SYNTHESIS AND CHARACTERIZATION OF ELECTROSPUN-BASED COMPOSITE FOR THE REMEDIATION OF PHARMACEUTICAL POLLUTANTS IN WASTEWATER

by

SISONKE SIGONYA (MAppSc)

21221323

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DECLARATION

I, **Sisonke Sigonya**, solemnly affirm that the thesis presented for the degree of Doctor of Philosophy in Chemistry at the Durban University of Technology is the culmination of my original research and has not been previously accepted in substance for any other degree. Furthermore, I confirm that it is not currently under consideration for any other academic qualification. I can unequivocally state that all the work contained within the thesis is my own, and I take full responsibility for its content and conclusions.

Student name: Sisonke Sigonya

Student signature: _____ Date:31.03.2024

Supervisor name: Dr T.H. Mokhothu

Supervisor signature: _____ Date:13.05.2024

Co-supervisor name: Dr T.R Makhanya

Co-supervisor signature: _____ Date:14.05.2024

Co-supervisor name: Professor P.M Mayer

Co-supervisor signature: _____ Date: 08.05.2024

Co-supervisor name: Dr T.C Mokhena

Co-supervisor signature: _ Date:14.05.2024

DEDICATION

To my dearest daughter, **Lunathi Ayolise Sigonya**

You are my greatest source of inspiration and motivation. Your unwavering support and infinite love have been my driving force throughout this challenging yet rewarding journey towards achieving my Doctor of Philosophy in Chemistry. I dedicate this thesis to you, with gratitude for your understanding and patience during the countless hours spent immersed in research and writing.

To my late grandparents,

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ABSTRACT

Pharmaceutical pollutants, including non-steroidal anti-inflammatory drugs (NSAIDs) and antiretroviral drugs (ARVs), pose a significant threat to aquatic environments, necessitating effective remediation strategies. This comprehensive study delves into the efficacy of nanotechnological approaches, with a special focus on adsorption, in addressing the persistent issue of pharmaceutical pollution in wastewater bodies. The research covers the synthesis and characterization of a multi-template molecularly imprinted polymer (MIP) targeting key pharmaceutical compounds, namely naproxen, ibuprofen, diclofenac, emtricitabine, tenofovir disoproxil, and efavirenz, for extraction from contaminated water sources.

Comparative analyses between the synthesized MIP and a commercial Solid Phase Extraction (SPE) cartridge showed comparative performance of the MIP and SPE cartridge in quantifying pharmaceutical compounds present in wastewater samples. The results highlighted both materials' consistent efficiency in the removal of pollutants, with selective pharmaceuticals exhibiting varying levels of removal efficiency during different treatment stages. Regressions analysis showcased high linearity (R^2 values ranging from 0.9980 to 0.9999), alongside remarkable recoveries (90.9 % to 100 %) for the MIP and method detection limits (MDLs) ranging from (0.14-1.08 μg L^{-1}) for all target pollutants. Recoveries for SPE samples ranged from (62 % to 98 %) with method detection limits at (0.7-4.68 μg L^{-1}).

The optimal conditions for efficient extraction of pharmaceutical compounds using the MIP were determined through a series of experiments, considering factors such as pH, mass, concentration, and contact time. Results showed high extraction efficiencies (>96%) and a notable adsorption capacity (>0.91 mg. g^{-1}) for both ARVs and NSAIDs, confirming the MIP's potential for successful removal of these pollutants from wastewater. Additionally, adsorption kinetics were studied, revealing a second-order rate model and adherence to the Freundlich adsorption isotherm.

Furthermore, this study incorporates synthesized MIP into the electrospinning technique, utilizing various polymer blends and optimized solvents to enhance the remediation process. The study explores the electrospun mats morphology, particularly those composed of polyvinyl alcohol (PVA) and polyethylene terephthalate (PET), examining their structural characteristics using techniques such as Fourier-transform infrared spectroscopy (FTIR), thermogravimetric

analysis (TGA), and adsorption time studies.

Through merging advanced nanotechnological techniques with electrospinning methodologies, this study presents a robust framework for combating pharmaceutical pollutants in wastewater. The incorporation of the MIP into electrospun mats, coupled with in-depth material characterization and adsorption studies, emphasizes the potential of this innovative approach for environmental remediation and drug purification processes. This research contributes valuable insights into the effective removal and quantification of pharmaceutical pollutants, emphasizing the pivotal role of electrospinning technologies in addressing environmental challenges.

In conclusion, this study sheds light on the potential of a multi-template MIP for the removal of ARVs and NSAIDs from contaminated water sources, showcasing its versatility and efficacy in enhancing water treatment processes, as well as its utility in drug purification and recovery processes. Overall, the research provides valuable insights into the complexities of pharmaceutical pollutant removal, emphasizing the significance of selecting appropriate extraction methodologies in wastewater treatment processes to ensure efficient and sustainable remediation practices.

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LIST OF ABBREVIATION

ACN	Acetonitrile
AOP	Adsorption, advanced oxidation process
ARV	Antiretroviral
ASAP	Accelerated surface area & porosimetry system.
APCI	Atmospheric pressure chemical ionization
BET	Brunauer-emmett-teller
BOD	Biological oxygen demand
CID	Collision-induced dissociation
CIP	Ciprofloxacin
CNT	Carbon nanotubes
COD	Chemical oxygen demand.
COOH	Carboxylic group
CP	Cross-polarisation
CuO	Copper oxide
DAD	Diode-array detection
DCM	Dichloromethane
DG0	Gibbs free energy
DH0	Enthalpy
DICLO	Diclofenac
DS0	Entropy

EDA	Electron donor acceptor
EFV	Efavirenz
EGDMA	Ethylene glycol dimethylacrylate
ELISA	Enzyme-linked immunosorbent assay
EMI	Emtricitabine
ESI	Electrospray ionization
ESI-MS	Electro spray ionization mass spectrometer
FLD	Fluorescence detection
FTIR	Fourier-transform infrared spectroscopy
GC-MS	Gas chromatography-mass spectrometry
HCl	Hydrochloric acid
HIV	Human immune virus
HLB	Hydrophilic-lipophilic balance
HPLC	High-performance liquid chromatography
IBU	Ibuprofen
KD	Distribution constant
KL	Langmuir constant
LC-MS	Liquid chromatography–mass spectrometry
LOD	Limit of detection
LOQ	Limit of quantification
MAS	Magic-angle-spinning

MAX	Mixed mode anionic exchange resin
MB	Methylene blue
MDLs	Method detection limits
MeOH	Methanol
MIMs	Molecular imprinted membranes
MIPs	Molecularly imprinted polymer
MIPC	Molecularly imprinted polymer composite
MOFs	Metal-organic frameworks
MRM	Multiple reaction monitoring
MS	Mass spectrometer
MWCNTs	Multi-walled carbon nanotubes
NAP	Naproxen
NIMs	Non imprinted membrane
NIPs	Non imprinted polymers.
NMR	Nuclear magnetic resonance

NRTI	Nucleoside/nucleotide reverse transcriptase inhibitors
NNRTI	Non-nucleoside reverse transcriptase inhibitors
NRF	National research fund
NSAIDs	Non-steroidal anti-inflammatory drugs
OH	Hydroxyl
OMCs	Ordered mesoporous carbons.
PES	Polyether sulfone
PET	Polyethylene terephthalate
PVA	Polyvinyl alcohol
PVDF	Polyvinylidene fluoride
Q-TOF	Quadrupole time-of-flight mass spectrometer
RPLC	Reverse phase liquid chromatography
rGO-MWCNTs	Reduced graphene oxide and multiwall carbon nanotubes.
RSD	Relative standard deviation
SEM	Scanning electron microscope.
SMX	Sulfamethoxazole
SPE	Solid phase extraction

SWCNTs Single-walled carbon nanotubes

TCD Tip to collector distance

TENO Tenofovir disoproxil

TFA Trifluoracetic acid

TGA Thermogravimetric analysis

TOF Time of flight

UHPLC Ultra-high-performance liquid chromatography

USA United states of America

USEPA United states environmental protection agency UV Ultraviolet

WWTPs Wastewater treatment plants

LIST OF PUBLICATIONS AND CONFERENCES

Publications:

i. **Sigonya, S.,** Mokhothu, T.H., Mokhena, T.C. and Makhanya, T.R., 2023. Mitigation of non-steroidal anti-inflammatory and antiretroviral drugs as environmental pollutants by adsorption using nanomaterials as viable solution—a critical review. Appl. Sci. 2023, 13(2), 772; ***PUBLISHED*** https://doi.org/10.3390/app13020772

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Preparation of electrospun molecular imprinted polymers for environmental remediation: A mini review. ***SUBMITTED***

Oral presentation Conferences:

i. **Sisonke Sigonya**, Mitigation of Non-Steroidal Anti-Inflammatory and Antiretroviral Drugs as Environmental Pollutants by Adsorption Using Nanomaterials as Viable Solution. The Scientistt GSASET2023 Conference Italy, Rome
ii. **Sisonke Sigonya,** Antimicrobial properties of PES/PVDF/CuO composite fibers. NIC annaual conference. Rhodes university Grahamstown
iii. **Sisonke Sigonya**, Optimization of extraction techniques for the isolation and pre-concentration of pharmaceuticals in aquatic environments. 39 Annual Trent Conference on Mass Spectrometry. Peterborough, Canada

1 CHAPTER 1: INTRODUCTION

Currently, pollution by pharmaceuticals has been a major concern due to their existence in the aquatic environment (Osman *et al.,* 2023; S. Singh *et al.,* 2021; Tran *et al.,* 2020). Pharmaceuticals are designed to elicit biological effects at low concentrations; thus, it is not surprising that many pharmaceuticals are persistent and have been detected in the aquatic environment demonstrating their potency and specificity in therapeutic applications. Consequently, their persistent nature and the ability to remain active even at trace levels raise concerns about environmental exposure. Numerous studies have documented the detection of these compounds in aquatic environments, where they can disrupt ecosystems and potentially harm aquatic organisms. (Ncube *et al.,* 2018; Ngubane *et al.,* 2019; Schoeman *et al.,* 2017; Sigonya *et al.,* 2022). Pharmaceuticals are organic and micropollutants that are recalcitrant to the conventional treatment of wastewater, with a low removal rate by the current technologies (Kasonga *et al.,* 2021; Tijani *et al.,* 2013). In several reports of environmental impact studies, NSAIDs and ARVs are two classes of pharmaceuticals amongst many that have been listed as high priorities due to their high consumption and potential risk to the environment and human health (Płuciennik-Koropczuk, 2014; Rimayi *et al.,* 2018). NSAIDs are used to treat pain and reduce inflammation. It is predicted that NSAID consumption will increase, and several of them can still pass through human metabolism and be excreted unchanged. Meanwhile, ARVs are used to suppress retroviral activity, thus halting the progression of HIV infection to AIDS. The consumption of ARVs is high compared to their detection in the environment, and they can affect human health indirectly through release into the environment. Exposure to ARVs in the environment, primarily via wastewater and agricultural runoff, may lead to endocrine disruption, which affects hormonal balance and can cause reproductive issues and developmental problems in fetuses. Long-term exposure has been associated with an increased risk of certain cancers and neurological effects, as well as gastrointestinal disturbances. Additionally, ARVs may contribute to kidney and liver damage over time, and their immunosuppressive effects could heighten susceptibility to infections (Isidori *et al.* 2009).

The basis of this study lies in the critical need for effective methods to address the growing concern of pharmaceutical pollutants in water systems. Understanding the capabilities of different techniques for pollutant remediation was essential in identifying the most efficient and sustainable solutions for water treatment. By examining the use of Molecularly Imprinted

Polymers (MIPs) for adsorption, this study aimed to harness the selectivity and affinity of MIPs towards specific pharmaceutical compounds, enhancing the removal efficiency of these pollutants from water sources. This research began by studying MIPs in isolation to elucidate their adsorption performance and specificity towards pharmaceutical pollutants. Subsequently, a comparative study was conducted between MIPs and a commercial Solid Phase Extraction (SPE) sorbent through SPE techniques, providing insights into the relative effectiveness and feasibility of using MIPs for pharmaceutical adsorption.

Lastly, this study focused on the development of composite materials by incorporating MIPs into various polymers and utilizing the electrospinning technique to create tailored MIP-based nanofibers. This approach aimed to optimize the adsorption efficiency and selectivity of MIPs for pharmaceutical pollutants in water. By systematically exploring and comparing these materials, this study seeks to advance the development of efficient and sustainable solutions for the removal and remediation of pharmaceutical contaminants from water systems.

Therefore, this study is focused on the development of molecularly imprinted polymer composite (MIPC) from the combination of polymers produced via electrospinning with MIPs for the effective removal of non-steroidal anti-inflammatory drugs (NSAIDs) and antiretroviral drugs (ARVs) in the aquatic environment. The specific objectives are: i) synthesize, characterize MIPs and, batch adsorption studies of MIP ii) apply the synthesized MIP in wastewater, iii) to develop a composite membrane of molecularly imprinted polymers using electrospun-based polymers varying polymers; iv) to characterize the formed composite membrane via various analytical and testing techniques such as NMR, FTIR, TGA, BET, SEM; v) to investigate the ability of the composite membrane to adsorb NSAIDs and ARVs and lastly, vi) to assess re-usability of the formed composite membrane and to evaluate it via the hybrid system process with existing conventional treatment of wastewater for the possibility of developing an alternative treatment technique.

In this thesis, the development, characterization, and application study of a novel molecularly imprinted polymer composite membrane (MIPC) in the remediation of pharmaceuticals such as NSAIDs and ARVs in wastewater were discussed. Often these pharmaceuticals enter aquatic environments through various pathways including wastewater discharge, agricultural runoff, and improper disposal practices. Once in water systems, these compounds can disrupt aquatic ecosystems, affecting the growth, reproduction, and survival of aquatic organisms and potentially leading to broader ecological imbalances. Current remediation methods, such as

activated carbon filtration, biological treatment, and advanced oxidation processes, have proven effective in reducing pharmaceutical concentrations in wastewater. However, these methods often have limitations, including high operational costs, incomplete removal of complex pharmaceutical mixtures, and secondary pollution issues. Electrospun-based polymers were used as the supporting material, and it had been proven as a cost-effective and straightforward technique for the synthesis of fibers with diameters ranging from nanometer to micrometer scale. Electrospun fiber has a high surface area to volume ratio, which is advantageous in terms of loading many functional groups, easy accessibility by solution, and a short pathway for mass transfer. The MIPs have been chosen as they possess high selectivity compared to non-imprinted polymers by having imprints complementary in shape and chemical functionality to the specific target molecule. This is achieved by removing the imprinted molecule from the polymer matrix to create specific binding sites. Usually, MIP is in the form of micro-sized particles, which are difficult to separate from the solution. To overcome this problem, MIP can be immobilized into solid-phase support to form MIPC and one of the common techniques is by incorporating MIP with a polymer matrix to form a thin film. This thin film MIPC can be enhanced by synthesizing or using better support to increase surface area or adding other functional compounds to increase its adsorption properties. Therefore, this has led to the idea of combining the electrospun-based polymer with the MIP technique in forming a composite and looking forward to the advantage of both technologies.

Water pollution and remediation have continuously surfaced as a growing worldwide issue. Large effluents including harmful pollutants, such as dyes, heavy metals, surfactants, personal care products, pharmaceuticals, and pesticides, from different sectors (e.g., agricultural, industrial, and municipal resources) have polluted the world's water supply. In recent years, extraordinary efforts have been made to address the obstacles of wastewater treatment. Rapidly expanding pharmaceutical companies and other activities have resulted in massive volumes of organic, inorganic, biodegradable, and non-biodegradable waste being discharged into the environment. Pharmaceuticals have recently been recognized as "emerging contaminants" that are significantly contaminating water streams and posing a substantial risk to aquatic life systems and humans (Carmalin Sophia *et al.*, 2016; Shen & Andrews, 2011) Contamination occurs in the environment not just via use and improper disposal, but also through numerous pharmaceutical manufacturing facilities. Pharmaceuticals have recently been found in wastewater, surface, ground, and drinking water, as well as the sea (Arora, 2019; Awwad *et al.*, 2013; Sigonya *et al.*, 2022). Antibiotics, antacids, steroids, antidepressants, analgesics, anti-

inflammatories, antipyretics, beta-blockers, lipid-lowering medications, tranquilizers, and antiretroviral drugs have all been identified as environmental pollutants, and they are classified as toxic materials. Figure 1-1 depicts the various commonly found classes of these pharmaceuticals in wastewater.

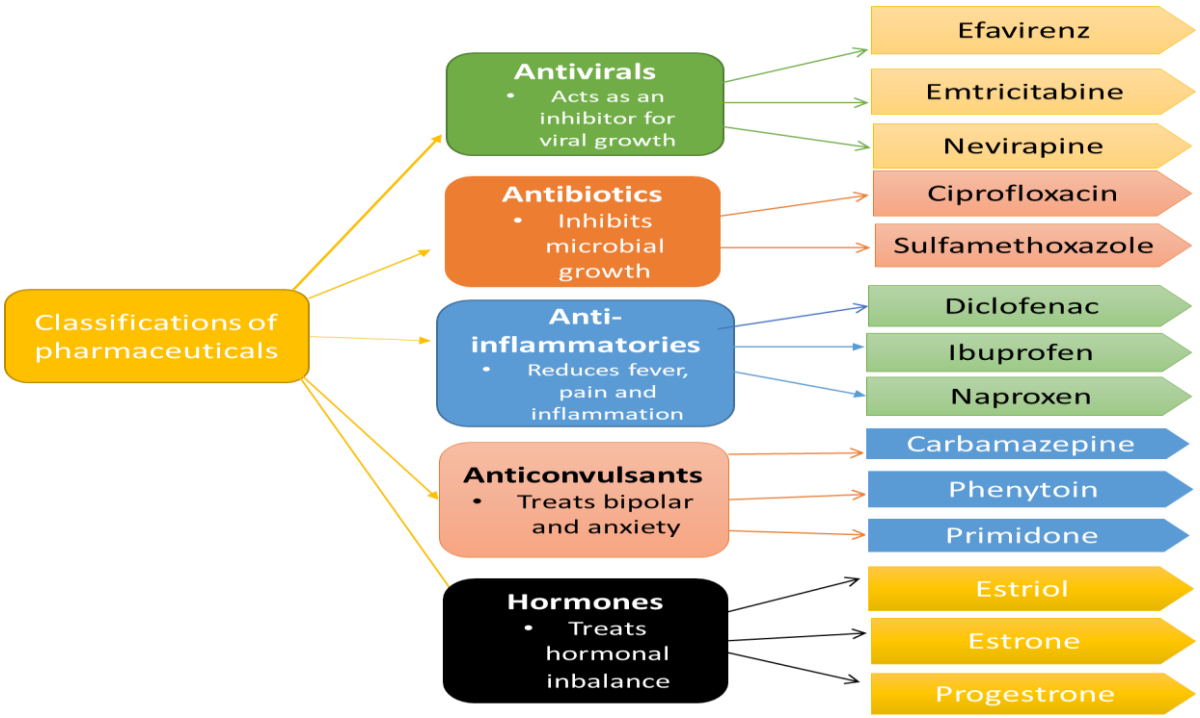


Figure 1-1. Classification of common pharmaceutical pollutants in wastewater

The most fundamental necessities for healthy living are a clean-living environment and safe drinking water. Clean water is necessary for residential use as well as industrial and agricultural purposes. Although water covers more than 70% of the planet, only 3% of it is fit for human consumption, with the remaining 97% being salty water (Rashid *et al.*, 2021). This life-sustaining asset is constantly being stressed by using hazardous chemicals in agricultural and industrial practices, as well as population increase, which has resulted in aquifer depletion, forcing us to venture out to face environmental challenges and to find innovative ways to remove these pollutants in water (Foster, 2017; Rashid *et al.*, 2021; Shafiq *et al.*, 2019). Several solutions have been developed to date to reduce wastewater discharges and mitigate the dangers of contaminants including physical, chemical, and biological methods.

1.1 Background

Molecularly imprinted polymers (MIPs) are synthetic polymers that can selectively recognize a given molecule or a family of molecules with a high degree of specificity. This is achieved by the polymer being constructed around a template molecule through covalent or non-covalent interactions. Subsequent removal of the template from the polymer leaves a cavity that is complementary to the template in terms of size, shape, and functional groups. This allows for the selective reuptake of the template or similar molecules via non-covalent interactions. One of the advantages that MIPs hold over natural adsorbents such as activated carbon and ion exchange resins is that they are cheaper to produce and can be used in a repeated manner with minimal reduction in shrinkage and effectiveness (Arabi *et al*. 2021). Despite the great potential of MIPs for the removal of substances in water, their application has often been limited to batch adsorption processes due to difficulties in producing MIP particles with acceptable mechanical strength and low-pressure drops for fixed bed column applications.

The occurrence of pharmaceuticals such as NSAIDs and ARVs in the environment has been a growing concern in recent years. The presence of these emerging pollutants can be attributed to their incomplete removal during wastewater treatment due to their diverse and complex structures. While there have been many reports on the permeation of these pharmaceuticals into natural water sources, only a limited number of studies have investigated their presence and impact in developing countries. This is of great concern as these countries often do not have the proper facilities for wastewater treatment and thus raw sewage is often discharged directly into water sources. It is well documented that ARVs have greatly improved the lives of HIV patients and the prevention of mother-to-child transmission. However, the discarding or excretion of unused or expired medication may lead to potential contamination of water sources in developing countries. This is also a concern for NSAIDs, which are often used to alleviate the symptoms of various illnesses.

1.2 Overview of current methods for wastewater treatment

Physical methods for removing contaminants from water include submerged membrane bioreactor, activated sludge treatment, constructed wetland, photocatalytic oxidation, catalytic ozonation, adsorption, advanced oxidation process (AOP), nanofiltration, reverse osmosis, ultra-filtration, ion exchange, and membrane separation. Chemical methods include electrolysis

and chemical precipitation. Biological approaches include bio-flocculation and phytoremediation, among others (Comerton *et al.,* 2008; Fuerhacker *et al.,* 2001; Kaya *et al.,* 2013; Oller *et al.,* 2011; Radjenović *et al.,* 2009; Stasinakis., 2008; Westerhoff *et al.,* 2005; Yoon *et al.,* 2010). Water treatment is often expensive since it is necessary to effectively remove the toxins contained in the wastewater to make the water clean and reusable. However, many wastewater treatment systems are built with the characterization and purification of effluents in mind, while neglecting the influence on overall treatment performance and the environment (Sigonya *et al.,* 2022). Conventional treatment procedures do not completely remove pollutants; instead, contaminants are concentrated or degraded into another phase as one of the drawbacks. Although different treatment methods have been studied, few of them are technologically and economically viable. However, the following are the disadvantages of the majority of the approaches listed above (i) intricate procedures; (ii) expensive initial investment and ongoing maintenance costs; (iii) development of secondary pollutants such as toxic sludge; and (iv) generation of by-products with higher toxicity than the original pollution. Adsorption is typically regarded as one of the favored methods for pharmaceutical removal due to its benefits of numerous adsorbents, high efficiency, ease of operation, good reversibility, and low cost (Carmalin Sophia *et al.,* 2016). The selection of adsorbents is critical in the adsorption process. A good adsorbent should have the following fundamental properties: high adsorption capacity, rapid adsorption rate, and ease of separation or recovery. The adsorption method that has been widely used to remove natural or synthetic organic contaminants from drinking water has numerous advantages: (i) adsorption can handle trace levels of pollutants.

(ii) it is efficient; (iii) it is simple to design or operate; (vi) it is toxicity-free; (v) it is suitable for batch and continuous processes; (vi) the adsorbent can be regenerated and reused several times; and (vii) it has a low initial capital cost for implementation (Mohanty *et al.,* 2006).

Several researchers have lately dedicated their efforts to finding adsorbents with large surface areas, cheap cost, and environmental friendliness. The researchers discovered effective adsorbents in nano-sized materials, which have been reported as important materials for removing pharmaceuticals, dyes, heavy metals, organic compounds, and other contaminants from wastewater (Rashid *et al.,* 2021).

Progressive development breakthroughs are being made to develop innovative wastewater treatment techniques and meet the needs of clean water (Ahmed & Haider, 2018; Rashid *et al.,* 2021). However, treating polluted discharged water thoroughly with available means has proven

difficult (Nguyen & Juang, 2019). Several wastewater treatment strategies have been published in the literature (Gerbersdorf *et al.,* 2015; Nasrollahzadeh *et al.,* 2021; Ngumba, Gachanja, *et al.,* 2016). They commonly involve physical, chemical, and biological processes that are thought to be successful enough for water treatment in a variety of ways such as colloids, organic matter, nutrients, and soluble pollutants (metals, organics, etc). A wide range of approaches can be applied, including traditional methods, proven recovery processes, and developing removal technologies. Their selection is influenced by a variety of criteria, such as dye concentration, sewage composition, process cost, and the presence of other contaminants in wastewater (Konig-Péter *et al.,* 2014; Shon *et al.,* 2006). Each treatment's unique characteristics might be advantageous in one aspect but restricting in another. Treatment procedures that have high installation and operating costs, longer processing times, and poor output, and those that emit harmful by-products after treatment, are frequently less suitable for industrial applications (Wong *et al.,* 2019). As a result, it is critical to develop an alternative treatment method that is capable of entirely degrading or removing desired pollutants. The advantages and disadvantages of wastewater treatment technologies are outlined thoroughly in a review by (Crini & Lichtfouse, 2019).

1.3 Pharmaceuticals Pollutants

1.3.1 Occurrence, Fate, and Removal Technologies of Pharmaceuticals in Water

Due to their widespread consumption, pharmaceuticals have been frequently detected in the aqueous environmental system around the world. These organic pollutants enter water systems primarily through three sources: urban, industrial, or hospital waste, and aquaculture facilities, with activities such as human excretion (sewage), improper disposal, leeching from landfills, and industrial drainage water, as shown in Figure 1-2 (Archer *et al.,* 2017). Wastewater effluents are discharged into the rivers and lakes and find their way to the sea (Collado *et al.,* 2014; Sigonya *et al.,* 2022) pharmaceuticals enter the food chain of marine organisms, causing harm to their metabolism. However, recent studies have shown that even after commercial wastewater treatment, residual amounts of pollutants remain in the water, causing harm to the organisms that consume this polluted water (Patel *et al.,* 2019). The widespread use of pharmaceuticals in the healthcare sector has resulted in significant aggregates of their unused or metabolized forms in the aqueous environment (De Andrade *et al.,* 2018). Non-volatile and polar drugs are not easily removed in water by the current technologies applied in the wastewater sector because the current technologies do not remove organic pollutants more than

they remove inorganic pollutants. Therefore, they are retained in various aquatic systems (De Andrade *et al.*, 2018). Furthermore, the use of drugs in animal therapeutics, such as growth promoters or feed additives, serves as another source of environmental contamination (see Figure1-2).

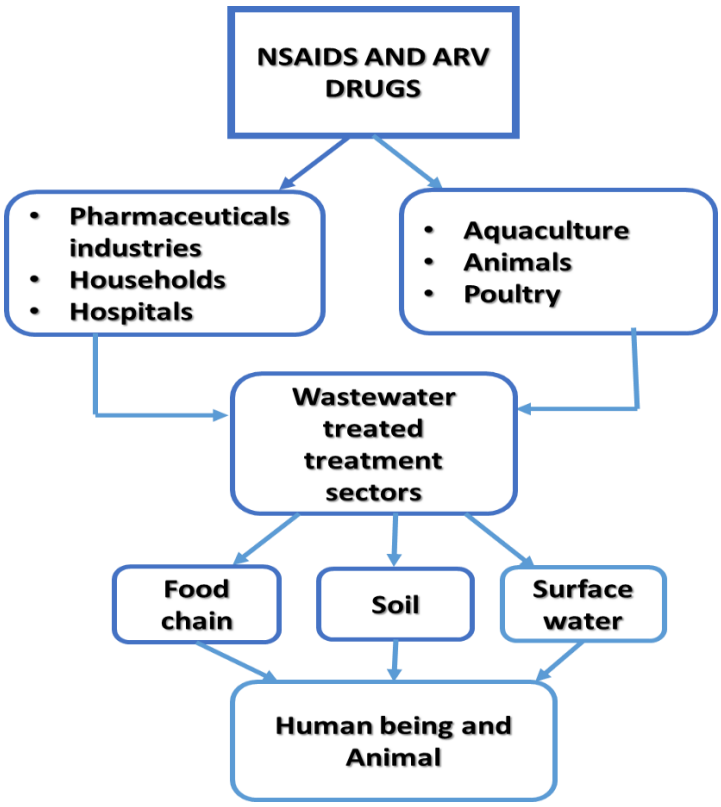


Figure 1-2. Sources of pharmaceuticals pollutants.

1.3.2 Non-Steroidal Anti-Inflammatory Drugs

Pharmaceuticals have become a major concern as emerging pollutants due to their low biodegradability, high persistence, and ease of bioaccumulation. Pharmaceutical drugs are widely used to improve the health of humans and animals. Antibiotics, analgesics, anti-inflammatory drugs, lipid regulators, hormones, and antiretroviral therapies are all commonly administered drugs. These biologically active compounds can be found in hospitals, pharmaceutical industries, and landfill effluents. The sources and trends of pharmaceutical pollutants are depicted in Figure 1-2. Pharmaceuticals, including nonsteroidal anti-inflammatory drugs (NSAIDs) and antiretroviral drugs (ARVs), have been increasingly utilized in many parts of the world, and their presence in the environment has sparked intense interest since many effluents from urban wastewater treatment plants (WWTPs) are polluted with these drug residues. NSAIDs are among the most used pharmaceutical products that are available

without a prescription as over-the-counter drugs (Sigonya *et al.,* 2022). The production and consumption of NSAIDs has increased substantially in the past years, thus introducing large amounts of these substances into the environment in an unutilized or metabolized form (Altman *et al.,* 2015; Dahane *et al.,* 2013; Island *et al.,* 2018). Diclofenac, ibuprofen, naproxen, ketoprofen, and salicylic acid are the most well-known classes of these drugs, with analgesic, anti-inflammatory, and antipyretic effects in humans (Ahmed, 2017). NSAIDs have been found in effluents, surface water, and seawater (Ngubane *et al.,* 2019; Sigonya *et al.,* 2022). Industrial and municipal wastewater are listed among the primary sources with huge potential to pollute groundwater supplies. NSAID compounds have a weak acidic character and a low adsorption into sludge. Ibuprofen is frequently metabolized within the liver, and its metabolites are biochemically active and toxic, especially to invertebrates and algae (Álvarez-Torrellas *et al.,* 2016). Conventional wastewater treatment methods are inadequate in removing or degrading many of these compounds, and they are only partially effective. NSAID residues persist in treated water and have been found to accumulate in drinking water. Although their concentrations in the environment are generally at trace amounts from (ng L^{-1} to µg L^{-1}), this amount may cause toxic effects (Baccar *et al.,* 2012; Weigel *et al.,* 2002) and they might concentrate, as a result. Trace levels of NSAIDs often correlate with their relative toxicities; for example, higher concentrations may be associated with significant ecotoxicological effects on aquatic organisms, while lower levels may still pose risks, particularly from highly potent compounds. Several techniques for removing these compounds from water are being developed. NSAIDs have been eliminated using various techniques such as adsorption, oxidation, heterogeneous photocatalysis, combined membrane, and electrochemical degradation. Among the techniques used to treat NSAID pollutants, adsorption is the method of choice due to the low-cost process with high removal efficiency (Ahmed, 2017).

Activated carbon with hydrophobicity, surface functionality, pore structure, high surface area, and high adsorptive capacity is used as an efficient adsorbent for water treatment, particularly for low pollutant concentration water remediation (Ahmed, 2017; Jedynak *et al.,* 2019). Antibiotics are the most studied pharmaceutical pollutants due to their relatively high concentrations in wastewater (Michael *et al.,* 2013; Yu *et al.,* 2016). Rare studies on NSAIDs removal from the aqueous phase using activated carbon can be found in the literature. Baccar *et al.,* (2012), studied the adsorption of ibuprofen, naproxen, ketoprofen, and diclofenac onto a low-cost activated carbon made from olive waste cakes. Low-cost carbonaceous materials, such as carbon black, were used as adsorbents for naproxen and ketoprofen (Jedynak *et al.,*

2019). Rakić *et al.* (2015), reported the adsorption of salicylic acid, acetylsalicylic acid, and diclofenac-sodium on activated carbons. Bhadra *et al.* (2016), investigated diclofenac sodium adsorption from aqueous solutions using surface-modified or oxidized activated carbons. As adsorbents of diclofenac from the aqueous phase, powdered activated carbon and activated carbon prepared from olive stones were used (Larous & Meniai, 2016). Chemically activated carbon materials derived from pine sawdust-*Onopordum acanthium L*. were investigated for their ability to remove diclofenac and naproxen from aqueous solutions (Álvarez-Torrellas *et al.,* 2016). Adsorbents for removing ibuprofen from the aqueous phase included a novel mesoporous activated carbon from an invasive weed, powdered activated carbons prepared from cork waste, chemically-surface-modified activated carbon cloths, and a commercial microporous-mesoporous granular activated carbon modified by oxidation (Guedidi *et al.,* 2013; Mestre *et al.,* 2007). Ibuprofen adsorption was studied by (Álvarez- Torrellas *et al.,* 2016) on commercial granular activated carbon, multi-walled carbon nanotubes, and two low-cost activated carbons obtained from peach stones and rice husk. On the other hand, the adsorption properties of ordered mesoporous carbons (OMCs) with uniform mesopores, high pore volume, and good chemical inertness were also investigated (Zhang *et al.,* 2017). From the overall studies mentioned above, there are common limitations to these methods, there is a high cost to recover the ash/carbon after use, and the use of H_2SO_4 to recover suggests water can easily dissolve or wash away the acid. They have a lower surface area for adsorption, and they are temperature-dependent. For instance, greater recoveries are often obtained at low temperatures. This suggests that better multi-layered adsorption membranes are needed with greater surface area and less temperature dependent and have great regeneration capacity.

1.3.3 Antiretroviral drugs

Although antiretroviral drugs are rarely reported in the literature, they are becoming increasingly common in countries and regions where ARVs and related drugs are widely used (Lofrano *et al.,* 2016; Wood *et al.,* 2015). Wood *et al.* (2015), reported that these drugs were detected in wastewater in ng L^{-1}. South Africa has the world's highest number of HIV/AIDS cases and the most extensive treatment program, benefiting over 7 million people. As a result, several research groups (Mosekiemang *et al.,* 2019; Ncube *et al.,* 2018; Peng *et al.,* 2014; Sigonya *et al.,* 2022) have reported the presence of ARV drugs in surface water, wastewater, river water, dam water, seawater and even drinking water. The potential health and environmental effects of these drugs in drinking water have not been thoroughly investigated. However, Sanderson and Colleagues., (Sanderson *et al.,* 2004), hypothesized that antiviral

drugs are among the most dangerous classes of drugs in terms of their toxicity to aquatic organisms such as algae, daphnia, and fish. Using trickling filters and anaerobic pond treatment, some conventional treatment methods for the removal of ARVs and related drugs have achieved removal efficiencies of 6–84% for nevirapine (Kebede *et al.,* 2020; Van Langenhove *et al.,* 2018) in wastewater. Nanomaterials have allowed nanotechnology to be used in water treatment plants. Materials on the nanoscale frequently exhibit unique physicochemical properties, such as a high surface-area-to-volume ratio, which promotes the high density of active sites required for removal processes. They also have a high surface reactivity due to the higher surface free energy.

Nanomaterials may be a breakthrough for the water treatment industry by utilizing these unique properties to address the inherent limitations of the current design. So far, several studies on wastewater treatment using nanomaterials have shown great promise. Nanoparticles (Afkhami *et al.,* 2010; Hua *et al.,* 2012), membranes (Kebede *et al.,* 2019; Zhang *et al.,* 2014)), carbon nanotubes (Ren *et al.,* 2011), nanocomposites (Bilal *et al.,* 2020; Kebede *et al.,* 2019; Lofrano *et al.,* 2016)(Bilal *et al.,* 2020; Kebede *et al.,* 2019; Lofrano *et al.,* 2016), and nanofibers (Bagbi *et al.,* 2019; Cui *et al.,* 2020) are some examples of materials used in adsorption processes. Unfortunately, only a few of the reported nanomaterials have been commercialized, with the majority still being developed in laboratories. Zero valent iron nanoparticles, for example, are commercially available and used for groundwater treatment in the United States (Karnik *et al.,* 2005). However, there are some drawbacks to using free nanoparticles in wastewater treatment plants, including: (i) their tendency to aggregate (Lofrano *et al.,* 2016), (ii) the difficulty of separating them after use (except for magnetic nanoparticles), and (iii) an unknown or incompletely understood impact on the aquatic environment and human health. T

he creation of nanofibrous membranes has proven to be an efficient and promising method of water treatment. Electro-spinning techniques, which are versatile, inexpensive, and effective, are commonly used to fabricate nanofibers. Nanofibers have been developed using a variety of polymer solutions (natural and synthetic). When compared to nanoparticles, polymer-based nanofibers can overcome the issues related to the recovery and reusability of the adsorption system. In addition, these fibers offer a platform to embed nanoparticles to afford their recovery and reusability. They have superior large surface-area-to-volume ratio properties, which is essential for affording nanosized materials that can improve the overall efficiency of the adsorbents. Furthermore, they have high interfacial reactivity, excellent mechanical properties,

environmental benefits, and are re- generable and reusable.

In general, pharmaceuticals are biologically active, recalcitrant, and bio-accumulative compounds (Sigonya *et al.*, 2022). Their low concentration (ng L^{-1} to g L^{-1} range) combined with metabolic novelty results in incomplete removal from WWTPs, and their exposure to the environment can result in endocrine disruption, aquatic toxicity, genotoxicity, and the development of pathogenic resistant bacteria (De Andrade *et al.*, 2018). These compounds are pseudo-persistent due to their continuous release because they are constantly replenished. Pseudo-persistent drugs have a greater environmental presence than other contaminants (Patel *et al.*, 2019). Furthermore, due to repeated contact of effluents from WWTPs, there is a high persistence of short half-live drugs in aqueous media. Because of their low volatility, such pollutants will primarily be dispersed through the environment via aqueous transport and food-chain dispersal.

In general, the alteration of pharmaceuticals is determined by their physiochemical properties and natural attenuation (Patel *et al.*, 2019). Table 1-1 depicts the physiochemical properties of common NSAIDs and ARV drugs in wastewater. The molecular weight, solubility in water, and pKa of target molecules are important factors that can influence the efficiency of separation in MIPs and NIPs. The molecular weight of the target molecule affects the design of the polymer and selection of functional monomers because larger molecules may require larger and more flexible binding sites to accommodate their structure, necessitating the use of specific functional monomers that can effectively interact through non-covalent forces, such as hydrogen bonding to ensure optimal selectivity and binding capacity in the final polymer matrix.

While the solubility in water and pKa values can impact the binding affinity and specificity of the polymer because the solubility determines how available the target molecule is in an aqueous environment, while the pKa affects the ionization state of the target compound at a given pH. When a pharmaceutical's solubility is high, it can lead to increased concentrations in solution, enhancing the likelihood of interaction with the MIP. Additionally, the ionization state dictated by pKa at a specific pH can affect the charge and overall conformation of the target molecule, thereby influencing the strength and specificity of its binding to the imprinted sites within the polymer. Ultimately, an effective MIP design must consider these factors to optimize binding efficiency and achieve selective removal of contaminants from complex mixtures.

The distribution coefficient (K_d) and the logarithm of the octanol-water partition coefficient (log K_{ow}) are parameters that influence the binding affinity and specificity of MIPs for target compounds. K_d represents the ratio of a compound's concentration in a solid phase (such as the MIP) to its concentration in a liquid phase (such as water), indicating how well the compound is retained by the polymer compared to its solubility in water. A higher K_d value reflects stronger binding interactions between the MIP and the target molecule.

On the other hand, log K_{ow} serves as an indicator of a compound's hydrophobicity; a higher log K_{ow} value suggests that the compound is more lipophilic and thus may preferentially partition into the organic phase versus the aqueous phase. This hydrophobic character can enhance the binding affinity of the target molecules to the hydrophobic sites in the MIP, leading to improved selectivity in complex aqueous environments, where molecules with higher lipophilicity are more efficiently captured. Together, K_d and log K_{ow} provide insight into the effectiveness of MIPs for specific contaminants, guiding the design and optimization of these polymers for enhanced performance in environmental remediation applications.

Understanding and considering these parameters helps to optimize the formation and performance of MIPs and NIPs for effective separation processes.

Table 1-1. Physiochemical properties of NSAIDs and ARV drugs present in wastewater.

Name of Pharmaceuticals	Chemical Formula	Molecular Weight (g/mol)	Water Solubility (mg L^{-1})	pKa	K_d	logKow
NSAIDs						
Diclofenac	$C_{14}H_{10}Cl_2NNaO_2$	318.1	4.8	4.15	0.2	4.51
Ibuprofen	$C_{13}H_{18}O_2$	206.29	21	4.91	3.7×10^{-7}	3.97
Naproxen	$C_{14}H_{14}O_3$	230.26	29.9	4.15	-	3.18
Ketoprofen	$C_{16}H_{14}O_3$	254.28	5	4.45	15	3.12
ARVs						
Efavirenz	$C_{14}H_9ClF_3NO_2$	315.6	0.093	10.2/12.52	-	4.7
Emtricitabine	$C_8H_{10}FN_3O_3S$	247.25	1.12×10^6	2.65	-	−0.43

Nevaripine	$C_{15}H_{14}N_4O$	266.29	0.705	2.80	-	3.89

1.3.4 Sample Preparation, Detection, and Analysis of NSAIDs and ARV Drugs

There have been numerous analytical techniques developed for the simultaneous quantification and detection of pharmaceutical compounds (Mlunguza *et al.*, 2019). Because of their diverse solubility, log K_{ow} values, polarity, pKa values, physical-chemical properties, and pollutants are present in low concentration in ecosystems. High solubility generally enhances recovery and detection efficiency during chromatographic analysis, while low solubility can hinder elution and lead to decreased sensitivity. Log Kow values indicate how compounds partition between aqueous and organic phases, affecting extraction techniques; hydrophobic drugs may be challenging to recover from water, while hydrophilic drugs will elute more readily in polar solvents. Polarity also plays a crucial role, as polar substances may exhibit stronger interactions with polar stationary phases, impacting retention times in chromatographic methods. Additionally, the pKa values determine the ionization state of the drugs at specific pH levels, influencing their solubility and detectability; ionized forms typically exhibit enhanced solubility in aqueous media, which can be leveraged for improved analytical outcomes. Optimizing procedures for analyzing multidrug residues remains a global challenge (Peng *et al.*, 2014). Because matrices are complex and have low concentrations, extraction is required prior to sample analysis, pre-concentration, and sample clean-up (Sigonya *et al.*, 2022). Solid-phase extraction (SPE) is usually the method of choice for extraction and pre-concentration NSAIDs and ARV drugs from various environmental matrices.

The effectiveness of SPE is determined by the elution solvent and sorbent type amongst others (Ngumba, Kosunen, *et al.*, 2016). Oasis HLB (lipophilic–hydrophilic balance), Oasis MAX (containing mixed mode and robust anion exchange groups), Strata-X (Phenomenex), Bond elute plexa, and molecular imprinted polymers (MIPs) are all commonly used sorbents in SPE. To retain polar and non-polar compounds, Oasis HLB contains divinylbenzene rings and N-vinyl-pyrrolidone groups (Dasenaki & Thomaidis, 2015). Three or more cartridges are typically used to pre-concentrate the samples, and polar solvents (acetonitrile and methanol) are typically used for elution (Zhou *et al.*, 2012).

Purification and comprehensive extraction procedures, such as liquid chromatography–mass spectrometry (LC- MS), are required to study the fate of these pharmaceuticals and their occurrence in wastewater, rivers, and sewage sludge. After pre-treatment with SPE, samples are analysed using various spectroscopic techniques such as liquid chromatography (LC) with fluorescence detection (FLD) and diode-array detection (DAD), high-performance liquid

chromatography (HPLC), ultra-high-performance liquid chromatography (UHPLC), tandem MS using triple quadrupole or ion trap MS, and so on (Petrie *et al.,* 2016). C8 and C18 columns with an elution mixture of acetonitrile/water or methanol/water are commonly used in HPLC to determine these pharmaceuticals (Patel *et al.*, 2019).

Acetic and formic acid additions are also used to improve the mobile phase's efficiency to increase analyte sensitivity and ionization for mass detection (Petrie *et al.,* 2016). Because of the high operating pressure, flow rate (mobile phase), reduced column length, and large particle surface area to achieve better resolution in a short separation time, LC-MS has several advantages over other techniques (Abafe *et al.*, 2018). MS, coupled with LC, is one of the most effective methods for analysing NSAIDs and ARV drugs and their residues, with a detection limit of ng L^{-1}. The majority of the techniques described focus on the parent compounds and rarely discuss their transformation products or residues. Hence, metabolites should be studied because they can be found in high concentrations with high toxicity, mobility, and persistence in the environment. So far, various approaches for detecting NSAIDs and ARV drugs in various environmental matrices have been proposed; they are broadly classified into polar and non-polar sorbents.

1.4 Importance of remediation methods for pharmaceutical pollutants

Pharmaceutical pollutants, including NSAIDs and Antiretroviral Drugs ARVs, pose a significant threat to aquatic ecosystems and human health due to their persistent presence in wastewater. Conventional wastewater treatment plants are often ineffective in removing these pharmaceutical compounds, leading to their accumulation in surface waters and groundwater. The importance of remediation methods for pharmaceutical pollutants lies in their potential to mitigate the adverse environmental and health impacts associated with these contaminants.

One of the key reasons for the importance of remediation methods is the potential ecological harm caused by pharmaceutical pollutants. NSAIDs and ARVs, which are designed to have biological effects on humans, can also impact non-target organisms in aquatic environments. Chronic exposure to low concentrations of these compounds has been linked to reproductive disorders, developmental abnormalities, and disruptions in the endocrine system of aquatic organisms (Isidori *et al*., 2009). Remediation methods that target the removal of pharmaceutical pollutants from wastewater can help reduce the risk of adverse effects on aquatic ecosystems and biodiversity.

Furthermore, pharmaceutical pollutants in wastewater can also pose risks to human health through the contamination of drinking water sources. The presence of residual NSAIDs and ARVs in drinking water supplies can lead to potential health risks for human populations, including antibiotic resistance, hormonal imbalances, and other adverse health effects. Effective remediation methods are essential to ensure the protection of public health and to minimize the exposure of vulnerable populations to pharmaceutical pollutants through drinking water consumption.

In addition to environmental and health considerations, pharmaceutical contaminants in wastewater present regulatory and societal challenges. Regulatory organizations worldwide are progressively recognizing the importance of stricter specifications and monitoring for pharmaceutical pollutants in wastewater effluents. Remediation solutions that can efficiently remove these substances from wastewater can assist industries and communities in meeting regulatory requirements while also demonstrating their commitment to environmental stewardship.

Overall, pharmaceutical pollutant remediation strategies are essential for addressing the complex challenges posed by the presence of NSAIDs and ARVs in wastewater. Researchers are actively developing and implementing effective treatment technologies to protect aquatic ecosystems, safeguard public health, and ensure compliance with regulatory standards.

1.5 Electrospun-based composites for pollutant remediation

Electrospinning has emerged as a versatile and efficient technique for the fabrication of nanofibrous materials with unique properties that make them ideal candidates for pollutant remediation applications (Haghi and Akbari, 2007, Rai and Biswas, 2010; Li and Xia, 2004). The use of electrospun-based composites in pollutant remediation offers several advantages over traditional remediation methods, making it a promising approach for tackling environmental pollution challenges. The key benefits and potential applications of these innovative materials in the field of environmental remediation are vast.

One of the primary advantages of electrospun-based composites is their high surface area-to-volume ratio, which is attributed to the nanofibrous structure of the materials. The large surface area provided by electrospun nanofibers enables enhanced pollutant adsorption and catalytic activities, making them highly efficient in removing contaminants from water (Ray *et al*., 2016; Zhu *et al*., 2021). This unique feature allows electrospun-based composites to achieve high

pollutant extraction efficiencies even at low concentrations, making them well-suited for applications in water treatment, air purification, and soil remediation (Gao *et al.,* 2022; R. Wang *et al.,* 2012; Zhu *et al.,* 2021).

Additionally, electrospun-based composites offer tunable properties that can be tailored to target specific pollutants based on their chemical composition and physical characteristics. By incorporating functional additives, such as nanoparticles, polymers, or MIPs, into a polymer solution to form nanofiber composites. Studies have shown composites with selective adsorption and catalytic properties for different types of pollutants (Awokoya *et al.,* 2013; Camiré *et al.,* 2020; Subramanian & Seeram, 2013). This versatility in material design enables the customization of electrospun-based composites for targeted pollutant removal, making them versatile tools for addressing diverse environmental challenges. Moreover, the scalability and cost-effectiveness of electrospinning technology further enhances the feasibility of using electrospun-based composites for pollutant remediation on a large scale. Electrospinning can be easily scaled up to produce bulk quantities of nanofibrous materials, making them suitable for industrial applications and wastewater treatment plants (Gutierrez *et al.,* 2017). The cost-effective nature of electrospinning technology, coupled with the availability of biocompatible and environmentally friendly polymers, makes electrospun-based composites an economically viable solution for pollutant remediation in various environmental settings.

The introduction of electrospun-based composites for pollutant remediation represents a paradigm shift in the field of environmental remediation, offering a sustainable and efficient approach to address pollution challenges. The unique properties of electrospun nanofibers, combined with the tunability and versatility of material design, make electrospun-based composites highly effective in removing pollutants from water, air, and soil. The scalability and cost-effectiveness of electrospinning technology further emphasizes the potential of electrospun-based composites as a practical and economically viable solution for pollutant remediation. As research in this field continues to advance, electrospun-based composites hold great promise for contributing to a cleaner and healthier environment.

1.6 Electrospinning as a potential technique

Electrospinning is a highly promising technique for the manufacture of membranes for the remediation of pharmaceutical pollutants in water due to several key advantages. Firstly, electrospinning allows for the creation of nanofibers with a high surface area-to-volume ratio. This high surface area enhances the contact between the adsorbent material (such as MIPs) and

the target pollutants, increasing the adsorption capacity and efficiency of the material. The small diameter of the nanofibers also provides a large number of active sites for adsorption, further enhancing the removal of pharmaceutical compounds from water. Moreover, electrospinning offers a great degree of tunability in terms of the properties of the nanofibers. By adjusting parameters such as polymer composition, fiber diameter, and surface functionalization, researchers can tailor the characteristics of the nanofibers to suit specific application requirements. This flexibility allows for the development of materials with optimized adsorption properties, improving the selectivity and efficiency of the remediation process. Additionally, the scalability and cost-effectiveness of the electrospinning process make it a practical technique for the large-scale production of adsorbent materials for water treatment (Zhang *et al.*, 2023). The simplicity of the setup and the possibility of using a wide range of polymers further contribute to the versatility and accessibility of this technique for environmental remediation applications.

A study by Shirazi *et al.*, (2022) highlights the potential of electrospinning as a suitable solution for water treatment is titled. Their review explored the use of electrospun nanofibrous materials, including those incorporated with functionalized nanoparticles and polymers, as effective adsorbents for the removal of various contaminants from water. The research showcased the high surface area, tunable properties, and enhanced adsorption capabilities of electrospun nanofibers, making them a promising option for water treatment applications. The study demonstrated the potential of electrospun nanofibrous materials in addressing water pollution challenges and offers insights into the development of advanced materials for efficient water remediation processes.

1.7 Problem Statement

Water pollution is one of the significant consequences of the rapid development in industrialization and population growth. Biological oxygen demand (BOD) and chemical oxygen demand (COD) are among the popular parameters employed to determine the level of water pollution. The existence of complicated organic material, harmful toxins, and several chemical substances in the water have increased the BOD and COD levels in the water sources (Yi *et al.*, 2020). BOD measures the amount of oxygen that microorganisms will consume while decomposing organic matter, thus indicating the biodegradability of pollutants, including pharmaceuticals; a high BOD suggests significant organic pollution that can deplete oxygen from aquatic environments. Conversely, COD quantifies the total quantity of oxygen required

to chemically oxidize all organic matter in a sample, providing a measure of the potential harmful effects of both biodegradable and non-biodegradable substances. In water treatment processes, understanding BOD and COD helps in designing appropriate treatment strategies to effectively remove pharmaceuticals, ensuring that both readily degradable and persistent compounds are adequately addressed. An important step in understanding the impact of pharmaceuticals on the environment and their effectiveness in removal is assessing the concentration of pharmaceuticals in sewage. Conventional wastewater treatment plants are not designed to biologically degrade these types of complex chemicals, and a significant fraction of these types of chemicals pass through sewage treatment plants into our natural water systems. NSAIDs and other acidic drugs like ARVs are common pharmaceutical compounds and have been detected at different concentrations in wastewater effluent sites. A study that was conducted by our research group in Durban, Kwa Zulu Natal wastewater treatment plants, rivers, estuaries and even the sea. Showed the presence of these pharmaceuticals pollutants in these water bodies (Sigonya *et al*. 2022). Due to their acidic nature, these pharmaceuticals are not easily extracted from water samples using standard solid-phase extraction techniques. An anion exchange resin was found to give poor recovery of these drugs because it preferentially retains the more highly concentrated inorganic anions that are present in environmental waters, resulting in irreparable membrane fouling. This leads to the findings that there is no standard method to effectively extract these compounds from water samples for analysis. With many pharmaceuticals having poor recovery rates using existing extraction methods, there is a need for an effective technique to remove these kinds of compounds from water.

1.8 Aims and Objectives

1.8.1 Aim

To develop a suitable multi-layered MIP-PVA filtration membrane, for the simultaneous adsorption of ARV drugs and NSAID pollutants in wastewater, by incorporating MIP into PVA via electrospinning process.

1.8.2 Objectives

- ✓ Synthesize a molecular imprinted and non-imprinted polymers via precipitation polymerization process.
- ✓ Apply the MIP in wastewater treatment.
- ✓ Compare the MIP material to a commercial adsorbent.
- ✓ Incorporate MIP into PVA *via* the electrospinning process.

- ✓ Characterize MIP and MIP-PVA using SEM, BET, FTIR, NMR and TGA
- ✓ Validate the MIP-PVA adsorption efficiency for ARVs and NSAIDs in water.
- ✓ Identify and quantify the target pharmaceuticals in wastewater using UHPLC.

This approach aligns with the current shift in water treatment methods towards membrane technology, which offers simplicity and lower operational costs. However, the high cost of MIP utilization has been a major drawback, preventing its implementation in industry. By using electrospinning methods to develop the MIP-membrane composite, this can reduce production costs and provide a continuous mode of membrane treatment with high mobility of the composite. This material can significantly reduce production costs by enabling the efficient fabrication of highly homogeneous and functional materials with minimal resource waste. This method allows for the production of thin, flexible membranes that are easier to scale and incorporate into existing treatment systems, reducing the need for expensive equipment and complex synthesis processes. Additionally, the continuous operation mode offered by these membranes enhances the treatment efficiency and longevity, potentially lowering operational costs over time, making MIP technologies more viable for industrial applications.

The development of MIP-based composite membranes has the potential to fulfil the need for a specific pollutant removal system. By producing an MIP that exhibits high selectivity and recognition ability towards certain pollutants, this can compete and replace some of the conventional treatment processes. The MIP will be integrated into a membrane to form a MIP-membrane composite for continuous treatment.

The goal is to develop water treatment technology using membrane processes that can remove a wide range of pharmaceutical compounds with less operational cost and complexity compared to currently available treatments such as advanced oxidation processes, ozone, and Fenton reactions.

To provide a practical solution for the issue associated with pollutant ingress into the aquatic environment, where the conventional wastewater treatment process is partially incapable of removing them, the aim is to impart new characteristics into the current membrane. Specifically, the aim is to enhance its recognition ability to selectively bind certain pollutants, thus working towards the development of a specific pollutant removal system using nanotechnology and molecular imprinting to address this issue. This study will be the first to report on MIP electrospun composites for the adsorption of NSAIDs and ARVs.

1.9 Thesis outline

- ✓ Chapter 1: Content of research.
- ✓ Chapter 2: Literature review (showing the relevant topics of environmental pollutants).
- ✓ Chapter 3: Detailed experimental work.
- ✓ Chapter 4: Results (tables and diagrams) are presented.
- ✓ Chapter 5: Discussion of the experimental results.
- ✓ Chapter 6: Conclusions (recommendations and main points based on the results presented)

2 CHAPTER 2: LITERATURE REVIEW

2.1 Source and effects of pharmaceutical pollutants in water.

Understanding the sources and effects of pharmaceutical pollutants in water is essential to address the environmental and public health risks associated with these contaminants. Pharmaceutical pollutants originate from improper drug disposal, human and animal excretion, and other pathways, leading to widespread contamination of water sources (Lantagne, Cardinali, and Blount 2010; Lin *et al*. 2023; Wen *et a*l. 2014). These pollutants can disrupt aquatic ecosystems by affecting the endocrine system of organisms, contributing to antibiotic resistance, and impacting the food chain. Moreover, chronic exposure to pharmaceuticals in drinking water poses potential health risks to humans, necessitating the development of remediation strategies and regulatory measures to safeguard public health and preserve water quality.

By identifying and mitigating the presence of pharmaceutical pollutants in water, this can work towards ensuring the long-term sustainability and safety of our water resources. The next section delves into the realm of emerging target pharmaceuticals, exploring how these compounds occur in water sources and the methods employed to identify and quantify their presence. Emerging target pharmaceuticals represent a growing concern in water quality management, and understanding their occurrence and measurement is crucial in effectively addressing their potential environmental and public health impacts.

2.1.1 Emerging pollutants (NSAIDs and ARVs)

Antiretroviral drugs (ARVs) are medications used to treat HIV infection by inhibiting the replication of the virus in the body. These drugs are typically taken daily at specific doses to effectively control the virus and reduce the risk of disease progression. Examples of ARVs include abacavir, nevirapine, tenofovir, and efavirenz. On the other hand, NSAIDs are a class of pharmaceutical drugs commonly used to reduce inflammation, pain, and fever. These drugs work by inhibiting the production of substances in the body that cause pain and inflammation. Some people living with HIV may require NSAIDs to manage conditions such as arthritis or other inflammatory disorders. Table 2-1 outlines the daily doses, maximum uses, and types of these medications for HIV treatment.

Table 2-1. Does and uses of NSAIDs and ARVs

Drug	Type	Administration	Dose	Maximum dose	Use	References
Naproxen	NSAID	Oral	50-150mg every 8 hours	200mg/day	Pain and inflammation relief	(Kaufman *et al.*, 2018)
Diclofenac	NSAID	Oral	200-800mg every 6 hours	3200mg/day	Fever, pain and inflammation relief	(Moore *et al.*, 2014)
Ibuprofen	NSAID	Oral	250-500mg every 12 houes	1000mg/day	Stiffness, pain and inflammation relief	(Moore *et al.*, 2014)
Aspirine	NSAID	Oral	325-650mg 4X/day	4000mg/ day	Clotting prevention, fever, pain, inflammation and pain relief	(Kaufman *et al.*, 2018)
Celecoxib	NSAID	Oral	200mg 1-2/day	400mg/day	Arthritis, pain and inflammation reduction	(K. H. Lee & Gritsenko, 2017)
Abacavir	NRTI	Oral	300mg	Daily	HIV/AIDs treatment	(Yuen *et al.*, 2008)
Emtricitabine	NRTI	Oral	300mg	Daily	HIV/AIDs treatment	(Modrzejew ski & Herman, 2004)
Efavirenz	NNRTI	Oral	600mg	Daily	HIV/AIDs treatment	(Cabrera Figueroa *et al.*, 2010)
Nevirapine	NNRTI	Oral	200 mg 2x/ day	400mg/day	HIV/AIDs treatment	(Cooper & van Heeswijk, 2007)
Tenofovir disoproxil	NRTI	Oral	300mg	daily	HIV/AIDs treatment	(Cabrera Figueroa *et al.*, 2010)

2.1.2 Occurrence and Quantification of NSAIDs and ARVs in Water:

When individuals take NSAIDs or ARVs, their bodies metabolize the drugs and some of the chemicals are expelled in their urine and feces. Pharmaceutical residues can then enter the sewage system via toilets and other sanitation facilities. Furthermore, drugs can enter water systems directly if they are improperly discarded by flushing them down the toilet or pouring them into sinks (Eggen *et al.,* 2010). NSAIDs and ARVs are identified from water systems using a variety of methods. These approaches may be divided into three categories: physical, chemical, and biological processes. Activated carbon adsorption, membrane filtration, and advanced oxidation processes (AOPs) are examples of physical approaches. To break down pharmaceuticals into less hazardous compounds, chemical procedures are utilized such as oxidation, reduction, or hydrolysis processes. Microorganisms or enzymes are used in biological processes to biodegrade pharmaceutical compounds. (Sigonya *et al.,* 2023, Natarajan *et al*., 2022; Wang & Chen, 2016)

2.2 Removal approaches of NSAIDs and ARVs:

Various analytical approaches are used to measure the amounts of NSAIDs and ARVs in water systems. High-performance liquid chromatography (HPLC), liquid chromatography-mass spectrometry (LC-MS), gas chromatography-mass spectrometry (GC-MS), and enzyme-linked immunosorbent assay (ELISA) are examples of these procedures. These methods allow for the identification and quantification of pharmaceutical compounds in low quantities. Detection limits for the techniques are typically as follows: HPLC ranges from ng/mL to μg/mL, LC-MS from pg/mL to ng/mL, GC-MS from pg/mL to ng/mL, and ELISA from pg/mL to ng/mL, allowing for effective identification and quantification of pharmaceutical compounds at low concentrations (Chen *et al*. 2021).

Solid-Phase Extraction (SPE) is one of the popular methods for extracting and purifying diverse chemicals from complicated matrices such as water samples. In the case of pharmaceuticals such as NSAIDs and ARVs, SPE can be used to remove them from water systems. Samples are typically prepared by filtering and pH correction to assure compatibility with the SPE technique. The selection of the proper SPE sorbent is critical for successful removal (Aini *et al.,* 2012). Adsorbents that are often employed for pharmaceutical elimination include activated carbon, silica gel, and polymeric resins. These sorbents have an affinity for the target

pharmaceuticals, allowing them to be absorbed from water (Larsson, Rabayah, and Jönsson 2013). SPE has several benefits, including excellent selectivity, adaptability, and the capacity to handle huge sample quantities (Andrade-Eiroa *et al.,* 2016). It should be emphasized, however, that SPE is a sample-specific technique, and the selection of sorbent as well as procedure optimization are critical for effective pharmaceutical removal.

On the other hand, MIPs have shown potential for the removal of multi-target pollutants of these NSAIDs and ARVs. However, the treatment of South African water may necessitate more investigation and evaluation, as the country has no standard stipulated for how much of these pharmaceutical drugs should be in the water systems. Several studies have shown that MIPs may successfully remove pharmaceuticals such as NSAIDs and ARVs from water systems in various regions (Lagha, 2011; Mbhele, Ncube *et al.,* 2018; Nkosi *et al.,* 2022). Comparative studies can be carried out to evaluate the performance of MIPs against other removal procedures used in South Africa. While MIPs have shown success in removing NSAIDs and ARVs from water systems, their specific efficacy in global waters must be continuously investigated further. For instance, a study by Nkosi *et al.* (2022) demonstrated the potential of multi-template molecular imprinted polymers for the efficient removal of NSAIDs. By utilizing multiple templates, the researchers achieved high extraction efficiency for all target compounds compared to their NIP counterparts.

This enhanced performance is attributed to the advantages of employing multiple templates synthesis, which enables the MIP to effectively recognize and bind to multiple target molecules. The adsorption kinetics were best suited with pseudo-second order, indicating chemisorption. Despite parallels in polymer characterization results for MIP and NIP, experiments on selectivity for MIP demonstrated a high selectivity towards one compound (gemfibrozil) than other compounds. A selectivity study diagram of templates in the presence of competitor for this study demonstrated significant adsorption efficiencies for the five targeted pharmaceuticals in the presence of two competitors. The order of the K_d values on MIP selectivity was gemfibrozil > ibuprofen > naproxen > fenoprofen > diclofenac, which could imply that the imprinting cavities of the compounds were created based on the interaction of shape, size, amount of hydrogen bonding, and functionality of the template. Some compounds were favoured over others even in multi-template MIPs.

2.3 Analysis techniques

This section will focus on the analysis techniques used to identify and quantify emerging target pharmaceuticals in water sources, as well as the characterization techniques used in this process. Given the growing concern surrounding these compounds and their potential impact on environmental and human health, understanding the methods for analyzing and characterizing them is essential for effective water quality management and remediation efforts.

2.3.1 Liquid chromatography with ultraviolet detection (LC-UV)

In the field of analytical chemistry, liquid chromatography with ultraviolet detection (LC-UV) instruments plays a crucial role in the identification and quantification of various compounds, including pharmaceutical pollutants. LC-UV instruments are recognized for their high sensitivity, selectivity, and versatility, making them indispensable tools in pharmaceutical analysis, environmental monitoring, and other research areas (Quintana *et al.,* 2004). In the present study, LC-UV was employed for the identification and quantification of pharmaceutical pollutants of interest. The ability of LC-UV instruments to separate complex mixtures, detect trace levels of analytes, and deliver precise quantitative results makes them suitable for the analysis of pharmaceutical compounds in environmental samples.

The importance of LC-UV instruments lies in their ability to provide reliable and accurate data, thereby helping with understanding the presence and behaviour of pharmaceutical pollutants in the environment. The instrument has a mobile phase mixture of two polar and apolar solvents which carries the solutes through the column. The ratio of the two solvents can be held constant (isocratic mode), or it can vary over time (gradient mode). The stationary phase is a solid silica particle coated with a polymer with the desired properties for the analytes in question.

There are two common types of chromatography: normal phase and reverse phase. The normal phase (NPLC), being an adsorption chromatography, involves polar interactions by retaining the analytes by reversible bonding on the stationary phase. On the contrary, the reverse phase (RPLC) being a polarity partition chromatography involves hydrophobic interactions by retaining the analytes by reversible dissolution in a column. There are also other types of interactions in chromatography such as ion exchange, affinity and steric exclusion (Hufsky *et al.,* 2014; Yar *et al.,* 2024)

Chromatography consists of several steps to obtain the desired results. First, the mobile phase flows and pumps push the solvents through the system at a rate programmed by the method. Once the sample is injected through the system, it travels with the mobile phase to the column head. Then, there is the separation of the compounds which is done physically on the stationary phase of the column. As analytes elute from the column, they are moved to the detector. Subsequently, they are detected by a signal generated by method-specific properties. Finally, the chromatographic data system translates the signal from the detected analytes into a chromatogram of the analyte signal versus retention time. The time measured is taken by the analyte to partition and interact with the stationary phase. A typical image of an LC-UV instrument is shown in Figure 2-1. Various studies have used this technique and have coupled it with mass spectrometers for higher sensitivity of the desired analyte

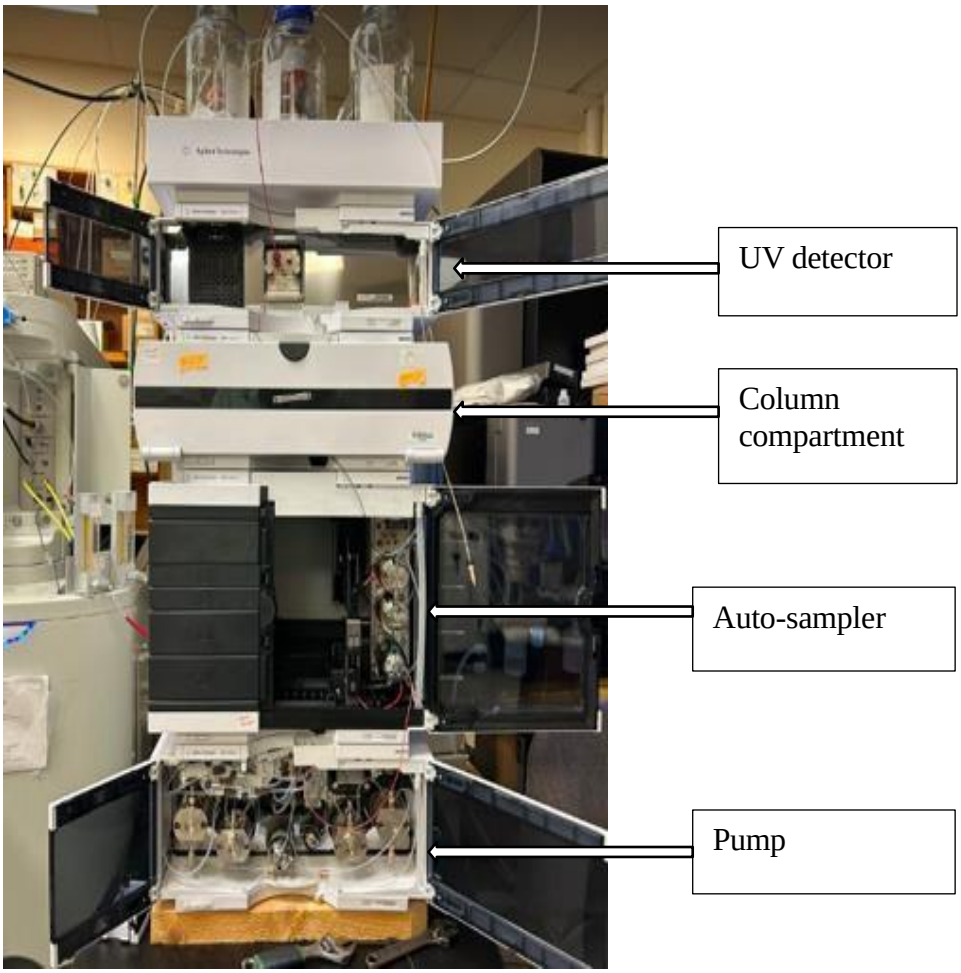


Figure 2-1. LC-UV auto-sampling instrument

2.3.2 Mass Spectrometry (MS)

Mass spectrometry allows the detection and identification of molecules by measuring their mass-to-charge ratio. This is a powerful and sensitive analytical technique for solid, liquid, or gaseous organic compounds with very good mass resolution. It is a popular detector as it makes it possible to determine the molar mass of each compound, to link the spectrum of a compound to its molecular structure, and to explain the mechanisms of bond fragmentation and to find the probable causes of the formation of ionic fragments. This technique allows qualitative and quantitative analysis with an extremely small detection limit e.g. nanogram, picogram (Weitzel *et al*. 2011). The mode of operation of this instrument is to produce ions from a sample usually denoted as (M+/ M-). Thereafter, it separates the molecular species based on their mass-to-charge ratio (m/z) and their abundance. The mass spectrometer (MS) is composed of an ionizer, a mass analyzer and a detector.

The ionizer is used to produce positive or negative ions. There are various types of ionizers depending on the sample to be analyzed: desorption-ionization (DI), electro-spray (ESI, IS), chemical ionization (CI), atmospheric pressure chemical ionization (APCI) and electron ionization (IE), matrix-assisted laser desorption/ionization (MALDI) and even more. The mass analyzer is used to separate the ions produced under the action of an electric or magnetic field. There are various types of analyzers classified by their resolution and mass range; for example, ion trap (Trap), cyclotron resonance (Orbitrap or FT-ICR), time of flight (TOF) and quadrupole (Q), and several others (Lössl, Snijder, and Heck 2014; McLafferty 1966). Finally, the detector is used to measure the number of electrons and increase the signal to obtain better sensitivity. The most used is the electron multiplier which amplifies the signal by the formation of excess electrons using lead-doped glass tubes (dynode) or using a Faraday cylinder. The signal can then be recorded, and the mass spectrum is produced. It is represented by the abundance of peaks (%) as a function of the mass-to-charge ratio (m/z). The compounds are identified by comparing the values obtained with those from a database and the result is expressed as a probability percentage (%).

To have better separation of compounds and thus improve the performance of the mass spectrometer, it is often coupled with another separation technique such as gas chromatography (GC), or high-performance liquid chromatography (HPLC). Additionally, there are various combinations between an ion source and a mass analyzer. The most common are ESI-Q, ESI-

/Q-TOF, MALDI-TOF. These combinations are selected and chosen based on their target performance and analytics. The performance of an MS is determined by the resolution (ability to separate ions of neighboring masses), accuracy (ability to measure the mass of the ion), sensitivity (ability to measure small masses) and mass range (mass measurement range). In this study the ESI- Q/TOF mass analyzer was used for effective identification and quantification of the compounds. The image of the mass ionizer used is shown in Figure 2-2. The Waters SYNAPT G1-HDMS Q-TOF instrument uses a combined quadrupole time-of-flight mass spectrometer (Q-TOF-MS) The first quadrupole (Q1) acts as a mass filter for ions selected based on their mass-to-charge ratio (m/z). This is followed by an ion mobility cell (not used in this research) followed by a collision cell where the ions collide with a neutral gas (nitrogen or argon), which leads to fragmentation of the ions by the process of collision-induced dissociation (CID). The resulting ions are then analyzed by a time-of-flight mass spectrometer.

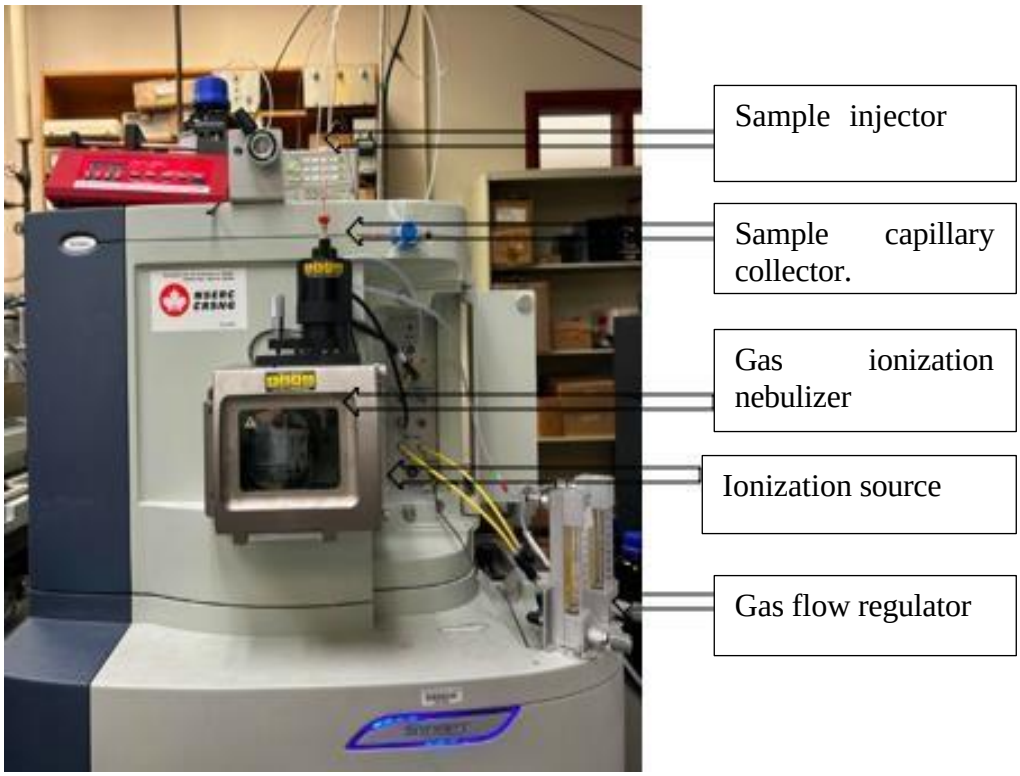


Figure 2-2. Electron spray Ionization Mass spectrometer

2.4 Tandem mass spectrometry (MS/MS)

Collision induced dissociation takes place in the transfer cell just prior to the TOF mass

spectrometer. When activated by collision, in which a portion of the ion's translational energy is converted to internal energy, the ion dissociates. These dissociation reactions tend to be very characteristic of ion structure. As a result, identification is more precise and accurate when using this kind of detector. Like mass spectrometry (MS), it allows qualitative and quantitative analysis. By applying a potential difference between the source and the collision cell, the technique can be amplified by increasing the kinetic energy of the chosen ions.

2.4.1 Solid phase extraction

Solid Phase Extraction (SPE) is a widely used analytical technique that has gained significant importance in various fields of research, including environmental monitoring, pharmaceutical analysis, and forensic science. SPE is a sample preparation method that utilizes a solid sorbent material to selectively extract target compounds from complex matrices (Madikizela, Mdluli, and Chimuka 2018). The technique has become a staple in modern analytical laboratories due to its ability to provide rapid, efficient, and selective extraction of target compounds.

2.5 Forms of SPE

There are several forms of SPE, each with its own advantages and disadvantages. Off-line SPE is the traditional method where the sample is loaded onto the SPE cartridge, and then the target compounds are eluted and analyzed. Off-line SPE is widely used in various analytical applications, including environmental monitoring and pharmaceutical analysis (Kuklenyik *et al*. 2011; Ötles and Kartal 2016). On-line SPE, on the other hand, involves connecting the SPE cartridge directly to the analytical instrument, allowing for real-time analysis and minimizing sample handling. Online SPE is particularly useful in applications where speed and automation are critical, such as in quality control and process monitoring.

2.5.1 Automated SPE

Automated SPE is another form of SPE that utilizes automated systems to perform all steps of the SPE process, including sample loading, washing, and elution. Automated SPE is widely used in high-throughput analytical laboratories, where speed and efficiency are essential. The use of automated systems eliminates the need for manual labour and reduces the risk of human error, making it an ideal choice for high-throughput applications (Lerch, Temme, and Daldrup 2014).

2.5.2 Dispersive SPE

Dispersive SPE is another form of SPE that involves mixing the sample with a sorbent material and then filtering it through a membrane. Dispersive SPE is particularly useful in applications where the target compounds are not strongly retained by the sorbent material. This method is often used in combination with other techniques, such as chromatography or spectroscopy, to provide a comprehensive analysis of the sample (Khezeli and Daneshfar 2017).

2.6 Benefits of Using SPE

The benefits of using SPE are numerous. The technique allows for the selective extraction of target compounds, reducing interference from matrix components and enhancing the sensitivity of the analytical method. SPE is also a rapid method, allowing for quick sample preparation and analysis. Additionally, SPE is a cost-effective alternative to traditional liquid-liquid extraction methods, reducing the amount of solvent required and minimizing waste generation.

2.6.1 Environmental Benefits

SPE reduces the use of organic solvents, making it a more environmentally friendly option. The use of solid-phase materials eliminates the need for large volumes of solvent, which reduces waste generation and minimizes the risk of environmental contamination. Additionally, SPE can be used in combination with other techniques, such as chromatography or spectroscopy, to provide a comprehensive analysis of the sample. However, MIPs offer notable environmental benefits, such as high selectivity for target contaminants, reusability, and low toxicity, making them a more efficient alternative to SPE. Unlike SPE, which can suffer from non-specific binding and often requires extensive conditioning and elution steps, MIPs are tailored to recognize and bind specific molecules, ensuring better adsorption efficiency.

In this study, solid phase extraction using a commercial sorbent was employed to compare with the synthesized MIP. In this method, one or more compounds in a mixture are isolated through extraction, absorption, or partitioning into the solid stationary phase of a chosen cartridge. MIPs-based SPE, also known as MISPE, has been utilized for many years and has been commercialized in certain circumstances including pharmaceuticals, food safety, environmental monitoring, biomedical applications, and rapid testing. The commercialized products are designed to extract specific compounds or biomarkers from complex samples, such as biological fluids, food, and environmental samples (Kataoka *et al.,* 2016; Tang *et al.,*

2016; Olayanju *et al.,* 2022). Its great applicability and throughput continue to draw interest. MIPs are widely used in all SPE modes due to their predictable structure, ability to build composites with other materials, ease of modification, and different morphologies including bulk, micro/nano sphere, membrane, and thin film. Researchers have made numerous attempts to synthesize preferred MIPs and innovate SPE methods to reduce steps, improve simplicity, cost-effectiveness, automation, miniaturization, time-saving, and environmental friendliness (Arabi *et al.*, 2020).

For instance, cartridges such as Bond Elut C18 are designed for hydrophobic compounds with an affinity for a fully porous silica-based stationary phase (Andrade-Eiroa *et al.,* 2010). The Bond Elut Plexa cartridges, on the other hand, retain non-polar compounds using a lipophilic neutral polymer absorbent based on divinylbenzene, making them suitable for the non-ionic extraction of acidic, neutral, or basic analytes (Ngubane *et al.* 2019). Commonly used cartridges include those containing a hydrophilic-lipophilic absorbent like Oasis HLB, which cater to a wide range of polar, non-polar, neutral, acidic, and basic compounds. This absorbent consists of N-vinylpyrrolidone (hydrophilic) and divinylbenzene (lipophilic) monomers.

In a few cases like this study where the sample matrix is complex, molecularly imprinted polymer cartridges are used to introduce selectivity during extraction. Through the synthesis of MIPs, small cavities specific to the target analyte are developed within the stationary phase, enabling the isolation of the desired compound. Various studies have utilized both MIP and commercial cartridges to isolate and preconcentrate target pharmaceutical compounds such as emtricitabine, naproxen, ibuprofen, diclofenac and efavirenz etc.

2.6 Adsorption

Adsorption is a type of physical method; it is commonly regarded as a cost-effective and dependable method of treating wastewater (Afroze and Sen, 2018). Adsorption is a mass transfer process in which solutes or removable species are transferred from a liquid phase to the surface of a solid phase (Abdullah *et al.*, 2011). Adsorbed substances are attached to the solid surface via physiochemical interactions. Adsorption has a removal effectiveness of up to 99.9% depending on the type of adsorbent used. The United States Environmental Protection Agency (USEPA) stated that the reverse osmosis (RO) and ion exchange adsorption method, among others, is one of the most effective and finest wastewater treatment procedures (Ezugbe and Rathilal, 2020). Adsorption is regarded as a well-developed technology for removing

pharmaceuticals from wastewater due to its simplicity and cost-effectiveness compared to other alternatives. Adsorbate migration happens in three successive phases in this process: (i) migration of adsorbate to the adsorbent's border shell, (ii) intraparticle diffusion into pores, and (iii) adsorption and desorption of solute. The rate of all these processes is determined by the properties of the adsorbate, adsorbent, and matrix (Sahay *et al*. 2023). Adsorption isotherms are used to calculate the material's maximum adsorption capacity. Adsorption isotherms are formed by graphing the adsorbed molecules per unit area of the contact vs. the equilibrium gas pressure or liquid solution concentration.

The most often used models for assessing pollutant adsorption are Langmuir and Freundlich's isotherms (Bazan-Wozniak and Pietrzak, 2020). Adsorbents should ideally have enough binding sites to provide effective adsorption of target contaminants. Bio-adsorbents, silica, alumina, activated carbon, clay, metal oxides, titania, and other traditional adsorbents are extensively used for pharmaceuticals and other pollutants removal (Prajapati *et al.,* 2020; Wadhawan *et al.,* 2020). Silica is an excellent adsorbent material due to its wide surface area, consistent pore size, and potential catalytic uses.

Mesoporous silica is frequently used as a support material due to its enormous surface area and superior accessibility for metals and metal oxides (Hussain *et al.,* 2012; Montes *et al.,* 2013). Nano-silica has been successfully employed in wastewater treatment since its efficacy is dependent on hydroxyl (OH) groups in many instances. Nano-alumina is also a great material for a variety of wastewater treatment applications. Alumina, on the other hand, has a limited adsorption capability (Ali & Ahmad, 2020). Nanomaterials have attracted substantial interest as adsorbents in wastewater purification due to their large specific surface area, reduced flocculent formation, and numerous accessible active sites for species binding. Furthermore, these adsorbents may be recycled and reused, making them both appealing and cost-effective.

2.7 Factors Affecting Adsorption

Initial concentration, contact time, adsorbent dosage, type of catalyst, irradiation time, pH, and temperature are some of the factors that influence the adsorption of pharmaceutical compounds by nanoparticles. The reaction rate is determined by the relative initial concentrations of absorbent and adsorbate (Jaria *et al.,* 2015). Higher concentrations of adsorbate result in lower removal efficiency of pharmaceutical compounds, while higher concentrations of adsorbent result in higher removal efficiency. The contact time between the adsorbent and the adsorbate is crucial in determining the removal efficiency of a specific nanomaterial. This is because it

provides information on the adsorbate's sorption kinetics for a given initial dosage of the adsorbent (Singh *et al.,* 2018). For instance, insight into the reaction rate and the sorption mechanism during adsorption involving mass transfer, diffusion, and reaction on the adsorbent surface (Krstić, 2021). In general, the amount of solute adsorption rises with increasing adsorbent concentration. This is as a result of higher adsorbent concentration, which translates to more active adsorption sites. However, the total solute adsorption per unit weight of an adsorbent might decrease when adsorbent concentration increases. This is due to interference produced by adsorbent active site interaction. Therefore, adsorption studies should incorporate the effect of dosage to obtain desired adsorption efficiency.

The optimal adsorbent dosage is mostly determined by the availability of active sites, which is linked to the existence of surface area and functional groups (Iftekhar *et al.,* 2018). In terms of the effects of pH, the pH of the solution is significant since it might affect the adsorption process. It affects the amount of adsorbate ionization and hence the surface properties of an adsorbent. The chemical equilibrium for estimating each adsorbate speciation should be within the pH range of 1-12 to understand adsorbent performance in solution (Iftekhar *et al.,* 2018). Yet, the temperature of the solution is the dominant influence on the adsorption process. Since it affects the adsorbent enlargement, adsorbate mobility, and the solid/liquid interface. The latter can be explained in terms thermodynamic parameters, such as Gibbs free energy (ΔG^o), enthalpy (ΔH^o), and entropy (ΔS^o). For instance, negative ΔG^o values indicate that the adsorption process is spontaneous, whereas positive ΔH^o values suggest that the process is endothermic. Furthermore, the amount of ΔH_0 appears to be connected to the kind of sorption, namely, physisorption (ΔH_0 50 kJ/mol) and chemisorption ($\Delta H_0 > 50$ kJ/mol) (Iftekhar *et al.,* 2017). In the of ΔS_0, the positive ΔS_0 values can be explained as an increase in entropy caused by the exchange of metal ions for more mobile ions during the adsorption process.

The affinity of pharmaceutical compounds is a key factor in regulating the mechanism of nanoparticles, and affinity is determined by the adsorbate molecules' properties. The higher the affinity of the adsorbate molecule for the adsorbent, the more likely the adsorption process will occur (Akhtar *et al.,* 2016). The electrostatic movement between the adsorbate and the adsorbent is governed by the electrostatic movement of ionic pharmaceutical compounds. It was discovered that the electrolyte solution could be used to modify the strength of absorbent–adsorbate interactions (Oba *et al.,* 2021).

Adsorbent and adsorbate physicochemical properties also have a significant impact on the

adsorption process. Changing the surface of the adsorbed using thermal or chemical activation procedures results in a more porous structure with more oxygenated functional groups (Bernal and Giraldo, 2018). The chemical composition and molecular structure change as a result of various activation processes, which are then used to remove specific pharmaceuticals. The adsorbate molecules attack the adsorbent's corners first, resulting in a variety of interactions (Singh *et al.,* 2021). This means that the more surface area a nanoparticle has, the better its chances of interacting with adsorbate molecules.

2.8 Mitigation of Pharmaceutical Pollutants by Nanomaterials

Over the last several years, there has been a growing interest in using nanotechnology-based remediation technologies. For pharmaceutical removal experiments, several sorbents have been used, including carbon nanotubes, silica nanoparticles, activated carbon, sorbents, metal-organic-frameworks, biochar, and synthetic adsorbents (Cho *et al.,* 2011; Hasan *et al.,* 2016; Rafati *et al.,* 2016; Lotfi *et al.*, 2019; Mondal *et al.*, 2020). Figure 2-3 shows the scheme of the adsorbents used. Nanomaterials are often defined as materials with at least one dimension less than 100 nm. These materials on the nanoscale have several novel size-dependent features, such as a high surface-to-volume ratio, reactivity, and efficiency. The use of nanomaterials in wastewater treatment can take many forms, including absorptive, catalytic membrane, bioactive nanoparticles, biomimetic membrane, polymeric and nanocomposite membrane, thin film composite, and so on.

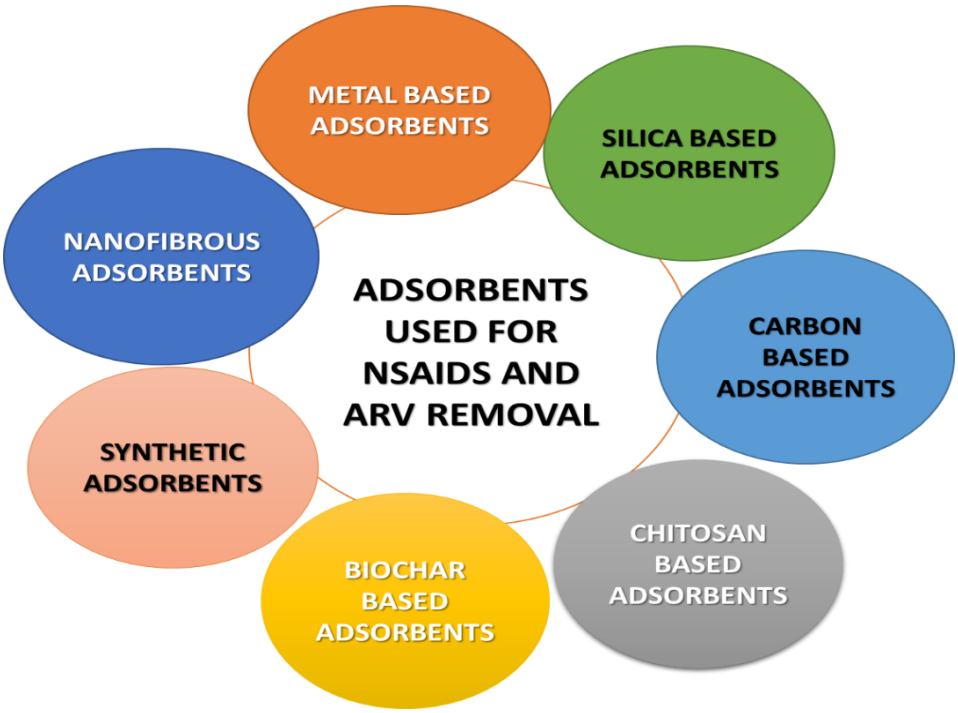


Figure 2-3. Scheme of various mechanisms used for the adsorption of NSAIDs and ARV drugs. on the surface of the absorbent.

2.9 Classification of Nano-Sorbents

In the upcoming section, the classification of nano-sorbents, focusing on the various nanosorbents that are utilized for removing pollutants in water is reviewed. Nano-sorbents have shown great promise in the field of water treatment, with a wide range of materials and structures being employed to effectively remove contaminants. Highlighting the diversity of nanosorbents and showcasing their use in water treatment highlighting the significant potential of nanotechnology in advancing water quality management practices.

2.9.1 Carbon-Based Nanomaterial

One of the most cost-effective techniques to remove pharmaceuticals from aqueous solutions is the use of carbonaceous materials as adsorbents (Cai *et al.*, 2018). Each carbon adsorbent has a unique structure and activity, and they all feature active surface functional groups, which is critical for the physicochemical characteristics of carbon materials and pharmaceutical adsorption (Yang *et al.*, 2019). Carbon nanotubes (CNTs) and graphene have received the most attention of all carbonaceous adsorbents due to their unusual surface properties (Cai *et al.*,

2018). Pharmaceutical adsorption on carbonaceous materials is primarily determined by interactions, such as hydrogen bonding, stacking, hydrophobic effects, electrostatic interactions, and covalent interactions. As a result, adsorbent surface parameters, such as porosity, surface area, and functional groups, have a significant impact on adsorption effectiveness. For example, graphene oxide was used for tetracycline, sulfamethoxazole (SMX), and ciprofloxacin (CIP) adsorption (Gao *et al.,* 2012; Chen *et al.,* 2015). The results show that graphene oxide effectively absorbed CIP and SMX at lower pH, with maximum sorption capacities of 379 and 240 mg g^{-1}, respectively. CIP sorption was primarily controlled by electrostatic attractions, whereas SMX sorption was primarily controlled by π-π EDA attraction on the basal planes of graphene oxide. Graphene nanoparticles were used to remove acetaminophen, reduced graphene oxide to remove ketoprofen and carbamazepine (Cai *et al.,* 2018), single-walled carbon nanotubes were used for carbamazepine and ketoprofen (Cai *et al.,* 2018; Zhao *et al.,* 2016), and multi-walled carbon nanotubes were for sulfamethoxazole, ketoprofen, thiamphenicol carbamazepine, diclofenac and ibuprofen, (Zhao *et al.,* 2016). The surface area of activated SWCNTs increased from 410.7 to 652.8 m^2 g^{-1}, while the surface area of MWCNTs increased from 157.3 to 422.6 m^2 g^{-1}. As a result, the activated SWCNTs and MWCNTs increased the adsorption capacity for the tested antibiotics (sulfamethoxazole, tetracycline) by 2–3 and 3–8 times, respectively. Adsorption occurred in the following order: SWCNTs > reduced graphene oxides > MWCNTs > graphene> graphite.

This arrangement corresponds to the arrangement of their surface areas and micro- pore volumes (Cai *et al.,* 2018). CNTs absorb various organic chemicals more efficiently than activated carbon. Organic compounds with carboxylic, hydroxyl, and amide functional groups form hydrogen bonds with the graphitic CNT surface, which donates electrons. CNTs have high adsorption competence for metal ions and are thus a good alternative to activated carbon (Akhtar *et al.,* 2016). For instance, using hydrothermal reduction and the chemical crosslinking method, a novel cyclodextrin immobilized the three-dimensional macrostructure of reduced graphene oxide, and multi-walled carbon nanotubes (CD/rGO- MWCNTs) were synthesized and used as an effective adsorbent for naproxen removal in aquatic environments (Feng *et al.,* 2022). The maximum naproxen adsorption capacity (qm) value of β-CD/rGO-MWCNTs stood at 132.09 mg g^{-1} (Feng *et al.,* 2022).

2.10 Current challenges and limitations in pharmaceutical pollutants remediation

The remediation of pharmaceutical pollutants from wastewater poses significant challenges and limitations due to the persistent presence of these contaminants in aquatic environments (Wilkinson *et al.,* 2016; Madikizela *et al.,* 2017). Various strategies have been employed to address this pressing issue; however, certain challenges hinder the effective removal of pharmaceuticals from water bodies.

One of the primary challenges in pharmaceutical pollutants remediation is the complex nature of these contaminants. Pharmaceutical compounds belong to diverse chemical classes, including antibiotics, analgesics, hormones, and antiretrovirals, making their removal a multifaceted task (Sanderson *et al.,* 2004). Each class of pharmaceuticals exhibits distinct physicochemical properties, solubility characteristics, and degradation pathways, complicating the development of universal remediation methods.

Moreover, the low concentration levels of pharmaceutical pollutants in wastewater present a major obstacle to their efficient removal. Traditional water treatment processes, such as coagulation-flocculation, sedimentation, and activated carbon filtration, are often ineffective in eliminating trace pharmaceutical residues from water (Vasilachi *et al.,* 2021; Yu *et al.,* 2014), as these methods are designed to target larger and more common pollutants. The detection and quantification of pharmaceutical compounds at such low levels pose significant analytical challenges and further impede remediation efforts (Nannou *et al.,* 2020). Furthermore, the occurrence of pharmaceutical pollutants in complex matrices, such as municipal and industrial wastewater, adds to the complexity of remediation processes. Co-occurrence with other contaminants, including heavy metals, microplastics, and organic pollutants, can interfere with the adsorption or degradation of pharmaceutical compounds, reducing the efficiency of treatment methods (Bilal *et al.,* 2020; Kasonga *et al.,* 2021; Majewsky *et al.,* 2016). The presence of matrix effects can alter the behaviour and fate of pharmaceutical pollutants in water, complicating their removal and posing challenges for accurate analysis.

In addition, the lack of specific regulations and guidelines for pharmaceutical pollutants in wastewater contributes to the limitations in their remediation. While certain countries have instituted guidelines for some pharmaceutical compounds (Sousa *et al.,* 2018), a comprehensive regulatory framework encompassing a wide range of pharmaceutical contaminants is lacking. The absence of stringent regulatory standards hinders the

implementation of effective remediation strategies and monitoring programs, leading to continued contamination of water sources.

Moreover, the emergence of novel pharmaceutical compounds and metabolites further adds to the challenges in pharmaceutical pollutant remediation. As new drugs enter the market and existing compounds undergo metabolic transformations, the identification and removal of these emerging contaminants become crucial. The limited availability of data on the fate, behaviour, and toxicity of emerging pharmaceutical pollutants complicates the design of remediation technologies tailored to address these evolving challenges.

In a nutshell, the remediation of pharmaceutical pollutants in wastewater faces several challenges and limitations, including the complex nature of pharmaceutical compounds, low concentration levels, co-occurrence with other contaminants, lack of regulatory standards, and the emergence of novel pollutants. Addressing these challenges requires integrated approaches that combine advanced analytical techniques, innovative remediation technologies, and robust regulatory frameworks. By addressing these limitations, effective strategies can be developed to mitigate the impact of pharmaceutical pollutants on aquatic ecosystems and human health. This study attempts to provide a molecularly imprinted polymer composite (MIPC) from the combination of polymers produced via electrospinning with MIPs as one of the pathways to remove these pharmaceuticals in aquatic environments.

2.11 Overview of electrospinning techniques and its applications in environmental pollutant removal

Electrospinning is a versatile and innovative technique used for the fabrication of nanofibrous materials. The process involves the application of an electric field to a polymer solution or melt, resulting in the formation of ultrafine fibers with diameters ranging from a few nanometers to several micrometers (Shabafrooz *et al.,* 2014). Electrospun nanofibers possess high surface area-to-volume ratios, small pore sizes, and unique morphologies, making them ideal candidates for various environmental applications, particularly in the field of pollutant removal. Advancements in electrospinning technology have led to the development of sophisticated electrospinning setups and methodologies, enabling precise control over fiber morphology, orientation, and functionalization (Li *et al.,* 2021; Teo & Ramakrishna, 2006). Researchers have explored the integration of electrospun nanofibers with various functional

materials, such as nanoparticles (Subramanian & Seeram, 2013), zeolites (Anis & Hashaikeh, 2016), graphene oxide (An *et al.,* 2014), and carbon nanotubes (Yeo & Friend, 2006), to enhance their pollutant removal capabilities.

The electrospun nanofibrous membranes or adsorbents exhibit exceptional adsorption capacities, rapid kinetics, and high selectivity towards a wide range of organic and inorganic pollutants present in water, air, and soil (Ray *et al.,* 2016). These nanofibrous materials have been employed for the removal of heavy metals, dyes, organic contaminants, microorganisms, and pharmaceuticals from environmental matrices (Fan *et al.,* 2019; Tian *et al.,* 2019; Zhao *et al.,* 2017). Additionally, electrospun nanofibers have been utilized in membrane technologies for water purification, gas filtration, oil spill cleanup, and environmental remediation applications.

In recent years, the field of electrospinning has witnessed significant advancements in terms of scalability, sustainability, functionalization, and hybridization with other materials. Figure 2-4 shows the road map electrospinning advancement has taken. Researchers have explored the use of eco-friendly polymers, natural fibers, and recyclable materials for electrospinning to address environmental concerns associated with traditional polymeric materials. The development of multifunctional nanofibrous composites with enhanced mechanical strength, chemical stability, and tailored surface properties has further expanded the scope of electrospinning in environmental pollutant removal applications.

Furthermore, the integration of smart materials, stimuli-responsive polymers, and nanocomposites into electrospun nanofibers have enabled the design of adaptive and self-healing membranes for pollutant sensing, monitoring, and remediation. These innovative electrospun materials offer prospects for real-time detection, selective adsorption, and controlled release of pollutants, paving the way for the development of next-generation environmental remediation technologies. The continuous evolution of techniques, coupled with advancements in nanomaterial science and environmental engineering, holds promise for addressing emerging challenges in environmental pollutant removal and sustainable resource management. By harnessing the unique properties and capabilities of electrospun nanofibers, researchers can contribute to the development of efficient, cost-effective, and eco-friendly solutions for mitigating environmental pollution and ensuring environmental sustainability.

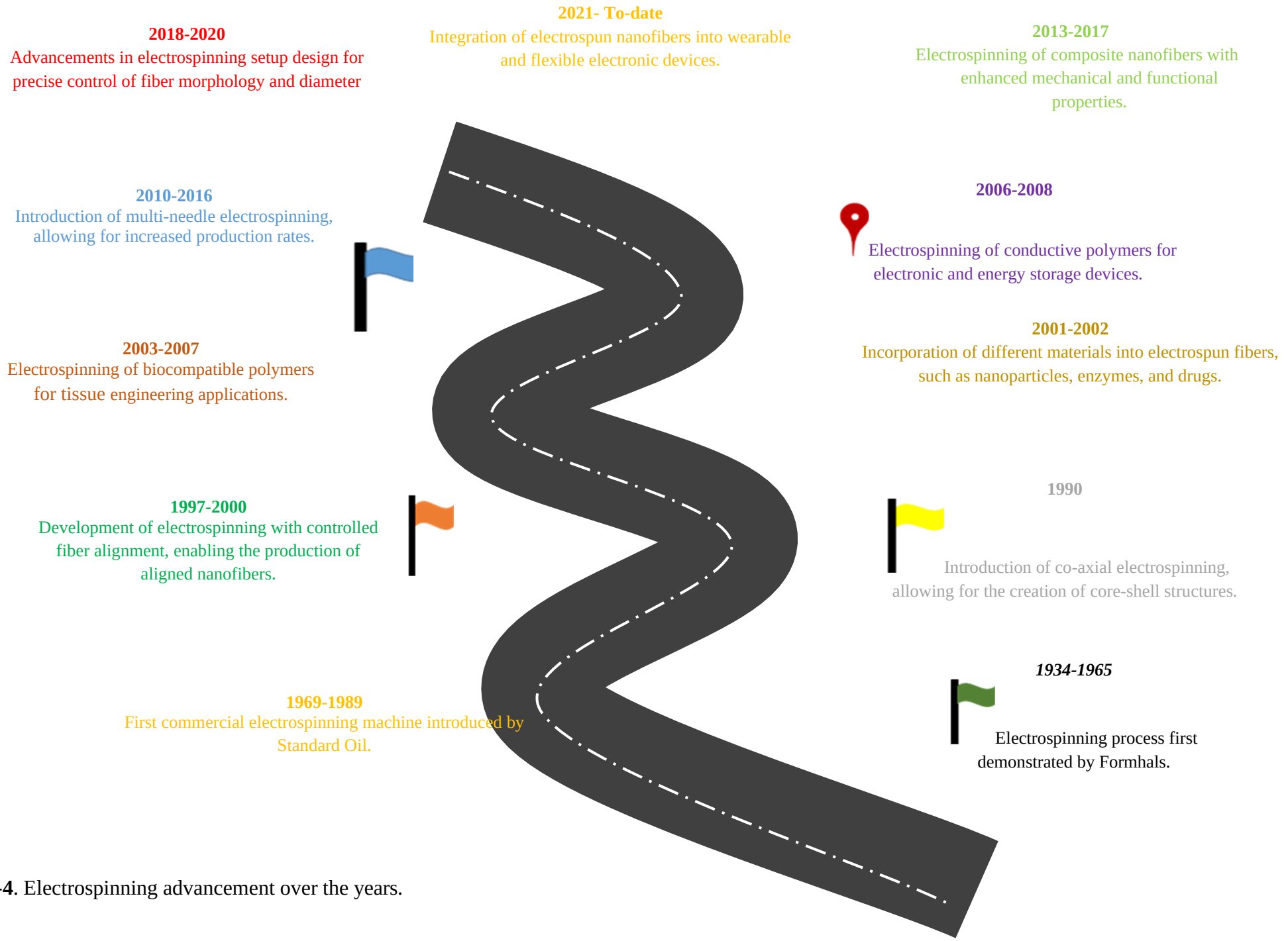


Figure 2-4. Electrospinning advancement over the years.

2.12 Molecularly imprinted polymers as selective adsorbents for pharmaceutical pollutants

Molecularly imprinted polymers (MIPs) have emerged as promising materials for the selective adsorption and removal of pharmaceutical pollutants from wastewater due to their high selectivity, stability, and tunability (Azizi & Bottaro, 2020; Gkika *et al.,* 2024). Pharmaceutical pollutants represent a significant environmental concern as they are often persistent, bioactive compounds that can have adverse effects on aquatic ecosystems. The development of efficient and selective adsorbents for the removal of pharmaceutical pollutants is crucial in water treatment processes to ensure the protection of human health and the environment.

Molecularly imprinted polymers are synthetic polymers that are designed to recognize and selectively bind to a specific target molecule based on the template molecule's shape, size, and functional groups. The process of imprinting results in the creation of recognition sites within the polymer matrix that specifically interact with the target molecule, leading to high selectivity and affinity for the adsorbate. MIPs can be synthesized through various polymerization techniques, including bulk polymerization, precipitation polymerization, and surface imprinting, allowing for the customization of their properties for specific applications.

Several studies have investigated the use of molecularly imprinted polymers as selective adsorbents for a range of pharmaceutical pollutants, including antibiotics, nonsteroidal anti-inflammatory drugs (NSAIDs), and hormones. For example, Bitas and Samanidou, (2018) developed a molecularly imprinted polymer for the selective adsorption of the antibiotic tetracycline, achieving high adsorption capacities and selectivity compared to non-imprinted polymers. Similarly, Lagha, (2011) reported the fabrication of a molecularly imprinted polymer for the removal of the NSAID ibuprofen from aqueous solutions, demonstrating high adsorption efficiency and selectivity. Concentrations of adsorbed pharmaceutical pollutants via MIPs have been reported to vary depending on the specific polymer formulation, target molecule, and experimental conditions. For instance, de Oliveira *et al.*, (2022) achieved adsorption capacities of 372.7 mg g^{-1} for estradiol: and 291.4 mg g^{-1} for ethinyl estradiol using a molecularly imprinted polymer synthesized via precipitation polymerization. Replicating the binding mechanisms observed in natural antibody-antigen interactions, MIPs offer a versatile and cost-effective solution for the selective removal of pharmaceutical pollutants from contaminated water sources.

Concisely, molecularly imprinted polymers have been presenting as a promising technology for the selective adsorption of pharmaceutical pollutants in water treatment applications. By harnessing the principles of molecular recognition and imprinting, MIPs offer high selectivity, efficiency, and stability for the removal of a wide range of pharmaceutical contaminants from wastewater. Further research into the design and optimization of MIPs as adsorbents for pharmaceutical pollutants continues to be investigated to enhance their performance and applicability in environmental remediation efforts.

2.13 Previous studies on electrospun-based composites for pollutant removal

Exploring previous studies that have utilized electrospun composites incorporating polymers with Molecularly Imprinted Polymers is essential for understanding the potential applications and benefits of this innovative material in pollutant remediation. Dyes are among the primary water pollutants that have been effectively targeted using electrospun MIPs, showcasing successful adsorption capabilities and inspiring further research in this area. However, the application of MIP-incorporated electrospun polymers for pharmaceutical pollutant removal remains relatively unexplored. This study aims to bridge this gap by investigating the use of MIP-containing electrospun nanofibers for the remediation of pharmaceutical pollutants, offering a novel approach to addressing this environmental challenge and expanding the potential applications of these advanced materials in water treatment technologies. By building upon the success of MIP-based adsorption for dyes demonstrating the effectiveness and versatility of MIP-incorporated electrospun composites.

2.13.1 Dyes

In this thesis, dyes are briefly reviewed as significant organic pollutants, drawing parallels with NSAIDs and ARVs based on their ubiquitous presence in wastewater. While our primary focus is not on studying dyes in isolation, we aim to highlight their similarities to NSAIDs and ARVs, as both groups comprise complex organic compounds that are resistant to typical biodegradation processes, leading to persistent environmental contamination. Additionally, dyes uniquely stand out as the only category of organic pollutants for which electrospun molecularly imprinted polymers composites have been explored for remediation. By examining their detection and quantification, we seek to draw insightful parallels with existing research for NSAIDs and ARVs, showing the need for using this nanocomposite material approach.

2.13.2 Electrospun MIMs and Dye Removal Techniques

To remove dyes from water, several approaches have been devised, ranging from physical procedures to complex chemical processes. Among the most prevalent approaches are Coagulation/Flocculation: Chemical coagulants are added to the water, causing the dye particles to agglomerate and become easier to remove by sedimentation or filtering (Ouakouak *et al.*, 2021). Adsorption is the process by which dye molecules bind to the surface of a solid substance. Adsorbents for dye removal that are often utilized include activated carbon, zeolites, and clay minerals (Shahadat, 2018; Shojaei & Esmaeili, 2022).

Membrane technologies including reverse osmosis, nanofiltration, and ultrafiltration may successfully remove dyes from water by physically separating them via a semipermeable membrane (Abid *et al.*, 2012). Advanced Oxidation Processes (AOPs) for the elimination of dyes, AOPs generate highly reactive oxidizing species such as hydroxyl radicals. AOPs incorporate techniques such as ozone oxidation, photocatalysis, and Fenton's reagent (Peramune *et al.*, 2022).

Electrospun MIMs (Molecularly Imprinted Membranes) have demonstrated promise in the removal of dyes from water systems. A study by Gao *et al.*, (2022) discovered that the inclusion of the template molecule methylene blue (MB) had no effect on the creation of nanofibers. Furthermore, the shape of the fiber was not disrupted by the molecular imprinting process, indicating that the electrospun nanofibrous membranes were extremely stable. The nanofibrous membranes were appealing because of their intrinsic porosity nature, with pore sizes varying from tens to hundreds of nanometers, allowing dye penetration and adsorption.

2.14 Polymers of interest

2.14.1 Polyvinyl alcohol (PVA)

Polyvinyl alcohol (PVA) is a synthetic polymer characterized by its excellent solubility in water, biocompatibility, and biodegradability. These properties make it a versatile material for various applications, particularly in the fields of water treatment and membrane technology (Jain, Singh, and Chauhan 2017). PVA’s unique structure, with hydroxyl groups that promote intermolecular hydrogen bonding, not only contributes to its functional properties but also provides avenues for further modification and enhancement to meet specific needs in water purification processes. PVA has gained attention in water treatment

applications due to its ability to form hydrogels, which can be engineered to efficiently filter and remove contaminants from water (Tian *et al*. 2019; Yang *et al*. 2021). One of the most promising aspects of PVA is its capacity to incorporate various additives or functional groups that enhance its adsorption properties, allowing it to selectively capture heavy metals, dyes, and other pollutants. Research has shown that PVA-based hydrogels can effectively immobilize pollutants through physical or chemical adsorption mechanisms, making them integral to advanced wastewater treatment systems (Zhao *et al*. 2017).

Additionally, PVA can be crosslinked or blended with other materials to improve its mechanical strength and stability during the water treatment process. This versatility enables the creation of hydrogels that can be tailored for specific contaminants, leading to more effective and targeted remediation strategies. For example, PVA hydrogels have been functionalized with materials such as metal oxides or carbon-based composites to create hybrid systems that enhance adsorption capacities and provide additional catalytic properties for pollutant degradation (Zulkiflee and Fauzi 2021).

PVA's good film-forming properties make it an excellent candidate for membrane fabrication. PVA-based membranes can be synthesized using various methods such as casting, phase inversion, or electrospinning, yielding structures with tailored pore sizes and permeation characteristics suitable for different applications. These membranes exhibit high permeability to water while retaining contaminants.

In the case of ARV drugs, a nanofiber from Mondia White/Poly vinyl alcohol (MW/PVA) blend and a first ever graphene-based material (graphene wool) were investigated (Kebede, Dube, and Nindi 2019). The effect of adsorbent dose on ARV and associated drugs elimination was by nanofiber MW/PVA was studied. According to the results obtained by Kebede and colleagues, a substantial decrease in drug removal was seen when the adsorbent dose was changed from 10 to 60 mg while other parameters remained constant. Understanding the polymer material helps to navigate the application of the polymer in water treatment.

2.14.2 Polyethylene terephthalate (PET)

Polyethylene terephthalate (PET) is a widely used synthetic polyester known for its strength, lightweight characteristics, and excellent chemical resistance. Commonly recognized for its application in the packaging industry, particularly in beverage bottles, PET also offers

promising potential in the fields of water treatment and membrane technologies (Mahalingam *et al*. 2015). Its structural properties and ability to undergo modifications make PET an attractive candidate for developing efficient solutions to address water pollution and enhance purification processes. The application of PET in water treatment revolves around its capacity to form composite materials or integrate with other filtering agents to enhance pollutant removal efficiency. Due to its robust structure, PET can be engineered into various forms, including fibers, membranes, and granules, allowing for diverse water treatment applications (Matos *et al*. 2023). PET materials can effectively adsorb contaminants such as heavy metals, organic pollutants, and dyes, particularly when modified with functional groups or combined with adsorptive materials like activated carbon or zeolites (Karim *et al*. 2022).

Moreover, PET has been explored in the development of novel filtration systems that leverage its durability and chemical stability. For instance, PET-based filters can be employed in reverse osmosis or ultrafiltration processes, effectively removing dissolved solids and micro-pollutants from water. The ability of PET to be recycled and repurposed for water treatment applications also contributes to sustainability efforts, addressing the growing demand for methods that lessen environmental impact while maintaining performance in pollutant removal (Karim *et al*. 2022; Matos *et al*. 2023).

PET's good mechanical and thermal stability makes it suitable for fabricating a variety of membranes used in water purification processes. PET membranes can be created using techniques such as phase inversion or electrospinning, providing tailored pore structures that facilitate selective permeability while effectively filtering out contaminants (Strain *et al.,* 2015). These membranes are particularly valuable in applications such as microfiltration and ultrafiltration, where they can separate particulate matter and microorganisms from water.

The adaptability of PET also enables the incorporation of nanomaterials or other functional additives to enhance membrane performance. For instance, embedding nanofillers such as graphene oxide or metal nanoparticles can improve the antibacterial properties of PET membranes, reducing the risk of biofouling and extending membrane lifespan (Mahalingam *et al*. 2015). Additionally, PET-based mixed matrix membranes, which combine PET with other polymers or materials, can be developed to optimize water passage characteristics while maintaining high rejection rates for contaminants. This literature review showed the removal of NSAIDs and ARVs through various methodologies, specifically focusing on MIPs, SPE, and electrospinning techniques utilizing PVA and PET. The integration of MIPs with

electrospun PVA and PET fibers presents a promising approach due to their high surface area, tunable pore structure, and selective binding capabilities, which enhance the efficiency of adsorbing targeted contaminants. By leveraging these advanced materials in the context of drug removal, this study aims to contribute valuable insights into sustainable and effective strategies for mitigating pharmaceutical pollution in environmental waters.

3 CHAPTER 3: MATERIALS AND METHODS

3.1 Chemicals

High purity (>98%) standards of target pharmaceutical compounds such as diclofenac (DICLO) salt, ibuprofen (IBU), naproxen (NAP), emtricitabine (EMI), efavirenz (EFV), tenofovir disoproxil (TENO), Polyvinyl alcohol (PVA), and Polyethylene terephthalate (PET) were all purchased from Sigma-Aldrich (Oakville, Canada). Hydrochloric acid (HCl) and formic acid (>98%) were also purchased from Sigma-Aldrich (Oakville, Canada).). The LC-MS-grade solvents acetonitrile (>99%), methanol (99, 5%), and acetic acid (>98%) were purchased from Fischer scientific (Ottawa, Canada). A 100 mg L^{-1} stock solution containing a mixture of the 6 target pharmaceutical compounds was prepared by dissolving the drugs in acetonitrile. A series of working standards in a concentration range of 0.1-10 mg L^{-1} was prepared in acetonitrile. Acetonitrile was the chosen solvent because of its relatively low polarity that enhances the solubility of hydrophobic and moderately polar compounds which the target NSAIDs and ARVs exhibit. Additionally, acetonitrile's high dielectric constant stabilizes ionic and polar species, assisting in the dissolution of these drugs. It's volatility and low boiling point allows for easy removal after the synthesis process. Together, these characteristics make acetonitrile a preferred choice for effectively solubilizing these pharmaceutical compounds.

3.2 Instrumentation

Water samples were filtered through 0.45 µm hydrophilic polypropylene Nalgene filtration bottle (75 mm x 100 circles) filter papers purchased from Apogent technologies (Canada). The pH of the water samples was measured with a Bante 900P portable multi-parameter water quality meter obtained from Bante instruments (Shanghai, China). For the extraction of the target compounds from the water samples, a vacuum SPE manifold sourced from Phenomenex (California, USA) attached to a vacuum pump purchased from Pall Corporations (Fribourg, Switzerland) was used. Agilent Bond Elute Plexa, (3mL, 200 mg) bought from Agilent technologies (Ontario, Canada). The UPLC instrument, purchased from Agilent technologies (Kyoto, Japan) model 1290 infinity II, with a high-speed binary pump (G7120A) as well as a multi-sampler (G716B). The compounds were separated using a C_{18} Poroshell 120 column (100mm x 2.1 mm x 5 µm) obtained from Phenomenex (California, USA) and this system was coupled to an ultraviolet (UV) detector as well as Synapt time of flight (TOF) electro spray ionization mass spectrometer (ESI-MS) detector.

3.3 LC-UV analysis procedures

Chromatographic separation was achieved by applying a mobile phase containing 0.1% formic acid in water (solvent A) and pure acetonitrile (solvent B). A multi-step gradient elution program was used by using 15% solvent B for the first 3 minutes at a flow rate of 0.5 mL min^{-1} and at 3.01 minutes ramped up to 60% solvent B until 7 minutes at a flow rate of 0.6 mL min^{-1} and 10 minutes changed to 15% solvent B and held at a flow rate of 0.5 mL min^{-1} to 5 minutes and thereafter changed back 1 mL min^{-1} for equilibration of the system. The total run time for the analysis was 15 min. The UV wavelengths were set according to the absorbance of each compound at 254 and 280 nm. Naproxen, ibuprofen, tenofovir disoproxil and efavirenz were monitored at 254 nm and emtricitabine and diclofenac were monitored at 280 nm. The chromatogram in Figure.3-1. is a representation of the separation of these compounds studied.

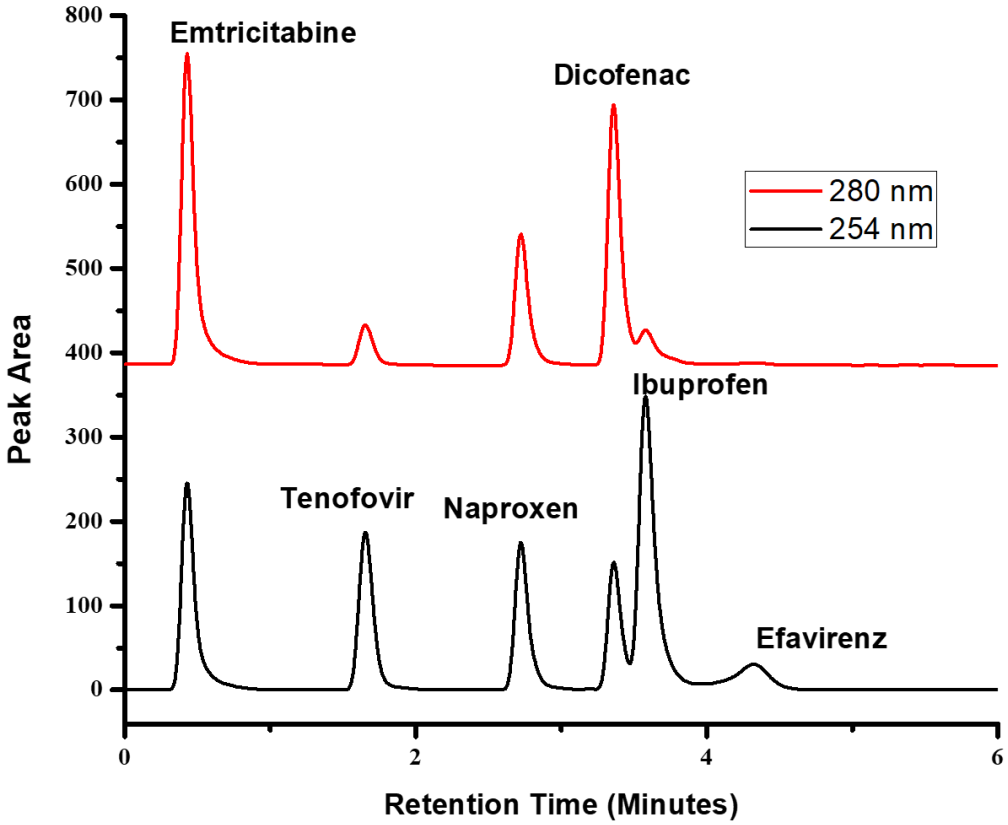


Figure 3-1. Retention time and peak area chromatogram.

3.4 ESI mass spectrometry procedure

The Waters Synapt G1 HDMS Q-TOF mass spectrometer was set up for analysis using electrospray ionization (ESI) mode for positive polarity analysis of five drugs and negative polarity for ibuprofen. The instrument parameters were optimized as follows: capillary voltage set to 3.50 kV, sampling cone voltage adjusted within -1 to 40 range, extraction cone voltage set between -0.8 to 20, syringe flow rate at 5 units, temperature set to 250 degrees Celsius for solvent removal, trap collision energy at 5.0, transfer collision energy at 3.0, detector range from 5 to 2200, mass range set to auto, and low mass resolution at 5.0. These settings were configured to ensure optimal ionization, transmission, and detection of the analytes in the sample for accurate mass spectrometry analysis using the Waters Synapt G1 HDMS Q-TOF instrument.

The mass spectrometry device was optimized based on each compound by directly injecting a standard solution of 1 ppm or 10 ppm depending on the target analyte into the instrument. The collision energy was optimized based on each compound, while the capillary potential was kept at 3.50 kV, the sample cone at 40 V, and the extraction cone at 2.0 V. source temperature was maintained at 80°C and desolation temperature at 250°C. Table 3-1 illustrates the reference data from other methods which will serve as comparisons to the results obtained from this method in Table 3-1.

Table 3-1.MS/MS optimization references from other methods

Mode	Analyte	Ion parent (m/z)	Ion Product (m/z)	Collision Energy (eV or V)	References
ESI (-)	**Naproxen**	229 ($[M-H]^-$)	185 169	-41 eV -11 eV	(Pietruk & Jedziniak, 2021)
	Ibuprofen	205 ($[M-H]^-$)	159 161	-11 eV -9 eV	(Pietruk & Jedziniak, 2021)
	Efavirenz	314 ($[M-H]^-$)	244	16,3 V	(Gouget *et al.,* 2020)
	Diclofenac sodium	294 ($[M-H]^-$)	250 214	11 V 20 V	(Mpanyakavili *et al.,* 2022)
	Emtricitabine	246 ($[M-H]^-$)	152 186 170	20 V	(Mpanyakavili *et al.,* 2022)

ESI (+)	**Diclofenac sodium**	296 ($[M+H]^-$)	250 215	18 eV 26 eV	(Pietruk & Jedziniak, 2021)
	Tenofovir Disoproxil furamate	542 ($[M+Na]^+$)	426 292	NA	(Sichilongo *et al.*, 2016)
	Emtricitabine	270 ($[M+Na]^+$)	152	10,2V	(Gouget *et al.*, 2020)

A method was developed to acquire the MS/MS spectra displaying the intensity (%) as a function of the m/z ratio for each compound. A comparative analysis of the MS/MS spectra for all compounds can be found in the supplementary appendix 1-1. An illustrative example of the MS/MS spectrum for tenofovir disoproxil fumarate is presented in Figure 3-2. Initially, emtricitabine was examined at a concentration of 1 mg L^{-1} and subjected to collision energies ranging from 5 eV to 15 eV for a duration of 1.5 minutes. Tenofovir disoproxil fumarate was also analyzed at a 1 mg L^{-1} concentration; however, this concentration was deemed inadequate as the peaks were not clearly identified at this concentration. A higher concentration of 10 mg L^{-1} was used. The collision energy for tenofovir disoproxil fumarate ranged from 5 eV to 15 eV over 1.5 minutes.

Similarly, naproxen, ibuprofen, and diclofenac were all analyzed at a concentration of 1 mg L^{-1}, which proved to be insufficient. Subsequently, concentrations of 10 mg L^{-1} were deemed more accurate for each compound. Naproxen, ibuprofen and diclofenac sodium were analyzed with collision energies ranging from 1 eV to 20 eV for a duration of 2.5 minutes each. Finally, efavirenz was evaluated at a concentration of 1 mg L^{-1} and exposed to collision energies ranging from 1 eV to 20 eV over 2.5 minutes as well. The optimization of collision energy for each analyte is detailed in Table 3-2, providing insights into the optimal conditions selected for MS/MS analysis of the respective compounds.

Table 3-2. Optimized MS/MS ion collision energies.

Analyte	**Retention time (Min)**	**Mass of molecule (g/mol)**	**Ion Parent (m/z)**	**Ions Product (m/z)**	**Collision Energy (eV)**
ESI (-)					
Naproxen	3,9	230.26	229($[M-H]^-$)	185 169	5 eV

Ibuprofen	5,4	206.29	205 ($[M-H]^-$)	159 161	5 eV
Efavirenz	5,5	315.68	314 ($[M-H]^-$)	244	10 eV
Diclofenac	5,2	296.15.	294 ($[M-H]^-$)	250 214	15 eV
ESI (+)					
Tenofovir Disoproxil	2,2	635.5	542 ($[M+Na]^+$)	426 292	10 eV
Emtricitabine	0,5	247.25	270 ($[M+Na]^+$)	152	10eV

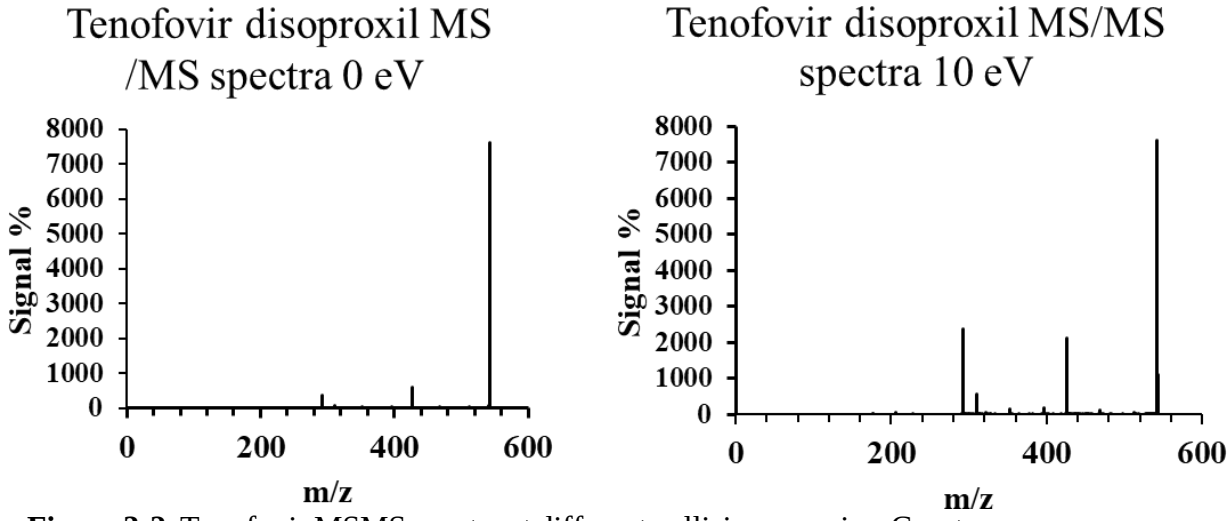


Figure 3-2: Tenofovir MSMS spectra at different collision energies. Courtesy

Emilie Drouin, University of Ottawa.

The graph displayed in Figure 3-2 illustrates the LC-MS/MS extracted ions detected at various retention times for EMI, TENO, NAP, DICLO, and EFV.

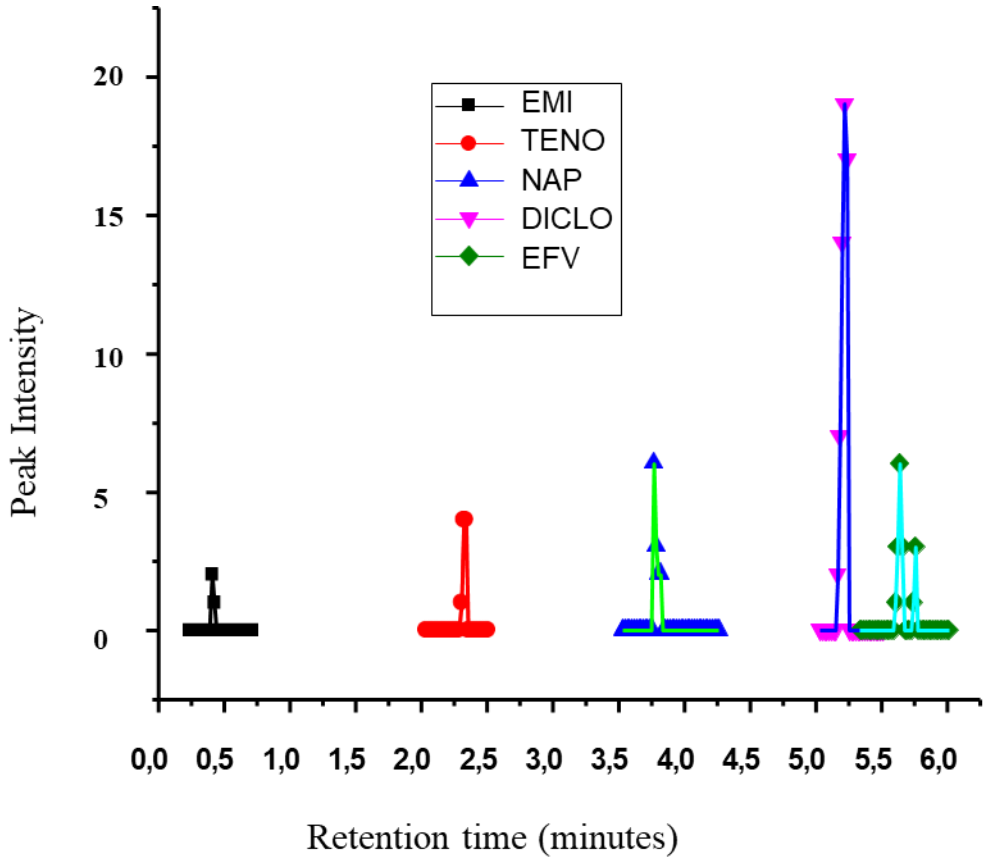


Figure 3-3 LC-MS/MS extracted ion chromatograms. Courtesy Emilie Drouin, University of Ottawa

3.5 Synthesis and characterization of MIPs

In the following section, the synthesis and characterization of Molecularly Imprinted Polymers (MIPs) and Non-Imprinted Polymers (NIP) for targeted pollutant removal in water will be discussed. Understanding the process of creating and analyzing these specialized polymers is crucial in harnessing their selectivity and efficiency in removing contaminants from water sources. By exploring the synthesis and characterization of MIPs and NIPs, this can help gain insight into their potential applications and effectiveness in water treatment processes.

3.5.1 Synthesis of Polymer

A method by Madikizela and Chimuka (2016) was adopted for the synthesis of the molecular imprinted polymers with minor changes. MIP bulk polymerization was carried out in two phases. In the first stage, 20 mg of 1,10-azobis-(cyclohexanecarbonitrile) was dissolved in 50 mL of toluene, followed by 1.51 mL of ethylene glycol dimethylacrylate. The flask was capped after being purged with nitrogen for 15 minutes. The reaction was then allowed to proceed for

8 hours with steady stirring in an oil bath set at 70°C. 0.33 mmol of EMI, TENO, NAP, DICLO, IBU, and EFV respectively were dissolved in acetonitrile (25 mL), then 0.25 mL 2-vinyl pyridine, 3.85 mL ethylene glycol dimethylacrylate, 60 mg 1, 10-azobis-(cyclohexanecarbonitrile), and 25 mL toluene were added. These components were added to the reaction product formed in the first stage. The mixture was sealed after being purged with nitrogen for 15 minutes. For 30 hours, the reaction was carried out in an oil bath set at 70°C. The resulting polymer was oven-dried to constant mass at 60°C overnight. The NIP was prepared the same way without the addition of templates.

3.5.2 Template Removal

The imprinted cavities of the templates were voided by performing a Soxhlet extraction process using the dried MIP. A 10% (v/v) mixture of acetic acid in methanol in a 250 mL flask was used to wash out the templates from the polymer. This process was repeated multiple times until the UPLC system could no longer detect the templates in the mixture. Furthermore, the polymer was washed with 100% pure acetonitrile to wash off the acetic acid residue. The NIP polymer was treated and washed under the same conditions as the MIP.

3.5.3 Grinding and Sieving Process of the Polymers

Both the MIP and NIP were milled and sieved into various particles using a 30-mesh hole stainless steel sieve with 595 μm holes. The particles below 595 μm were collected and used subsequent for the extraction experiments. Those above 595 μm were used for characterization. Figure 3-4 depicts the mechanism of interaction between the template and functional monomer. The functional monomer pyridine interacts with the templates through hydrogen bonding and π-π stacking interactions, assisting the formation of selective binding sites that mimics the structure of the target molecules.

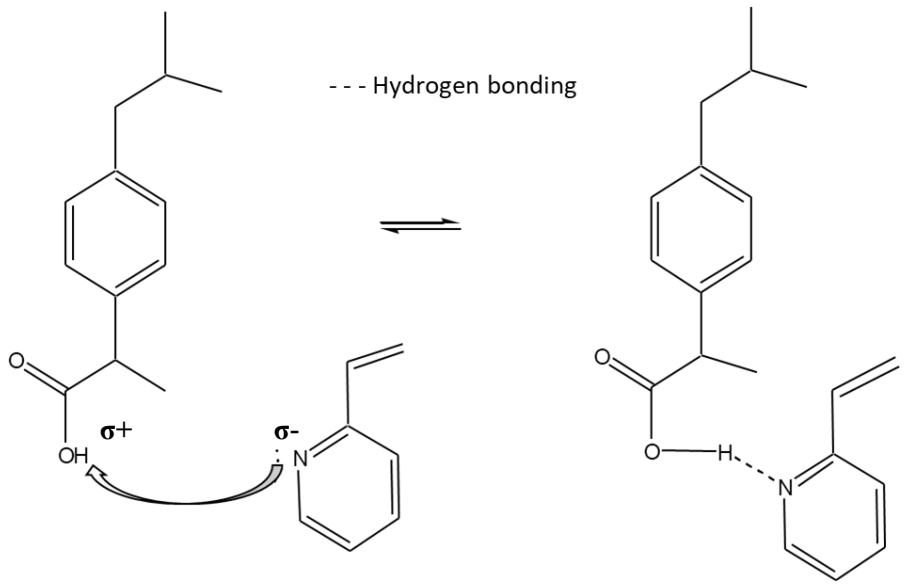


Figure 3-4. Proposed mechanism of template and functional monomer interaction.

3.6 Characterization Techniques

Ultra-high-performance liquid chromatography (UPLC) coupled with UV-VIS detection (LC-UV) and mass spectrometry (LC-MS) were used to perform the chromatographic separation and identification of the NSAIDs and ARVs. LC-UV was performed using an Agilent 1290 Infinity II ultra HPLC System with an Agilent poroshell 120, EC 1.9 μm, 2.1 × 100 mm, C8 reverse-phase column coupled with a binary pump G7120A and multisampling system from Agilent Technologies (Germany). For data analysis, the UV-VIS detector was set to 230 and 254 nm for the analysis of the templates and further coupled with an electrospray ionization (ESI) quadrupole time of flight (TOF) mass spectrometer (Waters Synapt G1) for further identification.

Solid state ^{13}C CP/MAS NMR was performed on a 4.7T Bruker AVANCE III at 200 MHz. The spectra were collected using a dual channel Bruker 7 mm HX probe with a 4 μs 1H pulse length. At room temperature, the cross-polarisation (CP) spectra were recorded with proton decoupling and a recycle delay of 2s. The ^{13}C CP/MAS experiment was conducted on solid glycine and was referred to 176.4 ppm. Cross-polarisation contact time was improved to 2.0 ms. Magic-angle-spinning (MAS) was carried out at a rate of 5,000 revolutions per second (5 kHz). Infrared spectra of the NIP and MIP were acquired on an Agilent Cary 670 Fourier- Transform infrared (FTIR) spectrometer.

Morphological images of the polymers were obtained with a JEOL JSM-7500F (Japan) field emission scanning electron microscope (SEM). Thermogravimetric analysis (TGA) was performed with a TGA 55 from TA Instruments. A platinum pan loaded with ~ 10 mg was used. The ramp rate was 10°C per minute from room temperature up to 500°C for the MIP and NIP. A Brunauer-Emmett-Teller (BET) instrument (Micromeritics Instruments Inc accelerated surface area & porosimetry System (ASAP) 2020) was used to characterize the surface area, pore size and pore volume of both polymers. The dry samples were loaded into a glass analysis tube for analysis. For activation of the as-synthesized samples, the tube was heated at 120°C under vacuum for 26 hours.

3.7 MIPs adsorption studies

The adsorption studies for both polymers were performed at room temperature using deionized water that had previously been spiked with 5 mg. L^{-1} emtricitabine, tenofovir, naproxen, diclofenac, ibuprofen, and efavirenz. The purpose of these experiment was to investigate the impact of pH (2.5-11), MIP mass (15-55 mg), and adsorption period (10-60 min) on extraction efficiency as well as the effect of concentration ranging from (5-50 mg L^{-1}). During the optimization, a single parameter was altered at a time, while the others remained constant. The mixture was agitated at room temperature for 20 minutes before being transferred to 3 mL SPE tubes, where the liquid fraction was discarded. Frits were used below and above the polymer to prevent sorbent loss. Each experimental extraction efficiency was calculated. Each experiment was carried out in triplicate. Using equation 1, the extraction efficiency, or the amount of each ARV and NSAID removed by MIP, was calculated as the difference between the spiking amount and the residual amount in solution after extraction. The adsorption capacity, or the maximum amount of each ARV and NSAID absorbed by a unit mass of MIP and NIP, was calculated using equation 2.

$$\text{Extraction efficiency } (\%) = \frac{(Co-Ce)}{Co} x100 \quad (1)$$

$$\text{Adsorption capacity } (\text{mg. g}^{-1}) \frac{(Co-Ce)}{W} V \quad (2)$$

Where C_0 represents the starting concentration (mg L^{-1}) before adsorption and C_e represents the final concentration (mg L^{-1}) after adsorption, V is the volume (L) of the solution, and W represents the mass of the polymer in (mg. g^{-1}) (Madikizela and Chimuka, 2016b; Mbhele *et*

al., 2018; Qwane *et al.,* 2020). For pseudo-first order and pseudo-second-order kinetic models, equations 3 and 4 were used to illustrate the adsorption method. The adsorption mechanism was described using the model with the highest R^2 value, where Q_e and Q_t are the adsorption capacity parameters (mg. g^1) at equilibrium and at time t (min), respectively. K_1 and K_2 are the Lagergren pseudo-first order and pseudo-second order (min^{-1}) sorption rate constants (Orimi *et al.,* 2020; Nkosi *et al.,* 2022).

$$\mathrm{Log}(Q_e - Q_t) = \mathrm{Log}Q_e - \frac{K_1 t}{2.303} \quad (3)$$

$$\frac{t}{Q_e} = \frac{1}{K_2 Q_2} + \frac{t}{Q_e} \quad (4)$$

The linearized forms of the Freundlich and Langmuir isotherms were used to describe the extent of adsorption and the isothermal analysis of the polymers, respectively. Where m denotes adsorption intensity or surface heterogeneity, C_e the target molecules adsorption capacity (mg. g^{-1}), Q_{max} the maximum adsorption capacity (mg. g^{-1}), and K_L the Langmuir adsorption equilibrium constant. The intercepts and slopes of the linear plots of C_e/Q vs C_e were used to calculate the constants K_L and Q_{max}. Equation 5 and 6.

$$\mathrm{Log}Q = \mathrm{m}\mathrm{Log}Ce + \mathrm{Log} \propto \quad (5)$$

$$\frac{C_e}{Q} = \frac{C_e}{Q_{max}} + \frac{1}{Q_{max} x K_L} \quad (6)$$

3.7.1 Selectivity experiments

The selectivity of the MIP for ARVs and NSAIDs was determined in batch rebinding experiments at room temperature using optimum conditions, which were deionized water (pH 7.0) previously spiked with 5 mg L^{-1} mixtures of emtricitabine, tenofovir disoproxil, naproxen, diclofenac, ibuprofen, efavirenz, and acetaminophen (competitor). The spiked solution (10 mLwas put into a flask with 55 mg of MIP. The resultant solution was agitated for 15 minutes (360 rpm) at room temperature before being placed into 3 mL SPE tube. Two polypropylene frits with pore sizes of 10 µm were placed below and above the MIP to prevent sorbent loss, and liquid portion were discarded. Following that, the concentration of unabsorbed compounds in solution and ran through the LC-MS system. The ARVs and NSAIDs were then

competitively absorbed from the mixture in the presence of acetaminophen. Using equation (7), the effect of imprinting on selectivity was estimated. Where K_d (mg. g^{-1}) is the distribution coefficient, C_0 is the initial solution concentration, C_e is the final solution concentration, V(mL)is the solution volume, and W(mg) is the polymer weight. Furthermore, in the presence of a competition, the selectively coefficient for the binding of ARVs and NSAIDs compounds was estimated using equation (8), where K is the selectivity coefficient. In addition, the MIPs selectivity coefficient (K′) as described in Equation 9.

$$K = \frac{C_0 - C}{W} V \quad (7)$$

$$K = \frac{K_d\,(\text{Template})}{K_d(\text{Competitor})} \quad (8)$$

$$K' = \frac{K_{MIP}}{K_{NIP}} \quad (9)$$

3.7.2 Swelling experiments

An empty 50 mL centrifuge tube was filled with 55 mg of the polymer and 10 mL of water. At room temperature, swelling was allowed to occur at different time intervals ranging from (10-60 minutes). The tube's contents were then centrifuged at 4000 rpm. Excess solvent was discarded, and the wet polymer mass was measured. Equation 10 was used to compute the swelling capacity. Where m_w is the mass of the wet polymer, m_d is the mass of the dry polymer.

$$\text{Swelling capacity} = \frac{Mw - Md}{Md} \times 100 \quad (10)$$

The swelling capacity is expressed in percentage (m/m). Understanding swelling behaviour helps predict how the MIP will behave in water, looking at aspects such as diffusion characteristics, mechanical stability, and the overall effectiveness of the imprinting process. This is essential for optimizing the performance of the composite material, ensuring that it maintains its desired properties in practical applications

3.8 Sample collection and pre-treatment.

Water samples were collected from 4 different sampling points located within the Ontario within the Robert O. Pickard Environmental Centre in Ottawa, Canada wastewater treatment

center. There sampling site GPS coordinates within the facility were N45°27’50.347’, W75°35’33.853. The sampling points were the influent, primary and secondary effluent and post chlorination effluent site. Samples were collected from the water surface in pre-cleaned 1 L amber glass bottles and kept in a cooler box with ice during transportation to the laboratory. They were filtered immediately for the removal of solid matter and thereafter stored in the refrigerator at 4ºC until analysis.

3.9 Solid-phase extraction of water samples

In this study, the analysis of samples was conducted adopting the method outlined by (Sigonya *et al.,* 2022), including their established protocols for the identification and quantification of pharmaceutical pollutants in wastewater treatment plants. The method employed herein builds upon their groundwork, ensuring a robust and consistent approach for the detection of NSAIDs and ARVs within our research context and follows the MIP adsorption results discussed.

At optimum conditions, the commercial SPE cartridges (3 mL, 200 mg styrene divinyl benzyl) were conditioned with 5 mL methanol and equilibrated with 5 mL ultrapure water adjusted to a pH 5.8, before loading the 50 mL water samples at a flow rate of 10 mL min^{-1}. The cartridges were dried under a gentle vacuum for 5 minutes. Elution of the retained compounds was performed with 3 mL methanol followed by 3 mL acetic acid in methanol (20:80) at a flow rate of 5 ml min^{-1}. The extracts were evaporated under a gentle stream of nitrogen gas at and temperature of 40ºC and then reconstituted with a 1 mL mixture of acetonitrile. Finally, the extracts were analyzed by LC-UV-MS.

3.10 Incorporation of MIP into polymer solutions (PVA and PET)

The PET solution was prepared by mixing 15% of PET with 4.0 mL of TFA in sealed vials and stirring for 3 hours at room temperature. Subsequently, a solution of molecularly imprinted polymers in 30 mL dichloromethane (DCM) was added to the PET solution. After 2 hours of agitation and ultrasonication, the same procedure was followed for PVA with a DH of 87-90% and PVA with a DH of 99%, where 7g of each polymer was dissolved in 40 mL of different solvents - including H2O (40 mL), ethanol (10 mL) and water (30 mL). The resulting solutions were then loaded into a plastic syringe connected to a syringe pump (KDS-200, Focus Co., Ltd., USA). The positive electrode of high-voltage power supply was attached to the metal needle tip (0.8 mm) of the syringe. The metal collector was covered with aluminum foil as a collector. An 18 kV voltage was applied with a tip-to-collector distance of 15 cm. The ambient

conditions were controlled at a temperature of 20˚C and a relative humidity of 40%. The fibrous membranes were then dried in a vacuum at room temperature to eliminate any residual solvent. NIMs were synthesized using the same method but without templates. The morphology and size of the polymer microspheres and electrospun membranes were characterized using scanning electron microscopy. Figure 3-5 is an electrospinning set up where d is the distance from tip to collector and V is the applied voltage.

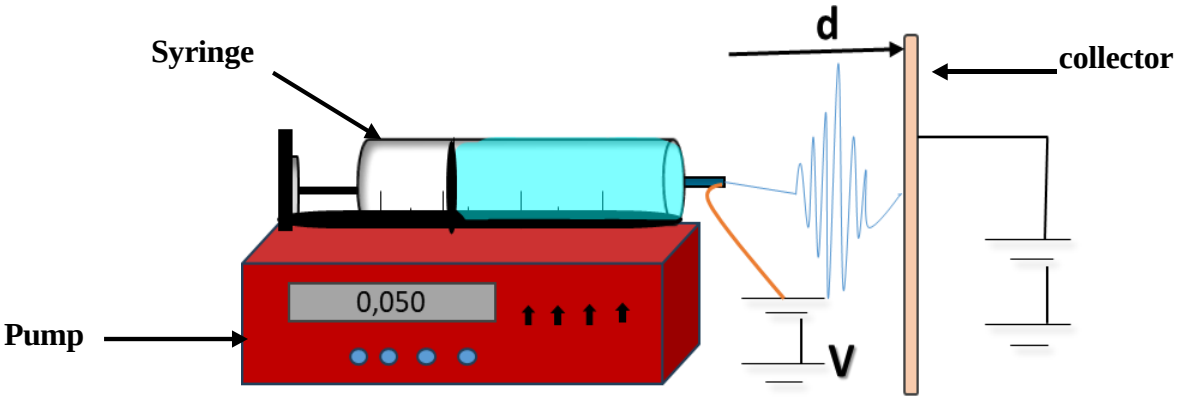


Figure 3-5. A laboratory schematic for an electrospinning experiment with a horizontal electrode arrangement.

3.10.1 Optimization of MIP amount

Molecularly imprinted polymer membranes of 10.0 mg, 20.0 mg, 30.0 mg, 40.0 mg, 50.0 mg and 60.0 mg were added into an aqueous solution containing EMI, TENO, NAP and DICLO (10 ppm, 20 mL). Then the samples were detected and analyzed after continuous stirring for 2h. The solution of 20 μL was removed for analysis with HPLC each time.

3.10.2 Optimization of adsorption time

Optimization of adsorption time is important for maximizing adsorption efficiency and capacity in various applications. By carefully adjusting the duration of contact between the composite material and the target substances, that can enhance the kinetics of adsorption, improve pollutant removal rates, and ensure the effective utilization of adsorption sites. Understanding the optimal adsorption time for PVA-MIP composites allows for tailored design of adsorption systems, leading to increased performance, cost-effectiveness, and environmental sustainability in applications such as water treatment.

Therefore, to study the adsorption time, molecularly imprinted polymer membranes (MIMs)

were introduced into an aqueous solution containing the 6 template molecules and continuously stirred. Samples were collected at various time intervals (every 10, 20, 30, 40, 50, 60 minutes, 12 hours, and 24 hours) and analyzed using HPLC starting from the initial time. Figure 3-6 shows the adsorption process used for the analysis of contact adsorption time by the material.

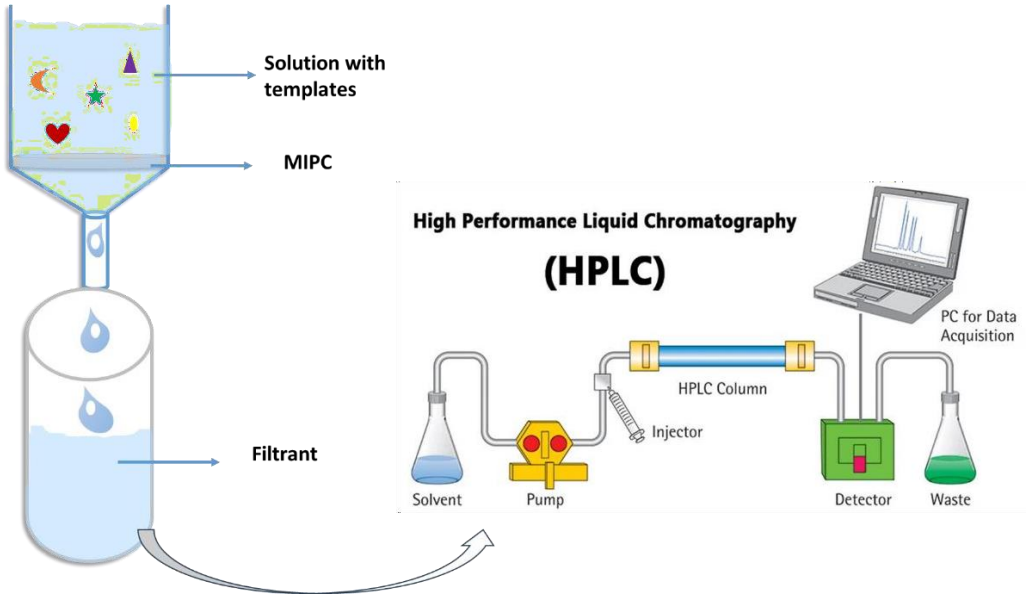


Figure 3-6. Molecular Imprinted Membrane analysis

4 CHAPTER 4: RESULTS AND DISCUSSION

4.1 Adsorption study of MIP for pharmaceutical pollutants in wastewater

In the following section, will discuss the adsorption study of MIP for pharmaceutical pollutants in Canadian wastewater treatment plants. This study aimed to explore the effectiveness of MIPs in removing pharmaceutical contaminants from wastewater, specifically in the context of Canadian treatment facilities. By investigating the adsorption properties of MIPs in this setting, we gain valuable insights into their potential as a sustainable and efficient solution for pharmaceutical pollutant removal in wastewater treatment processes.

4.1.1 Effects of pH

The pH of the water solutions was adjusted to facilitate the monomer-template interaction. The pH was measured in the (2.5-10) range (Figure 4-1) a mass of 55 mg and 50 mL volume were used and kept constant during this experiment. Various recoveries were observed for the target molecules, especially for emtricitabine, tenofovir disoproxil and naproxen. EMI has very stable recoveries throughout the various pH mediums with recoveries above 100 %, which was different with TENO which had low recoveries of 49, 49, 76 and 19 % across the pH range. EMI has a lower pKa, allowing it to remain predominantly in a protonated state in acidic conditions (like pH 4), which enhances its effective adsorption due to favourable interactions with the adsorbent material.

In contrast, TENO, with a higher pKa, exists mainly in a deprotonated (negatively charged) state at lower pH levels, resulting in reduced adsorption efficiency and lower recoveries due to repulsive interactions. At a pH of 4 TENO should be more in their neutral or protonated state that makes the adsorption with the material more effective based on its pKa. However, higher recoveries were seen from its more negative state at more neutral conditions at pH 7 (76 %). An electrostatic repulsion was expected in a neutral state due to the type of polymer adsorption material designed because the design of the polymer adsorption material is based on the idea that the imprinted polymer would primarily interact with charged or polar functional groups of the target molecule, potentially leading to repulsive forces when both the polymer and the molecule were in a neutral state. This expectation stems from the notion that, under certain conditions, like charges can repel each other, especially in the presence of similar functional groups. This was not observed because the molecular interactions dominated by non-electrostatic forces that is hydrogen bonding and hydrophobic interactions, which override repulsive electrostatic forces. Additionally, the spatial arrangement of the functional groups

within the polymer may have facilitated effective binding and minimized repulsion by promoting conformational adaptation. A slight decrease in recoveries was observed for other compounds like NAP which ranged above 100 % under acidic condition to 71 % under neutral condition. In a previous study (Nkosi *et al.*, 2022), it was found that above a pH of 4 the maximum adsorption efficiency decreased due to hydroxide ion interferences in the MIP cavities. Overall, a pH of 7 was opted for in this study as it gave the best overall performance for the six targets.

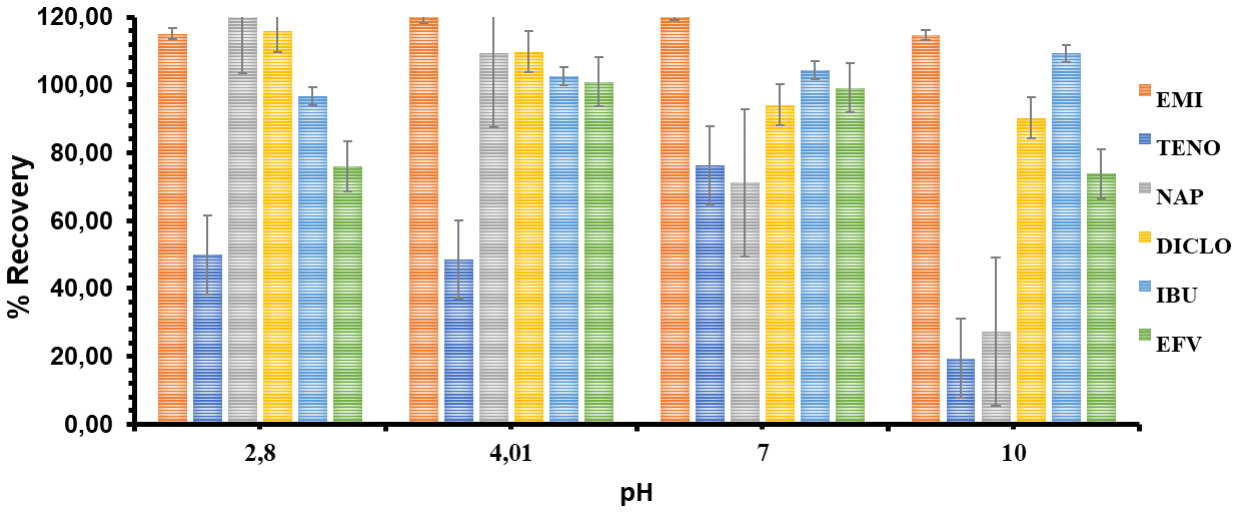


Figure 4-1. pH effects on the adsorption of ARVs and NSAIDs

4.1.2 Effects of polymer mass

Batch adsorption of the MIP was conducted with polymer masses ranging from 15-55 mg respectively, to find the optimum adsorption mass that will be used throughout the experiments whilst other parameters such as sample pH (7.0), target component concentration (5 mg. L^{-1}), and sample volume (10 mL) remained fixed. High recoveries were observed across all masses with extraction efficiencies ranging from >83%. Mass 55 mg as shown in Figure 4-2 had the best results for all target compounds as expected from its greater mass, and thus greater surface area. The MIP (Figure 4-2a) displayed had greater extraction efficiencies overall than the NIP (Figure 4-2b).

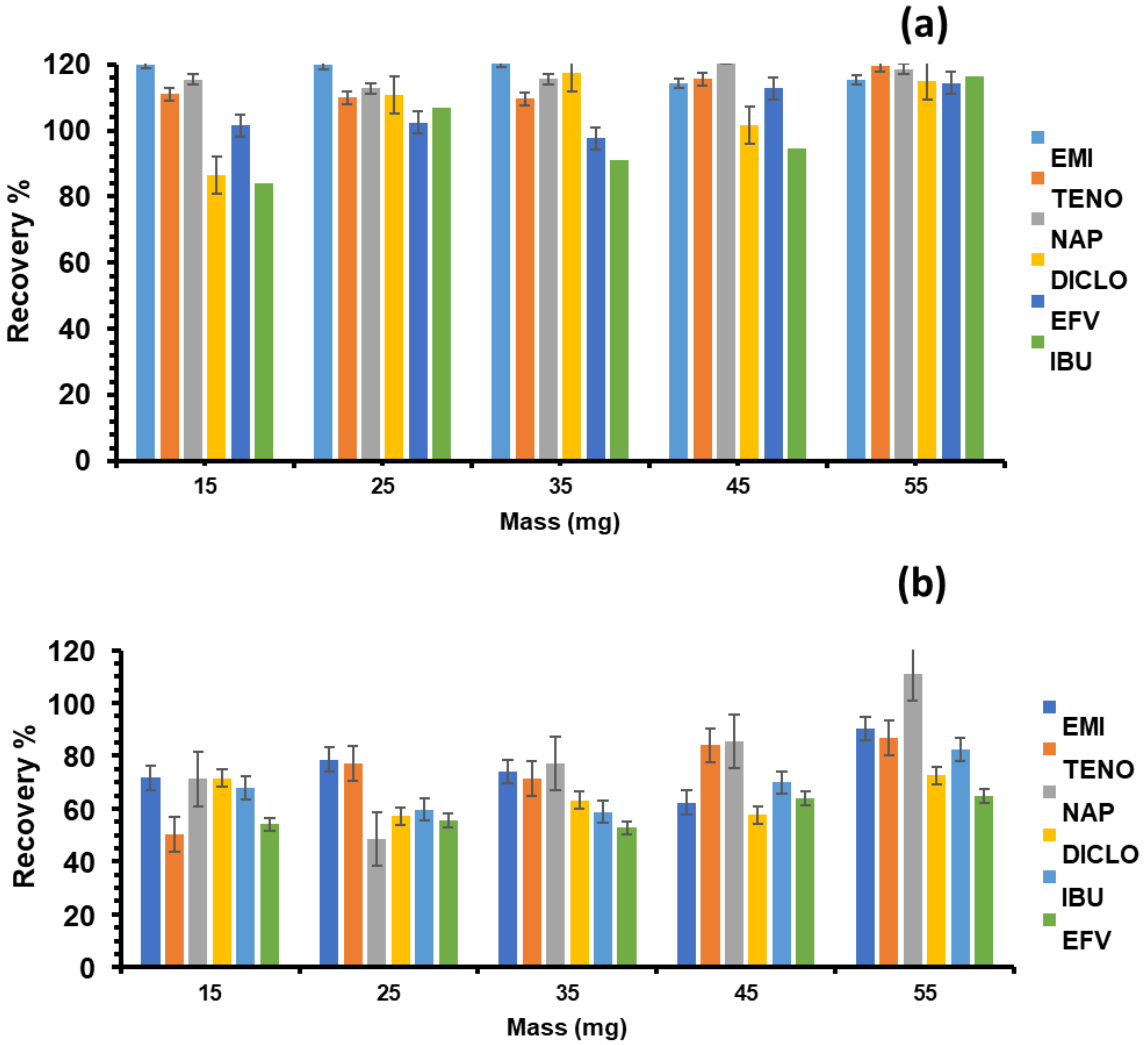


Figure 4-2. Mass effects of (a) MIP and (b) NIP for ARVs and NSAIDs recoveries.

4.1.3 Effects of initial concentration

As illustrated in Figures 4-3a & b, the adsorption capacity derived using Equation (2) is plotted as a function of the initial target molecule concentration in the range of 5 to 50 mg L^{-1} range. The results show a linear relationship between the two for the MIP; however, for the NIP, a decrease in concentration adsorption was observed for NAP and IBU as they reached equilibrium at 40 mg L^{-1}. This decrease was not observed for the MIP because it has the designed imprints of the template molecules recognizing the designed imprints of each template. Similar trends were observed in other multi-template studies for MIP adsorption (Archer *et al.*, 2017). High adsorption capacities of EMI and TENO, the two ARV drugs, were observed in the NIP with capacity of 49.05 and 22.85 mg. g^{-1}, respectively.

This might be due to the flexibility of the non-imprinted polymer to fit the size of these compounds with no steric hindrance. Also, as seen in the SEM and BET results above, the NIP has non- distinct cavities with a larger total pore volumes than the MIP, hence these two compounds with larger molecular weight have been adsorbed more in this material. (Figure 4-3).

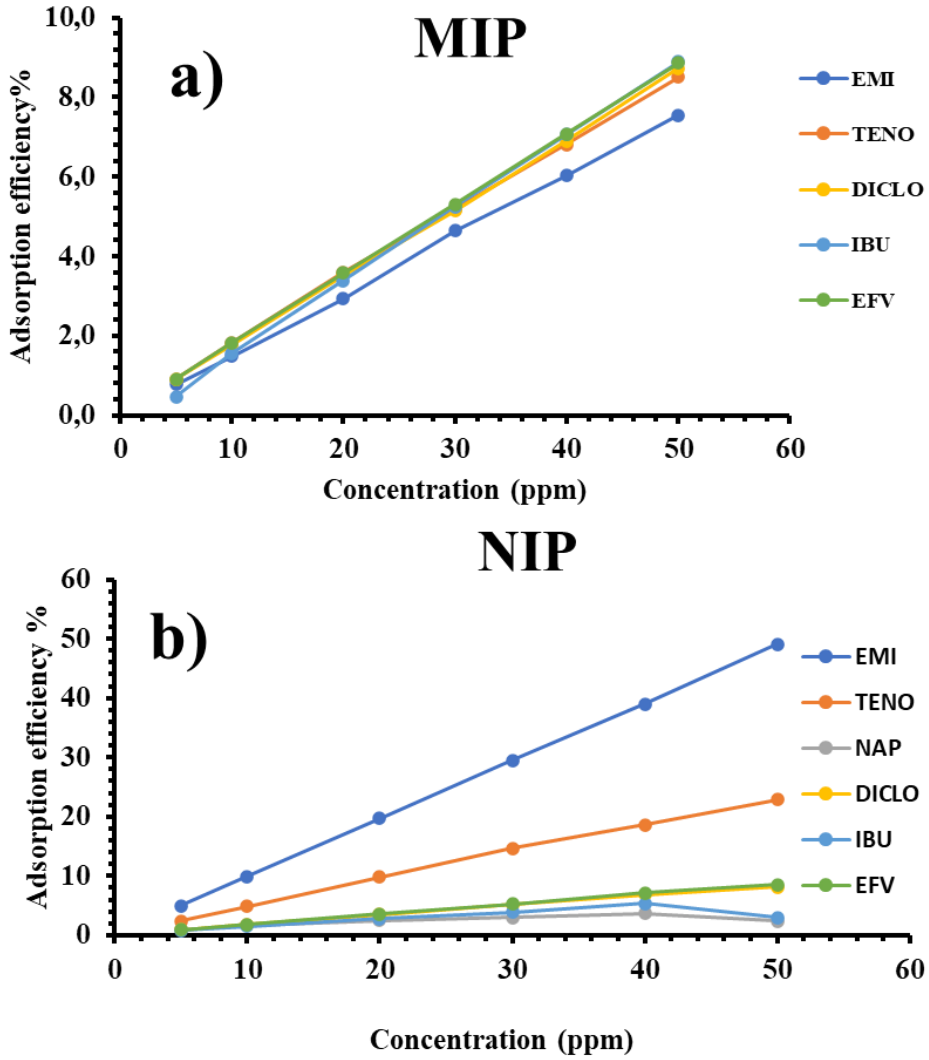


Figure 4-3. Effects of target initial concentration on the adsorption capacity with (a) MIP and (b) NIP.

4.1.4 Effects of contact time

The effect of contact time was explored by measuring the extraction efficiency as a function of time with a sample pH of 7.0, starting concentration (5 mg L^{-1}), adsorbent mass (55 mg), and sample volume (10 mL) were held constant (Figure 4-4). The initial 10 minutes of contact between the target molecule and the MIP showed a pronounced and rapid increase in adsorption. This rapid uptake can be attributed to the high affinity of the MIP for the imprinted sites corresponding to the template molecule. During this phase, a significant proportion of the target analyte was successfully bound to the polymer. As the contact time progressed, the rate of adsorption began to plateau, indicating that the available binding sites were becoming occupied, and the kinetics of the adsorption process started to slow. Extraction efficiencies greater than 96% were achieved within 10 minutes of interaction time. the following experiments. a contact duration of 10 minutes was used to ensure the regularity of target drug absorption from aqueous samples, in line with previous work (Bouzidi *et al.*, 2023; Sigonya *et al.*, 2023).

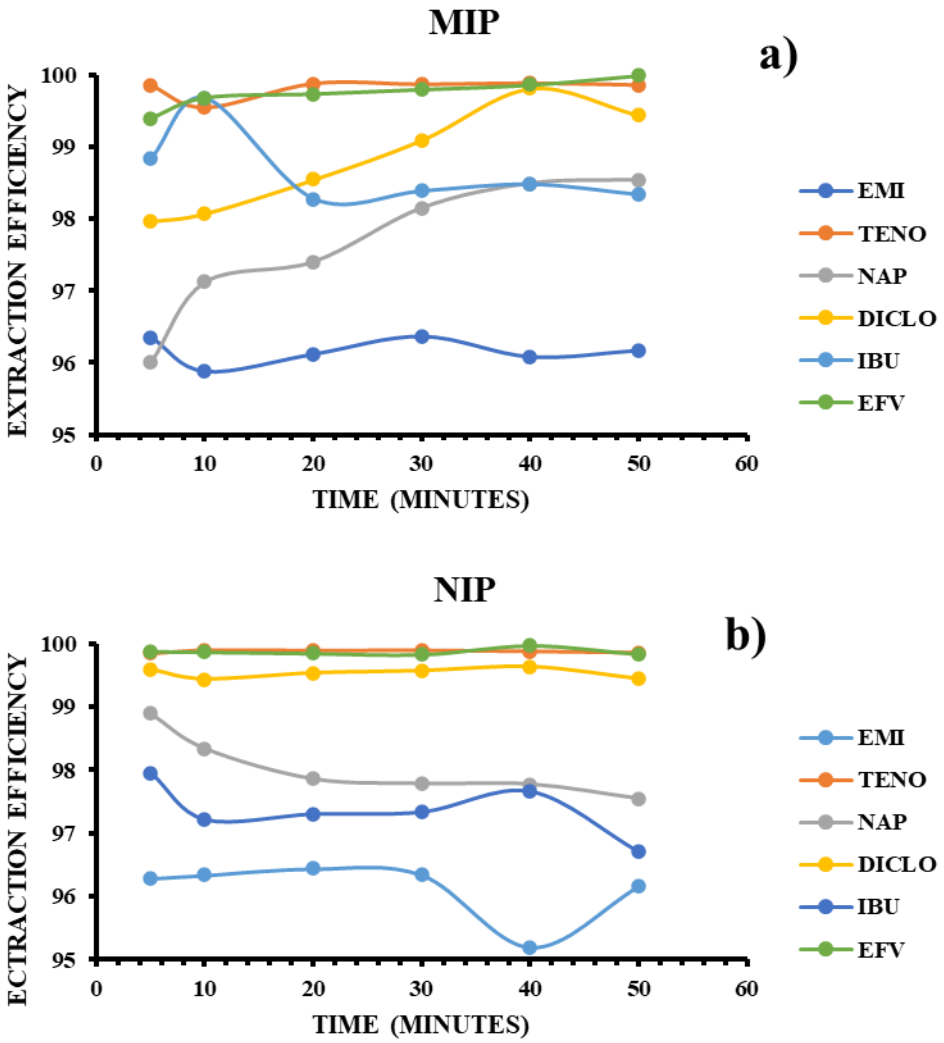


Figure 4-4. Extraction efficiency (a) MIP and (b) NIP based on template contact times.

4.2 Adsorption kinetics

This section delves into the adsorption kinetics and explores why studying these kinetics is important in water treatment. Adsorption kinetics play a pivotal role in understanding the rate at which contaminants are removed from water by adsorbent materials. By examining these kinetics valuable insights into the efficiency, performance, and effectiveness of adsorption processes, ultimately guiding the development of more efficient water treatment technologies.

4.2.1 Adsorption Isotherms

Adsorption isotherms may be used to describe how much material is adsorbed as a function of initial concentration at constant temperature, which in this case was ambient temperature. The

linear versions of the Langmuir and Freundlich isotherms were used to assess the adsorption data (Table 4-1). Based on the observed R^2, the Freundlich isotherm appears to be the best descriptor of the adsorption isotherm. The Freundlich isotherm, characterized by its non-linear nature, suggests a heterogeneity in the binding sites adsorption capacity of the polymer (Pereira *et al*. 2023). The preference for the Freundlich isotherm over the Langmuir, indicates that the adsorption process for both MIP and NIP surfaces is not limited to a single monolayer. Instead, it suggests the formation of multilayers of adsorbate molecules on the polymer surface.

Moreover, the affinity of both these polymer materials implies potential application including but not limited to separation purification processes. The values of 1/n for each drug provides insights into the surface characteristics, adsorption intensity, and nonlinearity in the adsorption process. Two groups of drug compounds can be discerned based on similarities in their 1/n values. Emtricitabine (1.1968) and ibuprofen (16.359) both exhibit heterogeneous surfaces, suggesting diverse adsorption sites possibly because of their physical properties as both have low molecular weight that is more effective in adsorption.

However, emtricitabine demonstrates a moderate adsorption intensity, implying a balanced adsorption process across different concentrations. Conversely, ibuprofen displays a low adsorption intensity, indicating less favourable adsorption conditions. Moreover, while emtricitabine shows moderate nonlinearity in adsorption as the 1/n value is greater than 1, ibuprofen demonstrates high nonlinearity, indicating a steep increase in adsorption capacity with decreasing concentration, which relates to the observations found in section 4.1.3 studying the effects of concentration at higher concentration ibuprofen has a decline in adsorption.

Similarly, tenofovir (0.302) and diclofenac (0.7003) present highly heterogeneous surfaces conducive to strong adsorption at low concentrations. Despite this similarity, both drugs exhibit a moderate adsorption intensity, suggesting favourable adsorption conditions. Moreover, their nonlinearity in adsorption is high, with a steep rise in adsorption capacity observed as concentration decreases.

Individually, naproxen (2.487) showcases considerable surface heterogeneity, potentially with varying adsorption sites. Its relatively high adsorption intensity suggests weaker adsorption at low concentrations, while moderate nonlinearity in adsorption implies a moderate increase in adsorption capacity with decreasing concentration as the Freundlich coefficient is greater than 1. In contrast, efavirenz (1.5028) demonstrates a relatively homogeneous surface with

consistent adsorption sites. The moderate adsorption intensity observed suggests a balanced adsorption process, while moderate nonlinearity in adsorption indicates a gradual increase in adsorption capacity with decreasing concentration.

The K_f values indicate the adsorption behaviour of the adsorbent material. For emtricitabine K_f =0.6943 and naproxen K_f =0.8050, moderate adsorption capacities are observed, suitable for efficient adsorption processes in wastewater treatment or purification applications. Conversely, for tenofovir disoproxil K_f=5.3002 and diclofenac K_f =4.3672, significantly higher adsorption capacities are evident, ideal for thorough removal of solutes or pollutants from solutions, such as in environmental remediation or industrial processes. Lastly, for K_f=0.0389 and K_f=0.0535, low adsorption capacities are observed, which may find utility in applications requiring selective adsorption or trace contaminant removal.

Table 4-1. Adsorption Isotherms

		Langmuir Isotherm (eq 6)		Freundlich Isotherm (eq 5)		
Polymer	**Compound**	**R^2**	**intercept**	**1/n**	**K_f**	**R^2**
MIP	Emtricitabine	0.6124	-0.1977	1.1968	0.6943	0.9869
	Tenofovir disoproxil	0.9709	-0.7240	0.302	5.3002	0.9150
	Naproxen	0.6227	-0.0942	2.487	0.8050	0.8139
	Diclofenac	0.8222	0.6402	0.7003	4.3672	0.9311
	Ibuprofen	0.9840	-1.4099	16.359	0.0389	0.7001
	Efavirenz	0.8525	-1.2718	1.5028	0.0535	0.9313
NIP	Emtricitabine	0.8854	1.1022	0.5594	15.929	0.9951
	Tenofovir disoproxil	0.7598	1.0834	0.7247	12.117	0.7425
	Naproxen	0.9856	0.277	0.4303	1.8958	0.9683
	Diclofenac	0.9592	0.6221	0.6456	4.1889	0.9840
	Ibuprofen	0.9585	0.0919	0.4199	1.2356	0.6853
	Efavirenz	0.8784	0.8577	0.7603	7.2061	0.9812

4.2.2 Kinetic modelling

The rate of ARV and NSAID adsorption by MIP and NIP was measured as a function of time. If second-order kinetics is used, the plot of t/Q vs t should provide a straight line. The values K_2 and Q_e were computed from the intercept and slope of the linear plots of C_e/Q vs Ce, respectively; the data is shown in Table 4-2. The kinetic modelling results showed that the adsorption process followed pseudo second order kinetics as they better obeyed a straight line. The adsorption capacities (Q_e) were 0.90, 0.83, 0.06, 0.83, 0.07, and 0.13 mg. g^{-1} for EMI, TENO, NAP, DICLO, IBU and EFV, respectively. These adsorption capacities were lower in the MIP than in the NIP. For instance, tenofovir disoproxil has adsorption capacity of 3.58 mg.

g^{-1} in the NIP compared to 0.83 mg. g^{-1} in the MIP. This could be due to the flexibility of the NIP with it having a smoother surface and larger pore size diameter than the MIP as mentioned earlier in the thesis. The pseudo-second-order kinetic model results fit well with the Freundlich isotherm.

Table 4-2. Calculated results of Kinetic Model

Polymer	Compounds	Pseudo-First Order		Pseudo-Second Order	
		R^2	R^2 min^{-1})	K_2 (mg. g^{-1}	Q_e (mg. g^{-1})
MIP	Emtricitabine	0.86	1.00	2.75	0.90
	Tenofovir disoproxil	0.61	1.00	3.47	0.83
	Naproxen	0.50	0.90	3.19	0.06
	Diclofenac	0.88	1.00	1.16	0.83
	Ibuprofen	0.86	0.83	0.07	0.07
	Efavirenz	0.86	1.00	2.07	0.13
NIP	Emtricitabine	0.84	0.98	0.56	0.92
	Tenofovir disoproxil	0.90	1.00	0.73	3.58
	Naproxen	0.75	0.99	0.43	2.91
	Diclofenac	0.63	1.00	0.65	3.75
	Ibuprofen	0.92	0.92	0.42	0.10
	Efavirenz	0.84	0.92	0.76	0.92

4.3 Swelling behaviour

Over a one-hour period, the swelling capacity (W) of the polymers was studied using the swelling experimental data explained earlier in section (2.6.2). Figure 4-5 depicts the polymers inflating rapidly after 10 minutes, then decreasing as they approached equilibrium and reaching a plateau between 50 and 60 minutes. The polymers reached equilibrium at 0.48 and 1.25 g. g^{-1} NIP and MIP, respectively. The swelling might be caused by the N-group of 2-vinyl pyridine, which was employed in the polymerization. These findings suggest that water penetrates the polymer network, reducing the osmotic pressure differential between the solution and the polymer and thereby slowing water diffusion (Madikizela & Chimuka, 2016b). Furthermore, the swelling of the MIP allows water to infiltrate into cavities, increasing interaction with the target analytes. The MIP's higher swelling capacity also implies the MIP is more prone to swelling in water than the NIP due to the specific imprints and the chemical nature of the imprints within the MIP that allows greater interaction with solvent. This is one of the desired outcomes of molecular imprinting since it gives polymer selectivity and recognition capabilities

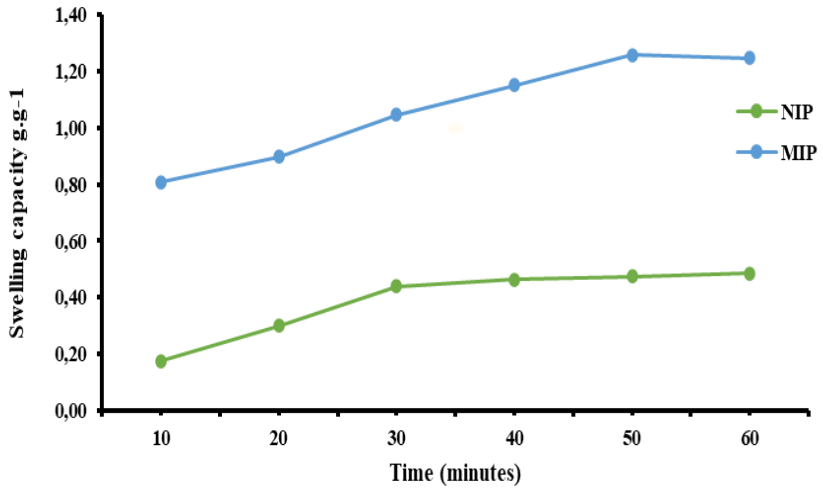


Figure 4-5. Swelling capacity of polymer as a function of time.

4.4 Selectivity studies

The selectivity of the MIP was determined using equations (7-9). Deionized water was spiked with 10 mg L^{-1} of each target compound in the presence of equivalent quantities of acetaminophen, which was utilized as a competitor in a multi-component process. Acetaminophen is a popular analgesic drug with physicochemical properties and size similar to the target compounds (Kaya *et al.*, 2013). It co-exists with all the mentioned target compounds in aquatic bodies. The competitor's molecular structure is similar to the target compounds in that they contain a carboxylic group. The hydrogen atom of the carboxylic group is predicted to interact with the nitrogen atom of 2-vinylpyridine which is our functional monomer as it should interact the same with acetaminophen. The MIP K′ values were compared to acetaminophen to determine the effect of imprinting on selectivity. The compounds binding capabilities on the MIP were found to be greater than those on the NIP. Table 4-3 summarizes the compound K_D, K, and K′ values. EMI, TENO, NAP, DICLO, IBU and EFV have K′ values of 1.08, 1.0, 1.0, 1.0, 1.06, and 1.05, respectively which are graphically represented in Figure 4-5. In aqueous samples, the selectivity of the MIP and NIP towards ARVs and NSAIDs in the presence of acetaminophen demonstrated that MIP has a slightly better selectivity towards the target compounds than the NIP.

Table 4-3. Template selectivity data in the presence of a competitor.

Templates	**K_d MIP (mg. g^{-1})**	**K_d NIP (mg. g^{-1})**	**K(MIP)**	**K(NIP)**	**K´**
Emtricitabine	1.78	1.65	1.16	1.06	1.08
Tenofovir disoproxil	1.78	1.77	1.44	1.44	1.00
Naproxen	1.77	1.76	1.14	1.14	1.00
Diclofenac	1.79	1.78	1.15	1.14	1.00
Ibuprofen	1.68	1.59	1.09	1.02	1.06
Efavirenz	1.81	1.74	1.17	1.12	1.05
Acetaminophen	1.56	1.55	-	-	-

The results indicated that the MIP also shows significant adsorption efficiencies for five targeted compounds in the presence of a competitor. The order of the K_d values on the selectivity of MIP was EFV> DICLO> TENO > EMI > NAP, IBU than acetaminophen which might imply that the imprinting cavities of the compounds were produced depending on the interplay of shape, size, quantity of hydrogen bonding, and functionality of the template. Some compounds are chosen over others even in multi-template MIPs. Based on these results efavirenz and diclofenac had higher K_d values suggesting a larger distribution and selectivity of these analytes possibly because of the larger molecular weight compared to the other templates. The provided K_d values ranging from approximately 1.68 to 1.81 suggest a low affinity between the target molecule and the MIPs these results are lower than those of Nkosi *et al*. (2022) whose K_d value were ranging between 1.0 to 3.9 for a bulk polymerization of NSAIDs. There common criteria for measuring distribution affinity are 1-10 g mL^{-1} is low affinity and anything above is moderate distribution affinity. These values indicate that the MIPs exhibit a consistent and reasonably slightly strong binding capability towards the target molecule across multiple measurements. While not exceptionally high, these K_d values signify significant and reliable binding interactions, making the MIPs promising candidates for various applications requiring selective binding, such as chemical sensing, separation, and purification processes. Further optimization and characterization may be pursued to enhance the binding affinity and specificity of these MIPs for targeted applications.

4.5 Comparative adsorbent data

Table 4-4 presents a comparative assessment of adsorbents, including sol-gel materials, activated carbon, graphene oxide nanoplatelets, and others, bulk polymerization MIPs stand out as a promising alternative due to their unique molecular recognition capabilities. While sol-gel materials like activated carbon and graphene oxide nanoplatelets exhibit high adsorption capacities, they often suffer from limitations such as limited selectivity and susceptibility to fouling (Ali *et al.*, 2024). For instance, activated carbon, despite its high adsorption capacity, lacks molecular specificity and may be prone to fouling, reducing its efficiency over time. Similarly, graphene oxide nanoplatelets, while offering moderate to high adsorption capacities, pose concerns regarding availability and potential toxicity. In contrast, MIPs offer tailored molecular recognition, allowing for precise binding to specific target molecules. This specificity ensures efficient removal from complex mixtures with minimal interference from other compounds. Moreover, MIPs demonstrate stability and can be regenerated and reused multiple times without significant loss of performance. Despite potential variations in adsorption capacities based on synthesis conditions, the advantages of molecular specificity and recyclability position MIPs as superior alternatives for applications requiring precise molecular recognition. Thus, MIPs offer a promising avenue for advancements in targeted adsorption tasks, overcoming the limitations posed by other materials.

Table 4-4. Comparison of the adsorption capacity and selectivity data found in pharmaceutical pollutants with other sorbents in literature.

Adsorbent	Adsorption capacity (mg. g^{-1})	Selectivity	Reference
Sol gel	28.38	-	(Liu *et al.*, 2018)
Raw zeolite	0.83	-	(Negarestani *et al.*,2023)
Activated carbon	90.9	-	(Farghal *et al.*, 2023)
Biosolid biochar	10.70	-	(Oh & Seo, 2016)
Graphene oxide nanoplatelet	38	-	(Hummadi *et al.*,2022)
Bulk polymerization MIP (NSAIDs)	1.230–1.249	1.12–2.4	(Nkosi *et al.*, 2022)
MIP(ARV)	5.98	4.4	(Qwane *et al.*, 2020)
Chitosan MIP	79.41	-	(Stachowiak et *al.*,2023)
Bulk polymerization MIP (NSAIDs/ARVs)	0.92-3.92	1.68 -1.81	This study

4.6 Application study of MIP in wastewater treatment

This section delves into the application study focusing on the MIP in wastewater treatment within Canadian wastewater facilities. Specifically, this section will explore the quantification of pharmaceutical pollutants present in the treatment plant utilizing the synthesized MIP. This approach highlights the effectiveness of MIP in targeting and removing specific contaminants, shedding light on its potential application in improving wastewater treatment processes and addressing pharmaceutical pollution in water systems.

4.6.1 Effects of sample volume

Sample effects were varied against the synthesized MIP, NIP and commercial SPE sorbent, to study the comparative adsorption of the synthesized material. This was essential due to the anticipated trace concentrations of target pharmaceuticals in environmental water samples, as high sample volumes are correlated with adsorption and pre-concentration parameters as well as the analytical method's sensitivity. The effect of sample volume on recoveries was investigated by extracting 25 mL and 50 mL deionized water samples that were spiked with a 5 mg L^{-1} mixture of the target pharmaceuticals at pH 7. Figure 4-6 shows the results obtained.

The 50 mL sample volume was chosen as the optimum because at 25 mL, the recovery of ibuprofen was found to be slightly lower compared to the 50mL in all the adsorption materials. With recoveries of 95.6 and 97.6 % IBU (MIP) respective to each sample volume. However, no significant changes were observed for the rest of the target compounds throughout the MIP, NIP and SPE sorbent. Recoveries ranging from 92-98.8% were obtained for the 50 mL sample volume (MIP), 87.2-98.8 % (NIP), while for commercial sorbent 95.6-99.9 % sample volume was observed. Choosing a lower sample volume helps with the efficiency of the experiment. It can be concluded that these materials are comparable in their adsorption of these analytes. The experiment was carried out in triplicates for all material time sample.

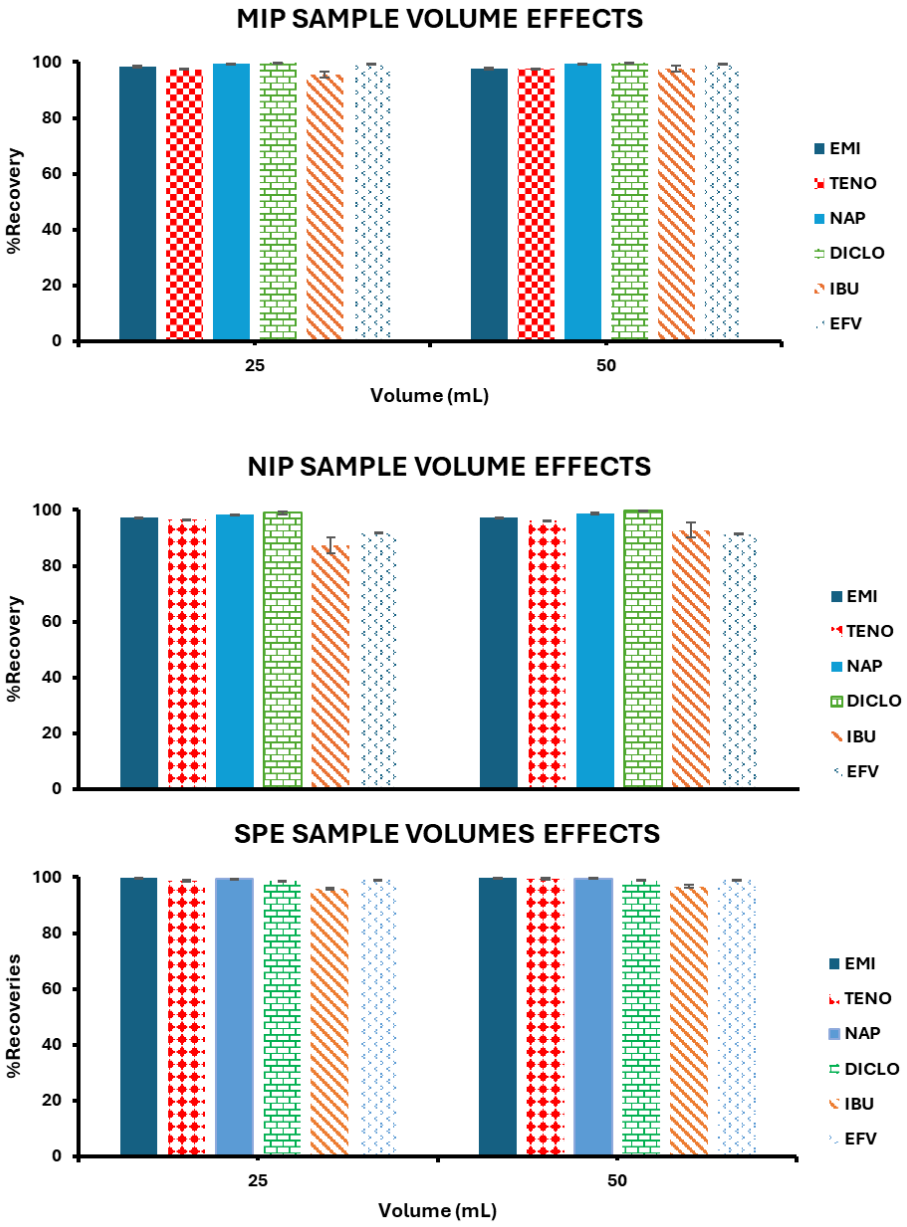


Figure 4-6. The effects of sample volume on percentage recovery.

4.6.2 Effects of elution solvent

The results of the elution solvent studies are shown in Figure 4-7. In this case, the elution solvent that gave high recoveries was investigated using different mixtures of solvents methanol (MeOH), acetonitrile (ACN), 10 % acetic acid in methanol (AA MeOH) and, 10% acetic acid in acetonitrile (AA ACN). The solvent elution study conducted in this research played a critical role in optimizing the recovery efficiency and selectivity of the removal of pharmaceuticals via MIPs and SPE. Furthermore, the solvent elution study provided valuable

insights into the binding affinities between the target pharmaceuticals and the MIPs and SPE sorbent, facilitating method validation and enhancing the reliability of our extraction process. For instance, solvents like MeOH and ACN have different affinities for the imprinted sites based on their dielectric constants and ability to disrupt the polymer matrix. The addition of acetic acid enhances elution by competing with the analyte for binding sites or altering the charge environment. Overall, the results of the solvent elution study have significant implications for improving the efficiency and effectiveness of MIPs and SPE-based extraction methods for pharmaceutical analysis.

The slightly better desorbing capabilities of 10 % AA MeOH for target pharmaceuticals in the adsorbents can be attributed to the ability of acetic acid to disrupt the specific interactions between the target pharmaceutical compounds and the sorbent material breaking of hydrogen bonds and hydrophobic interactions that hold the NSAIDs and ARVs in place on the MIPs or SPE sorbent, leading to a more efficient desorption process. Additionally, the unique chemical properties of acetic acid, such as its polar nature and acidity, may enhance the solubility of the pharmaceutical compounds in the solvent, further aiding in their effective elution from the sorbent material. These factors together contribute to the enhanced desorption performance of 10 % acetic acid in methanol compared to the other solvents tested in the study.

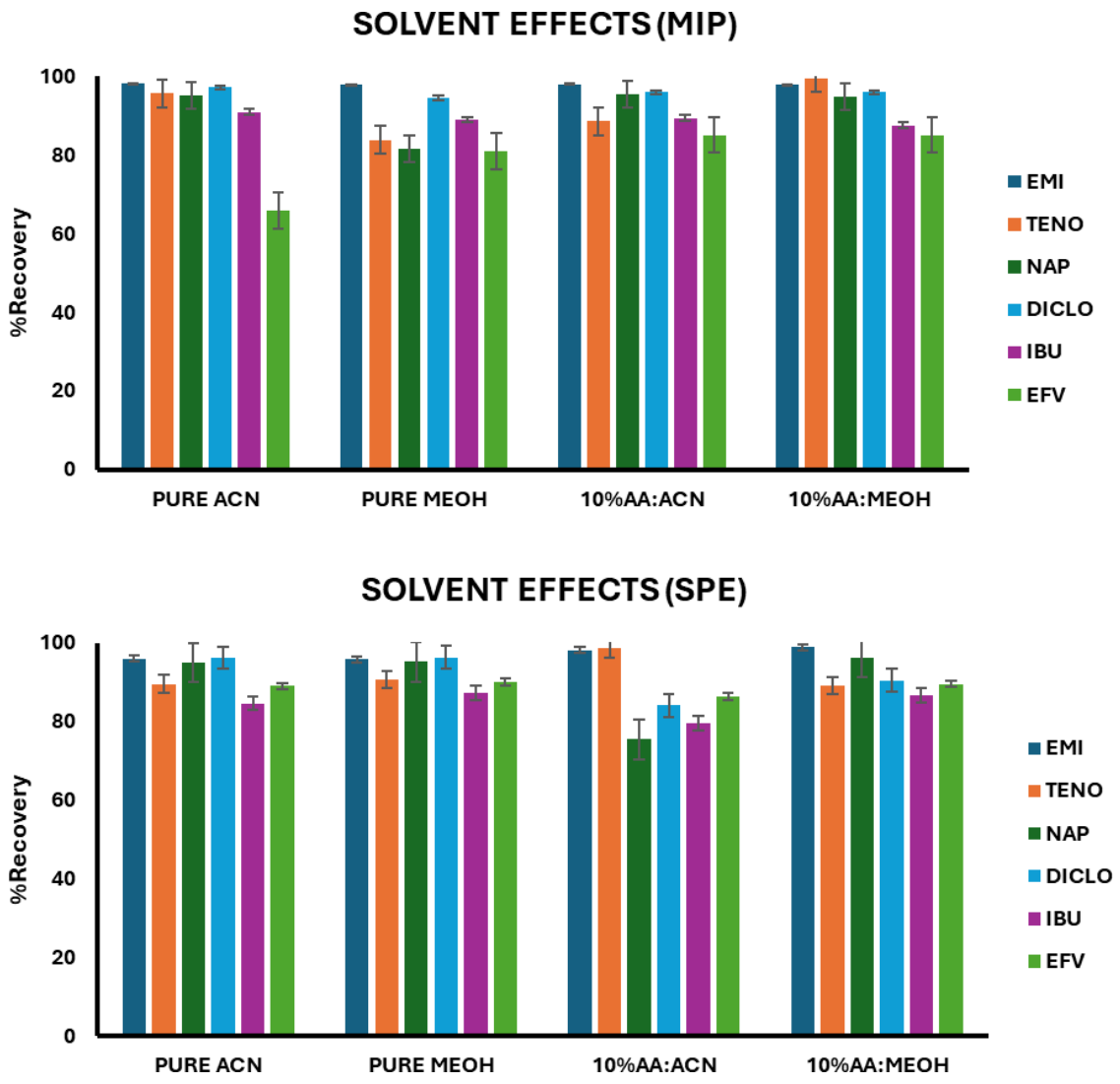


Figure 4-7. The effects of elution solvent

4.6.3 Regeneration studies

The regeneration of MIPs following the adsorption of NSAIDs and ARVs is an important aspect for efficient and sustainable analyses. In this study, the investigation of the regeneration efficiency of MIPs after the adsorption of the target pharmaceutical compounds was reported, focusing on the development of a robust regeneration protocol to ensure the long-term performance and cost-effectiveness of the MIP-based sorbents. Our results demonstrate the good regeneration capabilities of MIPs in selectively capturing NSAIDs and ARVs and their subsequent release under optimized conditions allowing for their reuse in multiple extraction cycles without significant loss of binding capacity or selectivity. The successful regeneration of the MIPs was confirmed through a series of characterization techniques, including adsorption-desorption studies, SEM imaging, and FTIR analysis, which all indicated the retention of the

MIP structure and functionality post-regeneration.

The excellent regeneration efficiency observed in our study can be attributed to several key factors, including the specific imprinting process used to create the MIPs, the choice of template molecules (NSAIDs and ARVs), and the optimization of elution conditions for targeted release of the pharmaceutical compounds. The strong and selective interactions between the MIPs and the template molecules facilitated their complete removal during the regeneration process, ensuring minimal carry over effects and contamination in subsequent extractions.

4.6.4 Quality assurance parameters of the method.

Linearity was assessed by plotting the concentration of each analyte against its corresponding peak area obtained in LC-MS analysis. The instrument's limit of detection (LOD) and limit of quantification (LOQ) were determined using the statistical equation of 3.3 and 10 times the standard error of the y-intercept divided by the slope of the calibration curve. To evaluate the impact of the sample matrix on recovery, deionized water, and post-chlorination water were spiked with a 10 µg L^{-1} concentration of target compounds. The sample was stirred for 15 minutes in separate flats containing MIP and NIP respectively. A separate spiked sample was prepared for SPE. The results, summarized in Table 4-5, indicated that the extraction process increased sensitivity and reduced the LOD to levels expected in environmental samples. Comparable recoveries were observed in deionized water and post-chlorination water. These findings suggest that the developed method was not significantly influenced by the sample matrix present in the real water.

Table 4-5. Quality assurance parameters

	Instrumental parameters		**Deionized water as a sample**		**Post-chlorination water as a sample**		
Compound	**LOD (mg L^{-1})**	**LOQ (mg L^{-1})**	**Linearity (R^2)**	**% Recovery**	**MDL (µg. L^{-1})**	**Linearity (R^2)**	**%Recovery± RSD**
Emtricitabine	0.24	0.75	0.9998	98±0.1	0.33	0.9987	95.9 ± 0.1
Tenofovir Disoproxil	0.23	0.72	0.9999	96±0.2	0.98	0.9996	90.9± 0.3
Naproxen	0.17	0.54	0.9999	98.8±0.3	1.08	0.9980	99.3± 0.3
Diclofenac	0.19	0.59	0.9999	99.8 ±0.4	0.26	0.9984	95.1± 0.1
Ibuprofen	25.95	78.6	0.9990	92.8±2.8	0.38	0.9995	92.2± 0.4
Efavirenz	1.34	4.07	0.9999	98.4± 0.1	0.14	0.9999	95.4± 0.1

4.7 Surface Chemistry of MIP and NIP material

This section delves into the surface chemistry of MIP and NIP materials, focusing on the properties of polymer materials utilized and the various characterizations of different polymer mats. By examining the surface chemistry of these polymer materials and exploring the diverse characterizations available, this study aims to gain a deeper understanding of their structural composition and behaviour in water treatment applications.

4.8 Nuclear magnetic resonance

The solid state ^{13}C CP/MAS NMR spectra for the MIP and NIP are shown in Figure 4-8. The baseline was adjusted, and the relevant peaks were identified between 0-200 ppm spectral regions. There seemed to be no dissimilarities between the chemical shifts and signal intensities of the polymers. This suggested that the polymer materials are chemically the same. Resonances were observed corresponding to the various methyl groups represented by the wide peak at 23 ppm. Other methylene groups were found at 47 and 65 ppm corresponding to the cross-linker agent used, as well as the carbonyl CO_2R group at 175 ppm were observed. Given the kind of polymer synthesis and mechanism of imprinting, which involves a considerable quantity of EGDMA and 2-VP, these results were anticipated.

All signals could be assigned in accordance with the estimated polymer design, and the appropriate peaks matched the results from previous studies (Madikizela & Chimuka, 2016a; Nkosi *et al.,* 2022; Qwane *et al.,* 2020). Nkosi *et al.,* 2022, reported the same chemical shifts as the used the process for the analysis of MIP and NIP of NSAIDs and using the same functional monomer. At the same time, carbonyl clustering in CO_2R is clearly visible at the far end, which is consistent with what is found in literature (Qwane *et al.,* 2020; Nkosi *et al.,* 2022).

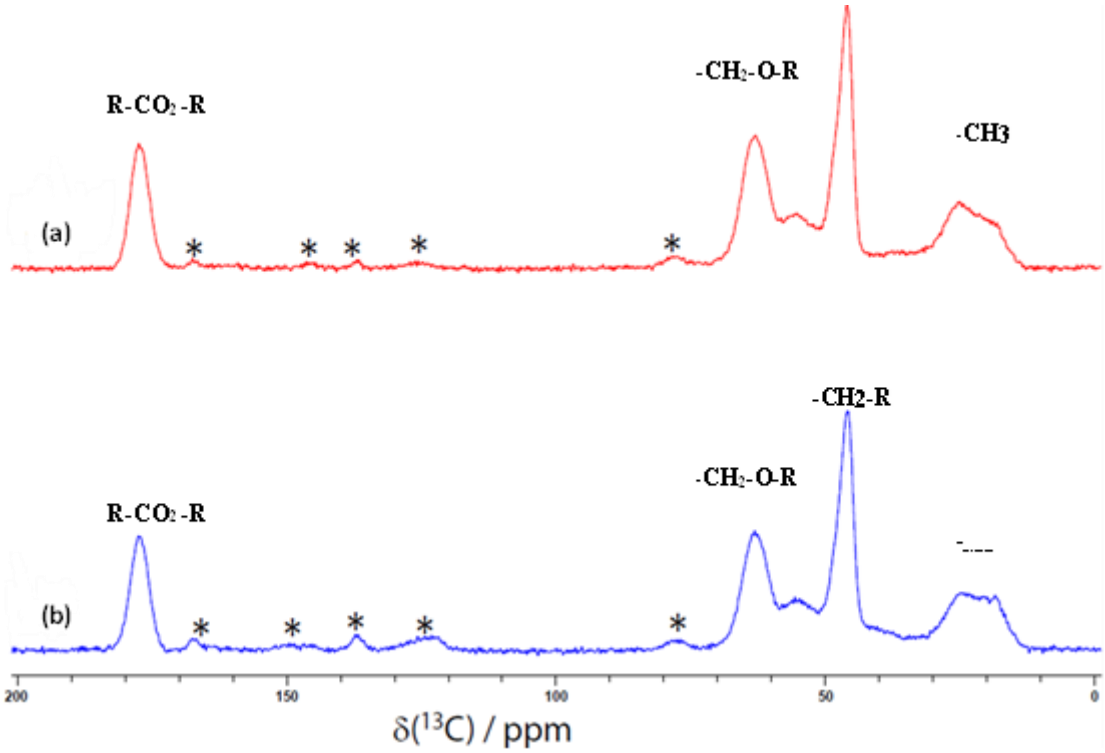


Figure 4-8. Solid-state 13C CP/MAS NMR spectra for (a) the MIP and (b) the NIP. * Denotes solvent peaks.

4.9 FTIR analysis

Figure 4-9 shows FTIR spectra of the synthesized and washed MIP and NIP. It can be observed that the IR spectra of the polymers are very similar in terms of bands, positions and shape, which is consistent with the fact that both polymers were created using the same monomer, cross-linker, and initiator. The interface between templates and monomer provided variable peaks in the spectra, with MIPs exhibiting a wide OH stretching vibration peak at 3500 cm^{-1}, the OH formed a bond that overlaps with that from the NH from the MIP, and this peak slightly smooths out in the NIP. These peaks are associated with the carboxylic group (COOH) of methacrylic acid. Because of the methylene group in 2-VP and EGDMA, the $-CH_2$ stretching peak was also seen at 2900 cm^{-1}. At 1700 cm^{-1}, the carbonyl group C=O stretching peak was seen in both MIP and NIP, which might have arisen from the template and cross-linking molecules. Weak bands from 1600 cm^{-1} to 1200 cm^{-1}, as well as the sharp band at 1100 cm^{-1} in the MIP spectrum indicate the existence of an aromatic ring from the 2-VP. All the notable peaks matched the data from previous studies (Nkosi *et al.*, 2022), where they reported the

same stretching's and presence of these functional groups around the same wavelength.

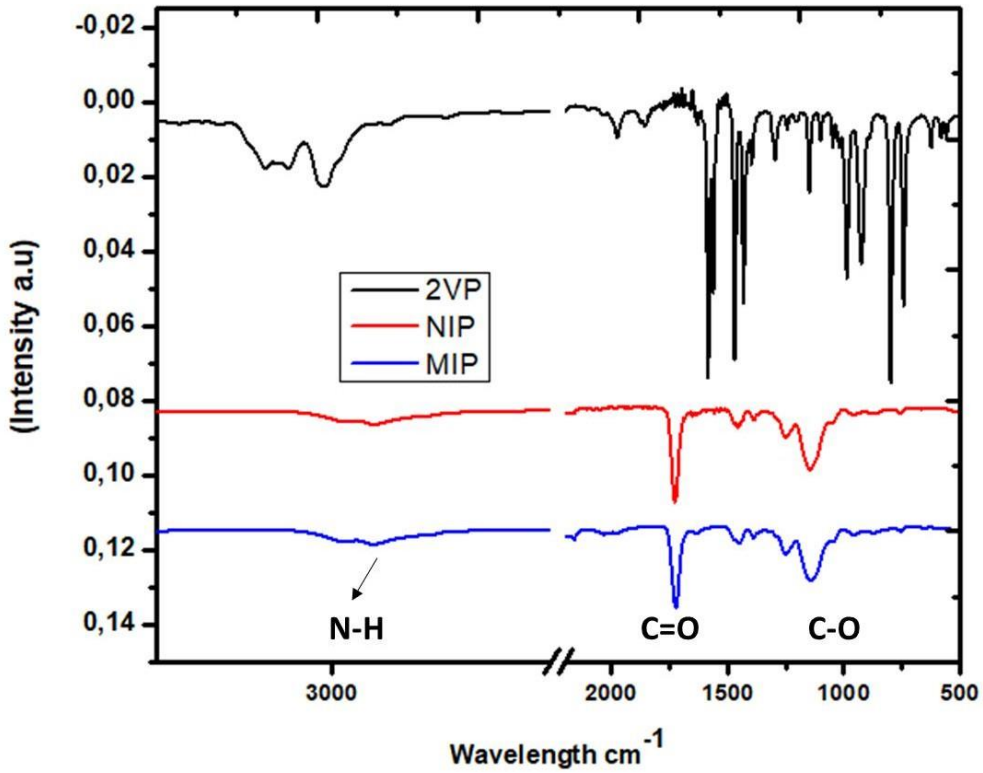


Figure 4-9. FTIR spectrum of the MIP, NIP, and the functional monomer 2-vinylpyridine (2-VP).

4.9 Morphology Analysis

4.9.1 SEM

The surface morphology and particle size of both the MIP and NIP were examined using SEM, as shown in Figure 4-10. The surface of the control polymer (NIP) was found to be smoother than that of the MIP as it did not have the target templated to form the desired cavities. Smaller pores are observed in the NIP images, due to the polymerization process that can create minor defects that are non-binding specific to create this porosity. Other factors such as the solvent and crosslinking effect density and can contribute to the porosity of the NIP as when these solvents are being evaporated, they might leave a void. The MIP, on the other hand, had a rough surface once the templates were removed. These rough surfaces can be attributed to the formation of cavities during the synthesis process and washing out of the template process; when these templates are removed, they form there desired specific binding pores (cavities) (Liu *et al.*, 2023; Zidarič *et al.*, 2023). A prior study found that the roughness of MIP particles

might result in a higher surface area than the control polymer (Sikiti *et al.*, 2014). As a result, the MIP outperforms the control polymer in adsorbing analytes of interest.

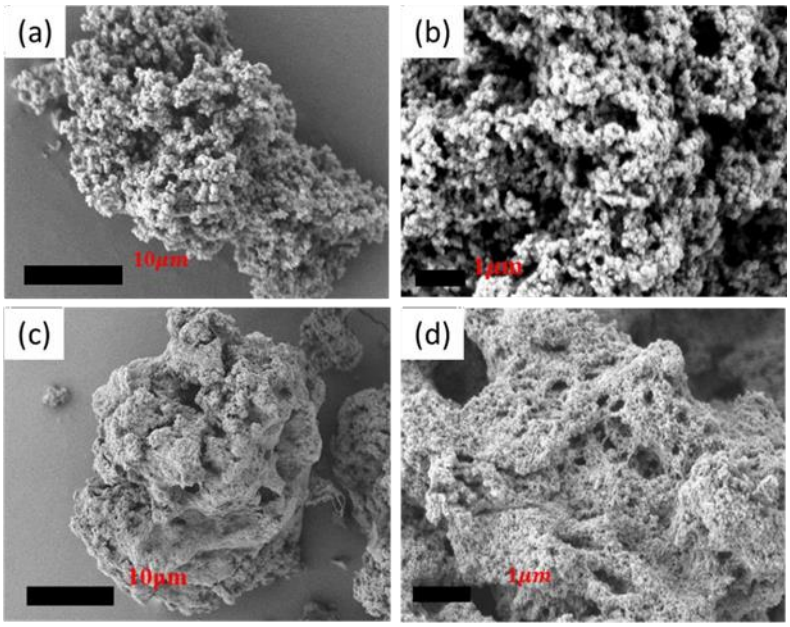


Figure 4-10.SEM surface morphologies: (a) NIP SEM image, (b) at high magnification of NIP (c) MIP SEM with expanded view in (d).at high magnification of MIP.

4.9.2 Brunauer, Emmett, and Teller (BET) Analysis

BET was used to study the surface area, surface volume and porosity of the MIP and NIP as tabulated in Table 4-6. The surface area of polymers has a considerable impact on compound adsorption. According to the BET data shown in Table 4-6, the MIP had a higher surface area, pore volume (425 m^2g^{-1}) and total area in pore (258 m^2g^{-1}) than the NIP with 347 and 201 m^2g^{-1} of surface area and total area in pore, respectively. This is consistent with the desired imprinting. With the NIP these areas are smaller because there were no target templates for specific binding; however, smaller cavities or voids are formed possibly by solvent evaporation or cross-linking density as mentioned earlier. The same pattern has been observed in a previous study of NSAID adsorption on similar polymers by Madikizela *et al.* (2016). It was reported that the synthesized MIP and NIP surface area were 282 and 232 m^2g^{-1}, respectively. Qwane *et al.* (2020) reported surface area results with the ARV drug abacavir imprinted MIP and its NIP analogue of 372 m^2g^{-1} for both the polymer materials. However, the surface area and total pore volume values are significantly larger in this study. Due to more target compounds are used in this study that are of different classes, therefore a larger surface area is required to

accommodate the six-target compared to the three-target and single-target they were investigating in their studies. Polymers with larger surface areas are more effective in adsorbing water pollutants. There are more binding sites that are scattered in the cavity, suggesting that there is greater imprinting impact for the MIP compared to the NIP. Also, looking at the total pore areas of the polymers, the MIP has a larger pore size area suggesting that there are more cavity imprints in the MIP as opposed to the NIP.

Table 4-6 BET polymer analysis.

Polymer	Surface area (m^2g^{-1})	Total pore volume (cm^3/g)	Average pore diameter (Å)	Total area in pores (m^2g^{-1})	Average particle size (nm)
MIP	425	0.345	44.2	258	14.1
NIP	347	0.393	45.3	201	17.3

4.9.3 Thermal Properties

Figure 4-11 shows the TGA curves of synthesized MIP and NIP. The TGA was performed to study the thermal stability, uniformity and binding affinity effects of the polymer materials in case that they are subjected to high temperature. The analysis was run over a 0 - 500°C temperature range. Two disintegration peaks are observed at slightly different temperatures for both the MIP and NIP suggesting the collapse of the material in both points. The initial backbone decomposition of both these polymers is observed at 275°C and 278°C respectively, as seen in Figure (4-11a & b), the backbone of both the washed MIP and NIP disintegrated, resulting in a considerable weight loss of nearly 90%. A similar polymer backbone collapse was observed at comparable temperatures of 280°C in a study by (Nkos*i et al.*, 2022) when they synthesized the polymers under the same circumstances utilizing the bulk polymerization process. The difference between the curves produced for washed NIP and washed MIP is that the MIP has a second decomposition peak between 371- 444°C that is below 15 mass % (compared to the same peak in the NIP that is over 30%). The discrepancy might be due to structural differences imposed during the template removal process of the MIP; there might be residual template molecules or template-related impurities in the MIP. These remaining molecules may interact with the polymer, affecting its thermal stability and resulting in the observed disintegration phases. During the imprinting process, the binding of template molecules to functional monomers may result in chemical bonds or interactions that affect the thermal stability of the polymer. These interactions might be missing from the NIP. It's possible

that the molecular imprinting process introduces structural heterogeneity within the MIP, leading to varying decomposition performances for different portions of the polymer. Thermal breakdown for both polymers is observed at 445°C. These findings are consistent with those found in the literature (Kasonga *et al.*, 2021; Sigonya *et al.*, 2023). As a result, the thermal stability of these polymers was regarded adequate because their applications are done at ambient temperature and revealed the slight irregularities of both the materials but showed uniformity in the synthesis process of these materials.

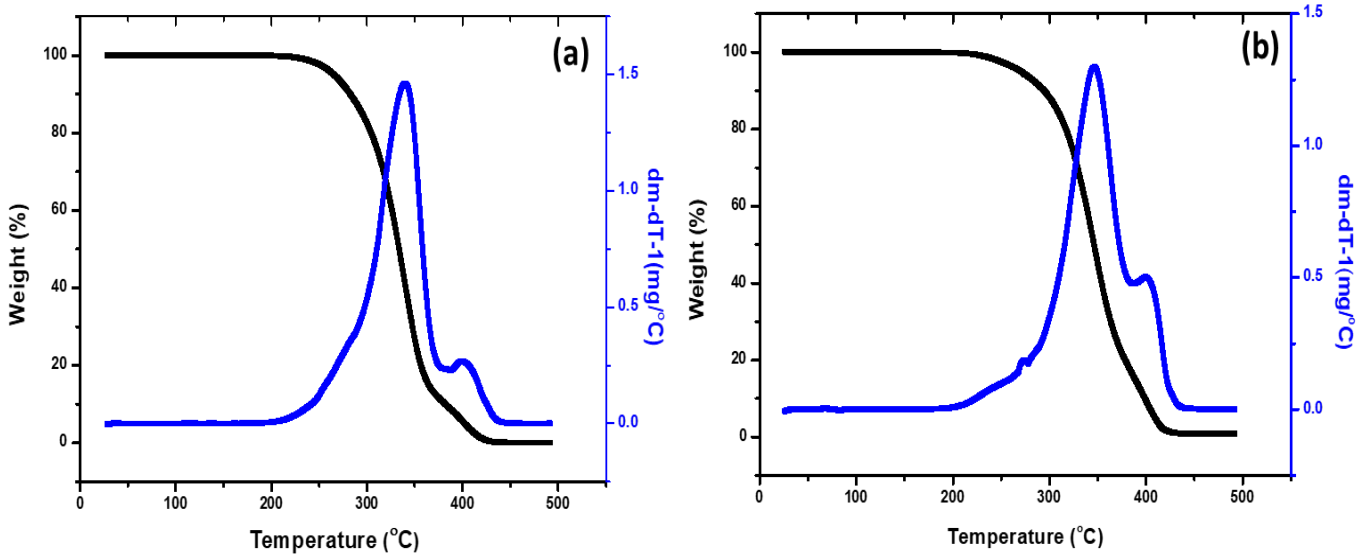


Figure 4-11. Thermal decomposition of (a) MIP and (b) NIP by TGA.

4.10 Environmental monitoring of target compounds

This section discusses the performance of each adsorption material used to the quantification of these pharmaceutical pollutants within the Robert O. Pickard Environmental Centre in Ottawa, Canada (N45°27’50.347’’, W75°35’33.853). The sites include influent, primary and secondary effluent and post-chlorination.

4.10.1 Pollutants in the wastewater treatment plant MIP

The concentrations of pharmaceutical compounds in wastewater samples collected from different treatment stages, including influent, primary effluent, secondary effluent, and post-chlorination, with a focus on MIPs as the adsorbent material as seen in Table 4-7. The results revealed varying concentrations of pharmaceuticals across different treatment stages and sites. In the influent, high concentrations of EMI (260 µg/L) and IBU (1034 µg/L) were observed, indicating significant input of these pharmaceuticals into the treatment plant high

concentrations are seen because this is untreated water. Interestingly, while TENO and DICLO were also present in notable amounts in the influent, NAP concentrations were below the detection limit (ND). During the primary effluent stage, concentrations of most pharmaceuticals increased, suggesting incomplete removal during initial treatment processes as well as an accumulation of these pollutants. However, the secondary effluent exhibited reduced concentrations of EMI, TENO, and IBU compared to the primary effluent, indicating some level of removal efficacy. Notably, NAP concentrations remained below the detection limit throughout the treatment stages. Furthermore, post-chlorination treatment resulted in further reductions in pharmaceutical concentrations, particularly for DICLO and EFV. Comparing the concentrations of pharmaceuticals across different treatment stages and sites highlights the effectiveness of the treatment processes in reducing pharmaceutical contamination. However, the persistence of certain compounds, such as EMI and IBU, underscores the need for enhanced treatment strategies, potentially involving advanced oxidation processes or additional adsorption techniques using MIPs.

Table 4-7. Real water sample site concentrations

Material	**Site**	**Compounds (µg. L^{-1})**					
		EMI	**TENO**	**NAP**	**DICLO**	**IBU**	**EFV**
MIP	Influent	260±0.03	49±0.02	ND	158±0.03	1034±0.30	14
	Primary effluent	316±0.02	54±0.02	288±0.17	104±0.04	88±0.29	32±0.02
	Secondary effluent	186	28±0.05	206	175±0.02	ND	32±0.06
	Post-chlorination	207±0.08	44±0.02	390±0.11	140±0.01	ND	8
NIP	Influent	208±0.03	15±0.01	ND	57	982	59±0.01
	Primary effluent	246	30±0.01	69±0.03	74	ND	86±0.04
	Secondary effluent	76	18±0.03	ND	155	206	46±0.01
	Post-chlorination	192	5±0.02	45	ND	424±0.12	22
	Influent	90±0.01	395	ND	286	988	46

	Primary effluent	917	567±0.68	580±0.03	ND	ND	49±0.01
SPE	Secondary effluent	55	392±0.22	450±0.02	ND	ND	47±0.06
	Post-chlorination	58±0.01	521±0.03	450±0.01	ND	ND	44±0.01

***ND= Not detected**

Comparable studies conducted in other countries have reported similar trends in pharmaceutical contamination levels. For instance, a study by de Oliveira *et al.*, (2022) in Brazil found concentrations of estradiol: 372.7 mg g^{-1} and ethinylestradiol: 291.4 mg g^{-1} compared to non-imprinted, which also achieved good results (estradiol: 315.5 mg g^{-1} and ethinylestradiol: 259.9 mg. g^{-1}). These in influent samples are consistent with our findings. Similarly, a study by Martinez-Sena *et al.*, (2016) in Spain reported concentrations of naproxen, ibuprofen and diclofenac respectively in 3 different sewage sites with of 0.031, 0.096,35µg L^{-1} naproxen, 0.05, 0.38, 150 µg L^{-1} ibuprofen, and 0.274, 0.047, 0.07 µg L^{-1} in influent samples, which are lower than those observed in this study. These cross-country comparisons emphasize the global prevalence of pharmaceutical contamination in wastewater and highlight the significance of targeted remediation strategies using MIPs. Additionally, our findings contribute to the collective understanding of pharmaceutical contamination dynamics in wastewater treatment plants and emphasize the potential of MIP-based approaches in mitigating this environmental challenge.

4.10.2 Pollutants in wastewater treatment plant commercial SPE sorbent

This study examined the concentrations of pharmaceutical compounds in wastewater samples collected from various treatment stages, focusing on the adsorption performance of SPE. Our findings revealed distinct concentrations of pharmaceuticals across different treatment stages and sites. Notably, in the influent samples, SPE exhibited lower adsorption capacities compared to MIP and NIP reported in previous analyses, indicating a reduced ability to selectively capture target compounds. Despite the relatively high concentrations of EMI and IBU in the influent (90 µg L^{-1} and 988 µg L^{-1}, respectively), the adsorption capacities of SPE remained comparatively lower. Furthermore, while significant reductions in pharmaceutical concentrations were observed in the primary effluent and subsequent treatment stages, the adsorption capacities of SPE remained consistently lower than those of MIPs and NIPs. This

discrepancy may be attributed to the inherent chemistry of SPE materials, which may lack the specific binding sites characteristic of MIPs or the affinity for certain compounds observed in MIPs. Additionally, the dynamic interactions between the analytes and SPE sorbents may differ from those in MIPs and NIPs, leading to lower adsorption efficiencies particularly notable in influent samples. For instance, in the influent samples, MIPs exhibited remarkable adsorption capacities of 260 μg L^{-1} for EMI, 49 μg L^{-1} for TENO, and 1034 μg L^{-1} for IBU as seen in Table 4-7. These values are than those of NIPs, which showed concentrations of 208 μg L^{-1}, 15 μg L^{-1}, and 982 μg L^{-1} for EMI, TENO, and IBU, respectively.

Furthermore, post-chlorination treatment appeared to strengthen the removal efficiency of MIPs, particularly evident for compounds like DICLO and IBU. For example, Liu and Dai (2018) reported adsorption capacities of 215 μg L^{-1} for EMI and 47 μg L^{-1} for TENO using MIP-based approaches, while Sun *et al*. (2019) achieved adsorption capacities of 180 μg L^{-1} for NAP and 150 μg L^{-1} for DICLO. Furthermore, our results are in line with Gao *et al*. (2020), who demonstrated the effectiveness of MIPs in selectively extracting EFV from water samples, with a reported adsorption capacity of 12.3 μg L^{-1}, corroborating our findings of elevated adsorption capacities for EFV by MIPs compared to NIPs. However, the observed variability in removal efficiencies for certain compounds, such as NAP and DICLO, highlights the need for further optimization of polymer properties or supplementary treatment strategies, as also indicated by (Schaffert & Wagner, 2008).

It's notable that certain drugs were not detected (ND) at various treatment stages despite their presence in the influent. This inconsistency suggests differential removal efficiencies for different compounds during the treatment process. This occurrence could be attributed to several factors, including the physicochemical properties of the compounds, their interactions with treatment processes, and the efficiency of the adsorption materials used. NAP and DICLO may have undergone degradation or transformation into by-products during treatment, resulting in their reduced concentrations or complete removal. Additionally, variations in compound solubility, volatility, and hydrophobicity can influence their behaviour during wastewater treatment, affecting their detection at different treatment stages. Understanding the mechanisms underlying the removal of pharmaceutical compounds and the factors influencing their fate within wastewater treatment plants is crucial for optimizing treatment processes and minimizing the release of potentially harmful contaminants into the environment.

The results reaffirm the better performance of MIPs over NIPs and SPE in selectively

removing pharmaceutical contaminants from real water samples, aligning with existing literature and emphasizing their potential in improving water quality during treatment processes.

4.11 Removal efficiencies from wastewater treatment plants

This section discusses briefly the removal efficiency of this wastewater treatment plant and draws a conclusion on the various methods of analysis used.

Table 4-8: Percent removal efficiencies for wastewater treatment plant

Compounds	Emtricitabine	Tenofovir	Naproxen	Diclofenac	Ibuprofen	Efavirenz
Removal efficiency	20	42	+35	11	100	42.8

+ shows accumulation

The removal efficiencies of the pharmaceutical pollutants in wastewater were varied using the MIP as an adsorbent. Table 4-8 shows the co-responding removal percentages of each pollutant respectively. Ibuprofen and efavirenz had high removal efficiencies of 100% and 42.8%, respectively. The chemical structures, pKa values, and logP values of the compounds were examined to understand the reasons behind these differences.

The high removal efficiency of ibuprofen from wastewater is attributed to its non-polar chemical structure, indicated by a logP value of approximately 3.5, which facilitates its partitioning into non-polar environments. Additionally, ibuprofen's low pKa value of around 4.4 means it largely exists in a non-ionized form, making it more amenable to removal through traditional wastewater treatment processes. Previous studies confirm that non-polar compounds with high logP values are effectively removed via physical-chemical treatment methods (Kosma *et al*., 2019; Papageorgiou *et al*., 2016). In contrast, efavirenz, with a logP value of about 4, exhibits a more hydrophobic nature and a higher pKa value of around 10.2, suggesting it is predominantly ionized and thus more resistant to removal by conventional methods. The lower removal efficiency of efavirenz aligns with findings indicating that hydrophobic compounds with high logP values also face challenges during wastewater treatment (Zhu *et al*., 2015).

Compounds such as emtricitabine, tenofovir, naproxen, and diclofenac demonstrate even lower removal efficiencies due to their distinct chemical structures and pKa values. Emtricitabine and tenofovir are highly polar, with logP values around -0.6 and 1.6, which indicates a tendency to

partition into water. Their relatively low pKa values (around 2-3) suggest they are mainly in non-ionized form, yet this alone may not suffice for effective removal during treatment. Naproxen and diclofenac, which possess acidic functional groups with pKa values of around 4.0 and 4.1, respectively, may also demonstrate reduced adsorption during treatment (Lee *et al*., 2019; Wang & Chen, 2016).

These observations highlight the limitations of traditional wastewater treatment processes, which primarily rely on physical-chemical methods such as sedimentation, filtration, and disinfection. These methods often struggle with the stable and hydrophobic nature of pharmaceuticals, emphasizing the need for alternative treatment technologies capable of effectively removing such persistent organic compounds from wastewater

4.12 Characterization of electrospun MIP composite material in terms of morphology, surface area and adsorption

4.12.1 Properties of polymer solutions

It is important to consider parameters, such as conductivity, viscosity, solvent, and temperature when electrospinning polymer solutions with a mixture of MIPs. These parameters play a significant role in the electrospinning process as they can affect the fiber formation, morphology, and properties of the final product (Wang *et al.*, 2012). Conductivity influences the electrostatic interactions during electrospinning, while viscosity determines the solution's ability to form stable fibers (Theron *et al.*, 2004). Temperature can impact the solution's rheological properties and the electrospinning process. Therefore, by understanding and optimizing these parameters, this can help enhance the electrospinning process and tailor the properties of the polymer-MIP fibers for specific applications.

Table 4-9 presents various parameters of polymer solutions, including the type of polymer, polymer mass, solvent used, solvent volume, conductivity, and viscosity. When analyzing the data, several trends can be observed across different types of polymers and their corresponding MIP and NIP forms. The viscosity measurements were taken at a standardized shear rate of 40 1/s for each sample. Analysis of the data reveals intriguing trends and variations among the different polymer-solvent systems. Firstly, looking at the conductivity values, it is evident that the conductivity of the solutions differs significantly based on the type of polymer and solvent used. For instance, PET solutions in TFA exhibit higher conductivity compared to those in TFA &DCM. This difference can be attributed to the nature of the solvents and their ability to

dissociate ions, leading to variations in conductivity levels.

TFA has a higher capability of dissociating ions, leading to increased conductivity in the solution as seen in Table 4-9. On the other hand, the viscosity is lower for the TFA & DCM mixture (3.9) compared to TFA alone (12.7). This suggests that the addition of DCM has reduced the viscosity of the solution, which is consistent with DCM being a less viscous solvent compared to TFA. DCM is a less polar solvent that does not readily dissociate into ions compared to TFA, which can lead to changes in the ionic mobility and charges present in the solution, ultimately affecting conductivity (Wang *et al*., 2021).

Additionally, DCM has different molecular interactions and solvation properties compared to TFA, which can influence the viscosity of the solution. The weak intermolecular forces in DCM allow the molecules to flow more easily past each other, reducing the resistance to flow and thereby lowering the viscosity of the solution. On the other hand, TFA is a polar solvent with stronger intermolecular forces due to the presence of polar functional groups. These stronger intermolecular interactions result in higher viscosity compared to non-polar solvents like DCM. The stronger intermolecular forces in TFA cause the molecules to have more difficulty sliding past each other, leading to increased resistance to flow and higher viscosity in the solution.

Secondly, the viscosity of the solutions also varied depending on the polymer and solvent combination used. In general, higher viscosity values are observed in PVA DH solutions compared to PET solutions. This difference could be due to the molecular structure of the polymers, where PVA tends to form more entangled chains, leading to increased viscosity. However, in our results there was no effect of temperature as the assessment was conducted at room temperature. Additionally, when comparing the MIP and NIP forms of the polymers, it is interesting to note that MIPs generally exhibit higher conductivity and viscosity values compared to their NIP counterparts. This can happen because of the molecular imprints in the polymer matrix, which alter the interaction of the polymer with the solvent, leading to changes in conductivity and viscosity. These interactions can influence the arrangement of polymer chains and solvent molecules, affecting the mobility of ions or charge carriers within the solution. Furthermore, the molecular imprints can create additional cross-linking points within the polymer matrix, resulting in a more rigid structure compared to NIPs. This increased rigidity can affect the flow properties of the solution, leading to higher viscosity values in MIP solutions. Additionally, the presence of molecular imprints can influence the overall structure and porosity of the polymer matrix, which can affect the solvation properties of the solvent

within the MIP. This alteration in the solvation environment can impact the flow behaviour and viscosity of the solution (Ardekani *et al.*, 2020).

Higher conductivity in polymer solutions improves electrospinnability by enhancing charge transfer and promoting the formation of a stable jet during electrospinning (Nayak *et al.*, 2013), as demonstrated through SEM images of PVA in both degrees using ethanol as a solvent. The fiber appears smoother, more elongated, and exhibits minimal to no bead formation (Figure 4-12). Conductive solutions tend to promote the formation of finer fibres with reduced bead formation (Deshawar *et al.*, 2020), leading to a more uniform fibre morphology. Therefore, polymer solutions with high conductivity, such as those observed in PET solutions in TFA, PET MIP in TFA, and PET NIP in TFA, are showing electrospun fibres with better quality and uniformity.

On the other hand, varying viscosity levels in the polymer solutions can also influence the electrospinning process and the resultant fibre morphology. Higher viscosity solutions exhibit increased resistance to jet elongation and may sometimes lead to the formation of thicker fibres with reduced alignment and uniformity. In contrast, lower viscosity solutions tend to facilitate the formation of finer fibres with improved alignment and reduced defects. PVA solutions have a higher viscosity compared to PET solutions. This difference in viscosity may affect the spinning process during electrospinning, leading to the formation of different morphologies. The higher viscosity of PVA solutions can result in smoother, more elongated fibers with less bead formation compared to fibers produced from PET solutions.

Table 4-9. Parameters of polymer solutions

Sample No.	Polymer	Polymer ratio (%)	Solvent	Solvent Volume (ml)	Conductivity (µS/cm)	Viscosity (mPa.s)
1.	PET	100	TFA	40	33.6	12.7
2.		100	TFA & DCM	30:10	11.64	3.9
3.	PVA DH (87-90%)	100	H_2O	40	1054	165.5
4.		100	H_2O & ethanol	30:10	987	229.6
5.	PET MIP	98.6/1.4	TFA	40	70.5	35.2
6.		98.6/1.4	TFA & DCM	30:10	24.35	-2.7
7.	PVA DH	98.6/1.4	H_2O	40	1190	154.9

8.	(87-90%) MIP	98.6/1.4	H_2O & ethanol	30:10	465	307.2
9.	PET NIP	98.6/1.4	TFA	40	72.9	18.3
10.		98.6/1.4	TFA & DCM	30:10	13.46	-0.7
11.	PVA DH (87-90%) NIP	98.6/1.4	H_2O	40	1082	167
12.		98.6/1.4	H_2O & ethanol	30:10	550	167.5

4.12.2 Viscosity vs shear rate polymer solution behaviour

Understanding the shear rate versus viscosity relationship of polymer solutions is important as it helps us understand the behaviour of the polymer solutions. The viscosity of a polymer solution varies with shear rate, a phenomenon known as shear-thinning behaviour. This behaviour influences the flow properties of polymer solutions in processing operations such as extrusion, spinning, and coating (Zhang *et al.*, 2022). By characterizing the rheological behaviour of polymer solutions, optimization formulation, processing parameters, and application properties, leading to the development of advanced materials with enhanced performance and efficiency can be achieved.

Therefore, a viscosity vs. shear rate graph was drawn to see the different behaviours of these solutions in different solvents and when an additive such as MIP and NIP is added to the polymer solution as shown in appendix 1-3. Several observations were made that shed light on the rheological behaviour of the polymer solutions studied. All solvents and polymer solutions without molecularly imprinted polymer and non-imprinted polymer additives exhibited Newtonian behaviour, suggesting a linear relationship between shear rate and viscosity. However, a notable exception was observed in the case of PVA 99 DH (Polyvinyl Alcohol 99 % degree of hydrolysis) solution, which displayed shear-thinning behaviour. This can be attributed to the unique structural properties of the PVA 99 DH polymer chains. PVA is known for its excellent film-forming and adhesive properties, as well as its ability to create strong hydrogen bonds with water molecules (Zulkiflee and Fauzi 2021). In this case of PVA with a high degree of hydrolysis (99%), PVA molecules have a linear structure with hydroxyl (-OH) groups along the backbone (Zhang *et al.,* 2022). At high shear rates, the polymer chains align in the direction of flow, causing the hydroxyl groups to interact with each other and form temporary hydrogen bonds, which reduces the resistance to flow.

This alignment and disruption of hydrogen bonds result in a decrease in viscosity as the shear rate increases. Moreover, in high-hydrolysis PVA solutions, the presence of a high number of hydroxyl groups along the polymer chain enhances the formation of hydrogen bonding between chains, leading to increased intermolecular interactions and higher viscosity at low shear rates. Opposite observations were made by (Vieira *et al.*, 2023). They noticed that at low viscosity there is high mobility. This was ascribed to their material, i.e. carboxymethyl cellulose (CMC) blended with PVA, and chemical crosslinking. This is a result of large number of hydrogen bonds and other weak interactions formed within the hybrid hydrogel network.

The increased hydrophilicity of the PVA 99 DH polymer chains leads to enhanced interactions with the surrounding solvent molecules, particularly water in this case. These interactions result in the formation of hydrogen bonds between the polymer chains and the solvent molecules, creating a network structure within the solution. Under low shear rates, this network structure remains stable, resulting in a higher apparent viscosity as seen in Table 4-9 at shear rate of 40, due to the resistance to flow offered by the entangled polymer chains and the hydrogen bonding network. However, as the shear rate increases in the system, the applied force causes the polymer chains to align and orient themselves along the direction of flow.

This reorientation of the polymer chains under shear stress disrupts the hydrogen bonds and weakens the physical entanglements within the solutions network, leading to a decrease in viscosity. The shear- thinning behaviour observed in the PVA 99 DH solution is a result of this structural rearrangement of the polymer chains in response to shear forces. Furthermore, the high degree of hydrolysis in PVA 99 DH may also contribute to an increased flexibility of the polymer chains, allowing for easier deformation and alignment under shear stress. This higher chain mobility facilitates the reduction in viscosity with increasing shear rate, as the polymer chains can flow more readily in response to the applied force. Similar shear thinning behaviour of PVA at 99 % DH was observed in a study by Reena *et al.* (2020) where they observed lower viscosity of the PVA: RF gel system that were attributed to a decrease in the semi-crystalline property of PVA due to the presence of salt and the alignment of chain segments of all the samples in the direction of applied stress.

The introduction of MIP and NIP additives into the polymer solutions had no significant impact on their rheological properties. Despite the majority of the MIP and NIP solutions maintaining Newtonian behaviour, the PVA 99 MIP and NIP solutions in both water and water-ethanol mixtures exhibited shear-thinning behaviour. This deviation from the expected rheological

response could be linked to the inherent complexity of the polymer-solvent matrix, as well as the presence of specific binding sites created by the molecular imprinting process. The resulting changes in intermolecular interactions and crosslinking densities within the polymer structure may have led to altered flow behaviour under shear stress.

Another factor that could have influenced the shear-thinning behaviour observed in the PVA 99 DH solution is the overall viscosity of the system. It is well established that shear-thinning behaviour is more commonly observed in thick or highly viscous solutions, where the rearrangement of polymer chains under shear stress results in decreased viscosity. In the case of the PVA 99 DH solution, the higher viscosity compared to other polymer solutions may have contributed to the observed shear-thinning behaviour. The polymer chains may have experienced more resistance to flow and exhibited a more pronounced response to changes in shear rate (Mongruel and Cloitre, 1999).

Bounoua *et al.,* (2016) observed similar behaviour to the rheological properties described in the study of polymer solutions with various solvents particularly the shear-thinning behaviour observed in the PVA 99 DH solution. They attributed it to the alignment and deformation of polymer chains under shear stress, leading to a decrease in viscosity. They also discussed how the interaction between polymer chains and solvent molecules can affect the rheological properties of the solution stating that for a given viscosity, suspensions in non-polar solvents there is much less shear thinning than suspensions in polar solvents. They also noted that shear thinning decreases when the viscosity of the suspending fluid increases. supporting the observations made in the study of polymer solutions with various solvents.

4.12.3 Effects of Voltage

The optimization of applied voltage in the electrospinning process plays an important role in controlling the formation and properties of nanofibers. By carefully adjusting the voltage, the morphology, diameter, alignment, and uniformity of the nanofibers produced can be influenced. In this experiment, the behaviour of polyvinyl alcohol (PVA) and polyethylene terephthalate (PET) nanofibers was studied at a constant flow rate, and tip-to-collector distance to investigate the impact of applied voltage on the electrospinning process. For the purpose of voltage effects both polymer solutions images will represent each voltage stage for the purpose of this discussion.

Experimental tests were conducted with a range of applied voltages spanning from 10 kV to 18

kV. The outcomes of these experiments are depicted in (Figure 4-12 a, b & c). The data revealed that the average diameter of fibers increased slowly as the voltage increased. At voltage 10 kV for PET/TFA solution a large number of beads with thin fibers were formed (Figure 4-12a & d). These fibers had a diameter of ~45 nm. This occurs because as the electric field strength is increased, the repulsive forces between the charges on the droplet surface also increase, which leads to a greater stretching force on the droplet, causing the fibers to become thinner. However, when voltage was increased to 15 kV, there was a significant proportion of fibers with diameters below 150 nm indicating the production of thicker fibers with less beads (Figure 4-12b & e). The electric field strength is directly proportional to the voltage applied. When increasing voltage, the electric field strength increases which leads to thinner fibers.

At the 18 kV of both PET and PVA polymers, the distribution of fiber diameters broadened, leading to the formation of thicker fibers. The observed results from the frequency distribution data and PET/ TFA showed varying patterns across different fiber diameter ranges exhibiting a more even distribution across the 75-200 nm range, (Figure 4-12c). Similar results were attained for PVA under the same experimental conditions (Figure Appendix 1- 4). A study by Faizal *et al.* (2020) showed similar behaviour when they varied voltage between 12 kV and 18 kV at 0.2 ml/hour. The fiber diameter was 36.90 ± 7.00 µm and the fibers had various size diameter of both thin and thick fibers with the use of a higher voltage as in this study.

The difference in polymers solutions led to distinct fiber diameter profiles, possibly due to variations in polymer chain length and cross-linking density because of differences in the length of the polymer chains and how tightly they are connected.in each polymer. For instance, PET/TFA with a low molecular weight ranging between 8000-31000 kDA showed a distribution skewed towards the larger fiber diameter ranges, with the 150-175 nm range having the highest frequency at higher voltage. Specifically, it was observed that a substantial proportion of thin fibers with diameters below 150 nm were evident when the applied voltage surpassed 15 kV. An increase in the applied voltage, corresponding to an increase in the electric field intensity, led to a heightened electrostatic repulsive force acting on the fluid jet, thereby promoting the formation of thicker smooth fibers (Larrondo & Manley, 1981).

Conversely, the expedited ejection of the jet from the Taylor cone results in a swifter removal of the solution from the capillary tip, consequently leading to an enlargement of the fiber diameter. Similarly, the use of PET with TFA as the solvent resulted in larger fiber diameters compared to the PVA materials, which may be attributed to differences in molecular weight,

structure and intermolecular interactions. In the case of PET, its molecular structure consists of repeating units of terephthalic acid and ethylene glycol, resulting in a linear polymer chain. This linear structure allows for stronger intermolecular interactions, such as Van der Waals forces, hydrogen bonding, and dipole-dipole interactions between adjacent polymer chains. These interactions give PET its high tensile strength and resistance to deformation (Grant, 2011). On the other hand, PVA has a more a larger but flexible molecular weight ranging between 30000-70000 Da, and structure due to the presence of hydroxyl groups on its backbone (Gaaz *et al.*, 2015).

This flexibility in structure results in weaker intermolecular interactions compared to PET, leading to the formation of smaller fiber diameters as the polymer chains are less constrained and can orient themselves more easily during fiber formation leading increased viscosity and lower conductivity as seen in section 4.12.1 property table which then affects the electrostatic forces acting on the solution. A more conductive solution will allow for better charge transfer between the spinneret and the collector, resulting in a more stable electrospinning process and finer, more uniform fibers. Therefore, the differences in molecular weight and structure and intermolecular interactions between PET and PVA play a significant role in the voltage applied.

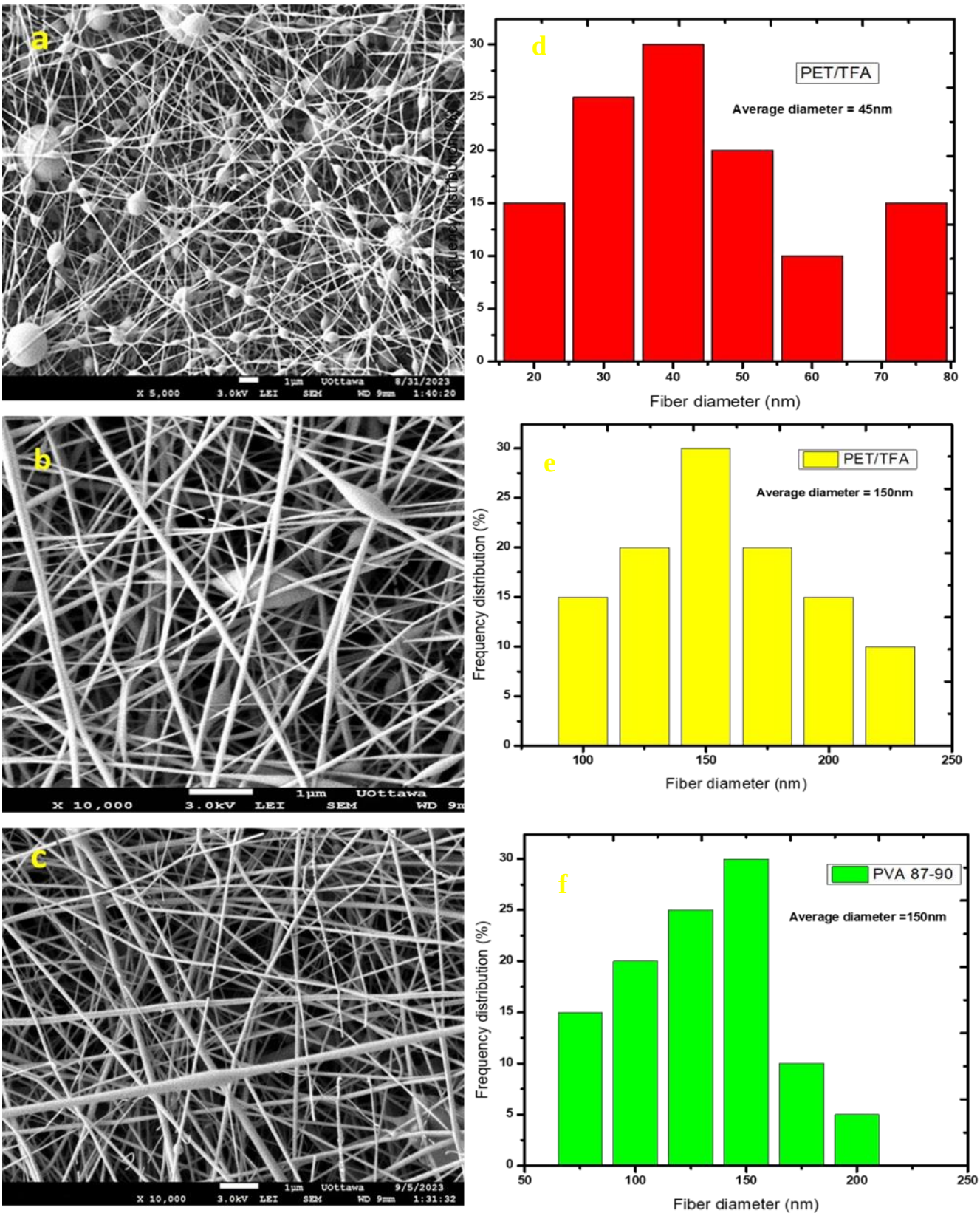


Figure 4-12. (a) PET TFA voltage 10 kV, (b) PVA H_2O voltage 15 kV, (c) PVA H2O 18 kV at 15cm tip-to-collector distance, 18G, 0.3mL/hr flowrate.

4.12.4 Effects of flowrate, needle and Tip to collector

Studying the effects of the flow rate, needle type, and tip-to-collector distance plays an essential role in influencing fiber formation during electrospinning. The flow rate dictates the rate of polymer solution ejection, affecting fiber thickness and uniformity. The needle type, particularly the sharpness and diameter, influencing the electric field intensity around the needle tip, impacting fiber morphology and diameter. The tip-to-collector distance determines the flight time of the polymer jet before deposition, affecting fiber diameter and morphology (Gündüz, 2023). The effects of flowrate, needle gauge, and tip-to-collector distance were investigated in the context of electrospinning experiments involving varying flowrates (ranging from 0.2 to 0.4 mL/hr), tip-to-collector distances (ranging from 8 to 15 cm), and different needles of gauges 18G, 23G, and 11G. To investigate the rest of the parameter effects, PVA only images were used as an example for the rest of the study. Therefore, discussions in this section will be made only for the PVA polymer solution.

4.12.4.1 Effects of flowrate

The choice of flow rate is important in the electrospinning process as it directly impacts the morphology, diameter, and alignment of the electrospun fibers. An optimal flow rate ensures a consistent, uniform spinning process, controlling the amount of polymer solution ejected from the spinneret and determining the rate at which the fibers are formed. Too high of a flow rate can lead to the formation of thicker fibers with potential bead defects, while a flow rate that is too low may result in unstable jet formation and irregular fiber deposition. The flowrate was investigated using a flowrate ranging between 0.2-0.4 mL/hr while all other parameters were held constant as seen in (Figure 4-13a, b &c).

At a flowrate of 0.2 mL/hr finer and more uniform fibers with a few beads were observed due to better stretching and alignment of the polymer chains giving enough time for solvent evaporation to occur (Figure 4-13a). The morphology of PVA nanofibers produced a flowrate of 0.3 mL/hr shown in (Figure 4-13b), a slightly higher polymer flow introduces more material, which led to moderately thicker fibers compared to the lower flow rate. The applied voltage continued to facilitate the stretching and alignment of the polymer chains, contributing to the formation of well-defined fibers with a higher aspect ratio.

However, the moderate increase in flow rate resulted in some irregularities along the fibers with fewer thin fibers formed. The results showed that the fibers were relatively thick, with an

average diameter of approximately 200 nm, and exhibited few observed beads as shown in Figure 4-13d. This morphology is not considered an issue, as the fibers are still suitable for use in various applications. The thick fibers and minimal bead formation are expected to influence the adsorption properties of the nanofibers. In contrast, the morphology at a flow rate of 0.4 mL/hr led to entanglements and irregularities in the resulting fibers, impacting the uniformity and quality of the fibers produced compared to the flowrate of 0.3 mL/hr.

The rapid polymer flowrate overwhelms the electrostatic forces exerted during spinning, the polymer chains do not have sufficient time to align and orient properly before solidification, resulting in the observed entanglements, kinks, and irregularities in the fibers as seen in Figure 4-13c. The thicker fibers produced at the flowrate 0.3 mL/hr may have improved mechanical properties, such as tensile strength and Young's modulus, compared to the thinner fibers produced at the lower flowrate. This is because the thicker fibers have a higher density of polymer chains, which can improve their mechanical properties hence this flowrate was chosen for future experiments.

Other researchers have also investigated the effect of flowrate on the morphology of PVA nanofibers. For example, a study by Singh *et al.* (2020) found that increasing the flowrate from 0.4 mL/hr to 0.6 mL/hr resulted in similar results with a significant increase in fiber diameter and bead formation. The authors attributed this to the increased polymer concentration at the tip of the needle, which led to the formation of larger droplets that solidified into thicker fibers.

Another study by (Baykara & Taylan, 2021) found that increasing the flowrate from 0.2 mL/hr to 0.4 mL/hr resulted in a decrease in fiber diameter and an increase in bead formation. The authors attributed this to the increased polymer solution velocity at the tip of the needle, which led to the formation of smaller droplets that solidified into thinner fibers. A higher flowrate resulted in an increased amount of polymer solution being delivered per unit time, which influenced the jet stability, stretching, and solidification processes during fiber formation.

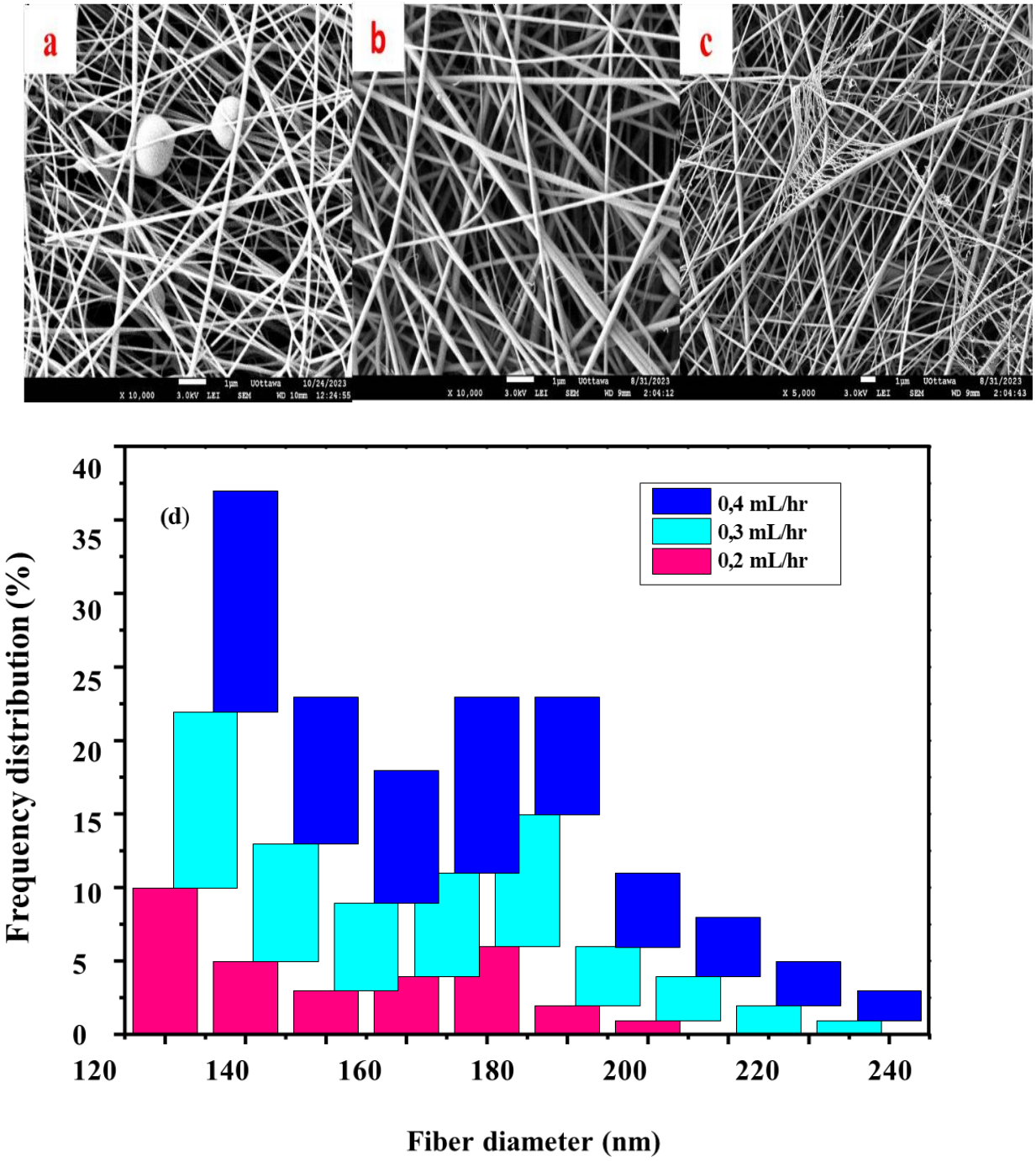


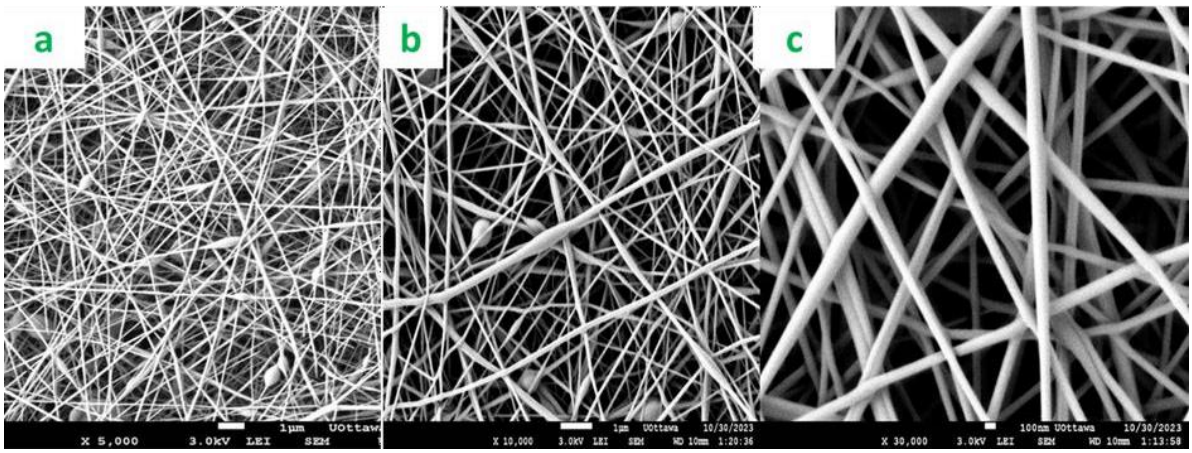
Figure 4-13.PVA/Water, 15 cm tip-to-collector distance, 18 G, 18 kV (a) flowrate = 0.2mL/hr, (b) flowrate = 0.3 mL/hr, (c)flowrate = 0.4 mL/hr, (d) frequency distribution

4.12.4.2 Needle effect.

The choice of needle gauge plays a crucial role in the electrospinning process, as it can significantly impact the morphology and properties of the resulting fibers. The effect of needle gauge on fiber diameter is investigated in this study, while all other parameters were held constant. In this study three needles, *viz*. 23 G with an inner diameter of 0.337 mm, 18 G with

an inner diameter of 0.838 mm, and 11 G with an inner diameter of 2.388 mm, were used to investigate the effect of needle size. The 23 G and 18 G needles produced fibers with smaller diameters due to the enhanced electric field intensity around the needle tip (Figure 4-14a, b &d). The enhanced electric field around the needle is caused by the sharpness and small radius of curvature of the needle tip, which results in a higher concentration of electric field lines. Xie and Zeng, (2012) made similar observations when they studied multi-needle electric field effect to achiever thin fiber diameters. They attributed to the strength of the electric field of the jets on the sides being too strong to form a stable Taylor cone.

This is in contrast to the 11G needle, which produced fibers with larger diameters. The electric field intensity around the needle tip is lower for the 11 G needle with a larger inner diameter compared to the smaller 23 G and 18 G needles. This is because the larger inner diameter of the 11 G needle results in a less sharp and less curved tip, leading to a more diffuse distribution of electric field lines and a lower intensity of the electric field in that region. the lower electric field intensity around the tip resulted in a more polymer solution being drawn-out leading to thicker uniform fibers being deposited onto the collector (Figure 4-15c). Additionally, the larger inner diameter needle was more effective in spinning polymer solutions with a mixture of the MIP and NIP.



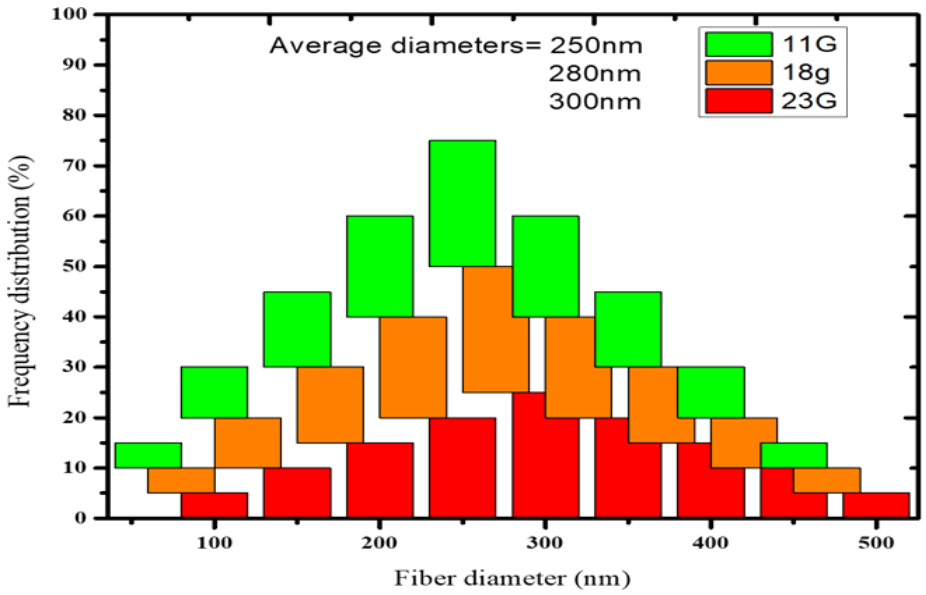


Figure 4-14.PVA/Water & ethanol,15cm tip-collector, 0.3mL/hr flowrate, 18kV (a)needle= 23 G, (b) needle= 18 G, (c) needle= 11 G and fiber diameter frequency graph

4.12.4.3 Tip-to-collector effect.

The tip-to-collector distance (TCD) also plays a crucial role in electrospinning process as it determines the flight time of the jet, the stretching of the polymer solution, and the deposition pattern on the collector. The shorter TCD led to a formation of beads due to the charged jet not having enough time to stretch and solidify before reaching the collector resulting (Figure 4-15a). In this case the TCD was kept at 8 cm with the resulting fibers having diameters below 100 nm. The resulting beaded fibres comes from the fact that the jet had no sufficient time for stretching because of short flight time. This led to no sufficient time for solvent to evaporate resulting in the formation of beads. However, the increase in the TCD created more space for the elongation and stretching and thus leading to smooth fibers without beads. When the TCD is 10 cm there is formation smooth fibers with less beads (Figure 4-15b).

The resulting fibers had an average diameter ranging from 300-350 nm. In the case of 15 cm TCD the fiber diameter was about 350 nm, as seen in Figure 4-15c. This can be attributed to enough time for solvent evaporation from the charged jet hence resulting in smooth fibers. In addition, the distance is sufficient to allow stretching of the jet. Purwar *et al*. (2016) reported that the shorter TCD lead to the formation of beads without fibrous structure being observed. The authors observed smooth fibers when the distance was increased from 3 cm to 8 cm, they attributed such behaviour to the charged jet being stretched enough prior to the deposition to the

collector. They indicated that shorter TCD led to shorter flight distance for the jet. This resulted into uneven stretching and incomplete solvent drying of the jet before reaching the collector, and thus resulting in beaded fibers.

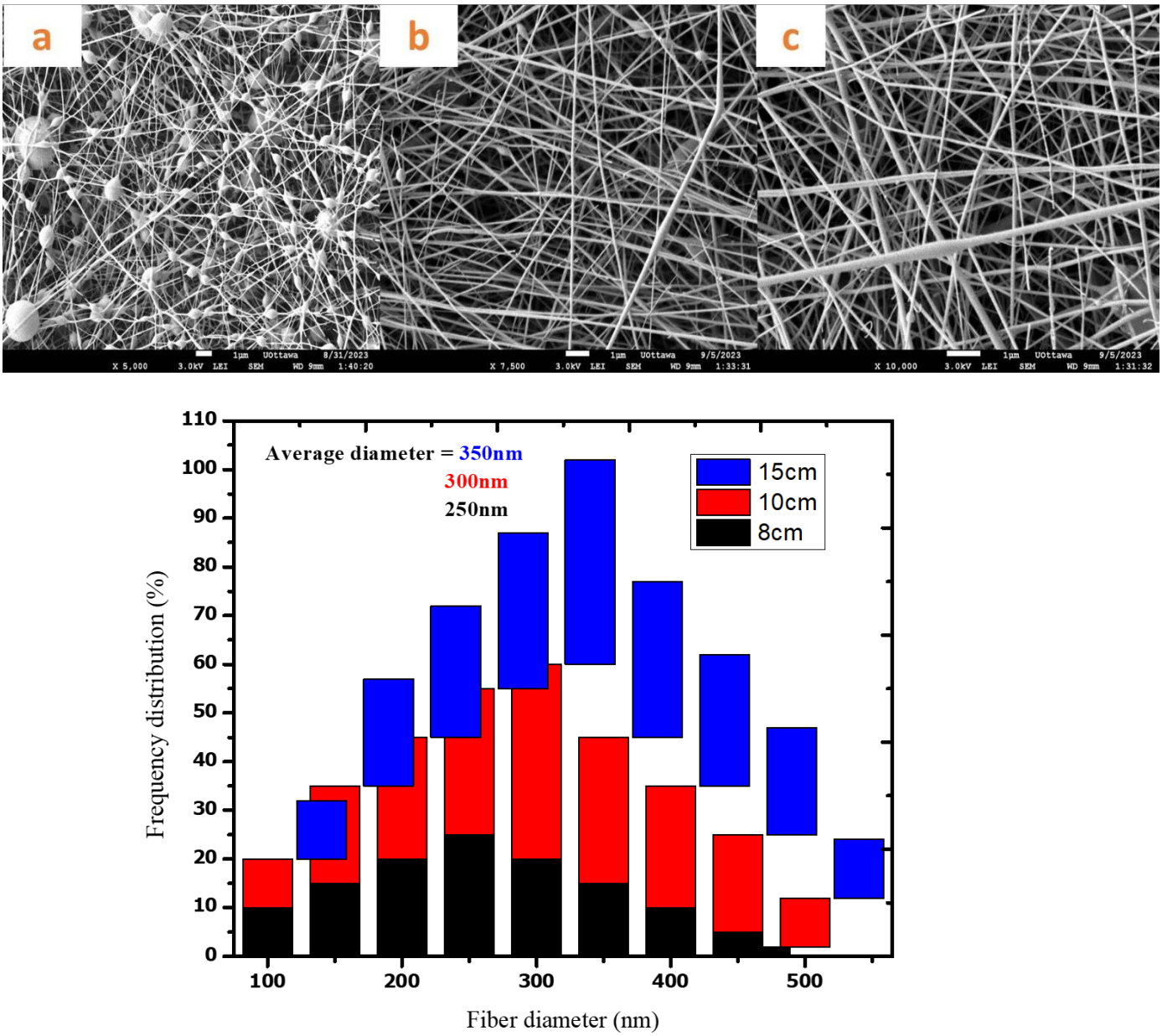


Figure 4-15.PVA/Water, 18G, 0.3min/min flow rate,18 kV (a) distance=8 cm, (b)distance=10 cm, (c)distance=15 cm and frequency and fiber diameter graph.

4.12.5 Effects of polymer solvent

The importance of studying the effects of the solvent used for polymer solutions, such as PVA and PET, lies in its significant impact on the properties, processing techniques, and environmental sustainability of the resulting materials. The choice of solvent influences the dissolution process of the polymer, molecular structure, and material properties, leading to

variations in mechanical, and thermal characteristics. Additionally, solvent selection affects processing parameters, such as fiber diameter and morphology, as well as environmental considerations like solvent recycling and waste generation. Understanding solvent-polymer interactions is essential for optimizing material performance, processing methods, and promoting eco-friendly manufacturing practices in the polymer industry (Mabesoone *et al.*, 2020). In this section of the study, the solvents used to dissolve PET and PVA were examined.

Therefore, this study investigated the impact of various solvents on PVA and PET polymers. The solvents used include water and a water-ethanol mixture (3:1 ratio) for PVA, and trifluoroacetic acid (TFA) and a TFA-dichloromethane (DCM) mixture (3:1 ratio) for PET. In the case of PVA in water, it was noted that water is a good solvent with good compatibility and hydrogen bonding capabilities with PVA, which helps in the effective dissolution of the polymer. Water is known to have lower surface tension compared to organic solvents which lead to improved fiber morphology and reduced bead formation during electrospinning process (Raza *et al.,* 2019). The fibers exhibited a smooth surface with minimal bead formation, showcasing fiber formation supported by hydrogen bonding as illustrated in Figure 4-16a.

The addition of ethanol to a PVA solution during electrospinning has multiple effects on the process and the resulting fiber formation. Ethanol acts as a plasticizer, reducing intermolecular forces and increasing polymer chain mobility, leading to decreased solution viscosity and improved spinnability (Kahvand & Fasihi, 2019). The lowered surface tension caused by ethanol helped reduce bead formation and enhance the uniformity of the fibers.

The presence of ethanol also influences the drying kinetics, promoting faster solvent evaporation (Figure 4- 16b). Water is a commonly used solvent for PVA due to its high solubility and non-toxic nature. The presence of ethanol in water can alter the solvent properties, such as viscosity and surface tension, affecting the solution's spinnability. Ethanol can enhance the processability of the PVA solution by improving the polymer-solvent interactions, resulting in uniform fiber production. Furthermore, the use of water-based solvents like water and ethanol in water for PVA samples contributes to the eco-friendliness of the spinning process, as water is a renewable and environmentally friendly solvent compared to organic solvents.

In the case of PET in TFA, TFA is a very strong solvent the use of it promoted chain entanglement and charge repulsion within this polymer producing beaded thin fibers (Figure 4-16c). As a solvent, TFA effectively dissolves PET, resulting in a homogeneous solution with a specific viscosity suitable for electrospinning. The controlled viscosity provided by TFA plays

an important role in the formation of fibers. The low viscosity of the solution affected the jet stability, stretching behaviour, and the ability of the fibers to solidify and maintain their shape during electrospinning the low viscosity does not viscosity provide enough resistance for the jet's elongation, leading to the formation of droplets that solidify into beads rather than fiber. Furthermore, the low conductivity of this solvent influenced the formation of the beaded structure.

The low conductivity led to poor ionization of the solution, resulting in a weak electrostatic force that is needed to draw and stretch the polymer solution into fibers. In this solution the was enhanced conductivity and electrospinnability of the solution as mentioned in section 4.12.1 (Table 4-9). The addition of DCM in this mixture affected the morphology of the fibre they were highly beaded with very thin fibers that broke under imaging (Figure 4- 16d). The addition of DCM further reduced the viscosity and conductivity of the solution that caused the morphology of the polymer mate to have increased bead formation.

TFA is a strong acid with high solvating power, commonly used for PET due to its ability to dissolve the polymer effectively (Karim *et al.*, 2022). However, TFA is challenging to handle due to its corrosive nature and toxicity. The addition of DCM in TFA modifies the solvent properties, such as volatility and evaporation rate, influencing the spinnability of the PET solution. A study by Mahalingam *et al.,* (2015) investigated the spinnability and solubility of PET with different solvents. They pointed out that PET is only spinnable when using TFA and/or DCM. The beaded fibers were formed with the use of TFA alone which corresponds with the observations in this study. However, the addition of DCM produced smooth nanofibers which is in contrast with this study's observation of increased bead and slightly elongated thin fibres.

The use of TFA-based solvents for PET samples, however, poses environmental considerations due to the toxicity and potential hazards associated with TFA. Proper waste management and handling protocols are essential to minimize environmental impact when using TFA-based solvents in polymer processing. Since the intended application is to treat wastewater sites the choice of solvents for polymer solutions becomes critical in terms of environmental consideration and eco-friendliness. In this research, the production of the electrospun polymer membrane must utilize environmentally sustainable methods to prevent the generation of detrimental by-products that could exacerbate the existing pressure on water resources. Therefore, PVA was used as the material of choice because it can be dissolved in water and

other eco-friendlier solvents. Conversely, TFA-based solvents like TFA and DCM in TFA for PET samples may raise concerns regarding their toxicity and potential environmental harm if not properly managed. Therefore, due to the environmental considerations and eco-friendliness associated with water-based solvents, further studies were conducted exclusively using polyvinyl alcohol to form the molecularly imprinted membranes (MIM) and nonimprinted membranes (NIM). The selection of PVA as the base polymer for these studies aligns with the goal of promoting sustainable practices in polymer processing and applications.

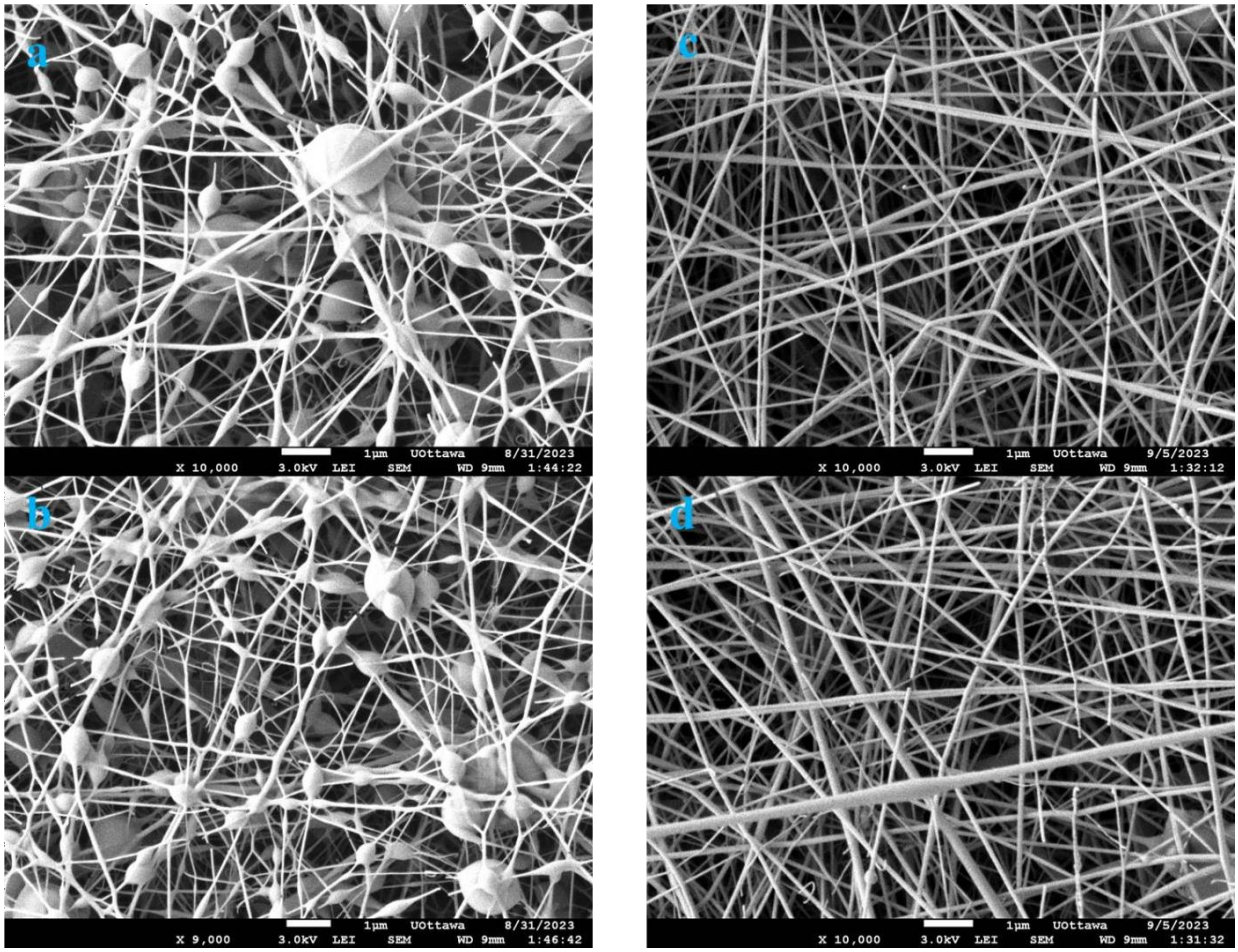


Figure 4-16: Solvent polymer effects (a) PET TFA, (b) PET TFA/DCM, (c) PVA H_2O, (d) PVA EtOH/H_2O

4.12.6 Effects of PVA polymer choice by degree of hydrolysis

Determining the optimal degree of hydrolysis for PVA was essential for achieving desirable material properties and processability. When comparing PVA with degrees of hydrolysis of 87-90% and 99%, considering their respective advantages and disadvantages crucial. Analyzing

the data presented in Table 4-10 and Section 4.12.1 (Table 4-9) for PVA solutions of different degrees of hydrolysis (DH) dissolved in water, PVA with a DH of 87-90% displayed better conductivity, spinnability, and viscosity when compared to PVA with a DH of 99% and thus resulting in formation of smooth fibers. The PVA solution with a DH of 87-90% exhibits lower conductivity (1054 µS/cm) compared to the 99% DH solution (839 µS/cm), which is beneficial for jet stretching during electrospinning and ensuring uniform thinner fiber deposition.

Furthermore, the PVA 87-90% solution demonstrates higher spinnability (165.5 mPa.s viscosity) compared to the 99% DH solution (2058.8 mPa.s viscosity), indicating better processability and fiber alignment. The lower viscosity of the 87-90% DH solution facilitates smoother jetting of the polymer solution, leading to the formation of well-defined and stable polymer mats. PVA with a lower degree of hydrolysis (87-90%) typically exhibits higher molecular weight chains and increased chain entanglements, and thus high viscosity. This is beneficial (Suleiman *et al.,* 2024).

On the other hand, PVA with a higher degree of hydrolysis (99%) offers better water solubility and compatibility due to a higher number of hydroxyl groups. However, the increased hydrophilicity of PVA 99% affecting its suitability for certain applications. For instance, filtration membranes have to exhibit certain mechanical performance, and high hydrophilicity may result in the reduction of mechanical strength and stability, and thus limit its application in wastewater treatment.

In terms of electrospinning to form polymer mats, looking at the polymer properties of PVA 87-90% mentioned in Section 4.12.1 and comparing them to those in Table 4-10 these results show that PVA with a lower degree of hydrolysis (87-90%) is preferred due to its superior mechanical properties and enhanced electrospinnability compared to PVA 99%. Research by Park *et al.* (2010) supported this finding, demonstrating that PVA 87-90% exhibited slightly higher mechanical strength and improved fiber formation during electrospinning than those below 87%. They further experienced the difficulty and poor electrospinnability of the PVA 99% as was experienced in this study, stating that the DH=99.9%, because of a combination of higher surface tension has the tendency to undergo gelation through a strong hydrogen bonding. Mostly beaded fibers were formed with DH=99% similar results were reported by (Zhang *et al.,* 2005).

Considering the advantages of PVA 87-90% in terms of mechanical strength and electrospinnability, a polymer mat of PVA 87-90% was selected to incorporate MIPs and NIPs

in the formation of PVA-MIP-based composites for the adsorption of select pharmaceuticals in water treatment applications. This choice was made to capitalize on the superior properties of PVA 87-90% for achieving improved performance and stability in pharmaceutical adsorption processes.

Table 4-10: PVA 99% polymer properties

Sample No	Polymer	Polymer ratio (%)	Solvent	Solvent Volume (ml)	Conductivity (µS/cm)	Viscosity (mPa.s)
1.	PVA DH (99%)	100	H_2O	40	839	2058.8
2.		100	H_2O & ethanol	30:10	425	249.8
3.	PVA DH (99%) MIP	98.6/1.4	H_2O	40	1386	2276.4
4.		98.6/1.4	H_2O & ethanol	30:10	666	586.6
5.	PVA DH (99%) NIP	98.6/1.4	H_2O	40	698	1316.2
6.		98.6/1.4	H_2O & ethanol	30:10	351	2314.8

4.13 Interpretation of the results from the adsorption and application studies

4.13.1 Material swelling studies.

The results obtained from the centrifugation experiment conducted on the PVA 87-90 DH electrospun MIM and NIM revealed an interesting trend in the weight of the materials over different time intervals. For the MIM, the weight decreased as the centrifugation time increased, starting at 2.864 g at 5 min and decreasing to 1.6483 g at 60 min before completely dissolving at 2 hours. On the other hand, the NIM also showed a decrease in weight over time, starting at 1.404 g at 5 min and diminishing to 0.136 g at 60 min before complete dissolution at 2 hours. This trend in weight loss can be explained based on the chemistry of PVA. PVA is a water-soluble polymer that swells in water and can dissolve when exposed to prolonged contact with water.

The decrease in weight of both MIM and NIM membranes over time can be attributed to the continuous hydration and swelling of PVA molecules in contact with water during centrifugation. This hydration causes the polymer chains to separate and dissolve, leading to the observed weight loss. Additionally, the presence of molecular imprints in the MIM could potentially affect the dissolution behaviour compared to the NIM, as the specific interactions between the imprinted sites and target molecules influence the swelling and dissolution properties of the membrane. Further investigation into the molecular imprinting process and

the effects of specific interactions on the dissolution behaviour could provide valuable insights for the development and optimization of PVA-based membranes for various applications. Figure 4-17 shows the swelling study graph.

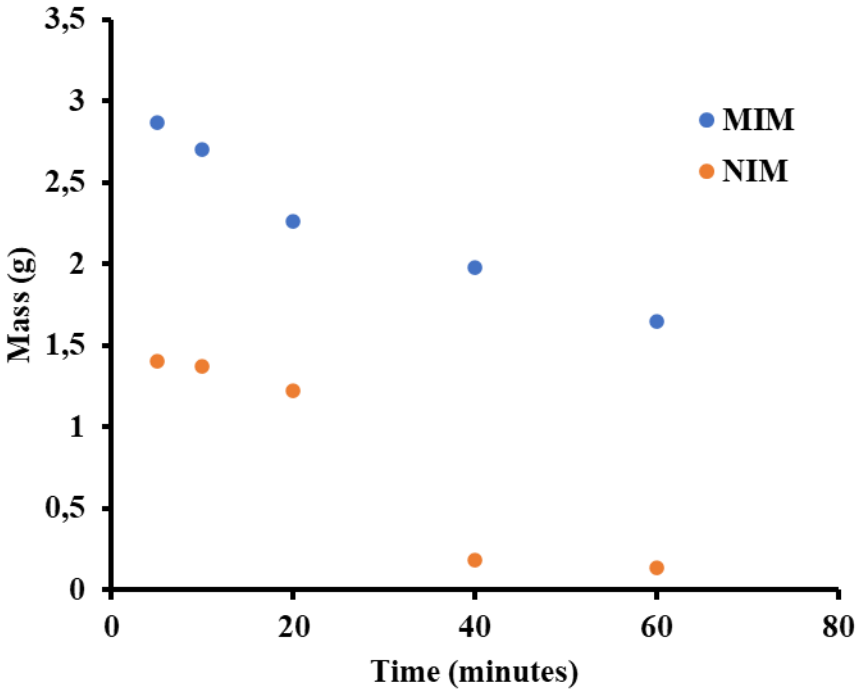


Figure 4-17. MIM and NIM swelling studies.

4.13.2 TGA spectra of polymer materials

Understanding the thermal stability of polymer materials is important for various applications. The choice of polymer material can significantly impact the adsorption efficiency, selectivity, and stability, making thermal stability a critical consideration. The thermal stability of a polymer material is important in adsorption applications because it determines the material's ability to withstand temperature fluctuations and maintain its adsorption properties over an extended period. A polymer material with a high thermal stability can ensure consistent performance and minimize the risk of thermal degradation.

A comparative discussion of the polymer materials formed in the TGA graphs in Figure 4-18(a, b &c) reveals distinct weight loss or degradation points in each material. While all the polymer materials exhibit thermal degradation, the temperature points at which this occurs differ significantly between them. For instance, PVA 99 EtOH: H_2O, a polyvinyl alcohol-based polymer, showed a relatively narrow temperature range for weight loss, with significant

degradation occurring between 100°C and 150°C due to the loss of water and ethanol. The most pronounced weight loss was observed around 150- 270 °C, as the temperature increases towards 270°C and beyond, the weight loss may indicate the breakdown of the polymer backbone and further degradation of the PVA molecules as seen in Figure 4-18c. The complete degradation observed at around 460°C suggests the decomposition of PVA into smaller molecular fragments, indicating the end of the thermal stability of the polymer. Overall, the weight loss at these specific temperature points can be linked to the evaporation of moisture or solvent molecules, as well as the thermal degradation of the PVA polymer chains.

In contrast, PET TFA, a polyethylene terephthalate-based polymer, displays a more extensive temperature range for weight loss, with significant degradation occurring between 230°C and 405°C. The initial weight loss around 150°C is likely due to the dehydration of PET, which is a common phenomenon observed in many polymer systems. The second weight loss peak around 405°C could be related to the thermal degradation of PET's molecular structure, possibly involving the breakdown of its ester linkages or the formation of volatile compounds. The complete degradation around 460°C is due to the destruction of the PET polymer chain, resulting in a significant loss of mass. In the case of PET-TFA, the weight loss at these temperatures could be influenced by the presence of TFA, which is known for its strong acid properties.

PET TFA/DCM, a blend of polyethylene terephthalate and dichloromethane, exhibits a similar temperature range for weight loss as PET TFA, with significant degradation occurring between the same temperature ranges as seen in Figure 4-18. However, the most pronounced weight loss is observed around 230°C and 400°C, which indicate different thermal degradation mechanisms compared to PET TFA. The presence of dichloromethane influences the thermal behaviour of this material at this temperature range. One possible reason for this is that DCM is a solvent that can affect the molecular structure and interactions within the polymer as mentioned in previous sections. When DCM is present in the polymer, it can disrupt the hydrogen bonding and π-π stacking interactions between the polymer chains, leading to a more open and flexible structure.

This increased flexibility can make the polymer more susceptible to thermal degradation, as the polymer chains can move more easily and break apart more easily. The MIP and NIP possess complex 3-dimensional structures formed as a polymer network by pyridine, which, makes them thermally stable polymer materials. The presence of the heterocyclic aromatic pyridine ring is a significant contributor to their stability, as it provides a rigid and planar structure that

is resistant to thermal degradation. When the MIP and NIP are mixed with polymer solutions, such as PVA or PET, they can shield the polymers from thermal degradation. This is evident in the TGA diagrams in Figure 4-18a&b, which show a delayed thermal degradation of the PVA-MIP and PET-MIP, as well as PVA-NIP and PET-NIP. There is about 21-51 % delayed degradation when the MIP is added to the PVA, and about 4-8 % delayed shift to PET-MIP materials. The MIP and NIP act as a thermal barrier, preventing

the polymer chains from undergoing thermal degradation. This shielding effect is attributed to the 3-dimensional structure of the MIP and NIP, which provides a protective environment for the polymer chains. The MIP exhibits a unique temperature range for weight loss with significant degradation occurring between 300°C and 460°C. The most pronounced weight loss is observed around 100°C and 280°C, suggesting a more gradual thermal degradation process of water and ethanol evaporation as well as the initial collapse of the MIP material as seen in the previous section 4.11.3 the collapse of the MIP backbone. This broader temperature range may indicate a more complex and variable thermal behaviour for this material compared to PVA 99 EtOH: H_2O as seen in Figure 4-18a.

In comparison to the other materials, PVA 99 EtOH: H_2O exhibits a relatively low temperature range for weight loss, indicating a more stable thermal behaviour. PET TFA and PET TFA/DCM exhibit broader temperature ranges for weight loss, suggesting more complex and variable thermal performances. MIP exhibits an intermediate temperature range for weight loss, indicating a more complex thermal behaviour compared to PVA 99 EtOH: H_2O but less complex than PET TFA and PET TFA/DCM. The NIP polymer mixture materials exhibit a unique thermal behaviour. Specifically, the NIP polymer mixture with PVA 99 EtOH: H_2O exhibits a distinct weight loss pattern, with significant degradation occurring between 100°C and 270°C. The most pronounced weight loss is observed around 270°C, suggesting a thermal degradation event.

In comparison to the other polymer materials, the NIP-polymer mixture with PVA 99 EtOH: H_2O exhibits a relatively high temperature range for weight loss, indicating a more complex thermal behaviour. This may be due to the presence of the NIP-polymer mixture, which can influence the thermal stability of the PVA 99 EtOH: H_2O. The NIP-polymer mixture with PET TFA exhibits a similar temperature range for weight loss as PET TFA alone, but with a more pronounced weight loss around 100°C and 260°C. This may indicate a synergistic effect between the NIP-polymer mixture and PET TFA as seen in Figure 4-18b. A study by Miranda

et al., (2017) found that when LA (lactic acid) was blended with PET powder, the weight loss began at 130°C, likely due to the evaporation of LA from the PET surface. As the processing steps progressed from pellets to preforms and bottles for the two-stage process, the weight loss at 250°C decreased. This decrease in weight loss was used as an indicator of the concentration of unbound LA, which was lower than the nominal loading. The two-stage preforms showed lower weight loss than pellets, consistent with previous studies on end groups and extraction. In contrast, the single-stage process preforms showed a higher weight loss at 250°C, with a total loss of 0.33% at 120°C. This suggests that LA in the PET matrix migrated during extraction in the single-stage process. This finding is supported by end-group analysis, which showed greater reaction between end groups to form LA-capped PET for the two-stage process.

In contrast, the NIP-polymer mixture with MIP exhibits a relatively low temperature range for weight loss, indicating a more stable thermal behaviour. The most pronounced weight loss is observed around 80°C, suggesting a thermal degradation event. The NIP-polymer mixture with PET TFA/DCM exhibits a complex temperature range for weight loss, with significant degradation occurring between 200°C and 400°C. The most pronounced weight loss is observed around 400°C and 460°C, suggesting multiple thermal degradation events. A study by (Yang *et al.*, 2021) revealed that PVA undergoes significant thermal degradation between 216°C and 320°C, resulting in a substantial weight loss due to the breakdown of its polymer backbone. Notably, the highest rate of weight loss occurred at 278°C. In contrast, a lower temperature of approximately 130.3°C led to a minor weight loss of around 5% due to dehydration.

When subjected to high temperatures, PVA decomposes completely, leaving no residue behind. This decomposition is attributed to oxidative processes involving organic substances in an air-containing atmosphere. Factors such as molecular weight, molecular structure, and degree of crystallinity can influence the degradation of PVA, while its state (molten or solid) also impacts its thermal degradation, resulting in distinct TG profiles. Which has similar findings to this study.

In conclusion, the comparative discussion of the polymer materials reveals distinct weight loss or degradation points in each material. The temperature ranges and points of weight loss differ significantly between the materials, indicating varying levels of thermal stability and complexity. While PVA 99 EtOH: H_2O exhibits a relatively stable thermal behaviour, PET TFA and PET TFA/DCM exhibit more complex thermal behaviours. MIP exhibits an

intermediate level of thermal complexity. Understanding these differences can inform the selection of appropriate polymer materials for specific applications where thermal stability is critical.

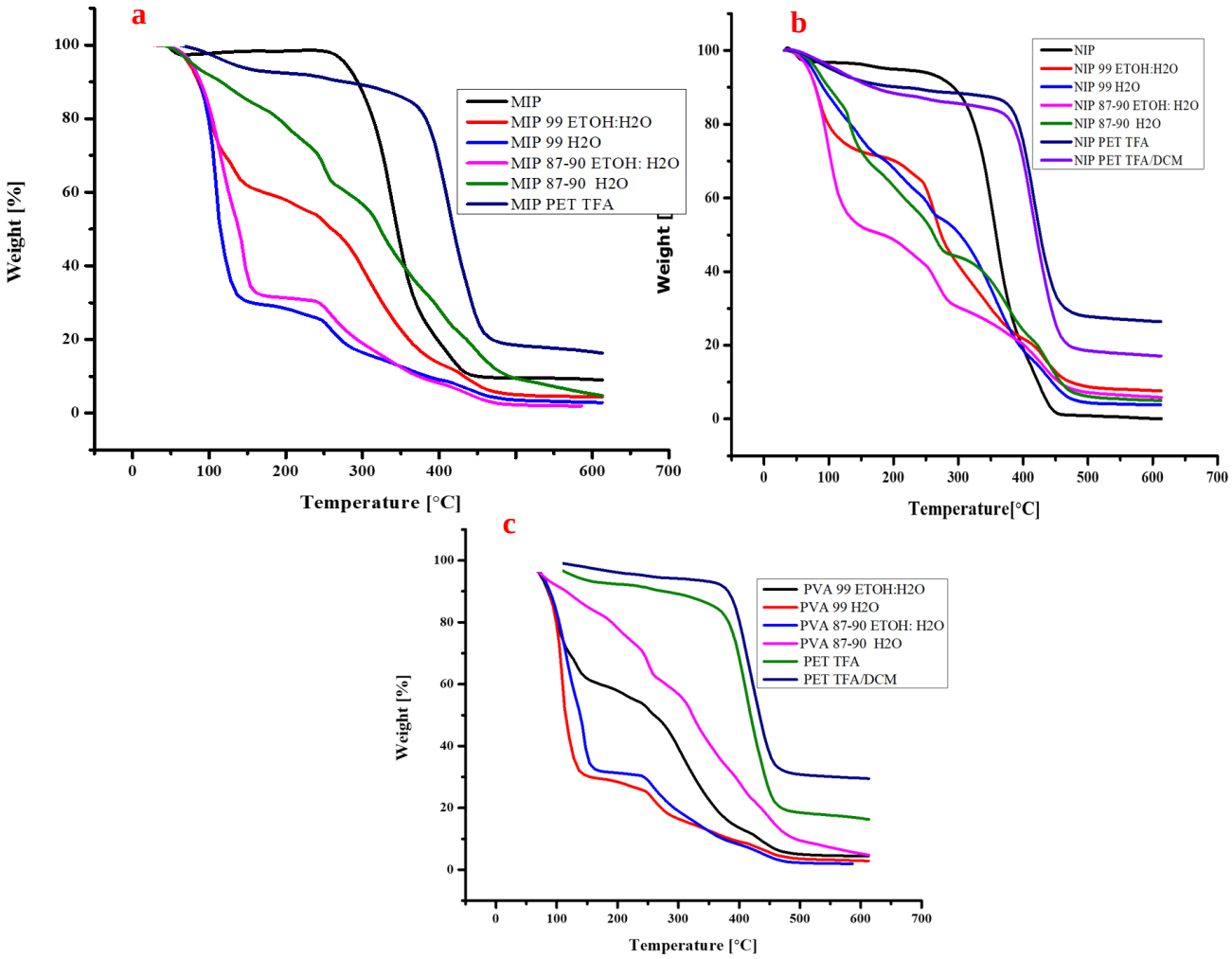


Figure 4-18: Thermal analysis of standard polymer materials, MIP and NIP additives to polymer solutions.

4.13.3 FTIR spectra of polymer materials

The FTIR characterization of PVA and PET in different solvents, including water, ethanol in water, TFA, and DCM in TFA, as well as solutions of polymers with MIP and NIP additives, provides a comprehensive understanding of the chemical interactions and functional group compositions present in the synthesized nanofiber structures. Analyzing the molecular bonding and characteristic peaks in the FTIR spectra allows for the identification of specific functional groups such as O-H, C-H, CH_2, C-O, and C-C, revealing the intricate molecular arrangements

and intermolecular connections within the polymer matrices. The detailed FTIR analysis offers important insights into the polymer-solvent interactions and polymer-polymer bonding, shedding light on the chemistry involved in the formation of nanofibers with designed properties and applications. The MIP and NIP functional groups present have been discussed alone in Section 4.9, therefore, this section they are only discussed in comparison to the other polymer solution.

Figure 4-19(a, b &c) illustrates the FT-IR results, showing the presence of various functional groups such as O-H, C-H, CH_2, C-O, and C-C in the synthesized nanofibers. Specifically, the stretching vibration of the O-H group was observed in the range of 3000-3800 cm^{-1}, with results showing a peak at 3275 cm^{-1}. The O-H symmetry stretch vibration appeared at a wavenumber of 3336 cm^{-1}. Furthermore, the vibration of the C-H group was detected at 2910 cm^{-1}, while the asymmetrical vibration of the C-H group occurred at 2900 cm^{-1}. The CH2 group vibration was found at 1430 cm^{-1}, with experimental results showing a peak at 1420 cm^{-1}. The C-H group vibrations were observed at 1330 and 1377 cm^{-1}, with a distinct peak at 1331 cm^{-1}. The absorption band at 1078 cm^{-1} indicated the presence of the C-O stretch in the nanofibers. Additionally, the vibration at 849 cm^{-1} denoted a C-C PVA stretch, with experimental results showing a peak at 857 cm^{-1}. These stretches and vibrations were consistent with those found by (Ullah *et al.*, 2020; Zhao *et al.*, 2017)

The FTIR spectra of PET in TFA and PET in TFA/DCM solutions in Figure 4-19c shows characteristic absorption bands corresponding to specific functional groups present in the polymer films which are ester groups, hydroxyl groups, and carboxylic acid groups. In the PET/TFA system, notable absorption peaks were observed at approximately 2959 cm^{-1}, indicative of C-H aliphatic groups. Another prominent peak at around 1718 cm^{-1} was attributed to the -C-O bond within the PET structure prominent absorption bands include the stretching vibration of the carbonyl group (C=O) in PET at around 1715 cm^{-1}. This peak indicates the presence of ester groups in the polymer chain, which are essential structural components of PET due to the ester linkages between terephthalate and ethylene glycol units in the polymer chain.

While peaks at approximately 1540 cm^{-1} and 1457 cm^{-1} suggested the presence of benzene rings disubstituted in the PET polymer. Additionally, peaks at approximately 1281 cm^{-1}, 1203 cm^{-1}, and 1121 cm^{-1} corresponded to the -C-C-O asymmetric stretch, the -O-C-C asymmetric stretch, and aromatic ring vibrations, respectively. A peak at 1073 cm^{-1} was associated with a

benzene para-substituted group in the PET structure, while another peak at 843 cm^{-1} indicated C-H vibrations within the aromatic structure peaks around 1380-1450 cm^{-1}, corresponding to the bending vibrations of the methyl ($-CH_3$) and methylene ($-CH_2-$) groups in PET. These peaks provide further evidence of the molecular structure of PET and can be used to confirm the presence of these alkyl groups within the polyester chain. Furthermore, a peak at 724 cm^{-1} was observed in the FTIR spectrum of PET in TFA, although the specific functional group responsible for this vibration was not explicitly identified. Similar stretching's and vibrations were found by (Nojavan *et al.*, 2024) while studying PET in combination with carbon nanotubes.

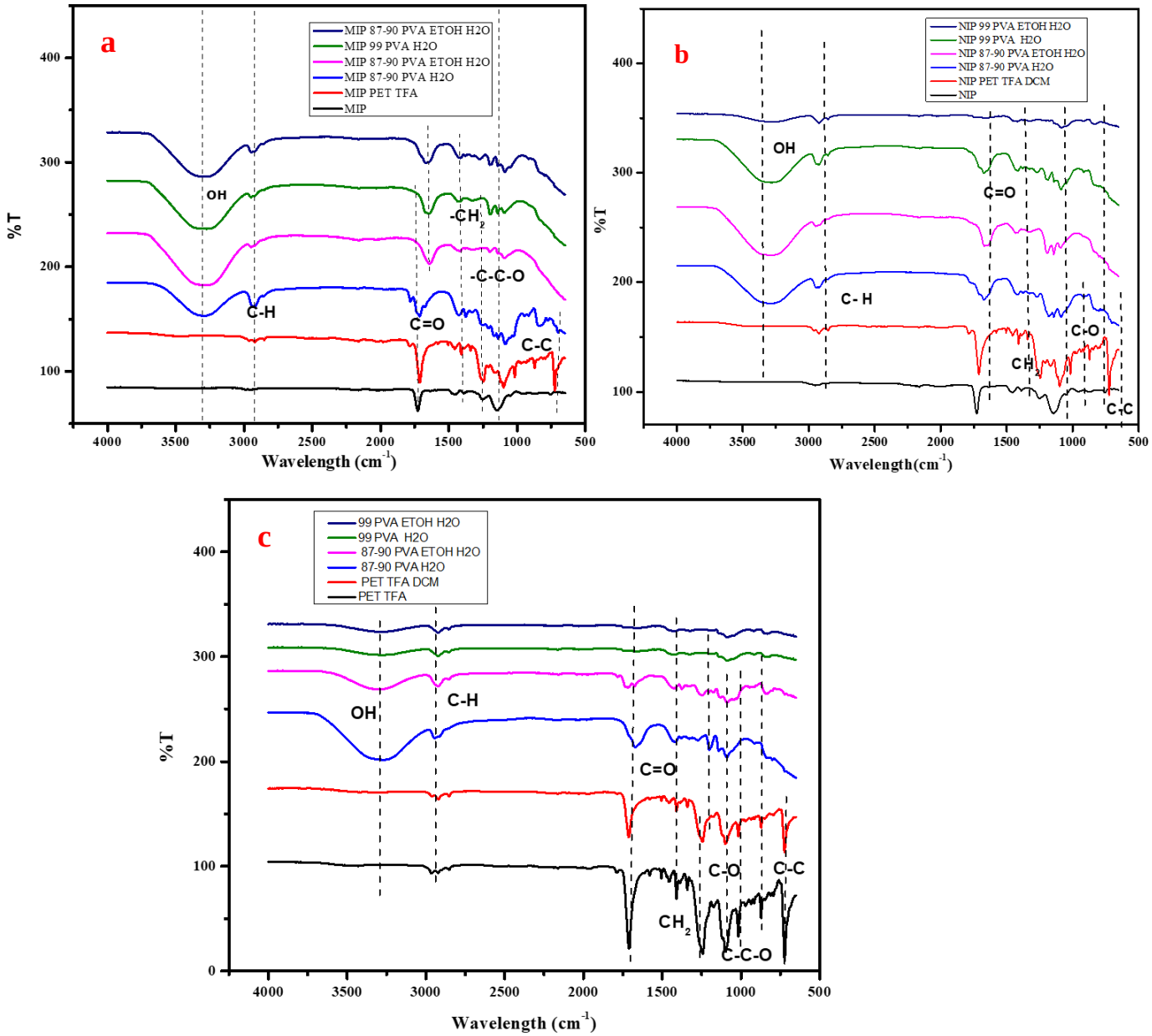


Figure 4-19 FTIR spectrums of PVA, PET solution with MIP and NIP additives and without

4.13.4 Adsorption time of the electrospun PVA-MIP and PVA-NIP composites.

The adsorption behaviour of various drugs (EMI, TENO, NAP, DICLO, IBU, EFV) on both molecularly imprinted membrane (MIM) and non-imprinted membrane (NIM) materials over different time intervals (5, 10, 20, 40, 60 minutes) was investigated. The data reveals the amount of each drug adsorbed onto the materials at each time point, providing insights into the adsorption kinetics of the drugs. Figure 4-20 portrays the pharmaceutical adsorption process using an electrospun-based PVA-MIP material over different time intervals. As expected, the results indicate a gradual increase in pharmaceutical adsorption as the time of contact between the material and the solution increases.

This is consistent with the typical behaviour of adsorption processes where the adsorption capacity of the material increases over time, eventually reaching a plateau where equilibrium is achieved. Starting with EMI, the graph shows that EMI exhibits higher adsorption onto MIM compared to NIM for all time intervals. Similar results were reported in a PET-MIP based material to adsorbent rhodamine blue dye in river water (Li *et al.*, 2012). This suggests that the MIM material may have specific recognition sites for EMI, enhancing its adsorption capacity. The trend is consistent across all drugs, indicating the effectiveness of molecular imprinting in enhancing selectivity and adsorption efficiency.

For TENO, NAP, DICLO, IBU, and EFV, similar trends are observed, with higher adsorption onto MIM compared to NIM. This consistent pattern further validates the benefits of molecular imprinting in enhancing adsorption performance. The data also reveals that the adsorption levels generally increase with time, indicating that a longer contact time results in higher drug uptake by both NIM and MIM. However, it is important to note that the adsorption capacity of the materials may be limited by factors such as stability and durability. In this context, the data shows that the PVA-MIP material dissolved completely after 60 minutes, highlighting the importance of material selection and stability in adsorption studies. The dissolution of the PVA-MIP material limits its practical utility as an adsorbent in water treatment applications, necessitating the need for material improvements to enhance stability and performance. One possible reason for this dissolution could be the sensitivity of PVA to prolonged exposure to the solution conditions. To overcome this issue of dissolution crosslinking the PVA material with other polymers that are hydrophobic might help to maintain the stability of the material. A study by Zhao *et al.* (2017) showed that crossing PVA with sericin improved the adsorption of organic dyes in water as well as heavy metals.

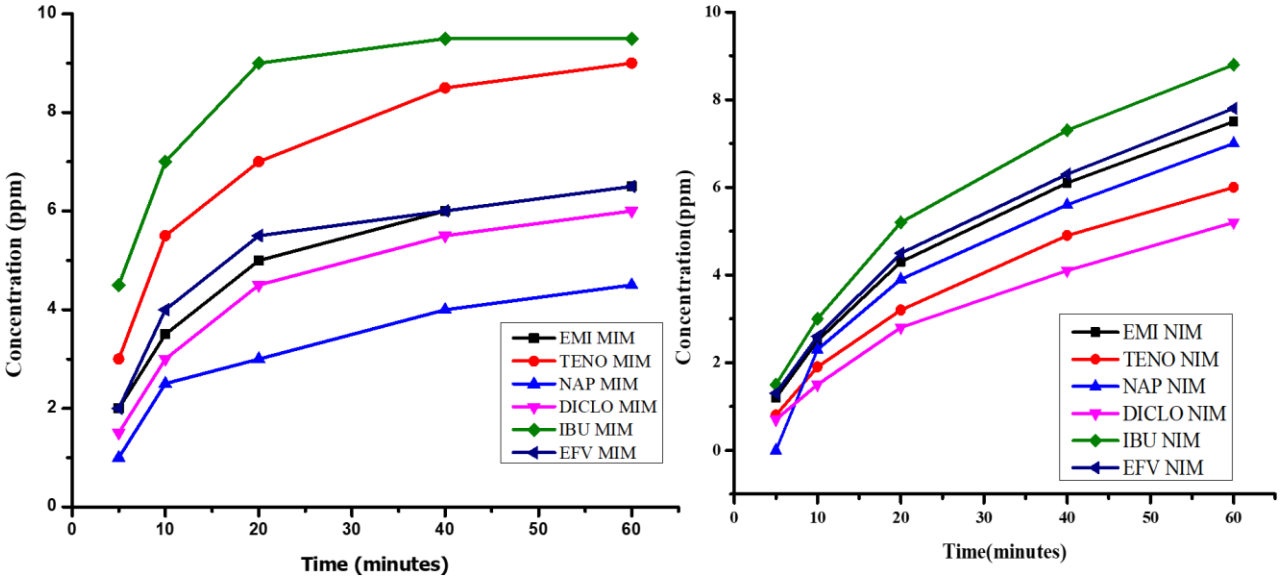


Figure 4-20: Adsorption capacity over time of MIP-PVA based MIM and NIM

4.13.5 Implications of the findings for future research and application

While this study revealed limitations in the stability of MIP-PVA-based materials for pharmaceutical adsorption, the data highlights that PVA can be effectively utilized in several other applications. One significant application of PVA is in the medical field, where it has been combined with different compounds such as glycerin, urea, sulfathiazole, methyl cellulose, ethylene dichloride, epoxy resin, and dimethyl sulfoxide for various purposes (Hirai *et al.*, 1994; Skinner & Waud, 1943; Waud, 1944). For instance, PVA films have been employed in the treatment of burns, as plombage material for thoracic surgery, and for fabricating hip disarticulation sockets. Additionally, PVA has been utilized in drug delivery systems, hydrogel development, polymer gel actuators, and as a material to improve paper strength (Li *et al.*, 2005; Reena *et al.*, 2020).

These diverse applications demonstrate the adaptability of PVA in addressing different medical and technological challenges. Moreover, PVA has also found applications in other fields such as civil engineering, soil science, chemistry, and electronics (Chemie, 1973; Patil *et al.*, 2011). For instance, PVA has been used in cement to reduce water loss during slurry preparation, for developing crust strength of silty soils, and in the preparation of polyvinyl cinnamate via esterification. In the electronics industry, PVA has been combined with polyacrylamide films to create semiconducting surface layers and has been utilized in supercapacitor applications through PVA/polyaniline thin films. These applications highlight the diverse capabilities of PVA and its significance in addressing various challenges in different sectors.

Despite the limitations observed in the study regarding the stability of PVA-based materials for pharmaceutical adsorption, the wide array of applications highlighted demonstrates that PVA remains a versatile and valuable material in various industries. The data serves as a testament to the importance of further research and development efforts to optimize the performance of PVA- based materials and unlock their full potential across different fields. By leveraging the unique properties of PVA and exploring innovative applications, the material can continue to contribute significantly to advancements in medicine, technology, and other sectors.

4.1 Evaluation of the adsorption performance of the electrospun MIP composite

When considering materials for water treatment applications, it is essential to choose a polymer that is not only strong and durable but also safe for use in drinking water. In this context, the PET/TFA polymer mats may not be the best choice due to several factors. One of the main concerns with using PET/TFA polymer mats is the presence of TFA solvent. TFA is a highly toxic and corrosive solvent that can have adverse effects on aquatic ecosystems if released into water bodies even though it is the best in dissolving PET. Therefore, using PET/TFA polymer mats in water treatment applications could potentially lead to contamination of the water, posing a risk to human health and the environment.

Additionally, the structure of the PET/TFA polymer mats may not be ideal for incorporating MIPs during the electrospinning process. The uniform beaded fibers formed with no pores make it difficult to incorporate MIP into the material effectively. This could result in reduced efficiency of the water treatment process and a lower capacity for removing target contaminants however further studies can be done for other applications that are not in water treatment.

Moreover, the blocking of the needle during the electrospinning process with PET/TFA polymer mats lead to longer experimental times and a less consistent product. This could increase production costs and hinder scalability for large-scale water treatment applications. While PET possesses several desirable qualities such as strength and durability, it was not the material of choice for further investigation in water treatment applications due to the limitations mentioned earlier. However, PET can still be utilized in other applications where its properties are better suited, such as in packaging materials, textiles, and medical devices.

On the other hand, PVA stands out as a more suitable material for other treatments and not water treatment applications. PVA is also considered safe for use in water treatment due to its non-toxic nature. PVA is biocompatible and non-toxic, making it safe for use in contact with drinking

water. This ensures that there are no harmful effects on human health when PVA is used in water treatment processes. Secondly, PVA's electrospinnability allows for the formation of fibers with a high surface area and uniform structure, enhancing the effectiveness of MIP incorporation for targeted contaminant removal. The large diameter fibers produced by PVA potentially contribute to improved adsorption capacity and efficiency in water treatment processes.

Furthermore, the ease of incorporating MIP into PVA during electrospinning makes the fabrication of MIPC materials more efficient and cost-effective. This streamlined process ensures a consistent and reliable product suitable for large-scale water treatment applications. In addition to water treatment, PVA-based MIPC materials can also find potential applications in drug delivery systems, sensors, and environmental remediation. The versatility and adaptability of PVA make it a valuable material for various fields where controlled release and selective adsorption properties are required.

Therefore, while PET has its own set of advantages, PVA emerges as the optimal choice for MIPC in water treatment applications in this study. Its biocompatibility, electrospinnability, ease of MIP incorporation, and safety for use in drinking water make PVA the superior option for enhancing the efficiency and effectiveness of water treatment processes. Further studies were conducted on the PVA 87-90 % DH only.

5 CHAPTER 5: CONCLUSION AND RECOMMENDATIONS

5.1 Summary of the key findings

The objectives of this study were to synthesize molecularly imprinted and non-imprinted polymers via precipitation polymerization. Then to use the synthesized MIP to study the adsorption efficiency of the material to adsorb selected target pharmaceuticals in Canadian wastewater treatment plants. A comparative study between the synthesized MIP and commercial adsorbent was done to assess the competitiveness of the MIP to commercial adsorbent. The material was found to successfully adsorb pharmaceutical pollutants such as emtricitabine, tenofovir disoproxil furmate, efavirenz, naproxen, diclofenac and ibuprofen in wastewater. Furthermore, the MIP was incorporated into a suitable polymer solution for electrospinning to form MIP-based membrane for possible application in wastewater sectors.

These materials were characterized using various techniques, such as NMR, FTIR, SEM, BET, and TGA to understand the structural morphologies, functional groups as well as the thermal stability of the materials. NMR and FTIR analyses showed successful incorporation of functional groups essential for selective adsorption, demonstrating differences between MIPs and NIPs in terms of molecular recognition capabilities. SEM provided image data of the unique morphologies of these composites, highlighting enhanced surface area and porosity in MIP, NIP, MIP-PVA and MIP-PET structures. BET analysis supported these results, quantifying increased surface areas and pore volumes conducive to adsorption.

Additionally, TGA assessed the thermal stability of the materials, suggesting that both MIP-PVA and MIP-PET composites maintain their integrity under high temperatures. Collectively, these characterization techniques underline the efficacy of MIP-based composites in the targeted removal of ARVs and NSAIDs, showing their potential for application in environmental remediation. The identification and quantification of the pharmaceuticals in Canadian wastewater using the synthesized MIP and commercial SPE adsorbent to assess the effectiveness of the MIP against commercial sorbent was successfully achieved. The comparable adsorption results are above 98% for both the MIP and SPE sorbent.

Various polymer solutions namely PET and PVA at different degrees of hydrolysis were studied to find the suitable polymer that can be compatible with MIP and NIP materials that are electrospinnable and environmentally friendly to use in water treatment. PVA at 87-90 DH was found to electrospinnable and eco-friendly than the other polymer materials studied and

was thus used to form a PVA-MIP based membrane via electrospinning. The adsorption efficiency of MIP and subsequent MIP-PVA for ARVs and NSAIDs, were successfully achieved with over 90% adsorption capacity in the first 10 minutes of analysis. The data analyzed showed varying concentrations of pharmaceutical compounds across different treatment stages and sites, indicating the effectiveness of the treatment processes in adsorbing pharmaceutical contaminants.

A comparative study between the formed molecular imprinted membrane and non-imprinted membrane was done. The adsorption behaviour of pharmaceutical drugs onto MIM and NIM materials over different time intervals demonstrated higher adsorption of the MIM compared to NIM, validating the benefits of molecular imprinting in enhancing selectivity and adsorption efficiency. However, the study also highlighted the limitations of the MIP-PVA material. Specifically, the MIM started experiencing dissolution after 60 minutes of contact with the solution. To address this issue, it was recommended to crosslink the PVA material with hydrophobic polymers to enhance stability and performance of the membrane.

Generally, this study showcased the potential of MIP-PVA composite materials in the remediation of pharmaceutical pollutants in wastewater. By incorporating nanotechnological approaches, electrospinning techniques, and in-depth material characterization, this study presented a robust framework for removing, identifying and quantifying pharmaceutical contamination in water sources. This study's findings emphasize the importance of efficient extraction methodologies and innovative approaches in addressing environmental challenges and ensuring sustainable water treatment processes. Moving forward, future research in this field could focus on further optimizing the stability and durability of MIP-PVA composite materials in water treatment.

It would be helpful to explore alternative polymers that are hydrophobic that can be mixed with PVA. Developing more adsorption techniques to improve the efficacy of pharmaceutical pollutant removal from wastewater will be helpful considering the water shortage the country faces. By building upon the findings of this study and continuing to innovate in the field of environmental remediation, researchers can contribute to the development of more effective and sustainable solutions for pharmaceutical pollution in water bodies.

5.2 Recommendations for further research on the development and optimization of electrospun MIP based composite for wastewater treatment.

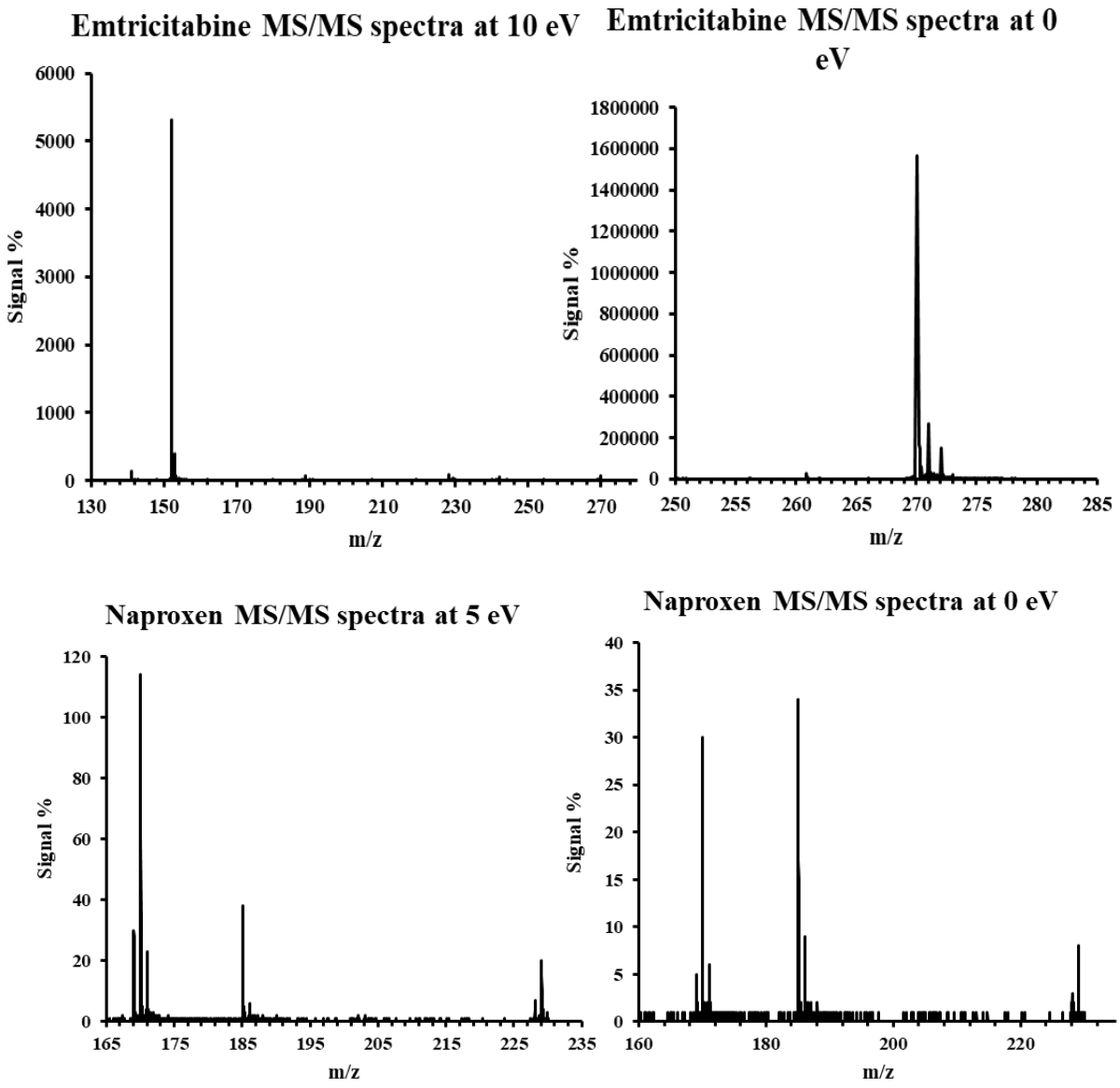
Future studies focusing on the improvement of Molecularly Imprinted Polymer (MIP)-Polyvinyl Alcohol (PVA) based composites could benefit from exploring novel techniques and materials to enhance their performance in adsorption applications. One recommendation for future research is to investigate the incorporation of PET into the composite material. PET is a versatile and durable polymer that could potentially enhance the structural integrity and adsorption capacity of the MIP-PVA composite. Additionally, PET is known for its high chemical resistance and mechanical strength, which could contribute to the overall stability and efficiency of the adsorbent material when using it with an eco-friendly solvent.

In terms of the solvent used for adsorption in wastewater treatment and other applications, it is crucial to consider environmentally friendly options that minimize the impact on the ecosystem. One strong and environmentally friendly solvent that could be explored for adsorption purposes is supercritical carbon dioxide ($scCO_2$). The $scCO_2$ is non-toxic, non-flammable, and readily available, making it an attractive option for environmentally conscious applications. In addition, $scCO_2$ has the advantage of being easily removed from the system after the adsorption process, leaving behind a pure product and minimizing solvent waste.

Furthermore, future studies could focus on optimizing the adsorption process by exploring different operating conditions, such as temperature, pressure, and flow rate, to maximize the adsorption efficiency of the MIP-PVA/PET composite. Additionally, the selectivity of the composite material can be further enhanced by fine-tuning the imprinting process and molecular recognition sites for specific pollutants or contaminants in wastewater. By tailoring the properties of the composite material and the adsorption process to the desired application, researchers can develop highly efficient and selective adsorbents for various environmental and industrial settings.

Overall, future studies in this field should aim to advance the development of sustainable and effective adsorbent materials by exploring innovative materials, incorporating environmentally friendly solvents, and optimizing the adsorption process. By integrating PET into the MIP-PVA composite and utilizing strong yet environmentally friendly solvents like $scCO_2$, researchers can create advanced adsorbents with improved performance and reduced environmental impact for applications in wastewater treatment and beyond.

6 Appendix


Emtricitabine MS/MS spectra at 10 eV
Signal %
m/z
Emtricitabine MS/MS spectra at 0 eV
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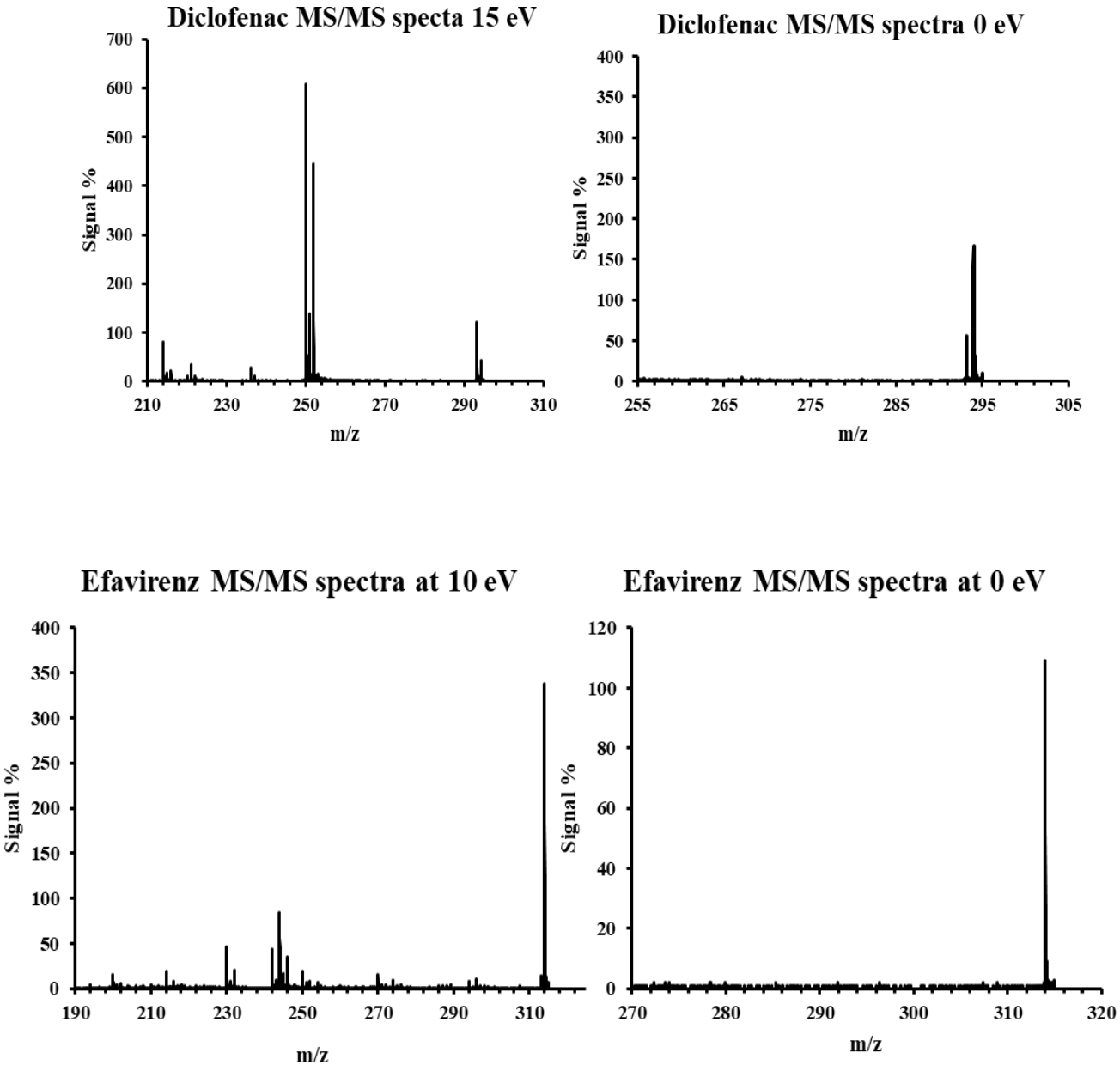
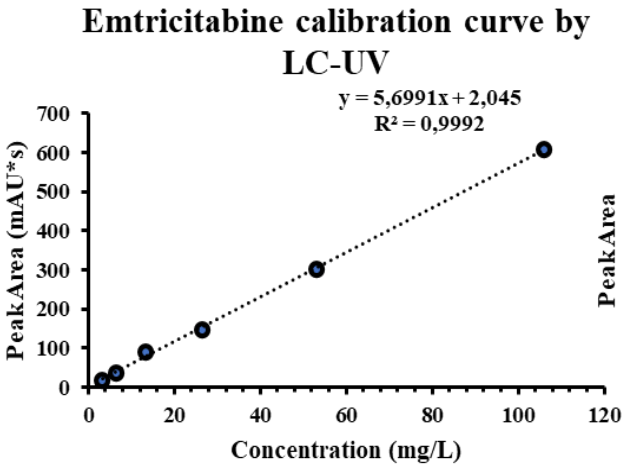
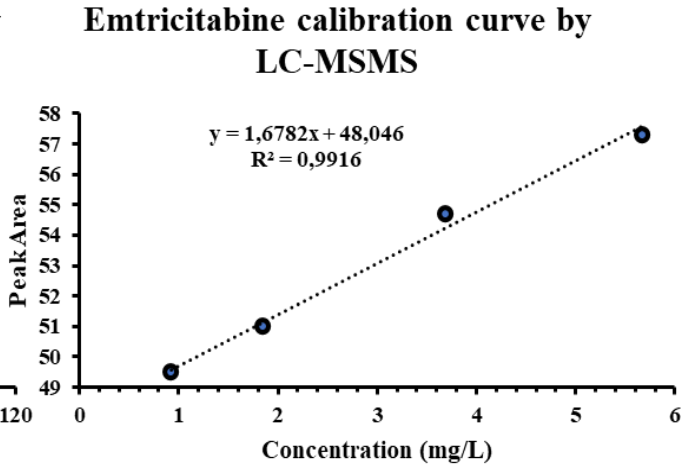
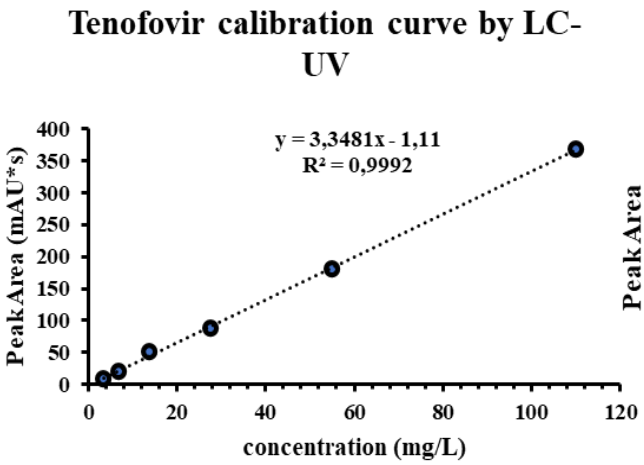
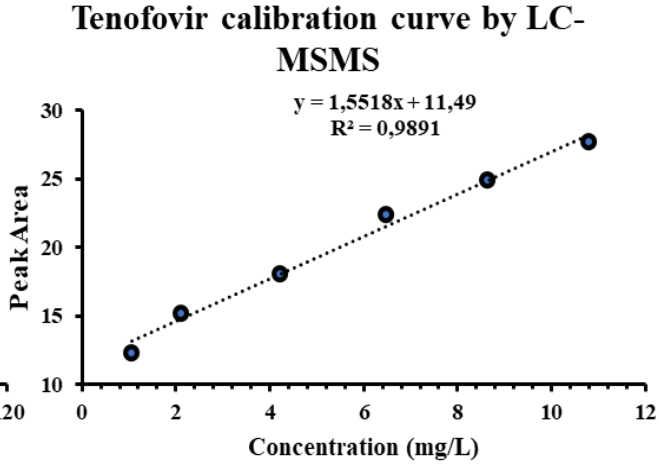


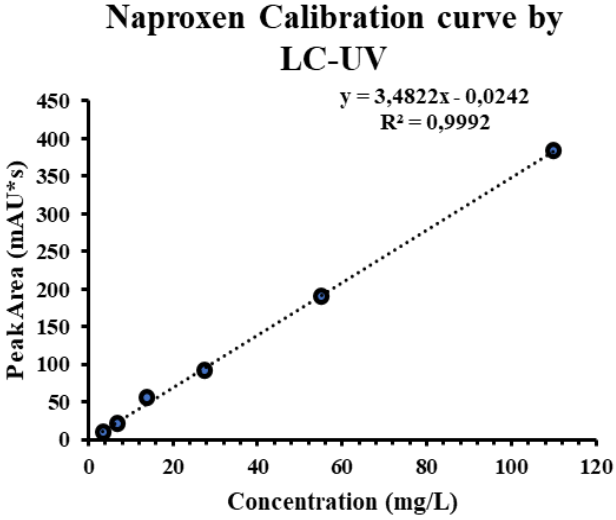
Appendix 1 -1: Comparison of MSMS optimization spectra of compounds at the chosen energy collision energy and of 0eV experiments courtesy of Emilie Drouin

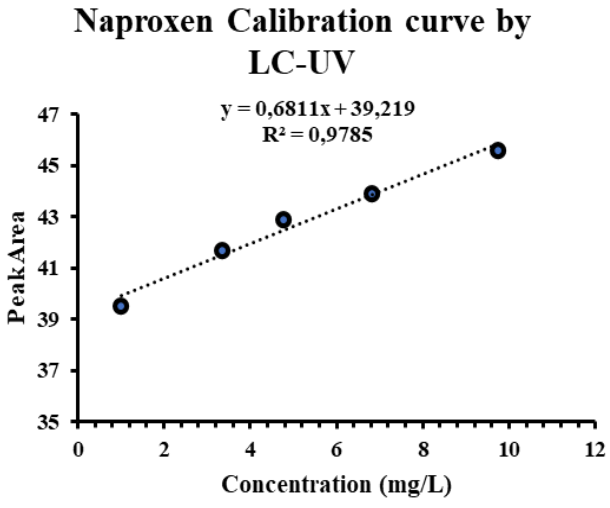

Emtricitabine calibration curve by LC-UV
y = 5,6991x + 2,045
R² = 0,9992
PeakArea (mAU*s)
Concentration (mg/L)

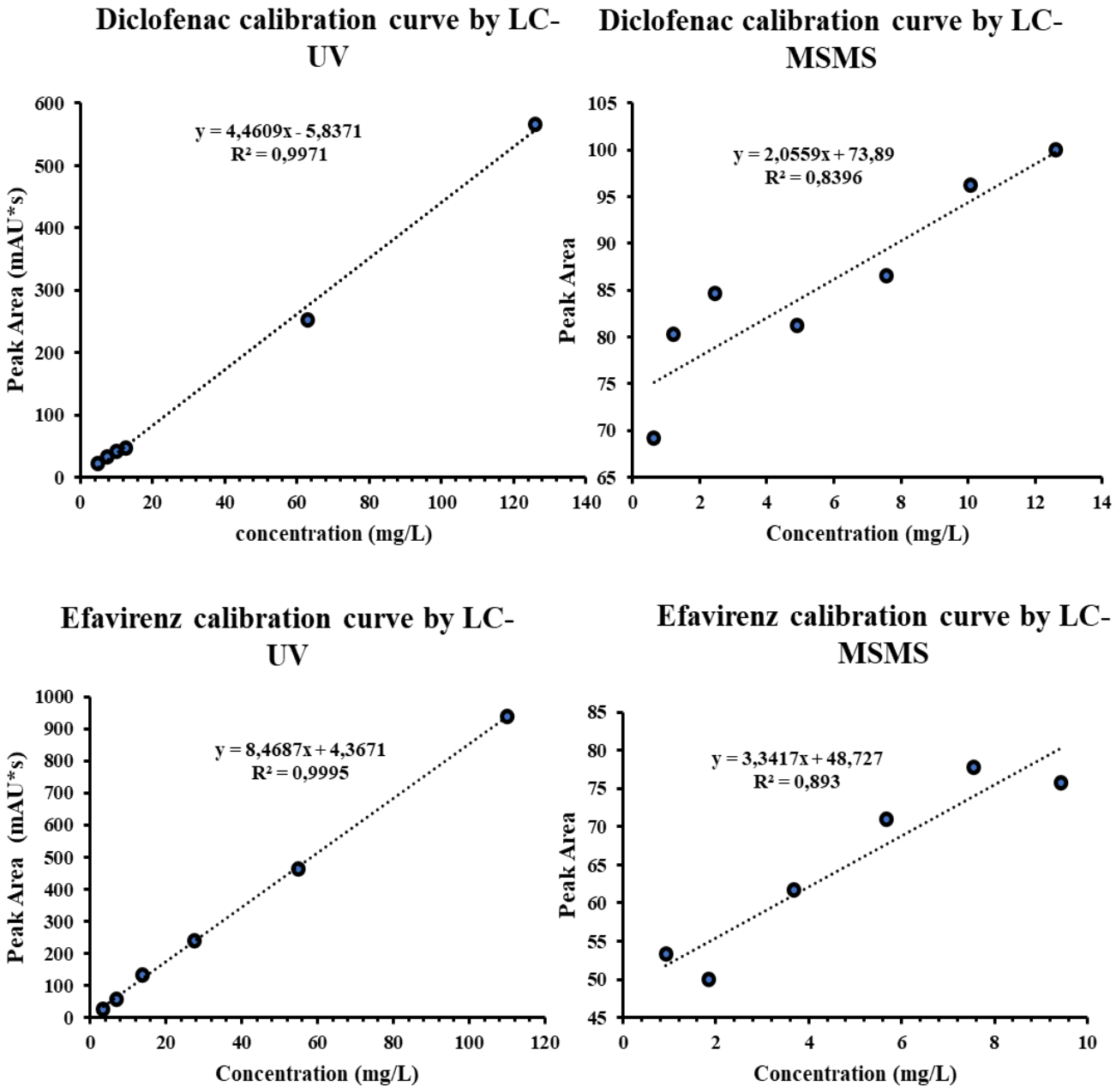

Emtricitabine calibration curve by LC-MSMS
y = 1,6782x + 48,046
R² = 0,9916
PeakArea
Concentration (mg/L)


Tenofovir calibration curve by LC-UV
y = 3,3481x - 1,11
R² = 0,9992
PeakArea (mAU*s)
concentration (mg/L)

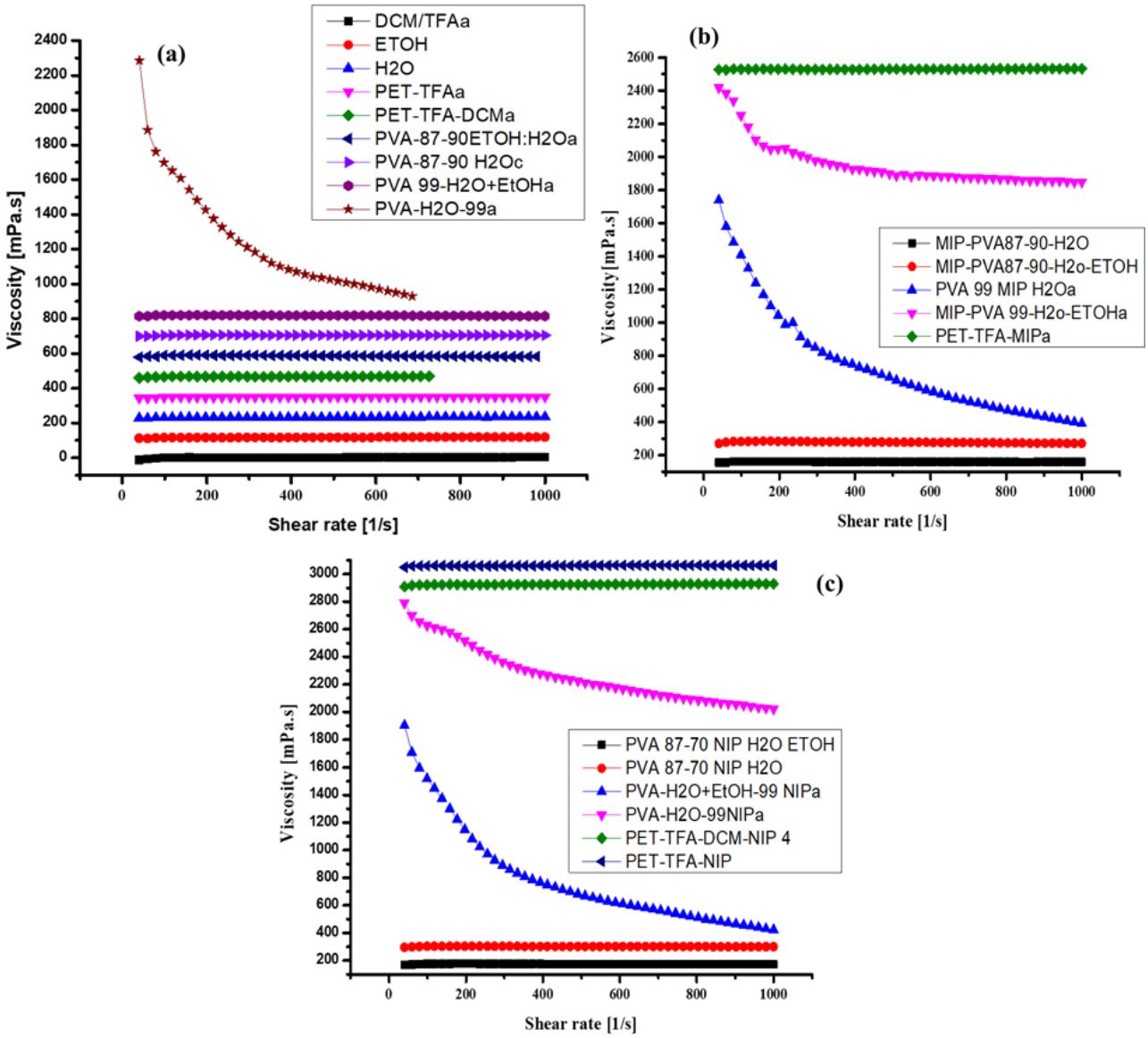

Tenofovir calibration curve by LC-MSMS
y = 1,5518x + 11,49
R² = 0,9891
PeakArea
Concentration (mg/L)


Naproxen Calibration curve by LC-UV
y = 3,4822x - 0,0242
R² = 0,9992
PeakArea (mAU*s)
Concentration (mg/L)

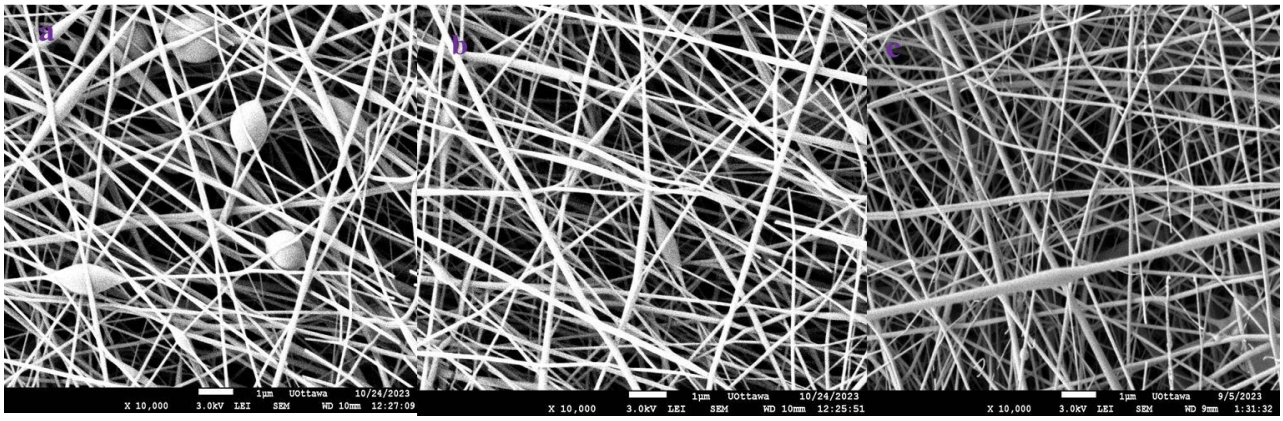

Naproxen Calibration curve by LC-UV
y = 0,6811x + 39,219
R² = 0,9785
PeakArea
Concentration (mg/L)



Appendix 1 -2: Comparative calibration curves of target compounds by LC-UV and LC-MSMS experiments courtesy of Emilie Drouin



Appendix 1- 3: Shear vs viscosity of Solvents, Pure Polymers solutions, Polymer solutions with MIP and NIP



Appendix 1- 4: PVA H_2O SEM images, Flowrate = 0.3 mL/min^{-1}, TCD= 15 cm, needle= 11 G, Voltage (a) 10kV, (b) 15 kV, (c) 18 kV.

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