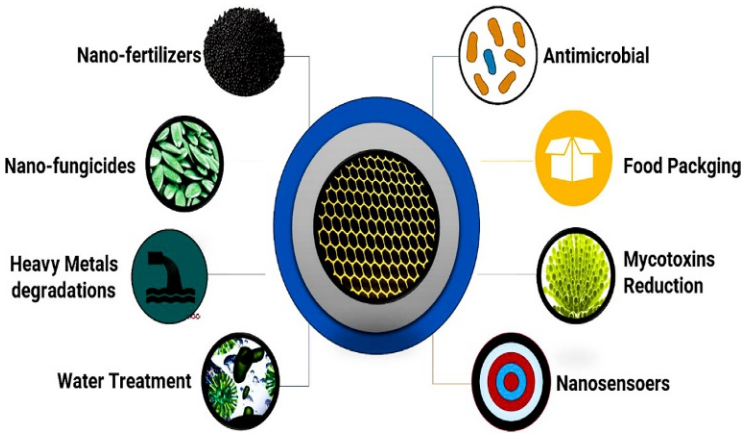

FIG. 2

Application of Cu-Nanocomposite in the agroecosystem.

CuO and ZnO. Fig. 2B shows the SEM images of CuO/ZnO; it is observed that the shape of CuO/ZnO was spheroidal. Fig. 2C infer that FTIR of CuO/ZnO; the functional groups involved in the CuO/ZnO formation.

4 Applications of copper nanocomposite

Copper nanocomposites have widespread applications in all disciplines of life sciences sectors. In biomedical applications, the metallic nanocomposite plays a dominant role either as a wound dressing or as an antimicrobial agent, disinfectant, and antifouling agent. Hebeish et al. (2011) designed cotton fabrics incorporated with Ag nanoparticles in the presence/absence of acrylate binder. The cotton fabrics restricted the growth of *E. coli* and *S. aureus* effectively. Tabesh et al. (2018) reported the antibacterial activity of the copper chitosan nanocomposite against methicillin-resistant *Staphylococcus aureus* and *E. coli*. Likewise, in another study, green synthesized CuO nanoparticles from *Sterculia foetida* were incorporated with glutaric acid, ethylene glycol, and acrylic acid (GEA) to form a hydrogel construct GEA-CuO nanocomposite. The nanocomposite exhibited effective inhibitory activity against the tested pathogens. In addition, the nanocomposite triggers apoptosis in the lung cancer cell line (A549) as evidenced by the MTT assay (Subashini et al., 2020). Hydroxyapatite-copper nanocomposite inhibited the growth of *E. coli* and *S. aureus*; the nanocomposite displays the least toxicity in osteoblast-like MG63 cells (Hadidi et al., 2017). These results indicate that Hydroxyapatite-Copper Nanocomposite is a safe biomaterial for bone implant in bone tissue engineering.

4.1 Applications of copper nanocomposite in the agroecosystem

The introduction of nano-based concepts in agriculture practices such as fertilizers, insecticides, pesticides, micronutrients, gene delivery, fruit ripening, and postharvest management is exponentially increasing in recent years due to their easy use and cost-effectiveness (Fig. 2). In this pipeline, the significance of Cu nanocomposites is to be addressed; many intriguing research developments in Cu nanocomposites in agriculture were achieved.

Chitosan-copper nanoparticles were synthesized and assessed its effect on finger millet plants. The study bestowed that Cu-chitosan nanoparticles were applied as a foliar spray, and subsequently it resulted in an increase in the yield of plant growth and profile. Moreover, the treated plant was challenged with *Pyricularia grisea* pathogen; the plant did not show any sign of blast disease (Sathiyabama and Manikandan, 2018). In another study, Cu-CNF was synthesized over activated carbon substrates and evaluated in the plant. The plant growth was improved by the sustainable release of Cu from CNF. Besides, the carbon substrates were easily translocated from roots to shoots to leaves. Gonza'lez Go'mez et al. (2017) fabricated a Cu-NP-dispersed chitosan-PVA-based hydrogel and assessed the efficacy in watermelon. As a result, the hydrogel enhances the utilization of water and nutrition by increasing the width of stomata in the leaf and increases the root and shoot length. Likewise, Cu-NP-dispersed chitosan-PVA-based nanocomposites were tested against tomato (*Solanum lycopersicum* L.) under stress conditions; the nanocomposite induces the expression of Jasmonic acid and Superoxide dismutase and also increases the plant growth. Choudhary et al. (2017) demonstrated that the Cu-chitosan nanocomposite will boost defense responses in curvularia leaf spot (CLS) disease in maize plants. Moreover, on treating the diseased plant with the Cu-chitosan nanocomposite, the plant can produce antioxidant (superoxide dismutase and peroxidase) and defense enzymes (polyphenol oxidase and phenylalanine ammonia-lyase) at higher concentrations indicating the defense response against the disease. Further, in pot and field experiments, the Cu-chitosan-treated plants exhibited disease-free and plant morphological features like height, stem diameter, root number and length, and chlorophyll content were promoted. Postharvest management is one of the primary tasks for researchers to prevent foods from decay and spoilage. In this aspect, a Cu-chitosan nanonet was designed and developed for the preservation of tomatoes. As a result, the tomatoes were preserved and the shelf life was extended up to 21 days. Noticeably, the Cu-chitosan net preserved tomatoes from microbial decay; significant variation was observed in physiological weight loss, respiration rate and fruit firmness was maintained during storage (Meena et al., 2020). Likewise, Juarez-Maldonado et al. (2016) demonstrated the effect of copper nanoparticles adsorbed on hydrogel in tomato fruits and seedlings. The hydrogel enhances tomato growth positively. Similarly, Cu nanoparticles embedded in PVA hydrogels stimulate the growth of capsaicin by 51% in the jalapeño pepper crop compared with untreated pepper plants. CuNPS-chitosan-polyacrylic acid hydrogel was applied to the onion plants as a foliar spray during the year 2016–17 at different seasons. The hydrogel increases the onion growth, chlorophyll content, and

other yields also at 75 ppm concentrations. Likewise, Mehta et al. (2021) documented the effect of chitosan-capped CuNPs in ginger (*Zingiber officinale*) under field conditions. The nanocomposite simulates the suppression of soft rot or rhizome disease caused by *Fusarium* or *Pythium* sp. Abd-Elsalam et al. (2018) studied the bimetallic blend BB (Zn–Cu) and Zn-chitosan, Cu-chitosan against the cotton seedling disease. The BB effectively suppresses the *Rhizoctonia solani* under greenhouse conditions. Moreover, the Cu nanocomposite combined with the *Trichoderma* strain also suppresses the cotton seedling disease under in vivo conditions.

Kumar et al. (2018) developed a nanofertilizer by producing polymer bimetallic carbon-containing bimetallic nanoparticles (Cu/Zn) dispersed in carbon nanofibers (CNF) encapsulated with PVA starch. The produced nanocomposite slowly releases the Cu/Zn micronutrients in a controlled manner and is easily translocated through roots to shoots to leaves. This method of producing polymer-metal-CNF is a newer approach and has immense potential in agricultural applications.

Inherently metals having antimicrobial properties; when the metal is reduced into nano form, it exhibits more activity than the parent one. Numerous studies have reported that metallic nanoparticles have innumerable antimicrobial activities against bacteria, viruses, pests, and nematodes. Nanoparticles combined with other materials (polymers, ceramics, metals) will boost up the antimicrobial activity and also the combination of materials will have the following advantages such as crystallinity, solubility, stability, and biodegradability. Generically, copper nanoparticles incorporated with polymer matrices (chitosan) exhibited enhanced activity against a broad range of microorganisms (Tamayo et al., 2016). Chitosan nanogels incorporated with Cu(II) exhibited strong antagonistic activity against the pathogenic fungus *Fusarium graminearum*. This is due to the synergistic effect of the chitosan–Cu (II) nanogel complex. Bogdanović et al. (2018) reported the copper nanoparticles designed with polyaniline to form a CuNPS-polyaniline nanocompoite. The nanocomposite remarkably exhibited inhibitory activity against *E. coli*, *S. aureus*, and *C. albicans* with a concentration of < 1 ppm within 2 h. Sumac extract was utilized as a reducing/stabilizing agent to fabricate copper nanoparticles. The synthesized copper nanoparticles were conjugated with chitosan; the so-called nanocomposite performed stupendous biocidal activity against the tested pathogens Xanthomonas perforans, Clavibacter michiganensis sub sp. *michiganensis, Erwinia amylovora,* and *Pseudomonas syringae* pv. *syringae* at different concentrations of 0.5 ppm, 1 ppm, 1.5 ppm. Aflatoxigenic protein from *A. flavus* is effectively controlled by CuNPs incorporated chitosan hydrogels effectively in a substantial manner. The effect of protein suppression depends on the fungal strain, nanocomposite, and medium used (Abd-Elsalam et al., 2020). Saharan et al. (2015) synthesized the Cu-chitosan nanocomposite against the diseases (early blight and Fusarium wilt) in tomato plants. The composite effectively suppressed *Alternaria solani* and *Fusarium oxysporum*. Further, the growth of the tomato plant was also significant after the application of the Cu nanocomposite. Vinceković et al. (2016) designed a microcapsule containing the Cu-ion-*Trichoderma viridae*-alginate. The results demonstrated that Cu ions improve the germination of *T. viridae* and

also deliver nutrients (Cu) to the plants. These nanocomposites act as protectants and also as micronutrients to the plant. Similarly, the Cu-chitosan nanocomposite dominantly inhibited the growth of the damping-off disease-causing fungi *R. solani* and *Pythium aphanidermatum* (Vanti et al., 2020). Abd-Elsalam et al. (2018) synthesized Cu/Zn chitosan and a Cu/Zn chitosan *Trichoderma longibrachiatum*-based nanocomposite. The Cu/Zn nanocomposite displays stupendous antifungal activity against the plant pathogenic fungi; while the Cu/Zn chitosan *Trichoderma longibrachiatum*-based nanocomposite suppressed the *Rhizoctonia solani* causative agent for cotton seedling diseases. Similarly, the chitosan-Cu < Cu-chitosan? > nanocomposite enhances the growth in the finger millet plant and also induces resistance against blast disease (Sathiyabama and Manikandan, 2018). The Cu-loaded thiamine-based composite acted as a growth stimulant and also protects the plants from virus and fungi in the chickpea plant (Muthukrishnan et al., 2019). The antibacterial activity of nanocomposites is primarily attributed to the use of biopolymers and nanoparticles which enhance the activity. These can be categorized into three phenomena: (i) fine dispersion of nanoparticles in the polymer matrices to increase the surface area, (ii) synergic interaction of nanoparticles with polymers, and (iii) sustained release of metallic ions from the polymer matrices to prolong the antibacterial activity (Bikiaris and Triantafyllidis, 2013; Bogdanović et al., 2015; Jayaramudu et al., 2019).

Nanomaterials conjugated with polymeric matrices are used as a tool for the removal of water pollutants and as a biological indicator of water pollution and contamination (Ahmad et al., 2020). In desalination plants, the copper nanoparticles were impregnated with chitosan membranes; the amino group in the chitosan can be easily protonated in the acidic media so that chitosan can easily interact with organic pollutants, and hence it can be easily removed (Sarma et al., 2019). Alzahrani (2018) demonstrated that the thin film membranes of CS-ZnO and CS-ZnO/CuO effectively removed the harmful dyes.

Pesticide contamination in water bodies and the soil deteriorates the ecosystem/adversely. Moreover, these pesticides indirectly accumulate in the vegetative parts and pose a great threat to human beings also. The Cu-based nanocomposite is effective in removing pesticides from the soil and aquatic water bodies as evidenced by the recent reports. Jaiswal et al. (2012) constructed a Cu-based chitosan nanocomposite to remove malathion pesticide from agricultural runoff. Cu ions act as an adsorption agent, forming a dithionate complex during the recovery process. Similarly, Cu-loaded diethylenetriamine cotton fibers were synthesized for the removal of Linuron pesticides from water. The nanocomposite effectively removes the pesticide with high adsorption efficiency. This is due to the amino groups present in the cotton fibers from a complex with Cu ions with greater affinity. As a result, the adsorbing efficiency is increased. Kumar and Verma (2018) fabricated CuNPs decorated with CNFs for the degradation of dichlorvos pesticide. The nanocomposite removes the pesticide by degrading the dichlorvos pesticide into carbon dioxide, water, phosphate, and chloride ions, which are nontoxic. Similarly, Cu/Fe NPs were decorated

with CNFs to remove the degradation of dichlorvos pesticide and also in the removal of chromium ions from water samples (Kumar and Verma, 2019). The nanocomposite effectively removes the chromium ions and the treated water was nontoxic and amicable for agriculture usage.

In the present scenario, environmental pollution and its management is the main concern for researchers. Versatile metallic nanocomposites were employed in tackling the environmental pollutants as adsorbents, photocatalysts, and sensors. Dye pollution is seriously alarming the environment; it primarily affects the water bodies and subsequently causes adverse effects in the ecosystem; therefore, it is necessitating removing the pollutant from the environment also. For instance, Karthikeyan et al. (2017) reported that the chitosan/Cu nanocomposite was effective in removing rhodamine B (RhB) and Congo red (CR) dyes pollutant dyes from an aqueous medium. Dura'n et al. (2019) synthesized a Cu-alumina chitosan-based membrane which effectively removes the methylene blue from wastewater. Similarly, a $CuFe_2O_4$ incorporated polyaniline-based nanocomposite was conceived to eradicate the methylene orange dye from water bodies. The nanocomposite effectively removes the dye due to the surface charge of the nanocomposite and dye. Motahharifar et al., 2020 devised a nanocomposite encompassing CuNPs –magnetic Fe_3O_4 chitosan as a catalyst for synthesizing different tetrazoles by the reaction of secondary or tertiary cyanamides with sodium azide in water under reflux conditions. High efficacy of phosphate removal from wastewaters was performed by the Cu-chitosan/Fe_3O_4 nanocomposite. The nanocomposite removes the phosphate with a high adsorption capacity of 88 mg/g^{-1} when compared with raw chitosan. CuNPs-chitosan-graphene oxide (GO) nanofibers is used as a material for detection and catalytic reduction of 4-nitrophenol (4-NP) in water samples (Khan et al., 2019a, b). The detection and reduction were extremely high by the nanocomposite materials. Likewise, the Cs/Cu_2O/CuO nanocomposite performed effective catalytic activity in the reduction of 4-nitrophenol, cationic, anionic dyes, and reactive dyes (Zayed et al., 2020) (see Fig. 3).

Food packaging and preservation by a nanocomposite is a new trend in this sector; various nano entities were employed for packaging and preservation. In this pipeline, a CuNPs-based nanocomposite was effectively used for the food packaging process. In a study demonstrated by Cioffi et al. (2005), Copper-fluoropolymer (Cu-CFx) nanocomposite films were developed to assess its efficacy against the food pathogens *Saccharomyces cerevisiae, Escherichia coli, Staphylococcus aureus,* and *Lysteria*. The aforementioned nanocomposite suggested the potentiality of packaging materials in food preservation. In a study reported by Mehta et al. (2021), the developed nanoformulation has the potential to be turned into valuable technology that will improve the shelf life and quality of fruits and vegetables during long-term storage. Green chitosan-capped copper NCs have shown considerable antifungal and antibacterial action against major agricultural plant diseases such as *Fusarium* sp., *Aspergillus* sp., *Alternaria alternata*, *Pythium* sp., and *Bacillus cereus*.

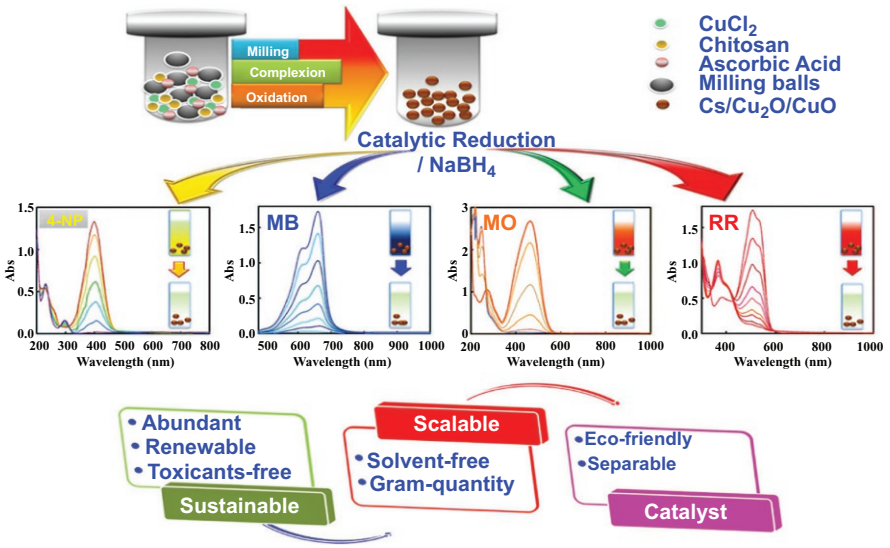

FIG. 3

The ball-milling preparation of the $Cs/Cu_2O/CuO$ nanocomposite.

Figure reprinted from Zayed, M.F., Eisa, W.H., Abd ElHameed, M.H., Abou Zeid, A.M., 2020. Spectroscopic investigation of the chitosan-supported Cu_2O/CuO nanocomposite; a separable catalyst for degradation of water pollutants. J. Alloys Compounds, 835, 155,306 with permission from Elsevier.

5 Future perspectives

Agriculture is adding fuel to the country's economy; the presently growing population demands the need for the production of agricultural products on a large scale. At the same time, crops are deteriorating due to pest attacks, lack of nutrients, microbial attack, and soil infertility. To meet these challenges and also increase production is a bottleneck factor for researchers. To alleviate all these problems, nanotechnology is a one-pot solution where nano-derived materials can act as pesticides/insecticides/micronutrients/growth regulators.

A metallic nanocomposite, especially a metal-polymer nanocomposite, has distinct features of biodegradability and biocompatibility which make it an ideal material to be used in crop protection and production. Customized nanomaterials might have the potential ability to be used in the agricultural sector, while conjugation of polymers with metallic nanoparticles will improve the release behavior, biocompatibility, ease of use.

For plant application studies, one must design the nanocomposite based on plant uptake, accumulation, and translocation ability. Carbon-based nanomaterials have a high translocation ability; henceforth, carbon-based nanocomposites can be developed in some plant application studies. Similarly, polymer chitosan also has high translocation capacity; further polymeric coating will change the surface charge and functionalization also.

Another important concern is toxicity; an engineered nanocomposite will impose toxicity. While applying an engineered nanocomposite in agriculture practices, it will leach into the environment and plants indirectly it will transform into humans. Commonly, CuNPs cause toxicity in plants, animals, and humans at higher concentrations. So when intending to apply in agriculture, it is strongly recommended to understand the toxic accumulation of Cu in plants. The toxic accumulation may vary depending on plant cells, species, and types of Cu nanomaterials used. To minimize the toxicity, the green synthesis of Cu nanomaterials can be developed from waste biomass. Also, conjugation of polymers with Cu nanoparticles will decrease the toxicity and also improve bioavailability, biodegradability, and translocation.

Nanomaterials are a powerful versatile tool to counteract stress, diseases, deliver micronutrients and fertile improver. But understanding the interaction of plant cells with nanocomposite is less explored; there is a need for more investigation regarding the interaction of nanomaterials with plant cells and translocation; only thereby we can develop a nanocomposite as an environmentally friendly agent for the protection and production of crops.

Recently, nanoparticles are being used as an elicitor to improve the production of bioactive compounds which might have a profound application in the medicine, agriculture, food, and pharmaceutical industries (Rivero-Montejo et al., 2021). Nevertheless, in the near future, the role of the Cu nanocomposite as an elicitor should be extensively studied and its potential effect on the ecosystem and health risk on humans should also be subjected to assessment.

6 Conclusion

This chapter manifests the functional role of the Cu nanocomposite and its application in the agroecosystem. CuNPs can be fabricated through physical, chemical, and biological methods in a simple reaction step. Likewise, the conjugation of metallic nanoparticles with polymers is addressed with adequate methodology and characterization. The use of Cu nanocomposites is having wide applications as antibacterial, antifungal, in the removal of dyes and pollutants, food packaging material, and agroecosystem applications in a lucrative manner. Therefore, it can be concluded that the Cu-based composite is having sound application in the agriculture sector and can be further developed into a safe entity material free from toxicity with improved plant protection and production.

References

Abd-Elsalam, K.A., Vasil'kov, A.Y., Said-Galiev, E.E., et al., 2018. Bimetallic blends and chitosan nanocomposites: novel antifungal agents against cotton seedling damping-off. Eur. J. Plant Pathol. 151, 57–72.

Abd-Elsalam, K.A., Alghuthaymi, M.A., Shami, A., Rubina, M.S., Abramchuk, S.S., Shtykova, E.V., Yu Vasil'kov, A., 2020. Copper-chitosan nanocomposite hydrogels against aflatoxigenic *Aspergillus flavus* from dairy cattle feed. J. Fungi 6, 112.

Ahmad, N., Sultana, S., Khan, M.Z., Sabir, S., 2020. Chitosan-based nanocomposites as efficient adsorbents for water treatment. In: Modern Age Wastewater Problems. Springer, Cham, pp. 69–83.

Alzahrani, E., 2018. Chitosan membrane embedded with ZnO/CuO nanocomposites for the photodegradation of fast green dye under artificial and solar irradiation. Anal. Chem. Insights 13. 1177390118763361.

Belessi, V., Lambropoulou, D., Konstantinou, I., Katsoulidis, A., Pomonis, P., Petridis, D., Albanis, T., 2007. Structure and photocatalytic performance of TiO2/clay nanocomposites for the degradation of dimethachlor. Appl. Catal. Environ. 733–4, 292–299.

Betancourt-Galindo, R.R., Puente-Urbina, P., Avila-Orta, B., Fernandez, C.R., Oliverio cadenas-pliego, Gregorio Lira-Saldivar, Ricardo García-Cerda, L.., 2014. Synthesis of copper nanoparticles by thermal decomposition and their antimicrobial properties. J. Nanomater. 2014. https://doi.org/10.1155/2014/980545.

Bhanjana, G., Dilbaghi, N., Kim, K.H., Kumar, S., 2017. Low temperature synthesis of copper oxide nanoflowers for lead removal using sonochemical route. J. Mol. Liq. 244, 506–551.

Bikiaris, D.N., & Triantafyllidis, K.S., 2013. HDPE/Cu-nanofiber nanocomposites with enhanced antibacterial and oxygen barrier properties appropriate for food packaging applications. Mater. Lett. 93, 1–4.

Bogdanović, U., Dimitrijević, S., Škapin, S.D., Popović, M., Rakočević, Z., Leskovac, A., Petrović, S., Stoiljković, M., Vodnik, V., 2018. Copper-polyaniline nanocomposite: role of physicochemical properties on the antimicrobial activity and genotoxicity evaluation. Korean J. Couns. Psychother. 93, 49–60. https://doi.org/10.1016/j.msec.2018.07.067. Epub 2018 Jul 24. PMID: 30274082.

Bogdanović, U., Vodnik, V., Mitrić, M., Dimitrijević, S., Škapin, S.D., Žunič, V., Budimir, M., Stoiljković, M., 2015. Nanomaterial with high antimicrobial efficacy–copper/polyaniline nanocomposite. ACS Appl. Mater. Interfaces 7, 1955–1966.

Chandrasekaran, R., Yadav, S.A., Sivaperumal, S., 2020. Phytosynthesis and characterization of copper oxide nanoparticles using the aqueous extract of *Beta vulgaris* L and evaluation of their antibacterial and anticancer activities. J. Clust. Sci. 311, 221–230.

Chepkasov, I.V., Gafner, Y.Y., Gafner, S.L., Bardahanov, S.P., 2016. Condensation of Cu nanoparticles from the gas phase. Phys. Met. Metallogr. 11710, 1003–1012.

Choudhary, R.C., Kumaraswamy, R.V., Kumari, S., et al., 2017. Cu-chitosan nanoparticle boost defense responses and plant growth in maize *Zea mays* L. Sci. Rep. 7, 9754.

Cioffi, N., Ditaranto, N., Torsi, L., Picca, R.A., Sabbatini, L., Valentini, A., Novello, L., Tantillo, G., Bleve-Zacheo, T., Zambonin, P.G., 2005. Analytical characterization of bioactive fluoropolymer ultra-thin coatings modified by copper nanoparticles. Anal. Bioanal. Chem. 381 (3), 607–616.

Dang, T.M.D., Le, T.T.T., Fribourg-Blanc, E., Dang, M.C., 2011. Synthesis and optical properties of copper nanoparticles prepared by a chemical reduction method. Adv. Nat. Sci.: Nanosci. Nanotechnol. 2 (1), 015009.

Das, S., Srivastava, V.C., 2017. Synthesis and characterization of ZnO/CuO nanocomposite by electrochemical method. Mater. Sci. Semicond. Process. 57, 173–177.

Dura'n, B., Hevia, S.A., Molero, L., Isaacs, M., Bonardd, S., Diaz Diaz, D., Leiva, A., Saldı'as, C., 2019. Novel 3D copper nanoparticles/chitosan/nanoporous alumina CCSA membranes with catalytic activity. Characterization and performance in the reduction of methylene blue. J. Clean. Prod. 210, 811–820.

Ealia, S.A.M., Saravanakumar, M.P., 2017. A review on the classification, characterisation, synthesis of nanoparticles and their application. In: IOP Conference Series: Materials Science and Engineering. vol. 263. IOP Publishing, p. 032019. No. 3.

Fedlheim, D.L., Foss, C.A., 2001. Metal Nanoparticles: Synthesis, Characterization, and Applications. CRC Press.

Gawande, M.B., Goswami, A., Felpin, F.X., Asefa, T., Huang, X., Silva, R., et al., 2016. Cu and Cu-based nanoparticles: synthesis and applications in catalysis. Chem. Rev. 1166, 3722–3811.

Gonza'lez Go'mez, H., Ramı'rez Godina, F., Ortega Ortiz, H., Benavides Mendoza, A., Robledo Torres, V., Cabrera De la Fuente, M., 2017. Use of chitosan–PVA hydrogels with copper nanoparticles to improve the growth of grafted watermelon. Molecules 22 (1031), 1–9.

Hadidi, M., Bigham, A., Saebnoori, E., Hassanzadeh-Tabrizi, S.A., Rahmati, S., Alizadeh, Z.M., et al., 2017. Electrophoretic-deposited hydroxyapatite-copper nanocomposite as an antibacterial coating for biomedical applications. Surf. Coat. Technol. 321, 171–179.

Hebeish, A., El-Naggar, M.E., Fouda, M.M., Ramadan, M.A., Al-Deyab, S.S., El-Rafie, M.H., 2011. Highly effective antibacterial textiles containing green synthesized silver nanoparticles. Carbohydr. Polym. 862, 936–940.

Jaiswal, M., Chauhan, D., Sankararamakrishnan, N., 2012. Copper chitosan nanocomposite: synthesis, characterization, and application in removal of organophosphorous pesticide from agricultural runoff. Environ. Sci. Pollut. Res. 19 (6), 2055–2062.

Jayaramudu, T., Varaprasad, K., Pyarasani, R.D., Reddy, K.K., Kumar, K.D., Akbari-Fakhrabadi, A., Mangalaraja, R., Amalraj, J., 2019. Chitosan capped copper oxide/copper nanoparticles encapsulated microbial resistant nanocomposite films. Int. J. Biol. Macromol. 128, 499–508.

Jeevanandam, J., 2018. Review on nanoparticles and nanostructured materials: history, sources, toxicity and regulations. Beilstein J. Nanotechnol. 9, 1050–1074.

Juarez-Maldonado, A., Ortega-Ortíz, H., Pérez-Labrada, F., Cadenas-Pliego, G., Benavides-Mendoza, A., 2016. Cu nanoparticles absorbed on chitosan hydrogels positively alter morphological, production, and quality characteristics of tomato. J. Appl. Bot. Food Qual. 89, 183–189.

Kalhor, M., Zarnegar, Z., 2019. Fe 3 O 4/SO 3 H@ zeolite-Y as a novel multi-functional and magnetic nanocatalyst for clean and soft synthesis of imidazole and perimidine derivatives. RSC Adv. 934, 19333–19346.

Khan, I., Saeed, K., Khan, I., 2019a. Nanoparticles: properties, applications and toxicities. Arab. J. Chem. 127, 908–931.

Karthikeyan, K.T., Nithya, A., Jothivenkatachalam, K., 2017. Photocatalytic and antimicrobial activities of chitosan-TiO_2 nanocomposite. Int. J. Biol. Macromol. 104, 1762–1773.

Khan, S.B., Ali, F., Akhtar, K., 2019b. Chitosan nanocomposite fibers supported copper nanoparticles based perceptive sensor and active catalyst for nitrophenol in real water. Carbohydr. Polym. 207, 650–662.

Khandel, P., Yadaw, R.K., Soni, D.K., et al., 2018. Biogenesis of metal nanoparticles and their pharmacological applications: present status and application prospects. J. Nanostruct. Chem. 8, 217–254.

Kumar, A., Verma, N., 2018. Wet air oxidation of aqueous dichlorvos pesticide over catalytic copper–carbon nanofiberous beads. Chem. Eng. J. 351, 428–440.

Kumar, A., Verma, N., 2019. Cu–Fe bimetal–carbon nanofiberous catalytic beads for enhanced oxidation of dichlorvos pesticide and simultaneous reduction of Cr(VI) inwet air. Catal. Today. https://doi.org/10.1016/j.cattod.2019.08.025.

Kumar, A., Saxena, A., De, A., Shankar, R., Mozumdar, S., 2013. Facile synthesis of size-tunable copper and copper oxide nanoparticles using reverse microemulsions. RSC Adv. 315, 5015–5021.

Kumar, R., Ashfaq, M., Verma, N., 2018. Synthesis of novel PVA–starch formulation-supported Cu–Zn nanoparticle carrying carbon nanofibers as a nanofertilizer: Controlled release of micronutrients. J. Mater. Sci. 5310, 7150–7164.

Kutláková, K.M., Tokarský, J., Peikertová, P., 2015. Functional and eco-friendly nanocomposite kaolinite/ZnO with high photocatalytic activity. Appl. Catal. Environ. 162, 392–400.

Machado, S., Pacheco, J.G., Nouws, H.P.A., Albergaria, J.T., Delerue-Matos, C., 2015. Characterization of green zero-valent iron nanoparticles produced with tree leaf extracts. Sci. Total Environ. 533, 76–81.

Mali, S.C., Dhaka, A., Githala, C.K., Trivedi, R., 2020. Green synthesis of copper nanoparticles using *Celastrus paniculatus* Willd. leaf extract and their photocatalytic and antifungal properties. Biotechnol. Rep. 27, e00518.

Manikandan, A., Yogasundari, M., Thanrasu, K., Dinesh, A., Raja, K.K., Slimani, Y., et al., 2020. Structural, morphological and optical properties of multifunctional magnetic-luminescent ZnO@ Fe_3O_4 nanocomposite. Phys. E: Low-Dimens. Syst. Nanostructures 124, 114291.

Meena, M., Pilania, S., Pal, A., Mandhania, S., Bhushan, B., Kumar, S., et al., 2020. Cu-chitosan nano-net improves keeping quality of tomato by modulating physio-biochemical responses. Sci. Rep. 101, 1–11.

Mehta, M.R., Mahajan, H.P., Hivrale, A.U., 2021. Green synthesis of chitosan capped-copper nano biocomposites: synthesis, characterization, and biological activity against plant pathogens. BioNanoSci. 11, 417–427.

Motahharifar, N., Nasrollahzadeh, M., Taheri-Kafrani, A., Varma, R.S., Shokouhimehr, M., 2020. Magnetic chitosan-copper nanocomposite: A plant assembled catalyst for the synthesis of amino-and N-sulfonyl tetrazoles in eco-friendly media. Carbohydr. Polym. 232, 115,819.

Murthy, H.C., Desalegn, T., Kassa, M., Abebe, B., Assefa, T., 2020. Synthesis of green copper nanoparticles using medicinal plant *Hagenia abyssinica* (Brace) JF. Gmel. leaf extract: antimicrobial properties. J. Nanomater. 2020.

Muthukrishnan, S., Murugan, I., Selvaraj, M., 2019. Chitosan nanoparticles loaded with thiamine stimulate growth and enhances protection against wilt disease in Chickpea. Carbohydr. Polym. 212, 169–177.

Okpala, C.C., 2013. Nanocomposites—an overview. Int. J. Eng. Res. 8, 17–23.

Patil, S., Chandrasekaran, R., 2020. Biogenic nanoparticles: a comprehensive perspective in synthesis, characterization, application and its challenges. J. Genet. Eng. Biotechnol. 181, 1–23.

Qiu, S., Dong, J., Chen, G., 1999. Preparation of Cu nanoparticles from water-in-oil microemulsions. J. Colloid Interface Sci. 2162, 230–234.

Rivero-Montejo, S.d.J., Vargas-Hernandez, M., Torres-Pacheco, I., 2021. Nanoparticles as novel elicitors to improve bioactive compounds in plants. Agriculture 11 (2), 134.

Rodrigues, A.C., Silva, E.L.D., Quirino, S.F., Cuña, A., Marcuzzo, J.S., Matsushima, J.T., et al., 2019. Ag@ Activated carbon felt composite as electrode for supercapacitors and a study of three different aqueous electrolytes. Mater. Res. 22 (1), e20180530.

Sadegh, H., Ali, G.A.M., Gupta, V.K., et al., 2017. The role of nanomaterials as effective adsorbents and their applications in wastewater treatment. J. Nanostruct. Chem. 7, 1–14.

Sadrolhosseini, A.R., Noor, A.S.B.M., Shameli, K., Mamdoohi, G., Moksin, M.M., Mahdi, M.A., 2013. Laser ablation synthesis and optical properties of copper nanoparticles. J. Mater. Res. 2818, 2629–2636.

Saharan, V., Sharma, G., Yadav, M., Choudhary, M.K., Sharma, S.S., Pal, A., Raliya, R., Biswas, P., 2015. Synthesis and in vitro antifungal efficacy of Cu-chitosan nanoparticles against pathogenic fungi of tomato. Int. J. Biol. Macromol. 75, 346–353. https://doi.org/10.1016/j.ijbiomac.2015.01.027. Epub 2015 Jan 21. PMID: 25617841.

Sakib, A.A.M., Masum, S.M., Hoinkis, J., Islam, R., Molla, M., Islam, A., 2019. Synthesis of CuO/ZnO nanocomposites and their application in photodegradation of toxic textile dye. J. Compos. Sci. 33, 91.

Saravanakumar, K., Shanmugam, S., Varukattu, N.B., MubarakAli, D., Kathiresan, K., Wang, M.H., 2019. Biosynthesis and characterization of copper oxide nanoparticles from indigenous fungi and its effect of photothermolysis on human lung carcinoma. J. Photochem. Photobiol. B Biol. 190, 103–109.

Sarkar, S., Guibal, E., Quignard, F., SenGupta, A.K., 2012. Polymer-supported metals and metal oxide nanoparticles: synthesis, characterization, and applications. J. Nanopart. Res. 142, 1–24.

Sarma, G.K., Sen, G., Bhattacharyya, S., K.G., 2019. Nanomaterials as versatile adsorbents for heavy metal ions in water: a review. Environ. Sci. Pollut. Res. 26, 6245–6278.

Sathiyabama, M., Manikandan, A., 2018. Application of copper-chitosan nanoparticles stimulate growth and induce resistance in finger millet *Eleusine coracana* (Gaertn.) plants against blast disease. J. Agric. Food Chem. 668, 1784–1790.

Selvi, K.T., Mangai, K.A., Priya, M., Sagadevan, S., 2021. Enhanced electrical and magnetic properties of CuO/MgO nanocomposites. Chem. Phys. Lett. 765, 138–320.

Shang, Y., Hasan, M., Ahammed, G.J., Li, M., Yin, H., Zhou, J., 2019. Applications of nanotechnology in plant growth and crop protection: a review. Molecules 2414, 2558.

Shantkriti, S., Rani, P., 2014. Biological synthesis of copper nanoparticles using *Pseudomonas fluorescens*. Int. J. Curr. Microbiol. App. Sci. 39, 374–383.

Shetty, P.K., 2004. Socio-ecological implications of pesticide use in India. Econ. Pol. Wkly, 5261–5267.

Subashini, K., Prakash, S., Sujatha, V., 2020. Polymer nanocomposite prepared using copper oxide nanoparticles derived from *Sterculia foetida* leaf extract with biological applications. Mater. Res. Express 711, 115,308.

Subhan, M.A., Chandra Saha, P., Uddin, N., Sarker, P., 2017. Synthesis, structure, spectroscopy and photocatalytic studies of nano multi-metal oxide MgO· Al2O3· ZnO and MgO· Al_2O_3· ZnO-curcumin composite. Int. J. Nanosci. Nanotechnol. 131, 69–82.

Suematsu, H., Nishimura, S., Murai, K., Hayashi, Y., Suzuki, T., Nakayama, T., Jiang, W., Yamazaki, A., Seki, K., Niihara, K., 2007. Pulsed wire discharge apparatus for mass production of copper nanopowders. Rev. Sci. Instrum. 785, 056105. https://doi.org/10.1063/1.2721419. PMID: 17552867.

Tabesh, E., Salimijazi, H., Kharaziha, M., Hejazi, M., 2018. Antibacterial chitosan-copper nanocomposite coatings for biomedical applications. Mater. Today: Proc. 57 (15), 806–15,812.

Tamayo, L., Azócar, M., Kogan, M., Riveros, A., Páez, M., 2016. Copper-polymer nanocomposites: an excellent and cost-effective biocide for use on antibacterial surfaces. Mater. Sci. Eng. C 69, 1391–1409.

Tarique, W.B., 2019. Synthesis and Characterization of Zno/Sno2 Nanocomposite Via a Two-Step Spray Pyrolysis Route. M.Sc. in physics, Department of Physics Bangladesh University of Engineering and Technology, Dhaka-1000, Bangladesh. 129 pp.

Tiwari, J.N., Tiwari, R.N., Kim, K.S., 2012. Zero-dimensional, one-dimensional, two-dimensional and three-dimensional nanostructured materials for advanced electrochemical energy devices. Prog. Mater. Sci. 574, 724–803.

Vanti, G.L., Masaphy, S., Kurjogi, M., Chakrasali, S., Nargund, V.B., 2020. Synthesis and application of chitosan-copper nanoparticles on damping-off causing plant pathogenic fungi. Int. J. Biol. Macromol. 156, 1387–1395.

Vinceković, M., Jalšenjak, N., Topolovec-Pintarić, S., Đermić, E., Bujan, M., Jurić, S., 2016. Encapsulation of biological and chemical agents for plant nutrition and protection: chitosan/alginate microcapsules loaded with copper cations and *Trichoderma viride*. J. Agric. Food Chem. 6443, 8073–8083.

Yadav, S., Vasu, V., 2016. Synthesis and characterization of copper nanoparticles, using combination of two different sizes of balls in wet ball milling. Int. J. Emerg. Trends Sci. Technol. 34, 2348–9480.

Zayed, M.F., Eisa, W.H., Abd ElHameed, M.H., Abou Zeid, A.M., 2020. Spectroscopic investigation of chitosan-supported Cu_2O/CuO nanocomposite; a separable catalyst for water-pollutants degradation. J. Alloys Compd. 835, 155,306.

Zhang, X.Y., Li, H.P., Cui, X.L., Lin, Y., 2010. Graphene/TiO 2 nanocomposites: synthesis, characterization and application in hydrogen evolution from water photocatalytic splitting. J. Mater. Chem. 2014, 2801–2806.

Further reading

Abd El-Aziz, M.E., Morsi, S.M.M., Salama, D.M., Abdel-Aziz, M.S., Abd Elwahed, M.S., Shaaban, E.A., Youssef, A.M., 2019. Preparation and characterization of chitosan/polyacrylic acid/copper nanocomposites and their impact on onion production. Int. J. Biol. Macromol. 123, 856–865.

Abd-Elsalam, K.V.'k., Said-Galiev, A., Rubina, E., Khokhlov, M., Naumkin, A., Alexander, S., Alghuthaymi, E., Mousa, 2017. Bimetallic blends and chitosan nanocomposites: novel antifungal agents against cotton seedling damping-off. Eur. J. Plant Pathol., 1–16. https://doi.org/10.1007/s10658-017-1349-8.

Akintelu, S.A., Folorunso, A.S., Folorunso, F.A., Oyebamiji, A.K., 2020. Green synthesis of copper oxide nanoparticles for biomedical application and environmental remediation. Heliyon 67, e04508.

Brunel, F., El Gueddari, N.E., Moerschbacher, B.M., 2013. Complexation of copper (II) with chitosan nanogels: towards control of microbial growth. Carbohydr. Polym. 92, 1348–1356.

Cele, T., 2020. Preparation of nanoparticles. In: Engineered Nanomaterials-Health and Safety. IntechOpen.

Ghali, A.E., Baouab, M.H.V., Roudesli, M.S., 2012. Aminated cotton fibers loaded with copper(II) ions for enhanced pesticide removal performance from water in a laboratory-scale batch. Ind. Crop Prod. 39, 139–148.

Herna'ndez-Herna'ndez, H., Jua'rez-Maldonado, A., Benavides-Mendoza, A., Ortega-Ortiz, H., Cadenas-Pliego, G., Sa'nchez-Aspeytia, D., Gonza'lez-Morales, S., 2018. Chitosan-PVA and copper nanoparticles improve growth and overexpress the SOD and JA genes in tomato plants under salt stress. Agronomy 8 (175), 1–10.

Mustafa, S.K., AlSharif, M.A., 2018. Copper (Cu) an essential redox-active transition metal in living system—a review article. Am. J. Anal. Chem. 901, 15.

Pavithran, S., Pappuswamy, M., Annadurai, Y., Armugam, V.A., Periyaswamy, T., 2020. Green synthesis of copper nanoparticles, characterization and their applications. J. Appl. Life Sci. Int., 10–24.

Pinedo-Guerrero, Z.H., Hernández-Fuentes, A.D., Ortega-Ortiz, H., Benavides-Mendoza, A., Cadenas-Pliego, G., 2017. Cu nanoparticles in hydrogels of chitosan-PVA affects the characteristics of post-harvest and bioactive compounds of Jalapeño pepper. Molecules 226, 926.

Shahryari, F., Rabiei, Z., Sadighian, S., 2020. Antibacterial Activity of Copper Nanoparticles Synthesized With Sumac Extract and Copper-Chitosan Nanocomposite Against Some Plant Pathogenic Bacteria in Laboratory., https://doi.org/10.22084/ab.2020.19130.1410.

Zavareh, S., Behrouzi, Z., Avanes, A., 2017. Cu (II) binded chitosan/Fe_3O_4 nanocomomposite as a new biosorbent for efficient and selective removal of phosphate. Int. J. Biol. Macromol. 101, 40–50.

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CHAPTER

24 Effect of copper-based nanoagrochemicals on plants and soil: A critical review

Shraddha Shahane and Arun Kumar

Department of Civil Engineering, Indian Institute of Technology Delhi, New Delhi, India

1 Introduction

CuO nanoparticles (CuO-NPs) are widely used in many agriculture sectors in the form of modified agro-products, such as pesticides, herbicides, fertilizers, additives for soil remediation, and growth regulators (Gogos et al., 2012; Xiong et al., 2017; Zhao et al., 2017b; Zuverza-Mena et al., 2015). The crops may be contaminated with CuO-NPs via roots in contaminated soils or foliar application of nanopesticides/nanofertilizers (Monica and Cremonini, 2009; Zhao et al., 2017b). As a result of the interaction of copper with plants and soil, the contaminated plant and soil might affect human health. Fig. 1 shows the different application methods of copper nanoagrochemicals (Foliar spray and soil amendment) and their interaction with plant and soil compartments.

Recently, a lot of research investigations on the toxicity of CuO NPs to plant germination, yield, and transpiration and translocation in plant tissues indicated negative impact of copper oxide nanoparticles (CuO NPs) on seed germination and plant growth of various crop plants, i.e., *Raphanus sativus* (Singh and Kumar, 2018), *Zea mays* (Wang et al., 2012), and cabbage (Xiong et al., 2017). The influence of Cu NPs or CuO NPs on different vegetables during their growth and development have been studied by many researchers via performing short-term (hydroponic and germination studies) (Hong et al., 2015) as well as long-term studies (full growth cycle studies or till maturity stage) (Singh and Kumar, 2018). The experimental study has been carried out to see the feasibility of using irrigation water contaminated with CuO NPs and a binary mixture of ZnO NPs + CuO NPs to grow spinach in soil media (Singh and Kumar, 2016). Few researchers have investigated the root uptake and translocation of NPs to aerial plant tissues (shoot portion) (Zhang et al., 2011). Kah et al. (2019) quantitatively highlighted information on the amounts and forms of Cu that may reach the soil after the application of copper nanoformulation (Kah et al., 2019).

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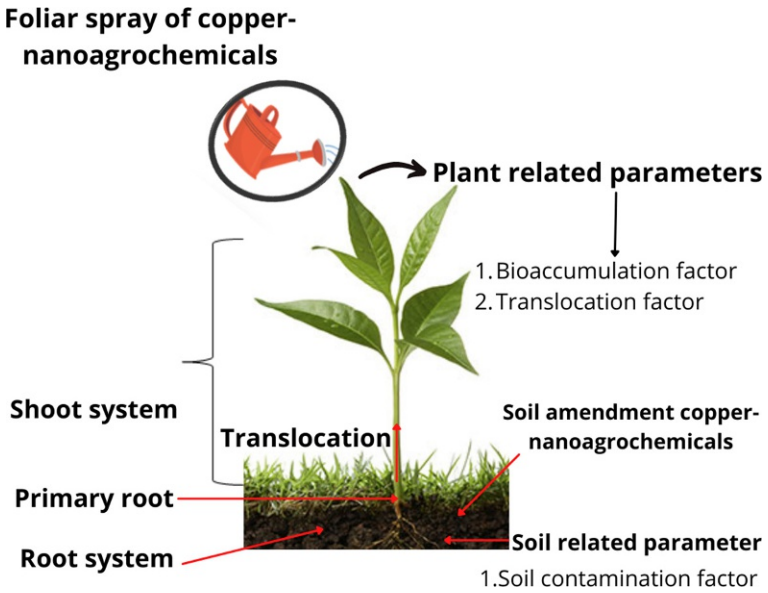

FIG. 1

Schematic representation showing overall application methods of copper nanoagrochemicals.

The long-term field study (mesocosm experiments) evaluating effects of frequent exposure of $Cu(OH)_2$ nanopesticides on the soil and sediment biodiversity of a target (terrestrial) and nontarget (wetland) ecosystems was also carried out (Carley et al., 2020). Zhang et al. (2020) performed studies on the impacts of copper nanopesticides $Cu(OH)_2$ at different agricultural application doses (0.5, 5, and 50 mg Cu kg^{-1}) on enzyme activities and bacterial communities of loamy soil over 21 days (Zhang et al., 2020). Peixoto et al. (2020) studied unintended consequences of commercial $Cu(OH)_2$ nanopesticides on nontarget soil microbial communities, suggesting nondesirable impact on the bacterial and fungal communities (Peixoto et al., 2020). Guan et al. (2020) conducted a study to assess the impact of CuO NPs on the changes in bacterial community structure and nitrogen-cycling-associated functions in a high pH soil and to correlate these changes with nitrate accumulation, changes in soil parameters, and plant growth over 28 days (Guan et al., 2020).

The studies on the behavior of CuO NPs in the soil-plant system were carried out by Burachevskaya et al. (2021). Burachevskaya et al. (2021) revealed that CuO NPs underwent a stronger transformation, and the Cu mobility was observed to increase within the soil profile. Furthermore, this study reported that the effect of high doses of macro- and nanosized CuO (2000 and 10,000 mg/kg) harmed the growth of the plant (spring barley).

Ecotoxicological impact of CuO NPs on the soil microbial community in biosolids-amended soil has been noted which indicated that low bioavailability of Cu^{2+} in CuO NPs exposures relative to $CuSO_4$ exposures (Samarajeewa et al., 2021).

The antifungal efficacy of synthesized copper sulfide nanoparticles (CuS NPs) and Kocide 3000 was studied against the pathogenic activity of *Gibberella fujikuroi* (Bakanae disease) in rice (*Oryza sativa*) (Shang et al., 2020).

Exposure of Cu NPs indicated high ecotoxicity to commonly found soil bacteria even at low concentrations through the loss of cell viability by increased oxidative stress by the generation of ROS (Sharma et al., 2021). Fischer et al. (2021) revealed toxic effects of CuO-NP toward a soil invertebrate (springtail *Folsomia candida*) at a low and realistic concentration range.

The quantitative agronomic and biochemical responses of tomato plants under salt stress with the foliar amendment of copper nanoparticles were performed by a group of researchers (Pérez-Labrada et al., 2019). The author preferred foliar application of copper nanoparticles on tomatoes under salinity which seems to induce stress tolerance to salinity by stimulating the tomato plant's antioxidant mechanisms (Pérez-Labrada et al., 2019). Spinach treated with a binary mixture of ZnO and CuO nanoparticles resulted in a higher reduction in fresh plant weight as compared to single NP exposure (Singh and Kumar, 2020). The reactive oxygen species (ROS) response of lettuce seedlings to biosynthesized ultrasmall CuO NPs (concentrations: 0.2–300 μg/mL) were captured by Pelegrino et al. (2020). So, the results indicated that low concentrations (≤20 μg/mL) of CuO NPs, provide beneficial effects to seedlings and plant growth (Pelegrino et al., 2020). A recent study was conducted on the evaluation of toxic interaction of zinc and copper oxide nanoparticles (concentrations: 0–1000 mg/L) on germination of radish revealed deleterious effects of NPs exposure more than 10 mg/L (Singh and Kumar, 2019).

The purpose of this study was (1) to compile the qualitative and quantitative information on the application of different copper-based nanoagrochemicals and their effects on plant growth along with copper accumulation in plant tissues and soil systems, (2) to estimate bioaccumulation factor (BAF) and translocation factor (TF) for copper stressed leafy vegetables related plants and effect of a variety of parameters on BAF and TF (variation in plant type, soil condition and exposure time), and (3) to estimate soil contamination factor in case of soil exposed to copper nanopesticides (Fig. 2).

2 Currently used copper nanoparticles-based pesticides

Integrating novel nanotechnology in the agriculture industry for the betterment of crop yield is still in its infancy but a number of products are already launched such as copper-based (Cu) nanopesticides used as a fungicide and bactericide in agriculture specifically for organic farming. The commercial pesticide, Kocide 3000, contains nanoparticles and micron-sized particles of Cu, and nanosheets composed of

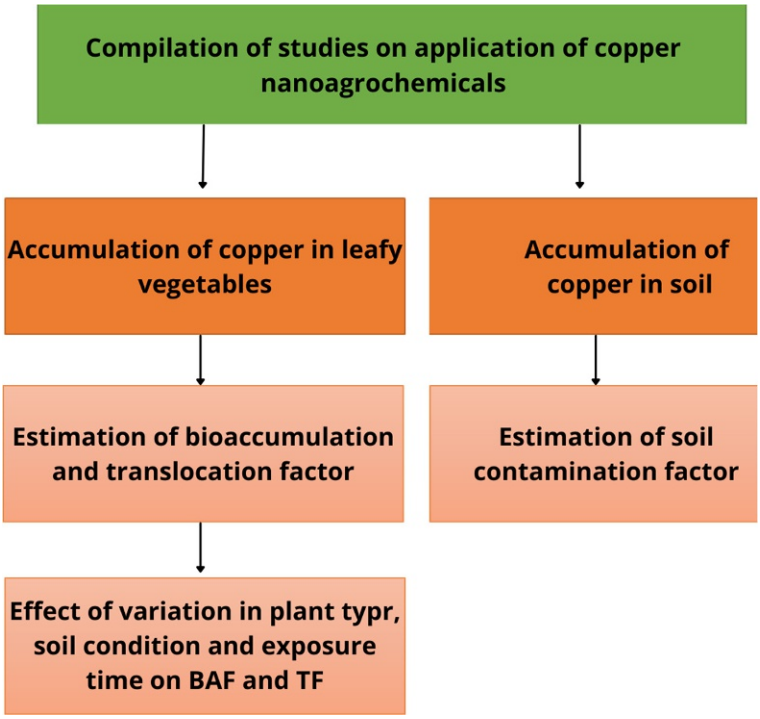

FIG. 2

Schematic representation for plant- and soil-related parameters.

$Cu(OH)_2$ and thus this nano-agrochemical containing copper as the active ingredient is considered as a nanopesticides, i.e., commercial pest control products (Adeleye et al., 2014; Zhao et al., 2017b).

3 Interaction of copper with plants

Copper is a redox-active metal known to speed up the generation of reactive oxygen species (ROS) through the Fenton and Harweiss reactions. ROS in plants exposed to abiotic or biotic stressors can damage cell structure, proteins, lipids, and genetic material. Antioxidant enzymes, such as dehydroascorbate reductase (DHAR), catalase (CAT), and ascorbate peroxidase (APX) protect plants from ROS damage. Every plant system has an antioxidant defense system that is activated by upregulation of the internal synthesis of some antioxidant enzymes.

Previous studies have shown that NPs applied to the root system can modulate the activity of stress enzymes. To determine the zinc, copper, and silver nanoparticle uptake and translocation from leaves to root, several research studies have been conducted on the response of edible plants to NPs (spinach, maize, and cucumber)

(Singh and Kumar, 2016; Zhao et al., 2016b, 2017a). A review of the literature suggests that NPs exist as colloids at low concentrations and may form small stable aggregates at moderate concentrations (Klaine et al., 2008). Ma et al. (2010) stated that genetic response is another most crucial factor which contributes to NP-plant interaction. Zhao et al. (2016a, b, c) evaluated the response of copper-stressed lettuce plants via foliar application of $Cu(OH)_2$ nanopesticides for 1 month and revealed the generation of oxidative stresses in lettuce plants (Zhao et al., 2016c).

The exposure of copper-containing nanopesticides may have visible symptoms or internal metabolite changes, which could have a significant impact on overall plant health. The compilation of data on the effect of different copper-based nanopesticides on edible plants was done using published data. In the current study, we have mainly focused on leafy vegetables while elaborating soil and plant-related parameters. Once nanoagrochemicals are applied to edible plants, there exists a possibility of an impact on plant health in terms of biomass, chlorophyll, and root and aerial length (shoot portion).

Table 1 summarizes a compilation of previously done studies including application mode of copper-based nanoagrochemicals, experimental condition, and effect on plant growth parameters. Zhao et al. (2017a) reported that foliar application of nano-enabled copper-based pesticide to maize resulted from diminished leaf chlorophyll content and biomass at 100 mg Cu $(OH)_2$ nanopesticides (Zhao et al., 2017a). Zhao et al. (2017b) performed studies on the assessment of the metabolic response of spinach treated with $Cu(OH)_2$ nanopesticides (foliar spray) at different concentrations (100 and 1000 mg/L), suggested a considerable reduction in defense-associated metabolites and changes in metabolite profiles of spinach leaves (Zhao et al., 2017b).

4 Plant-related parameters

4.1 Bioaccumulation factor (BAF)

Bioaccumulation factor (BAF; L/kg) indicates the ratio of accumulated copper in the aboveground (plant shoot) and underground part (root) to the applied dose of nanoagrochemicals. The bioaccumulation of nanopesticides in edible plant tissues and their effect on nutritional quality are of great importance because this relates to human health. This factor indicates uptake of contaminant and possible translocation throughout the plant and the ultimate accumulation in edible parts depending on media (hydroponic/soil incorporation). Therefore, in the case of copper-based nanoagrochemicals, BAF measures the amount of tendency of copper retention in plants.

Table 2 shows the comprehensive copper accumulation in leafy vegetable of plants in different forms (copper nanopesticides such as $Cu(OH)_2$ and CuPRO 2005), including CuO NPs and Cu NPs. The bioaccumulation factors in leafy vegetables including lettuce, spinach, and cabbage grown in the soil media contaminated with Cu-based nanoagrochemicals were estimated using the following equation:

$$\mathrm{BAF} = \frac{Cu_{plant\ tissues}}{Cu_{media}} \tag{1}$$

Table 1 Metal-based nanoformulations with uptake values of metals.

Original form of metal, plant, and specifications of Nanoproduct	Type of study and duration	Experimental conditions	Overall results related to growth analysis	References
$Cu(OH)_2$ (nanopesticides) **Plant:** Spinach H.D. 1532 ± 580 nm Copper content in Kocide 3000: 26.5 ± 0.9%	Pot study **Matrix:** soil **Harvesting period:** 4 weeks	**Concentration of nanopesticides:** 0.18 and 18 mg/plant or 100 and 1000 mg/L **Cu^{2+}:** (0.15, 15 mg/plant 10,1000 mg/L); Frequency: Trice a day for 1 week by foliar application	No considerable effect on photosynthetic pigment, altered the metabolic pathway in all exposed spinach plants. 18 mg of $Cu(OH)_2$ nanopesticides induced 29%–85% reduction in antioxidant metabolites	Zhao et al. (2017b)
Kocide 3000 (Dupont). Copper content in Kocide 3000 is 26.5 ± 0.9% **Plant:** Lettuce	Pot study **Matrix:** soil (sandy loamy) **Harvesting period:** 54 days	**Conc.** 0, 1050, and 1555 mg/L; foliar spray; Frequency of application: two times per week	Effect on nutritional quality of lettuce leaves	Zhao et al. (2016a)
nCuO, bulk CuO, nCu, bulk Cu, Kocide 3000 and CuPRO 2005. **Plant:** Cilantro	Pot study **Matrix:** soil **Duration of study:** 30 days	**Concentrations:** 0, 20, and 80 mg Cu/kg; Soil incorporation	20 mg/kg CuO applied to the soil reduced relative chlorophyll content by 26%	Zuverza-Mena et al. (2015)
Cu NPs **Plant:** Coriander (*Coriandrum sativum*)	Hydroponic study	**Concentrations:** 200, 400, and 800 mg/L; **Exposure period:** 7 days	Reduced root length, biomass and chlorophyll content; high levels of Cu in root than shoot.	Alquraidi et al. (2019)
CuO NPs **Plant:** Lettuce and Cabbage Particle size ranges from 40 to 60 nm	Pot study **Matrix:** Soil **Duration:** 15 days; **Germination period:** 2 weeks (hydroponic); 3 weeks plants (4 or 5) leaves/ plant to pot.	**Concentrations:** 0, 10, or 250 mg per plant **Exposure time:** 5, 10 or 15 days	Elevated Cu accumulation with increase in dose and exposure time (both plants).	Xiong et al. (2017)

Cu/CuO NPs **Plant:** Lettuce (*Lactuca sativa*)	Hydroponic culture **Duration of study:** 18 days	**Concentrations:** 10 and 20 mg/L	**Biomass:** 10 and 20 mg/L reduced root biomass by 54%, 66%, and 69% ($p \leq 0.05$) and leaves biomass by 51%, 54%, and 52% ($p \leq 0.002$), respectively. **Root length:** $CuSO_4 \cdot 5H_2O$ (10 mg/L), and nano-Cu/CuO at 10 and 20 mg/L reduced root length by 43%, 44%, and 51%, respectively; Observed visible toxicity symptoms In the first 2 days of treatment; plants treated with Cu/CuO NPs resulted reduced chlorophyll	Trujillo-Reyes et al. (2014)
CuO NPs **Plant:** Lettuce (*L. sativa*)	Pot study **Matrix:** Soil **Duration:** 30 days Foliar spray and soil irrigation	**Concentration:** 20 mg per plant	The elemental composition of roots was affected by the soil irrigation exposure for both Cu forms (NPs and salt). Neither Cu form added by soil incorporation was translocated to leaves. Cu concentration in leaves was mainly affected by foliar spray exposure for both Cu forms (NPs and salt)	Kohatsu et al. (2021)
CuO NPs **Plant:** Lettuce (*L. sativa*)	Hydroponic study Foliar spray Exposure duration: 5, 10, and 15 days	**Concentrations:** 100 and 1000 mg/L	Elevated Cu levels were observed in lettuce leaves (up to 6350 mg/kg), which was one magnitude greater than that in the roots (up to 525 mg/kg). Leaves to root translocation factors ranged from 1.80% to 15.6%. The CuO-NPs treatment severely inhibited lettuce growth and altered the nutrient status in plants.	Xiong et al. (2021b)
CuO NPs **Plant:** Lettuce (*L. sativa*)	Hydroponic study Foliar spray Exposure duration: 5,10, and 15 days	**Concentrations:** 100 and 1000 mg/L	Physiological results indicated that CuO-NPs adversely affected plant growth, photosynthesis, and enhanced reactive oxygen species (ROS) accumulation and antioxidant system activity. Gene expression analysis showed that the ATP-binding cassette (ABC) transporter family, heavy metal-associated isoprenylated plant proteins (HIPPs), endocytosis, and other metal ion binding proteins play important roles in CuO-NP accumulation by plant leaves	Xiong et al. (2021a)

Continued

Table 1 Metal-based nanoformulations with uptake values of metals—cont'd

Original form of metal, plant, and specifications of Nanoproduct	Type of study and duration	Experimental conditions	Overall results related to growth analysis	References
CuO NPs **Plant:** Spinach	Pot study **Matrix:** soil **Duration:** 45 days	**Concentration:** 400 mg/kg	With the 400 mg/kg nCuO weathered treatment (W), the shoot Cu concentration (36 mg/kg) was significantly higher than that of the corresponding control by 275% and higher than that of the corresponding ionic W treatment (12.5 mg/kg) by 188% ($p \leq 0.05$). At 20 days posttransplantation, (W) nCuO-exposed plants had ~56% lower carotenoid content relative to both W control and the UW counterpart ($p \leq 0.05$). The study reported that full life cycle of spinach plant the weathering process significantly deteriorates leaf pigment production under CuO exposure in particular and foliar health in general.	Rawat et al. (2021)
$Cu(OH)_2$ nanopesticide	Soil media (container)	**Concentration:** A single application [0.45 mg/kg (Cu) soil] and per season [19.86 mg/kg soil]	Nanopesticide exposure negatively impacted the bacterial and fungal community richness.	Peixoto et al. (2020)
$Cu(OH)_2$ Nanopesticide and Nano-$Cu(OH)_2$.	Soil media	**Concentration:** 0.5, 5 or 50 mg/kg	Both forms affected soil bacterial differently compared to $CuSO_4$, which could have resulted from the changes in bioavailable Cu concentration due to distinct nature of copper spiked (i.e., nano form vs. salt). Minor differences in the soil enzyme activity and bacterial community were observed between nanoformulation and conventional form, reflecting that effect of $Cu(OH)_2$ nanopesticide was primarily attributed to the presence of nano-$Cu(OH)_2$	Zhang et al. (2020)

Table 2 Summary of experimental conditions and outcomes of research studies on the application of copper-based nanoagrochemicals to leafy vegetables.

Plant	Form of copper	Soil type and portion of plants for BAF value	Concentration of copper compound/ solution type	Accumulation of Cu/Cu NPs/Cu^{2+} in plants	Calculated BAF ($L\,kg^{-1}$)	Reference
$Cu(OH)_2$						
Foliar spray						
Spinach	$Cu(OH)_2$ (nanopesticide)	Sand Leaves	100 and 1000 mg/L Suspension	Cu content: 377 ± 90.5 and 3021 ± 211.3 mg/kg DW	3.77 and 3.021	Zhao et al. 2017b)
Lettuce	$Cu(OH)_2$ (nano-pesticide)	Sandy loamy Leaves (photosynthesis tissues)	1050 and 1555 mg/L Suspension	Cu content:1353 and 2008 mg/kg DW	1.29 and 1.291	Zhao et al. (2016a)
Lettuce	$Cu(OH)_2$ (nano-pesticide)	Sandy loamy Vascular tissues	1050 and 1555 mg/L Suspension	Cu content: 823 and 1111 mg/kg DW	0.783 and 0.714	Zhao et al. (2016a)
UC*Lettuce	$Cu(OH)_2$ (nanopesticide)	Sandy loamy grassland Leaves (Vascular tissues)	1050, 1555, and 2100 mg/L Suspension	Cu content: 973 ± 145,1212 ± 139 and 1344 ± 73 mg/kg DW	0.926, 0.779, and 0.64	Zhao et al. (2016c)
UC*Lettuce	$Cu(OH)_2$ (nanopesticide)	Sandy loamy grassland leaves (Mesophyll tissues)	1050, 1555, and 2100 mg/L Suspension	Cu content: 1695 ± 113, 2157 ± 353, and 2296 ± 302 mg/kg DW	1.16142, 1.3871, and 1.093	Zhao et al. (2016c)
UC*Lettuce	$Cu(OH)_2$ (nanopesticide)	Sandy loamy grassland Root	1050, 1555, and 2100 mg/L Suspension	Cu content: 34.2 ± 1 2.7, 56.9 ± 22.5, and 34.9 ± 10.4 mg/kg DW	0.0325, 0.0365, and 0.0166	Zhao et al. (2016c)
Lettuce	$Cu(OH)_2$ (nanopesticide)	Sandy loamy grassland Leaves (Vascular tissues)	1050, 1555, and 2100 mg/L Suspension	Cu content: 823 ± 110, 1111 ± 80 and 1401 ± 137 mg/kg DW	0.783, 0.714 and 0.667	Zhao et al. (2016c)
Lettuce	$Cu(OH)_2$ (nanopesticide)	Sandy loamy grassland Leaves (Mesophyll tissues)	1050, 1555, and 2100 mg/L Suspension	Cu content: 1353 ± 324, 2008 ± 438, and 2501 ± 295 mg/kg DW	1.288, 1.608, and 1.190	Zhao et al. (2016c)
Lettuce	$Cu(OH)_2$ (nanopesticide)	Sandy loamy grassland Root	1050, 1555, and 2100 mg/L Suspension	Cu content: 19.5, 17.5, and 26.1 mg/kg	0.0185, 0.0112, and 0.0124	Zhao et al. (2016c)

Continued

Table 2 Summary of experimental conditions and outcomes of research studies on the application of copper-based nanoagrochemicals to leafy vegetables—cont'd

Plant	Form of copper	Soil type and portion of plants for BAF value	Concentration of copper compound/ solution type	Accumulation of Cu/Cu NPs/Cu^{2+} in plants	Calculated BAF ($L\,kg^{-1}$)	Reference
Sweet basil LAV	$Cu(OH)_2$ nanowires Suspension	Leaves	480 mg/L	Cu content: 265.4 mg/kg DW	0.55291	Tan et al. (2018)
Opal basil HAV	$Cu(OH)_2$ nanowires Suspension	Leaves	480 mg/L	Cu content: 387.7 mg/kg DW	0.80770	Tan et al. (2018)
Hydroponic study						
Lettuce	Cu $(OH)_2$ (nanopesticide)	Shoot	0, 5, 10, and 20 mg/L	At 5, 10, and 20 mg/L: Cu content: 20.0 ± 1.4, 52.4 ± 9/7, and 34.6 ± 5.1 (mg/kg)	4, 5.24, and 1.73	Hong et al. (2015)
Lettuce	Cu $(OH)_2$ (nanopesticide)	Root	0, 5, 10, and 20 mg/L	At 5,10, and 20 mg/L: Cu content: 2136.5 ± 54.3, 7674.1 ± 417.7, and 7505.3 ± 161.5 (mg/kg)	427.3, 767.41, and 375.265	Hong et al. (2015)
CuO NPs						
Soil incorporation						
Cilantro	CuO NPs	Plant	0, 20, and 80 mg/kg Cu	At 80 (Cu^{2+} uptake)164 mg/kg	2.05	Zuverza-Mena et al. (2015)
Spinach	CuO NPs	Clay loam Leaves	10, 100, and 1000 mg/L	At 10 mg/L: Cu^{2+} content: 150 mg/kg At 100 mg/L: 400 mg/kg At 1000 mg/L: 3480 ± 0.75 mg/kg	15, 4 and 3.48	Singh and Kumar (2016)
Foliar spray						
Lettuce	CuO NPs	Soil type not mentioned Leaves	10 and 250 mg per plant Suspension; 5 day exposure	Cu content: 669.31 ± 77.4 and 2731.67 ± 255 mg/kg DW	0.0234 and 0.001	Xiong et al. (2017)

Lettuce	CuO NPs	Soil type not mentioned Leaves	10 and 250 mg per plant Suspension; 10 day exposure	Cu content: 1065.99 ± 298 and 3314.75 ± 664 mg/kg DW	0.003 and 0.002	Xiong et al. (2017)
Lettuce	CuO NPs	Soil type not mentioned Leaves	10 and 250 mg per plant Suspension; 15 day exposure	Cu content: 2611.92 ± 282 and 6165.61 ± 1013 mg/kg DW	0.027 and 0.003	Xiong et al. (2017)
Cabbage	CuO NPs	Soil type not mentioned Leaves	10 and 250 mg per plant Suspension; 5 day exposure	Cu content: 396.19 ± 70.2 and 2752.28 ± 321 mg/kg DW	0.01 and 0.003	Xiong et al. (2017)
Cabbage	CuO NPs	Soil type not mentioned Leaves	10 and 250 mg per plant Suspension; 10 day exposure	Cu content:848.61 ± 108 and 2826.73 ± 722 mg/kg DW	0.03 and 0.113	Xiong et al. (2017)
Cabbage	CuO NPs	Soil type not mentioned Leaves	10 and 250 mg per plant Suspension; 15 day exposure	Cu content: 1386.47 ± 312 and 8292.27 ± 821 mg/kg DW	0.135 and 0.406	Xiong et al. (2017)
Lettuce	CuO NPs	Soil type not mentioned Root	10 and 250 mg per plant Suspension; 5 day exposure	Cu content: 154.16 ± 17.1 and 338.32 ± 21.5 mg/kg DW	0.005 and 0.0002	Xiong et al. (2017)
Lettuce	CuO NPs	Soil type not mentioned Root	10 and 250 mg per plant Suspension; 10 days exposure	Cu content: 96.88 ± 30.4 and 459.42 ± 40.2 mg/kg DW	0.00035 and 0.00031	Xiong et al. (2017)
Lettuce	CuO NPs	Soil type not mentioned Root	10 and 250 mg per plant Suspension; 15 day exposures	Cu content: 114.56 ± 16.4 and 238.18 ± 38 mg/kg DW	0.007 and 0.0003	Xiong et al. (2017)
Cabbage	CuO NPs	Soil type not mentioned Root	10 and 250 mg per plant Suspension	Cu content: 116.56 ± 5.9 and 358.91 ± 42.4 mg/kg DW	0.003 and 0.0004	Xiong et al. (2017)

Continued

Table 2 Summary of experimental conditions and outcomes of research studies on the application of copper-based nanoagrochemicals to leafy vegetables—cont'd

Plant	Form of copper	Soil type and portion of plants for BAF value	Concentration of copper compound/ solution type	Accumulation of Cu/Cu NPs/Cu^{2+} in plants	Calculated BAF ($L\,kg^{-1}$)	Reference
Cabbage	CuO NPs	Soil type not mentioned Root	10 and 250 mg per plant Suspension; 5 day exposure	Cu content: 172.34 ± 54 and 386.02 ± 121 mg/kg DW	0.007 and 0.0154	Xiong et al. (2017)
Cabbage	CuO NPs	Soil type not mentioned Root	10 and 250 mg per plant Suspension; 15 day exposure	Cu content: 68.56 ± 13.8 and 603.68 ± 48.2 mg/kg DW	0.006 and 0.029	Xiong et al. (2017)
Hydroponic study						
Lettuce	CuO NPs	Shoot	0, 5, 10, and 20 mg/L	At 5,10 and 20 mg/L: Cu content: 23.3 ± 0.9, 28.8 ± 5.7 and 25.6 ± 3.8 (mg/kg)	4.66, 2.88, and 1.28	Hong et al. (2015)
Lettuce	CuO NPs	Root	0, 5, 10, and 20 mg/L	At 5,10, and 20 mg/L: Cu content: 3555.8 ± 210.5, 9140.9 ± 99.4, and 9941.3 ± 531.0 (mg/kg)	711.16, 914.9, and 497.065	Hong et al. (2015)
Lettuce	CuO NPs	Foliar exposure Exposure duration: 5, 10, and 15 days	100 and 1000 mg/L	At 100 mg/L: 414–659 mg/kg At 1000 mg/L: 3100–6350 mg/kg	At 100 mg/L: 4.14–6.59 At 1000 mg/L: 3.1–6.35	Xiong et al. (2021a, b)
Hydroponic study						
Lettuce	Cu NPs	Shoot	0, 5, 10, and 20 mg/L	At 5,10, and 20 mg/L: Cu content: 30.2 ± 1.4, 45.8 ± 2.4, and 78.6 ± 1.8 (mg/kg)	6.04, 4.58, and 3.93	Hong et al. (2015)

Lettuce	Cu NPs	Root	0, 5, 10, and 20 mg/L	At 5,10 and 20 mg/L: Cu content: 6338.5 ± 731.3, 9373.9 ± 1061.3 and 13,318.8 ± 458.9 (mg/kg)	1267.7, 937.39, and 665.94	Hong et al. (2015)
Hydroponic study						
Lettuce	Cu/CuO nanomaterials	Organic soil	10 and 20 mg/L	3254 and 3362 mg/kg DW	325.5 and 168.1	Trujillo-Reyes et al. (2014)
Cu PRO 2005 (Based on nanocopper species)						
Lettuce	Nanocopper species	Shoot	0, 5, 10, and 20 mg/L	At 5,10, and 20 mg/L: Cu content: 24.6 ± 0.4, 33.3 ± 3.5, and 41.0 ± 3.8 (mg/kg)	4.92, 3.33, and 2.05	Hong et al. (2015)
Lettuce	Nanocopper species	Root	0, 5, 10, and 20 mg/L	At 5, 10, and 20 mg/L: Cu content: 3427.0 ± 265.3, 7313.4 ± 490.9, and 8459.5 ± 360.5 (mg/kg)	685.4, 731.34, and 422.975	Hong et al. (2015)

Note: UC indicates uncovered soil condition.*

where $Cu_{\ plant\ tissues}$ is the copper concentration in plant tissues (mg/kg or mg/L) and Cu_{media} is applied concentration of copper nanocompounds (mg/L or mg/kg).

4.1.1 Effect of plant types

There is a possibility of getting different bioaccumulation factor values for different leafy vegetables (under the same or different conditions). For example, spinach and lettuce upon $Cu(OH)_2$ nanopesticide exposure have shown different BAF values. The estimated BAF values for nanopesticide stressed spinach and lettuce were found to be in the range 1.291–3.77 L/kg (for higher to a lower dose, i.e., 100–1555 mg/L) (Zhao et al., 2016a, 2017b).

The estimated BAF value for spinach treated with 100 mg/L $Cu(OH)_2$ nanopesticide was 3.77 L/kg. Therefore, it can be concluded that the value of bioaccumulation factor for $Cu(OH)_2$ nanopesticide decreases with an increase in nanopesticide dose irrespective of soil condition. Another example which shows the variation in BAF values for different leafy vegetables is different BAF values for cabbage and lettuce treated with copper oxide nanoparticles at the same concentration (10 mg per plant) (Xiong et al., 2017).

This study provides information related to the application of four copper-based nanoformulations such as copper nanopesticides ($Cu(OH)_2$, CuPRO 2005), CuO NP, and CuNPs to leafy vegetables under soil matrix, hydroponic condition, and foliar spray for estimating values of BAF and TF. While elaborating the effect of variation of leafy vegetable type on BAF, the information related to $Cu(OH)_2$ nanopesticides was sufficient to compare the effect of variation in leafy vegetable type (spinach, lettuce, and cabbage) on BAF. Whereas, very little data is available on the application of other selected nanoagrochemicals and their effect on leafy vegetable growth. Most of the research has been conducted on lettuce plants exposed to $Cu(OH)_2$ nanopesticide. So, it was challenging to compare BAF values for the different green leafy vegetables under the same condition (soil/soilless media or foliar spray) treated with CuPRO 2005, CuO NPs, and Cu NPs. There is data available on the utilization of CuPRO 2005, CuO NPs, and Cu NPs to edible plants but the data showing accumulation of copper in different plant tissues is not adequate to make any conclusion related to the effect of variation of the plant on BAF values.

There is a need to monitor the accumulation data after the application of copper-based nanoagrochemicals in different plant tissues. Moreover, these types of studies must be supplemented with quantitative accumulation data depending on leafy vegetables, exposure time, concentration rather than giving the theoretical impact of copper nano formulations on overall plant health. This approach would help to estimate the BAF, TF, daily copper (NPs/ions) intake from ingestion of contaminated leafy vegetables and focusing human health risk assessment ideas.

4.1.2 Effect of concentration of nanoagrochemicals

BAF depends on the applied concentration of nanoagrochemicals. For example, in the case of lettuce plants exposed to Kocide 3000 ($Cu(OH)_2$) nanopesticides (1050–2100 mg/L), the estimated BAF values were found to be in the range of 0.66–0.78 L/kg (at 2100 and 1050 mg/L) which gives the evidence of change in BAF values with an applied concentration of nanoagrochemicals (Zhao et al., 2016a, 2016c).

This effect was also observed during the application of CuO nanoagrochemicals. BAF values for cabbage treated with copper oxide nanoparticles at varying concentrations (10 and 250 mg per plant, 5 days exposure) were found to be 0.003 and 0.0004 [unitless as the applied dose is in mg per plant: (mg/kg)/(mg/kg)], respectively (Xiong et al., 2017). A similar trend of bioaccumulation factor was observed for lettuce plants grown in soil media and treated with foliar spray of CuO NPs (Xiong et al., 2017). Singh and Kumar (2016) investigated the feasibility of the application of irrigation water contaminated with CuO NPs and its effect on spinach growth and uptake during 11 weeks (Singh and Kumar, 2016) and also reported the effect of concentration on BAF values. The estimated BAF values were found to be 15, 4, and 3.48 L/kg (with increasing concentrations of CuO NPs: 10, 100, and 1000 mg/L).

When Hong et al. (2015) exposed hydroponically grown lettuce plants to copper oxide nanoparticles at 5, 10, and 20 mg/L, the calculated values of bioaccumulation factor (for aerial portion) were found to be 6.04, 4.58, and 3.93 L/kg, respectively (Hong et al., 2015). In a study by Hong et al. (2015), the same results were observed for BAF values for the root section exposed to Cu NPs (Hong et al., 2015). The estimated BAF values for the underground portion of the plant were found to be higher than those obtained for shoot tissues (Table 2). These all the abovementioned studies indicated that the values of BAF decrease with an increase in nanoagrochemicals dose, irrespective of the application method of copper-based nanoagrochemicals expect for CuPRO 2005 and CuO NPs. However, these observations are contradictory to hydroponically grown lettuce exposed to 5 and 10 mg/L copper nanopesticides (CuPRO 2005), where BAF value at 10 mg/L for root portion (731.34 L/kg) was found to be higher than that obtained at the lowest CuPRO 2005 dose (BAF = 685.4 L/kg) (Hong et al., 2015).

4.1.3 Variation in BAF due to change in soil conditions (covered/uncovered)

Another important factor which could affect the bioaccumulation factor is the type of soil in which leafy vegetables are grown. For example, lettuce plants exposed to nanopesticides at different concentrations (1050, 1555, and 2100 mg/L) undercovered and uncovered soil conditions have shown variations in BAF values for leaves (vascular tissues). The observed BAF values for vascular tissue were ranging from 0.667 to 0.783 L/kg for uncovered and covered soil experiments for the same plant species (Zhao et al., 2016c). There have been very few studies which have revealed changes in bioaccumulation factor with respect to change in soil conditions for the same leafy vegetables (keeping other conditions same).

4.2 Translocation factor (TF)

Few literature studies have reported the use of translocation factor (TF) term instead of BAF for describing the metal uptake by food crops (Khan et al., 2013). The TF parameter is defined as the ratio of copper content in the shoot (mg/kg DW) to copper content in root (mg/kg DW) (Eq. (2)). Table 3 shows the TF values for leafy vegetables either (i) calculated using Eq. (2) or (ii) directly obtained from the published studies.

Table 3 Translocation factors calculated for few leafy vegetables.

Plant	Copper-based Nanoagrochemicals	Concentration	Translocation factor	References
Lettuce	$Cu(OH)_2$ (nanopesticide) (UC)	1050 mg/L	0.035	Zhao et al. (2016c)
Vascular tissues	$Cu(OH)_2$ (nanopesticide)(UC)	1555 mg/L	0.046	Zhao et al. (2016c)
	$Cu(OH)_2$ (nanopesticide)(UC)	2100 mg/L	0.025	Zhao et al. (2016c)
	$Cu(OH)_2$ (nanopesticide)(UC)	1050 mg/L	0.020	Zhao et al. (2016c)
Mesophyll tissues	$Cu(OH)_2$ (nanopesticide)(UC)	1555 mg/L	0.026	Zhao et al. (2016c)
	$Cu(OH)_2$ (nanopesticide)(UC)	2100 mg/L	0.015	Zhao et al. (2016c)
	$Cu(OH)_2$ (nanopesticide) (C)	1050 mg/L	0.023	Zhao et al. (2016c)
Vascular tissues	$Cu(OH)_2$ (nanopesticide)(C)	1555 mg/L	0.015	Zhao et al. (2016c)
	$Cu(OH)_2$ (nanopesticide)(C)	2100 mg/L	0.018	Zhao et al. (2016c)
	$Cu(OH)_2$ (nanopesticide)(C)	1050 mg/L	0.0144	Zhao et al. (2016c)
Mesophyll tissues	$Cu(OH)_2$ (nanopesticide)(C)	1555 mg/L	0.008	Zhao et al. (2016c)
	$Cu(OH)_2$ (nanopesticide)(C)	2100 mg/L	0.0104	Zhao et al. (2016c)
Lettuce	$Cu(OH)_2$ (nanopesticide)	10 mg/L	0.006	Hong et al. (2015)
	$Cu(OH)_2$ (nanopesticide)	15 mg/L	0.004	Hong et al. (2015)
	CuO NPs	5 mg/L	0.006	Hong et al. (2015)
	CuO NPs	10 mg/L	0.003	Hong et al. (2015)
	CuO NPs	15 mg/L	0.002	Hong et al. (2015)
	Cu NPs	5 mg/L	0.004	Hong et al. (2015)
	Cu NPs	10 mg/L	0.004	Hong et al. (2015)
	Cu NPs	15 mg/L	0.005	Hong et al. (2015)
	Cu PRO 2005	5 mg/L	0.007	Hong et al. (2015)
	Cu PRO 2005	10 mg/L	0.004	Hong et al. (2015)
	Cu PRO 2005	15 mg/L	0.004	Hong et al. (2015)
Lettuce				
5 days	CuO NPs	10 mg	**0.23**	Xiong et al. (2017)
5 days	CuO NPs	250 mg	0.13	Xiong et al. (2017)
10 days	CuO NPs	10 mg	**0.11**	Xiong et al. (2017)

10 days	CuO NPs	250 mg	0.16	Xiong et al. (2017)
15 days	CuO NPs	10 mg	**0.04**	Xiong et al. (2017)
15 days	CuO NPs	250 mg	0.04	Xiong et al. (2017)
Cabbage				
5 days	CuO NPs	10 mg	0.33	Xiong et al. (2017)
5 days	CuO NPs	250 mg	0.14	Xiong et al. (2017)
10 days	CuO NPs	10 mg	0.20	Xiong et al. (2017)
10 days	CuO NPs	250 mg	0.17	Xiong et al. (2017)
15 days	CuO NPs	10 mg	0.06	Xiong et al. (2017)
15 days	CuO NPs	250 mg	0.08	Xiong et al. (2017)
Lettuce				
5, 10, and 15 days	CuO NPs	100–1000 mg/L	0.018–0.156 (%)	Xiong et al. (2021b)

Note: 5, 10, and 15 days indicates exposure period.

$$\mathrm{TF} = \frac{Cu_{shoot}}{Cu_{root}} \tag{2}$$

4.2.1 Variation in TF due to change in leafy vegetable type

From the findings of the compiled studies, the variation in TF value with change in the type of leafy vegetables treated with CuO NPs was studied. Only one research study has given values of translocation factor for lettuce and cabbage, exposed to copper oxide nanoparticles. In the case of other copper nanoagrochemicals, there is a lack of accumulation data in plant tissues, such as shoot and root which is required in the estimation of a translocation factor value. There have been only limited studies whose findings can be used to understand the change in translocation values due to changes in plant type. Lettuce and cabbage treated with foliar spray of copper oxide nanoparticles (at 10 mg per plant, exposure period: 5 days) showed variation in TF value even at the same dose (Xiong et al., 2017) indicating that TF value depends on the interaction of nanoagrochemicals with plant species.

4.2.2 Variation in TF due to change in exposure time

The published research articles from the literature revealed that exposure time could be one of the factors influencing the translocation of copper (NPs or ionic part) within the same plant tissues (at the same dose of nanoagrochmical). In the case of lettuce treated with foliar spray of copper oxide NPs (250 mg per plant) for 5 and 15 days, observed translocation factor values were found to be 0.13 and 0.04, respectively, when other conditions were the same (Xiong et al., 2017). Similarly, this type of observation was also found in cabbage, treated with copper oxide nanoparticles at different exposure times. In the case of cabbage, the value of the translocation factor (at 15 days) was found to be less than that obtained at 5 days (Xiong et al., 2017). The data on translocation factor of exposure of other selected nanocopper-based compounds to leafy vegetables for different exposure intervals were missing.

4.2.3 Variation in TF due to change in soil conditions

The effect of soil exposure conditions on TF was also observed. For example, the exposure of lettuce plants to nanopesticides at different concentration values (1050, 1555, and 2100 mg/L) undercovered as well as uncovered soil conditions was observed to result in different translocation factor values for vascular tissues. The translocation factor values for vascular tissue at 1050 mg/L nanopesticides concentration were found to be 0.035 and 0.0144 for uncovered and covered soil experiments, respectively, for the same plant species (Zhao et al., 2016c), indicating the effect of soil conditions (covered/noncovered) on TF values. There have been few other studies which have revealed changes in estimated TF value with change in soil exposure conditions for the same leafy vegetable type. Research studies on the utilization of copper nanopesticides and their effect on translocation within plant tissues need to include copper (NPs/ionic) concentrations in root and shoot of leafy vegetables so that translocation can be easily studied. In the literature, there have been only 2–3 research papers which have given the idea of accumulation of copper in leafy vegetables after the application of copper nanopesticides and CuO NPs. But, still, this data are not adequate for discussing changes in translocation factor values with changes in plant and

soil conditions based on comparative studies (with certain same conditions). There is little data available on a quantitative accumulation of copper in leafy vegetables (in underground/aerial portion) exposed to Cu NPs under different soil types (sand or loam). It indicates a need for doing more studies in this direction.

4.2.4 Variation in TF value due to change in concentration of nanoagrochemicals

The effect of nanoagrochemicals concentration on TF was also observed. For example, Zhao et al. (2016c) suggested variation in translocation factor value with different doses of $Cu(OH)_2$ nanoagrochemicals to lettuce (Zhao et al., 2016c). The observed translocation factor values at 1050, 1555, and 2100 mg/L were found to be 0.023, 0.015, and 0.01, respectively (Vascular tissues, for covered soil condition). This kind of change was also observed in lettuce, exposed to CuO NPs at 10 and 250 mg/plant concentration levels (Xiong et al., 2017). Translocation values for hydroponically grown lettuce plants, exposed to 5, 10, and 20 mg/L CuO NPs and CuPRO 2005, were found to be different (Hong et al., 2015).

5 Soil contamination factor (SCF)

Soil contamination factor is calculated using the following equation, where Cu_{refer} is the value of copper concentration in the soil as background concentration (mg/kg) and Cu_{soil} is the copper concentration in the soil after application of nanoagrochemicals (mg/kg). We could calculate the soil contamination factor value only for $Cu(OH)_2$ nanopesticides (For covered and noncovered soil conditions), as there is no data available on the contamination of soil due to applications of CuPRO 2005, CuO NPs, and Cu NPs. The estimated values of soil contamination factors are presented in Table 4.

$$\mathrm{SCF} = \frac{Cu_{soil}}{Cu_{ref}} \tag{3}$$

Table 4 Estimated values of soil contamination factor during foliar application of $Cu(OH)_2$ nanopesticides (Model plant: Lettuce (Zhao et al., 2016c)).

Condition	Nanopesticides application rate (mg/L)	Copper concentration in soil at the end of experiment (mg/kg)	Calculated value of soil contamination factor
Uncovered	1050	50.3 ± 17.4 mg/kg DW	0.048
Uncovered	1555	44.1 ± 6.8 mg/kg DW	0.0283
Uncovered	2100	56.5 ± 15.6 mg/kg DW	0.0270
Covered	1050	37.1 ± 6.4 mg/kg DW	0.035
Covered	1555	38.3 ± 7.1 mg/kg DW	0.0246
Covered	2100	31 ± 1.4 mg/kg DW	0.0147

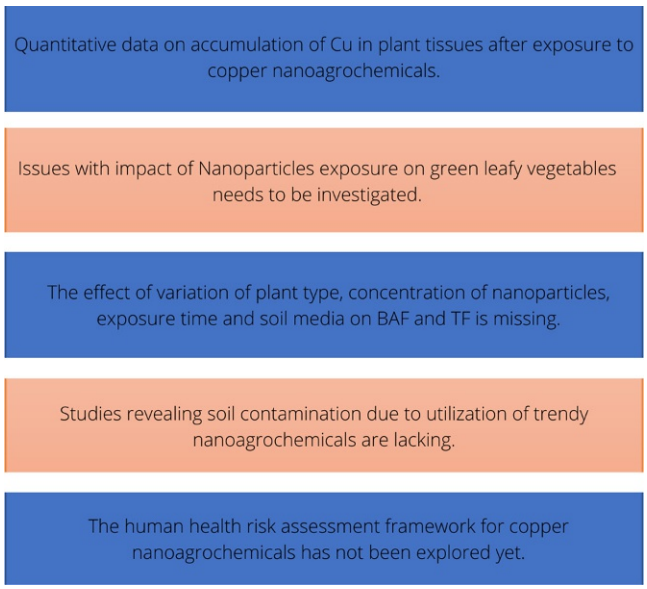

FIG. 3

Schematic representation showing identified knowledge gaps on the application of copper nanoagrochemicals in the future direction.

Fig. 3 shows identified knowledge gaps in this study. Out of these identified knowledge gaps, lack of accumulation data in plant tissues and soil contamination due to the exposure of copper nanoagrochemicals are of utmost importance. Therefore, detailed studies should be done on pot experiments with variation in leafy vegetables along with an accumulation of copper in plant tissues (metal ion content in shoot and root separately). Additionally, soil contamination due to exposure of each class of copper nanoagrochemicals must be studied in depth.

6 Summary and conclusions

Overall, the review of copper nanoagrochemicals indicated that bioaccumulation and translocation factors depend mainly on various parameters, such as type of copper nanoagrochemicals, a concentration at which edible plants are exposed, accumulation of copper in plant tissues, soil condition, and exposure type. Although qualitative data on the copper level in edible plant tissues are available, quantitative data of metal ion concentration was found to be lacking. Thus, this missing portion needs further detailed studies delivering quantitative data on the accumulation of nanoagrochemicals in plants. The changes in BAF and TF values due to changes in plant types, exposure time, concentration, and soil condition were discussed for four selected copper nanoagrochemicals. In the case of soil-related parameters, because of

insufficient data availability, we could estimate soil contamination factor only in the case of utilization of copper nanopesticides ($Cu(OH)_2$). This estimate could be used for determining probable NPs accumulation in edible plant tissues using values of bioaccumulation and translocation factors.

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References

Adeleye, A.S., Conway, J.R., Perez, T., Rutten, P., Keller, A.A., 2014. Influence of extracellular polymeric substances on the long-term fate, dissolution, and speciation of copper-based nanoparticles. Environ. Sci. Technol. 48, 12561–12568.

Alquraidi, A.O., Mosa, K.A., Ramamoorthy, K., 2019. Phytotoxic and genotoxic effects of copper nanoparticles in coriander (*Coriandrum sativum*-apiaceae). Plants 8.

Burachevskaya, M., Minkina, T., Mandzhieva, S., Bauer, T., Nevidomskaya, D., Shuvaeva, V., Sushkova, S., Kizilkaya, R., Gülser, C., Rajput, V., 2021. Transformation of copper oxide and copper oxide nanoparticles in the soil and their accumulation by *Hordeum sativum*. Environ. Geochem. Health 43(4), 1655–1672.

Carley, L.N., Panchagavi, R., Song, X., Davenport, S., Bergemann, C.M., McCumber, A.W., Gunsch, C.K., Simonin, M., 2020. Long-term effects of copper nanopesticides on soil and sediment community diversity in two outdoor mesocosm experiments. Environ. Sci. Technol. 54, 8878–8889.

Fischer, J., Evlanova, A., Philippe, A., Filser, J., 2021. Soil properties can evoke toxicity of copper oxide nanoparticles towards springtails at low concentrations. Environ. Pollut. 270, 116084.

Gogos, A., Knauer, K., Bucheli, T.D., 2012. Nanomaterials in plant protection and fertilization: current state, foreseen applications, and research priorities. J. Agric. Food Chem. 60, 9781–9792.

Guan, X., Gao, X., Avellan, A., Spielman-Sun, E., Xu, J., Laughton, S., Yun, J., Zhang, Y., Bland, G.D., Zhang, Y., 2020. CuO nanoparticles alter the rhizospheric bacterial community and local nitrogen cycling for wheat grown in a Calcareous soil. Environ. Sci. Technol. 54, 8699–8709.

Hong, J., Rico, C.M., Zhao, L., Adeleye, A.S., Keller, A.A., Peralta-Videa, J.R., Gardea-Torresdey, J.L., 2015. Toxic effects of copper-based nanoparticles or compounds to lettuce (*Lactuca sativa*) and alfalfa (*Medicago sativa*). Environ Sci Process Impacts 17, 177–185.

Kah, M., Navarro, D., Kookana, R.S., Kirby, J.K., Santra, S., Ozcan, A., Kabiri, S., 2019. Impact of (nano) formulations on the distribution and wash-off of copper pesticides and fertilisers applied on citrus leaves. Environ. Chem. 16, 401–410.

Khan, M.U., Malik, R.N., Muhammad, S., 2013. Human health risk from heavy metal via food crops consumption with wastewater irrigation practices in Pakistan. Chemosphere 93, 2230–2238.

Klaine, S.J., Alvarez, P.J.J., Batley, G.E., Fernandes, T.F., Handy, R.D., Lyon, D.Y., Mahendra, S., McLaughlin, M.J., Lead, J.R., 2008. Nanomaterials in the environment: behavior, fate, bioavailability, and effects. Environ. Toxicol. Chem. 27, 1825–1851.

Kohatsu, M.Y., Pelegrino, M.T., Monteiro, L.R., Freire, B.M., Pereira, R.M., Fincheira, P., Rubilar, O., Tortella, G., Batista, B.L., de Jesus, T.A., 2021. Comparison of foliar spray and soil irrigation of biogenic CuO nanoparticles (NPs) on elemental uptake and accumulation in lettuce. Environ. Sci. Pollut. Res. 28, 16350–16367.

Ma, X., Geiser-Lee, J., Deng, Y., Kolmakov, A., 2010. Interactions between engineered nanoparticles (ENPs) and plants: phytotoxicity, uptake and accumulation. Sci. Total Environ. 408, 3053–3061.

Monica, R.C., Cremonini, R., 2009. Nanoparticles and higher plants. Caryologia 62, 161–165.

Peixoto, S., Henriques, I., Loureiro, S., 2020. Long-term effects of Cu (OH) 2 nanopesticide exposure on soil microbial communities. Environ. Pollut. 269, 116113.

Pelegrino, M.T., Kohatsu, M.Y., Seabra, A.B., Monteiro, L.R., Gomes, D.G., Oliveira, H.C., Rolim, W.R., de Jesus, T.A., Batista, B.L., Lange, C.N., 2020. Effects of copper oxide nanoparticles on growth of lettuce (*Lactuca sativa* L.) seedlings and possible implications of nitric oxide in their antioxidative defense. Environ. Monit. Assess. 192, 1–14.

Pérez-Labrada, F., López-Vargas, E.R., Ortega-Ortiz, H., Cadenas-Pliego, G., Benavides-Mendoza, A., Juárez-Maldonado, A., 2019. Responses of tomato plants under saline stress to foliar application of copper nanoparticles. Plan. Theory 8, 151.

Rawat, S., Cota-Ruiz, K., Dou, H., Pullagurala, V.L.R., Zuverza-Mena, N., White, J.C., Niu, G., Sharma, N., Hernandez-Viezcas, J.A., Peralta-Videa, J.R., 2021. Soil-weathered CuO nanoparticles compromise foliar health and pigment production in spinach (*Spinacia oleracea*). Environ. Sci. Technol. https://doi.org/10.1021/acs.est.0c06548.

Samarajeewa, A.D., Velicogna, J.R., Schwertfeger, D.M., Princz, J.I., Subasinghe, R.M., Scroggins, R.P., Beaudette, L.A., 2021. Ecotoxicological effects of copper oxide nanoparticles (nCuO) on the soil microbial community in a biosolids-amended soil. Sci. Total Environ. 763, 143037.

Shang, H., Ma, C., Li, C., White, J.C., Polubesova, T., Chefetz, B., Xing, B., 2020. Copper sulfide nanoparticles suppress Gibberella fujikuroi infection in rice (*Oryza sativa* L.) by multiple mechanisms: contact-mortality, nutritional modulation and phytohormone regulation. Environ. Sci. Nano 7, 2632–2643.

Sharma, P., Goyal, D., Chudasama, B., 2021. Ecotoxicity of as-synthesised copper nanoparticles on soil bacteria. IET Nanobiotechnol. 15(2), 236–245.

Singh, D., Kumar, A., 2016. Impact of irrigation using water containing CuO and ZnO nanoparticles on S*pinach oleracea* grown in soil media. Bull. Environ. Contam. Toxicol. 97, 548–553.

Singh, D., Kumar, A., 2018. Investigating long-term effect of nanoparticles on growth of *Raphanus sativus* plants: a trans-generational study. Ecotoxicology 27, 23–31.

Singh, D., Kumar, A., 2019. Assessment of toxic interaction of nano zinc oxide and nano copper oxide on germination of *Raphanus sativus* seeds. Environ. Monit. Assess. 191, 703.

Singh, D., Kumar, A., 2020. Quantification of metal uptake in *Spinacia oleracea* irrigated with water containing a mixture of CuO and ZnO nanoparticles. Chemosphere 243, 125239.

Tan, W., Gao, Q., Deng, C., Wang, Y., Lee, W.-Y., Hernandez-Viezcas, J.A., Peralta-Videa, J.R., Gardea-Torresdey, J.L., 2018. Foliar exposure of Cu (OH) 2 nanopesticide to basil (*Ocimum basilicum*): variety-dependent copper translocation and biochemical responses. J. Agric. Food Chem. 66, 3358–3366.

Trujillo-Reyes, J., Majumdar, S., Botez, C.E., Peralta-Videa, J.R., Gardea-Torresdey, J.L., 2014. Exposure studies of core-shell Fe/Fe3O4 and Cu/CuO NPs to lettuce (*Lactuca sativa*) plants: are they a potential physiological and nutritional hazard? J. Hazard. Mater. 267, 255–263.

Wang, Z., Xie, X., Zhao, J., Liu, X., Feng, W., White, J.C., Xing, B., 2012. Xylem- and phloem-based transport of CuO nanoparticles in maize (*Zea mays* L.). Environ. Sci. Technol. 46, 4434–4441.

Xiong, T., Dumat, C., Dappe, V., Vezin, H., Schreck, E., Shahid, M., Pierart, A., Sobanska, S., 2017. Copper oxide nanoparticle foliar uptake, phytotoxicity, and consequences for sustainable urban agriculture. Environ. Sci. Technol. 51, 5242–5251.

Xiong, T., Zhang, S., Kang, Z., Zhang, T., Li, S., 2021a. Dose-Dependent physiological and transcriptomic responses of lettuce (*Lactuca sativa* L.) to copper oxide nanoparticles—insights into the phytotoxicity mechanisms. Int. J. Mol. Sci. 22, 3688.

Xiong, T., Zhang, T., Xian, Y., Kang, Z., Zhang, S., Dumat, C., Shahid, M., Li, S., 2021b. Foliar uptake, biotransformation, and impact of CuO nanoparticles in *Lactuca sativa* L. var. *ramosa* Hort. Environ. Geochem. Health 43, 423–439.

Zhang, Z., He, X., Zhang, H., Ma, Y., Zhang, P., Ding, Y., Zhao, Y., 2011. Uptake and distribution of ceria nanoparticles in cucumber plants. Metallomics 3, 816–822.

Zhang, X., Xu, Z., Qian, X., Lin, D., Zeng, T., Filser, J., Li, L., Kah, M., 2020. Assessing the impacts of Cu $(OH)_2$ nanopesticide and ionic copper on the soil enzyme activity and bacterial community. J. Agric. Food Chem. 68, 3372–3381.

Zhao, L., Huang, Y., Hannah-Bick, C., Fulton, A.N., Keller, A.A., 2016a. Application of metabolomics to assess the impact of Cu $(OH)_2$ nanopesticide on the nutritional value of lettuce (*Lactuca sativa*): enhanced Cu intake and reduced antioxidants. NanoImpact 3, 58–66.

Zhao, L., Huang, Y., Zhou, H., Adeleye, A.S., Wang, H., Ortiz, C., Mazer, S.J., Keller, A.A., 2016b. GC-TOF-MS based metabolomics and ICP-MS based metallomics of cucumber (*Cucumis sativus*) fruits reveal alteration of metabolites profile and biological pathway disruption induced by nano copper. Environ. Sci. Nano 3, 1114–1123.

Zhao, L., Ortiz, C., Adeleye, A.S., Hu, Q., Zhou, H., Huang, Y., Keller, A.A., 2016c. Metabolomics to detect response of lettuce (*Lactuca sativa*) to Cu $(OH)_2$ nanopesticides: oxidative stress response and detoxification mechanisms. Environ. Sci. Technol. 50, 9697–9707.

Zhao, L., Hu, Q., Huang, Y., Keller, A.A., 2017a. Response at genetic, metabolic, and physiological levels of maize (*Zea mays*) exposed to a Cu (OH) 2 nanopesticide. ACS Sustain. Chem. Eng. 5, 8294–8301.

Zhao, L., Huang, Y., Adeleye, A.S., Keller, A.A., 2017b. Metabolomics reveals Cu(OH)2 nanopesticide-activated anti-oxidative pathways and decreased beneficial antioxidants in spinach leaves. Environ. Sci. Technol. 51, 10184–10194.

Zuverza-Mena, N., Medina-Velo, I.A., Barrios, A.C., Tan, W., Peralta-Videa, J.R., Gardea-Torresdey, J.L., 2015. Copper nanoparticles/compounds impact agronomic and physiological parameters in cilantro (*Coriandrum sativum*). Environ Sci Process Impacts 17, 1783–1793.

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CHAPTER

25 Understanding the effect of copper-based nanoagrochemicals on nitrogen-fixation ability of blue-green algae: A review

Samridhi Rana and Arun Kumar

Department of Civil Engineering, Indian Institute of Technology Delhi, New Delhi, India

1 Introduction

The population of the world presently is 7.2 billion and it is anticipated to cross approximately 10 billion by the end of 2050 according to the studies done in the past. This increase also puts a burden on the agriculture sector. The possibility of increasing fertility and productivity of the plant with the help of management tools might help in ensuring food supply for all. One of the major questions that arises in today's agriculture practices is how we can enhance agricultural production to fulfill the present and future food requirements of people all around the globe by utilizing the available resources, without altering or harming the environment (Singh and Strong, 2016). The practice of sustainable agriculture and farming will be able to fulfill the growing need of food without harming the environment (Mason, 2003). It may also help in making the agricultural system more adaptable, self-dependent, and self-operating while maintaining productivity along with profitability (Adeleye et al., 2016).

Today, sustainable agriculture practices have anticipated the major role played by microorganisms to attain the security of the food without hampering the natural conditions. Since, cyanobacteria (CB) or blue-green algae can be called a favorable microbe, it plays a prominent role to enhance productivity in agricultural fields and alleviation of greenhouse gas (GHG) emissions (Singh et al., 2011). These bacteria can be considered as the vital biological mode in fixing degraded lands ecologically (Singh, 2014a), enhancing the capacity of water holding and porosity along with the cation exchange potential of soil. Problems associated with the establishment of inoculated strains (because of the competition with the native strains found in the soil) and inconsistency in the crop response due to environmental fluctuations have restricted the process of adoption by farmers all around the world (Lee and Watanabe, 1977; Whitton, 2006). Studies have attempted to enrich soil by the

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process of algalization (Kulasooriya, 1998; Singh and Bisoyi, 1989). These cyanobacteria provide profitable as well as ecologically beneficial alternative to the chemically synthesized fertilizers for the utmost goal of getting enhanced productivity, especially in rice cultivation. In the rice ecosystem ("Azolliculture"; Pabby et al., 2003; Whitton, 2000), the process of fixing nitrogen by free-living cyanobacteria is significantly to supply the nitrogen from the soil.

With the increasing use of nanoparticles (NPs) in different areas, the development in the fields related to nanotechnology has increased tremendously. Nanoparticles can be defined as particles that have at least one dimension ranging from 1 to 100 nm (Laurent et al., 2008). Nanoagrochemical can be called a combination of nanotechnology with agrochemicals, which resulted in the production of products such as nanofertilizers, nanopesticides, nanoinsecticides, nanoherbicides, and nanofungicides. Today, these nanoagrochemicals are popular because of their substantial effectiveness as compared to the traditional agrochemicals, thus making them more economically feasible as well as environmentally friendly. There are many studies about the toxicity of CuO nanoparticles (CuO·NPs) on the plant morphology, its germination process along with the quality, and the process, such as transpiration and translocation in plant tissues as well. Recently published studies on the toxicity of CuO nanoparticles have shown obstructive impact on germination of seed as well as on the growth of various crop plants, which includes lettuce (*Lactuca sativa*), rice (*Oryza sativa*), spinach (*Spinacia oleracea*), sweet potato (*Ipomoea batatas*), onion (*Allium cepa*), tomato (*Solanum lycopersicum*), soybean (*Glycine max*), carrot (*Daucus carota*), cotton-chickpea, barley (*Hordeum vulgare*), alfalfa (*Medicago sativa*), wheat (*Triticum aestivum*), mungbean (*Vigna radiate*), kidneybean (*Phaseolus vulgaris*), mustard (*Brassica juncea*), maize (*Zea mays*), cilantro (*Coriandrum sativum*), cucumber (*Cucumis sativus*), etc. (Rajput et al., 2018). The low cost of the cultivation, reduced time of production, and environment-friendly synthesis reduce the application of hazardous chemicals as well as make algae a very good alternative platform for NP synthesis (Khanna et al., 2019).

There exists a possibility of interaction of algae with nanoagrochemicals, such as CuO. Thus, it is important to understand its implication on different plants, such as rice. To understand this aspect, this study briefly elaborates the interaction and mechanism of nitrogen fixation by cyanobacteria, the effect of CuO NPs on the nitrogen fixation efficiency of the cyanobacteria, and their subsequent possible effect on the growth of plants especially on rice plant (Fig. 1 shows the outline of this study).

2 Use of blue-green algae in agriculture sector

The application of cyanobacteria or blue-green algae in the management of soil and management of the environment consists of the following: benefits in an economy such as reduction in the input cost, phosphorus bioavailability, water storage capacity, nutrient cycling, nitrogen fixation, and movement, environmental protection along with the pollution prevention and degradation of land mostly by the reduction

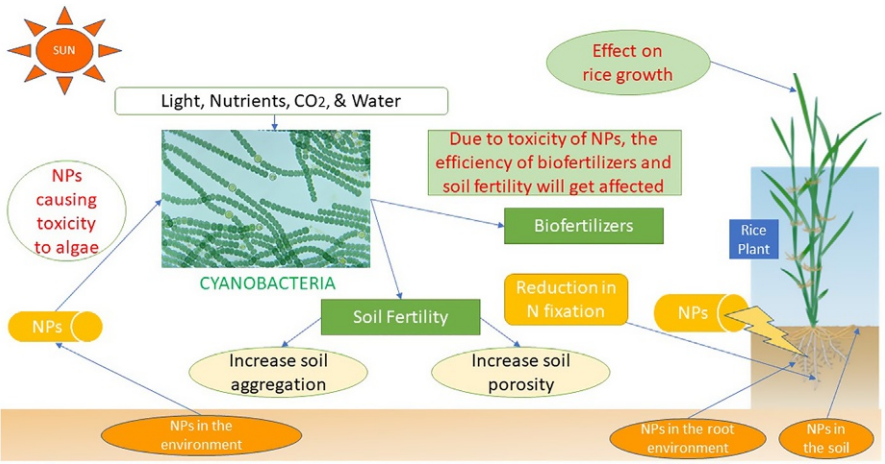

FIG. 1

Schematic representation of the outline of the effect of the interaction of algae with CuO on rice plant growth (NP-nanoparticles). It indicates that nanoparticles present in water interact with cyanobacteria as well as soil and are taken up by plant roots of rice plants. NP uptake by rice plants will affect the N fixation efficiency and growth of rice plants.

in the usage of chemicals in an agricultural field, and nutrients recycling followed by the soil fertility through reclamation by restoration (Prasad et al., 2014). The biosynthesis of NPs from blue-green algae can be either intracellular or extracellular, which is mostly dependent on the location where the formation of NPs is taking place (Chaudhary et al., 2020). Most of the paddy soils have organic population of cyanobacteria, which are a major source of combined nitrogen. The main significance of ecological observations on the abundance of cyanobacteria in the rice field soils of India became apparent when the heterocyst was considered N-fixing stations of heterocystous cyanobacteria and various nonheterocystous forms fixed nitrogen anaerobically (Kaushik et al., 2019). Agronomic trials conducted with rice crops commonly show that N contributed by cyanobacteria is of the order of 20–30 kg/ha. Thus, by using blue-green algae (BGA) in a rice field, a farmer can save to the extent of 20–30 kg N/ha without compromising with the normal yield. Fig. 2 shows the benefits of cyanobacteria in agro-ecosystem such as enhanced mobility and solubility along with plant growth stimulation.

2.1 For fixing nitrogen in soil environment

The most promising features of CB have the ability to photosynthesize and fix atmospheric nitrogen (N) in rice fields. Table 1 presents a list of CBs which help in fixing nitrogen in the field. Intrinsic fertility of tropical rice field soils has been attributed to the activity of diazotrophic cyanobacteria (Chakdar et al., 2012). Virtually,

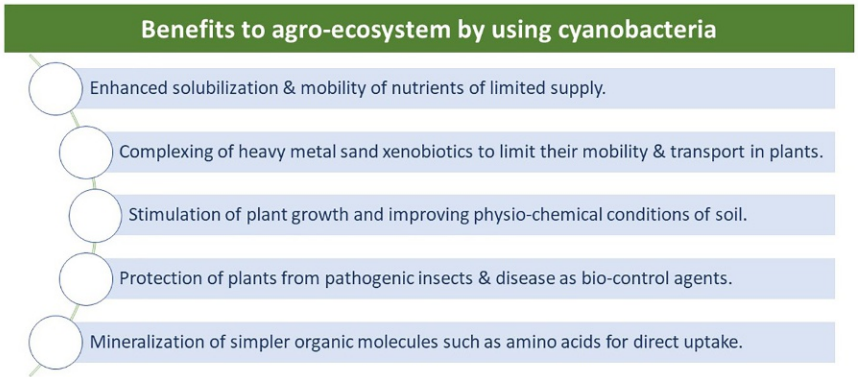

FIG. 2

Benefits of cyanobacteria to agro-ecosystem.

Table 1 Different forms of cyanobacteria which help in nitrogen fixing.

Forms of cyanobacteria	Species	Mechanism of fixing
Unicellular	*Dermocapsa, Synechococcus Aphanothece, Pleurocapsa, Xenococcus Chroococcidiopsis, Gloeocapsa (Gloeothece), Myxosarcina*	Without nitrogen
Filamentous heterocystous	*Anabaena, Rivularia, Scytonema, Scytonematopsis, Chlorogloeopsis, Cylindrospermum, Fischerella, Gloeotrichia, Westiellopsis, Hapalosiphon, Mastigocladus, Anabaenopsis, Aulosira, Calothrix, Camptylonema, Chlorogloea, Nodularia, Nostoc, Nostochopsis, Stigonema, Tolypothrix, Westiella*	It is used to separate N_2 fixation from oxygenic photosynthesis in space
Filamentous nonheterocystous	*Lyngbya, Microcoleuschthonoplastes, Pseudanabaena, Schizothrix, Myxosarcina, Oscillatoria, Plectonema, Boryanum, Trichodesmium*	N_2 fixation separation from oxygenic photosynthesis in respect to time

all dominant CBs inhabiting the rice fields is diazotrophic and it gives a mark on how rice has been grown for centuries without any external supply of N_2. It is found that the ability to fix N was found in heterocystous cyanobacteria, such as *Anabaena*, *Aulosira*, *Nostoc*, etc. along with the several nonheterocystous unicellular microbes which include *Gloeothece*, *Gloeocapsa*, *Aphanothece*, etc. as well as filamentous microbes, such as *Oscillatoria, Plectonema*, etc. blue-green algae.

In the nonheterocystous forms, it is found that the process of oxygenic photosynthesis is different from the process of nitrogen fixation. In temporal separation process, it was found that nitrogen fixation mostly happens in the period when it is dark and the process of photosynthesis occurs basically during the light. In a spatial separation, it was found that the central cells which are nonphotosynthetic usually engaged in the process of nitrogen fixation, while the cells which are present in the outer part are photosynthetically active. Apart from rice, other plants, such as sorghum, maize, vegetables, sugarcane, wheat, cotton, etc. are also considered to be responsive to the biofertilizer which has cyanobacteria (Abd-Alla et al., 1994).

Many blue-green algae or cyanobacteria are capable of utilizing atmospheric dinitrogen (N_2), and this process is known as nitrogen fixation (Mishra et al., 2019). Nitrate and nitrite ions are important sources of nitrogen, which later reduce into ammonia. Ammonia is taken up by the blue-green algae through the process of passive diffusion or as ammonium ions by a specific uptake system. The amino acids, such as glutamine, arginine, and asparagine act as a nitrogen source. In the process of biological nitrogen fixation, 2 mol of NH_3 are produced from 1 mol of N_2 gas, by utilizing 16 mol of ATP (adenosine triphosphate) with a supply of electrons, protons, and hydrogen ions as shown in the following equation:

$$N_2 + 8H^+ + 8e^- + 16ATP \rightarrow 2NH_3 + H_2 + 16ADP + 16Pi \quad (1)$$

The reaction stated above takes place only in prokaryotic organisms (such as bacteria and other related organisms) by utilizing a complex of enzymes that are known as nitrogenase. This enzyme includes two proteins—an iron protein and a molybdenum-iron protein. Blue-green algae (BGA) fix nitrogen under the anaerobic conditions in the specialized cells known as heterocyst which comprise 5%–10% of cells inside the filament (Fleming and Haselkorn, 1974). Cyanobacteria or blue-green algae have another mechanism for the process of protecting nitrogenase in which heterocyst fixes nitrogen which consists of only photosystem I. This system makes ATP by the reaction which is mediated by light whereas the other cells consist of both photosystem I and photosystem II which produce O_2 when the light energy is consumed to split H_2O to supply H_2 for the synthesis of organic compounds.

The main abiotic factors affecting the algae distribution in soils are solar radiation, pH, organic matter content, moisture, temperature, nutrients, as well as soil texture, which are less dominant. Usually, the higher the soil moisture, the temperature of the soil, and the penetration of the sunlight to the soil surface, the more will be the population of algae and its activities. Organic and inorganic nutrients of high levels also increase the growth along with the activity of the algae which is present terrestrially. The pH of the soil also contributes to the alteration of various activities of certain types of algae. Blue-green algae grows in the rice fields very rapidly which consists of organic matters in the soil in the huge amount along with the presence of water as well as the optimal conditions including temperature, organic sources along with pH in the fields of rice cultivation (Choudhury and Kennedy, 2004). It is said that the pH is one of the major factors in the growth, establishment, and a diversity of blue-green algae, which is generally preferred as

a slightly alkaline pH for the optimum growth amidst the soil properties (Kaushik, 1994). Blue-green algae, such as *Calothrix brevessima*, *Alosira ferrilissitiia,* etc., are ubiquitous in the rice fields of Kerala with the pH varying in the range 3.5–6.5. In a study by Subhashini and Kaushik (1981), the alkaline soil pH decreased when treated with blue-green algae. Also, in one of the studies done by Prasanna and Nayak (2007), the blue-green algae were found to be much in number at high pH in the rice fields. Blue-green algae are grown in soils that are highly alkaline to improve the physical and chemical properties of the soil. (Kaushik, 1994). In subsurface soil, blue-green algae associates with plant roots, producing root growth-stimulating hormones and enhancing the activities of microorganisms present or related to the roots (Issa et al., 2014).

BGA fixes the N mostly under combined nitrogen-deficient conditions and in the presence of combined N source, nitrogenase enzyme remains repressed or suspended similar to oxygen effect (i.e., reversible inhibition). Inoculation of rice fields with cyanobacteria lessens the nitrogen losses by via metabolization of nitrogen forms which are present in combined form. The combined nitrogen which is metabolized along with the biologically fixed nitrogen becomes available gradually by the process of exudation and decomposition of these algae. N fixed by CB will be available to rice plants only after it is released extracellularly into the surrounding environment, either as an extracellular product or by mineralization of their intracellular contents through microbial decomposition of fresh or dry algal mass which is incorporated into the soil. The amount of extracellular nitrogen which is liberated generally accounts for about 5%–50% of the total N fixed. As nitrogen fixation by blue-green algae vis-à-vis, it releases in the soil water system may be considered more useful for the production of the crop during vegetative growth stages of rice than that during a later stage.

Besides nitrogen contribution, cyanobacteria are beneficial to crop plants as they produce different growth-promoting or enhancing substances, such as auxins like indole-3-acetic acid, indole-3-propionic acid, etc., gibberellins, free amino acids, such as arginine, glycine, aspartic acid, serine, vitamin B12, threonine, glutamic acid, etc., along with the extra- and intracellular polysaccharides like xylose, galactose, etc. (Singh, 2014b). These substances have different benefits, such as improvement in the soil structure, as well as useful bacteria, chelation of heavy metals, and growth stimulation of crop plants (El-Enany and Issa, 2000).

2.2 For conditioning soil

Cyanobacteria also have great potential in the management of the environment as a soil conditioner. Organic amendments act by soil structure improvement, but also firmly influences the soil microflora. Rice field which is inoculated with BGA may help to fastly regenerate and help in soil structure improvement. Cyanobacteria during growth in soil excrete extracellularly different compounds, such as polysaccharides, peptides, lipids, etc. (Prasanna and Nayak, 2007), which possibly diffuse around the soil particles and bind them together as microaggregates.

Blue-green algae holds the potential to reclaim salinity-affected soils. BGA adapts and tolerates the stresses in the soils which are affected by salt such as deficiency of nutrients, salinity, and high pH. Blue-green algae (BGA) is adjusted in such a way to bear salt stress by the accumulation of organic solutes (Blumbald, 1983; Reed, 1984; Mackay, 1983) by optimizing inorganic ions (Miller et al., 1976) which contribute to the transport processes of iron (Apte and Thomas, 1984; Reed and Stewart, 1985; Apte, 1987) and several other adjustments metabolically (Blumwald and Tel-Or, 1984; Thomas and Apte, 1984).

Blue-green algae (BGA) due to their dual capability of photosynthesis and N_2 fixation also contribute to productivity (Fogg, 1973). By knowing the salt response in blue-green algae or cyanobacteria, it can be studied in understanding the detrimental effect of salinity on several crop plants (Pandhal, 2008). To reclaim soil, blue-green algae can be used, which are alkaline as they form a thick layer on the soil surface. Algal material is found to incorporate organic C and N and organic P along with the moisture to the soil which converts Na^+ to Ca^{2+}. Soil aggregation improvement and enhancement can be done by lowering pH and electrical conductivity and increasing hydraulic conductivity by blue-green algae (Kaushik and Subhashini, 1985). These changes improve the crop vigor as well as the yield in the soil (Kaushik and Subhashini, 1985; Subhashini and Kaushik, 1981).

3 Use of nanoagrochemicals in agriculture sector

Nanotechnology has a great potential to increase food production globally along with the enhanced quality of food and it reduces waste sustainably by the process of agricultural production (Prasad et al., 2017). The increased utilization of pesticides and fertilizers leads to environmental pollution, biodiversity loss, and agricultural pests along with the pathogen's emergence (Meena, 2020). For getting the solutions to the following problems, nanoformulations can be considered as targeted fertilizer that is released in a controlled manner with high specificity, which ultimately leads to the reduction in collateral damage (Seleiman et al., 2021). Therefore, in nanotechnology, food production and agriculture are considered to be the most important fields. From the literature, it was found that *Phormidium cyanobacterium* and *Spirulina* produce copper oxide (CuO) NPs (Hamida et al., 2020; Akintelu et al., 2020). Fig. 3 shows the schematic representation of the use of nanotechnology in the agriculture sector. According to the studies, sustainable agriculture demands very little use of agrochemicals for the protection of the environment. Table 2 gives a list of nanoagrochemicals used in the agriculture sector.

Copper (Cu) is one of the elements, which is naturally present in the Earth's Crust with a concentration of approximately 60 g/ton (Ojha et al., 2017) and is also known to play an important role in the mitochondrial respiration, mobilization of iron, signaling of a hormone, metabolism of cell wall and electron transportation (Yruela, 2009). Cu is generally toxic to plants and other organisms including algae, fish, mussels, and crustaceans (Braz-Mota et al., 2018). Currently, there is a lack of

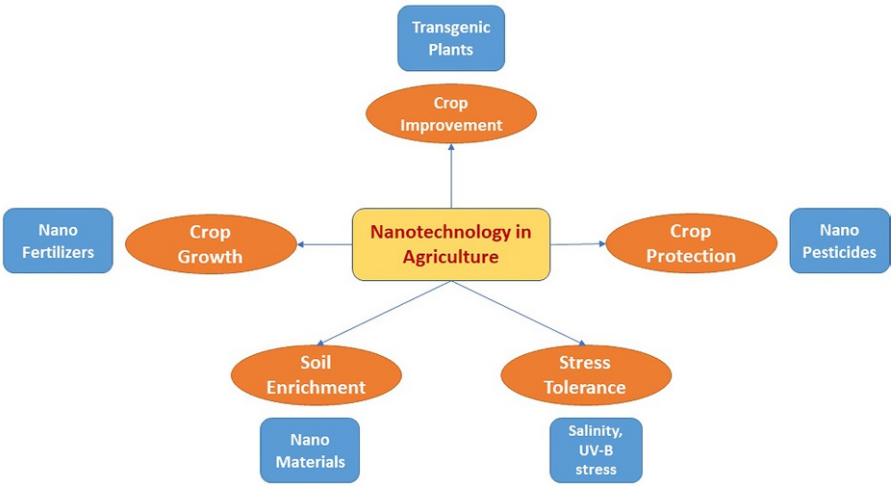

FIG. 3

Schematic representation showing the use of nanotechnology in agriculture.

Table 2 A list of studies on nano pesticides/herbicides and its application.

Carrier	Agent	Purpose	Method	References
Chitosan	Imazapic and imazapyr	Cytotoxicity assays	Encapsulation	Maruyama et al. (2016)
Silica	Piracetam, pentoxifylline, and pyridoxine	Brain tissue perfused	Suspension	Jampílek and Kráľová (2015)
Alginate	Imidacloprid	Cytotoxicity, sucking pest (leafhoppers)	Emulsion	Kumar et al. (2014)
Polyacetic acid-polyethylene glycol-polyacetic acid	Imidacloprid	Lethal concentration reduction	Encapsulation	Memarizadeh et al. (2014)
Carboxymethyl chitosan	Methomyl	Long-termcontrolled release	Encapsulation	Sun et al. (2014)
Chitosan/ tripolyphosphate	Paraquat	Lower cyto- and genotoxicity	Encapsulation	Grillo et al. (2014)

data on CuO-NPs concentration in the soil. It was found that the total Copper varies from 2 to 100 mg/kg in the soil which is considered to be unpolluted (Nagajyoti et al., 2010). Soil receive copper-based nanoparticles by the application of agricultural nano-products directly as well as by the industrial wastes (Adeleye et al., 2016; Rajput et al., 2018). The pesticides toxicity specifically due to copper-based

nanoparticles or copper-based nanopesticides make them the best choice so that they can be used as pathogens along with the pests in the plants. Copper-based fungicides have been used for centuries for contributing to soil contamination which is based on their copper ion content that allows them to perform or act as a reducing or oxidizing agent. The behavior of CuO nanoparticles on the plant cells is still not well studied to a satisfactory extent. The results which are present currently have no clear information regarding the effect and toxicity of CuO nanoparticles on the plants. Although it is said that nanopowders are successfully utilized as microfertilizers and pesticides (Selivanov and Zorin, 2001; Raikova et al., 2006). It can also be stated that the CuO nanoparticles exposure results in their uptake, bioaccumulation, along with the translocation in the plants such as mung bean as well as wheat plants according to the study done by Lee et al. (2008). It has been studied that the plants require Cu only in traces, hence, the increment in the CuO NPs concentration exerts toxic effect by penetrating directly inside the cell, or by oxidative impairment to structure of the cell as well as to the molecules (Nekrasova et al., 2011).

4 Effect of interaction of algae with CuO NPs on rice plant growth

There is a chance of copper interacting with algae in soil, which might induce the toxic effect. The following section presents a detailed description of this interaction and its implications on nitrogen fixation (Fig. 4).

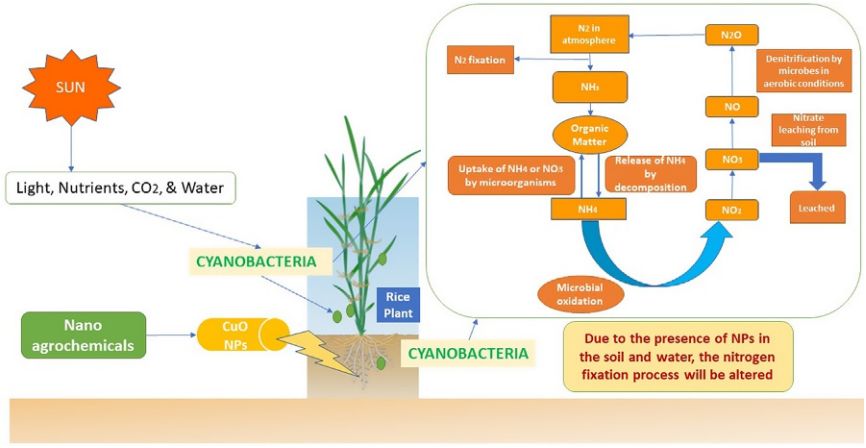

FIG. 4

The schematic representation showing the interaction of blue-green algae with rice plants and NPs along with the nitrogen fixation process.

4.1 Interaction of blue-green algae with copper nanoparticles

CuO NPs are known to attach to the surface of the algal cells externally, and also it was observed that between the CuO nanoparticles and cells of algae, heteroagglomeration takes place. CuO-NPs generally increment cell total by framing spans between the cells in the regions where the NPs had some aggregation. The CuO nanoparticles are attached to the surface of the blue-green algal cells. By the process of heteroagglomeration, physical damage, shading effect, internalization, oxidative stress, etc. can be seen to provide toxicity directly or indirectly. It will also release ions. Therefore, ions can be absorbed by algae, which could be converted to CuO intracellularly.

The main function of copper NPs is their ability to enter the plasma membrane which makes few alterations in the organelles. This condition causes oxidative stress which increases the enzyme activities such as POD, CAT, and SOD (Melegari et al., 2013). For ROS generation, chloroplasts and mitochondria play an important role in plant cells. Internal oxygen concentration (IOC) is found to be high during photosynthesis, and the chloroplasts are prone to the generation of ROS; therefore, this cytotoxic ROS can basically disrupt the organic process of metabolism because of which oxidative damage of lipids, nucleic acids, and proteins can be seen. In the results of flow cytometry, CuO NPs cause much bigger membrane damage than Cu^{2+} ions. Oxidative stress leads to the damage of membrane (Kamat et al., 2002)/physical interaction or penetration also (Huang et al., 2010). Therefore, it is important to know the amount of ROS generation inside the cells of algae after they are exposed to CuO NPs. Table 3 shows the summary of findings of studies done on the toxicity of CuO NPs to algae.

The copper nanoparticles which are exposed to the aquatic flora and fauna reflect the dysfunction in the photosystem. The amount of chlorophyll in *Lemna minor* decreases when there is an increment in the concentration of CuO nanoparticles at 100 mg/L (Song et al., 2016). Also, in the algae *Chlamydomonas reinhardtii*, the total chlorophyll reduction and decrease in carotenoids was found at the concentration of CuO NPs 1000 mg/L when they were exposed for about 72 h (Aruoja et al., 2009). For microalgae such as *Pseudokirchneriella,* Melegari et al. (2013) found that the concentration of 6.4 mg/L of CuO nanoparticles was sufficient to evoke the abnormalities in the performance of the photosynthetic system. In the study conducted by Perreault et al. (2014), the lower photosynthetic electron transport rate was seen in *Lemna gibba*. Also, the copper NPs (> 1 mg/L) suppress the photosynthesis process on *Elodea densa* (waterweed) whereas the low concentration such as < 0.25 mg/L has a positive effect on the photosynthesis (Nekrasova et al., 2011). A study has also shown that CuO-NPs alone, i.e., 0.004 g/L cause comparatively less toxicity to the alga *Chlamydomonas reinhardtii* than the CuO nanoparticles that have a coating of the polymer after 6 h of exposition (Perrault et al., 2012). The extent of toxicity is found to be significantly dependent on the density of the cell along with the more cell-dense cultures mitigation (Craig et al., 2020). The synthesis of NPs influences the size of the particle, surface area for generation of growth inhibition, morphological and density changes, and further deaths of blue-green algae at the nanoparticle-dependent

Table 3 Summary of findings on toxicity of CuO NPs to algae.

Reference	NP info	Experimental conditions	Parameters	Findings
Zhao et al. (2016)	CuO NPs (Cu NPs (10 mg/L) or Cu ions (0.6 mg/L))	*Chlorella pyrenoidos* algae; initial algal conc. = 1×10^6 cells/mL; NP conc. = 10–200 mg/L; Exposure times (0, 1, 2, 3, 4, and 5 days)	Characterization of NPs (size, morphology, hydrodynamic diameter); dissolution, zeta potential, growth inhibition, NPs and particles on the cell wall; membrane damage, ROS generation	72 h EC50 = 45.7 mg/L CuO nanoparticles attachment to the cells of algae and interaction with EPS (through light microscope and SEM observation.). More EPS production; Severe membrane damage
Chang et al. (2012)	CuO NPs ZnO NPs	Review of the toxicity mechanism of CuO and ZnO NPs on algae and other organisms	NA	NA
Nguyen et al. (2018)	CuO NPs ZnO NPs Pd, Ag, Pt NPs	*Chlamydomonas reinhardtii* algal culture	Characterization of NPs (size, morphology, dissolution, zeta potential, hydrodynamic diameter); growth inhibition, NPs and particles on the cell wall; membrane damage, ROS generation, chlorophyll content	All the NPs had a significant effect on algal growth rate; In terms of other biological effects, CuO NPs significantly cause cell membrane damage, and caused oxidative stress
Fazelian et al. (2020)	CuO, ZnO, Fe_2O_3 NPs	Green microalga *Nannochloropsis oculate*	NPs dispersion and characterization, microscopic analysis, chlorophyll content, fatty acid profile, protein concentration, FAME analysis, statistical analysis	CuO-NPs > ZnO-NPs > Fe_2O_3-NPs: growth of alga can be inhibited by the increasing concentration of NPs
Janani et al. (2020)	CuO NPs	Algal species *Lyngbya* sp.	Characterization of NPs, ROS determination, cytotoxic evaluation, antioxidant enzyme assay, etc.	0.1 μg/mL CuO NPs showed the growth inhibition of 47 ± 2% on *Lyngbya* sp. after the 5 days of incubation. Increased lipid peroxidation and generation of ROS in algal cells observed up on NPs exposure. The exposure of NPs suppressed the antioxidant defense system

concentration (Adochite and Andronic, 2021). The lower amount of toxicity that is presented by the plant-mediated NPs can be attributed to the high solubility as well as the release of ion of physically or chemically synthesized CuONPs. Consequently, CuONPs can be a powerful biocide toward several types of algae such as green algae, diatoms, and cyanobacteria because of their hazardous impact on photosynthesis and growth (Joonas et al., 2019). In one of the studies done by Aruoja et al. (2009), it was stated that the toxicity of CuO nanoparticles on the algae *Pseduokirchneriella subcapitata* is utilized for metal oxide formulation as a control. It was seen that at concentration EC50 = 0.71 mg Cu/L, CuO NPs were more soluble and more toxic than the control at concentration EC50 = 11.55 mg Cu/L. The observations have shown that the toxicities in the bulk form and nano-sized CuO were mostly influenced by the soluble copper ions which were similar to the conclusions drawn by Griffitt et al. (2007). Studies on the specific mechanism of CuO NP toxicity in cells of blue-green algae are still lacking (Mahana et al., 2020).

4.2 Toxicity of copper to rice plants growth

The previous section focuses on the toxicity of copper-related agrochemicals on rice plants and the present section focuses on the direct toxicity of copper-related agrochemicals on rice plants and presents information from published studies. The review indicates that CuO NPs affect the growth of rice plants and their seedlings. For example, one study reported that the CuO NPs significantly suppressed the growth rate of seedlings of rice plants as compared to the control in 7 days of exposure to 62.5, 125, and 250 mg/L under hydroponic conditions. Apart from that, physiological indexes, which are indicators of membrane damage due to antioxidants as well as antioxidant enzyme activity, can be estimated (Yang et al., 2020). CuO nanoparticles are reported to exhibit phytotoxicity by causing a various range of physiological effects, which are likely to have different toxic effects on different plants at different target concentrations. NPs have shown changes in the plants physiologically as well as physiochemically (Tarrahi et al., 2021). In the two studies, CuO nanoparticles were shown to inhibit the growth of maize at the concentration of 500 mg/L, whereas CuO NPs have a concentration less than 10 mg/L inhibited the biomass accumulation in the cotton plant. A negative influence of CuO nanoparticles has been found on the plants such as *Pisum sativum, Schoenoplectus tabernaemontani, Landoltia punctate*, *H. vulgare,* and *O. sativa* (rice) (Nair and Chung, 2014; Shaw and Hossain, 2013; Shaw et al., 2014). CuO NPs also inhibit the elongation of the root of freshly germinated maize as well as rice seedlings. The germination rate, root elongation, and accumulation of biomass are used to assess the phytotoxicity of CuO nanoparticles. Shaw and Hossain (2013) reported that CuO nanoparticles having concentration less than 50 nm have capability to reduce the germination of rice seedlings and the viability of root cells but have potential to increase H_2O_2 and malondialdehyde (MDA) levels as well as ascorbate peroxidase (APX) and glutathione reductase activities. Also, CuO NPs when they are present at a concentration as high as 1 g/L, have the potential to decrease the rate of photosynthesis, as well as the rate of transpiration along with

the photosynthetic pigment content and usually increase the content of MDA along with the proline in rice. Shi et al. (2017) report that in *Landoltia punctata* the CuO nanoparticles suspension can release up to 0.16 mg/L of Cu^{2+} ions which is insufficient to lead to the phytotoxicity of CuO NPs. In the study conducted by Zhang et al. (2014), it was found that the growth of *Schoenoplectus tabernaemontani* will not be affected by the concentration of 0.06 mg/L CuO NPs suspension.

Copper nanoparticles are considered to decrease the activity of PS II (photosystem II) due to the generation of ROS (Thit et al., 2017). Also, in conditions such as waterlogged in paddy fields or rice fields, it may influence nanoparticles accumulation, translocation mobility, dissolution, and bioavailability along with the transformation of nanoparticles. Peng et al. (2015) in their study observed the bioavailability along with the speciation of CuO nanoparticles in the paddy soil and also the transformation was found in the soil-rice system in the presence of CuO-NPs.

One of the studies has shown that the CuO nanoparticles have effectively decreased the redox potential in the soil along with that it has said that during the maturation phase of paddy soil it increases or alters the electrical conductivity. The bioavailability of CuO nanoparticles has shown a decreasing trend while there is rice growth, but also there was an increase in the cycles of drying-wetting. According to the studies, copper which is present in the root, plant leaves, as well as shoot of the plant was in the form of copper-citrate. It was observed that about one-third of the Cu (II) was transformed to Cu(I)-cysteine. Also, in the roots, it was about 15.7% found as Cu_2O and in the shoot section, it was 19% as Cu(I)-acetate. In chaff, it was found that about 30% of Cu in the form of Cu-citrate or Cu(I)-acetate but it was observed that in the polished phase of rice no CuO was reported. In one of the studies, it was found that in the rice grains copper was present in higher content in the form of copper and also there was the presence of sulfur (Cui et al., 2019). It was also found that sulfur fertilizers decrease the content of copper in the root along with the leaf of the rice plant. It was found that there was a higher biomass yield from the husk but also there was a presence of the high amount of copper in the form of copper-cysteine or copper-acetate in the rice grains. Therefore, it can be stated that the copper-based nanoparticles biotransformation mechanism consists of the combination of chemical and biochemical reactions including the soil components and living organisms.

The rice leaves when exposed to very high concentrations of CuO nanoparticles, turned to yellow gradually. There is a decrease in the content of chlorophyll when rice plants were exposed to CuO NPs. Also, photosynthesis in the seedlings of rice was found to be constrained as well as the growth of the plant was found to be inhibited.

According to the study by Zhou et al. (2021), it was found that polystyrene NPs can alter the growth of the roots of rice plants and give abiotic stress to the plant. It was found that the SOD activity was much higher in the rice roots when they are exposed to the concentration of CuO NPs (125 mg/L). In one of the studies done by Da Costa and Sharma (2016), it was found that the CuO NPs were accumulated inside the roots and leaf cells, especially the accumulation was seen in the chloroplast. In the content of Cu, there was an increase of 5.5-fold in the whole leaves which are

said to be treated with the CuO NPs concentration of 1000 mg/L as compared to the control plants. The Cu content which was having an increase of 76-fold was also observed in the whole roots which were treated with the Cu concentration of 100 mg/L. Although it was found that when the concentration is highest, accumulation in the whole root tissue of copper was only 9.4-fold as compared to the control plant. There was also a negligible effect of copper oxide nanoparticles in the seed germination because of selective permeability which is present in the seed coat. This selective permeability is said to protect the embryo from the toxicity of CuO NPs, which restrict the entry of nanoparticles until the emergence of the radicles and contact with the NPs directly in the growth medium. Wierzbicka and Obidzinska (1998) also reported the selective permeability of the metal NPs. In the same study, it was found that there was no significant change in the MDA content which indicated the absence of lipid peroxidation of cell membrane which can be a result of CuO NP treatment. Inside the leaves, the increment in the accumulation of the ascorbate suggested that there will be an oxidative response to the CuO NP treatment in the plants. The increased expression of APX and SOD (antioxidant enzymes), at the concentration of 10 and 100 mg/L of CuO nanoparticles indicated a process of protectiveness against the occurrence or development of oxidative stress in the plants. It has been stated that CuO NPs lowers the production of shoot biomass because of the accumulation due to dose-dependency in the grains (Martínez et al., 2021).

Uptake of CuO nanoparticles causes thylakoids per granum disruption when present or exposed to the 50 mg/L concentration with structural damage stronger as well as swelling on the exposure to the higher concentrations. Also, there was a decrease in the size as well as in the number of stomata but there was a significant increase in the size as well as in the number of trichomes. The evidence which were found suggested a mechanism of exclusion for CuO NPs at a root level, which ultimately leads to the reducing toxicity in shoots. Also, it was found that there was a prominent decline in the net CO_2 fixation, in quantum efficiency of PSII (Fv/Fm) along with the increased level of oxidative as well as the osmotic stress, and the higher expression or release of antioxidants such as APX and SOD.

In a study by Shaw and Hossain (2013), it was found that in comparison to control (91.6%) there was a significant reduction in the rate of germination with the increment in the concentration of CuO nanoparticles (with 0.5 mM CuO NP concentration having 78.6%, 1.0 mM having 75.6%, and 1.5 mM was having 71.6%). Also, it was observed that there was a significant decline in the seedling growth when treated with CuO NPs. Also, it was observed that the presence of CuO NPs enhanced the proline level in comparison to the control (No CuO NPs). The study also indicated that a higher concentration of nano-CuO than 0.5 mM was found to be very toxic for the growth of the seedling of the rice and their development. In the study done by Wu et al. (2012), the test was conducted to check the biological effects of various NPs of metal oxides, it was observed that the germination of the rice seedlings was severely affected in the presence of CuO NPs in the seeds of plants which include lettuce, radish, and cucumber seeds. Also, the significant increment in the activity of antioxidant enzymes of the ascorbate glutathione cycle under the nano-CuO stress is said to be a

significant indication of an increment in the ROS production along with the instant activation of the defence mechanism of the rice plant to combat the loss which is caused by the oxidative stress. In vivo detection of superoxides as well as of H_2O_2 as dark blue and deep brown spots in the leaves indicated the severe oxidative burst under the stress condition caused by nano-copper. It is now well known that the elevation in the levels of the antioxidant enzyme could be very much possibly associated with the mechanism of the plant stress tolerance (Gossett et al., 1994; Hernhdeza et al., 1995). Also, it was found that the high APX activity will be not sufficient to kill all the H_2O_2 produced in huge amounts under the stress condition caused by the CuO NPs. Also, there was a significant loss in the DHAR activity which supposedly renders the stressed cells in the futile recycling of antioxidant metabolites. Even the increase in the GSH/GSSG ratio will not be useful to prevent the cells from oxidative damages. There was also a decline in carotenoid production when the rice plants are under the stress of CuO NPs. Hossain et al. (2015) in their study stated that the treatment of the rice plant with CuO NPs has led to an increment in the enzyme antioxidant activity and it was found that it will also increase the MDA concentration. The CuO nanoparticles (NPs) modulate the performance of photosynthesis along with the antioxidative defence system which has demonstrated the restriction in root as well as in the growth of shoot with the reduction in the photosynthetic performance index in *H. vulgare* (Shaw et al., 2014). CuO nanoparticles are found to mediate the DNA damage along with the restriction of plant growth in *Raphanus sativus*, *Lolium perenne*, and *Lolium rigidum* (Atha et al., 2012). According to the study done by Singh et al. (2017), it was found that the CuO nanoparticles exposure has resulted in a very significant reduction in the chlorophyll pigment along with the sugar content of the plants. Also, CuO nanoparticles exposure has led to excess lipid peroxidation and SOD activity with the increment in the concentration of CuO nanoparticles in the plants.

Also, from the conclusion drawn by the various studies in the past, it can be stated that CuO nanoparticles were also able to make changes in the behavior of the network organization and mechanism of the stability of the PSII complex and affect the proper functioning of the photosynthetic organism such as blue-green algae. But due to the lack of studies in this direction, the proper mechanism of providing toxicity by CuO NPs to the BGA and other plants are still unclear.

4.3 Effect of toxicity of CuO NPs to algae on nitrogen fixation ability of algae

From the past studies, it can be concluded that most of the effects of nanoparticles on the cells which are living related to the generation of free radicals. These radicals lead to the damage of lipid as well as the damage of the cell membrane which also includes the death of the cell or the death of the organism (Garcia et al., 2014). Nitrogen is known to be the element that is present in the amplest form, and some metalloenzymes are necessary for the fixation of nitrogen. As the fixation of the nitrogen is dependent on the functional apparatus of the photosynthesis, which can

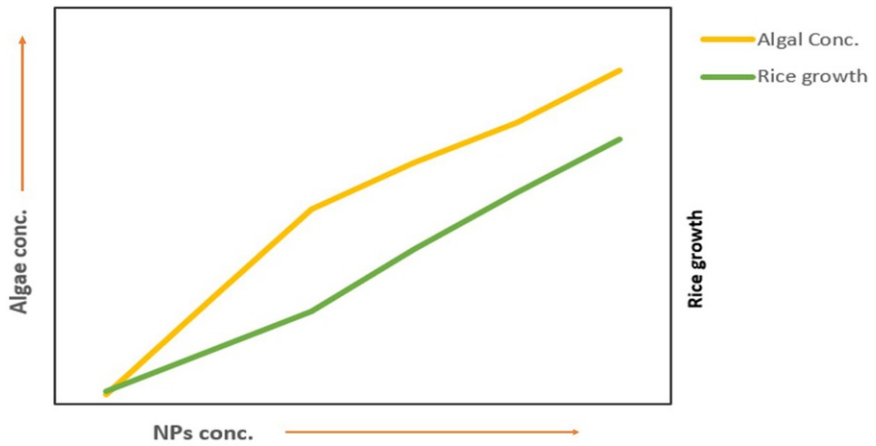

FIG. 5

Schematic representation showing the predicted rice growth and algal concentration in the presence of CuO NPs at different concentrations (theoretical only).

be sensitive to copper, such as *Calothrix elenkinii* is strongly influenced by the CuO nanoparticles. In one of the studies, an interesting observation was found that the acetylene reduction activity was also stimulated at all the different concentrations of CuO nanoparticles, with the period of optimum incubation. Copper (Cu) also has an important role in the respiratory proteins functioning which is required for the fixation of nitrogen (Delgado et al., 1998).

The rice plant fertility of the fields depends not only on the surface which is colonizing or having floating blue-green algae (BGA) and Azolla but also on the interactions of blue-green algae with the microflora directly as well as indirectly in the below-surface soil environment.

In Fig. 5, from all the previous data collected, it was found that when the NPs concentration is as low as 0.1 mg/L the algal concentration (Cyanobacteria), rice growth is not altered much whereas when the NPs concentration is as high as 1000 μg/L then there is a significant change in the concentration of algal and rice growth. The higher the NPs concentration, the higher will be the toxicity to the cyanobacterial growth and rice growth which can be investigated from the previous studies. So, the long-term dose-response curve is important to evaluate the toxicity and its mechanism to safeguard the rice plant from getting toxicity.

5 Summary and conclusions

This study focused on the interaction and toxicity of CuO NPs on blue-green algae (cyanobacteria) as well as their effect on rice plant growth. It was found that the presence of NPs in the soil and water environment will alter the rice plant growth

and alter its photosystem. Since cyanobacteria will also be affected by the toxicity of CuO NPs, there will be an alteration in their nitrogen fixation efficiency, which will ultimately affect the yield of rice. There are very few studies till date about the toxicity of NPs in plants, but there is no study about their interaction with plants and cyanobacteria. There is a need to understand the mechanism of toxicity and how it can be reduced so that the farmers can be benefitted by using nanoagrochemicals even if the soil and environment have NPs. This study will be helpful for scientists to study the growth of rice plants in the presence of NPs and blue-green algae and for agriculturists to know how to use nanoagrochemicals for plant growth and to study cyanobacteria for their agricultural studies. This chapter will be a link to agriculturists, farmers, and scientists.

The current toxicity studies which are related to the interactions with algae do not use realistic and environmentally relevant conditions and thus findings of these studies cannot be used to understand the effect of nanoparticles on algae and subsequently on lipid production. The constituents of water such as ions, humic acid, pH, solids affect the interaction of nanoparticles with algae and thus, these factors need to be explicitly considered in the understanding effect of nanoparticles and other emerging contaminants on algae and subsequently on lipid production. There is a lack of data to address the mixture toxicity issue in the realistic scenario as well as the impact of nanoparticles in lipid and energy production. More work is required in this direction for properly understanding the implications of emerging contaminants on algal-related energy production.

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References

Abd-Alla, M.H., Mahmoud, A.L.E., Issa, A.A., 1994. Cyanobacterial biofertilizer improved growth of wheat. Phyton 34 (1), 11–18.

Adeleye, A.S., Conway, J.R., Garner, K., Huang, Y., Yiming, S., Keller, A.A., 2016. Engineered nanomaterials for water treatment and remediation: costs, benefits, and applicability. Chem. Eng. J. 286, 640–662.

Adochite, C., Andronic, L., 2021. Aquatic toxicity of photocatalyst nanoparticles to green microalgae *Chlorella vulgaris*. Water 13 (1), 77.

Akintelu, S.A., Folorunso, A.S., Folorunso, F.A., Oyebamiji, A.K., 2020. Green synthesis of copper oxide nanoparticles for biomedical application and environmental remediation. Heliyon 6 (7), e04508.

Apte, S.K., 1987. Relationship between sodium influx and salt tolerance of nitrogen fixing cyanobacteria. Appl. Environ. Microbiol. 53 (8), 1934–1939.

Apte, S.K., Thomas, J., 1984. Sodium transport in filamentous nitrogen-fixing cyanobacteria. J. Biosci. 5, 225–234.

Aruoja, V., Dubourguier, H.-C., Kasemets, K., Kharu, A., 2009. Toxicity of nanoparticles of CuO, ZnO and TiO_2 to microalgae *Pseudokirchneriella subcapitata* Aruoja. Sci. Total Environ. 407 (4), 1461–1468.

Atha, D.H., Wang, H., Petersen, E.J., Cleveland, D., Holbrook, R.D., Jaruga, P., Dizdaroglu, M., Xing, B., Nelson, B.C., 2012. Copper oxide nanoparticle mediated DNA damage in terrestrial plant models. Environ. Sci. Technol. 46 (3), 1819–1827.

Blumbald, E., 1983. Studies of osmoregultion in salt adaptation of cyanobacteria with ESR spin probe techniques. Proc. Natl. Acad. Sci. U. S. A. 80, 2599–2602.

Blumwald, E., Tel-Or, E., 1984. Salt adaptation of the cyanobacterium *Synechococcus* growing in a continuous culture (Turbidostat). Plant Physiol. 74, 183–185.

Braz-Mota, S., Campos, D.F., MacCormack, T.J., Duarte, R.M., Val, A.L., Almeida-Val, V.M.F., 2018. Mechanisms of toxic action of copper and copper nanoparticles in two Amazon fish species: Dwarf cichlid (*Apistogramma agassizii*) and cardinal tetra (*Paracheirodon axelrodi*). Sci. Total Environ. 630, 1168–1180.

Chakdar, H., Jadhav, S.D., Dhar, D.W., Pabbi, S., 2012. Potential applications of blue-green algae. J. Sci. Ind. Res. 71, 13–20.

Chaudhary, R., Nawaz, K., Khan, A.K., Hano, C., Abbasi, B.H., Anjum, S., 2020. An overview of the algae-mediated biosynthesis of nanoparticles and their biomedical applications. Biomol. Ther. 10 (11), 1498.

Choudhury, A.T.M.A., Kennedy, I.R., 2004. Prospects and potentials for systems of biological nitrogen fixation in sustainable rice production. Biol. Fertil. Soils 39, 219–227.

Craig, J.D., Gabrielle, C.N., Davies, G.-L., Christie-Oleza, J.A., 2020. Mechanisms of silver nanoparticle toxicity on the marine cyanobacterium *Prochlorococcus* under environmentally relevant conditions. Sci. Total Environ. 747, 141229.

Cui, J.-L., Zhao, Y.-P., Lu, Y.-J., Chan, T.-S., Zhang, L.L., Tsang, D.CW., Li, X.D., 2019. Distribution and speciation of copper in rice (*Oryza sativa* L.) from mining-impacted paddy soil: implications for copper uptake mechanisms. Environ. Int. 126, 717–726.

Da Costa, M.V.J., Sharma, P.K., 2016. Effect of copper oxide nanoparticles on growth, morphology, photosynthesis, and antioxidant response in *Oryza sativa*. Photosynthetica 54 (1), 110–119.

Delgado, A., Anselmo, A., Novais, J., 1998. Heavy metal biosorption by dried powdered mycelium of *Fusarium flocciferum*. Water Environ. Res. 70, 370–375.

El-Enany, A.E., Issa, A.A., 2000. Cyanobacteria as a biosorbent of heavy metals in sewage water. Environ. Toxicol. Pharmacol. 8 (2), 95–101.

Fazelian, N., Movafeghi, A., Yousefzadi, M., Rahimzadeh, M., Zarei, M., 2020. Impact of silver nanoparticles on the growth, fatty acid profile, and antioxidative response of *Nannochloropsis oculata*. Acta Physiol. Plant. 42 (7), 1–14.

Fleming, H., Haselkorn, R., 1974. The program of protein synthesis during heterocyst differentiation in nitrogen-fixing blue-green algae. Cell 3 (2), 159–170.

Fogg, G.E., 1973. The Blue-Green Algae. Academic, London.

Garcia, N., Fu, F., Sedwick, P., et al., 2014. Iron deficiency increases growth and nitrogen-fixation rates of phosphorus-deficient marine cyanobacteria. ISME J. 9, 238–245.

Gossett, D.R., Millhollon, E.P., Lucas, M.C., 1994. Antioxidant response to NaCl stress in salt-tolerant and salt-sensitive cultivars of cotton. Crop. Sci. 34 (3), 706–714.

Griffitt, R.J., Weil, R., Hyndman, K.A., Denslow, N.D., Powers, K., Taylor, D., Barber, D.S., 2007. Exposure to copper nanoparticles causes gill injury and acute lethality in zebrafish (*Danio rerio*). Environ. Sci. Technol. 41 (23), 8178–8186.

Grillo, R., Rosa, A.H., Fraceto, L.F., 2014. Poly (ε-caprolactone) nano capsules carrying the herbicide atrazine: effect of chitosan-coating agent on physico-chemical stability and herbicide release profile. Int. J. Environ. Sci. Technol. 11 (6), 1691–1700.

Hamida, R.S., Ali, M.A., Redhwan, A., Bin-Meferij, M.M., 2020. Cyanobacteria–a promising platform in green nanotechnology: a review on nanoparticles fabrication and their prospective applications. Int. J. Nanomedicine 15, 6033.

Hernhdeza, J.A., Olmosa, E., Corpasb, F.J., Sevilla, F., de1 Riob, L.A., 1995. Salt-induced oxidative stress in chloroplasts of pea plants. Plant Sci. J. 105 (151167), 04047–04048.

Hossain, Z., Mustafa, G., Komatsu, S., 2015. Plant responses to nanoparticle stress. Int. J. Mol. Sci. 16 (11), 26644–26653.

Huang, C.-C., Aronstam, R.S., Chen, D.-R., Huang, Y.-W., 2010. Oxidative stress, calcium homeostasis, and altered gene expression in human lung epithelial cells exposed to ZnO nanoparticles. Toxicol. In Vitro 24 (1), 45–55.

Issa, A.A., Abd-Alla, M.H., Ohyama, T., 2014. Nitrogen fixing cyanobacteria: future prospect. In: Advances in Biology and Ecology of Nitrogen Fixation.

Jampílek, J., Kráľová, K., 2015. Application of nanotechnology in agriculture and food industry, its prospects and risks. Ecol. Chem. Eng. 22 (3), 321–361.

Janani, B., Al Farraj, D.A., Raju, L.L., Elshikh, M.S., Alkubaisi, N.A., Thomas, A.M., Das, A., Khan, S.S., 2020. Cytotoxicological evaluation of copper oxide nanoparticles on green algae, bacteria and crustacean systems. J. Environ. Health Sci. Eng. 18 (2), 1465–1472.

Joonas, E., Aruoja, V., Olli, K., Kahru, A., 2019. Environmental safety data on CuO and TiO_2 nanoparticles for multiple algal species in natural water: filling the data gaps for risk assessment. Sci. Total Environ. 647, 973–980.

Kamat, J.P., Devasagayam, T.P.A., Priyadarsini, K.I., Mohan, H., 2002. Reactive oxygen species mediated membrane damage induced by fullerene derivatives and its possible biological implications. Toxicology 155 (1–3), 55–61.

Kaushik, B.D., 1994. Algalization of rice in salt-affected soils. Ann. Agric. Res. 14, 105–106.

Kaushik, M.S., Kumar, A., Abraham, G., Dash, N.P., Singh, P.K., 2019. Field evaluations of agrochemical toxicity to cyanobacteria in rice field ecosystem: a review. J. Appl. Phycol. 31, 471–489.

Kaushik, B.D., Subhashini, D., 1985. Amelioration of salt affected soils with blue green algae II. Improvement in soil properties. Proc. Indian Natl. Sci. Acad. B51, 386–389.

Khanna, P., Kaur, A., Goyal, D., 2019. Algae-based metallic nanoparticles: synthesis, characterization and applications. J. Microbiol. Methods 163, 105656.

Kulasooriya, S., 1998. Cyanobacteria and *Azolla* as biofertilizer for rice. Cyanobacterial Biotechnology. Oxford Publishers and IBH.

Kumar, S., et al., 2014. Synthesis, characterization and on field evaluation of pesticide loaded sodium alginate nanoparticles. Carbohydr. Polym. 101, 1061–1067.

Laurent, S., Forge, D., Port, M., Robic, A., Vander Elst, L., Muller, R.N., 2008. Magnetic iron oxide nanoparticles: synthesis, stabilization, vectorization, physicochemical characterizations, and biological applications. Chem. Rev. 108 (6), 2064–2110.

Lee, W.M., An, Y.J., Yoon, H., Kweon, H.S., 2008. Toxicity and bioavailability of copper nanoparticles to the terrestrial plants mung bean (*Phaseolus radiatus*) and wheat (*Triticum aestivum*): plant agar test for water-insoluble nanoparticles. Environ. Toxicol. Chem. 27 (9), 1915–1921.

Lee, K.K., Watanabe, I., 1977. Problems of the acetylene reduction technique applied to water-saturated paddy soils. Appl. Environ. Microbiol. 34 (6), 654–660.

Mackay, M.A., 1983. Marine blue-green algae have a unique osmoregulatory system. Mar. Biol. 73, 301–307.
Mahana, A., Guliy, O.I., Mehta, S.K., 2020. Accumulation and cellular toxicity of engineered metallic nanoparticle in freshwater microalgae: current status and future challenges. Ecotoxicol. Environ. Saf. 208, 111662.
Martínez, G., Merinero, M., Pérez-Aranda, M., Pérez-Soriano, E.M., Ortiz, T., Begines, B., Alcudia, A., 2021. Environmental impact of nanoparticles' application as an emerging technology: a review. Materials 14 (1), 166.
Maruyama, C.R., Guilger, M., Pascoli, M., Bileshy-José, N., Abhilash, P.C., Fraceto, L.F., de Lima, R., 2016. Nanoparticles based on chitosan as carriers for the combined herbicides imazapic and imazapyr. Sci. Rep. 6, 19768.
Mason, J., 2003. Sustainable Agriculture. Landlinks Press.
Meena, R., 2020. Impact of agrochemicals on soil microbiota and management: a review. Land 9 (2), 34.
Melegari, S.P., Perreault, F., Costa, R.H.R., Popovic, R., Matias, W.G., 2013. Evaluation of toxicity and oxidative stress induced by copper oxide nanoparticles in the green alga *Chlamydomonas reinhardtii*. Aquat. Toxicol. 142, 431–440.
Memarizadeh, N., Ghadamyari, M., Adeli, M., Talebi, K., 2014. Preparation, characterization and efficiency of nanoencapsulated imidacloprid under laboratory conditions. Ecotoxicol. Environ. Saf. 107, 77–83.
Miller, D.M., et al., 1976. Ion metabolism in a halophilic blue-green alga, *Aphanothece halophytica*. Arch. Microbiol. 111, 145–149.
Mishra, A.K., Kaushik, M.S., Tiwari, D.N., 2019. Nitrogenase and hydrogenase: enzymes for nitrogen fixation and hydrogen production in cyanobacteria. Cyanobacteria. Academic Press.
Nagajyoti, P.C., Lee, K.D., Sreekanth, T.V.M., 2010. Heavy metals, occurrence, and toxicity for plants: a review. Environ. Chem. Lett. 8 (3), 199–216.
Nair, P.M.G., Chung, I.M., 2014. Impact of copper oxide nanoparticles exposure on Arabidopsis thaliana growth, root system development, root lignificaion, and molecular level changes. Environ. Sci. Pollut. Res. 21 (22), 12709–12722.
Nekrasova, G.F., Ushakova, O.S., Ermakov, A.E., Uimin, M.A., Byzov, I.V., 2011. Effects of copper (II) ions and copper oxide nanoparticles on *Elodea densa Planch*. Russ. J. Ecol. 42 (6), 458.
Nguyen, N.H., Padil, V.V.T., Slaveykova, V.I., Černík, M., Ševců, A., 2018. Green synthesis of metal and metal oxide nanoparticles and their effect on the unicellular alga *Chlamydomonas reinhardtii*. Nanoscale Res. Lett. 13 (1), 1–13.
Ojha, N.K., Zyryanov, G.V., Majee, A., Charushin, V.N., Chupakhin, O.N., Santra, S., 2017. Copper nanoparticles as inexpensive and efficient catalyst: a valuable contribution in organic synthesis. Coord. Chem. Rev. 353, 1–57.
Pabby, A., Prasanna, A., Nayak, S., Singh, P.K., 2003. Physiological characterization of the cultured and freshly isolated endosymbionts from different species of Azolla. Plant Physiol. Biochem. 41 (1), 73–79.
Pandhal, J., 2008. A cross-species quantitative proteiomic study of salt adaptation in a halotolerant environmental isolate using 15N metabolic labelling. J. Proteomics 8, 2266–2284.
Peng, H., Qi, W., Li, S., Ji, W., 2015. Modeling the phase stability of Janus, core-shell, and alloyed Ag-Cu and Ag-Au nanoparticles. J. Phys. Chem. C 119 (4), 2186–2195.
Perrault, F., Oukarroum, A., Melegari, S.P., Matias, W.G., Popovic, R., 2012. Polymer coating of copper oxide nanoparticles increases nanoparticles uptake and toxicity in the green alga *Chlamydomonas reinhardtii*. Chemosphere 87 (11), 1388–1394.

Perreault, F., Samadani, M., Dewez, D., 2014. Effect of soluble copper released from copper oxide nanoparticles solubilisation on growth and photosynthetic processes of *Lemna gibba* L. Nanotoxicology 8 (4), 374–382.

Prasad, R., Bhattacharya, A., Nguyen, Q.D., 2017. Nanotechnology in sustainable agriculture: recent developments, challenges, and perspectives. Front. Microbiol. 8, 1014.

Prasad, R., Kumar, V., Prasad, K.S., 2014. Nanotechnology in sustainable agriculture: present concerns and future aspects. Afr. J. Biotechnol. 13 (6), 705–713.

Prasanna, R., Nayak, S., 2007. Influence of diverse rice soil ecologies on cyanobacterial diversity and abundance. Wetl. Ecol. Manag. 15, 127–134.

Raikova, O.P., Panichkin, L.A., Raikova, N.N., 2006. Studies on the effect of ultrafine metal powders produced by different methods on plant growth and development. Nanotechnologies and information technologies in the 21st century. In: Proc. Int. Sci. Prac. Con, pp. 108–111.

Rajput, V., Minkina, T., Fedorenko, A., Sushkova, S., Mandzhieva, S., Lysenko, V., Duplii, N., Fedorenko, G., Dvadnenko, K., Ghazaryan, K., 2018. Toxicity of copper oxide nanoparticles on spring barley (*Hordeum sativum* distichum). Sci. Total Environ. 645, 1103–1113.

Reed, R.H., 1984. Osmotic adjustment in cyanobacteria from hypersaline environments. Arch. Microbiol. 138, 333–337.

Reed, R.H., Stewart, W.D.P., 1985. Evidence for turgor sensitive K+ influx in cyanobacteria *Anabaena variabilis* ATCC 29413 and *Synechocystis* PCC 6714. Biochim. Biophys. Acta 812, 155–162.

Seleiman, M.F., Almutairi, K.F., Alotaibi, M., Shami, A., Alhammad, B.A., Battaglia, M.L., 2021. Nano-fertilization as an emerging fertilization technique: why can modern agriculture benefit from its use. Plan. Theory 10 (1), 2.

Selivanov, V.N., Zorin, E.V., 2001. Sustained action of ultrafine metal powders on seeds of grain crops. Perspekt. Materialy 4, 66–69.

Shaw, A.K., Hossain, Z., 2013. Impact of nano-CuO stress on rice (*Oryza sativa L.*) seedlings. Chemosphere 93 (6), 906–915.

Shaw, A.K., Ghosh, S., Kalaji, H.M., Bosa, K., Brestic, M., Zivcak, M., Hossain, Z., 2014. Nano-CuO stress-induced modulation of antioxidative defense and photosynthetic performance of Syrian barley (*Hordeum vulgare* L.). Environ. Exp. Bot. 102, 37–47.

Shi, Y., Jiang, R., Liu, M., Fu, L., Zeng, G., Wan, Q., Mao, L., Deng, F., Zhang, X., Wei, Y., 2017. Facile synthesis of polymeric fluorescent organic nanoparticles based on the self-polymerization of dopamine for biological imaging. Mater. Sci. Eng. C 77, 972–977.

Singh, S., 2014a. A review on possible elicitor molecules of cyanobacteria: their role in improving plant growth and providing tolerance against biotic or abiotic stress. J. Appl. Microbiol. 117, 1221–1244.

Singh, J.S., 2014b. Cyanobacteria: a vital bio-agent in eco-restoration of degraded lands and sustainable agriculture. Clim. Change Environ. Sustain. 2 (2), 133–137.

Singh, P.K., Bisoyi, R.N., 1989. Blue-green algae in rice fields. Phykos 28, 181–195. Cyanobacterial Biofertilizers 457 for Rice.

Singh, H., Khattar, J.I.S., Ahluwalia, A.S., 2011. Cyanobacteria and agricultural crops. Vegetos 27 (1), 37.

Singh, A., Singh, N.B., Hussain, I., Singh, H., 2017. Effect of biologically synthesized copper oxide nanoparticles on metabolism and antioxidant activity to the crop plants *Solanum lycopersicum* and *Brassica oleracea* var. botrytis. J. Biotechnol. 262, 11–27.

Singh, J.S., Strong, P.J., 2016. Biologically derived fertilizer: a multifaceted bio-tool in methane mitigation. Ecotoxicol. Environ. Safety 124, 267–276.

Song, G., Hou, W., Gao, Y., Wang, Y., Lin, L., Zhang, Z., Mu, L., Ma, R., Niu, Q., Wang, H., 2016. Effects of CuO nanoparticles on *Lemna minor*. Bot. Stud. 57 (1), 3.

Subhashini, D., Kaushik, B.D., 1981. Amelioration of sodic soils with blue-green algae. Soil Res. 19 (3), 361–366.

Tarrahi, R., Mahjouri, S., Khataee, A., 2021. A review on in vivo and in vitro nanotoxicological studies in plants: a headlight for future targets. Ecotoxicol. Environ. Saf. 208, 111697.

Thit, A., Skjolding, L.M., Selck, H., Sturve, J., 2017. Effects of copper oxide nanoparticles and copper ions to zebrafish (*Danio rerio*) cells, embryos and fry. Toxicol. In Vitro 45, 89–100.

Thomas, J., Apte, S.K., 1984. Sodium requirement and metabolism in nitrogen-fixing cyanobacteria. J. Biosci. 6, 771–794.

Whitton, B.A., 2000. Soil and rice fields. The Ecology of Cyanobacteria. Kluwer.

Whitton, B.A., 2006. Soils and rice fields. In: Whitton, B.A., Potts, M. (Eds.), The Ecology of Cyanobacteria: Their Diversity in Time and Space. Kluwer Academic, Netherlands, pp. 233–255.

Wierzbicka, M., Obidzinska, J., 1998. The effect of lead on seed imbibition and germination in different plant species. Plant Sci. 137 (2), 155–171.

Wu, S.G., Huang, L., Head, J., Chen, D.R., Kong, I.C., Tang, Y.J., 2012. Phytotoxicity of metal oxide nanoparticles is related to both dissolved metals ions and adsorption of particles on seed surfaces. J. Pet. Environ. Biotechnol. 3 (4), 126.

Yang, H., Su, Z., Meng, X., Zhang, X., Kennedy, J.F., Liu, B., 2020. Fabrication and characterization of Pickering emulsion stabilized by soy protein isolate-chitosan nanoparticles. Carbohydr. Polym. 247, 116712.

Yruela, I., 2009. Copper in plants: acquisition, transport and interactions. Funct. Plant Biol. 36, 409–430.

Zhang, D., Hua, T., Xiao, F., Chen, C., Gersberg, R.M., Liu, Y., Ng, W.J., Tan, S.K., 2014. Uptake and accumulation of CuO nanoparticles and CdS/ZnS quantum dot nanoparticles by *Schoenoplectus tabernaemontani* in hydroponic mesocosms. Ecol. Eng. 70, 114–123.

Zhou, C.Q., Lu, C.H., Mai, L., Bao, L.J., Liu, L.Y., Zeng, E.Y., 2021. Response of rice (*Oryza sativa* L.) roots to nanoplastic treatment at seedling stage. J. Hazard. Mater. 401, 123412.

Chang, Y.-N., Zhang, M., Xia, L., Zhang, J., Xing, G., 2012. The toxic effects and mechanisms of CuO and ZnO nanoparticles. Materials 5 (12), 2850–2871.

Sun, C., et al., 2014. Encapsulation and controlled release of hydrophilic pesticide in shell cross-linked nanocapsules containing aqueous core. Int. J. Pharm. 463 (1), 108–114.

Zhao, J., et al., 2016. Interactions of CuO nanoparticles with the algae *Chlorella pyrenoidosa*: adhesion, uptake, and toxicity. Nanotoxicology 10 (9), 1297–1305.

CHAPTER

Advances in the applications of copper-based nanocomposites in wastewater treatment

26

Iffat Zareen Ahmad

Department of Bioengineering, Integral University, Lucknow, Uttar Pradesh, India

1 Introduction

The whole world requires unpolluted and freshwater for various life processes. Around 1.2 billion people face scarcity of fresh drinking water, around 2.6 billion people lack sanitation, and millions of individuals lose their lives yearly because of communicable diseases due to polluted water (Montgomery and Elimelech, 2007; Shannon et al., 2008). With the increasing human population and related environmental deprivation, the paucity of hygienic and potable water will be a chief concern, which is expected to rise in the coming years. To address these problems, novel strategies of water treatment are required. According to the predictions, the global population will reach 9 billion by 2050 and around 75% will face shortages of clean water by 2075 (Tlili et al., 2006; Kargari and Shirazi, 2014).

Many strategies of water purification have been utilized, for instance, distillation, chemical disinfection, sand filtration, reverse osmosis (RO), and membrane filtration. Among these approaches, membrane filtration is a comparatively latest method and it has some benefits such as scalability, less power intake, free of chemicals, and less working temperature (Tlili et al., 2007).

Nanotechnology is the sunrise technology that can make long-lasting water quality better, to make it available and sustainable. Different types of membranes such as nanofiltration (NF), RO, microfiltration (MF), and ultrafiltration (UF) have been used for water refinement (Theron et al., 2008; Khan et al., 2018a, 2018b, 2018c, 2018d, 2018e).

Desalination is one of the most important alternatives for attaining clean and safe water sources. Though it is quite costly, membrane-based desalination methods could be considered as they ensure better desalination competency, particularly, RO is applied for 41% of methods (Humplik et al., 2011). Factors that regulate the desalination price include getting the most out of the water flux through a membrane to reduce the fouling. Latest advances in membrane filtration machinery have led to energy effectiveness in RO plants (Fritzmann et al., 2007). NF has also been used

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and assessed for marine water desalination (Mohsen et al., 2003). Chapter objectives aim to give an account of various membrane-based separation and purification techniques used in water desalination and elaborate overview of the uses of copper-based nanostructures for water treatments.

2 Membrane technologies for water treatment

The process of desalination splits saline water into two parts—one with low salt concentration which can be said as treated water, and the other which has a much higher concentration than the feed water, which is generally denoted as brine concentrate. The membrane-based technologies are applied throughout the world for desalination. It needs the energy to operate and produce freshwater. Membrane technologies are highly efficient and can be categorized into the following types:

2.1 Advance membrane

Membrane technology is a widely used technology for water purification. This technology is not only used in industries but also in municipal wastewater treatment. One of the advanced membrane techniques consists of a number of carbon nanotubes. The water flows effortlessly through carbon nanotubes. Membranes can transform poor impure water into pure water which is fit for drinking. But they have some disadvantages also, that is, using membrane techniques for water purification requires more energy as compared to other techniques. But these membranes can remove salts and organic compounds from water as these impurities cannot pass through the membrane which results in fouling. Low-pressure membranes are very powerful for particulate contaminants while high-pressure membranes are very dominant for the effective removal of both organic and inorganic impurities.

2.2 Forward osmosis

Forward osmosis (FO) is one of the examples of membrane process and is the sustainable alternative to RO. FO has many benefits as low hydraulic pressure is required for this process. This process requires low consumption of energy and hence it is cheaper and is economically and technically feasible. FO has many applications such as generation of power, water desalination, and food processing also. It is suitable for the rejection of moderate to high organic impurities. There is relatively low membrane fouling in FO as compared to pressure-driven processes. This method can allow high water flux and the rejection rate of dissolved contaminants is also very high. The major difference between RO and FO is that the RO requires energy-intensive hydraulic pressure for their operation while FO requires only osmotic pressure for their operation.

2.3 Electrodialysis

Electrodialysis (ED) is a membrane process that is driven by voltage. An electrical potential is developed which drives the salts through a membrane, separating freshwater. ED was introduced on a commercial scale in the 1960s, almost 10 years earlier to RO. Although ED was initially considered as a desalination technique for seawater, it has normally been applied to desalination saline water.

2.4 Electrodialysis reversal technique

The Electrodialysis Reversal (EDR) technique was given by Buros (2000). The unit of EDR works on a similar principle as an ED unit, the only difference is that the structure of both the product and concentrate channels is similar. At numerous breaks in an hour, the polarity of the electrodes is reversed, triggering attraction of ions in the opposite direction through the membranes. Instantly after the reversal, the clean water is removed and the lines are flushed out to restore preferred water quality. The reversal procedure is advantageous in the breakdown and flushing of scales, slimes, and other deposits in the cells preventing their accumulation. Flushing aids in minimizing the difficulty of membrane fouling.

2.5 Reverse osmosis (RO)

RO is a comparatively latest technique that was made commercial in the year 1970s (Buros, 2000). Presently, RO is the most extensively used technique for desalination. In the RO procedure pressure is applied as the driving force to push salted water through a semipermeable membrane into the water and concentrated saline stream separately. RO is used for the removal of sodium and chloride. The procedural details include the phenomenon of osmosis which causes water to move from a dilute solution to a concentrated solution through a semipermeable membrane. By applying pressure the water flows in the opposite direction through the semipermeable membrane, leaving the salt. This procedure is known as the Reverse Osmosis (RO) process (Fig. 1).

2.6 Nanofiltration

NF is a technique based on the membrane that is utilized for the separation of divalent ions of salt like calcium, magnesium, and sulfate. The initiation of NF as a water treatment method is believed to be an advancement for the desalination process. NF membranes can separate turbidity, hardness, fluoride, and nitrate as well as a substantial portion of soluble salts. Desalination can be carried out with considerably less operating pressure and has developed into a highly energy-saving process. The transport properties of NF membrane, their process prediction and modeling are very important (Diawara, 2008).

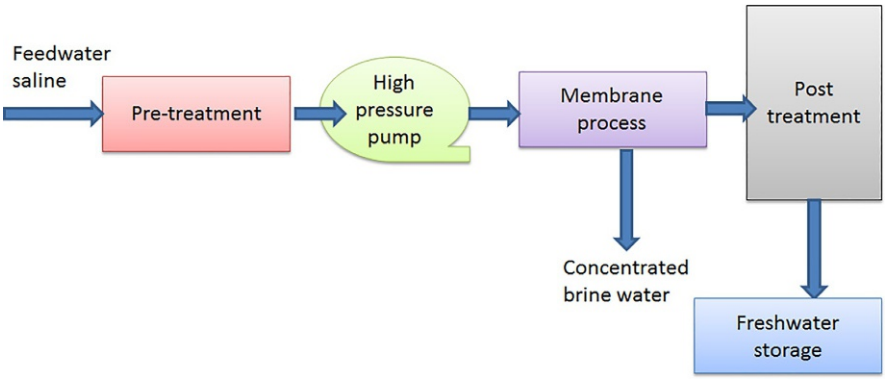

FIG. 1

The flowchart depicting the desalination of water by reverse osmosis process.

3 Advanced technologies of water desalination

The idea of freshwater production from brine water is not new, and for this purpose, new and advanced technologies with a variety of properties are emerging with time. These technologies arose on the basis of new contaminations found in water. In the earlier decades, only filtration and chlorination were sufficient for the desalination in municipal water treatment, but for the last 20 years, there is an extreme modification in the water desalination methodologies as currently there are different impurities found in water for which only chlorination and filtration is not able to purify the water. Here are some of the new emerging technologies for water desalination:

3.1 Microfluidic and nanofluidic concentration polarization technique

Concentration polarization occurs when there is a change in the concentration of a component in the boundary layer which is close to the surface of the membrane. In this system, multiple fluidic elements are linked in a series to identify substances present in a fluid. It is the process that arises in the junction of microfluidic and nanofluidic channels when an electric field is applied. The depletion layer is formed in this junction where charged particles repel each other. A larger nonporous membrane is more efficient in terms of energy used for water purification (Nandigana and Aluru, 2016).

3.2 Humidification and dehumidification water desalination

Humidification and dehumidification (HDH) water desalination is a thermal water purification technology that is based on nature's rain cycle. The main components used in this technology are (1) humidifier, (2) dehumidifier, and (3) heater. In the humidifier chamber, air is humidified in direct contact with saline water whereas in

the dehumidifier compartment moist air is in indirect contact with cold saline water. This method causes the condensation of water vapor to produce fresh drinking water. This technique is based on the first law of thermodynamics and there is a balance of mass and energy for the combined system. This technology is perfect for small-scale water desalination industries and it is very simple with low maintenance requirements. There are very less water vapors in the carrier gas and low energy recovery in this method. This process is simple but necessitates more research and development to increase its proficiency and performance (Elattar et al., 2020).

3.3 Microbial desalination cells

It is one of the recent techniques which produce electricity through the bioelectrochemical oxidation of organics present in wastewater. This technology eliminates the salinity of water and generates electric power from organic molecules and bacteria. The most significant factor of this technology is the speed of desalination which depends on the concentration of salt in the water. The process of desalination is also dependent on anode and cathode chambers. The electrons travel from anode to cathode through a wire which connects the two electrodes. The output of this technology can be increased by adding multiple ion exchange membranes between anode and cathode membranes. Another major concern in this method is the imbalance of pH. between the anode and cathode when there is more than one chamber between the electrodes (Al-Mamun et al., 2018).

4 Copper nanoparticles

Copper is characterized by high thermal and electrical conductivity as it is a ductile material belonging to a d-block element of the periodic table. The nanoparticles of copper with new properties are round and they look like a brown or black powder (Camacho-Flores et al., 2015). It has a very soft texture so has to amalgamate with other metals to form various alloys like that of brass (copper-zinc alloy) to be used in several applications. Copper nanoparticles are highly flammable and are known to be toxic for aquatic organisms.

4.1 Properties of copper NPS

(a) It has antimicrobial properties.
(b) It is used as a diet supplement.
(c) It is used to produce high strength metals and alloys.
(d) It is used as an efficient catalyst in several chemical reactions and for the synthesis of methanol and glycol.
(e) It is used as a sintering agent and in capacitor materials.
(f) It can also be used in conductive inks and pastes in place of expensive and expensive noble metals in different printed electronics, displays, etc.
(g) It is used as a lubricant additive for various nanometals.

5 Recent trends in water treatment using copper nanoparticles

Copper (Cu)-based nanomaterials have been deployed for the treatment of water as they have exhibited antibacterial and antifungal activities (Roberto Castro-Muñoz, 2020). They have also exhibited properties against viruses and algae (Ren et al., 2009; Varkey and Dlamini, 2012). The mechanism of its action possibly includes the interaction of Cu with the bacteria resulting in the production of reactive oxygen species (ROS), lipid peroxidation (LPO), protein oxidation and DNA degradation, resulting in the generation of superoxide anions (Tamayo et al., 2016). Further, $Cu^{2}+$ divalent ions may react with phosphorus or -SH groups present in biomolecules; they can act by disrupting biochemical processes, leading to the denaturation of protein (Ruparelia et al., 2008). Xu et al. (2012) and Xu et al. (2015) established the antimicrobial properties against *E. coli* by Cu NPs filled in PAN membranes. Xu et al. (2015) stated the use of cross-linked PAN-filled Cu(II) membranes to control the release of Cu^{2+}, which can be responsible for good antibacterial efficiency (Fig. 2).

Copper nanoparticles (CuNPs) were studied as a cheap alternative to the silver used in the case of paper filters for the purification of water. In this research study, the ecologically safe technique has been used for the direct in situ design of CuNPs in a paper by the reduction of adsorbed copper ions with ascorbic acid. It was a very

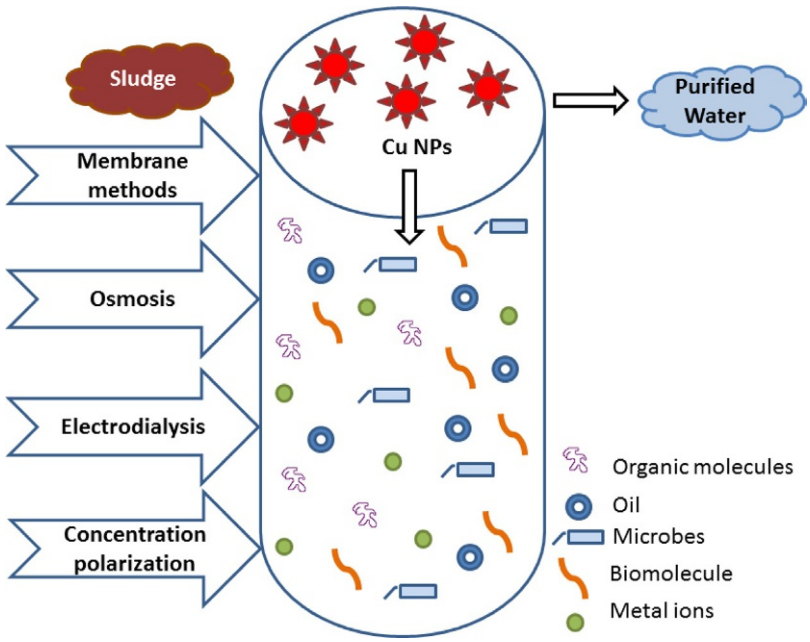

FIG. 2

Water purification techniques using copper nanoparticles.

quick method of copper nanoparticles synthesis. The characterization of paper sheets was done by x-ray diffraction (XRD), scanning electron microscopy (SEM), energy dispersive x-ray spectroscopy (EDX), and atomic absorption spectroscopy (AAS). The antibacterial property of the CuNP sheets was evaluated on *E. coli.* The effluent was evaluated for possible bacteria and the release of copper. The released copper in the treated water was less than the permissible limit for copper in potable water, that is, 1 ppm (Dankovich and Smith, 2014).

The nanosize has resulted in extraordinary features including better catalytic activity and adsorption efficiencies and high reactivity, therefore nanomaterials have been explored extensively for research and development purposes globally. Various studies have proved that nanomaterials can efficiently eliminate different contaminants from water and thus have been effectively applied in the treatment of water (Lu et al., 2016).

Biofouling might cause serious operational problems that can considerably damage membrane desalination methods. Of late, copper-based nanoparticles have been used as a potential antifouling agent in various membrane techniques owing to their high antimicrobial property and less price. Biocidal nanoparticles were coated on the surface of a thin-film composite RO membrane by using a novel and facile technique. The surface of the membrane was functionalized with CuNPs which made it applicable for RO desalination set up. The stacking of CuNPs on the membrane was confirmed by SEM imaging and X-ray photoelectron spectroscopy analysis, showing that the accumulated NPs comprised of copper element or copper oxide. There was a slight rise in the water and salt permeability. Further, there was also a slight increase in hydrophobicity. The in situ formed CuNPs discharged strong bactericidal properties, resulting in a 90% decline in the quantity of attached live *E. coli* bacteria on the membrane with a modified surface in comparison to the pristine RO membrane (Ben-Sasson et al., 2016).

In another study, CuNPs exhibited a facile and time-efficient process for salt permeation. CuNPs modified by polyethylenenimine (PEI) along with a high concentration of positive charges play a very vital function in the regulation of hydrophilicity and salt permeation (82% Na2SO4, 98% NaCl). Surface modification of nanomaterials proposes personalized control and targeted scheme of surface characteristics, bestowing materials with improved or different abilities including high hydrophilicity, exceptional specificity and penetrability, and greater antibacterial properties. In the research, the scientists designed dual schemes (two-step deposition/codeposition) that used mussel-inspired polydopamine (PDA) to intensely immobilize CuNPs onto a polymeric membrane with pores, linking the surface cracks from UF to lose NF. To check the optimized membrane characteristics, several characterization techniques were done including SEM, EDX, atomic force microscopy (AFM), water contact angle, and zeta potential estimations. The data showed an inclusive extraordinary function of surface characteristics and also a uniform nanoparticle dispersal, low coarseness, progressive hydrophilicity, and comparatively neutral charge. Codeposition of PDA and CuNPs displayed a facile and time-efficient method that accelerated a greater CuNP loading as compared to

the two-step strategy, as evident by SEM and AFM images. The incorporation of PEI-modified CuNPs with a high density of positive charges showed an essential unction in the refinement of the hydrophilicity and compatibility with PDA and in greatly neutralizing the negative charge of PDA, thus encouraging an exceptional permeation of salt (NaCl). In addition, CuNP/PDA-modified membranes showed great elimination of three categories of textile dyes, showing better NF performance. Moreover, the membranes functionalized with proteins exhibited clear antibacterial properties with a high reduction in live *E. coli* bacterial cells. This work demonstrated a quick, facile codeposition approach to accumulate multitasking coating onto a UF setup, which gives an enormous prospective for the fractionation of dye/salt mixtures. During the process, the Cu(II) formed octahedral complexes comprising the tertiary amine groups of G*x*-NH_2 EDA core PAMAM dendrimers at pH 7.0. The Cu(II) metal ion of each of these complexes present in the core seems to be coordinated to 2–4 dendrimer tertiary amine groups situated in the equatorial plane and 2 axial water molecules. Lastly, the data of the experiments along with the review of data was used to propose and estimate a prototype of Cu(II) removal by G*x*-NH_2 PAMAM dendrimers in water solutions. At less metal ion-dendrimer packings, the prototype delivers a better binding of Cu(II) in aqueous solutions of G4-NH_2 and G5-NH_2 PAMAM dendrimers at pH 7.0 (Junyong et al., 2016).

In another study, seven NPs were assessed for treating water formed from RO and multistep flash purification plants. The evaluated NPs were silver, copper, silver-copper, zinc oxide, magnesium oxide, silicon dioxide, and carbon nanotubes. The antibacterial efficacy of the NPs was studied by batch cultures in desalted water samples contaminated with *E. coli, Enterobacter, Salmonella*, and *Enterococci*. The Chick-Watson model was fixed to the inactivation data to assess the kinetic constant for every arrangement of NPs, type of water and microbe. The data showed that silver and silver-copper NPs gave the maximum decontamination efficacy among the studied NPs. Changes in the chemical properties of water samples seem to show evident variations in the antimicrobial efficiencies of copper and magnesium oxide NPs, but not in the case of other NPs.

CuNPs were synthesized by bringing a solution of 0.2 M $CuCl_2$ to 80°C in an oil bath with continuous stirring. After that, 0.6 M L-ascorbic acid solution was poured drop by drop into the container with continuous agitation. The mixture was kept at 80°C till a dark solution was formed. This solution was then centrifuged for 15 min. L-Ascorbic acid worked as both a reducing and a capping agent.

The synthesized NPs were morphologically characterized by transmission electron microscopy (TEM). The surface water was studied by Zetasizer Nano SZ particle analyzer equipment. A small droplet of suspended NPs was diluted in 10 mL distilled water. The diluted solution was then transferred to a 1.0 mL cell and placed in the equipment to estimate the surface charge of the NPs. The size of the particle was also evaluated by the Zetasizer Nano SZ analyzer, which measures particles as low as 0.3 nm in diameter (Al-Issai et al., 2019).

The thin-film composite reverse osmosis (TFC-RO) membranes were altered by the integration of copper and iron NPs to study antibiofouling and desalination properties.

CuNPs and a mix of an iron crystalline phase were attained by oxide-reduction-precipitation in the case of CuNPs and reduction reactions in the case of FeNPs. The characterization was done by XRD and TEM techniques. Modified membranes were attained by integrating these NPs during the interfacial polymerization process (PI). The characterization of the membranes was done by SEM EDX, AFM, and contact angle measurements. Antibacterial efficacy was done by studying Colony Forming Unit (CFU) using *E. coli* and antiadhesion activities were established by fluorescence microscopy. An enhancement in the roughness of the membrane was seen, affecting the desalination process. Moreover, both modifications showed a significant antibacterial and anti-adhesion effect and a decrement in CFU. But, the antiadhesion percentage and decrease in living or dead cells were more in the case of the membrane modified by copper (Ontiveros et al., 2019).

In recent times, NPs as adsorbents have gained significance due to their extraordinary characteristics. In this respect, the adsorption of acrylic acid from water was observed by using copper oxide (CuO) NPs. In this study, firstly, CuO-NPs was developed utilizing a basic precipitation method. CuO-NPs were characterized by Brunauer-Emmett-Teller (BET), Fourier transform infrared spectroscopy (FTIR), and SEM analyzers. CuO-NPs generated were in nanoscale size ranged between 140 and 180 nm. FTIR analysis also established the functional groups of CuO-NPs. Finally, the response of contact time, the concentration of acrylic acid, temperature, and CuO-NP dose on the adsorption of acrylic acid with CuO-NPs was seen. The ideal adsorption situations were attained at the contact time of 180 min, the concentration of acrylic acid of 10% (*w*/w), nanoparticle dose of 0.05 g, and temperature of 25°C. At these parameters, the highest adsorption efficiency of CuO-NPs for acrylic acid was attained which was 202.67 mg g^{-1}. This data established that the synthesized CuO-NPs showed the best adsorption activity for acrylic acid (Baylan et al., 2020).

In a study, new nanocomposites were simply synthesized by interpolating Cu nanoparticles into carboxylated/hydroxylated carbon nanotubes (CNT) accumulated on top of a traditional polymeric membrane. The As-prepared membrane has great pure water permeability and the ability to get rid of more than 90% of As (III) at transmembrane pressures below 0.01 bar, which is reasonable for gravity-driven membrane (GDM) filtration applications. In comparison to Fe-based materials described in the literature, the Cu/CNT nanocomposite membranes displayed strength in eliminating As (III) at a pH range of 5–9 and in the presence of chloride, nitrate, bicarbonate, sulfate, and natural organic matter. A mechanical investigation suggests that the filtration process involves direct adsorption of As (III) onto Cu/CNT composites. As (V) species were also produced due to oxidation of As (III) by dissolved oxygen under the catalysis of Cu and adsorbed by Cu/CNT composites. Overall, the novel Cu/CNT nanocomposite membranes exhibit promising potentials in As (III) removal from contaminated water (Luan et al., 2019).

Dried husk extract of *Zea mays* L. was used for the biosynthesis of copper oxide nanoparticles. It is the first time to obtain cubic CuO nanoparticles of red color applying this simple, environmentally friendly, green synthesis method. The thermal oxidation of CuO nanoparticles was carried out to get pure monoclinic CuO nanoparticles

at a temperature of 600°C. X-ray diffraction (XRD) technique was used to study the phases of the copper oxides and transmission electron microscope (HRTEM) was used to analyse the sizes of the nanoparticles which range from 10 to 26 nm, 36–73 nm and 30–90 nm for the unannealed Cu O, 300°C and 600°C annealed CuO respectively. The values of the bandgap energies were 2.0, 1.30 and 1.42 eV, respectively for the unannealed, 300°C, and 600°C annealed copper oxide nanoparticles as obtained from diffuse reflectance of the nanoparticles. The best result was obtained with 600°C annealed copper oxide nanoparticles which displayed 91% and 90% degradation capability for methylene blue dye (BM) and textile effluent (TE), respectively in visible light. While CuO_300 was more efficient to obstruct the growth of *Escherichia coli* 518,133 and *Staphylococcus aureus* 9144, CuO was good for *Pseudomonas aeruginosa* and *Bacillus licheniformis*. The data showed the photocatalytic and antimicrobial efficacy of the copper oxide NPs (Nwanya et al., 2019).

In an interesting study, the leaf extract of *Citrofortunella microcarpa* is used for the production of copper oxide nanoparticles (CuO-NPs) as a natural and eco-friendly reducing agent in addition to capping agents. The visual, organizational and morphological features of CuO-NPs are investigated by applying UV–vis spectroscopy, XRD, SEM, and FTIR. EDS and SEM confirmed the pureness and globular-like shape of CuO-NPs having a size range of 54–68 nm. The synthesis was confirmed by UV–vis spectroscopy displaying surface plasmonic resonance at 270–300 nm whereas XRD displayed monoclinic phase of synthetic NPs with space group C2/c. Additionally, the existence of functional groups accountable for synthesis was observed using FTIR. The manufactured CuONPs were applied as photocatalyst for decontamination of Rhodamin B (RhB) dye polluted water and showed 98% decomposition efficacy under UV light exposure. Therefore, this study exhibited a protocol for favorable cost-efficient, simple and eco-friendly biological synthesis of CuO photocatalyst which has shown to be a potent alternative for the treatment of water polluted with dye (Rafique et al., 2020).

Many copper nanostructures like sulfide of good quality, shape, and uniform size comprising of interconnecting nanosheets have been developed by a mixed solvent method. Copper chloride and thiourea have been used as precursors as a source of copper and sulfur for each experiment in the presence of some mixed solvents to attain different morphologies of CuS. The synthetic nanostructures were studied by X-ray powder diffraction (XRD) and all of the synthetic products were examined and were found to be the phase pure single-crystalline. SEM showed the uniform and separate nanoparticles. The Energy Dispersive Spectroscopy (EDS) spectrum then demonstrated that they don't possess any type of impurity. Ultraviolet-visible–near-infrared (UV–vis–NIR) transmittance spectrophotometer has been used to confirm the optical properties of the NPs. A study by an extended U·V absorption in the near-IR region showed the covellite phase of CuS. The most important aspect was that the prepared nanostructures exhibited an extraordinary photocatalyst activity in treating concentrated rhodamine B (RhB) dye in aqueous solutions in the presence of visible light with an outstanding reusage, proposing a potential application in wastewater treatment (Nabi et al., 2020).

The discharge of dairy plants was treated by synthetic copper oxide NPs combined with *Sophora Japonica* fruit in a study. It was used as a novel adsorbent, to work in a batch adsorption procedure. For the characterization of adsorbent, FTIR, XRD, and SEM were employed. The parameters of COD removal by the adsorbent were explored based on contact time, masses of the adsorbent, initial COD value and temperatures. The ideal conditions for maximum elimination percentage were contact time of 120 min, a temperature of 25°C, pH of 7.5, and 1 g of adsorbent. The initial range of COD values employed was 100–700 ppm and the range of COD removal in terms of percentage was 77%–95% (Al-Ananzeh, 2021).

A facile, cheap, microwave methodology for the synthesis of copper NPs was developed employing various counterions: sulfate, chloride, acetate, and nitrate. The synthesis was done by taking ethylene glycol as a reaction medium and sodium hypophosphite as a reducing agent. The products were characterized using FTIR, XRD, FE-SEM, EDS, XPS, DRS, and TEM. The results showed that the counter ions have a substantial effect on the products. The purest nanoparticles were developed by copper sulfate and copper chloride having an average particle size of 45 and 48 nm, respectively. All copper nanostructures produced exhibited good photocatalytic activity in the range of 95.0%–98.0% for the breakdown of safranin dye in the presence of UV radiation for 70 min (El-Berry et al., 2021).

In another research work, biological wastewater treatment using Fe^0-based NPs was shown. nZVI particles were added in the first step to a mixed bacterial community at three different concentrations (50, 1000, and 5000 mg/L) and the growth of bacteria was evaluated for 12 days. Also, the reactivity of nZVI was increased by the addition of a second metal to form the so-called bimetallic nanoparticles. Bacterial growth was enhanced by 53.84% and 84.61% when exposed to nZVI and Cu/nZVI treatment, respectively. The characterization by TEM and XRD displayed that Cu/nZVI NPs showed greater dispersibility and lesser agglomeration than only nZVI treatment. Also, COD removal efficiency was increased up to 33.21%, 55.30%, and 61.24% in control, nZVI, and Cu/nZVI reactors, respectively (Bensaida et al., 2021).

Wastewater decolorization was performed by the Fenton oxidation process employing Fe_3O_4/CuO and MnO_2-Fe_3O_4/CuO hybrid catalysts synthesized by coprecipitation and impregnation methods, respectively. The characterization of chemical structure, surface area, and porosity of hybrid nanoparticles was carried out by XRD, EDS, FE-SEM, and BET techniques. The results showed that the addition of MnO_2 to Fe_3O_4/CuO catalyst increased the rate of decolorization because of the greater surface area of the catalyst and narrower distribution of pore size, when compared with Fe_3O_4/CuO, and also the direct oxidation of methylene blue via Mn_4+ and Mn_3+. The maximum removal efficiency of methylene blue was by MnO_2-Fe_3O_4/CuO as compared with Fe_3O_4/CuO during 45 min reaction time (90% vs 79%). In addition, the catalytic performance was evaluated on the basis of reaction conditions including pH, dosage of hydrogen peroxide, and concentrations of catalyst and methylene blue (Ghasemi et al., 2021).

In another study, the degradation of reactive red was carried out by the combination of photocatalytic activity of plasma-functionalized Cu-doped TiO_2 NPs and the oxidization process of atmospheric pressure plasma jet. Cu-TiO_2 NPs were synthetized in the first part of the study by the sol-gel method. The characterization of the NPs was done by using XRD, XPS, and SEM measurements. XRD data showed the anatase phase as the main part which is the most photoactive form of TiO_2. The XPS data showed that the varied plasma treatments activated the generation of oxygen vacancies. In the second part of the study, the real breakdown of RR-198 by an Ar plasma treatment alone or combination with the plasma pretreated Cu-–TiO_2 NPs in an aqueous solution was explored. The breakdown of RR-198 was evaluated by employing UV–Vis spectroscopy and HPLC (Pandiyaraj et al., 2021).

Copper sulfide was studied as sorbent material for permanganate ions and the result was evaluated. The effect of pH, MnO_4- concentration, sorption time and temperature were explored. The data of this work showed that the concentration of sorbate as 1200 mg/L, pH of the solution as 1.5, time of sorption as 90 min, and temperature as 60°C are the ideal conditions for MnO4-sorption by CuS (Aljohani and AL-Aoh, 2021).

In another study, CuO NPs were produced by a microwave-assisted method using leaf extract of *Cordia africana* Lam. for reduction processes. The synthesized CuO NPs were characterized using XRD, FTIR, SEM, and EDS. The data showed that nanocrystals of the monoclinic CuO phase had an agglomerated morphology with 9 nm as crystallite size. The catalytic activity of CuO NPs was also studied on 4-nitrophenol (4-NP) reduction. The catalyst has displayed tremendous activity and the reaction was completed within 12 min. Further, the data showed that the Cu NPs which were synthesized at pH 7 displayed the best efficacy at the reduced time as compared to those obtained at higher pH values (Bekru et al., 2021).

6 Conclusion

Around 70% of the globe is bounded by water and water is required in every phase of day to day life. The requirement for water becomes more intense with a growing population and there is a need for safe and clean water due to increasing pollution. Conventional methods of water purification could not suffice to the growing demand for water. Therefore, advanced water treatment technologies are required to ensure the supply of high-quality potable water. In the present chapter, we have reviewed the role of nanotechnology in the desalination of water. There are reports on the applications of various nanomaterials for water purification. One of the significant advantages of using nanomaterials is that they can integrate all their properties, which results in a multifunctional system. In the same line, lately, copper-based nanomaterials have gained significance in the desalination of water due to their unique properties such as the nanosize and specifically the antimicrobial activity. Further research and studies are still needed to deal with the challenges and limitations of copper nanomaterials. Further improvement is required to improve its economic efficiency.

References

Al-Ananzeh, N.M., 2021. Treatment of wastewater from a dairy plant by adsorption using synthesized copper oxide nanoparticles: kinetics and isotherms modeling optimization. Water Sci. Technol. 83, 1591–1604.

Al-Issai, L., Elshorbagy, W., Maraqa, M.A., Hamouda, M., Soliman, A.M., 2019. Use of nanoparticles for the disinfection of desalinated water. Water 11, 559–579.

Aljohani, M.M., AL-Aoh, H.A., 2021. Adsorptive removal of permanganate anions from synthetic wastewater using copper sulfide nanoparticles. Mater. Res. Express 8, 035012.

Al-Mamun, A., Ahmad, W., Baawain, M.S., Khadem, M., Dhar, B.R., 2018. A review of microbial desalination cell technology: configurations, optimization and applications. J. Clean. Prod. 183, 458–480.

Baylan, N., İlalan, İ., İnci, İ., 2020. Copper oxide nanoparticles as a novel adsorbent for separation of acrylic acid from aqueous solution: synthesis, characterization, and application. Water Air Soil Pollut. 231, 465.

Bekru, A.G., Zelekew, O.A., Andoshe, D.M., Sabir, F.K., Eswaramoorthy, R., 2021. Microwave-assisted synthesis of CuO nanoparticles using *Cordia africana* Lam. Leaf extract for 4-nitrophenol reduction. J. Nanotechnol. 2021. 12 pages.

Bensaida, K., Eljamal, R., Sughihara, Y., Eljamal, O., 2021. The impact of iron bimetallic nanoparticles on bulk microbial growth in wastewater. J. Water Process. Eng. 40, 101825.

Ben-Sasson, M., Lu, X., Nejati, S., Jaramillo, H., Elimelech, M., 2016. In situ surface functionalization of reverse osmosis membranes with biocidal copper nanoparticles. Desalination 388, 1–8.

Buros, O.K., 2000. The ABCs of Desalting. International Desalination Association.

Camacho-Flores, B.A., Martínez-Álvarez, O., Arenas-Arrocena, M.C., Garcia-Contreras, R., Argueta-Figueroa, L., de la Fuente-Hernández, J., Acosta-Torres, L.S., 2015. Copper: synthesis techniques in nanoscale and powerful application as an antimicrobial agent. J. Nanomater. 2015, 415238.

Castro-Muñoz, R., 2020. The strategy of nanomaterials in polymeric membranes for water treatment: nanocomposite membranes. Tecnol. Cienc. del Agua 11, 410–436.

Dankovich, T.A., Smith, J.A., 2014. Incorporation of copper nanoparticles into paper for point-of-use water purification. Water Res. 63, 245–251.

Diawara, C.K., 2008. Nanofiltration process efficiency in water desalination. Sep. Purif. Rev. 3, 302–324.

Elattar, H.F., Nada, S.A., Al-Zahrani, A., Fouda, A., 2020. Humidification-dehumidification water desalination system integrated with multiple evaporators/condensers heat pump unit. Int. J. Energy Res. 44, 6396–6416.

El-Berry, M.F., Sadeek, S.A., Abdalla, A.M., Nassar, M.Y., 2021. Microwave-assisted fabrication of copper nanoparticles utilizing different counter ions: an efficient photocatalyst for photocatalytic degradation of safranin dye from aqueous media. Mater. Res. Bull. 133, 111048.

Fritzmann, C., Löwenberg, J., Wintgens, T., Melin, T., 2007. State-of-the-art of reverse osmosis desalination. Desalination 216, 1–76.

Ghasemi, H., Mozaffari, S., Mousavi, S.H., Aghabarari, B., Abu-Zahra, N., 2021. Decolorization of wastewater by heterogeneous Fenton reaction using MnO2-Fe3O4/CuO hybrid catalysts. J. Environ. Chem. Eng. 9, 105091.

Humplik, T., Lee, J., O'Hern, S.C., et al., 2011. Nanostructured materials for water desalination. Nanotechnology 22, 292001. 2011.

Junyong, Z., Uliana, A., Wang, J., Yuan, S., Li, J., Tian, M., Volodin, K.S.A., Lin, J., Bernaerts, K., Zhang, Y., Bruggen, B.V., 2016. Elevated salt transport of antimicrobial loose nanofiltration membranes enabled by copper nanoparticles via fast bioinspired deposition. J. Mater. Chem. A 4, 13211–13222.

Kargari, A., Shirazi, M.M.A., 2014. Water desalination: solar-assisted membrane distillation. In: Capehart, B.L. (Ed.), Encyclopedia of Energy Engineering and Technology, second ed. CRC Press, Boca Raton, FL, USA, pp. 1–15.

Khan, I., Tlili, I., Imran, M.A., Miraj, F., 2018a. MHD fractional Jeffrey's fluid flow in the presence of thermo diffusion, thermal radiation effects with first order chemical reaction and uniform heat flux. Results Phys. 10, 10–17.

Khan, I., Ali Abro, K., Mirbhar, M.N., Tlili, I., 2018b. Thermal analysis in Stokes' second problem of nanofluid: applications in thermal engineering. Case Stud. Therm. Eng. 12, 271–275.

Khan, Z., Khan, I., Ullah, M., Tlili, I., 2018c. Effect of thermal radiation and chemical reaction on non-Newtonian fluid through a vertically stretching porous plate with uniform suction. Results Phys. 9, 1086–1095.

Khan, Z., Rasheed, H.U., Tlili, I., Khan, I., Abbas, T., 2018d. Runge-Kutta 4th-order method analysis for viscoelastic Oldroyd 8-constant fluid used as coating material for wire with temperature dependent viscosity. Sci. Rep. 8, 14504.

Khan, Z.A., Ul Haq, S., Khan, T.S., Khan, I., Tlili, I., 2018e. Unsteady MHD flow of a Brinkman type fluid between two side walls perpendicular to an infinite plate. Results Phys. 9, 1602–1608.

Lu, H., Wang, J., Stoller, M., Wang, T., Bao, Y., Hao, H., 2016. An overview of nanomaterials for water and wastewater treatment. Adv. Mater. Sci. Eng. 2016, 4964828.

Luan, H., Teychene, B., Huang, H., 2019. Efficient removal of As (III) by Cu nanoparticles intercalated in carbon nanotube membranes for drinking water treatment. Chem. Eng. J. 355, 341–350.

Mohsen, M.S., Jaber, J.O., Afonso, M.D., 2003. Desalination of brackish water by nanofiltration and reverse osmosis. Desalination 157, 167.

Montgomery, M.A., Elimelech, M., 2007. Water and sanitation in developing countries including health in the equation. Environ. Sci. Technol. 41, 17–24.

Nabi, G., Tanveer, M., Tahir, M.B., Kiran, M., Rafique, M., Khalid, N.R., Alzaid, M., Fatima, N., Nawaz, T., 2020. Mixed solvent based surface modification of CuS nanostructures for an excellent photocatalytic application. Inorg. Chem. Commun. 121, 108205.

Nandigana, V.V.R., Aluru, N.R., 2016. Concentration polarization at micro-/nanofluidic interfaces. In: Bhushan, B. (Ed.), Encyclopedia of Nanotechnology. Springer, Dordrecht, Netherlands, pp. 486–493.

Nwanya, A.C., Razanamahandry, L.C., Bashir, A.K.H., Ikpo, C.O., Nwanya, S.C., Botha, S., Ntwampe, S.K.O., Ezema, F.I., Iwuoha, E.I., Maaza, M., 2019. Industrial textile effluent treatment and antibacterial effectiveness of *Zea mays* L. Dry husk mediated bio-synthesized copper oxide nanoparticles. J. Hazard. Mater. 375, 281–289.

Ontiveros, M.A., Quintero, Y., Llanquilef, A., Morel, M., Martínez, L.A., García, G.A., Garcia, A., 2019. Anti-biofouling and desalination properties of thin film composite reverse osmosis membranes modified with copper and iron nanoparticles. Materials 12, 2081.

Pandiyaraj, K.N., Vasu, D., Ghobeira, R., Tabaei, P.S.E., De Geyter, N., Morent, R., Pichumani, M., Padmanabhanan, P.V.A., Deshmukh, R.R., 2021. Dye wastewater degradation by the synergetic effect of an atmospheric pressure plasma treatment and the photocatalytic activity of plasma-functionalized Cu–TiO2 nanoparticles. J. Hazard. Mater. 405, 124264.

Rafique, M., Shafiq, F., Gillani, S.S.A., Shakil, M., Tahir, M.B., Sadaf, I., 2020. Eco-friendly green and biosynthesis of copper oxide nanoparticles using *Citrofortunella microcarpa* leaves extract for efficient photocatalytic degradation of Rhodamin B dye form textile wastewater. Optik 208, 164053.

Ren, G., Hu, D., Cheng, E.W.C., Vargas-Reus, M.A., Reip, P., Allaker, R.P., 2009. Characterisation of copper oxide nanoparticles for antimicrobial applications. Int. J. Antimicrob. Agents 33, 587–590.

Ruparelia, J.P., Chatterjee, A.K., Duttagupta, S.P., Mukherji, S., 2008. Strain specificity in antimicrobial activity of silver and copper nanoparticles. Acta Biomater. 4, 707–716.

Shannon, M.A., Bohn, P.W., Elimelech, M., Georgiadis, J.G., Mariñas, B.J., Mayes, A.M., 2008. Science and technology for water purification in the coming decades. Nature 452, 301–310.

Tamayo, L., Azócar, M., Kogan, M., Riveros, A., Páez, M., 2016. Copper-polymer nanocomposites: an excellent and cost-effective biocide for use on antibacterial surfaces. Mater. Sci. Eng. C 69, 1391–1409.

Theron, J., Walker, J.A., Cloete, T.E., 2008. Nanotechnology and water treatment: applications and emerging opportunities. Crit. Rev. Microbiol. 34, 43–69.

Tlili, I., Timoumi, Y., Ben Nasrallah, S., 2006. Numerical simulation and losses analysis in a Stirling engine. Int. J. Heat Technol. 24, 97–105.

Tlili, I., Timoumi, Y., Ben Nasrallah, S., 2007. Thermodynamic analysis of Stirling heat engine with regenerative losses and internal irreversibilities. Int. J. Engine Res. 9, 45–56.

Varkey, A.J., Dlamini, D., 2012. Point-of-use water purifcation using clay pot water flters and copper mesh. Water SA 38, 721–726.

Xu, J., Feng, X., Chen, P., Gao, C., 2012. Development of an antibacterial copper (II)-chelated polyacrylonitrile ultrafiltration membrane. J. Membr. Sci. 413–414, 62–69.

Xu, J., Zhang, L., Gao, X., Bie, H., Fu, Y., Gao, C., 2015. Constructing antimicrobial membrane surfaces with polycationcopper(II) complex assembly for efficient seawater softening treatment. J. Membr. Sci. 491, 28–36.

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CHAPTER

27 Synthesis of copper nanostructures: Antimicrobial applications and environmental remediation of emerging agrochemicals

Kubra Ulucan-Altuntas

Department of Environmental Engineering, Yildiz Technical University, Davutpasa, Istanbul, Turkey

1 Introduction

Agriculture is one of the main activities that play an important role in the development of societies, contribute to the national economy, and form the backbone of many sectors. The aggressive spread of agrochemicals (i.e., pesticides, herbicides, insecticides, fertilizers) used to increase crop yields in the agricultural field has caused complications such as reduced soil fertility and formation of pathogens with antimicrobial resistance (Onder Erguven et al., 2021). These chemicals, which pose threats to both the environment and human health, can damage beneficial microorganisms in the soil unintentionally, and cause various diseases by biological accumulation. In this regard, both the remediation of existing accumulated pollutants and the use of nanoparticles against pathogens are new and important advancements for the agricultural sector (Mehta et al., 2021).

Recently, metal nanoparticles have attracted great interest in nanoscale science and technology due to their electronic, optical, and magnetic properties as well as their chemical and physical properties. They are used in many areas such as chemical and biological sensors, photonic and electronic devices, and catalysis (Aygün and Cann, 2005; Zhang and Zhang, 2008). Noble metal nanoparticles such as gold, silver, titanium, and platinum are more widely used in the food industry and agricultural activities as antifungal and antimicrobial agents. However, nanomaterials prepared from inexpensive Earth-abundant metals have the potential to be used as a substitute for expensive and rare metals in many chemical processes, including water and wastewater treatment. In the last decade, the synthesis of metal oxide nanoparticles, such as zinc, iron, copper, and magnesium, and their use for different purposes has gained great attention from many researchers (Cabir et al., 2017; Ulucan-Altuntas

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and Kuzu, 2019; Varank et al., 2020). Among these metals, copper nanoparticles (Cu NPs) exhibit antimicrobial properties against various microorganisms, making them widely used in areas such as medical purposes, personal care products, and the food industry (Jahan et al., 2020; Ren et al., 2009).

Low cost and readily available copper (Cu) is a transition metal with high thermal and electrical conductivity. Because of these properties, Cu NPs find a place in many applications such as electrocatalyst and photocatalyst in the removal of organic substances. Cu exhibits various oxidation states (Cu0, CuI, CuII, and CuIII), enabling both one- and two-electron redox processes. The fact that copper is rapidly oxidized by agents such as oxygen and water, has led researchers to use copper-based nanoparticles and support materials such as copper oxide (CuO_x) nanoparticles. Besides, to prevent oxidation, the use of capping agents in the synthesis of Cu NPs emerges to be applied against undesirable oxidation states during synthesis. Also, their synthesis with different metal oxides increases both their stability and catalytic properties. It has gained great attention on synthesizing nanocomposites by using supporting material to enhance the antimicrobial and photocatalytic effects of Cu-based nanoparticles. For example, chitosan is a natural polysaccharide and has antimicrobial properties. Chitosan-based metal oxide nanocomposites can be considered promising candidates, especially for antifungal activity (Chouhan and Mandal, 2021).

This book chapter provides a literature review of recent advances in the synthesis of Cu NPs and their usage in the environmental remediation of agrochemicals. The synthesis of Cu and CuO_x-based nanoparticles and also their nanocomposites with different metal oxide, carbon-based nanoparticles, and polymers are described and the current situation of Cu NPs nanostructures applications on antimicrobial activity and photocatalytic activity is discussed.

2 Synthesis of copper nanostructures

In this section, basic information about copper and copper oxide nanoparticles, which are widely applied in the literature, and synthesis methods of copper and copper-based nanoparticles (Fig. 1), such as composite-nanostructures supported by different composites, are explained.

2.1 Copper and copper oxide-based nanoparticles

The methods generally used in the preparation of metal nanoparticles are also used in the synthesis of Cu-based nanoparticles. These nanoparticles are often synthesized using the "bottom-up" method, where the nanoparticle is synthesized from atomic level to nanoscale, or by using the "top-down" method, where the bulk is separated from the solid into smaller components.

The synthesis of Cu and copper oxide nanoparticles is mainly conducted using a combination of reduction, hydrolysis, condensation, and oxidation reactions. For

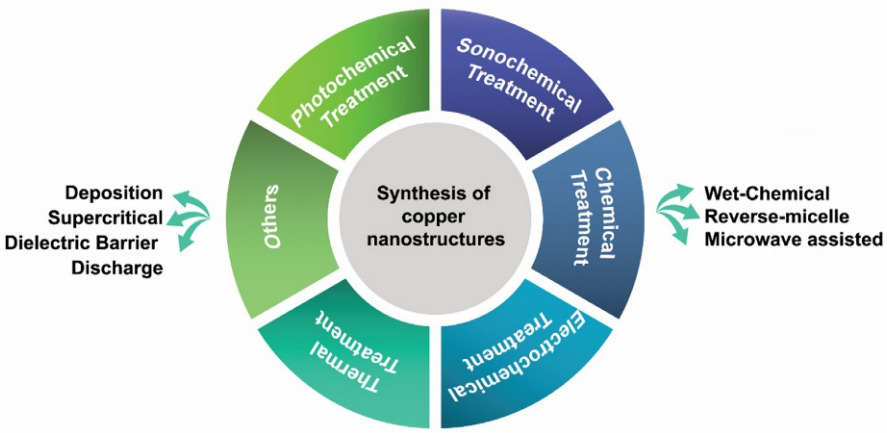

FIG. 1

Main synthesis methods for copper nanostructures.

example, it is generally reduced using a Cu^{+} and Cu^{2+} source. However, for the synthesis of CuO_x NPs, hydrolysis of the copper source followed by its dehydration and oxidation can be performed. Although "wet-chemical processes" are the most used process in synthesizing copper-based nanoparticles, various methods have been developed in which heat treatments, photochemical techniques, electrochemical synthesis, sonochemical methods, and cold plasma are applied. Various synthesis methods are examined in Table 1. Among these methods, the wet chemical reduction method has advantages such as controlling the reaction and rapid production. In the wet synthesis method, which is a chemical process, as in other metal nanoparticles such as nZVI, generally, Cu salts (i.e., $CuSO_4$, $CuCl_2$) are reduced by providing electrons with a reducing agent. In the reduction process (1) the medium of the solvent, (2) the reducing agent, and (3) the capping agent are important. It is seen that organic solvents are generally used as solvent media. The reducing agents used are chemicals such as sodium borohydride (Dharmadasa et al., 2013), hydrazine (Singh et al., 2010; Songping and Shuyuan, 2006), and 1,2-hexadecanediol (Mott et al., 2007). Various capping agents are used for stabilizing and preventing the oxidation of nanoparticles during the chemical reaction. For this purpose, surfactants such as polyethylene glycol (PEG), polyvinylpyrrolidone (PVP), sodium dodecyl sulfate (SDS), and hydroxypropyl methylcellulose (HPMC) enable the synthesis of CuO NPs in the form of nanocubes or spherical shapes with core-shell properties (Jayaramudu et al., 2021; Sekar et al., 2021; Wan et al., 2019). El-Berry et al. (2020) reported the method by which they synthesized copper nanoparticles using different capping agents in a simple and controllable manner. They examined the effects of SDS, PEG 2000, and PEG 4000, which they used as capping agents, on the size and morphology of Cu NPs. They reported that they obtained pure Cu NPs by using PEG 4000 in 28 nm size. Vaseem et al. (2011) used cetyltrimethylammonium bromide (CTAB) as a capping agent to stabilize Cu NPs in their study, spherically synthesized at 10–50 nm in size.

Table 1 Synthesizing methods for Cu and Cu oxide-based nanoparticles.

Synthesized method	Particle	Cu precursor	Reducing agent and stabilizer	Particle size	References
Wet-chemical	Cu NPs	$Cu(NO_3)_2$	Sodium borohydride Tergitol NP-9	10–15 nm	Dharmadasa et al. (2013)
	Cu_2O	Copper acetate dihydrate	Glucose	18–32 nm	Sabbaghan et al. (2015)
	Cu NPs	$CuCl_2$	Sodium borohydride PVP	19–240 nm various size	Lagrow et al. (2014)
	Cu NPs	Copper(II) acetylacetonate	1,2-hexadecanediol	2–25 nm	Mott et al. (2007)
	Cu Nos	$CuSO_4$	Ethylene glycol SDS and polyethylene glycol	28 nm spherical	El-Berry et al. (2020)
	Cu NPs	$Cu(NO_3)_2$	Hydrazine hydrate and starch	5 nm spherical	Singh et al. (2010)
	Cu NPs	$Cu(NO_3)_2$	Hydrazine hydrate and CTAB	10–50 nm spherical	Vaseem et al. (2011)
	Cu NPs hydrogel	$CuSO_4$	HPMC and ascorbic acid	38 nm cubic	Jayaramudu et al. (2021)
	Cu NPs hydrogel	$CuSO_4$	Chitosan	8 nm spherical	Jayaramudu et al. (2020)
Green synthesis	Cu NPs	$CuSO_4$	L-Ascorbic acid	< 2 nm	Xiong et al. (2011)
	Cu nanofluid	$CuSO_4$	Glucose	50 nm	Shenoy and Shetty (2013)
	Cu NPs	$CuCl_2$	Aconitic acid and pluronic	3–4 nm spherical	Zhao et al. (2020)
	Cu NPs	$CuSO_4$	Ascorbic acid and CTAB	90 nm spherical	Biçer and Şişman (2010)
	Cu NPs	$CuSO_4$	*Carica papaya* leaves extracts	77 nm spherical	Dulta et al. (2021)
	Cu NPs	$Cu(NO_3)_2$	Ammonia and *Solanum tuberosum* (starch)	54 nm spherical	Keihan et al. (2017)

	Ag-Cu @ZnO	$CuNO_3$	Acacia caesia extract	12 nm	Manjari et al. (2020)
	Cu-doped ZnO NPs	$Cu(NO_3)_2$	Leaf extracts of *Abutilon indicum*, clerodendrum infortunatum, *Clerodendrum inerme*	20 nm	Khan et al. (2018)
Reverse micelle	Atomic Cu clusters	$CuSO_4$	Sodium borohydride SDS Isopentanol	2.9 ± 1.1 nm	Vázquez-Vázquez et al. (2009)
	Cu NPs	$CuCl_2$	Ascorbic acid Triton X-100	< 20 nm	Wang et al. (2014)
Microwave-assisted treatment	CuO	$CuSO_4$	Hydrazine hydrate *Psidium guajava* leaves extract	13.07 ± 3.43 nm	Sreeju et al. (2016)
		$CuSO_4$	*Citrus sinensis* fruit extract	10.2 nm spherical	Jahan et al. (2020)
Electrochemical synthesis	Fe/Cu/Sn film	Copper acetate	Diethanolamine Dimethylamine borane complex and PEG 3000		Panzeri et al. (2021)
		$CuSO_4$	Methyl viologen	Various size	Kokorekin et al. (2017)
Thermal treatment	Cu NPs	$CuSO_4$	Sodium hydroxide	10–30 nm Rod	ALOthman et al. (2021)
Sonochemical treatment	Cu-CuO_x NPs	$CuSO_4$	Acsorbic acid	170–200 nm	Shui et al. (2013)
Supercritical conditions	Cu NPs	$CuSO_4$	Ethylenediamine tetraacetic acid disodium salt	14–85 nm	Zhou et al. (2015)
Atomic layer deposition	Cu nanocoil	$Cu\ (thd)_2$	–	80–120 nm	Yu et al. (2018)
Dielectric barrier discharge	Cu/Pd	$Cu\ (NO_3)_2$	–	5–9 nm	Di et al. (2017)
	Cu	CuO	–	35 nm	Di et al. (2014)
Pulsed wire discharge	Cu		–	20–70 nm	Jiang and Yatsui (1998)

There is an increasing interest in green chemistry applications to reduce the use of hazardous and environmentally harmful solvents in nanoparticle synthesis and to promote sustainable environmentally friendly solutions. In this regard, it is seen that water is used as a solvent, and plant-based materials such as L-ascorbic acid (Xiong et al., 2011), glucose (Shenoy and Shetty, 2013), tea extract (Keihan et al., 2017), and *Carica papaya* leaves extracts (Dulta et al., 2021) are used as a reducing agent, and starch (Singh et al., 2010; Keihan et al., 2017) is used as a capping agent. Zhao et al. (2020) reported a facile green synthesis method for Cu nanoparticles by using $CuCl_2$, aconitic acid, and pluronic as Cu precursor, reducing agent, and stabilizer, respectively. They reported that the dimensions of the synthesized Cu nanoparticles were approximately 3–4 nm and that they had a catalytic effect in the removal of nitrophenols in their study, which they stated were spherical. The reverse micelle method, which enables the formation of smaller nanoparticles compared to other methods, is based on the formation of microemulsions in water and oil with the use of lipophilic surfactants. To accelerate the reaction during the synthesis of Cu NPs, there are methods in which microwave is used as an energy source. Cu NPs are synthesized by irradiating microwaves onto the reaction mixture, which converts the electromagnetic energy into heat. Compared to traditional heating methods, the microwave method offers advantages such as fast energy transfer and noncontact processing. Jahan et al. (2020) used fruit extracts for the synthesis of nontoxic Cu NPs by microwave method. Spherical Cu NPs with diameters of 6.93–20.70 nm were synthesized. Similarly, Bhattacharjee and Ahmaruzzaman (2015), used l-arginine for the synthesis of two-dimensional CuO nanoleaves using microwave energy.

Sonification creates high temperatures and pressures locally and accelerates reactions with the help of acoustic cavitation. In this regard, high temperatures used in the synthesis of Cu NPs using ultrasonic frequencies will enable local synthesis. Moghimi-Rad et al. (2010) used ethylene glycol as capping agents in the synthesis of ultrasound-assisted Cu NPs and obtained Cu NPs of approximately 108 nm in size. In the electrochemical synthesis method, which is an inexpensive and easily applicable method, a salt solution containing Cu is added into the electrolytic cell where electrodes that will function as anode and cathode are placed, and Cu NPs are synthesized by agglomeration under electrical current or by electrical deposition (Kumar et al., 2011; Panzeri et al., 2021).

Recently, there has been an increasing interest in using cold plasma methods to efficiently synthesize metal ions. Compared to traditional methods, the separation and reduction of catalysts can be achieved with cold plasma, which is easier, faster, and more energy-efficient, and environmentally friendly (Di et al., 2017). Instead of chemicals used as reductants in the cold plasma method, which allows the synthesis of smaller metal nanoparticles, Cu NPs can be synthesized from CuO by creating dielectric barrier discharge in argon and hydrogen gas environment (Di et al., 2014). Another cold plasma method used in metal nanoparticle synthesis is pulsed wire discharge (Jiang and Yatsui, 1998). Emphasizing that a high rate of production can be achieved with this method, Murai et al. (2007) reported that the Cu NPs coated with oleic acid were approximately 25 nm in size and remained intact for months.

In short, Cu NPs can be synthesized in different shapes and sizes such as spherical, cubic, depending on the experimental conditions, the chemicals used, capping agents, and where the required energy is supplied (i.e., thermal, microwave, ultrasound, cold plasma) (Fig. 1). Although production with green chemistry is an important approach in terms of producing fewer waste chemicals, there are a limited number of studies on synthesis with cold plasma that does not generate waste.

2.2 Copper-based supported nanostructures

Cu NPs can be produced with various support materials to suit the process to be applied. In this regard, carbon- and polymer-based supporting materials, metal oxide-based support materials, or natural products such as bentonite and zeolite are reported in synthesizing Cu-based supported nanostructures. The synthesis methods of these mentioned materials are summarized in Table 2.

Although it has been known for many years that the physicochemical properties of carbon materials provide the use of these substances as catalysts in the transformation of organic and inorganic substances, the synthesis of 2D carbons with high surface area (i.e., graphene oxide) has increased the interest in this process called carbocatalysis. Among the carbon-based Cu NPs, the most researched support material is activated carbon (AC), an inexpensive material. Boruban and Esenturk (2018) synthesized AC-supported Cu NPs, in which the activated carbon was, mixed with $CuCl_2$ solution after being purified with acid. By adding NaOH to this Cu implanted AC solution, $Cu(OH)_2$ formation was observed and then calcified to obtain AC-supported CuO nanostructure.

The carbon nanotubes (CNTs) have unique hollow geometry capable of incorporating metals into their structure with high surface functionalization. CNTs synthesized with metal oxides gain great attention because of their large surface area and excellent mechanical properties. In the study by Aktürk et al. (2018), they synthesized Cu-CeO_2 nanoparticles on multiwall carbon nanotubes (MWCNTs), which were synthesized separately and purified with acid before deposition. Graphene, another excellent material based on carbon, is used as an excellent support material with high surface area and high thermal and electrical conductivity. In the synthesis of graphene, graphene oxide, and reduced graphene oxide-supported Cu nanostructures, generally, graphene-based nanoparticles are subsequently reacted with Cu precursor. Kim et al. (2021) declared a simple one-step method for synthesizing reduced graphene oxide (rGO)-supported Cu nanoparticles. In the method, Cu-rGO nanoparticles were synthesized by adding hydrazine hydrate after the graphene oxide was synthesized by the modified Hummers' method and after the copper sulfate reacted at a low temperature such as 70°C using the precursor. Among carbon-based nanomaterials, carbon quantum dots (QDs) have attracted great interest from researchers for the last decade due to their advantages such as low toxicity and superior chemical properties. It has a high potential for use in bioimaging, photocatalyst, and drug delivery (Nazri et al., 2021). Li et al. (2012) investigated their photocatalytic properties. It is seen that they produce carbon QDs and then coat them on Cu_2O using polyvinylpyrrolidone to synthesize carbon QDs loaded Cu_2O.

Table 2 Synthesizing methods for Cu-based supported nanostructure.

Cu-based supported nanoparticles	Synthesized method	Cu precursor	Reducing agent and stabilizer	Particle size	References
AC-CuO	Chemical-thermal	$CuCl_2$	NaOH	230 nm	Boruban and Esenturk (2018)
AC-Cu	Wet chemical	$CuCl_2$	Na_2SO_3	–	Khan et al. (2013)
AC-Cu	Wet-chemical	CuI	–	80–300 nm	Sharghi et al. (2009)
Cu-CeO_2-coated MWCNTs	Electrochemical deposition	$CuSO_4$	–	Needle shape	Aktürk et al. (2018)
Cu-MWCNTs	Electrochemical deposition	$CuCl_2$	–	10–15 nm	Aslan et al. (2016)
C-supported Cu-Pt	Microwave treatment	$CuCl_2$	Ethylene glycol	2.31 nm	Song et al. (2020)
Cu/C	Wet chemical	$CuCl_2$	Hydrazine hydrate naphthalene	–	Zhao et al. (2021)
Cu-rGO	Wet chemical	$CuSO_4$	Sodium borohydride	90 nm	Fakhri et al. (2014)
Cu-rGO	Wet chemical	$CuSO_4$	Hydrazine hydrate	5 nm–spherical	Kim et al. (2021)
Carbon QDs loaded CuO	Thermal	$CuSO_4$	NaOH	22 nm × 700 nm nanosheet	Muthulingam et al. (2021)
Carbon QDs loaded CuO	Microwave	$CuCl_2$	Ammonium citrate	3.4 nm spherical	Che et al. (2019)
Carbon QDs loaded Cu_2O	Wet chemical	$CuSO_4$	Polyvinylpyrrolidone glucose	Spherical	Li et al. (2012)
La_2O_3-supported Cu NPs	Thermal treatment	Copper Asetate	–	30 nm	Shi et al. (2010)
Cu-ZrO_2	Thermal treatment	$Cu(NO_3)_2$	–	6–33 nm	Dolgikh et al. (2011)
Cu-ZnO nanorods	Wet chemical	$Cu(NO_3)_2$	Ethylene glycol	3–8 nm	Lin et al. (2009)
Iron oxide-supported copper oxide nanoparticles	Wet chemical	$CuCl_2$	–	20–30 nm	Shelke et al. (2014)
Cu/Ti pillared Bentonite	Wet chemical	$Cu(NO_3)_2$	–	–	Tomul et al. (2016)

Bentonite-supported Cu NPs	Wet chemical	$CuSO_4$	*Thymus vulgaris* L. leaf extract	Various sizes	Issaabadi et al. (2017)
TiO_2 doped Cu on clinoptilolite	Photo/ electrochemical-thermal method	Cu electrode	–	Various sizes	Castañeda-Juárez et al. (2019)
Cu-supported on Y-Zeolite	Wet chemical	$Cu(NO_3)_2$	–	61.9 nm	de Andrade et al. (2020)
Zeolite supported Cu NPs	Wet chemical	$Cu(NO_3)_2$	N_2H_4	8 nm	Subramanian and Pitchumani (2012)
Cu-supported on conducting polymer	Wet chemical	$CuCl_2$	N_2H_4	5–6 nm	Pham et al. (2012)
Chitosan capped-copper nanobiocomposites	Green synthesis	$CuSO_4$	Ascorbic acid	–	Mehta et al. (2021)
Chitosan-supported Cu NPs	Wet chemical	$CuSO_4$	Sodium tripolyphosphate	374 nm	Saharan et al. (2015)
Alumina-supported Pd/Cu aloy NPs	Dielectric barrier discharge	$Cu(NO_3)_2$	Ascorbic acid	6.2 nm	Di et al. (2015)
Cu with oleic acid coating	Pulsed wire discharge	Cu wire	–	25 nm	Murai et al. (2007)
Polyaniline carbon nanotube composite	Electrochemical treatment	$CuCl_2$	Trisodium citrate	13–58 nm	Chauhan et al. (2011)
CuO/TiO2/PANI	Wet chemical	$Cu(NO_3)_2$	Sodium borohydride	40 nm spherical	Nekooie et al. (2021)

Conductive polymers are interesting materials for synthesizing nanocomposite photocatalysts by using their water-insoluble, nontoxic, easy, and inexpensive synthesis. Polyaniline is a leading conductive polymer, especially with metal oxide nanoparticles. Free electrons in the structure of zircon increase the photocatalytic effect. Nekooie et al. (2021) synthesized the polyaniline nanocomposite as they collected CuO/TiO_2. They achieved sonification by adding aniline and HCl to the CuO/TiO_2 solution, which they synthesized with the help of $NaBH_4$. They were vigorously mixed at 60°C for 3 h to achieve polymerization. Chitosan, a biopolymer, is an environmentally friendly, natural material against plant pathogens, and nanostructures created with metals attract great attention in the field of agriculture. Chitosan-supported Cu NPs, on the other hand, are cheap compared to other metals and an important nanostructured due to the nature of Cu. Saharan et al. (2015) synthesized the chitosan-supported Cu NPs by adding the Cu solution dropwise into the chitosan solution prepared based on ionic gelation with sodium tripolyphosphate. Also, studies have shown that ascorbic acid and NaOH are added as capping agents (Usman et al., 2012).

To increase the effects of photocatalysts, natural materials with high porosity are used as supporting materials (Tomul et al., 2016). Castañeda-Juárez et al. (2019) synthesized TiO_2-doped Cu nanoparticles using the photo/electrochemical-thermal method. They deposited copper on clinoptilolite with 0.5–1 A current intensity under UV light in the electrochemical cell, where copper was used as a sacrificial electrode. As an example of the wet chemical method, De Andrade, et al. (2020) synthesized zeolite-supported Cu by calcinating the mixed solution of zeolite and copper nitrate at 500°C.

3 Applications of Cu NPs in agrochemical remediation

Agrochemicals are chemicals used in the agricultural field to obtain more products. Among these, biodegradable pesticides that are passed as emerging pollutants remain in nature for many years without degradation. In addition, emerging man-made compounds, which reaches groundwater, can mix with the soil through irrigation water and adsorbed by the plants. The most common methods for removing agrochemicals are adsorption and degradation via the use of photocatalysts. The use of nanoparticles in adsorption and degradation is advantageous due to their thermal resistance and large and reactive surface areas. The use of nanoparticles against pathogenic microorganisms in the agricultural field is one of the most researched topics over the past few years. In this section, antimicrobial applications of Cu NPs and their use against emerging compounds are discussed.

3.1 Antimicrobial applications

The fact that infections by pathogenic microorganisms have caused significant losses in agricultural products in the past has led researchers to develop a series of chemical agents to prevent this situation. It is important to produce low-cost materials that

do not cause permanent pollution, have low toxicity, are safe, and easy to use, both for nature and for humans and animals. In this regard, copper has been applied for the first time in 1885 (Lamichhane et al., 2018), but the accumulation of copper in the soil causes long-term pollution, and it also mixes with groundwater and reduces water quality.

The properties of micron-sized nanoparticles improve especially when they are synthesized as nano and quantum dot (QDs), increasing the catalytic effect. The small size and high surface area of the nanoparticles enable them to penetrate microbial membranes more effectively, allowing them to have higher antibacterial activity than particles of micron sizes (Lamichhane et al., 2018). The synthesized Cu NPs and nanostructures were reported to be effective against phytopathogenic fungi and also for use as possible fungicide in several studies. It is also stated that they could be utilized in fungicide formulations to prepare new pesticides. Asghar et al. (2018) reported the effective antifungal activity of Cu NPs against *Aspergillus flavus* and *Aspergillus parasiticus* fungal species. Mahapatra et al. (2008) investigated their antimicrobial effect on pathogenic bacteria such as, *Pseudomonas aeruginosa, and Salmonella paratyphi*, which they synthesized with the wet chemical method. They also reported that CuO NPs passes through bacterial cell membrane and kills the bacteria by damaging their vital enzymes. Azam et al. (2012) investigated the effects of CuO nanoparticles of different sizes against Gram-negative *(E. coli and P. aeruginosa)* and Gram-positive bacteria *(B. subtilis* and *S. aureus)*. They reported that the inhibitory property of Cu NPs against the aforementioned bacteria depends on particle size and concentrations. They stated that 20-nm Cu NPs, the lowest particle size they synthesized, limited the growth of bacteria by passing through the pores of the bacteria. Antibacterial activity is not still fully established (Jayaramudu et al., 2021), however, another mechanism that is thought to be effective is by producing reactive oxygen species (ROS), inhibiting DNA replication and amino acid synthesis by microorganisms (Pelgrift and Friedman, 2013; Dizaj et al., 2014; Román et al., 2020; Jayaramudu et al., 2021). Fig. 2 shows possible removal mechanisms of Cu-based nanostructures.

Chitosan, a natural hydrophilic polysaccharide, is an important biodegradable substance investigated in terms of antipathogenic and seed preparation due to its antimicrobial activity. They have advantages such as being biodegradable, nontoxic to humans, and having a wide antifungal activity (Brunel et al., 2013; Saharan et al., 2015, Saharan et al., 2013). Research on metal nanoparticles with high surface area and smaller particle sizes supported with chitosan has taken off recently. The fact that chitosan is biodegradable makes it an important carrier for metal nanoparticles. Brunel et al. (2013) reported that chitosan and Cu NPs have a synergistic effect in inhibiting *Fusarium graminearum*. Similarly, Saharan et al. (2015) reported in their study that chitosan-supported Cu NPs have both high antifungal activity and accelerated the growth of tomato seedlings against phytopathogenic fungi. They reported that when chitosan-supported Cu NPs were added at a concentration of 0.12%, they inhibited the spore germination of *Alternaria solani* and *Fusarium oxysporum* fungi by 61.5% and 83%, respectively.

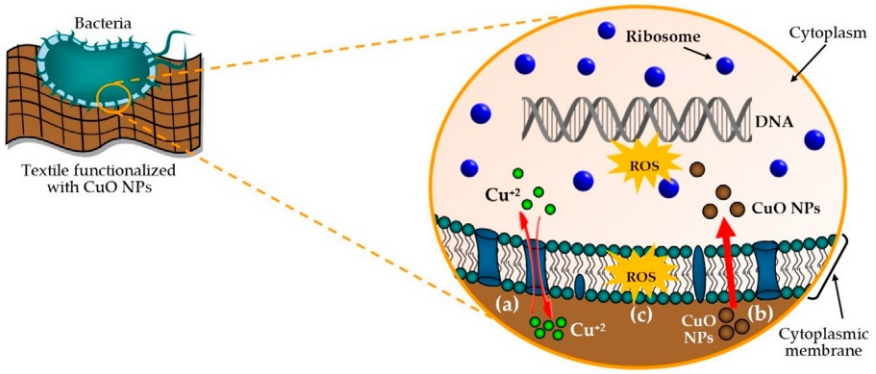

FIG. 2

Diagrammatic representation of the mechanisms of the antimicrobial activity of textile materials functionalized with CuO NPs: (A) release of copper ions, (B) contact of CuO NPs with bacteria, and (C) reactive oxygen species.

Reprinted from the reference Román, L.E., Gomez, E.D., Solís, J.L., Gómez, M.M., 2020. Antibacterial cotton fabric functionalized with copper oxide nanoparticles. Molecules 25(24), 5802. with permission from MDPI Publisher, Licensee MDPI, Basel, Switzerland. This article is an open-access article distributed under the terms and conditions of the Creative Commons Attribution (CC BY) license (http://creativecommons.org/licenses/by/4.0/).

3.2 Adsorption and photocatalytic applications

The contamination of aquifers with agricultural chemicals poses a serious threat to public health and the environment. Pesticides are the high percentage of persistent organic pollutants (POPs) whose use and environmental releases are prohibited by the Stockholm Convention, which entered into force in 2004 (Ulucan-Altuntas and Debik, 2020). POPs added to the main list are increasing with the meetings held every year. Among the first pesticides included in the list are DDT and its derivatives, which is an insecticide widely, used worldwide. Ortíz and Velasco (2019) investigated soil degradation of DDT derivatives, endrin, and endosulfan with nano-zero valent iron-copper (Fe/Cu) nanoparticles in their study. They stated that the presence of Cu NPs for DDT derivatives DDD, DDE, and endrin increased the degradation efficiency from 8 to 4 days. Another organochlorine compound limited by the Stockholm convention is heptachlor. Heptachlor is a toxic component and is still found in surface waters, groundwater, and soil, which was important for use in agricultural areas before it was banned. Mahmoud et al. (2020) studied the degradation of heptachlor with Fe/Cu nanoparticles in 30 min with a degradation efficiency of 99.3%. Similarly, atrazine, detected in groundwater, was a herbicide used before it was banned in 2004 to prevent the broadleaf unwanted plant weeds. Santacruz-Chávez et al. (2015) determined that they achieved 60% atrazine mineralization with the Cu/TiO_2 nanoparticle they synthesized. Parada et al. (2019) reported in their study on atrazine degradation that atrazine dissipation in sandy loam soil decreased with the presence of Cu NPs.

Kalidhasan et al. (2017) mentioned the improvement in the degradation of atrazine with the smaller size of Cu NPs size. They demonstrated atrazine degradation in an aqueous environment with the addition of hydrogen peroxide by 90% degradation in 30 min and 99% degradation in less than 1 h. In the study investigating the degradation of Chlorpyrifos, an insecticide with organophosphorus, with nano zero-valent iron-Cu (Fe/Cu) nanoparticles, it is stated that 90% degradation is achieved and 12.2% chloride is removed (Graça et al., 2020). Manjari et al. (2020) synthesized silver (Ag)-Cu-doped ZnO by green synthesis method to use as a catalyst to degrade 4-nitrophenol, which is used in the manufacturing of fungicides and insecticides. They reported the synergistic effect of Ag and Cu nanoparticles doped on ZnO.

Perfluorooctanesulfonic acid (PFAS) is a man-made chemical and is another chemical that is prohibited by the Stockholm Convention due to its use and release caused by industries producing fire-fighting foam, Teflon pan, etc. Due to its mixing with underground and surface waters, it can be classified as an emerging agrochemical encountered in agricultural areas by irrigation water and soil. On the catalytic treatment of perfluorooctanoate (PFOA), which is the most common type, with Cu NPs, Lee et al. (2017) reported that 65% of the biomimetic reductive system was eliminated by producing extraordinary reactive radicals in the presence of titanium (III) citrate and vitamin B12. Zhao et al. (2018) investigated PFOA degradation in their study using Fe/Cu nanoparticles embedded carbon aerogel as a cathode in the electro-Fenton process. They reported that they almost completely remove PFOA as total organic carbon (TOC).

It is encountered in various studies in the literature that magnetic nanoparticles of copper ferrite ($CuFe_2O_4$), an alternative catalyst, are used as activators in advanced oxidation processes. Li et al. (2017) used copper ferrite used in persulfate activation for 4-nitrophenol removal and it was reported that it was degraded at a rate of 89% after 1 h reaction time. Various nanostructures produced with graphene and its derivatives (i.e., GO, rGO) are shown as promising composite catalysts. GO nanosheets have been used as a support material to increase the effect of copper ferrite and Zangiabadi et al. (2020) reported that imidacloprid was almost completely degraded with the GO/CdS-$CuFe_2O_4$. Imidacloprid, used as an alternative to lindane, is a toxic herbicide. Saharan et al. (2021) prepared CuO nanocomposite by carbon nanofibers (CNF) to investigate the ultrasonic-assisted degradation of a pesticide (dichlorophenoxyacetic acid) and reported higher than 90% degradation in 10 min.

Nekooie et al. (2021) investigated the novel copper oxide/titanium dioxide/polyaniline (CuO/TiO2/PANI) nanocomposite, which is a toxic pesticide in the aquatic environment, and stated that they achieved 95% degradation in 90 min under visible light. In addition, they proposed the scheme in Fig. 3 for chlorpyrifos degradation with this nanocomposite, which they synthesized for the *Z*-scheme photocatalytic mechanism. Accordingly, electrons produced under the light in CuO are transferred to HOMO orbitals in PANI, increasing the efficiency of photo-generated electrons and holes in PANI. This situation increases the superoxide reaction produced in the LUMO orbital of PANI. Besides, H_2O can react with the photo-generated holes of CuO and generate OH radicals, which is a strong oxidant that can react with

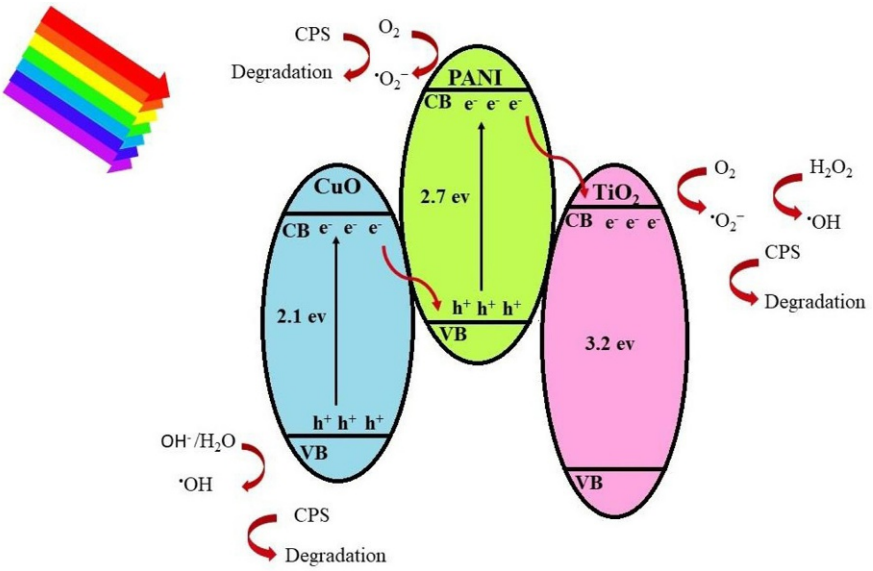

FIG. 3

Schematic representation of degradation mechanism of CuO and TiO_2 supported on PANI.
Reprinted from the reference of Nekooie, R., Shamspur, T., Mostafavi, A., 2021. Novel CuO/TiO2/PANI nanocomposite: Preparation and photocatalytic investigation for chlorpyrifos degradation in water under visible light irradiation. J. Photochem. Photobiol. A Chem. 407, 113038. (Copyright Elsevier).

chlorpyrifos and its by-products (Fig. 3). The studies of nanostructures of Cu NPs are summarized in Table 3 and show that these nanoparticles are a promising material, especially in persistent agrochemicals degradation.

4 Conclusion and future perspectives

The continuous and improper use of agrochemicals creates both environmental and health problems for humans and animals. There is a need for a greener approach to sustainable agriculture than persistent pesticides. Cu NPs have antimicrobial properties that can replace pesticides and remove the existing spread of recalcitrant agrochemicals. Synthesizing Cu NPs with green chemistry will reduce chemical wastes that will harm nature during production and will become a natural product when used for improvement. Besides, the use of chitosan as supporting material in the field of agroscience emerges to increase the antimicrobial effect of Cu NPs. Biopolymer property can be useful for sustainable agriculture. Furthermore, the spread of emerging agrochemicals can be degraded with the use of Cu NPs structures. To use nanoparticles on a large scale in agricultural applications, more data on the health problems that may arise are needed, when the nanoparticles are up taken by plants and their influence on groundwater.

Table 3 Reported applications of Cu NPs in agrochemical remediation.

Target pollutant	Cu-based nanoparticle	Removal efficiency	Process/removal mechanism	References
Aspergillus flavus *Aspergillus parasiticus*	Cu NPs	77.2% and 83.1% of aflatoxins reduction	Antifungal activity	Asghar et al. (2018)
Pseudomonas aeruginosa, *Salmonella paratyphi*	CuO		Antibacterial activity	Mahapatra et al. (2008)
E. coli and P. aeruginosa B. subtilis and S. aureus	CuO		Antibacterial activity	Azam et al. (2012)
Fusarium graminearum	Chitosan-supported Cu NPs		Antibacterial activity	Brunel et al. (2013)
Alternaria solani and *Fusarium oxysporum*	Chitosan-supported Cu NPs	61.5% and 83% inhibition with 0.12% of NPs	Antibacterial activity	Saharan et al. (2015)
Staphylococcus aureus *Aspergillus*	Cu NPs		Antifungal activity	Lee et al. (2017)
E. coli	CuO supported on polyethersulfone-cellulose acetate-silver oxide nanocomposite	82% bacterial growth inhibition in 24 h	Antibacterial activity	Gul et al. (2017)
Alternaria alterneta, *Rhizoctonia solani* *Aspergillus flavus*	Chitosan-supported Cu NPs	100% inhibition	Antibacterial activity	Kaur et al. (2015)
Staphylococcus aureus *Salmonella typhi*, *Escherichia coli*, *Klebsiella pneumonia* *Pseudomonas aeruginosa*	Mafenide acetate load Cu NPs	–	Antibacterial activity	Selvaraj et al. (2021)
Fusarium sp., *Aspergillus* sp., *Alternaria alternata*, *Pythium* sp., *Bacillus cereus*	Chitosan capped-copper nanobiocomposites	–	Antifungal activity	Mehta et al. (2021)
Bacillus cereus and Escherichia coli	Iodine-stabilized Cu nanoparticle chitosan composite	–	Antibacterial activity	Mallick et al. (2012)
4,4-Dichloro-diphenyl-trichloroethane (DDT)	Fe-Cu/SBA-15	92.3% at 4 h	Fenton-like catalytic reaction	Nguyen et al. (2018)
DDT and derivates	Fe/Cu bimetallic nanoparticle	Degradation efficiency increased from 8 days to 4 days (soil)	Photocatalytic	Ortíz and Velasco (2019)

Continued

Table 3 Reported applications of Cu NPs in agrochemical remediation—cont'd

Target pollutant	Cu-based nanoparticle	Removal efficiency	Process/removal mechanism	References
2,4-Dichlorophenol	$Cu_2(OH)PO_4$/rGO	87.1% in 6 h	Photocatalytic activity under infrared light	Zhang et al. (2018)
Heptachlor	Fe/Cu bimetallic nanoparticle	%99.3 in 30 min (aqueous)		Mahmoud et al. (2020)
Atrazine	Cu NPs	99% in less than 1 h (aqueous)	Photocatalytic	Kalidhasan et al. (2017)
Atrazine	Cu NPs	(Soil)	Photocatalytic activity	Parada et al. (2019)
Atrazine	Cu/TiO_2	60% (aqueous)	Photocatalytic activity	Santacruz-Chávez et al. (2015)
Atrazine	$Cu\text{-}BaTiO_3$	100% in 40 min	Photocatalytic activity	Basaleh and Mohamed (2020)
Chlorpyrifos	Fe/Cu	90%		Graça et al. (2020)
Perfluorooctanoate	Cu NPs	65% of PFOA	Adsorption and photocatalytic activity	Lee et al. (2017)
Perfluorooctanoate	Fe/Cu	(TOC) removal (88%–99%) in 240 min	Electrocatalytic	Zhao et al. (2018)
p-Nitrophenol	$CuFe_2O_4$	89% in 1 h (aqueous)	Persulfate-activated catalytic oxidation	Li et al. (2017)
p-Nitrophenol	CuO supported on polyethersulfone-cellulose acetate-silver oxide nanocomposite	100% in 44 min	Catalytic activity	Gul et al. (2017)
p-Nitrophenol	Cu NPs supported on CNT	99.5% in 80 min (aqueous)	Catalytic activity	Li et al. (2020)
p-Nitrophenol	Cu NPs supported on pistachio shell	100% in 3 min	Photocatalytic activity	Taghizadeh and Rad-Moghadam (2018)
Dichlorophenoxyacetic acid	GO decorate $CuFe_2O_4$	90% in 10 min	Ultrasonic-assisted degradation	Zangiabadi et al. (2020)
Chlorpyrifos	CuO/TiO_2/PANI	95% in 90 min (aqueous)	Photocatalytic under visible light	Nekooie et al. (2021)
Nitrate	Fe/Pd/Cu	85%	Denitrification	Liu et al. (2014)
Nitrate	Fe/Cu	76% Flow 0.125 mm/s (140 min[a])	Denitrification	Mossa Hosseini et al. (2011)
Nitrogen	Cu/Pd supported on N-doped mesoporous carbon	91% in 30 h	Electrocatalytic nanodenitrification	Wang et al. (2020)

[a] *Values are calculated according to given data.*

References

Aktürk, M., Karabiberoğlu, Ş.U., Dursun, Z., 2018. Fabrication of Cu−CeO $_2$ coated multi-wall carbon nanotube composite electrode for simultaneous determination of guanine and adenine. Electroanalysis 30, 238–249.

ALOthman, Z.A., Badjah, A.Y., Alduhaish, O.M., Rathinam, K., Panglisch, S., Ali, I., 2021. Synthesis, characterization, kinetics and modeling studies of new generation pollutant keto-profen removal in water using copper nanoparticles. J. Mol. Liq. 323, 115075.

Asghar, M.A., Zahir, E., Shahid, S.M., Khan, M.N., Asghar, M.A., Iqbal, J., Walker, G., 2018. Iron, copper and silver nanoparticles: green synthesis using green and black tea leaves extracts and evaluation of antibacterial, antifungal and aflatoxin B1 adsorption activity. LWT—Food Sci. Technol. 90, 98–107.

Aslan, E., Akin, I., Patir, I.H., 2016. Enhanced hydrogen evolution catalysis based on cu nanoparticles deposited on carbon nanotubes at the liquid/liquid interface. ChemCatChem 8, 719–723.

Aygün, S., Cann, D., 2005. Hydrogen sensitivity of doped CuO/ZnO heterocontact sensors. Sens. Actuators B 106, 837–842.

Azam, A., Ahmed, A.S., Oves, M., Khan, M.S., Memic, A., 2012. Size-dependent antimicrobial properties of CuO nanoparticles against gram-positive and -negative bacterial strains. Int. J. Nanomedicine 7, 3527–3535.

Basaleh, A.S., Mohamed, R.M., 2020. Synthesis and characterization of Cu-BaTiO3 nanocomposite for atrazine remediation under visible-light radiation from wastewater. J. Mater. Res. Technol. 9, 9550–9558.

Bhattacharjee, A., Ahmaruzzaman, M., 2015. Facile synthesis of 2-dimensional CuO nanoleaves and their degradation behavior for Eosin y. Mater. Lett. 161, 20–25.

Biçer, M., Şişman, I., 2010. Controlled synthesis of copper nano/microstructures using ascorbic acid in aqueous CTAB solution. Powder Technol. 198, 279–284.

Boruban, C., Esenturk, E.N., 2018. Activated carbon-supported CuO nanoparticles: a hybrid material for carbon dioxide adsorption. J. Nanopart. Res. 20, 1–9.

Brunel, F., El Gueddari, N.E., Moerschbacher, B.M., 2013. Complexation of copper(II) with chitosan nanogels: toward control of microbial growth. Carbohydr. Polym. 92, 1348–1356.

Cabir, B., Yurderi, M., Caner, N., Agirtas, M.S., Zahmakiran, M., Kaya, M., 2017. Methylene blue photocatalytic degradation under visible light irradiation on copper phthalocyanine-sensitized TiO2 nanopowders. Mater. Sci. Eng. B Solid-State Mater. Adv. Technol. 224, 9–17.

Castañeda-Juárez, M., Martínez-Miranda, V., Almazán-Sánchez, P.T., Linares-Hernández, I., Santoyo-Tepole, F., Vázquez-Mejía, G., 2019. Synthesis of TiO 2 catalysts doped with Cu, Fe, and Fe/Cu supported on clinoptilolite zeolite by an electrochemical-thermal method for the degradation of diclofenac by heterogeneous photocatalysis. J. Photochem. Photobiol. A Chem. 380, 111834.

Chauhan, N., Narang, J., Rawal, R., Pundir, C.S., 2011. A highly sensitive non-enzymatic ascorbate sensor based on copper nanoparticles bound to multi walled carbon nanotubes and polyaniline composite. Synth. Met. 161, 2427–2433.

Che, Y., Pang, H., Li, H., Yang, L., Fu, X., Liu, S., Ding, L., Hou, J., 2019. Microwave-assisted fabrication of copper-functionalized carbon quantum dots for sensitive detection of histidine. Talanta 196, 442–448.

Chouhan, D., Mandal, P., 2021. Applications of chitosan and chitosan based metallic nanoparticles in agrosciences-A review. Int. J. Biol. Macromol. 166, 1554–1569.

de Andrade, T.S., Souza, M.M.V.M., Manfro, R.L., 2020. Hydrogenolysis of glycerol to 1,2-propanediol without external H2 addition in alkaline medium using Ni-Cu catalysts supported on Y zeolite. Renew. Energy 160, 919–930.

Dharmadasa, R., Jha, M., Amos, D.A., Druffel, T., 2013. Room temperature synthesis of a copper ink for the intense pulsed light sintering of conductive copper films. ACS Appl. Mater. Interfaces 5, 13227–13234.

Di, L., Zhang, X., Xu, Z., 2014. Preparation of copper nanoparticles using dielectric barrier discharge at atmospheric pressure and its mechanism. Plasma Sci. Technol. 16, 41–44.

Di, L., Xu, W., Zhan, Z., Zhang, X., 2015. Synthesis of alumina supported Pd-Cu alloy nanoparticles for CO oxidation via a fast and facile method. RSC Adv. 5, 71854–71858.

Di, L.B., Duan, D.Z., Park, D.W., Ahn, W.S., Lee, B.J., Zhang, X.L., 2017. Cold plasma for synthesizing high performance bimetallic PdCu catalysts: effect of reduction sequence and Pd/Cu atomic ratios. Top. Catal. 60, 925–933.

Dizaj, S.M., Lotfipour, F., Barzegar-Jalali, M., Zarrintan, M.H.K. Adibkia., 2014. Antimicrobial activity of the metals and metal oxide nanoparticles. Mater. Sci. Eng. C, 278–284. https://doi.org/10.1016/j.msec.2014.08.031.

Dolgikh, L.Y., Pyatnitskii, Y.I., Reshetnikov, S.I., Deinega, I.V., Staraya, L.A., Moroz, É.M., Strizhak, P.E., 2011. Effect of crystalline modification of the support on the reduction and catalytic properties of Cu/ZrO2 catalysts in the steam reforming of bioethanol. Theor. Exp. Chem. 47, 324–330.

Dulta, K., Gözde, A.K., Chauhan, P., Chauhan, P.K., 2021. Biogenic production and characterization of CuO nanoparticles by Carica papaya leaves and its biocompatibility applications. J. Inorg. Organomet. Polym. Mater. 31, 1846–1857.

El-Berry, M.F., Sadeek, S.A., Abdalla, A.M., Nassar, M.Y., 2020. Facile, controllable, chemical reduction synthesis of copper nanostructures utilizing different capping agents. Inorg. Nano-Met. Chem. 51, 1418–1430.

Fakhri, P., Jaleh, B., Nasrollahzadeh, M., 2014. Synthesis and characterization of copper nanoparticles supported on reduced graphene oxide as a highly active and recyclable catalyst for the synthesis of formamides and primary amines. J. Mol. Catal. A Chem. 383–384, 17–22.

Graça, C.A.L., Mendes, M.A., Teixeira, A.C.S.C., de Velosa, A.C., 2020. Anoxic degradation of chlorpyrifos by zerovalent monometallic and bimetallic particles in solution. Chemosphere 244, 125461.

Gul, S., Rehan, Z.A., Khan, S.A., Akhtar, K., Khan, M.A., Khan, M.I., Rashid, M.I., Asiri, A.M., Khan, S.B., 2017. Antibacterial PES-CA-Ag2O nanocomposite supported cu nanoparticles membrane toward ultrafiltration, BSA rejection and reduction of nitrophenol. J. Mol. Liq. 230, 616–624.

Issaabadi, Z., Nasrollahzadeh, M., Sajadi, S.M., 2017. Green synthesis of the copper nanoparticles supported on bentonite and investigation of its catalytic activity. J. Clean. Prod. 142, 3584–3591.

Jahan, I., Erci, F., Isildak, I., 2020. Facile microwave-mediated green synthesis of non-toxic copper nanoparticles using Citrus sinensis aqueous fruit extract and their antibacterial potentials. J. Drug Delivery Sci. Technol. 61, 102172.

Jayaramudu, T., Varaprasad, K., Reddy, K.K., Pyarasani, R.D., Akbari-Fakhrabadi, A., Amalraj, J., 2020. Chitosan-pluronic based Cu nanocomposite hydrogels for prototype antimicrobial applications. Int. J. Biol. Macromol. 143, 825–832.

Jayaramudu, T., Varaprasad, K., Pyarasani, R.D., Reddy, K.K., Akbari-Fakhrabadi, A., Carrasco-Sánchez, V., Amalraj, J., 2021. Hydroxypropyl methylcellulose-copper

nanoparticle and its nanocomposite hydrogel films for antibacterial application. Carbohydr. Polym. 254, 117302.
Jiang, W., Yatsui, K., 1998. Pulsed wire discharge for nanosize powder synthesis. IEEE Trans. Plasma Sci. 26, 1498–1501.
Kalidhasan, S., Ben-Sasson, M., Dror, I., Carmieli, R., Schuster, E.M., Berkowitz, B., 2017. Oxidation of aqueous organic pollutants using a stable copper nanoparticle suspension. Can. J. Chem. Eng. 95, 343–352.
Kaur, P., Thakur, R., Barnela, M., Chopra, M., Manuja, A., Chaudhury, A., 2015. Synthesis, characterization and *in vitro* evaluation of cytotoxicity and antimicrobial activity of chitosan-metal nanocomposites. J. Chem. Technol. Biotechnol. 90, 867–873.
Keihan, A.H., Veisi, H., Veasi, H., 2017. Green synthesis and characterization of spherical copper nanoparticles as organometallic antibacterial agent. Appl. Organomet. Chem. 31, e3642.
Khan, N.A., Hasan, Z., Min, K.S., Paek, S.M., Jhung, S.H., 2013. Facile introduction of Cu+ on activated carbon at ambient conditions and adsorption of benzothiophene over Cu+/ activated carbon. Fuel Process. Technol. 116, 265–270.
Khan, S.A., Noreen, F., Kanwal, S., Iqbal, A., Hussain, G., 2018. Green synthesis of ZnO and Cu-doped ZnO nanoparticles from leaf extracts of Abutilon indicum, Clerodendrum infortunatum, Clerodendrum inerme and investigation of their biological and photocatalytic activities. Mater. Sci. Eng. C 82, 46–59.
Kim, K., Chaudhari, K.N., Kim, S., Kim, Y., Shin, K.S., 2021. Facile single-step synthesis of Cu-rGO nanocomposite through simultaneous reduction process and its peroxidase mimic activity. J. Ind. Eng. Chem. 95, 388–396.
Kokorekin, V.A., Gamayunova, A.V., Yanilkin, V.V., Petrosyan, V.A., 2017. Mediated electrochemical synthesis of copper nanoparticles in solution. Russ. Chem. Bull. 66, 2035–2043.
Kumar, S., Saini, D., Lotey, G.S., Verma, N.K., 2011. Electrochemical synthesis of copper nanowires in anodic alumina membrane and their impedance analysis. Superlattice. Microst. 50, 698–702.
Lagrow, A.P., Sinatra, L., Elshewy, A., Huang, K.W., Katsiev, K., Kirmani, A.R., Amassian, A., Anjum, D.H., Bakr, O.M., 2014. Synthesis of copper hydroxide branched nanocages and their transformation to copper oxide. J. Phys. Chem. C 118, 19374–19379.
Lamichhane, J.R., Osdaghi, E., Behlau, F., Köhl, J., Jones, J.B., Aubertot, J.N., 2018. Thirteen decades of antimicrobial copper compounds applied in agriculture. A review. Agron. Sustain. Dev. 38, 28.
Lee, Y.C., Chen, Y.P., Chen, M.J., Kuo, J., Lo, S.L., 2017. Reductive defluorination of perfluorooctanoic acid by titanium(III) citrate with vitamin B12 and copper nanoparticles. J. Hazard. Mater. 340, 336–343.
Li, H., Liu, R., Liu, Y., Huang, H., Yu, H., Ming, H., Lian, S., Lee, S.T., Kang, Z., 2012. Carbon quantum dots/Cu 2O composites with protruding nanostructures and their highly efficient (near) infrared photocatalytic behavior. J. Mater. Chem. 22, 17470–17475.
Li, J., Ren, Y., Ji, F., Lai, B., 2017. Heterogeneous catalytic oxidation for the degradation of p-nitrophenol in aqueous solution by persulfate activated with CuFe2O4 magnetic nanoparticles. Chem. Eng. J. 324, 63–73.
Li, C.x., Huang, R.t., Shi, X.y., 2020. Biosynthesis of Cu nanoparticles supported on carbon nanotubes and its catalytic performance under different test conditions. J. Chem. Technol. Biotechnol. 95, 1511–1518.
Lin, Y.-G., Hsu, Y.-K., Chen, S.-Y., Lin, Y.-K., Chen, L.-C., Chen, K.-H., 2009. Nanostructured zinc oxide nanorods with copper nanoparticles as a microreformation catalyst. Angew. Chem. Int. Ed. Engl. 48, 7586–7590.

Liu, H., Guo, M., Zhang, Y., 2014. Nitrate removal by Fe/Pd/Cu nano-composite in groundwater. Environ. Technol. 35, 917–924.

Mahapatra, O., Bhagat, M., Gopalakrishnan, C., Arunachalam, K.D., 2008. Ultrafine dispersed CuO nanoparticles and their antibacterial activity. J. Exp. Nanosci. 3, 185–193.

Mahmoud, A.S., Ismail, A., Mostafa, M.K., Mahmoud, M.S., Ali, W., Shawky, A.M., 2020. Isotherm and kinetic studies for heptachlor removal from aqueous solution using Fe/Cu nanoparticles, artificial intelligence, and regression analysis. Sep. Sci. Technol. 55, 684–696.

Mallick, S., Sharma, S., Banerjee, M., Ghosh, S.S., Chattopadhyay, A., Paul, A., 2012. Iodine-stabilized Cu nanoparticle chitosan composite for antibacterial applications. ACS Appl. Mater. Interfaces 4, 1313–1323.

Manjari, G., Saran, S., Radhakrishanan, S., Rameshkumar, P., Pandikumar, A., Devipriya, S.P., 2020. Facile green synthesis of Ag–Cu decorated ZnO nanocomposite for effective removal of toxic organic compounds and an efficient detection of nitrite ions. J. Environ. Manage. 262, 110282.

Mehta, M.R., Mahajan, H.P., Hivrale, A.U., 2021. Green synthesis of chitosan capped-copper nano biocomposites: synthesis, characterization, and biological activity against plant pathogens. Bionanoscience 11, 417–427. https://doi.org/10.1007/s12668-021-00823-8.

Moghimi-Rad, J., Zabihi, F., Hadi, I., Ebrahimi, S., Isfahani, T.D., Sabbaghzadeh, J., 2010. Effect of ultrasound radiation on the size and size distribution of synthesized copper particles. J. Mater. Sci. 45, 3804–3811.

Mossa Hosseini, S., Ataie-Ashtiani, B., Kholghi, M., 2011. Nitrate reduction by nano-Fe/Cu particles in packed column. Desalination 276, 214–221.

Mott, D., Galkowski, J., Wang, L., Luo, J., Zhong, C.J., 2007. Synthesis of size-controlled and shaped copper nanoparticles. Langmuir 23, 5740–5745.

Murai, K., Watanabe, Y., Saito, Y., Nakayama, T., Suematsu, H., Jiang, W., Yatsui, K., Shim, K.H., Niihara, K., 2007. Preparation of copper nanoparticles with an organic coating by a pulsed wire discharge method. J. Ceram. Process. Res. 8, 114–118.

Muthulingam, S., Greeshma, K.P., Uthirakumar, A.P., Thamizselvi, R., 2021. Surfactant-free synthesis of carbon quantum dots adorned copper oxide nanocomposites and their photocatalytic activity of commercial dyes beneath sunlight and Uv light sources. Environ. Nanotechnol. Monit. Manag. 15, 100427.

Nazri, N.A.A., Azeman, N.H., Luo, Y., Bakar, A.A.A., 2021. Carbon quantum dots for optical sensor applications: a review. Opt. Laser Technol. 139, 106928. https://doi.org/10.1016/j.optlastec.2021.106928.

Nekooie, R., Shamspur, T., Mostafavi, A., 2021. Novel CuO/TiO2/PANI nanocomposite: preparation and photocatalytic investigation for chlorpyrifos degradation in water under visible light irradiation. J. Photochem. Photobiol. A Chem. 407, 113038.

Nguyen, T.T., Le, G.H., Le, C.H., Nguyen, M.B., Quan, T.T.T., Pham, T.T.T., Vu, T.A., 2018. Atomic implantation synthesis of Fe-Cu/SBA-15 nanocomposite as a heterogeneous Fenton-like catalyst for enhanced degradation of DDT. Mater. Res. Express 5, 115005. https://doi.org/10.1088/2053-1591/aadce1.

Onder Erguven, G., Tatar, Ş., Serdar, O., Yildirim, N.C., 2021. Evaluation of the efficiency of chlorpyrifos-ethyl remediation by Methylobacterium radiotolerans and Microbacterium arthrosphaerae using response of some biochemical biomarkers. Environ. Sci. Pollut. Res. 28, 2871–2879.

Ortíz, I., Velasco, A., 2019. Degradation of DDT, endrin, and endosulfan in polluted-soils by zero-valent iron (Fe0) and zero-valent iron-copper (Fe0-Cu0) treatments. Rev. Mex. Ing. Quim. 18, 875–888.

Panzeri, G., Dell'Oro, R., Sansotera, M., Marchionna, S., Parravicini, J., Acciarri, M., Binetti, S., Magagnin, L., 2021. Design and characterization of a chloride-free organic copper solution: electrochemical synthesis of Zn/Cu/Sn precursor stack for CZTS-based photoconversion devices. Electrochim. Acta 372, 137857.

Parada, J., Rubilar, O., Diez, M.C., Cea, M., Sant'Ana da Silva, A., Rodríguez-Rodríguez, C.E., Tortella, G.R., 2019. Combined pollution of copper nanoparticles and atrazine in soil: effects on dissipation of the pesticide and on microbiological community profiles. J. Hazard. Mater. 361, 228–236.

Pelgrift, R.Y., Friedman, A.J., 2013. Nanotechnology as a therapeutic tool to combat microbial resistance. Adv. Drug Deliv. Rev. 65, 1803–1815.

Pham, L.Q., Sohn, J.H., Kim, C.W., Park, J.H., Kang, H.S., Lee, B.C., Kang, Y.S., 2012. Copper nanoparticles incorporated with conducting polymer: effects of copper concentration and surfactants on the stability and conductivity. J. Colloid Interface Sci. 365, 103–109.

Ren, G., Hu, D., Cheng, E.W.C., Vargas-Reus, M.A., Reip, P., Allaker, R.P., 2009. Characterisation of copper oxide nanoparticles for antimicrobial applications. Int. J. Antimicrob. Agents 33, 587–590.

Román, L.E., Gomez, E.D., Solís, J.L., Gómez, M.M., 2020. Antibacterial cotton fabric functionalized with copper oxide nanoparticles. Molecules 25 (24), 5802.

Sabbaghan, M., Beheshtian, J., Niazmand Liarjdame, R., 2015. Preparation of Cu2O nanostructures by changing reducing agent and their optical properties. Mater. Lett. 153, 1–4.

Saharan, V., Mehrotra, A., Khatik, R., Rawal, P., Sharma, S.S., Pal, A., 2013. Synthesis of chitosan based nanoparticles and their in vitro evaluation against phytopathogenic fungi. Int. J. Biol. Macromol. 62, 677–683.

Saharan, V., Sharma, G., Yadav, M., Choudhary, M.K., Sharma, S.S., Pal, A., Raliya, R., Biswas, P., 2015. Synthesis and in vitro antifungal efficacy of Cu-chitosan nanoparticles against pathogenic fungi of tomato. Int. J. Biol. Macromol. 75, 346–353.

Saharan, P., Kumar, V., Mittal, J., Sharma, V., Sharma, A.K., 2021. Efficient ultrasonic assisted adsorption of organic pollutants employing bimetallic-carbon nanocomposites. Sep. Sci. Technol. https://doi.org/10.1080/01496395.2020.1866608.

Santacruz-Chávez, J.A., Oros-Ruiz, S., Prado, B., Zanella, R., 2015. Photocatalytic degradation of atrazine using TiO2 superficially modified with metallic nanoparticles. J. Environ. Chem. Eng. 3, 3055–3061. Elsevier Ltd.

Sekar, K., Chuaicham, C., Balijapalli, U., Li, W., Wilson, K., Lee, A.F., Sasaki, K., 2021. Surfactant- and template-free hydrothermal assembly of Cu2O visible light photocatalysts for trimethoprim degradation. Appl. Catal. Environ. 284, 119741.

Selvaraj, S., Karuppaiah, A., Karthik, S., Sankar, V., 2021. Synthesis and toxicity assessment of copper-based nano composite cream: an approach to enhance the antibacterial effect of mafenide acetate. Inorg. Nano-Met. Chem. 51, 27–37.

Sharghi, H., Khalifeh, R., Doroodmand, M.M., 2009. Copper nanoparticles on charcoal for multicomponent catalytic synthesis of 1,2,3-triazole derivatives from benzyl halides or alkyl halides, terminal alkynes and sodium azide in water as a "green" solvent. Adv. Synth. Catal. 351, 207–218.

Shelke, S.N., Bankar, S.R., Mhaske, G.R., Kadam, S.S., Murade, D.K., Bhorkade, S.B., Rathi, A.K., Bundaleski, N., Teodoro, O.M.N.D., Zboril, R., Varma, R.S., Gawande, M.B., 2014. Iron oxide-supported copper oxide nanoparticles (nanocat-Fe-CuO): magnetically recyclable catalysts for the synthesis of pyrazole derivatives, 4-methoxyaniline, and ullmann-type condensation reactions. ACS Sustain. Chem. Eng. 2 (7), 1699–1706. https://doi.org/10.1021/sc500160f.

Shenoy, U.S., Shetty, A.N., 2013. A simple solution phase synthesis of copper nanofluid using single-step glucose reduction method. Synth. React. Inorg., Met.-Org., Nano-Met. Chem. 43, 343–348.

Shi, R., Wang, F., Tana, Li, Y., Huang, X., Shen, W., 2010. A highly efficient Cu/La2O3 catalyst for transfer dehydrogenation of primary aliphatic alcohols. Green Chem. 12, 108–111.

Shui, A., Zhu, W., Xu, L., Qin, D., Wang, Y., 2013. Green sonochemical synthesis of cupric and cuprous oxides nanoparticles and their optical properties. Ceram. Int. 39, 8715–8722.

Singh, M., Sinha, I., Premkumar, M., Singh, A.K., Mandal, R.K., 2010. Structural and surface plasmon behavior of Cu nanoparticles using different stabilizers. Colloids Surf. A Physicochem. Eng. Asp. 359, 88–94.

Song, P., Lei, Y., Hu, X., Wang, C., Wang, J., Tang, Y., 2020. Rapid one-step synthesis of carbon-supported platinum–copper nanoparticles with enhanced electrocatalytic activity via microwave-assisted heating. J. Colloid Interface Sci. 574, 421–429.

Songping, W., Shuyuan, M., 2006. Preparation of micron size copper powder with chemical reduction method. Mater. Lett. 60, 2438–2442.

Sreeju, N., Rufus, A., Philip, D., 2016. Microwave-assisted rapid synthesis of copper nanoparticles with exceptional stability and their multifaceted applications. J. Mol. Liq. 221, 1008–1021.

Subramanian, T., Pitchumani, K., 2012. Transfer hydrogenation of carbonyl compounds and carbon-carbon multiple bonds by zeolite supported Cu nanoparticles. Cat. Sci. Technol. 2, 296–300.

Taghizadeh, A., Rad-Moghadam, K., 2018. Green fabrication of cu/pistachio shell nanocomposite using Pistacia Vera L. hull: an efficient catalyst for expedient reduction of 4-nitrophenol and organic dyes. J. Clean. Prod. 198, 1105–1119.

Tomul, F., Turgut Basoglu, F., Canbay, H., 2016. Determination of adsorptive and catalytic properties of copper, silver and iron contain titanium-pillared bentonite for the removal bisphenol A from aqueous solution. Appl. Surf. Sci. 360, 579–593.

Ulucan-Altuntas, K., Debik, E., 2020. Dechlorination of dichlorodiphenyltrichloroethane (DDT) by Fe/Pd bimetallic nanoparticles: comparison with nZVI, degradation mechanism, and pathways. Front. Environ. Sci. Eng. 14, 17. https://doi.org/10.1007/s11783-019-1196-2.

Ulucan-Altuntas, K., Kuzu, S.L., 2019. Modelling and optimization of dye removal by Fe/Cu bimetallic nanoparticles coated with different Cu ratios. Mater. Res. Express 6, 1150a4.

Usman, M., Ibrahim, N., Shameli, K., Zainuddin, N., Yunus, W., 2012. Copper nanoparticles mediated by chitosan: synthesis and characterization via chemical methods. Molecules 17, 14928–14936.

Varank, G., Guvenc, S.Y., Çebi, A., Can Güven, E., 2020. Central composite design for the advanced treatment of biologically treated leachate nanofiltration concentrate using zero-valent copper and iron activated persulfate. Desalin. Water Treat. 208, 434–447.

Vaseem, M., Lee, K.M., Kim, D.Y., Hahn, Y.B., 2011. Parametric study of cost-effective synthesis of crystalline copper nanoparticles and their crystallographic characterization. Mater. Chem. Phys. 125, 334–341.

Vázquez-Vázquez, C., Bañobre-López, M., Mitra, A., López-Quintela, M.A., Rivas, J., 2009. Synthesis of small atomic copper clusters in microemulsions. Langmuir 25, 8208–8216.

Wan, L., Zhou, Q., Wang, X., Wood, T.E., Wang, L., Duchesne, P.N., Guo, J., Yan, X., Xia, M., Li, Y.F., Jelle, A.A., Ulmer, U., Jia, J., Li, T., Sun, W., Ozin, G.A., 2019. Cu2O nanocubes with mixed oxidation-state facets for (photo)catalytic hydrogenation of carbon dioxide. Nat. Catal. 2, 889–898.

Wang, A., Chen, L., Xu, F., Yan, Z., 2014. In situ synthesis of copper nanoparticles within ionic liquid-in-vegetable oil microemulsions and their direct use as high efficient nanolubricants. RSC Adv. 4, 45251–45257.

Wang, J., Teng, W., Ling, L., Fan, J., Zhang, W.X., Deng, Z., 2020. Nanodenitrification with bimetallic nanoparticles confined in N-doped mesoporous carbon. Environ. Sci. Nano 7, 1496–1506.

Xiong, J., Wang, Y., Xue, Q., Wu, X., 2011. Synthesis of highly stable dispersions of nanosized copper particles using L-ascorbic acid. Green Chem. 13, 900–904.

Yu, L., Wan, G., Qin, Y., Wang, G., 2018. Atomic layer deposition assisted fabrication of high-purity carbon nanocoil for electrochemical energy storage. Electrochim. Acta 268, 283–294.

Zangiabadi, M., Saljooqi, A., Shamspur, T., Mostafavi, A., 2020. Evaluation of GO nanosheets decorated by CuFe2O4 and CdS nanoparticles as photocatalyst for the degradation of dinoseb and imidacloprid pesticides. Ceram. Int. 46, 6124–6128.

Zhang, H., Zhang, M., 2008. Synthesis of CuO nanocrystalline and their application as electrode materials for capacitors. Mater. Chem. Phys. 108, 184–187.

Zhang, C., Du, Z., Zhou, R., Xu, P., Dong, X., Fu, Y., Wang, Q., Su, C., Yan, L., Gu, Z., 2018. Cu2(OH)PO4/reduced graphene oxide nanocomposites for enhanced photocatalytic degradation of 2,4-dichlorophenol under infrared light irradiation. RSC Adv. 8, 3611–3618.

Zhao, H., Qian, L., Chen, Y., Wang, Q., Zhao, G., 2018. Selective catalytic two-electron O2 reduction for onsite efficient oxidation reaction in heterogeneous electro-Fenton process. Chem. Eng. J. 332, 486–498.

Zhao, K., Wang, J., Kong, W., Zhu, P., 2020. Facile green synthesis and characterization of copper nanoparticles by aconitic acid for catalytic reduction of nitrophenols. J. Environ. Chem. Eng. 8, 103517.

Zhao, R., Dong, W., Teng, J., Wang, Z., Wang, Y., Yang, J., Jia, Q., Chu, C., 2021. Activated charcoal supported copper nanoparticles: a readily available and inexpensive heterogeneous catalyst for the N-arylation of primary amides and lactams with aryl iodides. Tetrahedron 79, 131858.

Zhou, L., Wang, S., Ma, H., Ma, S., Xu, D., Guo, Y., 2015. Size-controlled synthesis of copper nanoparticles in supercritical water. Chem. Eng. Res. Des. 98, 36–43.

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CHAPTER

Copper-based metal-organic framework for environmental applications 28

Alviya Sultana[a], Rishabh Anand Omar[b], Neetu Talreja[c], Divya Chauhan[d], R.V. Mangalaraja[c], and Mohammad Ashfaq[c,e]

[a]*School of Sciences, Monash University, Subang Jaya, Malaysia*

[b]*Center for Environmental Science and Engineering, Indian Institute of Technology Kanpur, Kanpur, India*

[c]*Advanced Ceramics and Nanotechnology Laboratory, Department of Materials Engineering, Faculty of Engineering, University of Concepción, Concepción, Chile*

[d]*Department of Chemical and Biomedical Engineering, University of South Florida, Tampa, FL, United States*

[e]*School of Life Science, BS Abdur Rahaman Institute of Science and Technology, Chennai, India*

1 Introduction

Nowadays, the development of industrialization is continuously increasing with the increase in global population. The industrial by-products have pretentious the environments by perilous waste (heavy metal ions, dyes, and microorganism), dangerous gases, and smokes. Therefore, there is a need to remove such toxic compounds from the water system. In this context, nanomaterials have potential ability to remove various compounds using adsorption, incineration, and chemical oxidation. Numerous metals, metal oxides, and carbon-based materials [carbon nanotubes (CNTs), carbon nanofibers (CNFs), and activated carbon] have been used for various end applications including treatment of water from heavy metal ions, pharmaceutical compounds, sensors, dye, and killing or inhibiting bacteria. The CNTs and CNFs are extensively used in various applications such as drug delivery, wound healing, sensor, energy, and agriculture due to their extraordinary characteristics such as small size, high surface area, nontoxic, and easy functionalization (Afreen et al., 2020, 2018; Chauhan et al., 2020, 2021; Omar et al., 2019b, a; Ashfaq et al., 2019, 2016, 2017a, 2014, 2013, 2017b, 2018; Talreja et al., 2014, 2016, 2021; Singh et al., 2013; Tripathi et al., 2016; Kumar et al., 2018; Mustafa et al., 2011; Bhadauriya et al., 2018; Sasidharan et al., 2021). However, relatively difficult to produce uniform pore size was observed. In this context, metal-organic frameworks (MOFs) have the potential ability to resolve such associated issues.

The MOFs or porous coordination polymers or crystalline porous materials that are composed of clusters are interconnected with organic ligands. Fig. 1 shows the

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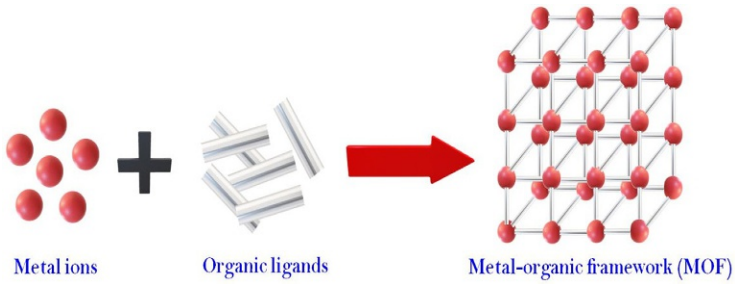

FIG. 1

A schematic illustration of MOFs.

schematic illustration of MOFs. The earliest application of the MOFs was heterogeneous catalyst due to its characteristics, mainly porosity. The MOFs is another class of porous materials that are similar to catalytic porous materials such as aluminosilicate zeolites. Zeolite was a commercially used catalyst due to strong, pure inorganic materials, and porosity that might be a suitable candidate under tremendous conditions, thereby enhancing catalytic activity. Moreover, the uniform pores and channels lead to their catalytic selectivity. However, the MOFs also have catalytic activity like zeolites. However, large surface area, uniform pore size distribution, and cavity size differ in various aspects in comparison to zeolites. (1) MOFs contain organic ligands, therefore can be easily synthesized in different varieties. (2) They have higher thermal stability in comparison to zeolites. (3) Most MOFs have permanent porosity like zeolites, whereas some collapse when a solvent is removed. The persistence porosity after solvent evaporation is essential for gas-phase catalysis or gas storage and gas separation applications. MOFs have intrinsic advantages because they can be easily tuned based on metal ions or organic ligands that provide an organic microenvironment and behave like enzymes. Moreover, an extraordinary active site might be created within the frameworks that are intricate from other methods (Lee et al., 2009; Yaghi et al., 1995; Baumann et al., 2019; Wang and Astruc, 2020; Liu et al., 2020; Parmar et al., 2021). Numerous synthesis processes of the Cu-MOFs using a variety of organic ligands such as ditropic, tritopic, tetratropic, hexatropic, octatopic, desymmetrized, N-heterocyclic linkers, and metallo have been used for the formation of MOFs. On the other hand, numerous catalysts such as Lewis acid catalysis (like alkene oxidation, and oxidation coupling), homogenous catalysts (like metallophophirin, Schiff base complexes, binapthyl complex), and MOFs encapsulated microcatalyst have developed different catalyst-based MOFs. The chemical and physical characteristics of the MOFs can be easily tuned based on metal ions and organic ligands that might be suitable for storage and release of Cu ions. Therefore, copper-based MOFs (Cu-MOFs) are excellent materials for various end applications like environmental remediation, gas separation, gas storage, medicine, wound healing, drug delivery, agriculture, and sensor. In recent times, MOFs have shown peroxidase-like enzymatic activities. For example, Fe-based MOFs (Fe-MOFs) have been used to detect ascorbic acid and

H_2O_2. Moreover, peroxidase-like enzymatic activities were also determined in another transitional metal-based catalyst. Moreover, the application of chromogenic reaction using MOFs is limited but still has gained great interest toward the development of colorimetric detection of metal ions, glucose, peroxidase, bacteria, ascorbic acid, and H_2O_2. In this context, Cu-MOFs have gained great interest due to their suitable candidate for various end applications. However, Cu-MOFs are likely unstable at physiological conditions that limit their direct applicability toward biological applications. In this context, the selection of ligands or the amount of ligands used in Cu-MOFs or different synthesis processes is very important to combat such associated issues. The incorporation of the Cu within MOFs provides high stability that shows synergistic effects toward high catalytic activity, thereby highly sensitive for the detection of heavy metal ions, bacteria, ascorbic acid, and gases. The interconnected porous frameworks within the MOFs provide a space for guest molecules, thereby increasing the host-guest interaction which further enhances the sensitivity. However, the sensitivity of analysts mainly depends on the binding ability of analysts and MOFs. Therefore, Cu-MOFs have the potential ability to remove various contaminants from water as well as sensing of these analysts (Wang et al., 2017). This book chapter summarizes the different methods for the synthesis of Cu-MOFs and their application of environmental remediation application. Finally, we will also discuss the other application of the Cu-MOFs and future prospects.

2 Heavy metal ions in the environments

Usually, the contaminations of heavy metal ions (HMI) through the precipitation or ion exchange within the soil that leach out into the water bodies, subsequently reach into the human body. This HMI is nonbiodegradable that enhances different kinds of challenges for remediation (Kumar et al., 2011; Saraswat et al., 2012; Khare et al., 2013; Kumar and Talreja, 2019). For example, a study devoted HMI from the fingernail of the students of both children and adults with respect to the class. The data were determined by Fe, Cu, and Mg, and K that was present in the fingernails of the children. The study suggested that the HMI was present in the soil as well as fingernails of the children (Okoro et al., 2018). HMI has been identified as one of the leading issues in both terrestrial and water bodies. HMI is the solemn environmental pollution because of their toxic response. HMI pollutants were recognized as one of the foremost issues in both environments (terrestrial and aquatic). These contaminations become more complicated or challenging issues due to their toxicity, bioaccumulation, and diligence in natural conditions in the environments including human bodies. Numerous techniques such as adsorption, coprecipitation, ion exchange, membrane filtration, chemical precipitation, and electrodialysis have been used for the removal of HMI. Among all of them, the adsorption process is a widely used, simple, and economically viable process. Usually, MOFs remove HMI by using simple weak hydrogen bonding. Fig. 2 shows the schematic representation of the MOFs that easily remove HMI via a simple hydrogen process.

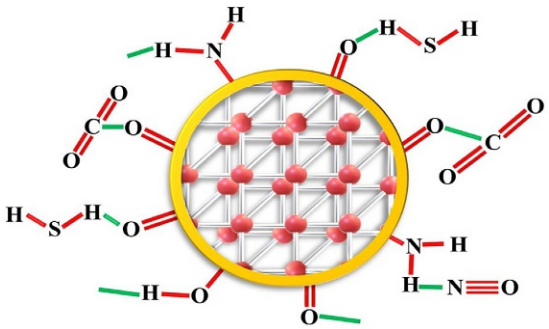

FIG. 2

A schematic representation of MOFs that shows adsorption over MOFs by weak hydrogen bonding.

3 Cu-MOFs in the removal of HMI

HMI was released into the environments that rose considerable menace to environments as well as public health because of their accumulation within the body. It is important to mention here, industrial activities play one of the main roles in the contamination of HMI into the environments, thereby HMI is a fastidious area of research, globally. Mining, coal combustion, disposal of the waste product are a few of the main sources for the contamination of HMI that releases into the surrounding soil, drinking water, water bodies, and rocks. Therefore, there is a need to develop newer materials or MOFs for the removal or recovery of the HMI from wastewater. As discussed earlier in the text, there are various processes used for the removal and recovery of the HMI. Among all of them, adsorption is simple, low cost, and easy process, thereby gains the considerable interest of the researchers. Numerous materials such as activated carbon, CNTs, CNFs, and MOFs have been used for the recovery and removal of HMI from water. Recently, MOFs have gained considerable interest from researchers due to their high stability, chemical reactivity, highly porous structure, large surface area, and are easily functionalized, thereby are extensively used in the removal and recovery of HMI from water. For example, Ke et al. synthesized thiol-based 3D-Cu-MOFs for the removal of Hg ions from water. The data suggested that the prepared thiol-based 3D-Cu-MOFs effectively removed Hg ions with high adsorption (~714 mg/g) ability. Moreover, the prepared thiol-based 3D-Cu-MOFs shows high sorption affinity toward Hg ions (Ke et al., 2011). Zou et al. synthesized Cu-based MOFs (HKUST-1) by microwave irradiation process for the selective removal of Pb, Cd, Hg, and Cr ions from water samples. The data suggested that the prepared HKUST-1 have high porosity, high surface area, and higher chemical stability. Moreover, the incorporation of polyoxometalate in HKUST-1 filled the pore of MOFs that creates stability of the MOFs. Interestingly, prepared HKUST-1 effectively adsorbed all HMI with high sorption ability (Zou et al., 2013). Chakraborty et al. synthesized Cu-based 3D-based MOFs (Cu-3D-MOFs) using a

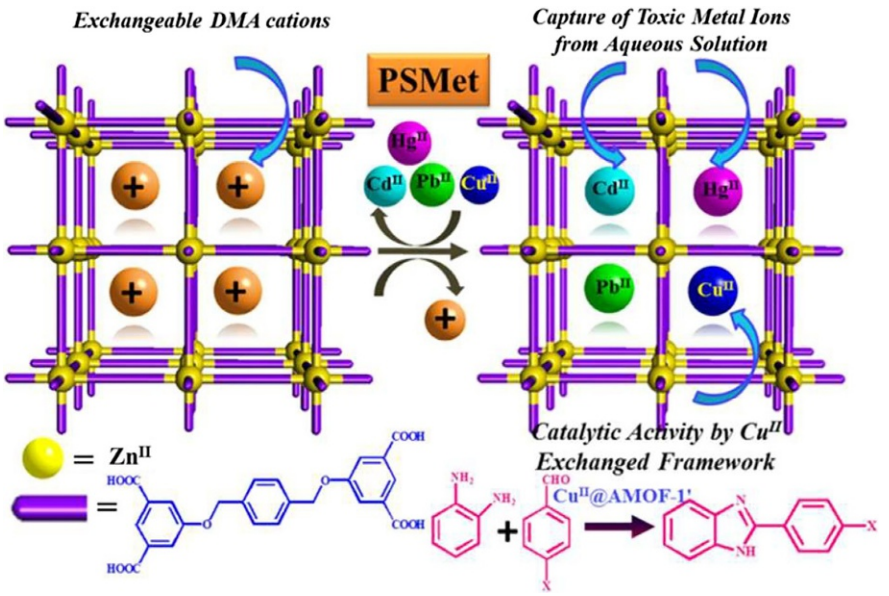

FIG. 3

A Schematic representation of Cu-3D-MOFs and its application to remove HMI.

The image was taken from Chakraborty, A., Bhattacharyya, S., Hazra, A., Ghosh, A. C. Maji, 2016. Postsynthetic metalation in an anionic MOF for efficient catalytic activity and removal of heavy metal ions from aqueous solution. Chem. Commun. 52(13), 2831–2834 with permission from The Royal Society of Chemistry 2016.

flexible tetracorboxylate linker for the removal of Hg, Pb, and Cd ions. The data suggested that the Cu-3D-MOFs show a new way of capturing HMI with high removal efficiency (Chakraborty et al., 2016). Fig. 3 shows the schematic representation of Cu-3D-MOFs and their application to remove HMI. Xu et al. synthesized Cu-MOFs using rigid ligands (5-aminoisopthalic acid) for the adsorption of volatile organic carbons. The data suggested that the prepared Cu-MOFs effectively capture formaldehyde gases (Xu et al., 2018). Ming et al. synthesized luminescent amino-functionalized Cu-MOFs using the solvothermal method for fluorescent detection of ferric ions. The data suggested that the prepared amino-functionalized Cu-MOFs have high fluorescent activity against ferric ions that have the potential ability for the detection of environmental pollution (Ming et al., 2019). Yusuff et al. synthesized Cu-MOFs using solvothermal process for the removal of Cd ions. The data suggested that the prepared Cu-MOFs have effectively removed Cd ions from water (Yusuff et al., 2019). Hasankola et al. synthesized two types of MOFs Cu-BTC and Zn-BTC for the removal of Pb ions. The data suggested that the Cu-BTC have better performance compared with that of the Zn-BTC (Hasankola et al., 2019). In general, the Cu-MOF-based materials have a high surface area, high porosity, and high chemical stability. Moreover, the adsorption of HMI onto the Cu-MOFs-based materials is due to the simple weak hydrogen bonding.

4 Cu-MOFs for the removal of dyes

Dyes are a synthetic substance that binds to material and imparts color to it. Chemically they are ionic, organic compounds with aryl rings. Dyes are distributed into an array of categories, based on their solubility and chemical properties. Among them, reactive dyes are the most popular and utilized ones due to their bonding with natural fibers. Besides, dyes are extensively utilized by plastic, paper, leather, printing, etc. industries (Sokolowska-Gajda et al., 1996). With the increasing use of cellulosic fibers, over 7×10^5 tons of dye is produced annually and the colorful effluents from these industries which carry, teratogenic and carcinogenic organic dye compounds with it, and are dumped into water bodies (Crini, 2006; Siddiqui et al., 2018; Allen et al., 2005). These compounds being resistant to oxidants and light, are hard to degrade naturally and persists in our ecosystem, posing serious threats to aquatic as well as human life (Tsai et al., 2007; Inthorn et al., 2004). Dye removal from wastewater could be performed in three classical ways, i.e., biological, physical, and chemical. The physical adsorption method for dye removal is generally considered the most efficient method because it quickly lowers the concentration of dissolved dyes. For this purpose, activated carbon is the most widely used adsorbent for the removal of dyes in an aqueous solution. Their popularity is due to its porosity and therefore, high adsorption capacities owing to its high surface area. Nevertheless, the use of activated carbon as an adsorbent for water/wastewater treatment remains a costly affair, due to its high cost and regeneration cost (Rattanapan et al., 2017; Zhao et al., 2013). Thus, low-cost and effective alternatives are of growing interest.

Amidst various developments, MOFs are emerging as a promising alternative for wastewater treatment, due to their high porosity, stability, and specific interaction with adsorbent. Moreover, as reported recently, they can be manipulated easily by tuning of light-harvesting properties of homo dinuclear Co(II) and Ni(II) complexes, in order to improve their photocatalytic properties and hence, their probable utilization in degradation of organic pollutants (Khan et al., 2019). Lately, Cu(II) metal-organic framework based on tetrazole ligand comprising [Cu(Metet)]n, synthesized by solvothermal method, has been reported to show tremendous adsorption capacity for methylene blue dye. Structural analysis of the material revealed its porous nature which removed the dye by carrying it away and absorbing it into the pores of the metal-organic framework. The linear structure of methylene blue made it easily accessible into the porous network, therefore the adsorption phenomenon of [Cu(Metet)] n (MOF-1) was immensely enhanced. Another metalloprphyrin Cu_5-cluster-based MOF referred to as LIFM-WUZ-3, showed astounding adsorption capacities for methylene blue and crystal violet. The material possessed a unique 2D + 3D or 3D anionic microporous structure, which is thermally and chemically quite stable. The structure possesses frl-type 3D MOF and a layered 2D hydrogen bond organic framework (HOF) intertwined together to form an anionic framework with 1D spindle-like channels. The presence of anionic frame selectively adsorbed cationic dyes from the aqueous solution, by the ion exchange process. Moreover, the presence of spindle-like channels allowed adsorption and separation of small-sized dye molecules. Since

two factors contribute to the adsorption process, i.e., porosity and ion exchange, the adsorption capacity ranks highest among such MOFs. Most interestingly, both the MOF adsorbent and the target dye could be recycled by the release of adsorbed dyes in saturated NaCl solution of CH_3CN (Wang et al., 2018). Another cationic dye, Malachite Green is reported to be removed effectively from aqueous solution by copper (II) MOF synthesized from 1,2,4,5-benzenetetracarboxylic acid and copper (II) acetate (Ebrahimi et al., 2017).

Besides porous materials, nonporous MOFs are also known widely for dyes removal through available free functional groups which are involved in H-bonding with dye molecules. The latest report announces the development of a novel Cu-MOF in conjunction with graphene oxide (GO) (Dadashi Firouzjaei et al., 2020). GO offers low-cost, high flexibility toward modification which makes it an efficacious candidate for drawing out various organic dyes of both cationic as well as anionic nature including azo-dyes such as Acid Orange 8 (AO8) and Direct Red 23 (DR23), from aqueous solutions (Khurana et al., 2017; Konicki et al., 2017). On account of abundant oxygen-containing functional groups on GO, the material possesses high reactivity toward other compounds (Zhu et al., 2010). Graphene oxide and Cu-MOF combination obtained by immobilizing Cu-MOF on GO via ultrasonication method (GO-Cu-MOF), exhibited enhanced adsorption capacity for methylene blue in comparison to Cu-MOF (Dadashi Firouzjaei et al., 2020). *p*-Nitrophenol (PNP), a toxic phenolic compound, was effectively removed by a copper-based MOF, i.e., HKUST-1(Andrew Lin and Hsieh, 2015). The high adsorption capacity of the MOF could be attributed to the affinity between planar aromatic rings of PNP and HKUST-1 as well as, presence of partially-charged central metal ion (Cu), which interacted with negatively charged oxygen from NO_2 of PNP via ionic interaction and covalent bonding (Andrew Lin and Hsieh, 2015). A water-stable and recyclable MOF (Cu-btc-1) which is $[Cu_2(Hbtc)_2(H_2O)_2(\mu_2\text{-}H_2O)]H_2O$, where H_3btc = benzene-1,2,4-tricarboxylic acid, is been reported for its excellent efficiency in separating methylene blue (MB) from methyl orange (MO) and rhodamine (Rh−B) in the aqueous phase. The underlying mechanism of Cu-btc-1 actions involves various interactions such as electrostatic attraction/repulsion, π–π interactions, H-bonding and weak Van der Waals interactions.

In general, capabilities, designing, tuneability, various interactions with adsorbents, as shown by present MOFs could open new directions toward a cleaner environment and flourishing aquatic life by removing hazardous materials from water/wastewater.

5 Cu-MOFs-based sensor for the detection of HMI

Researchers continue focusing on the development of ultrasensitive electrochemical sensors by using technological advancement in terms of design, and high conducting materials for a selective and sensitive sensor for HMI. In this context, various porous materials are modified by using transitional metals to enhance the electrical conductivity, high surface area, and biocompatibility. Moreover, a native enzyme was also

used for ultrasensitive detection of HMI. However, poor stability, time-consuming separation, and purification limit their applicability toward real-time applications. Therefore, there is a need to develop a novel catalyst that might behave like enzymes to enhance the electrochemical signal of sensitivity. In this regard, researchers continue looking toward newer mimetic catalysts with higher sensitivity, high stability, and excellent tunability compared with that of natural enzymes. For this, MOFs might be potential ability to resolve such issues associated with natural enzymes that catalyzed ascorbic acid, glucose, and H_2O_2. However, an appropriate selection of the metal ions might be necessary to enhance the catalytic performance or detection of HMI. Numerous Cu-MOFs have been developed and used for the detection of HMI. For example, Dong et al. synthesized 1,3,5-benzenetricarboxylic acid copper $[Cu_3(BTC)_2]$-based MOFs for the electrochemical detection 2,4-dichlorophenol. The data suggested that the prepared Cu-MOFs-based sensor have high sorption ability, extraordinary electron transfer, high sensitivity, high stability, and low detection limit (Dong et al., 2016). Li et al. synthesized Cu-MOFs-graphene composite for the detection of dihydroxybenzene isomers water. The data suggested that the prepared Cu-MOFs-graphene composite effectively detect hydroquinone and catechol from water (Li et al., 2018). Arul et al. synthesized size-controlled Cu-MOFs incorporated with graphene oxide (Cu-MOFs-GO) by using an ultrasonic-assisted approach for the electrochemical detection of nitride in water samples. The data suggested that the prepared Cu-MOFs-GO effectively detect nitride ions from the water sample (Arul et al., 2020). Singh et al. synthesized Cu-MOFs by using a simple solvothermal process for the electrochemical detection of Hg ions in tuna fish. The data suggested that the produce Cu-MOFs have exceptional characteristics in terms of structural, optical, and electrochemical, thereby effectively detects Hg ions from fish (Singh et al., 2020). Zhang et al. synthesized Cu-MOFs-based DNA sensor for electrochemical detection of Hg ions. The data suggested that the prepared Cu-MOFs-based DNA sensor acted as a mimetic catalyst. The produced Cu-MOFs-based DNA sensor is effectively used for the ultrasensitive detection of Hg ions. Fig. 4 shows graphical representation of the electrochemical sensor for the detection of Hg ions. The aforementioned studies suggested that the Cu-MOFs-based electrode materials might be advantageous for the detection of HMI as the Cu-MOFs behave like a mimetic enzyme that easily catalyze. Moreover, Cu-MOFs-based electrode materials provide higher stability as compared with that of natural enzymes.

6 Cu-MOFs-based sensor for the detection of bacteria

Bacterial infection is one of the leading causes of death in humans nowadays, thereby sensitive and selective detection of bacteria or pathogenic microorganism is a necessity to combat such infections related to bacteria. Usually, a culture-based process is used for the detection of microorganisms that might be cost-effective. However, a relatively time-consuming process and a skilled person are required. In this context, polymerase chain reaction (PCR) might be beneficial that have the advantage of low

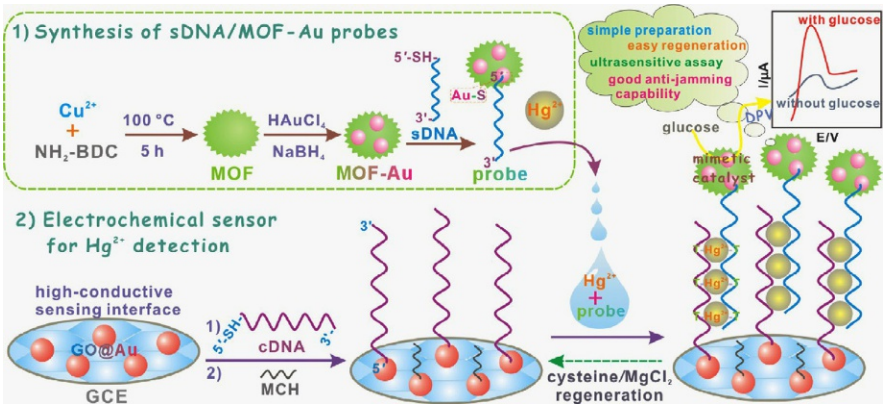

FIG. 4

Graphical representation of the electrochemical sensor for the detection of Hg ions.

Image reprinted from Zhang, X., Jiang, Y., Zhu, M., Xu, Y., Guo, Z., Shi, J., Han, E., Zou, X. Wang, 2020. Electrochemical DNA sensor for inorganic mercury(II) ion at attomolar level in dairy product using Cu(II)-anchored metal-organic framework as mimetic catalyst. Chem. Eng. J. 383, 123182 with the permission from© 2019 Elsevier B.V. All rights reserved.

detection limit and high sensitivity. However, PCR-based techniques require sophisticated instruments and also a professional person to perform the experiments that limit their applicability. Such associated issue might be resolved by using electrochemical, fluorescent, and colorimetric detection of pathogenic microorganism that has various advantageous like ultralow sensitivity, rapid, and accurate. Numerous studies suggested that Cu-MOFs have been used for the detection of microorganisms using electrochemical, fluorescent, and colorimetric-based sensors (François et al., 2010; Loesche et al., 1992; Wellinghausen et al., 2009; Cheng et al., 2016). For example, Wang et al. synthesized Cu-MOFs-based NPs by using a solvothermal process. The synthesized Cu-MOFs NPs were within the range of 550 nm. The data suggested that the prepared Cu-MOFs-based NPs showed peroxidase-like activity that catalyzed 3,3′,5,5′-tetramethylbenzidine to generate yellow color in the presence of H_2O_2. The enzymatic activity of the prepared Cu-MOFs-based NPs depends on the solution pH, temperature, and reaction time. The presence of the amine group on the surface of Cu-MOFs-based NPs facilitate the modification of microorganism (*S. aureus*) that changes the color (Wang et al., 2017). Gupta et al. synthesized Cu(BTC) PANI or Cu-MOFs for electrochemical sensing of *E. coli*. The prepared Cu(BTC) PANI-based framework effectively detects *E. coli* bacteria with low sensitivity 2 CFU/Ml (Gupta et al., 2019). Ren and his team synthesized Cu-MOFs loaded on chitosan film for the inhibition bacteria. The data suggested that the prepared Cu-MOFs loaded on chitosan film was effectively used for the inhibition of bacteria. The in vivo analysis suggested that the prepared Cu-MOFs loaded on chitosan film killed bacteria and promoted the regeneration of vessels (Ren et al., 2019). In general, the detection of bacteria using Cu-MOFs-based electrode materials mainly depend on

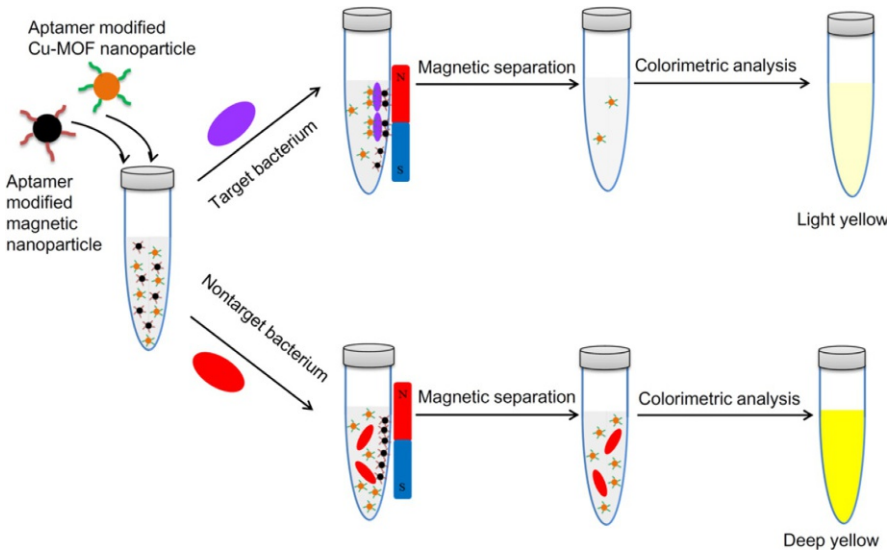

FIG. 5

Graphical representation of colorimetric detection of bacteria using Cu-MOFs.

The image was taken from Wang, S., Deng, W., Yang, L., Tan, Y., Xie, Q., Yao, S., 2017. Copper-based metal–organic framework nanoparticles with peroxidase-like activity for sensitive colorimetric detection of Staphylococcus aureus. ACS App. Mater. Interfaces, 9(29), 24440–24445 with the permission from American Chemical Society.

the three factors (1) conductivity of the electrodes, (2) surface functional group of electrode materials, and (3) mimetic behavior of electrode materials, thereby Cu-MOFs-based electrode materials efficiently detect bacteria even at a lower concentration (Fig. 5).

7 Cu-MOFs-based sensor for the detection of pharmaceutical compounds

The uses of antibiotics are increasing with the increasing number of infectious diseases, globally. The excessive use of antibiotics gains attention due to the presence of antibiotics in the wastewater. One of the major concerns of the researchers is that these antibiotics accumulate within the environments because of their unrelenting nature. The studies suggested that exposure to antibiotics affects the growth of microflora and fauna as well as human health. Therefore, there is the need to develop materials for the removal of antibiotics or pharmaceuticals compounds from water. Numerous studies have suggested that various Cu-based MOFs have been used for the removal or detection of antibiotics or pharmaceutical compounds from water. For example, Wang et al. synthesized Cu-MOFs (PDA/DMF) by using a

solvothermal process. The data suggested that the produced Cu-MOFs shows high peroxidase activity that easily detects dopamine from urine and pharmaceutical samples (Wang et al., 2019). Azhar et al. synthesized Cu-based MOFs (HKSUT-1) for the removal of sulfonamide antibiotics from wastewater. The data suggested that the prepared HKSUT-1 have a high adsorption ability (384 mg/g). The higher adsorption ability of HKSUT-1 materials was observed due to the π-π stacking, and hydrogen bonding (Azhar et al., 2016). Wu et al. synthesized magnetic Cu-based MOFs (Fe3O4/HKUST-1) for the removal of fluoroquinolone antibiotics. The data suggest that the Fe3O4/HKUST-1 shows high sorption ability, rapid kinetics, and can be easily separated from water. The higher sorption ability of Fe3O4/HKUST-1 is due to the presence of π-π stacking and hydrogen bonding (Wu et al., 2018). Tran et al. synthesized highly porous HKUST-1-based Cu-Cu_2O-CuO-C/Cu-MOFs for the removal of ciprofloxacin and tetracycline antibiotics from water. The data suggest that the HKUST-1-based Cu-Cu_2O-CuO-C/Cu-MOFs have high sorption ability. The higher sorption ability is due to the highly porous structure, presence of π-π stacking, and hydrogen bonding (Tran et al., 2020). Similarly, the data suggested that the Cu-MOF-based electrode materials might be effective against pharmaceutical compounds due to the highly porous structure, presence of π-π stacking, and hydrogen bonding. Table 1 shows different Cu-MOF-based materials for the removal and detection of analytes. The data suggest that the Cu-MOF-based materials show higher loading efficiency as well as lowest detection limit in different environmental pollutes.

8 Conclusion and prospects

In the summary, there is an alarming situation or exigency to control environmental pollutions like HMI, pharmaceuticals compounds, and bacterial infection. A pollutant like HMI comes from natural sources and contaminates groundwater as well as water bodies. The removals of these pollutants are necessary to provide safe drinking water and a healthy environment for society. Numerous materials such as activated carbon, CNTs, CNFs, and polymeric nanocomposite have been developed for the removal of these contaminants. Researchers are still searching for newer materials that have a uniform pore, high surface area, and high chemical stability. Recently, MOFs continuously gains interest because of the uniform pore, high surface area, high chemical stability, and mimetic behavior. Cu-MOFs are extensively used in various end applications especially in the removal and detection of environmental pollution. The adsorption of the pollutants onto the Cu-MOFs was observed mainly due to the highly porous structure, high surface area, and weak hydrogen bonding. Interestingly, Cu-MOFs-based electrode materials also show the sensitive and selective detection of environmental pollution due to the mimetic behavior of the materials. A lot of Cu-MOFs-based materials have been developed and many more remain to be developed for higher removal as well as the lowest detection limit of the environmental pollution.

Table 1 Different Cu-MOF-based materials for the removal and detection of analytes.

S.No.	Materials	Analysts	Detection method	Detection limit	References
1.8.	HKUST-1	Pb ions Cd ions Hg ions Cr ions	Adsorption	98.18 mg/g 32.45 mg/g 0.650 mg/g 38.25 mg/g	Zou et al. (2013)
2.	Cu-3D-MOFs	Hg ions Pb ions Cd ions	Adsorption	98.7% removal 97.6% removal 98.2% removal	Chakraborty et al. (2016)
3.	$[Cu_3(BTC)_2]$-based MOFs	2,4 Dichlorophenol	Electrochemical	0.4 to 1.0 μM	Dong et al. (2016)
4.	HKSUT-1	Sulfonamide	Adsorption	384 mg/g	Azhar et al. (2016)
5.	Cu-MOF-based NPs	*S. aureus*	Colorimetric	20 CFU/mL	Wang et al. (2017)
6.	Fe3O4/HKUST-1	Ciprofloxacin Norfloxacin	Adsorption	538 mg/g 513 mg/g	Wu et al. (2018)
7.	Cu-MOFs-graphene composite	Hydroquine and catechol	Electrochemical	1×10^{-6} to 1×10^{-7} M 5.9×10^{-7} to 3.3×10^{-7} M	Li et al. (2018)
8.	Cu-MOFs (PDA/DMF)	Dopamine	Colorimetric	0.169 mM	Wang et al. (2019)
9.	Amino functionalized Cu-MOFs	Ferric ions	Fluorescent	1.56 μM	Ming et al. (2019)
10.	Cu-MOFs	Hg ions	DNA sensor	0.1 aM–100 nM	Zhang et al. (2020)
11.	Cu-MOFs loaded on chitosan film	Bacteria	Local therapy	–	Ren et al. (2019)
12.	Cu-MOFs	Cd ions	Adsorption	219 mg/g	Yusuff et al. (2019)
13.	Cu-BTC Zn-BTC	Pb ions	Adsorption	333 mg/g 312 mg/g	Hasankola et al. (2019)
14.	Cu(BTC) PANI	*E. coli*	Electrochemical	2 CFU/mL	Gupta et al. (2019)
15.	Cu-MOFs	Hg ions	Electrochemical	0.1–50 nm	Singh et al. (2020)
16.	Cu-MOFs-GO	Nitride	Electrochemical	1.47 nM	Arul et al. (2020)
17.	HKUST-1-based Cu-Cu_2O-CuO-C	Ciprofloxacin Tetrcyclin	Adsorption	67.5 mg/g 112.25 mg/g	Tran et al. (2020)

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References

Afreen, S., Omar, R.A., Talreja, N., Chauhan, D., Ashfaq, M., 2018. Carbon-based nanostructured materials for energy and environmental remediation applications. In: Prasad, R., Aranda, E. (Eds.), Approaches in Bioremediation: The New Era of Environmental Microbiology and Nanobiotechnology. Springer International Publishing, Cham, pp. 369–392.

Afreen, S., Talreja, N., Chauhan, D., Ashfaq, M., 2020. Chapter 15—Polymer/metal/carbon-based hybrid materials for the detection of heavy metal ions. In: Abd-Elsalam, K.A. (Ed.), Multifunctional Hybrid Nanomaterials for Sustainable Agri-Food and Ecosystems. Elsevier, pp. 335–353.

Allen, S., Koumanova, B., Keir, D., 2005. Decolourozation of water/wastewater using adsorption (review). J. Univ. Chem. Technol. Metallurgy 40 (3), 175–192.

Andrew Lin, K.-Y., Hsieh, Y.-T., 2015. Copper-based metal organic framework (MOF), HKUST-1, as an efficient adsorbent to remove p-nitrophenol from water. J. Taiwan Inst. Chem. Eng. 50, 223–228.

Arul, P., Gowthaman, N.S.K., John, S.A., Lim, H.N., 2020. Ultrasonic assisted synthesis of size-controlled Cu-metal–organic framework decorated graphene oxide composite: sustainable electrocatalyst for the trace-level determination of nitrite in environmental water samples. ACS Omega 5 (24), 14242–14253.

Ashfaq, M., Singh, S., Sharma, A., Verma, N., 2013. Cytotoxic evaluation of the hierarchical web of carbon micronanofibers. Ind. Eng. Chem. Res. 52 (12), 4672–4682.

Ashfaq, M., Khan, S., Verma, N., 2014. Synthesis of PVA-CAP-based biomaterial in situ dispersed with Cu nanoparticles and carbon micro-nanofibers for antibiotic drug delivery applications. Biochem. Eng. J. 90, 79–89.

Ashfaq, M., Verma, N., Khan, S., 2016. Copper/zinc bimetal nanoparticles-dispersed carbon nanofibers: a novel potential antibiotic material. Mat. Sci. Eng. C 59, 938–947.

Ashfaq, M., Verma, N., Khan, S., 2017a. Carbon nanofibers as a micronutrient carrier in plants: efficient translocation and controlled release of Cu nanoparticles. Environ. Sci. Nano 4 (1), 138–148.

Ashfaq, M., Verma, N., Khan, S., 2017b. Highly effective Cu/Zn-carbon micro/nanofiber-polymer nanocomposite-based wound dressing biomaterial against the *P. aeruginosa* multi- and extensively drug-resistant strains. Mater. Sci. Eng. C 77, 630–641.

Ashfaq, M., Verma, N., Khan, S., 2018. Novel polymeric composite grafted with metal nanoparticle-dispersed CNFs as a chemiresistive non-destructive fruit sensor material. Mater. Chem. Phys. 217, 216–227.

Ashfaq, M., Talreja, N., Chuahan, D., Srituravanich, W., 2019. Carbon nanostructure-based materials: a novel tool for detection of Alzheimer's disease. In: Ashraf, G.M., Alexiou, A. (Eds.), Biological, Diagnostic and Therapeutic Advances in Alzheimer's Disease: Non-Pharmacological Therapies for Alzheimer's Disease. Springer Singapore, Singapore, pp. 71–89.

Azhar, M.R., Abid, H.R., Sun, H., Periasamy, V., Tadé, M.O., Wang, S., 2016. Excellent performance of copper based metal organic framework in adsorptive removal of toxic sulfonamide antibiotics from wastewater. J. Colloid Interface Sci. 478, 344–352.

Baumann, A.E., Burns, D.A., Liu, B., Thoi, V.S., 2019. Metal-organic framework functionalization and design strategies for advanced electrochemical energy storage devices. Commun. Chem. 2 (1), 86. 1-14.

Bhadauriya, P., Mamtani, H., Ashfaq, M., Raghav, A., Teotia, A.K., Kumar, A., Verma, N., 2018. Synthesis of yeast-immobilized and copper nanoparticle-dispersed carbon nanofiber-based diabetic wound dressing material: simultaneous control of glucose and bacterial infections. ACS Appl. Bio Mater. 1 (2), 246–258.

Chakraborty, A., Bhattacharyya, S., Hazra, A., Ghosh, A.C., Maji, T.K., 2016. Post-synthetic metalation in an anionic MOF for efficient catalytic activity and removal of heavy metal ions from aqueous solution. Chem. Commun. 52 (13), 2831–2834.

Chauhan, D., Afreen, S., Talreja, N., Ashfaq, M., 2020. Chapter 8—Multifunctional copper polymer-based nanocomposite for environmental and agricultural applications. In: Abd-Elsalam, K.A. (Ed.), Multifunctional Hybrid Nanomaterials for Sustainable Agri-Food and Ecosystems. Elsevier, pp. 189–211.

Chauhan, D., Talreja, N., Ashfaq, M., 2021. Chapter 13—Nanoadsorbents for wastewater remediation. In: Abd-Elsalam, K.A., Zahid, M. (Eds.), Aquananotechnology. Elsevier, pp. 263–280.

Cheng, D., Yu, M., Fu, F., Han, W., Li, G., Xie, J., Song, Y., Swihart, M.T., Song, E., 2016. Dual recognition strategy for specific and sensitive detection of bacteria using aptamer-coated magnetic beads and antibiotic-capped gold nanoclusters. Anal. Chem. 88 (1), 820–825.

Crini, G., 2006. Non-conventional low-cost adsorbents for dye removal: a review. Bioresour. Technol. 97 (9), 1061–1085.

Dadashi Firouzjaei, M., Akbari Afkhami, F., Rabbani Esfahani, M., Turner, C.H., Nejati, S., 2020. Experimental and molecular dynamics study on dye removal from water by a graphene oxide-copper-metal organic framework nanocomposite. J. Water Process Eng. 34, 101180.

Dong, S., Suo, G., Li, N., Chen, Z., Peng, L., Fu, Y., Yang, Q., Huang, T., 2016. A simple strategy to fabricate high sensitive 2,4-dichlorophenol electrochemical sensor based on metal-organic framework Cu3(BTC)2. Sens. Actuators B 222, 972–979.

Ebrahimi, A.K., Sheikhshoaie, I., Mehran, M., 2017. Facile synthesis of a new metal-organic framework of copper (II) by interface reaction method, characterization, and its application for removal of Malachite Green. J. Mol. Liq. 240, 803–809.

François, P., Scherl, A., Hochstrasser, D., Schrenzel, J., 2010. Proteomic approaches to study Staphylococcus aureus pathogenesis. J. Proteomics 73 (4), 701–708.

Gupta, A., Bhardwaj, S.K., Sharma, A.L., Kim, K.-H., Deep, A., 2019. Development of an advanced electrochemical biosensing platform for E. coli using hybrid metal-organic framework/polyaniline composite. Environ. Res. 171, 395–402.

Hasankola, Z.S., Rahimi, R., Safarifard, V., 2019. Rapid and efficient ultrasonic-assisted removal of lead(II) in water using two copper- and zinc-based metal-organic frameworks. Inorg. Chem. Commun. 107, 107474.

Inthorn, D., Singhtho, S., Thiravetyan, P., Khan, E., 2004. Decolorization of basic, direct and reactive dyes by pre-treated narrow-leaved cattail (*Typha angustifolia Linn.*). Bioresour. Technol. 94 (3), 299–306.

Ke, F., Qiu, L.-G., Yuan, Y.-P., Peng, F.-M., Jiang, X., Xie, A.-J., Shen, Y.-H., Zhu, J.-F., 2011. Thiol-functionalization of metal-organic framework by a facile coordination-based post-synthetic strategy and enhanced removal of Hg2+ from water. J. Hazard. Mater. 196, 36–43.

Khan, M.S., Khalid, M., Ahmad, M.S., Ahmad, M., Ashafaq, M., Rahisuddin, Arif, R., Shahid, M., 2019. Synthesis, spectral and crystallographic study, DNA binding and molecular docking studies of homo dinuclear Co(II) and Ni(II) complexes. J. Mol. Struct. 1175, 889–899.

Khare, P., Talreja, N., Deva, D., Sharma, A., Verma, N., 2013. Carbon nanofibers containing metal-doped porous carbon beads for environmental remediation applications. Chem. Eng. J. 229, 72–81.

Khurana, I., Saxena, A., Bharti, Khurana, J.M., Rai, P.K., 2017. Removal of dyes using graphene-based composites: a review. Water Air Soil Pollut. 228 (5), 180.

Konicki, W., Aleksandrzak, M., Moszyński, D., Mijowska, E., 2017. Adsorption of anionic azo-dyes from aqueous solutions onto graphene oxide: equilibrium, kinetic and thermodynamic studies. J. Colloid Interface Sci. 496, 188–200.

Kumar, D., Talreja, N., 2019. Nickel nanoparticles-doped rhodamine grafted carbon nanofibers as colorimetric probe: naked eye detection and highly sensitive measurement of aqueous Cr^{3+} and Pb^{2+}. Korean J. Chem. Eng. 36 (1), 126–135.

Kumar, V., Talreja, N., Deva, D., Sankararamakrishnan, N., Sharma, A., Verma, N., 2011. Development of bi-metal doped micro- and nano multi-functional polymeric adsorbents for the removal of fluoride and arsenic(V) from wastewater. Desalination 282, 27–38.

Kumar, R., Ashfaq, M., Verma, N., 2018. Synthesis of novel PVA–starch formulation-supported Cu–Zn nanoparticle carrying carbon nanofibers as a nanofertilizer: controlled release of micronutrients. J. Mater. Sci. 53 (10), 7150–7164.

Lee, J., Farha, O.K., Roberts, J., Scheidt, K.A., Nguyen, S.T., Hupp, J.T., 2009. Metal-organic framework materials as catalysts. Chem. Soc. Rev. 38 (5), 1450–1459.

Li, J., Xia, J., Zhang, F., Wang, Z., Liu, Q., 2018. An electrochemical sensor based on copper-based metal-organic frameworks-graphene composites for determination of dihydroxybenzene isomers in water. Talanta 181, 80–86.

Liu, J., Chen, M., Cui, H., 2020. Recent progress in environmental applications of metal-organic frameworks. Water Sci. Technol. 83 (1), 26–38.

Loesche, W.J., Lopatin, D.E., Stoll, J., van Poperin, N., Hujoel, P.P., 1992. Comparison of various detection methods for periodontopathic bacteria: can culture be considered the primary reference standard? J. Clin. Microbiol. 30 (2), 418–426.

Ming, F., Hou, J., Huo, D., Zhou, J., Yang, M., Shen, C., Zhang, S., Hou, C., 2019. Copper-based metal–organic framework nanoparticles for sensitive fluorescence detection of ferric ions. Anal. Methods 11 (34), 4382–4389.

Mustafa, S., Khan, H.M., Shukla, I., Shujatullah, F., Shahid, M., Ashfaq, M., Azam, A., 2011. Effect of ZnO nanoparticles on ESBL producing Escherichia coli & Klebsiella spp. East. J. Med. 16 (4), 253–257.

Okoro, H.K., Ayika, S.O., Ngila, J.C., Tella, A.C., 2018. Rising profile on the use of metal-organic frameworks (MOFs) for the removal of heavy metals from the environment: an overview. Appl. Water Sci. 8 (6), 169.

Omar, R.A., Afreen, S., Talreja, N., Chauhan, D., Ashfaq, M., 2019a. Impact of nanomaterials in plant systems. In: Prasad, R. (Ed.), Plant Nanobionics: Volume 1, Advances in the Understanding of Nanomaterials Research and Applications. Springer International Publishing, Cham, pp. 117–140.

Omar, R.A., Afreen, S., Talreja, N., Chauhan, D., Ashfaq, M., Srituravanich, W., 2019b. Impact of nanomaterials on the microbial system. In: Prasad, R. (Ed.), Microbial Nanobionics: Volume 1, State-of-the-Art. Springer International Publishing, Cham, pp. 141–158.

Parmar, B., Bisht, K.K., Rajput, G., Suresh, E., 2021. Recent advances in metal–organic frameworks as adsorbent materials for hazardous dye molecules. Dalton Trans. 50 (9), 3083–3108.

Rattanapan, S., Srikram, J., Kongsune, P., 2017. Adsorption of methyl orange on coffee grounds activated carbon. Energy Procedia 138, 949–954.

Ren, X., Yang, C., Zhang, L., Li, S., Shi, S., Wang, R., Zhang, X., Yue, T., Sun, J., Wang, J., 2019. Copper metal–organic frameworks loaded on chitosan film for the efficient inhibition of bacteria and local infection therapy. Nanoscale 11 (24), 11830–11838.

Saraswat, R., Talreja, N., Deva, D., Sankararamakrishnan, N., Sharma, A., Verma, N., 2012. Development of novel in situ nickel-doped, phenolic resin-based micro–nano-activated carbon adsorbents for the removal of vitamin B-12. Chem. Eng. J. 197, 250–260.

Sasidharan, V., Sachan, D., Chauhan, D., Talreja, N., Ashfaq, M., 2021. Three-dimensional (3D) polymer—metal-carbon framework for efficient removal of chemical and biological contaminants. Sci. Rep. 11 (1), 7708.

Siddiqui, S.I., Ravi, R., Rathi, G., Tara, N., ul-Islam, S., Chaudhry, S.A., 2018. Decolorization of textile wastewater using composite materials T2. In: Nanomaterials in the Wet Processing of Textiles T3. Wiley Online Books, pp. 187–218.

Singh, S., Ashfaq, M., Singh, R.K., Joshi, H.C., Srivastava, A., Sharma, A., Verma, N., 2013. Preparation of surfactant-mediated silver and copper nanoparticles dispersed in hierarchical carbon micro-nanofibers for antibacterial applications. N. Biotechnol. 30 (6), 656–665.

Singh, S., Numan, A., Zhan, Y., Singh, V., Van, H., Nam, T., N. D., 2020. A novel highly efficient and ultrasensitive electrochemical detection of toxic mercury (II) ions in canned tuna fish and tap water based on a copper metal-organic framework. J. Hazard. Mater. 399, 123042.

Sokolowska-Gajda, J., Freeman, H.S., Reife, A., 1996. Synthetic dyes based on environmental considerations. Part 2: iron complexes formazan dyes. Dyes Pigm. 30 (1), 1–20.

Talreja, N., Kumar, D., Verma, N., 2014. Removal of hexavalent chromium from water using Fe-grown carbon nanofibers containing porous carbon microbeads. J. Water Process Eng. 3, 34–45.

Talreja, N., Verma, N., Kumar, D., 2016. Carbon bead-supported ethylene diamine-functionalized carbon nanofibers: an efficient adsorbent for salicylic acid. CLEAN—Soil Air Water 44 (11), 1461–1470.

Talreja, N., Ashfaq, M., Chauhan, D., Mera, A.C., Rodríguez, C.A., 2021. Strategic doping approach of the Fe–BiOI microstructure: an improved photodegradation efficiency of tetracycline. ACS Omega 6 (2), 1575–1583.

Tran, T.V., Nguyen, D.T.C., Nguyen, T.T., Le, H.T.N., Nguyen, C.V., Nguyen, T.D., 2020. Metal-organic framework HKUST-1-based Cu/Cu2O/CuO@C porous composite: rapid synthesis and uptake application in antibiotics remediation. J. Water Process Eng. 36, 101319.

Tripathi, K.M., Tyagi, A., Ashfaq, M., Gupta, R.K., 2016. Temperature-dependent, shape variant synthesis of photoluminescent and biocompatible carbon nanostructures from almond husk for applications in dye removal. RSC Adv. 6 (35), 29545–29553.

Tsai, W.-T., Hsu, H.-C., Su, T.-Y., Lin, K.-Y., Lin, C.-M., Dai, T.-H., 2007. The adsorption of cationic dye from aqueous solution onto acid-activated andesite. J. Hazard. Mater. 147 (3), 1056–1062.

Wang, Q., Astruc, D., 2020. State of the art and prospects in metal–organic framework (MOF)-based and MOF-derived nanocatalysis. Chem. Rev. 120 (2), 1438–1511.

Wang, S., Deng, W., Yang, L., Tan, Y., Xie, Q., Yao, S., 2017. Copper-based metal-organic framework nanoparticles with peroxidase-like activity for sensitive colorimetric detection of *Staphylococcus aureu*s. ACS Appl. Mater. Interfaces 9 (29), 24440–24445.

Wang, Z., Zhang, J.-H., Jiang, J.-J., Wang, H.-P., Wei, Z.-W., Zhu, X., Pan, M., Su, C.-Y., 2018. A stable metal cluster-metalloporphyrin MOF with high capacity for cationic dye removal. J. Mater. Chem. A 6 (36), 17698–17705.

Wang, J., Hu, Y., Zhou, Q., Hu, L., Fu, W., Wang, Y., 2019. Peroxidase-like activity of metal–organic framework [Cu(PDA)(DMF)] and its application for colorimetric detection of dopamine. ACS Appl. Mater. Interfaces 11 (47), 44466–44473.

Wellinghausen, N., Siegel, D., Gebert, S., Winter, J., 2009. Rapid detection of Staphylococcus aureus bacteremia and methicillin resistance by real-time PCR in whole blood samples. Eur. J. Clin. Microbiol. Infect. Dis. 28 (8), 1001–1005.

Wu, G., Ma, J., Li, S., Guan, J., Jiang, B., Wang, L., Li, J., Wang, X., Chen, L., 2018. Magnetic copper-based metal organic framework as an effective and recyclable adsorbent for removal of two fluoroquinolone antibiotics from aqueous solutions. J. Colloid Interface Sci. 528, 360–371.

Xu, W.-Q., He, S., Lin, C.-C., Qiu, Y.-X., Liu, X.-J., Jiang, T., Liu, W.-T., Zhang, X.-L., Jiang, J.-J., 2018. A copper based metal-organic framework: synthesis, modification and VOCs adsorption. Inorg. Chem. Commun. 92, 1–4.

Yaghi, O.M., Li, G., Li, H., 1995. Selective binding and removal of guests in a microporous metal–organic framework. Nature 378 (6558), 703–706.

Yusuff, A.S., Popoola, L.T., Babatunde, E.O., 2019. Adsorption of cadmium ion from aqueous solutions by copper-based metal organic framework: equilibrium modeling and kinetic studies. Appl. Water Sci. 9 (4), 106.

Zhang, X., Jiang, Y., Zhu, M., Xu, Y., Guo, Z., Shi, J., Han, E., Zou, X., Wang, D., 2020. Electrochemical DNA sensor for inorganic mercury(II) ion at attomolar level in dairy product using Cu(II)-anchored metal-organic framework as mimetic catalyst. Chem. Eng. J. 383, 123182.

Zhao, D., Zhang, W., Chen, C., Wang, X., 2013. Adsorption of methyl orange dye onto multiwalled carbon nanotubes. Procedia Environ. Sci. 18, 890–895.

Zhu, Y., Murali, S., Cai, W., Li, X., Suk, J.W., Potts, J.R., Ruoff, R.S., 2010. Graphene and graphene oxide: synthesis, properties, and applications. Adv. Mater. 22 (35), 3906–3924.

Zou, F., Yu, R., Li, R., Li, W., 2013. Microwave-assisted synthesis of HKUST-1 and functionalized HKUST-1-@H3PW12O40: selective adsorption of heavy metal ions in water analyzed with synchrotron radiation. Chemphyschem 14 (12), 2825–2832.

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CHAPTER

29 Ecological effects of copper NPs: Advantages and drawbacks regarding current and potential applications

Hermes Pérez-Hernández[a], Selvia García-Mayagoitia[b], Patricio Andrés Torres-Gómez[b], Rafael G. Campos-Montiel[c], and Fabián Fernández-Luqueño[b]

[a]*El Colegio de la Frontera Sur (CONACYT), Agroecología, Unidad Campeche, Campeche, Mexico*

[b]*Sustainability of Natural Resources and Energy Programs, Cinvestav-Saltillo, Ramos Arizpe, Coahuila, Mexico*

[c]*ICAP—Instituto de Ciencias Agropecuarias, Universidad Autónoma del Estado de Hidalgo, Tulancingo, Hidalgo, México*

1 Introduction

During the few last years, the use of nanosized materials (NMs) or nanotechnology-based products has expanded; subsequently, the risk of soil, air, or water contamination by NMs has also increased. NMs will produce better daily or specialized use products regarding functionality, weight, energy consumption, and maybe a cleaner environment. The shape and size of nanoparticles (NPs) are well known for the main characteristics determining their unique magnetic, electronic, optical, and catalytic properties (Khaldari et al., 2021). Besides, copper oxide NPs (CuO NPs) are used worldwide in various technological areas due to their unique electric, thermal, mechanical, catalytic, and magnetic properties. Therefore, CuO NPs are one of the most synthesized NMs for coating, cosmetics, antimicrobial agents, medical applications, and agricultural, environmental, industrial, and medical fields; estimates are that production could increase from 0.27 million tons (2012) to 1.663 million tons by 2020 (Rajput et al., 2019). This will increase their discharge into the soil, air, or water, potentially threatening organisms and ecosystems (Seena and Kumar, 2019).

CuO NP use has increased in different applications, particularly in antifouling paints and pesticides (Keller et al., 2017). Therefore, CuO NPs are directly spread to the environment, resulting in increased direct exposure toward not just target organisms or ecosystems but also potential collateral damage. However, it has to be stated

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that CuO NPs have been used to reduce environmental pollution; therefore, these NMs also have outstanding potential to dissipate pollutants, break down contaminants, and recover degraded sites. Besides being nonpolluting, eco-friendly, cheap, and green synthesis procedures for CuO NPs have been designed with excellent potential in textile dyes' catalytic degradation (Sharma et al., 2018). Contrary to this, Seena and Kumar (2019) provided a novel insight regarding the potential risk of short-term exposure to environmentally realistic concentrations of CuO NPs (0.00, 0.04, 0.08, and 0.12 mg L^{-1}) for a short period (24, 48, 72, and 96 h) on the ecological performance of *Articulospora tetracladia*, a cosmopolitan aquatic fungal decomposer.

According to Ijaz et al. (2020), the synthesis of CuO NPs can be made by two approaches such as top-down and bottom-up. CuO NPs have been produced by mechanical or ball-milling methods, which are inexpensive methods to produce NPs from bulk. Also, laser ablation, sputtering methods, and biological synthesis have been used to produce CuO NPs (Akintelu et al., 2020). Biological synthesis is included in the bottom-up synthesis. This eco-friendly and green technology involves the use of plant extracts and bacteria, fungi, or yeast.

This chapter describes and discusses the advantages and drawbacks of current and potential applications, emphasizing the newest publication on this topic. Barreto et al. (2021) studied the CuO NPs effects in the physiology of *Ankistrodesmus densus*, a cosmopolitan green microalga. This research focused on environmental NPs levels, so the concentration range was 0.0003–0.635 mg L^{-1} during a 72-h exposure assay. They found that environmental CuO NPs concentrations affect viral functions in *A. densus*, which could imply facing problems related to the increasing delivery of engineered CuO NPs in ecosystems in the near future. Akintelu et al. (2020) described CuO NPs' biomedical applications and their use in environmental remediation. Therefore, the anticancer, antioxidant, antibacterial CuO NPs properties were discussed and found to efficiently dissipate pollutants during effluent treatment.

This chapter aims to discuss and highlight recent findings regarding the ecological effects of CuO NPs, emphasizing recently published manuscripts on the advantages and disadvantages of its use.

2 Classification and synthesis of copper nanomaterials

2.1 Classification

NMs are divided into three categories based on their origin: natural, incidental, and engineered. According to other classifications, there are metal NPs, their oxides, bimetallic, and other inorganic NPs. These NMs could have one of the four-dimensional structures: zero, one, two, and three dimensions (Fig. 1; Din and Rehan, 2017).

2.2 Traditional and biological synthesis

There are several methods of synthesis of NMs of Cu and Cu oxides (CuO): traditional methods, i.e., empty deposition, emulsion, polyol method, thermal

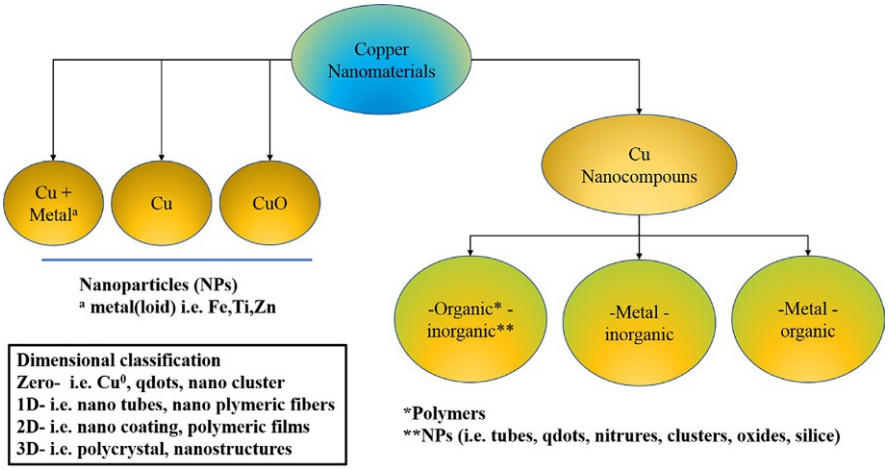

FIG. 1

Classification of copper nanomaterials by chemical nature and dimensional structure.

decomposition, wet precipitation, chemical reduction, electrochemical reduction, precipitation, sol-gel, Pechini, oxidative hydrolysis, etc. (Table 1) and biological methods, i.e., plant and spice extracts, fungi use, etc. (Table 2). There are also nanocompounds (organic-inorganic, metal-inorganic, metal-organic), polymer matrix (inorganic materials), and nanolaminates, among others (Calvillo-Anguiano, 2019).

CuO NPs have several diverse applications such as being a highly efficient and suitable heterogeneous catalyst for different organic transformations (Behrouz, 2017). CuO NPs are also antibacterial agents to reduce *Staphylococcus aureus, Bacillus cereus*, and *E. coli*. CuO NPs are an excellent option for purifying water and improving human health issues (Tohidiyan et al., 2017). Besides, conductive gold and copper-gold microstructures with susceptible and selective properties were manufactured with potential application in the design and fabrication of new nonenzymatic biosensors (Panov et al., 2017; Behrouz, 2018). Besides, it is well known that ion track filters (ITFs) used as templates have various advantages for synthesizing micro/nanostructures, whiskers, fibrils, quantum wires, and dots (Saineetha et al., 2020). Regarding the removal of pollutants, thin 2D metal-organic framework (MOFs) nanosheets (MNS) were prepared through complexation between 2-methylimidazole and Cu (II) by a one-step, cost-effective route. This MNS was used to immobilize Uranium (VI) from MOFs' aqueous nuclear industry solution as nanosheets (Duan et al., 2019). Cupper NPs derived from *Cynomorium coccineum* L. plant extract was used for diverse purposes such as dye removal, antioxidant, diabetic, antiinflammatory, antibacterial, and energy storage systems, among others (Sebeia et al., 2020). A brief description of the eco-friendly synthesis of copper NPs is shown in Fig. 2.

Table 1 Traditional methods of CuO NPs synthesis.

Precursor	Solvent	Catalyst/Ligand	Size (nm)	Method	Reference
Cu $(CH_3COO)_2$	Methanol	H_2L	40–50	Ultrasonic irradiation	Tohidiyan et al. (2017)
NMs [Cu(L)] Complex			20–30	Thermal decomposition	
$CuCl_2$	H_2O	NaOH/ $KNaC_4H_4O_6$	25	Laser-inducing metal deposition	Panov et al. (2017)
Au (PPh_3) Cl	DMF				
$[bmin]N_3$	DMF	Nano CDSCS		Thermal/TLC monitoring	Behrouz (2018)
$CuSO_4$	Ion-free water and H_2SO_4		30	Electrochemical	Saineetha et al. (2020)
$CuSO_4$	$H_2SO_4 + Na_2SeO_3$		23–28	Template synthesis using ITFs	
Cu (II)	MeOH + H_2O	MeimiH	20–25	One-step chemical solution	Duan et al. (2019)
Cu $(NO_3)_2$	Acid benzendicarboxylic	Phenanthroline	27	Ultrasonic irradiation	Fard et al. (2020)

H_2L = Ligand; MeimiH = co-ligands for 2, based methanol; CDSCS = Copper doped silica cuprous sulfate; DMF = Solvent; TBT = Tetra n butyl titanate; ITFs = Ion track filters.

Table 2 Biological method of CuO NPs synthesis.

Precursor	Extract/ reducing agent/ compound	Size (nm)	Method	Reference
Cu $(CH_3COO)_2$	Cotton fabric	10.6	Aqueous bath	Rezaie et al. (2018)
$CuCl_2$	*Tinospora cardifolia*	63	Mixture stirred	Sharma et al. (2019)
$CuCl_2$	*Euphorbia falcata*	5–10	Mixture stirred	Motahharifar et al. (2020)
Cu NPs	Fe_3O_4-chitosan		Mixture stirred/ precipitation	
$CuSO_4$	*Cynomorium coccineum*	14.2	Mixture stirred	Sebeia et al. (2020)

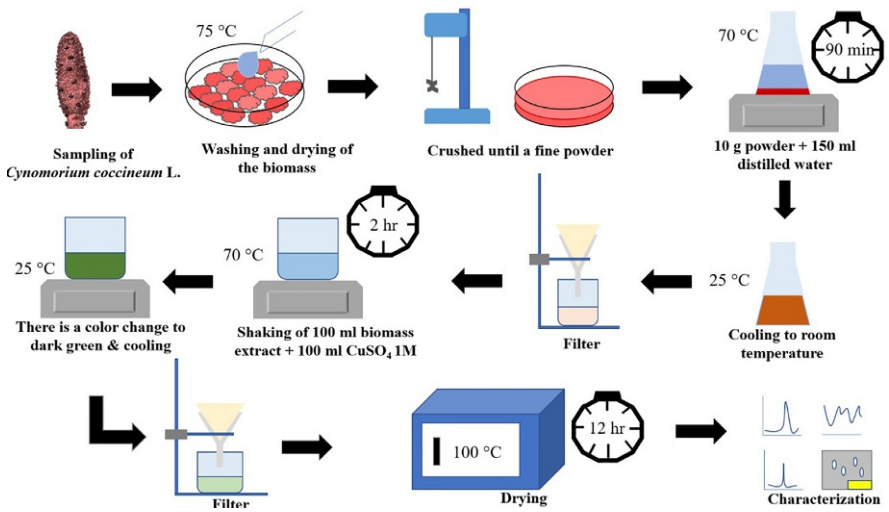

FIG. 2

Brief representation of an eco-friendly synthesis of copper NPs from plant biomass.

2.3 Eco-friendly cost-effective synthesis

Using the catalyst heterogeneous (recyclable and reused easily), room temperature, and using ethylene glycol as a solvent makes an eco-friendly system of Cu NPs compound synthesis with 1,2,3 triazole that has an essential use in the pharmaceutic industry as a potent agent for treating different diseases and disorders (Chetia et al., 2018).

Synthetized Cu NPs in a blanched cotton fabric without chemicals is optimal for obtaining eco-friendly NPs at low cost. A study showed that these NPs have photocatalytic properties for removing dye solution in the presence of UV or sunlight,

which means that textiles with Cu NPs can eliminate the color of the dye solution or stains by oxidation absorbing UV or sunlight. It has been reported that CuO NPs can degrade Rhodamine B, Methyl orange, and Methyl red (Rezaie et al., 2018).

Conventional preparation of cheap metal NPs supported on polyanilines (PANIs) inevitably requires chemical oxidants such as $(NH_4)_2S_2O_8$ that generate solid wastes; however, by using H_2O_2 as a green oxidant, nano Cu@PANIs with better catalyst activity in C–N coupling reactions is the better option. These eco-friendly materials can be used as sensors, catalysis, and for drug development, among others (Chen et al., 2019).

In textiles with applied Cu NPs obtained by green synthesis, laundry durability assessment was performed to determine the retention power of Cu NPs on the fabric. It was found that fabric was 65% efficacious for Gram-positive bacteria and 50.5% efficacious for Gram-negative bacteria (Sharma et al., 2019). The synthesis with plant extracts reduced costs and is eco-friendly because sources are abundantly available, cost-effective, and conveniently applicable. The extracts were prepared with distilled water, cooled to room temperature, and then filtrated with a filter paper (Sebeia et al., 2020).

Tetrazoles are a versatile member of five-membered nitrogen heterocycles with unique properties applied in medicinal chemistry as lipophilic spacers, ligands for complex preparation antitumor agents, antihypertensive drugs, etc. The Cu NPs@Fe_3O_4-chitosan showed excellent catalytic efficiency for synthesizing various tetrazoles in high yields; these compounds were made with via green synthesis (Motahharifar et al., 2020). With the speedy progress of electronic products, massive quantities of waste electric and electronic equipment had been gendered in recent years. Recycling and recovering valuable waste materials with common eco-friendly cost methods is the best choice, and copper NPs have been used for this work (El-Nasr et al., 2020).

3 Environmental uses of copper nanomaterials

Copper nanomaterials (Cu NMs) are used in many technologies, including catalysts, electronics, magnetic storage, solar energy conversion, wood preservation, and antimicrobial activity products (Fig. 3). Also, it has uses in agriculture as a pesticide with fungicide, algaecide, and herbicide activity (Ma et al., 2019). Important copper forms include carbonates, hydroxides, some oxide phases, and zero-valent metal, and its dissolution to commonly assumed bioavailable is the activity mode of these NMs. The environmental and safety concerns are significant because of the potential large-scale production and their high redox activity and toxicity reported from in-vitro studies (Ma et al., 2019; Ameh and Sayes, 2019; Solano et al., 2021).

The Cu NMs that use copper oxides such as CuO and Cu_2O are well known for their p-type semiconductors with a narrow band gap, making them of interest as solar absorbers and solar back contact materials (Isherwood, 2017). They are also excellent candidates for heterogeneous catalytic reactions, energy conversion, biosensing, etc.

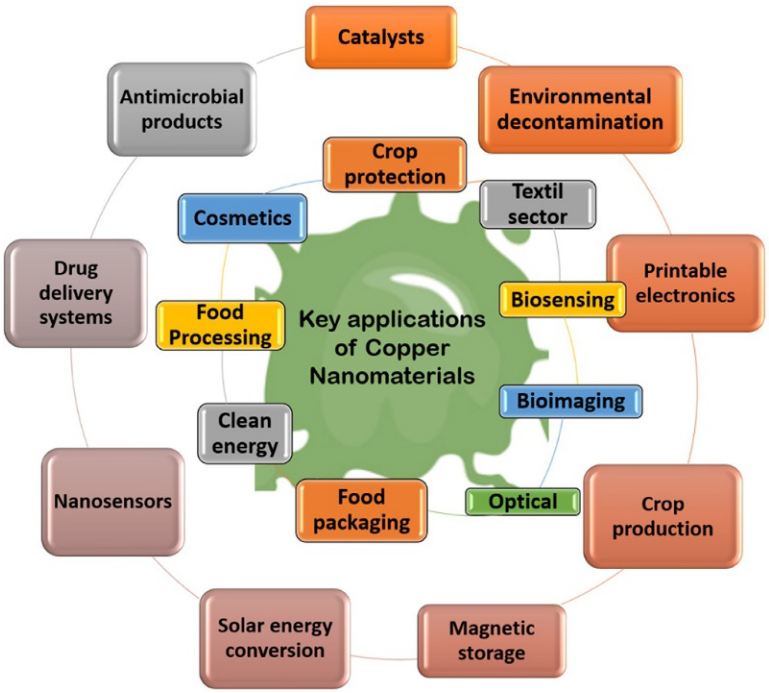

FIG. 3

Key applications of different kinds of nanomaterials based on copper.

There have been different methods developed to prepare these NMs such as chemical reduction, sonochemical reduction, and radiation-based methods, which have already been mentioned in the literature (Khalaj et al., 2018).

The application of Cu NMs in the environment is increasingly in the interest of many researchers. Different types of modified Cu NMs are applied for the degradation or removal of contaminants from polluted environments such as nanoscale zero-valents. It is mainly used for in situ removal of nitrate from surface water and water refinery hydrogen energy production of methyl orange and dichloromethane of the groundwater. The catalytic activity is related to its morphological, optical, and electrical properties (Khalaj et al., 2018).

There exist limited information regarding the antimicrobial activity of CuO NPs. These NMs are cheaper than silver, can be easily mixed with polymers, and are relatively stable in chemical and physical properties. Besides, highly ionic nanoparticulate metal oxides from Cu such as CuO NPs are precious antimicrobial agents that can be prepared with extremely high surface areas and unusual crystal morphologies (Djellabi et al., 2020).

In this chapter, different reports of the uses of copper NPs are discussed, such as how they can be helpful to decontaminate the environment such as water and soil. Nonetheless, its application in photocatalytic activities is also valuable, where copper

enhances the catalytic activity using a photoelectrolysis cell and where the Cu and its oxides are used as semiconductor materials. Also, with regard to the use of copper for its antibacterial properties, as reported, its properties work against Gram-positive and Gram-negative bacteria, depending on how the NPs interact with the cell wall.

3.1 Environmental decontamination

One of the critical pollutants in water is nitrate (NO_3^-), which is the most abundant ground and surface water pollutant due to extensive fertilization of agricultural soils, millions of tons of livestock manure delivery to the environment, and the discharge of untreated or inefficiently treated wastewater. The NO_3^- content is limited in drinking, ground, and surface water through specific regulations due to its effect on human health (Lucchetti et al., 2017). Lucchetti et al. (2017) investigated the photocatalytic reduction of NO_3^- to nitrogen using copper-loaded titania (P25) NPs using glycerol as a sacrificial agent and UV-A/Vis radiation. It was shown that total N removal efficiencies over 90% were achieved for NO_3^- concentrations up to $0.15\,g\,L^{-1}$ (Lucchetti et al., 2017).

Cu_2O, CuO, or CuO_2 are commonly used to dissipate pollutants in wastewater (Fig. 4). CuO_2 is commonly used as a photocatalyst for splitting seawater and degrading its organic pollutants such as dyes. Dyes are delivered by textile industries, paper and ink manufacturing, cosmetics, and pharmaceuticals, among other activities. Congo red, Methylene blue, Rhodamine B, and Methyl orange are common dyes used in the industry (Thakur et al., 2020). Therefore, an amount of dye comes from the textile industries and is discharged into the dying water effluents. Conventional

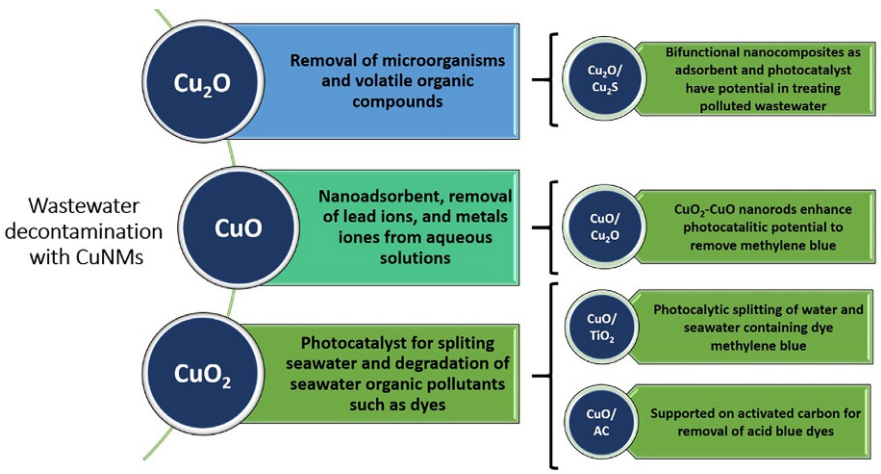

FIG. 4

Copper nanomaterials where oxygen combines with copper to form copper (I) oxide (Cu_2O), copper (II) oxide (CuO), and copper dioxide (CuO_2), which are used to dissipate pollutant.

wastewater treatment methods include biological, coagulation, and chemical oxidation. One alternative for this conventional wastewater treatment is an advanced oxidation process in which photocatalysis has been widely used (Thakur et al., 2020).

For years, Simamora et al. (2012) showed that the photocatalytic splitting of water and seawater containing the dye methylene blue (MB) on CuO-supported nanosized TiO_2 (2.5% CuO/TiO_2-NPs) was very active for photocatalytic splitting of water and seawater in the presence of MB at 10 ppm. It is shown that after 5 h of UV–Vis irradiation on the photocatalyst in water and seawater, 86% and 99% of MB was degraded, respectively. Also, it seems that this photocatalyst can degrade more than 90% of MB in seawater within 2 h UV–Vis light irradiation, which is more effective than 5.0% CuO/TiO_2-NPs, concluding that with a lower amount of CuO, the results are favorable for the degradation of MB (Simamora et al., 2012). More recent studies by Thakur et al. (2020) observed that Cu-capped Cu_2O NPs (Cu-Cu_2O) exhibits photocatalytic mineralization up to 99% to decontaminate water polluted with Congo red dye.

Elsewhere, the synthesis of CuO NPs loaded on activated carbon (CuO NPs-AC) was made using a simple, low-cost, and efficient procedure. AC is a widely used dye removal technique because of its high mechanical and chemical stability with the least cost that acts as a mild reducing agent and catalyst. This material was applied to remove acid blue 129 (AB 129), an acidic dye, during the dyeing of several raw materials used in the textile industry. It was observed that CuO NP-AC with a concentration of 0.045 g when the AB 129 was increased from 10 to 60 mg L^{-1}, the removal percentage decreases from 99.8% to 85.4%. The efficiency of these NMs showed good capacity absorbency of 65.36 for removing AB 129 from aqueous solutions in a short time of $\leq$25 min (Nekouei et al., 2015).

In a study, CuO NPs were immobilized into a porous matrix of sodium alginate, obtaining a granulated CuO nanoadsorbent used in the removal of Zr(IV), Co(II), Pb(II), and U(VI) from aqueous solutions during water and wastewater treatment. It was found that nanostructured CuO granules are an effective adsorbent and that the effect of time on the removal of lead ions reached the maximum value after 5 h, but not after that. These results could be found because most adsorbent sites were vacant at the onset of the experiment, and the solute concentration gradient was high (Ahmadi et al., 2012). Also, recent studies showed that a combination of engineered nanomaterials (ENMs) was efficient in removing arsenic and microbes from water (Priyadarshni et al., 2020). First, the findings demonstrated the successful synthesis of biochar stabilized iron and copper oxide NPs from rice husk (biochar @ Fe and biochar @ Cu). Besides, the combination of both NPs eliminated As^{III} and As^{V} with an efficiency of 95%. The authors suggest that pH, time, and interfering ions are key factors in removing contaminants when ENMs are used as absorbents. Also, this study demonstrated efficiency for the elimination of pathogenic bacteria from the water. The authors suggest using ENMs combined with biochar as a novel sustainable decontamination technology (Priyadarshni et al., 2020).

CuO NPs obtained using the reactive magnetron sputtering technique had an average size of 8 nm with 84.3 m^2/g surface area. These NPs were an effective

nanoadsorbent for the removal of Cr (VI) ions from wastewater. The removal efficiency of CuO NPs decrease with an increase in the concentration of Cr (VI) ions, with an adsorption efficiency of 15.6 mg g^{-1}. It confirms monolayer adsorption over the CuO NPs surface (Gupta et al., 2016).

The uses of Cu NPs and Cu oxides are promising materials for different pollutants in the environment. They are widely used in wastewater sources, which are most commonly polluted with different kinds of contaminants and the most problematic environmental pollution from different industries such as pharmaceuticals. These NMs are effective for most pollutants, especially at the beginning of the adsorption experiments where the material has the vacancies to adsorb the different contaminants, including dyes and metallic ions.

3.2 Antibacterial properties

Almost all bacteria cause infections. Frequently, the source of infections are from touched surfaces that are likely to harbor bacteria; these surfaces are the clinic settings, doorknobs, push plates, handles, and taps; most of these are often made of stainless steels and aluminum (Al) alloys, partially due to their appearance or low cost. Many tests show that methicillin-resistant *Staphylococcus aureus* (MRSA), *Escherichia coli,* and other bacteria can survive on stainless steel and aluminum surfaces for an extended period (Bhatta et al., 2018; Katzenberger et al., 2021). The use of antimicrobial Cu materials as environmental surfaces can reduce bacterial levels (Amaro et al., 2021).

Cu is an essential trace element for humans and most other forms of life, including bacteria. In the case of bacteria, Cu can penetrate the bacterial envelope, and in excess, Cu ions cause a cascade of adverse events in bacterial cells, leading to their death. The antibacterial actions include oxidative damage by reactive oxygen species (ROS), loss of cell envelope integrity, leakage of small solutes, and interference with other essential elements, such as Zn and Fe. Cu surfaces can inactivate microbes, including *E. coli* and *C. difficile*. Water and humidity are essential factors for bacterial growth and biofilm formation. Therefore, some characteristics of an organism and its surrounding environment affect bacterial cells' survival on surfaces amended with nanoparticulated Cu (Banerjee et al., 2020).

Alotaibi et al. (2020), through aerosol application, deposited thin films of Cu-doped TiO2 anatase NPs on glass substrates to evaluate microbial effectiveness. The results showed that under UVA irradiation of 4 h, photocatalytic activity of the NPs was observed for the elimination of *S. aureus* and *E. coli*. In previous studies, Nie et al. (2010) used Cu plates, Al plates, and Cu-dotted oxide coatings against different bacteria and measured bacterial reductions (BR) for 2–3 h. After 1 h of the experiment's onset, the Cu-dotted oxide coating inactivated bacteria quicker than the Cu plate. The coating eliminated 97% of bacteria after 3 h. The antibacterial activity of the Cu plate against *E. coli* was very effective after 3 h. The significant difference in the 1 h test results between the Cu plate and the Cu-dotted oxide coating was their surface morphologies (Nie et al., 2010).

In another study, it was found that certain Gram-positive bacteria form endospores that can resist heat, radiation, desiccation, and denaturing chemicals, among other extreme conditions. Bacillus or Clostridia's endospores pose a real challenge to aseptic procedures (Grass et al., 2011).

Therefore, Ramyajuliet et al. (2020) synthesized Cu NPs by mixing copper chloride (CuCl2) and *Marsilea quadrifolia* extract from the perspective of biological synthesis. The authors found that the synthesized NPs (25 nm) were toxic to Gram-positive bacteria, *Bacillus thuringiensis*, and *Streptococcus faecalis.* Also, in previous studies, only one report was found in which the viable spores were diminished by c.a. 100% in 3 h in solid copper, while complete inactivation of spores in 1 or 2 days has also been reported. It is clear that endospores are more resilient to contact killing by copper than Gram-vegetative cells but killing may still occur and thus warrant the strategic use of copper to curb the spreading of *Clostridium difficile* (Grass et al., 2011).

A study using CuO nanorods (CuO NR) showed antibacterial activity against *Bacillus, Saccharomyces, Escherichia,* and *Klebsiella* bacteria. The CuO NR was more effective in Gram-negatives strains than the Gram-positive bacteria. Cu^{2+} ions can disrupt bacterial cell membranes and gain entry to disrupt enzyme function. Therefore, it was elucidated that the CuO NR showed effective antimicrobial activity (Christy et al., 2013). Also, recent studies show that both Cu NPs and dissolved copper ($CuCl_2$) are effective against *Saccharomyces cerevisiae* mutants. Possibly, the toxic effects are generated by oxidative stress (Chen et al., 2020).

It is revealed in the viability tests with copper oxides using *Enterococcus hirae* during the wet plating protocol experiment that there was no apparent cell death on glass, $(2–3) \times 10^8$ bacteria were killed within 300 min on pure copper. Cu_2O exhibited essentially the same antimicrobial activity as pure copper. In contrast, Cu_2O showed a decreased antibacterial activity, with still 10^3 cells surviving after 300 min of exposure, suggesting that the Cu_2O, as expected, is predominant on dry copper surfaces exposed to ambient conditions due to the oxidation of the copper (Hans et al., 2013).

Razeeb et al. (2014) mentioned the effect of the morphology on the antibacterial activity, and the properties of novel vertically aligned nanotubular Cu arrays (NT-Cu) having ultrafine pores (~25 nm) were investigated These NMs were evaluated using selected pathogens: Gram-positive *S. aureus*, Gram-negative *E. coli*, *Shigella sonnei*, *Salmonella enterica,* and yeast *Candida albicans*. The results showed that NT-Cu had the most effective performance against *S. aureus*, where the antimicrobial action was observed after 2, 4, and 6 h of the experiment. At the end of the experimental trial, over 99.99% of the *S. aureus* was inactivated. After 4 h of exposure, it was observed that, for *E. coli*, *S. sonnei*, *S. enterica,* and *C. albicans*, the log red was 1.67, 1.24, 0.99, and 1.01 respectively, corresponding to a reduction in the microbial population by 98%, 94%, 90%, and 90% for *E. coli*, *S. sonnei*, *S. enterica,* and *C. albicans,* respectively (Razeeb et al., 2014). The studies of Yaqub et al. (2020) showed other relevant results of the efficiency of Cu NPs against *Pseudomonas aeruginosa* and *E. coli.*

The uses of Cu NMs have antibacterial properties; it has been studied many years before in different reports. These studies include the application on surfaces from hospitals and clinics or laboratories, which is also essential in the food industry. All in these spaces are susceptible to contamination with different microorganisms, and it is essential to use NMs with these antimicrobial properties. As explained before, Cu has the property to enter the microbial cell and interact with its cell machinery. Finally, the obtained results were almost the complete reduction of the microbial population on the surface.

3.3 Photocatalytic applications

Cu_2O is a simple p-type oxide semiconductor with a theoretical 18% solar to fuel conversion efficiency. It is essential to mention that the potential levels of the self-reduction from Cu_2O to Cu and self-oxidation to CuO are all within the band gap, which limits the stability of Cu_2O in aqueous solution, and thus the energy conversion efficiency improves (Huang et al., 2015; Jung et al., 2019).

In the search for semiconductor photoelectrodes, it is essential to mention that these materials should necessitate high efficiency, long-term stability, low cost, and no toxicity. Copper-based chalcogenides exhibited p-type semiconductor character and have been widely used for solar cells with efficiencies higher to 20%, i.e., high efficiency. In different studies, various copper-based chalcogenides such as $CuInS_2$, $CuGaSe_2$, Cu(*In*, *Ga*)Se_2 (CIGS), and Cu_2ZnSnS_4 (CZTS) films were examined as photocathodes for photoelectrochemical (PEC) water splitting. Most of the copper chalcopyrite and kesterite semiconductors have narrow band gaps such as $CuInS_2$ (1.5 eV), $CuInSe_2$ (1.0 eV), $CuGaSe_2$ (1.7 eV), and CZTS (1.5 eV), enabling better harvesting of visible and even near-infrared light (Chen et al., 2016).

Jacobsson et al. (2013) demonstrated the use of CIGS ($CuIn_xGa_{1-x}Se_2$) for the photoreduction of water into molecular hydrogen with high efficiency. To get efficient results, researchers must rely on a solid-state pn-junction, as in a conventional solar cell configuration, by depositing CdS and ZnO on top of the CIGS material. These materials increase the photocurrent with an order of magnitude and values as high as 6 mA/cm^2 but are not catalytic with respect to water reduction. Also it was demonstrated in a PEC setup that CIGS is one of the more promising materials for solar hydrogen production, with only one problem: the lack of stability in water under illumination (Jacobsson et al., 2013). In addition, recent results on the photocatalytic hydrogen generation from the activity of Cu NPs can be seen in several research studies and review articles (Carrasco-Jaim et al., 2020; Ghosh et al., 2020).

The role of Cu as a photocatalyst, in conclusion, is that it is an NM typically used with other metals or nonmetals, which enhances its properties for photoreduction in the photoelectrolysis cell (Huang et al., 2015). These materials are utilized as photoelectrodes. In other words, a photocathode is used to reduce the copper oxide in the electrolyte to produce hydrogen from the cell as a resulting product reaction. Research in this field is still ongoing for advances in materials that enhance these cells' performance.

4 Agricultural application of copper nanomaterials

Food safety and quality are just some of the leading global concerns due to population growth. However, in future agriculture, nanotechnology has been glimpsed, promising to increase production, improve crop quality and safety, and decrease production costs due to the change in the use of chemicals by nanofertilizers, nanopesticides, and nanoherbicides. Furthermore, several reports and investigations suggested that the use of NMs in agriculture is efficient since, once deposited in the soil (near the base of the plant stem), foliar application, through irrigation (León-Silva et al., 2018), or under hydroponic conditions (Abu-Elsaad and Hameed, 2019), the NPs are absorbed by plants in a precise and controlled manner, which makes possible a greater efficiency compared to traditional chemical formulas. Besides, this technology includes nanotools and nanosensors, proposed to monitor, identify, and detect environmental changes, deficiencies, and excesses of nutrients, contaminants, or diseases in crops (Duhan et al., 2017).

Therefore, in the following subsections, we will discuss several examples of the positive effects caused by Cu NPs, particularly on the physiological and chemical changes in plants and changes in symbiotic relationships with beneficial bacteria and fungi. In this context, due to the controversies of effects (positive and negative), we will highlight and discuss the study scenarios where the experiments have been carried out (laboratory, greenhouse, and field) with different culture media, the latter being one of the main factors considered to be controversial, since many experimental conclusions suggest the use of NMs at a commercial level, even when previous investigations are carried out in artificial culture media and in the laboratory.

4.1 Nanofertilization

Cu is considered an essential microelement for crops since its participation is critical in synthesizing chlorophyll *a*nd metabolic changes of proteins and carbohydrates. However, excess or poor application of conventional fertilizers can cause death in plants and may affect beneficial plant microorganisms (Salas-Leiva et al., 2021). Even with conventional applications, it is reported that only a meager amount of the elements reaches the target site., i.e., fertilizers are lost by leaching, runoff, evaporation, or microbial degradation (Sabir et al., 2014). Therefore, several investigations have evaluated nanofertilizers' addition in a simple way, such as the nutrients themselves. However, other research suggests that, for better effective dispersal and delivery, NMs should be covered and transported by a matrix that covers or integrates within a hollow-structured nanocapsule (nanocarriers) (Kah et al., 2018).

For years, Cu has been considered a fungicide, but research results from more than a decade ago until today have offered valuable knowledge for understanding the effects of nanofertilizers on edible plants. Recently, Cu NPs have been compared with other nanometer-sized metals to evaluate their positive or phytotoxic efficiency on morphological and biochemical properties in edible plants. For example, in a potted wheat study, TiO_2 and Fe_2O_3 were nontoxic to plants, whereas Cu NPs inhibited

grain growth and development, which increased Cu amounts by up to 30% to control. Furthermore, Cu NPs decreased amino acid levels in grains such as isoleucine, leucine, threonine, and histidine but not for TiO_2 and Fe_2O_3 NPs (Wang et al., 2019).

In the context of the use of NMs to improve stress in plants by salinity, Pérez-Labrada et al. (2019), in a study with tomato plants (*Solanum lycopersicum* L.var. "Huno F1", Harris Moran), showed that under greenhouse conditions with artificial soil, the foliar application of Cu NPs ($250\,mg\,L^{-1}$) promoted growth of the plant and fresh and dry weight of the aerial biomass. However, the results were similar to the control. Nevertheless, with Cu NPs, the yield was higher compared to plants under saline stress (50 mM NaCl). Variables, such as the content of vitamin C and lycopene, were higher with the application of NPs. Therefore, stress caused damage to the plant, but this condition was mitigated by applying Cu NPs. Furthermore, tomato plants with NPs under salinity apply stress tolerance by activating antioxidant mechanisms.

Similarly in previous studies by Hernández-Hernández et al. (2018), in greenhouse conditions on artificial soil under saline stress, the effect of NPs chitosan-polyvinyl alcohol (chitosan-PVA) and the mixture of NPs Cu with chitosan-PVA on *S. lycopersicum* was evaluated on tomato plants of the same variety. On one hand, without saline stress, all the treatments including control showed no difference in performance. In contrast, under stress conditions, the chitosan-PVA + Cu NPs mixture obtained a higher yield. However, it was 6% lower compared to the same mixture without stress conditions. On the other hand, chitosan-PVA increased the content of chlorophyll (a, b, and total) and enzymatic activity, while the mixture of chitosan-PVA with Cu NPs activated the enzymatic defense mechanism of tomato plants. Also, chitosan-PVA and chitosan-PVA + Cu increased the content of vitamin C and lycopene, respectively. This suggests that the use of the mixture may be an option to improve the quality of the tomato fruit.

In another case study, Cu NPs evaluated in pot-grown, drought-stressed corn plants showed positive effects. Under normal conditions, the results showed that, at 7 and 21 days, the Cu NPs (30–40 nm) at a concentration of 450 mL of 69.4 μM Cu NPs increased the height of plants compared to control plants. They also presented an increase in chlorophyll and carotenoids' content with a decrease in ROS compared to plants treated with water under conditions of drought stress at 21 days. At the end of the experiment (21 days), Cu NPs increased seed number and grain yield under stress conditions within the findings. Therefore, the authors suggest that NPs hold promise for drought-tolerant plants' production (Nguyen et al., 2020).

Green synthesis has been another option in nanotechnology for the creation of NMs as fertilizers. For example, studies of Cu NPs ion reductions and the combined effect with Zn NPs (both with average size < 100 nm) from basil extract (*Ocimum basilicum* L.) caused changes in chlorophyll a, b, and total concentrations and phenolic and flavonoid content on the same plant. The concentration that caused a significant effect on different morphological characteristics in the basil was 4000 ppm of NPs of Zn + 2000 ppm of NPs of Cu. The authors suggest that, with the combined effect of both NMs, the necessary amount of micronutrients is obtained to obtain a

quality plant (Abbasifar et al., 2020). Likewise, synthesis of Cu NPs (40 nm) from *Azadirachta indica A. Juss.* leaf extract, after 8 weeks, was shown to induce callus formation in four wheat varieties (*Oryza sativa* L.) at a concentration of 10 mg L^{-1} when compared with the control, while, at high doses of 20 mg L^{-1}, the callogenesis decreases. The researchers suggest that low doses of Cu NPs may hold promise for in-vitro propagation use since copper is an essential nutrient in plant growth and is involved in critical physiological processes (Anwaar et al., 2016). Saratale et al. (2018) reviewed other examples of green synthesis of NPs from plants and organic wastes for agricultural and environmental application.

From a commercial point of view, manufacturers such as Urth Agriculture, Aqua-Yield Operations, LLC; Bio-Nano Technology, Giza, Egypt, GreenEarth-NanoPlant, FL, USA; and Land Green & Technology Co., Ltd., Taiwan, among others are recognized for releasing nanofertilizers to the market, which, in some cases, the composition of materials is unknown. The review article by He et al. (2019) mentioned more details of products' names and trade specifications.

4.2 Pests and diseases control

The literature mentions that 1% of traditional pesticides kill pest organisms or pathogens while the rest (99%) harm beneficial and nontarget organisms. Also, with the constant applications of chemical pesticides, the organisms become resistant, or in the worst case, new pests emerge (Khan and Rizvi, 2017). Since ancient times, copper has been used as a fungicide in various crops, with ionic forms such as Cu^{2+} and Cu^{1+} causing toxicity, thus affecting the activity of various enzymes and, consequently, the appearance or germination of fungi and bacteria (Gogos et al., 2012).

Therefore, the main reason for incorporating nanopesticides and nanofungicides in agriculture is to achieve better protection of plants since nanoformulations regularly increase bioavailability by increasing the active substance's solubility or lowering the toxic effect on nontarget organisms (Kah et al., 2018). In this sense, nanoplaguicides or nanofungicides must penetrate and remain active in the target organism and not generate resistance; remain benign for plants, superior organisms such as mammals, and soil biota (macrofauna, mesofauna, and microfauna); be profitable to industrialize; and, above all, provide a new mode of action (Benelli, 2016).

For example, some years ago, it was demonstrated under greenhouse conditions that after 7 days of evaluation, the effect of CuO NPs at low concentrations was more effective than commercial pesticides for the control of *Phytophthora infestans*, which was considered a pest of the tomato crop. They did not cause toxic effects on the plant (Giannousi et al., 2013). In a recent study, Quiterio-Gutiérrez et al. (2019) showed that with the combined application at low and high doses of Se NP (10 and 20 mg L^{-1}) and Cu NP (10 and 50 mg L^{-1}) in tomato plants (*S. lycopersicum* L. var. "El Cid F1", Harris Moran), no apparent combative effects on *Alternaria Solani* were observed when NP treatments were compared, even without positive effects on plant growth. However, NPs increased leaf chlorophyll content, enzyme activity, and antioxidant capacity, suggesting that plants better tolerate stress caused by *A. solani.*

Other efforts to find ideal combinations of NMs and synthetic compounds under laboratory conditions have been studied. For example, Malandrakis et al. (2020) revealed that two phenotypes of *Botrytis cinerea* showed resistance to the fungicides benzimidazoles (BEN-R), thiophanate methyl (TM), and carbendazim. However, the combined action of Cu NPs and TM showed effectiveness in fighting resistance in both in-vitro and in-vivo tests (application on apples) on *B. cinerea*. This suggests that the combination of Cu NPs with fungicides can be a sustainable strategy by reducing the use of fungicides.

Nanocapsules are another option in pest control, as they are substance carriers or active NMs. Dorri et al. (2018), when evaluating Cu nanocapsules for the control of bean, *Tetranychus urticae* Koch (Acari: Tetranychidae) to 120 days exposure; the results showed that copper nanocapsules at a concentration of $5.5\,g\,L^{-1}$ significantly decreased the population of the pest to one organism compared to the control treatment (49 organisms).

For this chapter, the objective was to present the ecological effects, advantages, and disadvantages of Cu NPs. A work published by Zhao et al. (2016) showed that when $Cu(OH)_2$ nanoinsecticides were applied in foliar form for 30 days (the highest concentration of application was $1555\,mg\,L^{-1}$), the content of Cu in the leaves after the evaluation presented a maximum of $2008\,mg\,kg^{-1}$. In fact, the ordinary contents of Cu in plant tissues are of $10\,\mu g\,g^{-1}$ dry weight (Baker and Senef, 1995). The antioxidants dehydroascorbic acid and cis-caffeic acid decreased by as much as 33% and 8%, respectively. Research suggests that, despite the pest control's positive effects, application rates affect human health after consuming vegetables with excess Cu NMs.

On the other hand, among the new advances in nanotechnology for the control of pests and diseases is the green synthesis of Cu NPs from plants and microorganisms, which some consider less expensive and cleaner for the environment (Singh et al., 2016). The work of de Oliveira et al. (2018) presents a series of examples of botanical pesticides and their advantages and limitations in the control of pests and diseases. Among the advantages, they mention that they are more efficient, have low toxicity for nontarget organisms, do not contaminate soil and water, do not develop resistance, are easy to store, and are low cost and friendly to the environment. For example, the Cu NPs biosynthesized (48 nm average size) from *Pseudomonas fluorescens* MAL2 caused toxicity in the pest beetle (*Tribolium castaneum*) at a concentration of 37 ppm (LC_{50}) after 5 days of exposure. The authors suggest that biosynthesized Cu NPs could be potential biocontrol agents with an ecological and economical approach to control stored grain pests (El-Saadony et al., 2020). Also, in reports by He et al. (2019), some trade names of organic nanopesticides are mentioned as well as specifications of the products.

On the other hand, one of the drawbacks of biosynthesis is that considerable amounts of raw material (plants, organisms) are required. Besides, information is needed to identify all the mechanisms and synthesis processes that occur in various molecules and metabolites involved in developing bionanomaterials (He et al., 2019). In particular, much research work and new methodologies are required to

find feasible and desirable nanometric sizes and shapes in agriculture (Singh et al., 2016). Therefore, it is a matter of time and research effort to find the ideal and effective methods to obtain promising NMs in the fight against pests and crop diseases in a sustainable way, and in this way being able to avoid harmful effects on human health due to the effects of nanopesticides and nanofertilizers and other sources of contagion where Cu NPs are involved. Other examples of Cu NPs on morphological characteristics in plants and on plant diseases are shown in Table 3.

4.3 Nanosensors and other uses

According to Chhipa (2019), nanosensors are structured devices such as NPs nanotubes, nanowires, or nanocrystals used in the agricultural field to control, detect, and monitor nutrients, chemicals, or any substance in the soil and water that promotes the growth and development of plants and beneficial organisms. Furthermore, biosensors are used to detect diseases and abiotic changes in the soil and water (temperature, humidity, pH, among others).

The use of various NMs as efficient nanosensors is mentioned by Duhan et al. (2017). Nevertheless, regarding nanosensors based on copper NMs, there is little information on agriculture and the environment. One of the few cases reported in the literature is that of Huang et al. (2019). To generate a sensor for organophosphate pesticides in agricultural fields, through a fluorescence assay based on the inhibition of acetylcholinesterase (AChE) activity and copper-catalyzed (Cu NPs) click chemical reaction, the authors found that during the reaction, thiocholine (TCh) is formed with a thiol group; as a consequence, when reacting with Cu ions from the Cu NPs, high fluorescence is observed. However, in the presence of organophosphorus pesticides, TCh activity is inhibited, resulting in high Cu release and consequently decreased fluorescence signal. Therefore, the results suggest that, with the magnification of the signal mediated by Cu, sensitivity is improved, allowing a practical nanometric methodology to detect pesticides in irrigation water or generate environmental protection in the future. In this line, Guo and Zhao (2019) discuss using colorimetric and fluorescent nanosensors based on nanomaterials formed in situ. The use of Cu NPs and other NMs is mentioned in this literature. Specifically, it is argued that with in-situ analytes, directly or indirectly, nanomaterials are created by controlling the concentration of stabilizing agents, reducing agents, or metal ions, producing a fluorescence activation or deactivation response.

Sulfide ion (S^{2-}) is a toxic pollutant present in wastewater and natural waters. In this sense, the group of Zhang et al. (2019), by synthesizing copper nanoclusters (CuNCs) using silk fibroin protein (SF) as a reducing agent, showed that the fluorescent intensity of SF@ CuNCs gradually increased with increasing S^{2-} concentrations. The authors suggest that the essays are a simple, reliable, and eco-friendly method for detecting the sulfide ion contaminant. From an agricultural point of view, the contaminant may be in irrigation water.

Other uses of Cu NPs were reported by Maruthupandi et al. (2020); they demonstrated that the synthesis of 1-thio-β-D-glucose (TG) and copper nanocluster (CuNC)

Table 3 Effects of Cu NPs on morphological characteristics in plants and on plant diseases.

Cu NPs Shape	Effects	Culture medium	References
Molybdenum disulfide loaded with copper NPs (MoS_2-Cu NPs)	The application of NPs (4–32 $\mu g\,mL^{-1}$) produced an increase in the chlorophyll content and improved the rice plant's growth. Also, it exhibited antibacterial activity of 19.0 times more against the plant pathogen *Xanthomonas oryzae* pv. *oryzae* (Xoo) compared to commercial pesticides.	To evaluated *X. oryzae*, it was incubated in Luria-Bertani (LB) broth medium, and the rice seedlings evaluated by the hydroponics system.	Li et al. (2020a, 2020b)
Cu NPs	The application of NPs at 0.2, 2, and 20 $\mu g\,mL^{-1}$) produced enhanced plant growth (*Lactuca sativa* L.)	Petri dishes with filter paper	Pelegrino et al. (2020)
CuO NPs	The synthesis of Cu NPs (1.5 to 20 nm) from *Adiantum lunulatum* at a concentration of 0.01 and 0.025 $mg\,mL^{-1}$ CuO NPs caused positive changes in the seed germination percentage, root length, and seedling vigor index of *Lens culinaris*. Also, at a concentration of 0.25 $mg\,mL^{-1}$, the defense enzymes in the plants were activated.	Petri dishes	Sarkar et al. (2020)
Cu NPs stabilized with starch	The NPS (< 20 mn) at low concentrations (5 $mg\,L^{-1}$) caused an increase in secondary metabolites in the herb *Bacopa monnieri* (L.) Pennell. In contrast, at high concentrations (100 $mg\,L^{-1}$), plants expressed increased ROS	Hydroponic culture	Lala (2020)
Hybrid NP, copper-zinc (Cu/Zn)	Hybrid NP (40–100 nm) reduced the growth of *Xanthomonas perforans* (bacteria that causes the bacterial stain in tomato) at concentrations of 200, 500, and 1000 $\mu g\,mL$. Besides, the results showed that after transplantation at a concentration of 500 $\mu g\,mL$, the treated plants reduced the severity of the disease compared to control plants.	Nutrient agar medium	Carvalho et al. (2019)

(TG-CuNCs), with the preparation of a paper kit and a smart device, is a potential method for in-situ monitoring of Hg^{2+} and S^{2-} ions. In another case, regarding the use of Cu NPs to detect food-borne pathogens, Duan et al. (2020) reported a new fast and sensitive method by synthesizing copper-based metal-organic framework NPs (Cu MOF NPs) functionalized with aptamers. The method involved a colorimetric process. In this sense, the organic structure of copper and aptamers acted as signal probes. In *Escherichia coli*, it allows the peroxidase substrate to be catalyzed to generate a colorimetric signal.

Although the significant effects of Cu NPs on the morphological and biochemical properties of plants are known in the fight against pest organisms and diseases, recent potential effects as components of nanosensors, for the detection of diseases in plants, during postharvest, and detection of pollutants in the environment, there are still doubts about the interactions and mechanisms that Cu NMs can be activated with the properties of the soil, within plant cells, mechanisms that are activated in different beneficial microorganisms in the soil, among others. Therefore, we must be careful to recommend the use of copper-based NPs for agricultural and environmental use. We believe that a lot of information is needed to offer a realistic and rigorous recommendation that includes healthy agriculture without putting the environment and humans at risk.

5 Copper nanomaterials toxicity

In contrast to the positive effects in the field of agriculture and environmental remediation, several manuscripts (review articles, research, book chapters, among others) have argued and defended that the practical application of the NMs should be based on detailed experiments, with results indicating the evidence of null or minimal adverse effects on nontarget organisms, including edible and inedible plants, host plants of natural enemies, pollinators, macroinvertebrates, decomposers of organic matter (earthworms, isopods, collembola, etc.), and microorganisms such as bacteria and fungi that fulfill various functions in the cycling of nutrients, increasing soil fertility, maintaining a mutualistic relationship with plants, etc. In general, the scientific, social, and human interest is that NMs must not contaminate food, compromise human health, or deteriorate the environment (Pérez-Hernández et al., 2020; Yusefi-Tanha et al., 2020).

Therefore, we present recent studies showing the adverse effects of Cu NMs on microorganisms, macroinvertebrates, and damage to mammalian and human cells for this section. When we searched the "Web Science" database (2010–20, until May 30), within the subject field, we found at least 288 articles that reported adverse effects caused by Cu NPs: 219 to plants, 32 on soil bacteria and fungi, and 37 articles including in-vitro laboratory studies of cells and effects in mammals and humans.

Numerous reports have demonstrated contradictory effects on plants due to the application of Cu NPs; most of the experiments were carried out in laboratories, on artificial soils, and in controlled environments (Kah et al., 2018). Also, it has been

documented that the physicochemical characteristics of Cu NPs, in combination with the soil's physicochemical factors, cause toxic effects on edible and inedible plants and soil microbial communities, as well as repercussions in the mechanism of biotransformation (Rajput et al., 2019). Indeed, in laboratory work (Petri dishes), Lee et al. (2008) evaluated the NPs of Cu on mung bean (*Phaseolus radiatus* L.) and wheat (*Triticum aestivum* L.) plants. The results showed that the NPs were toxic to both plants during seedling growth, being more sensitive for *P. radiatus* (EC50, 335 mg L^{-1}) than for *T. aestivum* (EC50, 570 mg L^{-1}).

Furthermore, the authors observed a low translocation of Cu toward the stems, possibly due to root damage. In current studies using edible plants, it was shown that the synthesis of three CuO NPs compounds, at a size of 25 nm at 500 mg kg^{-1} dry soil, activated a defense mechanism with the expression of antioxidants such as superoxide dismutase (SOD), catalase (CAT), guaiacol peroxidase (POX), and ascorbate peroxidase (APX) in *Glycine* max (cv. Kowsar) cultivated in the soil for 120 days. Besides, lower seed yield was observed compared to Cu NPs with sizes of 50 and 250 nm. The results show that the Cu NPs can be introduced into the roots and distributed in the plant tissues at a smaller size, causing biochemical and morphological repercussions in the plants (Yusefi-Tanha et al., 2020). Similarly, Wang et al. (2020) observed in a study with Petri dishes for 7 days, the Cu NPs at a concentration of 2000 mg L^{-1} inhibited seed germination, plant growth, root length, and fresh biomass, with an increase of Cu in the root. Also, the generation of oxidative stress in roots and shoots was observed.

In an in-vitro experiment, it was shown that the NPs of Ni, Zn, and Cu at concentrations of 1000 mg L^{-1} cause damage to the root and shoot length, with a decrease in chlorophyll content, lipid peroxidation, and phenolic level of *Abelmoschus esculentus* (okra). Therefore, the results suggest that CuO NPs have growth inhibitor and biochemical effects in edible plants (Baskar et al., 2020). In another study, under hydroponic conditions, results showed that Cu NPs (< 50 nm) at a concentration of 250 mg L^{-1} suppressed growth in rice plants (*Oryza sativa* L.). A decrease in the chlorophyll and carotenoid content was observed (Yang et al., 2020).

As mentioned in another section, Cu NPs for use as fertilizers and fungicides have been explored. Nevertheless, these have demonstrated damaging effects. In this sense, the study of Hortin et al. (2019) reported that Cu NPs (100 mg Cu NPs kg^{-1} sand) damaged wheat plants (*T. aestivum* L. v. Deloris) compared to control. Besides, the Cu concentration compared to the control increased 2.0 and 177 times in roots and shoots, respectively. Another important finding is that the bacteria responded to the presence of Cu NPs in the rhizosphere (they alter the enzymatic activity and organic acids), which affects the morphological and biochemical changes in plants. The results suggest that, beyond the effects observed in plants, it is essential to take into account the properties of the soil and the microbial mass when evaluating the NPs effects of Cu for agricultural use.

Cu NPs deposited in agricultural soils through irrigation water, from biosolids of water treatment plants, sediments of the river, and nanofertilizers, can be consumed and cause toxicity to soil macroinvertebrates. However, toxicity can increase

when the NMs are covered by various soil organic compounds (de Santiago-Martín et al., 2016). For example, in an experiment that lasted 14 days in fresh soil, Tatsi et al. (2018) showed that COOH-coated Cu NPs (1000 mg kg^{-1} dry soil) were the most toxic compared to $CuSO_4$. Furthermore, the Cu concentrations were 10 times higher compared to the control. In aged soil, Cu NPs coated with CuO NH^{4+} were the most toxic ENM compared to controls. However, Cu accumulation was minor in earthworms than in the fresh soil study. In a more recent study, it was revealed that NPs could bind to other substances. Li et al. (2020a, 2020b) reported that Cu NPs (maximum concentration of 250 mg kg^{-1}) facilitate the absorption of the bifenthrin insecticide (100 μg kg^{-1}) by earthworms, which results in damage to organisms, confirmed by the expression of ROS, SOD, and malondialdehyde (MDA).

In the context of trophic chains, there is also evidence of the accumulation of Cu NPs. Servin et al. (2017) reported the trophic transfer of Cu NPs of the plant (*Lactuca sativa*) to crickets (*Acheta domestica*) and subsequently to lizards (*Anolis carolinensis*). The authors observed that the most significant accumulation occurred in the primary consumers (crickets) and less in the secondary consumers (lizards). The study suggests that CuO NPs may undergo transformation processes in soil upon weathering that subsequently affect NPs' availability in terrestrial food chains. Along these same lines, another author suggests that the dissolution involved in the transformation process depends on the soil's physicochemical properties. The arguments demonstrated by Sekine et al. (2017) revealed that low pH soils promote rapid dissolution (3 days) of Cu NPs, while at high pH, NPs persist over time (4 months) due to slow dissolution. This condition is also related to organic matter. Therefore, studies show that soil acidity or alkalinity dictates the fate and availability of NPs to soil organisms.

Concerns about contamination of aquatic sites by Cu NPs have also been documented. Nemati et al. (2019) revealed that the transfer of Cu NPs could occur in real scenarios. In their laboratory experiments, a diet that contained Cu NPs and was consumed by *Artemia salina* for 21 days was accumulated by *Amatitlania nigrofasciata*. The authors suggest that manufactured Cu NMs can be transferred in the food chain through water exposure. This may affect humans, as millions of people are consumers of shellfish from rivers, lakes, and the sea. In fact, in a recent study, it was shown that, under laboratory conditions, Cu NPs suppressed the proliferation and viability of normal and carcinoma lung cells, caused DNA damage, activated ROS, and consequently generated an oxidative state (Fahmya et al., 2020). Fig. 5 shows the possible destinations of Cu NMs, including soil, organisms, plants, and possible accumulation in humans.

Also, researchers have evaluated the CuO NPs in rats. In a 14-day study, it was confirmed that female rats that consumed Cu NPs (maximum concentrations 2000 mg kg^{-1}) orally (catheter procedure) showed liver damage but not in animals tested with copper microparticles (CuO MP). Likewise, the results confirmed liver regeneration at the end of the study period (Maciel-Magalhães et al., 2020). Another investigation in rats showed that Cu NPs cause changes in weight at 6 days at 250 and 500 mg kg^{-1}. Also, at 14 days, an increase in the content of plasma protein,

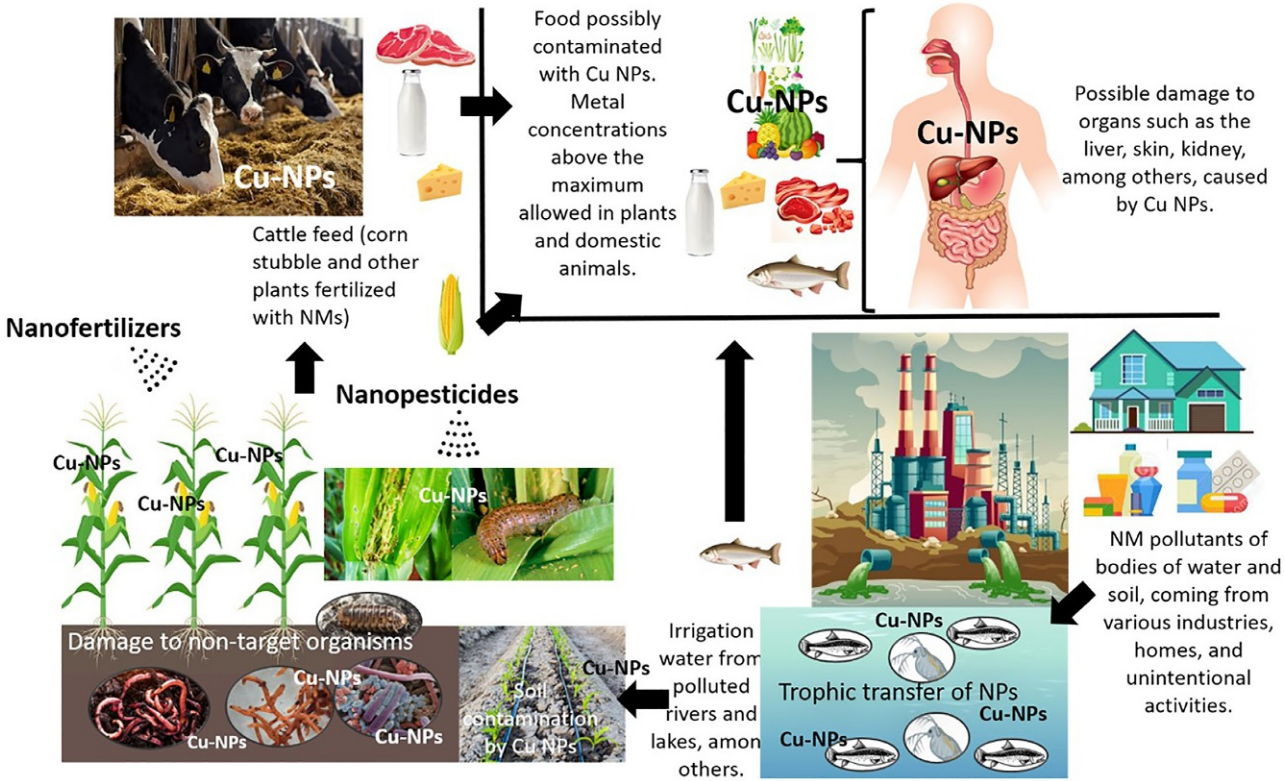

FIG. 5

Schematic representation of the fates of Cu NPs, including soil, organisms, plants, and possible accumulation in humans.

magnesium, and triglycerides at concentrations of 500 mg kg^{-1} was observed. Likewise, anxiety index changes were observed at high concentrations (Ouni et al., 2019). Investigations with human cells reported that Cu NPs induced apoptosis and suppressed the proliferation of human extravillous trophoblast cells in a time- and dose-dependent manner (Zhang et al., 2018). Due to the antimicrobial action of Cu NPs in the biomedical field, this same line has raised doubts and concerns about the possible effects of exposure on human skin. In a 24-h study, using a Franz static diffusion cell model, it was shown that Cu NPs could pass through the first layers of the skin, possibly arriving at reaching the receptor fluid of the stratum corneum (Zanoni et al., 2019). Therefore, the toxicology perspectives in the short, medium or long-term depend on various factors, including the physicochemical characteristics of the CuO NPs, concentration, mode of exposure, the animal model, and evaluation characteristics (Naz et al., 2020).

Reports indicate that many agricultural, urban, industrial, and natural areas are prone to metal contamination of copper. In this sense, several works on soil remediation were carried out to solve this problem. Bio- and nanoremediation are efficient in the degradation, elimination, and removal of Cu NPs. For example, to generate efforts to decontaminate water bodies, taking advantage of advances in biotechnology and the use biological products, Salvadori et al. (2014) developed a biological process using dead biomass from the yeast *Rhodotorula mucilaginosa* for the synthesis of NPs of metallic Cu. This biological remediation process had a dual role, acting as reducing and stabilizing agents during the formation of Cu NP and in the absorption of copper ions, which was promising.

Although some reports include Cu NPs as metallic oxides to degrade, eliminate, immobilize, etc., certain metals and organic substances (Trujillo-Reyes et al., 2014), there are many more reports that evaluate different NMs for the decontamination of excess copper of different sizes, including nanometer size, of soils and waters. For example, in a field experiment, Xing et al. (2016) found that the apatites in order of effectiveness, microhydroxyapatite (MAP), nano-hydroxyapatite (NAP), and ordinary particle apatite (OAP) at the same dose of 25.8 t ha^{-1} are potentially promising for Cu adsorption. Mandal et al. (2020) reported that a combination of graphene (GO) and zero nanovalent iron (nZVI) integrated with biochar (BC) has a much higher removal efficiency (> 65%) compared to that of BC and GO @ BC after 14 days. Also, a conversion of the metal to accessible and less toxic forms was observed. The previous examples are just a few of many investigations in the "Web Science" database on copper decontamination. Indeed, we found at least 385 documents evaluating different materials, including NMs for soil and water decontamination of copper (the search within the topic field [2010–20, until 30 May]).

For this section, we conclude that, despite the current and future potential benefits and that Cu NPs cause and may cause in agriculture, as well as other benefits not discussed here in areas such as the medical, electronics, textile industry, and sectors cosmetics, among others, it is confirmed that the applications of Cu NPs as nanofertilizer and nanopesticides can generate direct or indirect adverse effects in plants and indirectly on beneficial microorganisms essential in the symbiotic relationship with

plants. On the other hand, soil macroinvertebrates play an essential ecological role since they improve the soil's quality and fertility, participate in the nutrient cycle, and decompose organic matter, among others. However, the concerns go beyond what is proven at the ground level about plants' different physiological and biochemical parameters. The cases reported here concerning the trophic transfer of copper NMs indicate that they can bioaccumulate in plants and animals, and consequently, in humans, since we are large consumers of those products. Therefore, the investigations that generate knowledge and seek responses to processes and mechanisms that occur in the soil, when they come into contact with the NMs, must be rigorous and not just thinking of improving the morphological and biochemical properties of the crops, but also avoiding the damages caused to the environment and human health.

6 Conclusions

It is well known that environmental concentrations of Cu NPs are still low. However, these low environmental rates of Cu NPs could still rise because Cu nanometric materials are produced on an industrial scale for their intensive use in various devices, daily products, and medicines, all of which pose a risk to ecological communities and human and environmental health. Also, there are still no specific technologies for proper Cu NPs management or disposal. The synthesis of these NMs and their application has been set back because of the high cost of reagents, equipment, and associated environmental and social hazards, i.e., the Cu NPs production cost and retail price are the main factors restricting their wider use. Therefore, scientists still need to conduct more in-depth research to understand how Cu NPs can increase their potential applications and current performance in different processes or products. It is necessary to further study the effect of Cu NPs on the aquatic, terrestrial, or aerial environment.

Also, the use of computational sciences, alongside other disciplines, will shape the eco-friendly application of Cu NPs and reduce the environmental effect to promote wider use of these NMs with better performance and null or reduced collateral effects.

Quantitative characterization and ecological or environmental monitoring of CuO NPs is still limited due to the lack of detection methods and long-period trials. Therefore, studies regarding the effects of these NMs on plants and organisms must move forward to find evidence and confirm that the benefits of nanotechnology upon application outweigh their environmental risks. Therefore, NMs' collateral damage on human and ecological health should be reckoned before the nanomaterials are delivered to the environment.

The combined approaches regarding nanotechnology's advantages and drawbacks may provide a better holistic understanding and management of risks. ALSO, the adverse effect of cupper nanomaterials on organisms will induce ecological adverse events. Although several impressive results have been achieved in the secure application of copper NPs, research toward toxicological effects and additional disadvantages of these NMs remain in their infancy. Therefore, significant improvements are still required to make these materials fully competitive, safe, cheaper, and eco-friendly.

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References

Abbasifar, A., Shahrabadi, F., ValizadehKaji, B., 2020. Effects of green synthesized zinc and copper nano-fertilizers on the morphological and biochemical attributes of basil plant. J. Plant Nutr. 43 (8), 1104–1118.

Abu-Elsaad, N.I., Hameed, R.E.A., 2019. Copper ferrite nanoparticles as nutritive supplement for cucumber plants grown under hydroponic system. J. Plant Nutr. 42, 1645–1659.

Ahmadi, S.J., Sadjadi, S., Hosseinpour, M., 2012. Adsorption behavior of toxic metal ions on nanostructured CuO granules. Sep. Sci. Technol. 47, 1063–1069.

Akintelu, S.A., Folorunso, A.S., Folorunso, F.A., Oyebamiji, A.K., 2020. Green synthesis of copper oxide nanoparticles for biomedical application and environmental remediation. Heliyon 6 (7), e04508.

Alotaibi, A.M., Williamson, B.A.D., Sathasivam, S.S., Kafizas, A., Alqahtani, M., Sotelo-Vazquez, C., Buckeridge, J., Wu, J., Nair, S.P., Scanlon, D.O., Parkin, I.P., 2020. Enhanced photocatalytic and antibacterial ability of Cu-doped anatase TiO_2 thin films: theory and experiment. ACS Appl. Mater. Interfaces 12 (13), 15348–15361.

Amaro, F., Morón, A., Díaz, S., Martín-González, A., Gutiérrez, J.C., 2021. Metallic nanoparticles—friends or foes in the battle against antibiotic-resistant bacteria? Microorganisms 9 (2), 364.

Ameh, T., Sayes, C.M., 2019. The potential exposure and hazards of copper nanoparticles: a review. Environ. Toxicol. Pharmacol. 71, 103220.

Anwaar, S., Maqbool, Q., Jabeen, N., Nazar, M., Abbas, F., Nawaz, B., Hussain, T., Hussain, S.Z., 2016. The effect of green synthesized CuO nanoparticles on callogenesis and regeneration of *Oryza sativa* L. Front. Plant Sci. 7, 1330.

Baker, D.E., Senef, J.P., 1995. Copper. In: Alloway, B.J. (Ed.), Heavy Metals in Soils. Blackie Academic and Professional, London, pp. 179–205.

Banerjee, D., Shivapriya, P.M., Gautam, P.K., Misra, K., Sahoo, A.K., Samanta, S.K., 2020. A review on basic biology of bacterial biofilm infections and their treatments by nanotechnology-based approaches. Proc. Natl. Acad. Sci. India, Sect. B Biol. Sci. 90, 243–259.

Barreto, D.M., Tonietto, A.E., Lombardi, A.T., 2021. Environmental concentrations of copper nanoparticles affect vital functions in *Ankistrodesmus densus*. Aquat. Toxicol. 231, 105720.

Baskar, V., Safia, N., Preethy, K.S., Dhivya, S., Thiruvengadam, M., Sathishkumar, R., 2020. A comparative study of phytotoxic effects of metal oxide (CuO, ZnO and NiO) nanoparticles on in-vitro grown *Abelmoschus esculentus*. Plant Biosyst. https://doi.org/10.1080/11263504.2020.1753843.

Behrouz, S., 2017. Highly efficient three-component synthesis of 5-substituted-1H-tetrazoles from aldehydes, hydroxylamine, and tetrabutylammonium azide using doped nanosized copper (I) oxide (Cu_2O) on melamine–formaldehyde resin. J. Saudi Chem. Soc. 21, 220–228.

Behrouz, S., 2018. Copper-doped silica cuprous sulfate: a highly efficient heterogeneous nano-catalyst for one-pot three-component synthesis of 1-H-2-substituted benzimidazoles from 2-bromoanilines, aldehydes, and [bmim] N3. J. Saudi Chem. Soc. 22, 261–268.

Benelli, G., 2016. Plant-mediated biosynthesis of nanoparticles as an emerging tool against mosquitoes of medical and veterinary importance: a review. Parasitol. Res. 115, 23–34.

Bhatta, D.R., Hamal, D., Shrestha, R., Subramanya, S.H., Baral, N., Singh, R.K., Nayak, N., Gokhale, S., 2018. Bacterial contamination of frequently touched objects in a tertiary care hospital of Pokhara, Nepal: how safe are our hands? Antimicrob. Resist. Infect. Control 7, 97.

Calvillo-Anguiano, A.K., 2019. Evaluación de la viabilidad celular y la actividad antimicrobiana de nanopartículas de cobre. Universidad Autónoma de San Luis Potosí, Maestría.

Carrasco-Jaim, O.A., Huerta-Flores, A.M., Torres-Martínez, L.M., Moctezuma, E., 2020. Fast in-situ photodeposition of Ag and Cu nanoparticles onto $AgTaO_3$ perovskite for an enhanced photocatalytic hydrogen generation. Int. J. Hydrogen Energy 45 (16), 9744–9757.

Carvalho, R., Duman, K., Jones, J.B., Paret, M.L., 2019. Bactericidal activity of copper-zinc hybrid nanoparticles on copper-tolerant *Xanthomonas perforans*. Sci. Rep. 9, 20124.

Chen, Y., Feng, X., Liu, M., Su, J., Shen, S., 2016. Towards efficient solar-to-hydrogen conversion: fundamentals and recent progress in copper-based chalcogenide photocathodes. Nanophotonics 5, 524–547.

Chen, Y., Zhang, Q., Jing, X., Han, J., Yu, L., 2019. Synthesis of Cu-doped polyaniline nanocomposites (nano Cu@ PANI) via the H_2O_2-promoted oxidative polymerization of aniline with copper salt. Mater. Lett. 242, 170–173.

Chen, X., Zhang, R., Sun, J., Simth, N., Zhao, M., Lee, J., Ke, Q., Wu, X., 2020. A novel assessment system of toxicity and stability of CuO nanoparticles via copper super sensitive *Saccharomyces cerevisiae* mutants. Toxicol. In Vitro 104969.

Chetia, M., Gehlot, P.S., Kumar, A., Sarma, D., 2018. A recyclable/reusable hydrotalcite supported copper nano catalyst for 1,4-disubstituted-1,2,3-triazole synthesis via click chemistry approach. Tetrahedron Lett. 59, 397–401.

Chhipa, H., 2019. Chapter 6—Applications of nanotechnology in agriculture (Orgs.). In: Gurtler, V., Ball, A.S., Soni, S. (Eds.), Methods in Microbiology. Nanotechnology. vol. 46. Academic Press, pp. 115–142 (S.l.).

Christy, A.J., Jegatha Christy, A., Nehru, L.C., Umadevi, M., 2013. A novel combustion method to prepare CuO nanorods and its antimicrobial and photocatalytic activities. Powder Technol. 235, 783–786.

de Oliveira, J.L., Campos, E.V.R., Fraceto, L.F., 2018. Recent developments and challenges for nanoscale formulation of botanical pesticides for use in sustainable agriculture. J. Agric. Food Chem. 66, 8898–8913.

de Santiago-Martín, A., Constantin, B., Guesdon, G., Kagambega, N., Sébastien, R., Cloutier, R.G., 2016. Bioavailability of engineered nanoparticles in soil systems. J. Hazard. Toxic Radioact. Waste 20 (1), B4015001.

Din, M.I., Rehan, R., 2017. Synthesis, characterization, and applications of copper nanoparticles. Anal. Lett. 50, 50–62.

Djellabi, R., Ali, J., Zhao, X., Saber, A.N., Yang, B., 2020. CuO NPs incorporated into electron-rich TCTA@PVP photoactive polymer for the photocatalytic oxidation of dyes and bacteria inactivation. J. Water Process Eng. 36, 101238.

Dorri, H., Khaghani, S., Moghadam, A., Ghanbari, D., Bihamta, M., 2018. The effect of copper nanocapsules on the control of two spotted spider mite (Tetranychusurticae). J. Nanostruct. 8 (3), 316–324.

Duan, S., Wu, L., Li, J., Huang, Y., Tan, X., Wen, T., Hayat, T., Alsaedi, A., Wang, X., 2019. Two-dimensional copper-based metal−organic frameworks nano-sheets composites: one-step synthesis and highly efficient U (VI) immobilization. J. Hazard. Mater. 373, 580–590.

Duan, N., Yang, W., Wu, S., Zou, Y., Wang, Z., 2020. A visual and sensitive detection of *Escherichia coli* based on aptamer and peroxidase-like mimics of copper-metal organic framework nanoparticles. Food Anal. Methods. https://doi.org/10.1007/s12161-020-01765-9.

Duhan, J.S., Kumar, R., Kumar, N., Kaur, P., Nehra, K., Duhan, S., 2017. Nanotechnology: the new perspective in precision agriculture. Biotechnol. Rep. 15, 11–23.

El-Nasr, R.S., Abdelbasir, S., Kamel, A.H., Hassan, S.S., 2020. Environmentally friendly synthesis of copper nanoparticles from waste printed circuit boards. Sep. Purif. Technol. 230, 115860.

El-Saadony, M.T., Abd El-Hack, M.E., Taha, A.E., Fouda, M.M.G., Ajarem, J.S., Maodaa, S.N., Allam, A.A., Elshaer, N., 2020. Ecofriendly synthesis and insecticidal application of copper nanoparticles against the storage pest *Tribolium castaneum*. Nanomaterials 10, 587.

Fahmya, H.M., Ebrahim, N.M., Gaber, M.H., 2020. In-vitro evaluation of copper/copper oxide nanoparticles cytotoxicity and genotoxicity in normal and cancer lung cell lines. J. Trace Elem. Med. Biol. 60, 126481.

Fard, M.J.S., Hayati, P., Masoudiasl, A., Janczak, J., 2020. A facile route for the synthesis of new 1D copper (II) coordination polymer as precursors for preparation of nano structures: crystallography and Hirshfeld surface analysis. J. Mol. Struct. 1200, 127020.

Ghosh, S., Keshri, S.R., Bera, S., Basu, R.N., 2020. Enhanced solar hydrogen generation using CueCu2O integrated polypyrrole nanofibers as heterostructured catalysts. Int. J. Hydrogen Energy 45 (11), 6159–6173.

Giannousi, K., Avramidis, I., Dendrinou-Samara, C., 2013. Synthesis, characterization and evaluation of copper based nanoparticles as agrochemicals against *Phytophthora infestans*. RSC Adv. 3 (44), 21743.

Gogos, A., Knauer, K., Bucheli, T.D., 2012. Nanomaterials in plant protection and fertilization: current state, foreseen applications, and research priorities. J. Agric. Food Chem. 60 (39), 9781–9792.

Grass, G., Rensing, C., Solioz, M., 2011. Metallic copper as an antimicrobial surface. Appl. Environ. Microbiol., 1541–1547.

Guo, Y., Zhao, W., 2019. In situ formed nanomaterials for colorimetric and fluorescent sensing Coord. Chem. Rev. 387, 249–261.

Gupta, V.K., Chandra, R., Tyagi, I., Verma, M., 2016. Removal of hexavalent chromium ions using CuO nanoparticles for water purification applications. J. Colloid Interface Sci. 478, 54–62.

Hans, M., Erbe, A., Mathews, S., Chen, Y., Solioz, M., Mücklich, F., 2013. Role of copper oxides in contact killing of bacteria. Langmuir 29, 16160–16166.

He, X., Deng, H., Hwang, H.M., 2019. The current application of nanotechnology in food and agriculture. J. Food Drug Anal. 27, 1–21.

Hernández-Hernández, H., González-Morales, S., Benavides-Mendoza, A., Ortega-Ortiz, H., Cadenas-Pliego, G., Juárez-Maldonado, A., 2018. Effects of chitosan-PVA and Cu nanoparticles on the growth and antioxidant capacity of tomato under saline stress. Molecules 23 (1), 178.

Hortin, J.M., Anderson, A.J., Britt, D.W., Jacobson, A.R., McLean, J.E., 2019. Soil derived fulvic acid and root exudates, modified by soil bacteria, alter CuO nanoparticle-induced root stunting of wheat: via Cu complexation. Environ. Sci. Nano 6, 3638–3652.

Huang, Q., Ye, Z., Xiao, X., 2015. Recent progress in photocathodes for hydrogen evolution. J. Mater. Chem. A 31, 15824–15837.

Huang, N., Qin, Y., Li, M., Chen, T., Lu, M., Zhao, J., 2019. A sensitive fluorescence assay of organophosphorus pesticides using acetylcholinesterase and copper-catalyzed click chemistry. Analyst 144, 3436–3441.

Ijaz, I., Gilani, E., Nazir, A., Bukhari, A., 2020. Detail review on chemical, physical and green synthesis, classification, characterizations and applications of nanoparticles. Green Chem. Lett. Rev. 13 (3), 59–81.

Isherwood, P.J.M., 2017. Copper zinc oxide: investigation into a p-type mixed metal oxide system. Vacuum 139, 173–177.

Jacobsson, T.J., Jesper Jacobsson, T., Platzer-Björkman, C., Edoff, M., Edvinsson, T., 2013. $CuInxGa_1-xSe_2$ as an efficient photocathode for solar hydrogen generation. Int. J. Hydrogen Energy 38, 15027–15035.

Jung, C., Lim, T., Bae, H., Ha, J.S., Martinez-Morales, A.A., 2019. Cu_2O photocathode with faster charge transfer by fully reacted Cu seed layer to enhance performance of hydrogen evolution in solar water splitting applications. ChemCatChem 11 (17), 4377–4382.

Kah, M., Kookana, R.S., Gogos, A., Bucheli, T.D.A., 2018. Critical evaluation of nanopesticides and nanofertilizers against their conventional analogues. Nat. Nanotechnol. 13, 677–684.

Katzenberger, R.H., Rösel, A., Vonberg, R.P., 2021. Bacterial survival on inanimate surfaces: a field study. BMC. Res. Notes 14 (1), 97.

Keller, A.A., Adeleye, A.S., Conway, J.R., Garner, K.L., Zhao, L.J., Cherr, G.N., Hong, J., Gardea-Torresdey, J.L., Godwin, H.A., Hanna, S., Ji, Z.X., Kaweeteerawat, C., Lin, S.J., Lenihan, H.S., Miller, R.J., Nel, A.E., Peralta-Videa, J.R., Walker, S.L., Taylor, A.A., Torres-Duarte, C., Zink, J.I., Zuverza-Mena, N., 2017. Comparative environmental fate and toxicity of copper nanomaterials. NanoImpact 7, 28–40.

Khalaj, M., Kamali, M., Khodaparast, Z., Jahanshahi, A., 2018. Copper-based nanomaterials for environmental decontamination—an overview on technical and toxicological aspects. Ecotoxicol. Environ. Saf. 148, 813–824.

Khaldari, I., Naghavi, M.R., Motamedi, E., 2021. Synthesis of green and pure copper oxide nanoparticles using two plant resources via solid-state route and their phytotoxicity assessment. RSC Adv. 11 (6), 3346–3353.

Khan, M.R., Rizvi, T.F., 2017. Application of nanofertilizer and nanopesticides for improvements in crop production and protection. In: Ghorbanpour, M., Manika, K., Varma, A. (Eds.), Nanoscience and Plant-Soil Systems. Soil Biology. vol. 48. Springer, Cham, Switzerland, pp. 405–427.

Lala, S., 2020. Enhancement of secondary metabolites in *Bacopa monnieri* (L.) Pennell plants treated with copper-based nanoparticles in vivo. IET Nanobiotechnol. 14 (1), 78–85.

Lee, W.-M., An, Y.-J., Yoon, H., Kweon, H.-S., 2008. Toxicity and bioavailability of copper nanoparticles to the terrestrial plants mung bean (*Phaseolus radiatus*) and wheat (*Triticum aestivum*): plant agar test for water-insoluble nanoparticles. Environ. Toxicol. Chem. 27 (9), 1915.

León-Silva, S., Arrieta-Cortes, R., Fernández-Luqueño, F., López-Valdez, F., 2018. Design and production of nanofertilizers. In: López-Valdez, F., Fernández-Luqueño, F. (Eds.), Agricultural Nanobiotechnology. Springer, Cham, pp. 17–31.

Li, Y., Liu, Y., Yang, D., Jin, Q., Wu, C., Cui, J., 2020a. Multifunctional molybdenum disulfide-copper nanocomposites that enhance the antibacterial activity, promotes rice growth and induces rice resistance. J. Hazard. Mater. 394, 122551.

Li, M., Xu, G., Yang, X., Zeng, Y., Yu, Y., 2020b. Metal oxide nanoparticles facilitate the accumulation of bifenthrin in earthworms by causing damage to body cavity. Environ. Pollut. 263 (Pt. A), 114629.

Lucchetti, R., Onotri, L., Clarizia, L., Di Natale, F., Di Somma, I., Andreozzi, R., Marotta, R., 2017. Removal of nitrate and simultaneous hydrogen generation through photocatalytic reforming of glycerol over "in situ" prepared zero-valent nano copper/P25. Appl. Catal. Environ. 202, 539–549.

Ma, C., Borgatta, J., De La Torre-Roche, R., Zuverza Mena, N., White, J.C., Hamers, R.J., Elmer, W.H., 2019. Time-dependent transcriptional response of tomato (*Solanum lycopersicum* L.) to Cu nanoparticle exposure upon infection with *Fusarium oxysporum* f. sp *lycopersici*. ACS Sustain. Chem. Eng. 7 (11), 10064–10074.

Maciel-Magalhães, M., Medeiros, R.J., Bravin, J.S., Patricio, B.F.C., Rocha, H.V.A., Paes-de-Almeida, E.C., Santos, L.M.G., Jacob, S.C., Savignon, T.C.M., Amendoeria, F.C., 2020. Evaluation of acute toxicity and copper accumulation in organs of wistar rats, 14 days after oral exposure to copper oxide (II) nano- and microparticles. J. Nanopart. Res. 22, 2.

Malandrakis, A.A., Kavroulakis, N., Chrysikopoulos, C.V., 2020. Synergy between Cu-NPs and fungicides against *Botrytis cinereal*. Sci. Total Environ. 703, 135557.

Mandal, S., Pu, S., He, L., Ma, H., Hou, D., 2020. Biochar induced modification of graphene oxide & nZVI and its impact on immobilization of toxic copper in soil. Environ. Pollut. 259, 113851.

Maruthupandi, M., Thiruppathi, D., Vasimalai, N., 2020. One minute synthesis of green fluorescent copper nanocluster: the preparation of smartphone aided paper-based kit for on-site monitoring of nanomolar level mercury and sulfide ions in environmental samples. J. Hazard. Mater. 392, 122294.

Motahharifar, N., Nasrollahzadeh, M., Taheri-Kafrani, A., Varma, R.S., Shokouhimehr, M., 2020. Magnetic chitosan-copper nanocomposite: a plant assembled catalyst for the synthesis of amino- and N-sulfonyl tetrazoles in eco-friendly media. Carbohydr. Polym. 232, 115819.

Naz, S., Gul, A., Zia, M., 2020. Toxicity of copper oxide nanoparticles: a review study. IET Nanobiotechnol. 14 (1), 1–13.

Nekouei, F., Nekouei, S., Tyagi, I., Gupta, V.K., 2015. Kinetic, thermodynamic and isotherm studies for acid blue 129 removal from liquids using copper oxide nanoparticle-modified activated carbon as a novel adsorbent. J. Mol. Liq. 201, 124–133.

Nemati, T., Sarkheil, M., Johari, S.A., 2019. Trophic transfer of CuO nanoparticles from brine shrimp (*Artemia salina*) nauplii to convict cichlid (*Amatitlania nigrofasciata*) larvae: uptake, accumulation and elimination. Environ. Sci. Pollut. Res. 26, 9610–9618.

Nguyen, D.V., Nguyen, H.M., Len, T., Nguyen, K.H., Le, H.M., Nguyen, A.T., Dinh, N.T.T., Hoang, S.A., Ha, C.V., 2020. Copper nanoparticle application enhances plant growth and grain yield in maize under drought stress conditions. bioRxiv. https://doi.org/10.1101/2020.02.24.963132.

Nie, Y., Kalapos, C., Nie, X., Murphy, M., Hussein, R., Zhang, J., 2010. Superhydrophilicity and antibacterial property of a Cu-dotted oxide coating surface. Ann. Clin. Microbiol. Antimicrob. 9, 25.

Ouni, S., Askri, D., Jeljeli, M., Abdelmalek, H., Sakly, M., Amara, S., 2019. Toxicity and effects of copper oxide nanoparticles on cognitive performances in rats. Arch. Environ. Occup. Health. https://doi.org/10.1080/19338244.2019.1689376.

Panov, M.S., Vereshchagina, O.A., Ermakov, S.S., Tumkin, I.I., Khairullina, E.M., Skripkin, M.Y., Mereshchenko, A.S., Ryazantsev, M.N., Kochemirovsky, V.A., 2017. Non-enzymatic

sensors based on in situ laser-induced synthesis of copper-gold and gold nanosized microstructures. Talanta 167, 201–207.

Pelegrino, M.T., Kohatsu, M.Y., Seabra, A.B., Monteiro, L.R., Gomes, D.G., Oliveira, H.C., Rolim, W.R., de Jesus, T.A., Batista, B.L., Langen, C.N., 2020. Effects of copper oxide nanoparticles on growth of lettuce (*Lactuca sativa* L.) seedlings and possible implications of nitric oxide in their antioxidative defense. Environ. Monit. Assess. 192, 232.

Pérez-Hernández, H., Fernández-Luqueño, F., Huerta-Lwanga, E., Mendoza-Vega, J., Álvarez-Solís, J.D., 2020. Effect of engineered nanoparticles on soil biota: do they improve the soil quality and crop production or jeopardize them? Land Degrad. Dev., 1–18. https://doi.org/10.1002/ldr.3595.

Pérez-Labrada, F., López-Vargas, E.R., Ortega-Ortiz, H., Cadenas-Pliego, G., Benavides-Mendoza, A., Juárez-Maldonado, A., 2019. Responses of tomato plants under saline stress to foliar application of copper nanoparticles. Plants (Basel) 8 (6), 151.

Priyadarshni, N., Nath, P., Nagahanumaiah, Chanda, N., 2020. Sustainable removal of arsenate, arsenite and bacterial contamination from water using biochar stabilized iron and copper oxide nanoparticles and associated mechanism of the remediation process. J. Water Process Eng. 37, 101495.

Quiterio-Gutiérrez, T., Ortega-Ortiz, H., Cadenas-Pliego, G., Hernánde-Fuentes, A.D., Sandoval-Rangel, A., Benavides-Mendoza, A., Cabrera-de la Fuente, M., Juárez-Maldonado, A., 2019. The application of selenium and copper nanoparticles modifies the biochemical responses of tomato plants under stress by *Alternaria solani*. Int. J. Mol. Sci. 20 (8), 1950.

Rajput, V., Minkina, T., Ahmed, B., Sushkova, S., Singh, R., Soldatov, M., Laratte, B., Fedorenko, A., Mandzhieva, S., Blicharska, E., Musarrat, J., Saquib, Q., Flieger, J., Gorovtsov, A., 2019. Interaction of copper-based nanoparticles to soil, terrestrial, and aquatic systems: critical review of the state of the science and future perspectives. In: de Voogt, P. (Ed.), Reviews of Environmental Contamination and Toxicology Volume 252. Reviews of Environmental Contamination and Toxicology (Continuation of Residue Reviews). vol. 252. Springer, Cham.

Ramyajuliet, M., Priyanka Beulah, G., Tresina, P., Doss, A., Mohan, V., 2020. Biogenic synthesis of copper nanoparticles using aquatic pteridophyte *Marsilea quadrifolia* Linn. rhizome and its antibacterial activity. Int. J. Nano Dimens. 11 (4), 337–345.

Razeeb, K.M., Podporska-Carroll, J., Jamal, M., Hasan, M., Nolan, M., McCormack, D.E., Quilty, B., Newcomb, S.B., Pillai, S.C., 2014. Antimicrobial properties of vertically aligned nano-tubular copper. Mater. Lett. 128, 60–63.

Rezaie, A.B., Montazer, M., Rad, M.M., 2018. Environmentally friendly low cost approach for nano copper oxide functionalization of cotton designed for antibacterial and photocatalytic applications. J. Clean. Prod. 204, 425–436.

Sabir, A., Yazar, K., Sabir, F., Kara, Z., Yazici, M.A., Goksu, N., 2014. Vine growth, yield, berry quality attributes and leaf nutrient content of grapevines as influenced by seaweed extract (*Ascophyllum nodosum*) and nanosize fertilizer pulverizations. Sci. Hortic. 175, 1–8.

Saineetha, A., Sharma, S., Reddy, A.V.D., Jayarambabu, N., Kumar, N.V.M., Rao, K.V., Kumar, K.V., 2020. Template assisted electrochemical synthesis and micro-structural characterization of copper and copper selenide based polymer thin films as nano ensembles applications. Mater. Today 26, 130–133.

Salas-Leiva, J., Salas-Leiva, D.E., Tovar-Ramírez, D., Herrera-Pérez, G., Tarango-Rivero, S., Luna-Velasco, A., Orrantia-Borunda, E., 2021. Copper oxide nanoparticles slightly affect diversity and metabolic profiles of the prokaryotic community in pecan tree (*Carya illinoinensis*) rhizospheric soil. Appl. Soil Ecol. 157, 103772.

Salvadori, M.R., Ando, R.A., Oller do Nascimento, C.A., Corrêa, B., 2014. Intracellular biosynthesis and removal of copper nanoparticles by dead biomass of yeast isolated from the wastewater of a mine in the brazilian Amazonia. PLoS One 9 (1), e87968.

Saratale, R.G., Saratale, G.D., Shin, H.S., Jacob, J.M., Pugazhendhi, A., Bhaisare, M., Kumar, G., 2018. New insights on the green synthesis of metallic nanoparticles using plant and waste biomaterials: current knowledge, their agricultural and environmental applications. Environ. Sci. Pollut. Res. 25, 10164–10183.

Sarkar, Y., Chakraborty, N., Chatterjee, A., Bhattacharjee, A., Dasgupta, D., Acharya, K., 2020. Green synthesized copper oxide nanoparticles ameliorate defence and antioxidant enzymes in *Lens culinaris*. Nanomaterials 10, 312.

Sebeia, N., Jabli, M., Ghith, A., Saleh, T.A., 2020. Eco-friendly synthesis of *Cynomorium coccineum* extract for controlled production of copper nanoparticles for sorption of methylene blue dye. Arab. J. Chem. 13, 4263–4274.

Seena, S., Kumar, S., 2019. Short-term exposure to low concentrations of copper oxide nanoparticles can negatively impact the ecological performance of a cosmopolitan freshwater fungus. Environ. Sci.: Processes Impacts 21 (12), 2001–2007.

Sekine, R., Marzouk, E.R., Khaksar, M., Scheckel, K.G., Stegemeier, J.P., Lowry, G.V., Donner, E., Lombi, E., 2017. Aging of dissolved copper and copper-based nanoparticles in five different soils: short-term kinetics vs. long-term fate. J. Environ. Qual. 46 (6), 1198–1205.

Servin, A.D., Pagano, L., Castillo-Michel, H., De la Torre-Roche, R., Hawthorne, J., Hernandez-Viezcas, J.A., Loredo-Portales, R., Majumdar, S., Gardea-Torresday, J., Dhankher, O.P., White, J.C., 2017. Weathering in soil increases nanoparticle CuO bioaccumulation within a terrestrial food chain. Nanotoxicology 11, 98–111.

Sharma, P., Pant, S., Poonia, P., Kumari, S., Dave, V., Sharma, S., 2018. Green synthesis of colloidal copper nanoparticles capped with *Tinospora cordifolia* and its application in catalytic degradation in textile dye: An ecologically sound approach. J. Inorg. Organomet. Polym. Mater. 28 (6), 2463–2472.

Sharma, P., Pant, S., Dave, V., Tak, K., Sadhu, V., Reddy, K.R., 2019. Green synthesis and characterization of copper nanoparticles by *Tinospora cardifolia* to produce nature-friendly copper nano-coated fabric and their antimicrobial evaluation. J. Microbiol. Methods 160, 107–116.

Simamora, A.-J., Hsiung, T.-L., Chang, F.-C., Yang, T.-C., Liao, C.-Y., Paul Wang, H., 2012. Photocatalytic splitting of seawater and degradation of methylene blue on CuO/nano TiO_2. Int. J. Hydrogen Energy 37, 13855–13858.

Singh, P., Kim, Y.J., Zhang, D., Yang, D.C., 2016. Biological synthesis of nanoparticles from plants and microorganisms. Trends Biotechnol. 34 (7), 588–599.

Solano, R., Patiño-Ruiz, D., Tejeda-Benitez, L., Herrera, A., 2021. Metal-and metal/oxide-based engineered nanoparticles and nanostructures: a review on the applications, nanotoxicological effects, and risk control strategies. Environ. Sci. Pollut. Res., 1–20. Online First https://doi.org/10.1007/s11356-021-12996-6.

Tatsi, K., Shaw, B.J., Hutchinson, T.H., Handy, R.D., 2018. Copper accumulation and toxicity in earthworms exposed to CuO nanomaterials: effects of particle coating and soil ageing. Ecotoxicol. Environ. Saf. 166, 462–473.

Thakur, A., Kumar, A., Kumar, P., Nguyen, V.H., Vo, D.V.N., Singh, H., Pham, T.D., Truc, N.T.T., Sharma, A., Kumar, D., 2020. Novel synthesis of advanced cu capped Cu_2O nanoparticles and their photocatalytic activity for mineralization of aqueous dye molecules. Mater. Lett. 276, 128294.

Tohidiyan, Z., Sheikhshoaie, I., Khaleghi, M., Mague, J.T., 2017. A novel copper (II) complex containing a tetradentate Schiff base: synthesis, spectroscopy, crystal structure, DFT study, biological activity and preparation of its nanosized metal oxide. J. Mol. Struct. 1134, 706–714.

Trujillo-Reyes, J., Peralta-Videa, J.R., Gardea-Torresdey, J.L., 2014. Supported and unsupported nanomaterials for water and soil remediation: are they a useful solution for worldwide pollution? J. Hazard. Mater. 280, 487–503.

Wang, Y., Jiang, F., Ma, C., Rui, Y., Tsang, D.C.W., Xing, B., 2019. Effect of metal oxide nanoparticles on amino acids in wheat grains (*Triticum aestivum*) in a life cycle study. J. Environ. Manage. 241, 319–327.

Wang, W., Liu, J., Ren, Y., Zhang, L., Xue, Y., Zhang, L., He, J., 2020. Phytotoxicity assessment of copper oxide nanoparticles on the germination, early seedling growth, and physiological responses in *Oryza sativa* L. Bull. Environ. Contam. Toxicol. 104, 770–777.

Xing, J., Hu, T., Cang, L., Zhou, D., 2016. Remediation of copper contaminated soil by using different particle sizes of apatite: a field experiment. Springer Plus 5, 1182.

Yang, Z., Xiao, Y., Jiao, T., Zhang, Y., Chen, J., Gao, Y., 2020. Effects of copper oxide nanoparticles on the growth of rice (*Oryza Sativa* L.) seedlings and the relevant physiological responses. Int. J. Environ. Res. Public Health 17 (4), 1260.

Yaqub, A., Malkani, N., Shabbir, A., Ditta, S.A., Tanvir, F., Ali, S., Naz, M., Kazmi, S.A.R., Ullah, R., 2020. Novel biosynthesis of copper nanoparticles using *Zingiber* and *Allium* sp. with synergic effect of doxycycline for anticancer and bactericidal activity. Curr. Microbiol. 77 (9), 2287–2299.

Yusefi-Tanha, E., Fallah, S., Rostamnejad, A., Pokhrel, L.R., 2020. Particle size and concentration dependent toxicity of copper oxide nanoparticles (CuONPs) on seed yield and antioxidant defense system in soil grown soybean (*Glycine max* cv. Kowsar). Sci. Total Environ. 115, 136994.

Zanoni, I., Crosera, M., Ortelli, S., Blosi, M., Adami, G., Larese, F.F., Costa, A., 2019. CuO nanoparticles penetration through intact and damaged human skin. New J. Chem. https://doi.org/10.1039/c9nj03373d.

Zhang, C.H., Wang, Y., Sun, Q.Q., Xia, L.L., Hu, J.J., Cheng, K., Wang, X., Fu, X.X., Gu, H., 2018. Copper nanoparticles show obvious in vitro and in vivo reproductive toxicity via ERK-mediated signaling pathway in female mice. Int. J. Biol. Sci. 14 (13), 1834–1844.

Zhang, G., Wann, R., Shi, L., Zhang, C., Zhang, Y., Zhou, Y., Dong, C., Li, G., Shuang, S., 2019. Aggregation/assembly induced emission based on silk fibroin-templated fluorescent copper nanoclusters for "turn-on" detection of S^{2-}. Sens. Actuators B 279, 361–368.

Zhao, L., Huang, Y., Hannah-Bick, C., Fulton, A.N., Keller, A.A., 2016. Application of metabolomics to assess the impact of $Cu(OH)_2$ nanopesticide on the nutritional value of lettuce (*Lactuca sativa*): enhanced Cu intake and reduced antioxidants. NanoImpact 3–4, 58–66.

CHAPTER

Copper nanoparticle-based sensors for environmental pollutions 30

Khemchand Dewangan[a], Tushar Kant[b], and Kamlesh Shrivas[b]

[a]*Department of Chemistry, Indira Gandhi National Tribal University, Amarkantak, Madhya Pradesh, India,*

[b]*School of Studies in Chemistry, Pt. Ravishankar Shukla University, Raipur, Chhattisgarh, India*

1 Introduction

In this 21st century, rampant urbanization and the emergence of countless factories have been introduced uninvited hazardous substances into the environment, which is a major cause of unsafe and unhygienic water sources, food contaminations, and poor air quality. The entry of these harmful substances into the ecological systems causes a large number of hospitalizations and demises across the world (Benedict et al., 2017; Pandey et al., 2021; Somayaji et al., 2020; Uyttendaele et al., 2015; Viator et al., 2015; Zhao et al., 2021); thus their remediation and management seem a serious and global challenge (Anastas and Zimmerman, 2021; Zamora-Ledezma et al., 2021). It has already been recognized that contaminated drinking water can vastly increase waterborne diseases. Furthermore, irrigation of contaminated water in agricultural lands results in foodborne illnesses that can affect the entire living organisms (Haroon et al., 2021). For instance, the presence of toxic heavy metal ions in the air, soil, and water is well known for their toxicity to humans, animals, and other living organisms. They can affect the nervous system, kidneys, bone, liver, and some of them are diagnosed as cancer genic elements (Crisponi and Nurchi, 2015; Egorova and Ananikov, 2017). Moreover, several emerging studies show that interactions between pollutants and plants/microbiomes can change the biological mechanisms in the regulatory living cell due to pollutants may lead to straight effects on pathogens during a critical phase of infection or reproduction (Claus et al., 2016; Mallakpour et al., 2021; Marazziti et al., 2021). For example, at the end of 2019 coronavirus disease (COVID-19) was firstly diagnosed, which spread worldwide speedily and infected a large number of people. It was identified as an acute infectious respiratory disease caused by coronavirus. More recently, Dutheil and groups proposed a model that predicted the mortality rate of COVID-19 may become more adverse because of increasing air pollution (Dutheil et al., 2020).

To tackle the pollution complications, there are several modern instruments techniques such as atomic absorption spectrometry (AAS), inductively coupled plasma

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(ICP) spectrometry, voltammetry, surface-enhanced Raman scattering (SERS), mass spectrometry, X-ray fluorescence (XRF), spectrophotometry, and many other techniques have been applied for the quantitative/qualitative determination of pollutant species in different types of samples. Most of these techniques are sophisticated and expensive that require very tedious and time-consuming sample preparation and needed well-trained people to handle these instruments for sample analysis. Also, these techniques are found to be cumbersome to apply at the sample sources (fields) for the determination of target analyte; therefore they are not appropriate for in-field testing of pollutants present in water and territories.

From the last two decades, nanoparticles and nanotechnology-based diagnostics tools have been received significant attention as alternative tools for the sensing and detection of different types of pollutants/adulterators (Chen and Park, 2016; Dewangan et al., 2020; Kumar and Prasad, 2021; Sathish Kumar et al., 2021; Yao et al., 2018). In addition, they offer user-friendly, point-of-need, in-field-testing, and cost-effectively strategies for a variety of applications (Monisha et al., 2021; Shrivas et al., 2020a). Recent advancement of nanotechnology allows us to control the size, shape, composition, and porosity of nanomaterials for our condition and requirement, which have great advantages in numerous kinds of applications. For example, nanoscale size of metals [e.g., gold (Au), silver (Ag), copper (Cu)] (Talebzadeh et al., 2019), metal oxides (Dewangan et al., 2012), metal nitrides (Dewangan et al., 2021), nanocarbons (e.g., carbon nanotubes, graphene) (Ahlawat et al., 2021; Bhattacharya and Samanta, 2016; Tajik et al., 2020), quantum-dots (Guo et al., 2020), and many other pure and hybrid nanostructured materials (Dewangan et al., 2020) are extensively being used in the fields of electronics, optics, and energy including biology, agricultural activity, and environmental remediation. Since this book chapter deals with nanostructured metallic Cu and their sensing mechanism of environmental contamination with special reference in the agrochemicals and agroecosystems, thus we will limit our discussion to this aspect only.

2 General aspect of bulk and nanoscale size Cu element

Cu is a moderately rich element in the earth's crust and it is one of the ancient known metals used by humans in several regions from thousands of years ago. Its high electrical and thermal conductivity, as well as malleability properties compared to analogous other metals, make it useful for a variety of fields such as electrical industries, building materials, home and kitchen appliances, etc. In addition, many different alloys of Cu are beneficial involving brass, bronze for making coins, jewelry, thermocouple, and other purposeful objects as tabulated in Fig. 1. Moreover, several Cu compounds are also fabricated for a diversity of applications in the fields of agriculture, coating, medicines, etc. (Gale and Stos-Gale, 1982; Mason, 1975).

For example, the Bordeaux mixture is a basic Cu hydroxide and is made from copper sulfate ($CuSO_4$), lime [$Ca(OH)_2$], and water. It is an effective fungicide and bactericide spray for preventing fungus on plants (Robinson, 1923). Also, there was

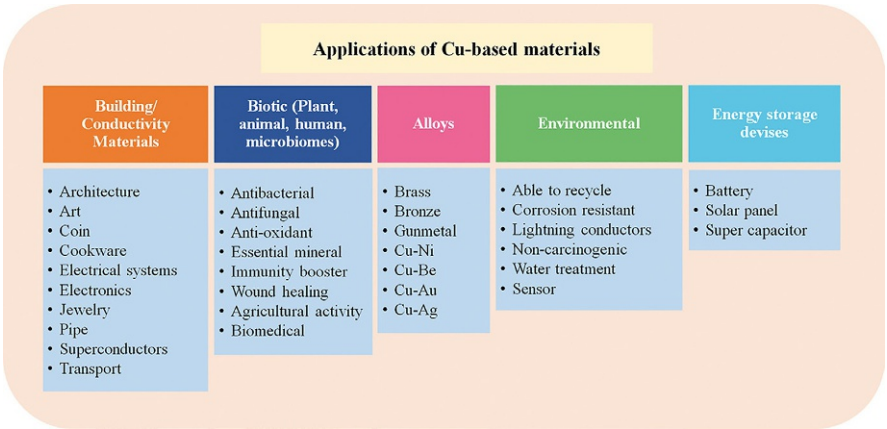

FIG. 1

Applications of Cu-based materials.

great interest in a variety of mixed Cu-based oxide as high-temperature superconductor material, for this work G. Bednorz and A. Müller were honored with the Nobel Prize for physics in the year 1987. Moreover, Cu is an essential nutrient for humans, animals, and plants at a certain level and is recognized to control central functions in iron mobilization, mitochondrial and hormone mechanism, cell wall metabolism, and electron transport processes. In addition, Cu is also known for one of the potential applications in human health as the antiseptic and antimicrobial activities as early as 3000 BCE and described in the Hippocrates (Roberto, 2006) books and the Ayurveda antique book "Susruta-Samhita" (Sharma, 2015).

On account of the solid background of bulk-Cu utilities, a variety of Cu-nanoparticles (CuNPs) with different morphologies such as particles, spheres, rods, wires, cubes, rings, plates have been successfully fabricated. These NPs generally facilitate and suffer a range of reactions due to the wide range of available oxidation states (0, +I, and +II) of Cu metal. Additionally, CuNPs exhibit unique thermal, optical, electronics, mechanical, catalytic, and relatively nontoxicity properties, which provide them the great possibility for useful applications in nanotechnologies such as the catalyst, sensors, energy storage devices, electronic along with various correlated areas such as biology, medical, and environment (Bhanushali et al., 2015; Ghuglot et al., 2021; Li et al., 2021; Rai et al., 2018; Xu et al., 2015; Zhao et al., 2018). The main restriction in the development of CuNPs is its inherent oxidation tendency to form Cu_2O or CuO under atmospheric conditions. To protect from oxygen, water, and other chemical entities of CuNPs, various research groups have been attempted to cover the surface of NPs and provide sufficient stability under ambient conditions using surface-capping agents or hybridization with other nanosystems (Bhanushali et al., 2015; Gawande et al., 2016; Ravi Kumar et al., 2015).

3 Scope of this chapter

In this chapter, the uses of CuNPs as sensing materials for the detection of environmental pollutants are summarized. The synthetic approaches through appropriate examples of CuNPs are discussed. Basic ideas of the relevant structural and morphology characterization techniques such as X-ray diffraction (XRD), scanning electron microscopy (SEM), transmission electron microscopy (TEM), energy dispersive X-ray (EDX) spectroscopy, ultraviolet-visible (UV–Vis) spectroscopy, X-ray photoelectron spectroscopy (XPS), and atomic absorption spectroscopy (AAS) are remarked. We hope that a detailed outline of the well-established wet-chemical procedures for the synthesis of CuNPs and their sensing applications would be helpful to a wide community of academicians and scientists researching in the fields of nanosensors, nanobiosensors, agrochemicals (nanofertilizers, nanopesticides) along with associated biology and environmental applications.

4 Methods of preparation of CuNPs

Generally, different shapes and sizes of nanomaterials are fabricated using top-down and bottom-up strategies, and sometimes a combination of both strategies (Cao, 2004). The top-down technique is based on breaking a bulk-sized material into nanoscale and giving the desired shape through physical approaches such as lithography, grinding, milling, cutting, laser beam processing, etc. Another way of nanofabrication is the bottom-up approach, which applies physical/chemical energy existing at the atomic level precursor to build up nanostructures by assembling in the solution/gas phase. However, there are advantages/disadvantages with both methodologies; the bottom-up approach has been extensively used because it offers more scope for controlling the structural morphology of the resulting nanomaterials. Thus, in this section, we highlight ubiquitously used bottom-up approaches for the synthesis of CuNPs nanomaterial.

To prepared CuNPs, the bottom-up techniques are simple chemical route strategies and classified into wet-chemical, sol-gel, polyol-process, microemulsion, solvothermal, thermal treatment, electrodeposition, etc., (Bhanushali et al., 2015; Gawande et al., 2016; Liu et al., 2020b; Ravi Kumar et al., 2015; Zhao et al., 2018). Among these, a few of the very well-recognized methods are listed with references in Table 1. These methods mainly focused on chemical treatment strategies. As an extension of these procedures, some of the advanced methods are also reported for improvement in terms of selectivity of shape and size of nanomaterials. Here, we briefly summarized some of the very imperative examples for the production of CuNPs. A well-established "wet chemical" method for the synthesis of metallic CuNPs mostly involves the reduction of Cu salts [e.g., $CuCl_2$, $CuSO_4$, $Cu(NO_3)_2$] in the presence of reducing agents and suitable stabilizers. Generally, reducing compounds employed are citric acid, glucose, sodium borohydride, hydrazine, ascorbic acid, etc., which provide electrons for the reduction of Cu^{+}/Cu^{2+} to Cu^{0}. For illustration, Yu and

Table 1 Reported some mostly used bottom-up synthesis approaches of CuNPs.

S. no.	Methods	Shape of CuNPs	Precursor	Reducing agent/ stabilizer	Solvent	References
1	Wet chemical	Spherical/rod	$CuSO_4$	Hydrazine/ poly(allylamine)	Water	Wang and Asefa (2010)
2		Particle	$Cu(NO_3)_2$	Diethanolamine	Diethanolamine	Wen et al. (2012)
3		Particle	$Cu(NO_3)_2 \cdot 3H_2O$	L-ascorbic acid/ poly(acrylic acid)	Water	Abiraman et al. (2020)
4		Wire	$Cu(NO_3)_2 \cdot 3H_2O$	Hydrazine hydrate	Water and ethylenediamine	Xu et al. (2016)
5	Solvothermal	Coil	CuCl	PVP-co-vinyl acetate)	NMP + water	Liu et al. (2015)
6		Hollow microsphere	$Cu(CH_3COO)_2$	Glucose, acrylic acid, and NH_3	Water	Wang et al. (2014)
7		Necklace-like microcable	$CuCl + CuCl_2 \cdot 3H_2O$	PVP	Water	Zhan and Yu (2008)
8	Microwave assisted	Sphere	Cu-II acetylacetonate	Benzyl alcohol	Benzyl alcohol	Dar et al. (2012)
9		Particle	$CuCl_2$	–	Ethylene glycol	Kawasaki et al. (2011)
10	Emulsion method	Particle	Cu-$(AOT)_2$	AOT (dioctyl sodium sulfosuccinate)	–	Lisiecki and Pileni (1993)
11		Disk	$Cu(NO_3)_2$	Span 80, Twin 80, and oleic acid/hydrazine	*n*-Butanol and paraffin	Sun et al. (2011)
12	Sol-gel	Particles	$Cu(NO_3)_2 \cdot 3H_2O$	Citric acid	Water	Jiang et al. (2009)
13	Polyol process	Particle	$CuSO_4 \cdot 5H_2O$	Sodium phosphinate monohydrate/PVP	Diethylene glycol	Park et al. (2007)
14		Wire	CuCl and KBr	oleylamine	Ethylene glycol	Yin et al. (2014)
15	Thermal decomposition	Particle	$Cu(N_2H_3COO)_2 \cdot 2H_2O$	–	Water	Dhas et al. (1998)
16		Particle/rod/cube	Cu-II acetylacetonate	1,2-hexadecanediol/ oleic acid and oleylamine	Octylether	Mott et al. (2007)
17		Particle	Cu oxalate	Oleylamine triphenylphosphene	Oleylamine	Salavati-Niasari et al. (2008)
18		Particle	Cu-II oleate	Oleic acid	Phenyl ether	Betancourt-Galindo et al. (2014)
19		Cube	CuCl + octadecylamine	Trioctylphosphine	Oleylamine	Yang et al. (2014)

researchers synthesized well-stabilized Cu nanowires using Cu-nitrate as starting materials and hydrazine as a reducing agent (Xu et al., 2016). Also, they study their oxidation kinetics in gas and liquid phases. Moreover, CuNPs were synthesized by simple chemical reduction of Cu-ions in alkaline media using amino acids as stabilizing components (Yu et al., 2015).

Another most useful synthetic approach for the preparation of nanomaterials with controlled size and shape is known as the solvothermal/hydrothermal technique (Shi et al., 2013; Dewangan et al., 2012). In the solvothermal process, the reaction mixture is treated in an autoclave reactor made of an outer shell with high-quality stainless steel and an inner shell chamber with Teflon polytetrafluoroethylene (PTFE). To prepare CuNPs, the Cu salt/organometallic-Cu compound act as a precursor material that is dissolved along with appropriate additives in a suitable solvent (e.g., water, alcohol). Subsequently, this mixture is solvothermal treated at optimized reaction temperature and reaction time for preparation of desired nanostructured. For example, the hollow structure of the Cu microsphere is prepared by hydrothermal treatment of a homogeneous aqueous solution made of Cu-acetate, glucose, and acrylic acid (Wang et al., 2014). While, Cu nanocoils were produced using *N*-methyl-2-pyrrolidone (NMP) and water mixture as solvent through a solvothermal process (Liu et al., 2015). Likewise, of hydrothermal techniques, a large-scale of Cu nanowires was cooked in the electric pressure cooker using cupric chloride and glucose as the precursor and reducing agent, respectively. Oleic acid and oleylamine are used as dual capping agents. The reaction temperature was maintained at 116°C for different time lengths (2 – 12 h) (Li et al., 2014).

The sol-gel technique is a versatile synthetic approach for the preparation of metal oxide NPs involving two-step processes; first preparation of sol and second its successive conversion to gel by evaporation of the solvent (Niederberger, 2007). As for the metal NPs concern, sol-gel and its modified routes are not much studied. However, Yang and his group reported a combined sol-gel strategy with auto-combustion for the preparation of metallic CuNPs (Jiang et al., 2009). They have first prepared sol by adding Cu-nitrate and citric acid into water, and adjusted pH to 7.0 with an aqueous ammonia solution. The resultant solution mixture was heated at 95°C to evaporate the solvent and change a dehydrated gel. Then obtained gel was activated in the auto-combustion tube under the Ar/N_2 atmosphere at 300°C. Finally, after cooling down to room temperature, CuNPs were obtained.

The reverse micelle method is an alternative approach to prepare various nanostructured materials (Ganguli et al., 2010). In this approach, water-in-oil (W/O) or oil-in-water (O/W) type microemulsion is formed by dispersing two immiscible liquids in the presence of appropriate surface-active agents (emulsifiers/surfactants). The final geometry of micelles is controlled by the size of the polar part and length of the hydrocarbon chain of surfactant. Finally, the Cu salt is dissolved in this microemulsion, which serves as nanoreactor templates for the preparation of CuNPs. As an example to obtain CuNPs, first a W/O microemulsions system was prepared by a surfactant (sodium dodecyl sulfate, SDS), cosurfactant (isopentanol), oil phase (cyclohexane), and the aqueous phase (aqueous solution of $CuSO_4$). Then the aqueous

solution of sodium borohydride was added dropwise into the microemulsion, which produces nanosized metallic Cu (Qiu et al., 1999).

The polyol process is another extensively used chemical approach for the shape-controlled synthesis of metal and oxide NPs (Cao, 2004; Fiévet et al., 2018)NPs. In this process, the high boiling polyol solvents such as ethylene glycol, triethylene glycol, diethylene glycol, tetraethylene glycol, polyethyleneglycol, and many others were employed for the reduction of metal ions. To synthesize Cu NPs, the polyol process is suitable because it can protect the surface of NPs against atmospheric corrosion and oxidation. Initially, CuO and EG system was performed to produce microscale Cu particles (Fievet et al., 1989), subsequently modified polyol processes have been developed for the preparation of shape-controlled CuNPs with/without external reducing agents and stabilizers. For example, Cu nanowires were produced by refluxing the CuCl, KBr, oleylamine, and EG reaction mixture under the anhydrous condition at 198°C for 1 h (Yin et al., 2014).

Microwave-assisted nanofabrication (Kumar et al., 2020) is an efficient novel route, which uses microwave electromagnetic radiations to carry out chemical reactions and has been also applied to produce nanostructured metallic Cu. In this procedure, microwave energy is transformed into heat energy, which accelerates the reactions with several benefits as compared to conventional heating such as contactless heating, rate enhancement, as well as the high yield of the products with a controlled distribution of particle size. Additionally, a key advantage of the microwave irradiation technique is that it can be hybridized with other processes such as chemical reduction, polyol, emulsion, solvothermal, sonochemical, etc. For instance, simply microwave irradiation in Cu(II)-acetylacetonate and benzyl alcohol solution produce air-stable highly crystalline Cu nanospheres (Dar et al., 2012). On the other hand, an improved microwave-assisted polyol method is used for the preparation of metallic CuNPs by reduction of Cu(II)-sulfate with sodium hypophosphite in ethylene glycol (Zhu et al., 2004). Likewise, Kawasaki and groups prepared fluorescent Cu nanocrystals in a nonaqueous solvent through microwave-assisted polyol method without employing any external surfactant (Kawasaki et al., 2011).

In the solution chemistry, mostly thermal decomposition of the metal-organic complex such as metal-carbonyl (Peng et al., 2006), metal-acetylacetonate (Mott et al., 2007), and metal-oleate (Park et al., 2004) is carried out in high boiling solvents to produce NPs. Generally, at high temperatures, metal-organic compounds decompose and short-burst into metal nuclei and grow as fine and dispersed particles in the solvent. To control the growth rate and protect the surface of growing nuclei, appropriate surfactants are added to the reaction mixture. In this typical preparation technique of CuNPs, Cu(II)-acetylacetonate, Cu(II)-oxalate, Cu(II)-oleate, and other salts along with surfactants such as oleylamine, oleic acid, triphenylphosphene, poly(*N*-vinylpyrrolidone) (PVP), etc. (Gawande et al., 2016) are thermally treated. For instance, Zhong et al. demonstrated that the thermal decomposition of Cu(II)-acetylacetonate in the presence of 1,2-hexadecanediol as a reducing agent along with oleic acid and oleylamine as capping agents in the octylether solvent produces monodispersed and stable and metallic nano-Cu. By tuning the reaction temperature,

reaction time, and capping agent concentration, rod, and cube-shaped CuNPs can be prepared (Mott et al., 2007). In contrast, CuNPs were synthesized in an aqueous media by refluxing of copper(II) hydrazine carboxylate complex at 80°C in inert atmosphere (Dhas et al., 1998). This reaction proceeded through thermally decomposition and reduction of the complex by changing the blue color reaction mixture into red.

Apart from abovementioned bottom-up chemical techniques, there are many other approaches such as green synthesis (Gopalakrishnan and Muniraj, 2021; Jahan et al., 2021), biosynthesis (Brumbaugh et al., 2014), electrochemical (Kumar et al., 2011), photochemical (Shimotsuma et al., 2007), sonochemical (Haas et al., 2006), chemical vapor deposition (Choi and Park, 2004), and other related strategies (Gawande et al., 2016) have been extensively used for the preparation of CuNPs.

5 Characterization of CuNPs

Crystal structure, surface topography, composition, and other physicochemical properties of CuNPs are characterized using various commonly used instruments and techniques. The detailed discussion of instrumentation is beyond the scope of this chapter; therefore, a brief summary of different characterization techniques often used is discussed here. X-ray diffraction (XRD) is a nondestructive and versatile analytical technique that enables the determination of crystallinity and crystal structure of CuNPs including lattice constants, phase-purity, anisotropic growth, and the preferred orientation of polycrystalline materials. Electron microscope techniques such as scanning electron microscopy (SEM) and transmission electron microscopy (TEM) are the most important tools for the surface morphology imagining of NPs. The use of advanced studies of TEM such as high resolution-TEM (HRTEM) imaging and selected area electron diffraction (SAED) patterns provide crystallographic information along with grain boundary, dislocation, and defects present in the NPs. The energy dispersive X-ray (EDX) spectroscopy generally allied with SEM and TEM is employed for studying the qualitative/quantitative elemental composition of NPs. In principle, X-ray photoelectron spectroscopy (XPS) is known as a surface characterization technique and has been found very useful to analyze surface chemistry of the NPs to determine the surface elemental composition, chemical state, and electronic state of the elements. In the context of CuNPs, they can be used to confirm the presence of Cu^0, Cu^+, or Cu^{2+} oxidation state in the sample.

At the nanoscale level, metallic Cu has unique optical and electronic features, therefore spectrophotometry has become an alternative useful tool for characterization and applications purposes. Thus, CuNPs exhibit local surface plasmon resonance (LSRP) due to a collective oscillation of conduction electrons and show peaks under irradiation of ultraviolet-visible (UV–Vis) light like gold and silver NPs. For example, based on the preparation conditions and dimensions of Cu nanowires, LSPR peaks of 590 nm (Liu et al., 2003), 570 nm (Zhang et al., 2006), and 620 nm (Cao et al., 2003) have been reported. Moreover, surface areas and pore size distribution of NPs are measured by gas adsorption/desorption.

6 Applications CuNP-based sensors for environmental pollutants

The sensor is an analytical device that responds against physiochemical properties change during the interactions between the interest of the subject (chemical, temperature, pressure, etc.) and the active component of the sensor. For example, a chemical sensor transforms chemical information such as composition, presence of a particular element or ion, concentration, chemical activity, partial pressure, etc., into useful signals (Hulanicki et al., 1991). Based on the physical or chemical properties summarized in Table 2, a variety of sensor devices has been fabricated for applications in miscellaneous fields such as medicine, environmental remediation, home and public securities, food analysis, etc. In the following paragraphs, the use of CuNPs as the active material in sensing devices to detect various kinds of hazardous components present in the environment is highlighted.

6.1 Optical properties-based sensors

The study of colorimetric absorption and fluorescence phenomena of CuNPs is the most promising method for the detection of toxic components present in the water and territorial ecosystems. Advancement in the optics and use of Cu nanomaterials have improved performances including factors such as affordability, user-friendly, rapidness, and miniaturization of optoelectronic devices (Jeong et al., 2020; Wang et al., 2017). Moreover, multianalyte zones for different functions can be designed for the sensing of multicomponents in a single device.

6.1.1 Metal and anion sensors

Citrate-capped CuNPs were used as colorimetric sensors for the detection of Hg^{2+} by measuring the change of characteristic absorption peak of CuNPs observed at 260 nm. Authors provide evidence that CuNPs reduced Hg^{2+} and led to the formation of Hg–Cu amalgam (Li et al., 2019). In the same manner, Soomro et al. developed the use of cysteine capped CuNPs for selective detection of mercury ions (Hg^{2+}) from river water samples (Soomro et al., 2014). For this, $CuCl_2$ was used as a precursor, as

Table 2 Type of interactions between the analytes and the active materials.

Type of interactions	Type of analytical signals	Devices based-on
Physical interaction	Optical, thermal, electrical, mass	Optical Electrochemical Thermometric Electrical Mass sensitivity Magnetic α, β, and γ radioactivity
Chemical interaction	Chemical reaction	
Biochemical interaction	Biochemical reaction	

well as cysteine and hydrazine monohydrate employed as the capping and reducing agents, respectively. The resultant NPs exhibit red color that changes to yellow by the addition of Hg^{2+} ions. It was also noticed that the LSPR band of NPs depends on the size and shape, capping agents, and surrounding medium of the solution. In this experiment, the addition of Hg^{2+} induced aggregation of CuNPs was indicated by a red-shift of the LSPR band in the visible region using spectrophotometry and TEM studies. The linearity range for the determination of Hg^{2+} was measured 0.5–3.5 μM with a limit of detection (LOD) value of 43 nM. Other research groups used cysteine functionalized CuNPs for detection of chromium ions (Cr^{4+}) in the aqueous solution using quenching properties of fluorescence emission observed at 490 nm (Cui et al., 2015). Laghari et al. demonstrated the application of ranolazine (rano)-derived CuNPs for selective detection of arsenic (As^{3+}). Rano-Cu NPs were synthesized in the presence of hydrazine and ranolazine where the hydrazine is used as a reducing agent and $CuCl_2$ is used as a precursor molecule. The sensing principle is based on the color change of rano-CuNPs after the addition of As^{3+} from brick red to dark green that can be visualized by naked eyes (Laghari et al., 2019).

Selective detection of sulfide ion (S^{2-}) was demonstrated using mercaptosuccinic acid (MPA) stabilized CuNPs in food additives (Wang et al., 2020). Here, Cu^{2+}@MPA-CuNPs display aggregation-induced fluorescence emission, which is quenched in the presence of S^{2-} due to the destruction of the aggregated structure. Momeni et al. developed a fluorescence-based method for selective and sensitive detection of cyanide ion (CN^-) in water samples using CuNPs as a fluorescent probe. CuNPs were prepared using ascorbic acid as a reducing and capping agent with an average size of 10 nm having a blue emission at 440 nm. The linear range for determination of CN^- in water is found in the range of 0.5–18 μM with the LOD value of 0.37 μM (Momeni et al., 2017).

6.1.2 Chemical and biomolecules sensors

MPA stabilized CuNPs were used as colorimetric probes for sensing hydrogen peroxide (H_2O_2) without the use of chromogenic reagents. Researchers explained that a sequential oxidation process of CuNPs leads as a probe for the colorimetric and spectroscopic detection of H_2O_2 and other reactive oxygen species in a wide sampling range (Du et al., 2017). Ghoto and his team studied the application of CuNPs for colorimetric sensing of dithiocarbamate pesticides present in the environment plus vegetables and fruit juice samples. The color change of cetyltrimethylammonium bromide (CTAB) capped CuNPs was monitored with the interaction pesticide (Ghoto et al., 2019). Chen et al. demonstrated the preparation of poly-thymine30 (PolyT30) DNA templated CuNPs and applied them as the fluorescence assays for selective detection of organophosphorus pesticides through the use of tyrosinase enzymatic controlled reaction (Chen et al., 2019). Fluorescence and mass spectroscopy-based bimodal technique was developed for accurate and selective detection of the explosive 2,4,6-trinitrotoluene (TNT) using poly(thymine)-CuNPs. This methodology exhibits excellent sensitivity and is capable to detect TNT at the subpart per trillion levels (Hu et al., 2018).

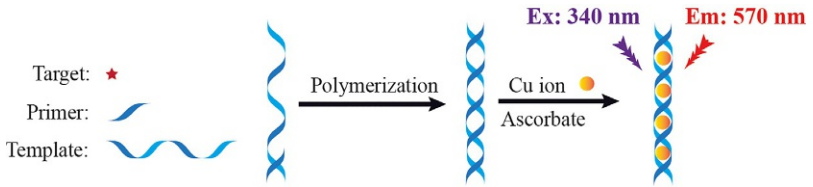

FIG. 2

Schematic illustration of template formation dsDNA and fluorescent emission using CuNPs.

Reproduced with permission from Qing, Z., Qing, T., Mao, Z., He, X., Wang, K., Zou, Z., Shi, H., He, D., 2014. dsDNA-specific fluorescent copper nanoparticles as a "green" nano-dye for polymerization-mediated biochemical analysis. Chem. Commun. 50, 12746–12748. Copyright (1996) Royal Society of Chemistry.

Recently, Liu and research groups prepared monodispersed Cu nanoclusters that show excellent tetraenzyme mimic activities. Based on peroxidase and ascorbic acid oxidase enzymatic activities, they developed novel colorimetric glutathione and fluorimetric ascorbic acid sensors, respectively (Liu et al., 2020a). Wang and research groups employed CuNP-based DNA-specific fluorescent as an environment-friendly nano-dye for the polymerization-mediated biochemical analysis. As shown in Fig. 2, corresponding target species triggered polymerization reaction yielding complementary double-stranded DNA (dsDNA) template, which used to develop CuNPs fluorescence signal. The same research group effectively applies this procedure for the detection of *E. coli* bacteria, nucleic acid, Hg^{2+}, S^{2-}, and Pb^{2+} (Chen et al., 2012; Liu et al., 2012; Qing et al., 2014). Recently, Tsai and research groups applied dsDNA templated Cu-nanoprobe for quick detection of tuberculosis (Tsai et al., 2019). Moreover, several studies have been reported to use CuNPs as fluorescent nanoprobe in the fields of imaging of cancer cells (Zhou et al., 2016; Wang et al., 2015), renal clearance (Yang et al., 2015), microRNA biosensor (Cui et al., 2020), and other biomedical research. Aghajani et al. used the aerosol direct writing method for deposition of CuNPs (size distribution is below 20 nm) patterns on the silicon substrate. This method allows to the creation of surface-enhanced Raman scattering (SERS) printed substrates for highly sensitive and selective SERS-based sensor applications (Aghajani et al., 2020).

6.2 Electrochemical properties based sensors

The high electrical conductivity and metallic nature of CuNPs make them a potential candidate to use as an active material for the fabrication of electrochemical sensors. The oxidation-reduction redox processes occurring between the target analyte and active material are recorded with various electrochemical techniques such as cyclic voltammetry (CV), chronopotentiometry, and electrochemical impedance spectroscopy (EIS). For example, Zhang et al. used Cu nanodendrimer to decorate Au-electrode for the determination of L-tyrosine in the aqueous solution using CV

and EIS techniques (Zhang et al., 2008). In another approach, CuNPs were electrochemically deposited on the Cu-disk surface, which is used as a sensor for analyzing chemical oxygen demand (COD) in the different water sources with a linear range of 4.8–600 mg L^{-1} and LOD 3.6 mg L^{-1} (Yang et al., 2011). Also, Stortini et al. reported that Cu-nanowires decorated polycarbonate membrane performs as a better electrochemical sensor for the detection of nitrate in terms of durability and reproducibility (Stortini et al., 2015). Jiang et al. prepared nonenzymatic electrodes by depositing CuNPs on the graphene surface for glucose sensing. The interaction effect between CuNPs and graphene sheets responds very quickly to glucose oxidation in the alkaline medium with the LOD value of 0.12 μM (Jiang et al., 2017). CuNPs decorated with carbon nanotubes were used to fabricate sensors by dip coating on the surface of glassy carbon electrodes for the detection of methimazole (Karim-Nezhad et al., 2018) and nicotine (Goodarzi et al., 2015). Recently, Miao et al. demonstrated that the dsDNA templated CuNPs could be applied for the detection of microRNA by amplified electrochemical technique (Miao et al., 2018). Similarly, poly(thymine)-templated CuNPs were used as biomarkers for the electrochemical detection of prostate cancer (Zhu et al., 2016). In other work, Sheng et al. described machine learning electrochemical sensors for the detection of maleic hydrazide using CuNPs in onion, rice, potato, and cotton leaf samples with good stability, selectivity with detection limits (Sheng et al., 2019).

6.3 Other sensors

Apart from the optical and electrochemical sensors, CuNPs have been studied for various other kinds of sensors. For example, Sun and coworkers prepared ultralight pressure sensors utilizing pours Cu-nanowire aerogel (Xu et al., 2017). When pressure is applied to the aerogel, it induces structural geometry change of aerogel that transforms into a corresponding change of electrical resistance; therefore, this work opens a multipurpose application in the fields of electronic skin, wearable devices, etc. In another approach, conductive nanoink made of Cu nanowires was printed on a silicon wafer or alumina ceramic by direct writing method. The high-temperature studies of printed electrodes provide stable and high electrical conductivity, which can be utilized for the preparation of high-temperature flexible electronic sensors (Li et al., 2020, 2021). Likewise, CuNPs are deposited on the cellulose to yield a highly conductive paper platform for the applications of lightweight and next-generation flexible electronic sensors (Pinto et al., 2020; Yang et al., 2019). More recently, Shrivas et al. demonstrated the use of Cu@Ag core-shell NPs for food safety monitoring of phenthoate pesticide using a smartphone-assisted paper-based sensor as shown in Fig. 3 (Shrivas et al., 2020b). There was an enhancement of signal intensity when bimetallic NPs used as a sensing material on the paper substrate compared to individual use of citrate-capped AgNPs. The working principle for selective detection of phenthoate is attributed to the selective interaction of pesticide with Cu@Ag NPs caused the color change from yellow to pink.

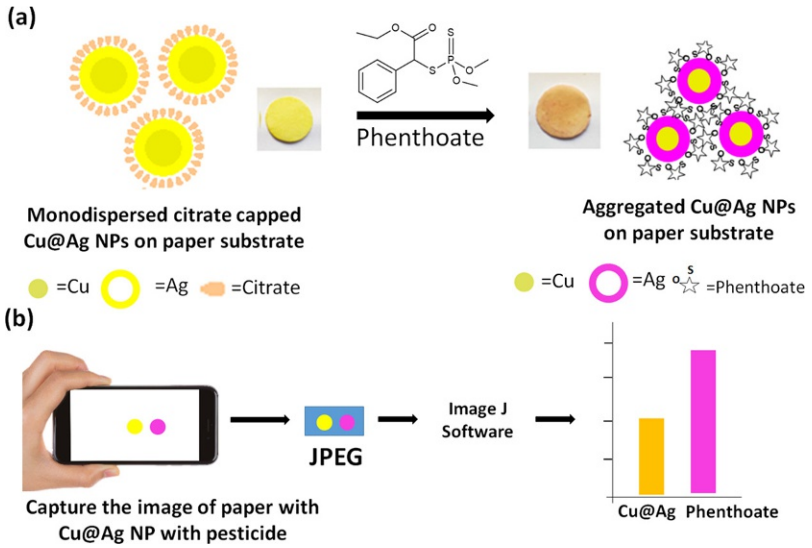

FIG. 3

(A) Mechanism for detection of phenthoate on paper-based sensor where the monodispersion and aggregation of Cu@Ag NPs before and after the addition of phenthoate and (B) procedure for the determination of the signal intensity of Cu@Ag NPs and with phenthoate by smartphone-assisted paper-based sensor.

Reproduced with permission from Shrivas, K., Monisha, Patel, S., Thakur, S.S., Shankar, R., 2020. Food safety monitoring of the pesticide phenthoate using a smartphone-assisted paper-based sensor with bimetallic Cu@Ag core-shell nanoparticles. Lab Chip 20, 3996–4006. Copyright (2001) Royal Society of Chemistry.

7 CuNPs-based sensor applications in agrochemicals and agroecosystems

The use of nanomaterials in the sector of agrochemical involves agricultural activities such as fertilizers, pesticides, and soil condition, which play a significant role in plant growth and protection, plant-pathogen diagnosis, and disease management. Also, smart nano-drug delivery systems for gene modification/transfer in molecular genetic nanotechnology are stimulating several areas of agriculture (DeRosa et al., 2010; Kah, 2015; Scott et al., 2018; Sebastian et al., 2020; Shang et al., 2019). In addition, their applications in the sustainable environment involve the development of green energy resources, water and air purification, pollutant sensing and controlling, food safety and packaging, and net nutrient balance including green synthesis of NPs. Moreover, nanomaterials are emergent systems in the areas of veterinary science such as animal health, poultry farming, drug and vaccination, food supplements, etc.

In this context, the potential impact of CuNPs on human health along with biotic (plant/microbes/animals) and the environment in aquatic and nonaquatic systems they have been widely used due to their broad application range and less-toxic nature. As a result, they can be utilized as nanofertilizers, nanoherbicides, nanopesticides, nanosensors, water treatment, textile, food preservation along with related other agricultural, biomedical, and environmental applications. For example, nano Cu at $50\,\mu g\,mL^{-1}$ concentration has unique genotoxicity and is more effective in *E. coli* and *lactobacillus* bacteria compared to microsize Cu (Kaweeteerawat et al., 2015). This study shows that nano-Cu generates substantial reactive oxygen species in different mechanisms, which is responsible for DNA damage and cell growth inhibition of microbes. Sathiyabama and Manikandan employed Cu-chitosan NPs as a foliar spray on finger millet plants to enhance growth profile and control blast disease (Sathiyabama and Manikandan, 2018). In the same way, root fungal disease in tomato plants can be suppressed through the foliar treatment of nanoscale Cu (Shen et al., 2020). Pradhan and groups studied the effect of polymer encapsulated CuNPs on mung bean plants and their result exhibits that CuNPs improve biochemical and biophysical properties compared to widely used copper sulfate (Kaweeteerawat et al., 2015). In another report, CuNPs synthesized by eco-friendly bacteria display an excellent insecticidal activity against grains storage pest control (El-Saadony et al., 2020). Verma and groups synthesized yeast-immobilized CuNPs dressing material for diabetic wounds and simultaneously prevent bacterial infection and control glucose levels (Bhadauriya et al., 2018). Very recently, Mandal and coworkers reported that nanocomposite of CuNPs and graphene can be used as an effective antiviral coating material against infectious respiratory RNA viruses such as influenza and corona, which are generally transmitted through breathing droplets or contaminated surfaces (Das Jana et al., 2020).

Despite the useful applications of CuNPs, several studies indicate that uncontrolled and extensive use of nanoscale Cu poses a negative impact on ecosystems (Ameh and Sayes, 2019; Pang et al., 2021; Sharma et al., 2021). For example, CuNPs presence in the water prompts toxic effect in rainbow trout fish by inducing ionoregulatory that affects sodium-pump activity in the brain (Shaw et al., 2012). At present, it is not clear how CuNPs affect soil-plant and soil-microbial systems that may result in major problems on crops production, environment, and health-related issues (Adeleye et al., 2016; Anjum et al., 2015). There are many other research articles available on the toxicity of CuNPs including review articles and book chapters (Conway et al., 2015; Keller et al., 2017; Rajput et al., 2019; Wang et al., 2013). Therefore, it is in-depth studies required to explore CuNPs toxicity and mechanism on ecosystems, the interaction of soil-microbes, the bioaccumulation in plants as well as their toxic behavior and biotransformation as reported by Avellan and group (Avellan et al., 2020).

8 Conclusion and future trends

A brief discussion was made of the frequently used wet-chemical routes for the synthesis of CuNPs. The strategies of protection of the surface of metallic CuNPs are

comprehensively highlighted. The use of CuNPs for sensing devices is an ultimate way to take advantage of the inherent unique physical and chemical properties available at the nanosize Cu. This chapter critically demonstrates the characterization, sensing mechanism, and applications of CuNPs as a sensor for the quantitative determination of different types of toxic substances from environmental, biological, foods samples, etc. However, due to the lack of a complete profile of their toxicity uncontrolled uses are still risky for ecosystems and biomedical points of view. Therefore, future research must be formulated by assessing existing risks toward green synthesis, distribution schemes, including release and detection policy.

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References

Abiraman, T., Rajavelu, K., Rajakumar, P., Balasubramanian, S., 2020. Sub 1 nm poly(acrylic acid)-capped copper nanoparticles for the synthesis of 1,2,3-triazole compounds. ACS Omega 5, 7815–7822.

Adeleye, A.S., Oranu, E.A., Tao, M., Keller, A.A., 2016. Release and detection of nanosized copper from a commercial antifouling paint. Water Res. 102, 374–382.

Aghajani, S., Accardo, A., Tichem, M., 2020. Aerosol direct writing and thermal tuning of copper nanoparticle patterns as surface-enhanced Raman scattering sensors. ACS Appl. Nano Mater. 3, 5665–5675.

Ahlawat, J., Masoudi Asil, S., Guillama Barroso, G., Nurunnabi, M., Narayan, M., 2021. Application of carbon nano onions in the biomedical field: recent advances and challenges. Biomater. Sci. 9, 626–644.

Ameh, T., Sayes, C.M., 2019. The potential exposure and hazards of copper nanoparticles: a review. Environ. Toxicol. Pharmacol. 71, 103220.

Anastas, P.T., Zimmerman, J.B., 2021. Moving from protection to prosperity: evolving the U.S. environmental protection agency for the next 50 years. Environ. Sci. Technol. 55, 2779–2789.

Anjum, N.A., Adam, V., Kizek, R., Duarte, A.C., Pereira, E., Iqbal, M., Lukatkin, A.S., Ahmad, I., 2015. Nanoscale copper in the soil–plant system—toxicity and underlying potential mechanisms. Environ. Res. 138, 306–325.

Avellan, A., Simonin, M., Anderson, S.M., Geitner, N.K., Bossa, N., Spielman-Sun, E., Bernhardt, E.S., Castellon, B.T., Colman, B.P., Cooper, J.L., Ho, M., Hochella, M.F., Hsu-Kim, H., Inoue, S., King, R.S., Laughton, S., Matson, C.W., Perrotta, B.G., Richardson, C.J., Unrine, J.M., Wiesner, M.R., Lowry, G.V., 2020. Differential reactivity of copper- and gold-based nanomaterials controls their seasonal biogeochemical cycling and fate in a freshwater wetland mesocosm. Environ. Sci. Technol. 54, 1533–1544.

Benedict, K.M., Reses, H., Vigar, M., Roth, D.M., Roberts, V.A., Mattioli, M., Cooley, L.A., Hilborn, E.D., Wade, T.J., Fullerton, K.E., Yoder, J.S., Hill, V.R., 2017. Surveillance for waterborne disease outbreaks associated with drinking water—United States, 2013–2014. MMWR Morb. Mortal. Wkly Rep. 66, 1216–1221.

Betancourt-Galindo, R., Reyes-Rodriguez, P.Y., Puente-Urbina, B.A., Avila-Orta, C.A., Rodríguez-Fernández, O.S., Cadenas-Pliego, G., Lira-Saldivar, R.H., García-Cerda, L.A., 2014. Synthesis of copper nanoparticles by thermal decomposition and their antimicrobial properties. J. Nanomater. 2014, 980545.

Bhadauriya, P., Mamtani, H., Ashfaq, M., Raghav, A., Teotia, A.K., Kumar, A., Verma, N., 2018. Synthesis of yeast-immobilized and copper nanoparticle-dispersed carbon nanofiber-based diabetic wound dressing material: simultaneous control of glucose and bacterial infections. ACS Appl. Bio Mater. 1, 246–258.

Bhanushali, S., Ghosh, P., Ganesh, A., Cheng, W., 2015. 1D copper nanostructures: progress, challenges and opportunities. Small 11, 1232–1252.

Bhattacharya, S., Samanta, S.K., 2016. Soft-nanocomposites of nanoparticles and nanocarbons with supramolecular and polymer gels and their applications. Chem. Rev. 116, 11967–12028.

Brumbaugh, A.D., Cohen, K.A., St. Angelo, S.K., 2014. Ultrasmall copper nanoparticles synthesized with a plant tea reducing agent. ACS Sustain. Chem. Eng. 2, 1933–1939.

Cao, G., 2004. Nanostructures and Nanomaterials Synthesis, Properties and Applications. Imperial College Press, London.

Cao, X., Yu, F., Li, L., Yao, Z., Xie, Y., 2003. Copper nanorod junctions templated by a novel polymer–surfactant aggregate. J. Cryst. Growth 254, 164–168.

Chen, J., Park, B., 2016. Recent advancements in nanobioassays and nanobiosensors for foodborne pathogenic bacteria detection. J. Food Prot. 79, 1055–1069.

Chen, J., Liu, J., Fang, Z., Zeng, L., 2012. Random dsDNA-templated formation of copper nanoparticles as novel fluorescence probes for label-free lead ions detection. Chem. Commun. 48, 1057–1059.

Chen, J., Han, T., Feng, X., Wang, B., Wang, G., 2019. A poly(thymine)-templated fluorescent copper nanoparticle hydrogel-based visual and portable strategy for an organophosphorus pesticide assay. Analyst 144, 2423–2429.

Choi, H., Park, S.-H., 2004. Seedless growth of free-standing copper nanowires by chemical vapor deposition. J. Am. Chem. Soc. 126, 6248–6249.

Claus, S.P., Guillou, H., Ellero-Simatos, S., 2016. The gut microbiota: a major player in the toxicity of environmental pollutants? NJP Biofilms and Microbiomes 2, 16003.

Conway, J.R., Adeleye, A.S., Gardea-Torresdey, J., Keller, A.A., 2015. Aggregation, dissolution, and transformation of copper nanoparticles in natural waters. Environ. Sci. Technol. 49, 2749–2756.

Crisponi, G., Nurchi, V.M., 2015. Metal ion toxicity. In: Scott, R.A. (Ed.), In Encyclopedia of Inorganic and Bioinorganic Chemistry. John Wiley & Sons, Ltd, pp. 1–14.

Cui, M., Song, G., Wang, C., Song, Q., 2015. Synthesis of cysteine-functionalized water-soluble luminescent copper nanoclusters and their application to the determination of chromium(VI). Microchim. Acta 182, 1371–1377.

Cui, J., Han, H., Piao, J., Shi, H., Zhou, D., Gong, X., Chang, J., 2020. Construction of a novel biosensor based on the self-assembly of dual-enzyme cascade amplification-induced copper nanoparticles for ultrasensitive detection of microRNA153. ACS Appl. Mater. Interfaces 12, 34130–34136.

Dar, M.I., Sampath, S., Shivashankar, S.A., 2012. Microwave-assisted, surfactant-free synthesis of air-stable copper nanostructures and their SERS study. J. Mater. Chem. 22, 22418–22423.

Das Jana, I., Kumbhakar, P., Banerjee, S., Gowda, C.C., Kedia, N., Kuila, S.K., Banerjee, S., Das, N.C., Das, A.K., Manna, I., Tiwary, C.S., Mondal, A., 2020. Copper nanoparticle–graphene composite-based transparent surface coating with antiviral activity against influenza virus. ACS Appl. Nano Mater. https://doi.org/10.1021/acsanm.0c02713.

DeRosa, M.C., Monreal, C., Schnitzer, M., Walsh, R., Sultan, Y., 2010. Nanotechnology in fertilizers. Nat. Nanotechnol. 5, 91.

Dewangan, K., Sinha, N.N., Chavan, P.G., Sharma, P.K., Pandey, A.C., More, M.A., Joag, D.S., Munichandraiah, N., Gajbhiye, N.S., 2012. Synthesis and characterization of self-assembled nanofiber-bundles of V_2O_5: their electrochemical and field emission properties. Nanoscale 4, 645–651.

Dewangan, K., Shrivas, K., Kurrey, R., 2020. Chapter 9—hybrid nanomaterials as chemical sensors. In: Abd-Elsalam, K.A. (Ed.), multifunctional Hybrid Nanomaterials for Sustainable Agri-Food and Ecosystems. Elsevier, pp. 213–239.

Dewangan, K., Singh, D., Patel, S.K.S., Shrivas, K., 2021. Temperature-programmed nitridation of monodispersed VO*x* nanoparticles into nanocrystalline superconducting oxygen-doped vanadium nitride. New J. Chem. 45, 6129–6135.

Dhas, N.A., Raj, C.P., Gedanken, A., 1998. Synthesis, characterization, and properties of metallic copper nanoparticles. Chem. Mater. 10, 1446–1452.

Du, Y., Fang, J., Wang, H., Yang, Y., 2017. Inducible sequential oxidation process in water-soluble copper nanoclusters for direct colorimetric assay of hydrogen peroxide in a wide dynamic and sampling range. ACS Appl. Mater. Interfaces 9, 11035–11044.

Dutheil, F., Baker, J.S., Navel, V., 2020. COVID-19 as a factor influencing air pollution? Environ. Pollut. 263, 114466.

Egorova, K.S., Ananikov, V.P., 2017. Toxicity of metal compounds: knowledge and myths. Organometallics 36, 4071–4090.

El-Saadony, M.T., Abd El-Hack, M.E., Taha, A.E., Fouda, M.M.G., Ajarem, J.S., Maodaa, S.N., Allam, A.A., Elshaer, N., 2020. Ecofriendly synthesis and insecticidal application of copper nanoparticles against the storage pest tribolium castaneum. Nanomaterials 10, 587.

Fievet, F., Lagier, J.P., Blin, B., Beaudoin, B., Figlarz, M., 1989. Homogeneous and heterogeneous nucleations in the polyol process for the preparation of micron and submicron size metal particles. Solid State Ion. 32-33, 198–205.

Fiévet, F., Ammar-Merah, S., Brayner, R., Chau, F., Giraud, M., Mammeri, F., Peron, J., Piquemal, J.Y., Sicard, L., Viau, G., 2018. The polyol process: a unique method for easy access to metal nanoparticles with tailored sizes, shapes and compositions. Chem. Soc. Rev. 47, 5187–5233.

Gale, N.H., Stos-Gale, Z.A., 1982. Bronze age copper sources in the mediterranean: a new approach. Science 216, 11–19.

Ganguli, A.K., Ganguly, A., Vaidya, S., 2010. Microemulsion-based synthesis of nanocrystalline materials. Chem. Soc. Rev. 39, 474–485.

Gawande, M.B., Goswami, A., Felpin, F.-X., Asefa, T., Huang, X., Silva, R., Zou, X., Zboril, R., Varma, R.S., 2016. Cu and cu-based nanoparticles: synthesis and applications in catalysis. Chem. Rev. 116, 3722–3811.

Ghoto, S.A., Khuhawar, M.Y., Jahangir, T.M., Mangi, J.U.D., 2019. Applications of copper nanoparticles for colorimetric detection of dithiocarbamate pesticides. J. Nanostruct. Chem. 9, 77–93.

Ghuglot, R., Titus, W., Agnihotri, A.S., Krishnakumar, V., Krishnamoorthy, G., Marimuthu, N., 2021. Stable copper nanoparticles as potential antibacterial agent against aquaculture pathogens and human fibroblast cell viability. Biocatal. Agric. Biotechnol. 32, 101932.

Goodarzi, Z., Maghrebi, M., Zavareh, A.F., Mokhtari-Hosseini, Z.-B., Ebrahimi-hoseinzadeh, B., Zarmi, A.H., Barshan-tashnizi, M., 2015. Evaluation of nicotine sensor based on copper nanoparticles and carbon nanotubes. J. Nanostruct. Chem. 5, 237–242.

Gopalakrishnan, V., Muniraj, S., 2021. Neem flower extract assisted green synthesis of copper nanoparticles—optimisation, characterisation and anti-bacterial study. Mater. Today 36, 832–836.

Guo, X., Huang, J., Wei, Y., Zeng, Q., Wang, L., 2020. Fast and selective detection of mercury ions in environmental water by paper-based fluorescent sensor using boronic acid functionalized MoS_2 quantum dots. J. Hazard. Mater. 381, 120969.

Haas, I., Shanmugam, S., Gedanken, A., 2006. Pulsed sonoelectrochemical synthesis of size-controlled copper nanoparticles stabilized by poly(N-vinylpyrrolidone). J. Phys. Chem. B 110, 16947–16952.

Haroon, M., Al-Saadi, A.A., Iqbal, M.A., 2021. Comparative exposure assessment of potential health risks through the consumption of vegetables irrigated by freshwater/wastewater: Gujranwala, Pakistan. Chem. Res. Toxicol. https://doi.org/10.1021/acs.chemrestox.0c00277.

Hu, J., Wang, C., Liu, R., Su, Y., Lv, Y., 2018. Poly(thymine)-CuNPs: bimodal methodology for accurate and selective detection of TNT at sub-ppt levels. Anal. Chem. 90, 14469–14474.

Hulanicki, A., Glab, S., Ingman, F., 1991. Chemical sensors definitions and classification. Pure Appl. Chem. 63, 1247–1250.

Jahan, I., Erci, F., Isildak, I., 2021. Facile microwave-mediated green synthesis of non-toxic copper nanoparticles using Citrus sinensis aqueous fruit extract and their antibacterial potentials. J. Drug Delivery Sci. Technol. 61, 102172.

Jeong, S., Liu, Y., Zhong, Y., Zhan, X., Li, Y., Wang, Y., Cha, P.M., Chen, J., Ye, X., 2020. Heterometallic seed-mediated growth of monodisperse colloidal copper nanorods with widely tunable plasmonic resonances. Nano Lett. 20, 7263–7271.

Jiang, Y., Yang, S., Hua, Z., Huang, H., 2009. Sol–gel autocombustion synthesis of metals and metal alloys. Angew. Chem. Int. Ed. 48, 8529–8531.

Jiang, J., Zhang, P., Liu, Y., Luo, H., 2017. A novel non-enzymatic glucose sensor based on a cu-nanoparticle-modified graphene edge nanoelectrode. Anal. Methods 9, 2205–2210.

Kah, M., 2015. Nanopesticides and nanofertilizers: emerging contaminants or opportunities for risk mitigation? Front. Chem. 3, 64.

Karim-Nezhad, G., Khorablou, Z., Dorraji, P.S., 2018. A promising electrochemical sensing platform based on copper nanoparticles-decorated polymer in carbon nanotube electrode for monitoring methimazole. J. Iran. Chem. Soc. 15, 905–913.

Kawasaki, H., Kosaka, Y., Myoujin, Y., Narushima, T., Yonezawa, T., Arakawa, R., 2011. Microwave-assisted polyol synthesis of copper nanocrystals without using additional protective agents. Chem. Commun. 47, 7740–7742.

Kaweeteerawat, C., Chang, C.H., Roy, K.R., Liu, R., Li, R., Toso, D., Fischer, H., Ivask, A., Ji, Z., Zink, J.I., Zhou, Z.H., Chanfreau, G.F., Telesca, D., Cohen, Y., Holden, P.A., Nel, A.E., Godwin, H.A., 2015. Cu nanoparticles have different impacts in Escherichia coli and lactobacillus brevis than their microsized and ionic analogues. ACS Nano 9, 7215–7225.

Keller, A.A., Adeleye, A.S., Conway, J.R., Garner, K.L., Zhao, L., Cherr, G.N., Hong, J., Gardea-Torresdey, J.L., Godwin, H.A., Hanna, S., Ji, Z., Kaweeteerawat, C., Lin, S., Lenihan, H.S., Miller, R.J., Nel, A.E., Peralta-Videa, J.R., Walker, S.L., Taylor, A.A., Torres-Duarte, C., Zink, J.I., Zuverza-Mena, N., 2017. Comparative environmental fate and toxicity of copper nanomaterials. NanoImpact 7, 28–40.

Kumar, A., Prasad, K.S., 2021. Role of nano-selenium in health and environment. J. Biotechnol. 325, 152–163.

Kumar, S., Saini, D., Lotey, G.S., Verma, N.K., 2011. Electrochemical synthesis of copper nanowires in anodic alumina membrane and their impedance analysis. Superlattice. Microst. 50, 698–702.

Kumar, A., Kuang, Y., Liang, Z., Sun, X., 2020. Microwave chemistry, recent advancements, and eco-friendly microwave-assisted synthesis of nanoarchitectures and their applications: a review. Mater. Today Nano 11, 100076.

Laghari, G.N., Nafady, A., Al-Saeedi, S.I., Sherazi, S.T.H., Nisar, J., Shah, M.R., Abro, M.I., Arain, M., Bhargava, S.K., 2019. Ranolazine-functionalized copper nanoparticles as a colorimetric sensor for trace level detection of As^{3+}. Nanomaterials 9, 83.

Li, S., Chen, Y., Huang, L., Pan, D., 2014. Large-scale synthesis of well-dispersed copper nanowires in an electric pressure cooker and their application in transparent and conductive networks. Inorg. Chem. 53, 4440–4444.

Li, Q., Wu, F., Mao, M., Ji, X., Wei, L., Li, J., Ma, L., 2019. A dual-mode colorimetric sensor based on copper nanoparticles for the detection of mercury-(ii) ions. Anal. Methods 11, 4014–4021.

Li, Z., Khuje, S., Chivate, A., Huang, Y., Hu, Y., An, L., Shao, Z., Wang, J., Chang, S., Ren, S., 2020. Printable copper sensor electronics for high temperature. ACS Appl. Electron. Mater. 2, 1867–1873.

Li, Z., Chang, S., Khuje, S., Ren, S., 2021. Recent advancement of emerging nano copper-based printable flexible hybrid electronics. ACS Nano. https://doi.org/10.1021/acsnano.1c02209.

Lisiecki, I., Pileni, M.P., 1993. Synthesis of copper metallic clusters using reverse micelles as microreactors. J. Am. Chem. Soc. 115, 3887–3896.

Liu, Z., Yang, Y., Liang, J., Hu, Z., Li, S., Peng, S., Qian, Y., 2003. Synthesis of copper nanowires via a complex-surfactant-assisted hydrothermal reduction process. J. Phys. Chem. B 107, 12658–12661.

Liu, J., Chen, J., Fang, Z., Zeng, L., 2012. A simple and sensitive sensor for rapid detection of sulfide anions using DNA-templated copper nanoparticles as fluorescent probes. Analyst 137, 5502–5505.

Liu, Y., Liu, X., Zhan, Y., Fan, H., Lu, Y., 2015. Copper nanocoils synthesized through solvothermal method. Sci. Rep. 5, 16879.

Liu, C., Cai, Y., Wang, J., Liu, X., Ren, H., Yan, L., Zhang, Y., Yang, S., Guo, J., Liu, A., 2020a. Facile preparation of homogeneous copper nanoclusters exhibiting excellent tetraenzyme mimetic activities for colorimetric glutathione sensing and fluorimetric ascorbic acid sensing. ACS Appl. Mater. Interfaces 12, 42521–42530.

Liu, J., Fu, J., Zhou, Y., Zhu, W., Jiang, L.-P., Lin, Y., 2020b. Controlled synthesis of EDTA-modified porous hollow copper microspheres for high-efficiency conversion of CO_2 to multicarbon products. Nano Lett. 20, 4823–4828.

Mallakpour, S., Azadi, E., Hussain, C.M., 2021. The latest strategies in the fight against the COVID-19 pandemic: the role of metal and metal oxide nanoparticles. New J. Chem. 45, 6167–6179.

Marazziti, D., Cianconi, P., Mucci, F., Foresi, L., Chiarantini, I., Della Vecchia, A., 2021. Climate change, environment pollution, COVID-19 pandemic and mental health. Sci. Total Environ. 773, 145182.

Mason, J.A., 1975. Ancient Civilizations of Peru. Viking Penguin.

Miao, P., Zhang, T., Xu, J., Tang, Y., 2018. Electrochemical detection of miRNA combining T7 exonuclease-assisted cascade signal amplification and DNA-templated copper nanoparticles. Anal. Chem. 90, 11154–11160.

Momeni, S., Ahmadi, R., Safavi, A., Nabipour, I., 2017. Blue-emitting copper nanoparticles as a fluorescent probe for detection of cyanide ions. Talanta 175, 514–521.

Monisha, Shrivas, K., Kant, T., Patel, S., Devi, R., Dahariya, N.S., Pervez, S., Deb, M.K., Rai, M.K., Rai, J., 2021. Inkjet-printed paper-based colorimetric sensor coupled with smartphone for determination of mercury (Hg^{2+}). J. Hazard. Mater. 414, 125440.

Mott, D., Galkowski, J., Wang, L., Luo, J., Zhong, C.-J., 2007. Synthesis of size-controlled and shaped copper nanoparticles. Langmuir 23, 5740–5745.

Niederberger, M., 2007. Nonaqueous sol–gel routes to metal oxide nanoparticles. Acc. Chem. Res. 40, 793–800.

Pandey, A., Brauer, M., Cropper, M.L., Balakrishnan, K., Mathur, P., Dey, S., Turkgulu, B., Kumar, G.A., Khare, M., Beig, G., Gupta, T., Krishnankutty, R.P., Causey, K., Cohen, A.J., Bhargava, S., Aggarwal, A.N., Agrawal, A., Awasthi, S., Bennitt, F., Bhagwat, S., Bhanumati, P., Burkart, K., Chakma, J.K., Chiles, T.C., Chowdhury, S., Christopher, D.J., Dey, S., Fisher, S., Fraumeni, B., Fuller, R., Ghoshal, A.G., Golechha, M.J., Gupta, P.C., Gupta, R., Gupta, R., Gupta, S., Guttikunda, S., Hanrahan, D., Harikrishnan, S., Jeemon, P., Joshi, T.K., Kant, R., Kant, S., Kaur, T., Koul, P.A., Kumar, P., Kumar, R., Larson, S.L., Lodha, R., Madhipatla, K.K., Mahesh, P.A., Malhotra, R., Managi, S., Martin, K., Mathai, M., Mathew, J.L., Mehrotra, R., Mohan, B.V.M., Mohan, V., Mukhopadhyay, S., Mutreja, P., Naik, N., Nair, S., Pandian, J.D., Pant, P., Perianayagam, A., Prabhakaran, D., Prabhakaran, P., Rath, G.K., Ravi, S., Roy, A., Sabde, Y.D., Salvi, S., Sambandam, S., Sharma, B., Sharma, M., Sharma, S., Sharma, R.S., Shrivastava, A., Singh, S., Singh, V., Smith, R., Stanaway, J.D., Taghian, G., Tandon, N., Thakur, J.S., Thomas, N.J., Toteja, G.S., Varghese, C.M., Venkataraman, C., Venugopal, K.N., Walker, K.D., Watson, A.Y., Wozniak, S., Xavier, D., Yadama, G.N., Yadav, G., Shukla, D.K., Bekedam, H.J., Reddy, K.S., Guleria, R., Vos, T., Lim, S.S., Dandona, R., Kumar, S., Kumar, P., Landrigan, P.J., Dandona, L., 2021. Health and economic impact of air pollution in the states of India: the global burden of disease study 2019. Lancet Planet. Health 5, e25–e38.

Pang, C., Skjolding, L.M., Selck, H., Baun, A., 2021. A "point-of-entry" bioaccumulation study of nanoscale pigment copper phthalocyanine in aquatic organisms. Environ. Sci. Nano 8, 554–564.

Park, J., An, K., Hwang, Y., Park, J.G., Noh, H.J., Kim, J.Y., Park, J.H., Hwang, N.M., Hyeon, T., 2004. Ultra-large-scale syntheses of monodisperse nanocrystals. Nat. Mater. 3, 891–895.

Park, B.K., Jeong, S., Kim, D., Moon, J., Lim, S., Kim, J.S., 2007. Synthesis and size control of monodisperse copper nanoparticles by polyol method. J. Colloid Interface Sci. 311, 417–424.

Peng, S., Wang, C., Xie, J., Sun, S., 2006. Synthesis and stabilization of monodisperse Fe nanoparticles. J. Am. Chem. Soc. 128, 10676–10677.

Pinto, R.J.B., Martins, M.A., Lucas, J.M.F., Vilela, C., Sales, A.J.M., Costa, L.C., Marques, P.A.A.P., Freire, C.S.R., 2020. Highly electroconductive nanopapers based on nanocellulose and copper nanowires: a new generation of flexible and sustainable electrical materials. ACS Appl. Mater. Interfaces 12, 34208–34216.

Qing, Z., Qing, T., Mao, Z., He, X., Wang, K., Zou, Z., Shi, H., He, D., 2014. dsDNA-specific fluorescent copper nanoparticles as a "green" nano-dye for polymerization-mediated biochemical analysis. Chem. Commun. 50, 12746–12748.

Qiu, S., Dong, J., Chen, G., 1999. Preparation of cu nanoparticles from water-in-oil microemulsions. J. Colloid Interface Sci. 216, 230–234.

Rai, M., Ingle, A.P., Pandit, R., Paralikar, P., Shende, S., Gupta, I., Biswas, J.K., da Silva, S.S., 2018. Copper and copper nanoparticles: role in management of insect-pests and pathogenic microbes. Nanotechnol. Rev. 7, 303–315.

Rajput, V., Minkina, T., Ahmed, B., Sushkova, S., Singh, R., Soldatov, M., Laratte, B., Fedorenko, A., Mandzhieva, S., Blicharska, E., Musarrat, J., Saquib, Q., Flieger, J., Gorovtsov, A., 2019. Interaction of copper-based nanoparticles to soil, terrestrial, and aquatic systems: critical review of the state of the science and future perspectives. In: Reviews of Environmental Contamination and Toxicology. vol. 252. Springer, Switzerland, pp. 51–96. Cham.

Ravi Kumar, D.V., Woo, K., Moon, J., 2015. Promising wet chemical strategies to synthesize cu nanowires for emerging electronic applications. Nanoscale 7, 17195–17210.

Roberto, M., 2006. Copper in medicine and personal care: a historical overview. In: Hostynek, J.J., Maibach, H.I. (Eds.), Copper and the Skin. CRC Press, Boca Raton, pp. 149–160.

Robinson, R.H., 1923. Powdered Bordeaux mixture. Ind. Eng. Chem. 15, 941–942.

Salavati-Niasari, M., Davar, F., Mir, N., 2008. Synthesis and characterization of metallic copper nanoparticles via thermal decomposition. Polyhedron 27, 3514–3518.

Sathish Kumar, V., Vidhyasri, R., Dhevasenaa, P.R., Ganeshbabu, O., 2021. Reduction of toxic elements in marine environment using nano adsorbent materials. Mater. Today 37, 1554–1557.

Sathiyabama, M., Manikandan, A., 2018. Application of copper-chitosan nanoparticles stimulate growth and induce resistance in finger millet (eleusine coracana gaertn.) plants against blast disease. J. Agric. Food Chem. 66, 1784–1790.

Scott, N.R., Chen, H., Cui, H., 2018. Nanotechnology applications and implications of agrochemicals toward sustainable agriculture and food systems. J. Agric. Food Chem. 66, 6451–6456.

Sebastian, A., Nangia, A., Prasad, M.N.V., 2020. Chapter 18—advances in agrochemical remediation using nanoparticles. In: Prasad, M.N.V. (Ed.), Agrochemicals Detection, Treatment and Remediation. Butterworth-Heinemann, pp. 465–485.

Shang, Y., Hasan, M.K., Ahammed, G.J., Li, M., Yin, H., Zhou, J., 2019. Applications of nanotechnology in plant growth and crop protection: a review. Molecules (Basel, Switzerland) 24, 2558.

Sharma, P.V., 2015. Sushruta Samhita, volume 1: Sutrasthana. Chaukhambha Orientalia, Varanasi.

Sharma, P., Goyal, D., Chudasama, B., 2021. Ecotoxicity of as-synthesised copper nanoparticles on soil bacteria. IET Nanobiotechnol. 15, 236–245.

Shaw, B.J., Al-Bairuty, G., Handy, R.D., 2012. Effects of waterborne copper nanoparticles and copper sulphate on rainbow trout, (Oncorhynchus mykiss): physiology and accumulation. Aquat. Toxicol. 116-117, 90–101.

Shen, Y., Borgatta, J., Ma, C., Elmer, W., Hamers, R.J., White, J.C., 2020. Copper nanomaterial morphology and composition control foliar transfer through the cuticle and mediate resistance to root fungal disease in tomato (solanum lycopersicum). J. Agric. Food Chem. 68, 11327–11338.

Sheng, Y., Qian, W., Huang, J., Wu, B., Yang, J., Xue, T., Ge, Y., Wen, Y., 2019. Electrochemical detection combined with machine learning for intelligent sensing of maleic hydrazide by using carboxylated PEDOT modified with copper nanoparticles. Microchim. Acta 186, 543.

Shi, W., Song, S., Zhang, H., 2013. Hydrothermal synthetic strategies of inorganic semiconducting nanostructures. Chem. Soc. Rev. 42, 5714–5743.

Shimotsuma, Y., Yuasa, T., Homma, H., Sakakura, M., Nakao, A., Miura, K., Hirao, K., Kawasaki, M., Qiu, J., Kazansky, P.G., 2007. Photoconversion of copper flakes to nanowires with ultrashort pulse laser irradiation. Chem. Mater. 19, 1206–1208.

Shrivas, K., Ghosale, A., Bajpai, P.K., Kant, T., Dewangan, K., Shankar, R., 2020a. Advances in flexible electronics and electrochemical sensors using conducting nanomaterials: a review. Microchem. J. 156, 104944.

Shrivas, K., Monisha, Patel, S., Thakur, S.S., Shankar, R., 2020b. Food safety monitoring of the pesticide phenthoate using a smartphone-assisted paper-based sensor with bimetallic Cu@Ag core–shell nanoparticles. Lab Chip 20, 3996–4006.

Somayaji, R., Neradilek, M.B., Szpiro, A.A., Lofy, K.H., Jackson, M.L., Goss, C.H., Duchin, J.S., Neuzil, K.M., Ortiz, J.R., 2020. Effects of air pollution and other environmental exposures on estimates of severe influenza illness, Washington, USA. Emerg. Infect. Dis. 26, 920–929.

Soomro, R.A., Nafady, A., Sirajuddin, Memon, N., Sherazi, T.H., Kalwar, N.H., 2014. L-cysteine protected copper nanoparticles as colorimetric sensor for mercuric ions. Talanta 130, 415–422.

Stortini, A.M., Moretto, L.M., Mardegan, A., Ongaro, M., Ugo, P., 2015. Arrays of copper nanowire electrodes: preparation, characterization and application as nitrate sensor. Sens. Actuators B 207, 186–192.

Sun, L., Zhao, Y., Guo, W., Tao, X., Zhang, Z., 2011. Microemulsion-based synthesis of copper nanodisk superlattices. Appl. Phys. A Mater. Sci. Process. 103, 983–988.

Tajik, S., Dourandish, Z., Zhang, K., Beitollahi, H., Le, Q.V., Jang, H.W., Shokouhimehr, M., 2020. Carbon and graphene quantum dots: a review on syntheses, characterization, biological and sensing applications for neurotransmitter determination. RSC Adv. 10, 15406–15429.

Talebzadeh, S., Queffélec, C., Knight, D.A., 2019. Surface modification of plasmonic noble metal–metal oxide core–shell nanoparticles. Nanoscale Adv. 1, 4578–4591.

Tsai, T.-T., Chen, C.-A., Yi-Ju Ho, N., Yang, S., Chen, C.-F., 2019. Fluorescent double-stranded DNA-templated copper nanoprobes for rapid diagnosis of tuberculosis. ACS Sens. 4, 2885–2892.

Uyttendaele, M., Jaykus, L.-A., Amoah, P., Chiodini, A., Cunliffe, D., Jacxsens, L., Holvoet, K., Korsten, L., Lau, M., McClure, P., Medema, G., Sampers, I., Rao Jasti, P., 2015. Microbial hazards in irrigation water: standards, norms, and testing to manage use of water in fresh produce primary production. Compr. Rev. Food Sci. Food Saf. 14, 336–356.

Viator, C., Blitstein, J., Brophy, J.E., Fraser, A., 2015. Preventing and controlling foodborne disease in commercial and institutional food service settings: a systematic review of published intervention studies. J. Food Prot. 78, 446–456.

Wang, Y., Asefa, T., 2010. Poly(allylamine)-stabilized colloidal copper nanoparticles: synthesis, morphology, and their surface-enhanced Raman scattering properties. Langmuir 26, 7469–7474.

Wang, Z., von dem Bussche, A., Kabadi, P.K., Kane, A.B., Hurt, R.H., 2013. Biological and environmental transformations of copper-based nanomaterials. ACS Nano 7, 8715–8727.

Wang, A.-X., Chu, D.-Q., Wang, L.-M., Mao, B.-G., Sun, H.-M., Ma, Z.-C., 2014. Template-free hydrothermal synthesis of copper hollow microspheres: microstructure, formation mechanism and compression plasticity. RSC Adv. 4, 7545–7548.

Wang, C., Cheng, H., Sun, Y., Lin, Q., Zhang, C., 2015. Rapid sonochemical synthesis of luminescent and paramagnetic copper nanoclusters for bimodal bioimaging. ChemNanoMat 1, 27–31.

Wang, Z., Chen, B., Rogach, A.L., 2017. Synthesis, optical properties and applications of light-emitting copper nanoclusters. Nanoscale Horiz. 2, 135–146.

Wang, D., Wang, Z., Wang, X., Zhuang, X., Tian, C., Luan, F., Fu, X., 2020. Functionalized copper nanoclusters-based fluorescent probe with aggregation-induced emission property for selective detection of sulfide ions in food additives. J. Agric. Food Chem. 68, 11301–11308.

Wen, Y., Huang, W., Wang, B., Fan, J., Gao, Z., Yin, L., 2012. Synthesis of cu nanoparticles for large-scale preparation. Mater. Sci. Eng. B 177, 619–624.

Xu, W.-H., Wang, L., Guo, Z., Chen, X., Liu, J., Huang, X.-J., 2015. Copper nanowires as nanoscale interconnects: their stability, electrical transport, and mechanical properties. ACS Nano 9, 241–250.

Xu, L., Yang, Y., Hu, Z.-W., Yu, S.-H., 2016. Comparison study on the stability of copper nanowires and their oxidation kinetics in gas and liquid. ACS Nano 10, 3823–3834.

Xu, X., Wang, R., Nie, P., Cheng, Y., Lu, X., Shi, L., Sun, J., 2017. Copper nanowire-based aerogel with tunable pore structure and its application as flexible pressure sensor. ACS Appl. Mater. Interfaces 9, 14273–14280.

Yang, J., Chen, J., Zhou, Y., Wu, K., 2011. A nano-copper electrochemical sensor for sensitive detection of chemical oxygen demand. Sens. Actuators B 153, 78–82.

Yang, H.-J., He, S.-Y., Chen, H.-L., Tuan, H.-Y., 2014. Monodisperse copper nanocubes: synthesis, self-assembly, and large-area dense-packed films. Chem. Mater. 26, 1785–1793.

Yang, S., Sun, S., Zhou, C., Hao, G., Liu, J., Ramezani, S., Yu, M., Sun, X., Zheng, J., 2015. Renal clearance and degradation of glutathione-coated copper nanoparticles. Bioconjug. Chem. 26, 511–519.

Yang, Y., Huang, Q., Payne, G.F., Sun, R., Wang, X., 2019. A highly conductive, pliable and foldable cu/cellulose paper electrode enabled by controlled deposition of copper nanoparticles. Nanoscale 11, 725–732.

Yao, S., Swetha, P., Zhu, Y., 2018. Nanomaterial-enabled wearable sensors for healthcare. Adv. Healthc. Mater. 7, 1700889.

Yin, Z., Lee, C., Cho, S., Yoo, J., Piao, Y., Kim, Y.S., 2014. Facile synthesis of oxidation-resistant copper nanowires toward solution-processable, flexible, foldable, and free-standing electrodes. Small 10, 5047–5052.

Yu, J.-C., Zhao, F.-G., Shao, W., Ge, C.-W., Li, W.-S., 2015. Shape-controllable and versatile synthesis of copper nanocrystals with amino acids as capping agents. Nanoscale 7, 8811–8818.

Zamora-Ledezma, C., Negrete-Bolagay, D., Figueroa, F., Zamora-Ledezma, E., Ni, M., Alexis, F., Guerrero, V.H., 2021. Heavy metal water pollution: a fresh look about hazards, novel and conventional remediation methods. Environ. Technol. Innov. 22, 101504.

Zhan, Y.-J., Yu, S.-H., 2008. Necklace-like Cu@cross-linked poly(vinyl alcohol) core−shell microcables by hydrothermal process. J. Am. Chem. Soc. 130, 5650–5651.

Zhang, X., Zhang, D., Ni, X., Zheng, H., 2006. One-step preparation of copper nanorods with rectangular cross sections. Solid State Commun. 139, 412–414.

Zhang, X., Wang, G., Liu, X., Wu, H., Fang, B., 2008. Copper dendrites: synthesis, mechanism discussion, and application in determination of L-tyrosine. Cryst. Growth Des. 8, 1430–1434.

Zhao, S., Han, F., Li, J., Meng, X., Huang, W., Cao, D., Zhang, G., Sun, R., Wong, C.-P., 2018. Advancements in copper nanowires: synthesis, purification, assemblies, surface modification, and applications. Small 14, 1800047.

Zhao, J., Wu, E., Zhang, B., Bai, X., Lei, P., Qiao, X., Li, Y.-F., Li, B., Wu, G., Gao, Y., 2021. Pollution characteristics and ecological risks associated with heavy metals in the Fuyang river system in North China. Environ. Pollut. 281, 116994.

Zhou, M., Tian, M., Li, C., 2016. Copper-based nanomaterials for cancer imaging and therapy. Bioconjug. Chem. 27, 1188–1199.

Zhu, H.-T., Zhang, C.-Y., Yin, Y.-S., 2004. Rapid synthesis of copper nanoparticles by sodium hypophosphite reduction in ethylene glycol under microwave irradiation. J. Cryst. Growth 270, 722–728.

Zhu, Y., Wang, H., Wang, L., Zhu, J., Jiang, W., 2016. Cascade signal amplification based on copper nanoparticle-reported rolling circle amplification for ultrasensitive electrochemical detection of the prostate cancer biomarker. ACS Appl. Mater. Interfaces 8, 2573–2581.

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Copper Nanostructures: Next-Generation of Agrochemicals for Sustainable Agroecosystems

Edited by Kamel A. Abd-Elsalam

Copper Nanostructures: Next Generation of Agrochemicals for Sustainable Agroecosystems provides a detailed examination of how copper-based nanomaterials are being used to help create sustainable agricultural systems.

A volume in the Nanobiotechnology for Plant Protection series

This book explores the impact of a large variety of copper-based nanostructures on agri-food sectors. There is increased interest in this subject in both academic and industrial sectors, where the opportunities that nanotechnology can provide are being embraced.

The book is divided into six main parts. Part One highlights the green synthesis of copper nanoparticles, production mechanisms, eco-safety, and future perspectives. Part Two highlights the increasing importance of copper nanomaterials in plant protection applications. Part Three describes the use of copper nanostructures in plant science applications, such as multifunctional copper-based nanocomposites and their agroecosystem applications; the impact of copper-based nanoparticles on economically important plants; copper nanoparticles in soil, uptake, mechanism of toxicity, and biotransformation in plants; and copper-/carbon-based nanostructured materials as a growth stimulator of plants. Part Four is devoted to one of the most innovative topics of nanobiotechnology, which concerns antimicrobial applications. In this part, current approaches are summarized for using copper nanomaterials as antimicrobials and antibacterials. Part Five describes copper nanostructure applications, including copper nanostructures as antimicrobial agents against animal pathogens; safety considerations of copper nanoparticles in food, feed, and additives; and finally, applications of copper nanoparticles against plant and animal parasitic nematodes. Part Six summarizes the current applications of copper nanomaterials in agroecosystems, such as copper nanoparticles as nanosensors, their negative ecological effects, estimation risks of exposure to copper-based agrochemicals, understanding their interaction with blue-green algae, and wastewater treatment.

The book provides information on the design and application of ecologically safe formulations, for protecting cultivated crops against insects and pathogen-causing diseases, plant science, antimicrobial applications, and agroecosystem applications as well as veterinary applications.

Key Features

- Assesses the impact of a large variety of copper-based nanostructures on agri-food sectors
- Discusses how the properties of a variety of copper-based nanomaterials make them effective for agricultural applications
- Explains the challenges for mass production of copper-based nanomaterials

About the Editor

Kamel A. Abd-Elsalam is a Research Professor at the Plant Pathology Research Institute, Agricultural Research, Egypt

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