

MEMORANDUM

To: Ms. N. Muller: Acting Chief Librarian
From: Dr D. F. Naude
Date: 6 May 2003

RE: MASTER'S DEGREE IN TECHNOLOGY : HOMOEOPATHY
Copy of abstract
Miss P. Rielly - Student No: 9802296

Herewith one bound copy and one ring bound copy of the dissertation from the above student, for library purposes.

Please acknowledge receipt

Dr D.F. Naude
Research Co-ordinator
DEPARTMENT OF HOMOEOPATHY

THE EFFICACY OF HOMOEOPATHIC ILEX PARAGUENSIS IN THE
TREATMENT OF NOCTURNAL ENURESIS IN CHILDREN BETWEEN FIVE
AND EIGHTEEN YEARS, RESIDING IN CHILDREN'S HOMES.

By

Patricia Rielly

Dissertation submitted in partial compliance with the requirements for the
Master's degree in Technology : Homoeopathy , in the Faculty of Health
Sciences at the Durban Institute of Technology.

I, Patricia Rielly, do hereby declare that this dissertation is representative of my
own work, both in conception and execution.

.....

16.04.2003

Date of signature

APPROVED FOR FINAL SUBMISSION

.....
f supervisor

01.05.03

Date of signature

Dr. C.M. Hall

B.Sc. (PU for CHE); M. Tech: Hom (TN)

Signature of joint supervisor

Dr. D. F. Naude

M. Tech. Hom (TN)

16/04/03

Date of signature

I DEDICATE THIS STUDY TO MY PARENTS
FOR YOUR LOVE, SUPPORT AND ENCOURAGEMENT.

THANK YOU.

ACKNOWLEDGEMENTS

I extend sincere appreciation to Dr. Corne Hall for supervising this study, and Dr David Naudé for co-supervision.

Special gratitude to Nicholas Nell for his constant support and encouragement.

ABSTRACT

The purpose of this study was to evaluate the efficacy of *Ilex paraguensis* 6x in the treatment of nocturnal enuresis. It was part of a group research project, which intended to explore the effectiveness of a homoeopathic complex (*Cantharis vesicatoria* 12ch, *Equisetum hyemale* 12ch, *Sarsaparilla* 12ch, *Staphysagria* 12ch, *Uva ursi* 12ch); as well as the homoeopathic *simillimum* in the treatment of the above-mentioned disorder.

The research focuses on children between the ages of five and eighteen living in various children's homes in Durban. The incidence of nocturnal enuresis in these institutions is high and poses a real problem to both the institutions and the affected children.

Nocturnal enuresis is categorised into primary and secondary enuresis. Primary nocturnal enuresis is defined as the failure to achieve dryness consistently and accounts for more than 90 percent of all cases of enuresis (Ullom-Minnich, 1996: 2259). Secondary enuresis refers to the return of incontinence after an extended period of dryness (Ullom-Minnich, 1996: 2259). For the purpose of this study this distinction was largely ignored as homoeopathic treatment is not reliant on a detailed diagnosis for its efficacy. The children were however screened for chronic urinary tract infections as well as other neurological and systemic causes

e.g. diabetes mellitus. Each child received a full physical examination as well as a detailed homoeopathic case taking. The aim of the above was to exclude any clear aetiologies as well as to establish the homoeopathic simillimum.

The sample comprised twenty-six children, five received placebo, and twenty-one received *Ilex paraguensis*. This study was part of a larger group research, which comprised of sixty-eight children divided into four groups. Three trial groups of fifteen, sixteen and twenty-one children each, and one placebo group of sixteen children i.e. the placebo group was shared.

An observation period of two weeks with the completion of enuresis diaries was used as a baseline for statistical analysis. The following two weeks formed the treatment period with each child receiving a single powder each evening before bed. The remaining four weeks formed the post treatment observation period. Upon completion of the trial, placebo group children were offered free treatment and those who wished to continue with treatment were referred to the Homoeopathic Day Clinic.

Results were analysed using descriptive and non-parametric statistical procedures. The average number of wet nights was used and the results analysed both within and across the groups. The Mann-Whitney U test was applied to the inter group comparison and the Wilcoxon's Signed Rank test was applied to the intra group comparison.

No statistically significant improvement was noted in either the placebo or treatment group. There was also no statistically significant difference between the two groups. This indicated an absence of response to homoeopathic treatment with *Ilex paraguensis*.

This study failed to demonstrate any clinical improvement in symptoms of nocturnal enuresis. Possible wider psychodynamic improvements or clinical improvements over a longer time period were not measured in this study. Further research could be aimed to assess these areas, before final conclusions can be made about the efficacy of homeopathic *Ilex paraguensis* in the management of nocturnal enuresis.

CONTENTS

Dedication	ii
Acknowledgments	iii
Abstract	iv
Table Of Contents	vii
List of Tables	xii
List of Figures and Graphs	xiv
Definitions Of Terms	xv
1 INTRODUCTION	1
1.1 Introduction	1
1.2 Problem Statement	2
1.2.1 First Objective	2
1.2.2 Second Objective	3
1.2.3 Third Objective	3
1.3 Impact of enuresis	3
1.4 Motivation for research	4
2 REVIEW OF THE RELATED LITERATURE	6
2.1 Introduction	6

2.2	Definition	6
2.3	Anatomy and Physiology of the urinary system	7
2.4	Epidemiology	8
2.5	Aetiology	9
2.6	Treatment	11
2.6.1	Introduction	11
2.6.2	Pharmacological Therapy	11
2.6.2.1	Imipramine hydrochloride	12
2.6.2.2	Anticholinergic therapy	12
2.6.2.3	Desmopressin acetate (DDAVP)	12
2.6.3	Non-pharmacological Therapy	13
2.6.3.1.	Acupuncture therapy	13
2.6.3.2	Chiropractic treatment	13
2.7	Homeopathic treatment	15
2.7.1	Ilex Paraguensis	16
2.7.1.1	Medicinal action and uses	17
2.7.1.2	Chemical composition	17
2.7.1.3	Clinical trial using Ilex paraguensis	18
2.8	Placebo	19
2.9	Conclusion	19

3 MATERIALS AND METHODS	21
3.1 The data	21
3.2 The research methodology	21
3.2.1 Subjects	21
3.2.2 Inclusion criteria	22
3.2.3 Exclusion criteria	23
3.3 Experimental design	23
3.3.1 Initial assessment	24
3.4 The process of randomisation	25
3.5 Homeopathic consultation	27
3.6 Medicine preparation	27
3.7 Treatment and Measurement	28
3.7.1 Observation period	28
3.7.2 Treatment period	29
3.7.3 Follow-up-period	29
3.8 Data analysis	30
3.8.1 Interpretation of data	30
3.9 Ethical considerations	31
3.9.1 Use of placebo	31
3.9.2 Confidentiality	31
3.9.3 Language considerations	32
3.9.4 Side effects of treatment	32
3.9.5 Consent and assent	32

3.9.5 Consent and assent	32
4 THE RESULTS	33
4.1 Introduction	33
4.1.1 Problem statement	35
4.1.1.1 First objective	35
4.1.1.2 Second objective	36
4.1.1.3 Third objective	36
4.1.2 Abbreviations	36
4.2 Criteria for admissibility of data	37
4.3 Descriptive statistics	38
4.4 The analysed data	43
4.4.1 Non-parametric hypothesis testing	43
4.4.1.1 Statistical procedure 1 and 2	43
4.4.1.2 Statistical procedure 3	46
5 DISCUSSION	50
5.1 Indication for the remedy	51
5.2 Posology	51
5.3 Observation Period	52
5.4 Measurement of Improvement	53
5.5 Clinical homoeopathy	54

6 CONCLUSION AND RECOMMENDATIONS	55
7 REFERENCES	58
8 APPENDICES	63
Appendix 1: Case taking form for enuresis research	63
Appendix 2: Minor assent form	71
Appendix 3: Patient information sheet	73
Appendix 4: Parent/guardian Consent Form	81
Appendix 5: Wet night Diary	85
Appendix 6: Drug Side Effects	86
Appendix 7: Research procedure	87

LIST OF TABLES

Table 3.1 Table of gender and age distributions between treatment and placebo groups for <i>Ilex paraguensis</i> trial	26
Table 4.1 Illustration of the different periods of the study.	37
Table 4.2 Comparison based on the percentage differences between the baseline period and the trial period for the treatment and placebo groups.	42
Table 4.3 Comparison of the improvement in the control and the experimental groups based on the percentage differences between the baseline period and the post-trial observation period.	43
Table 4.4 Sample analysis of the placebo group comparing the average number of wet nights of the baseline period to the average number of wet nights of each week of the study using Wilcoxon's Signed Rank test.	44

Table 4.5 Sample analysis of the treatment group comparing the average number of wet nights of the baseline period to the average number of wet nights of each week of the study, using Wilcoxon's Signed Rank test. 45

Table 4.6 Statistical comparison between the placebo and treatment groups for the baseline period using the Mann- Whitney U test. 47

Table 4.7 Statistical comparison between the placebo and treatment groups for the trial period using the Mann- Whitney U test. 47

Table 4.8 Statistical comparison between the placebo and treatment groups for the post-trial observation period using the Mann- Whitney U test. 48

Table 4.9 Statistical comparison between the placebo and treatment groups for each week of the trial using the Mann- Whitney U test. 49

LIST OF FIGURES AND GRAPHS

Fig 4.1 Summary of Results	34
Fig 4.2 Gender distribution of the subjects.	38
Fig 4.3 Age distribution of the subjects (5-8 yrs, 9-12 yrs, 13-18 yrs)	39
Fig 4.4 Age distribution of the subjects.	40
Fig 4.5 Comparison of the average number of wet nights in the placebo and the treatment group.	41

DEFINITIONS OF TERMS

Acupuncture: the Chinese practice of piercing specific areas of the body along peripheral nerves with fine needles to relieve pain, to induce surgical anesthesia, and for therapeutic purposes (Dorland, 1989).

Chiropractic: a system of therapeutics that attributes disease to dysfunction of the nervous system, and attempts to restore normal function by manipulation and treatment of the body structures, especially those of the vertebral column (Dorland, 1989).

Diaphoretic: pertaining to, characterised by, or promoting diaphoresis (Dorland, 1989).

Diuretic: increasing urine excretion or the amount of urine (Dorland, 1989).

Homeopathy: a system of therapeutics based on the administration of minute doses of drugs which are capable of producing in healthy persons symptoms like those of the disease treated (Dorland, 1989).

Placebo: an inactive substance or preparation given to satisfy the patient's symbolic need for drug therapy, and used in controlled studies to determine the efficacy of medicinal substances (Dorland, 1989).

Potency: The term used to indicate the number of serial dilution (either centesimal or decimal) and succussion steps that a remedy has undergone in its manufacture (Das, 1998).

Potentisation: according to Das (1998), homeopathic potentisation is a process by which the medicinal properties which are latent in natural substances, become activated and developed by a procedure of succussion or trituration.

Proving: a drug proving is a systematic and orderly process of investigation of the pathogenetic power of medicine by administering it in different healthy human beings of both sexes, ages and of various constitutions (Das, 1998).

Simillimum: a homeopathic remedy specifically chosen from the entire range of homeopathic remedies, and the pathogenetic action matches the symptom picture of the patient (Das, 1998).

Success: a reduction of 50% or more in the wet night frequency (Leboeuf et al. 1991).

Succussion: a method of potentiising soluble substances by repeated and vigorous shaking of the substance in a liquid carrier (Das, 1998).

Tincture: an alcoholic or hydro-alcoholic solution prepared from animal or vegetable drug or a chemical substance (Dorland, 1989)

CHAPTER 1

INTRODUCTION

1.1 Introduction

The word 'enuresis' is derived from the Greek word "*enourein*" – to void urine. Nocturnal enuresis, or bedwetting, has puzzled physicians for many centuries with medical literature dating back to the Papyrus Ebers BC (Glicklich, 1951). Today, enuresis is defined as "involuntary discharge of urine after the age by which bladder control should have been established.... usually five years (Ullom-Minnich, 1996:2296).

Nocturnal enuresis occurs in 20% of the population (Cendron, 1999:2). Authors from various texts concur with Marla et al. (1996:2259), that 10-20% of five year olds, 5-7% of ten year olds and 2-4% of twelve to fourteen year old children are affected.

Nocturnal enuresis is categorised into primary and secondary enuresis. Primary nocturnal enuresis is defined as the failure to achieve dryness consistently and accounts for more than 90 percent of all cases of enuresis (Ullom-Minnoch, 1996:2259). Secondary enuresis refers to the return of incontinence after an extended period of dryness (Ullom-Minnoch, 1996:2259).

1.2 Problem statement

The objective of the study was to evaluate the efficacy of homoeopathic *Ilex paraguensis* 6x in the treatment of nocturnal enuresis with respect to the number of wet nights per week in children between ages five and eighteen years in children's homes. Improvement was measured as the decrease in the average number of wet nights in a week. From this evaluation, an understanding of the role this method of treatment plays in the management of primary nocturnal enuresis can be gained.

In order to statistically evaluate the effect of the homoeopathic *Ilex paraguensis* three objectives were identified. These allow hypothesis testing to be applied using the relevant statistical procedures.

1.2.1 First Objective

The first objective proposed to evaluate the response of the treatment group to homoeopathic *Ilex paraguensis*, in order to evaluate the role this remedy played in the management of nocturnal enuresis. Wilcoxon's Signed Rank test was used to compare the intra-group data from this group.

1.2.2 Second Objective

The second objective proposed to evaluate the response of the placebo group to placebo treatment, in order to evaluate the role placebo played in the management of nocturnal enuresis. Wilcoxon's Signed Rank test was used to compare the intra group data from this group.

1.2.3 Third Objective

The third objective proposed to compare the responses of the treatment and placebo groups in order to evaluate the efficacy of homoeopathic *Ilex paraguensis* in the treatment of nocturnal enuresis. The Mann-Whitney U test was used for the inter-group comparisons performed.

1.3 Impact of enuresis

Enuresis is a humiliating and potentially psychologically damaging condition for sufferers, with no clear aetiology (Cortina, 1994: 220). Further, current medical treatment of nocturnal enuresis is expensive and has a low efficacy rate (Jalswal, 1989: 332). Lasting cure rates in nocturnal enuresis, using the alarm, imipramine or desmopressin, have been quoted as 43%, 17% and 22%, respectively (van Gool *et al.* 2002:1). In addition the drugs used have side effects, which may

outweigh their potential benefits in treating enuresis Appendix 6. (Cendron, 1999:2; Klauber, 1998:28).

1.4 Motivation for the research

Homoeopathic research on enuresis is scanty, making this an area that needs to be addressed. A study using *Ilex paraguensis* for the treatment of nocturnal enuresis was conducted by Cortina (1994:220-222). The results, however, were compromised by a number of methodological flaws. This study aimed to test the results of the previous research.

According to Cortina (1994:220-222) the mental picture of *Ilex paraguensis* presented the following features: depression, exaggerated reflexes, anxiety, lack of concentration, irritability, sleepiness, aggressiveness, mental and physical restlessness, talkativeness and taciturnity. He felt therefore that *Ilex paraguensis* would benefit children from broken homes who often presented with these types of symptoms. The psychodynamic school of thought see enuresis as a response to environmental stress, usually considered to reflect an underlying emotional disturbance (Butler and Golding, 1986:70). In their research on enuresis Butler and Golding concluded that bedwetting was associated independently with the number of children in the household, low social class, number of cigarettes smoked by mother, lack of father figure, presence of a step-parent and mobility of the family. They also found that boys were more likely than girls to wet their

beds. The high incidence of these associated factors in the children's homes increases the psychodynamic susceptibility of the children in the homes to enuresis. The social stresses experienced by these children manifest in behaviours such as aggression, irritability, anxiety, lack of concentration, restlessness, disruptive behaviour, talkativeness and taciturnity (Butler and Golding, 1986:70). Thus we can see that *Ilex paraguensis*, from a homoeopathic perspective, is indicated by more than just its action on urinary symptoms. This research thus aimed to test this idea in the context of the children's home.

This research was part of a greater research project, involving two other researchers. They were also researching enuresis; one using homeopathic *simillimum* (Bloch, 2002), and the other using a complex (*Cantharis vesicatoria* 12ch, *Equisetum hyemale* 12ch, *Sarsaparilla* 12ch, *Staphysagria* 12ch, *Uva ursi* 12ch) (Lockyear, 2002). The research was designed in such a way that the researchers shared a common placebo group.

This research provides a basis for further research involving homeopathy and enuresis. It also provides possible alternatives for the treatment of enuresis on a sustainable non-invasive level. This study was based on the assumption that enuresis is treatable, as it is part of a non- organic symptom complex. It was assumed that *Ilex paraguensis* would be efficacious in treating enuresis and that a two-week treatment period would be sufficient to show a response to treatment.

CHAPTER 2

REVIEW OF THE RELATED LITERATURE

2.1 Introduction

The following literature review focuses on the available literature regarding nocturnal enuresis, the physiology of this condition, and the current medical and homoeopathic trends towards the management and treatment of the condition. *Ilex paraguensis* and its use in treating enuresis will also be discussed.

2.2 Definition

Enuresis may be defined as "involuntary discharge of urine after the age by which bladder control should have been established... usually five years" (Ullom-Minnich, 1996:2259). Nocturnal enuresis is described by Norgaard et al. (1998:1) as the voiding of urine in bed at night without the child noticing it. Most authors further subdivide enuresis into primary and secondary types. "Primary enuresis is the failure to achieve dryness consistently

and accounts for more than 90 percent" whereas "secondary enuresis refers to the return of incontinence after an extended period of dryness" (Ullom-Minnich, 1996:2259). Norgaard et al. (1998:2) suggest that secondary enuresis should include an extended period of dryness of 6 months or more. According to Medel et al. (1998:50) nocturnal enuresis should be further classified into mono-symptomatic and complicated types depending on whether bedwetting is the only symptom or is associated with urinary tract infections, diurnal incontinence or urgency. Thus for the purposes of this research mono-symptomatic primary and secondary enuresis will be considered thereby separating children with a definable aetiology from those without.

2.3 Anatomy and physiology of the urinary system

The urinary system consists of the kidneys, the ureters, the bladder and the urethra. These structures form a functional unit, which collects transports, and eliminates metabolic waste products as urine. The functional component that is central to primary nocturnal enuresis is the urinary bladder.

The urinary bladder is a hollow organ with thick muscular walls. It's shape, size, relations and position vary with the amount of urine it contains and with the age of the person. The bladder walls are chiefly composed of smooth muscle arranged in three layers: the external and internal layers of longitudinal fibres and the middle layer of circular fibres. Toward the neck of the bladder these fibres

form the involuntary internal sphincter. This sphincter, in its contracted state, prevents emptying of the bladder (Moore, 1992)

The bladder receives both sympathetic and parasympathetic innervation. The sympathetic innervation is received from T11, T12, L1 and L2 nerves. These fibres are inhibitory to bladder emptying. The parasympathetic supply is received from the pelvic splanchnic nerve (S2, S3 and S4). These fibres are inhibitory to the internal sphincteric muscle of the bladder and motor to the detrusor muscle, thus stimulating bladder emptying (Moore, 1992). On stretching of the bladder wall (i.e. filling) the parasympathetic component is activated, the internal sphincter is relaxed and the bladder contracts. This only results in urination if the voluntary sphincter (external sphincter) is relaxed. Control of this sphincter is learnt in the first few years of life (Toffler et al., 1991).

2.4 Epidemiology

There are no epidemiological studies in South Africa on the subject of enuresis. Authors from various texts concur with Marla et al. (1996:2259), that 10-20% of five year olds, 5-7% of ten year olds and 2-4% of twelve to fourteen year old children are affected. Cendron and Klauber (1998:26) report a spontaneous resolution rate of 15%, which is supported by other authors. Cendron (1999:2) further states that an estimated five to seven million children are affected in the

United States. The above figures suggest a notable prevalence despite the lack of local verification.

2.5 Aetiology

The aetiology of primary nocturnal enuresis has been widely debated but is not yet completely understood. Primary nocturnal enuresis is a diagnosis of exclusion and all other causes of bedwetting must be ruled out, (Cendron 1999:2). Causes of secondary enuresis include neurogenic, bladder and associated spinal cord abnormalities, urinary tract infections, and the presence of posterior urethral valves in boys or an ectopic ureter in girls. Posterior urethral valves cause significant voiding symptoms, such as straining to void and diminished urinary stream. An ectopic ureter causes constant wetting (Cendron 1999:2).

The aetiology of primary nocturnal enuresis remains somewhat controversial (Ullom-Minnich, 1996:2259), and the condition appears to be multifactorial (Cendron, 1999:2). In addition, the well-recognised spontaneous resolution rate clouds the search for causative mechanisms. Finally, the various treatment approaches and modalities are influenced by the patient's family environment and by the background and prejudices of the patient, the parents and the physician (Cendron, 1999:2).

Butler and Golding (1986:79) found a significant correlation between enuresis and social class, single parent, and mobility of family. The prevalence of bedwetting was higher in the manual social classes. There was a trend within urban areas such that the rate of enuresis was highest in 'poor' neighbourhoods, and lowest in the 'well-to-do' areas (Butler and Golding, 1986:71). These differences are, of course, largely to be expected from the social class distribution.

There was a positive association with household mobility: the more times the child had moved house, the more likely was he or she to wet the bed. A strong association was shown with the number of other children in the household. 'Only' children had a very low prevalence of bedwetting, whereas children with four or more siblings had twice the risk (Butler and Golding, 1986:75).

Even more relevant to this research was the association found with the parental situation; the children of unsupported single parents having the highest prevalence. This prevalence was even higher if the single parent was the father. Children in children's homes had a sixty percent chance of bedwetting (Butler and Golding, 1986:75).

Butler and Golding (1986:76) conclude in their study that low social class and separation from a natural parent are of major importance in the aetiology of enuresis.

Other possible aetiologies of primary nocturnal enuresis include developmental delay, genetics, sleep disorder, behaviour and psychogenic disorders (Cendron, 1999:2), constipation, increased diuresis at night due to low levels of antidiuretic hormone (Ullom-Minnich 1996: 2261) and endocrine problems (Norgaard et al. 1991).

2.6 Treatment

2.6.1 Introduction

The treatment of and therapeutic approach to nocturnal enuresis is complicated by the multifactorial nature of the condition, lack of clear aetiology and paucity of pathophysiological understanding (Cendron, 1999;2). The treatment can be divided into two broad categories, pharmacological and non-pharmacological. The main treatments are outlined.

2.6.2 Pharmacological therapy

Drug therapy is reserved for children over the age of seven. It works either by increasing the bladder capacity or decreasing the urine produced by the kidneys (Cendron, 1999:7).

2.6.2.1 Imipramine hydrochloride

This drug has been used for approximately 25 years. It is hypothesised to either alter the sleep and arousal mechanism, affect sympathetic innervation of the bladder, increase the secretion of anti-diuretic hormone or a combination of these (Cendron, 1999:9). Success rates range from 25 to 50% with a 30% relapse rate (Ullom-Minnich, 1996:2259). Side effects are common and range from insomnia to personality changes and nervousness, as well as the danger of overdose (Cendron, 1999:9) (see Appendix 6).

2.6.2.2 Anticholinergic therapy

Studies done on the effectiveness of Oxybutynin and Hyoscyamine are limited. They appear to act on smooth muscle, causing the bladder capacity to contract (Ullom-Minnich, 1996; 2264). Side effects range from constipation to dizziness and tremors (Cendron, 1999:9). Cendron and Klauber(1998) demonstrated a 60% success rate in a study using Hyoscyamine and Desmopressin combined. The relapse rate however was high, pointing to palliation rather than cure.

2.6.2.3 Desmopressin Acetate (DDAVP)

Desmopressin is an antidiuretic, decreasing urine production at night by raising ADH levels. The success rate varies between studies, but all confirm limited if

any side effects. Desmopressin is fast acting and thus useful in cases of parental intolerance or to avoid embarrassment if a child is sleeping away from home. In a 7-year follow up study on the effect of Desmopressin Lackgren et al. (1998) demonstrated a significant cure rate, which was maintained after the termination of the therapy. The children outgrowing bedwetting naturally could have affected the cure rate, or as a result of the attention they received. It is presently the drug of choice. In a Cochrane review looking at trials using Desmopressin in enuresis Glazener (2001:2) concluded that Desmopressin rapidly reduced the number of wet nights per week, but that there was some evidence that this was not sustained after treatment stopped.

2.6.3 Non-pharmacological therapy

According to Ullom-Minnich (1996), non-pharmacological treatments are usually used in combination with one another or in conjunction with pharmacological treatments. Ullom-minnich (1996) evaluates each approach. The alarm system is approximately 70% effective with a relapse rate of 30%. Bladder stretching, in which the child has to withhold urination for increasing amounts of time has an improvement rate of 60% but is time consuming and requires motivation. Dry bed training, which includes night waking, cleanliness training, positive practice and the alarm has an 85 to 100% success rate and is considered a good treatment option. Hypnosis has a 40- to 70% success rate but is expensive.

2.6.3.1 Acupuncture therapy

In a study by Serel et al. (2001) on fifty children suffering from nocturnal enuresis the results showed that treatment using acupuncture appeared to be efficacious both in terms of the percentage dry nights at the end of treatment and in relation to the stability of results.

2.6.3.2 Chiropractic treatment

In a single blind placebo controlled study involving thirty children, Grobler (1996) had a success rate of 40% of subjects in the treatment group. These results suggested a statistically significant clinical effect of chiropractic therapy in the treatment of functional nocturnal enuresis. The study could have shown more significant results if the follow up period used was extended. A further improvement could have been recorded if the adjustments used to treat the patients were chosen on a more individual basis (Grobler, 1996).

Gemmell and Jacobson (1989), published a review of research done on enuresis and concluded that the patients' enuresis resolved with the use of manipulation and that this happened in a manner that could not be attributed to time or placebo effect.

2.7 Homeopathic Treatment

Homoeopathy is a system of medicine devised at the end of the eighteenth century by a German physician, Samuel Hahnemann. The foundation principles of homoeopathy were laid down after extensive experimentation and scientific observation. These principles are: The law of similars (a substance in dilution cures what it can produce in a healthy subject), the minimum dose (the least amount necessary to effect a cure based on the fact that the medicinal action of a substance is facilitated by successive dilution and succussion) and the totality principle (disease and health are manifest on all levels of the organism – physical, emotional and mental). (Vithoulkas, 1980). The understanding and application of these principles has been developed over the last two centuries, by homoeopathic physicians around the world.

Homoeopathic remedies are sourced from a wide range of substances, both artificial and natural; animal, vegetable and mineral. A substance is serially diluted either centesimally (1:99) or decimally (1:9)(Das, 1998). Between each dilution stage the remedy undergoes a vigorous shaking process known as succussion, which aids the dilution process as well as facilitating the transfer of medicinal information to the macrostructure of the water/alcohol mix that acts as diluent (Vithoulkas, 1980).

Homoeopathic treatment is aimed at correcting a basic bio-energetic pattern

which is manifested by a symptom complex. The symptom complex is the totality of the symptoms (physical, emotional and mental) which distinguish the patients state from a healthy state. (Vithoulkas, 1980). This form of treatment relies on physical doses of therapeutic substances as well as serially diluted and potentised remedies. Treatment with a particular remedy is indicated by the degree of similarity of the patient's symptom complex to the remedy picture (symptomatology created by the remedy). The response of the patient to the remedy is directly proportional to the degree of similarity between the remedy picture (totality of symptoms produced by the substance in a healthy person) and the patient's symptom complex.

2.7.1 *Ilex paraguensis*

Ilex paraguensis belongs to the Aquifoliaceae family and originates in South America. Mate tea is an infusion of the leaves of *Ilex paraguensis*. Its name "Yerba" signifies the herd "par excellence", and the consumption in South America is vast, as it is drunk at every meal and hour (Grieve, 2002). "Mate" is derived from the name of the vessel in which it is infused in the manner of tea, burnt sugar or lemon juice being added. It is sucked through a tube, usually of silver, with a bulb strainer at the end, and the cup is passed around (Grieve, 2002). Common names for the plant include mate`, yerba mate`, Jesuit's tea, Brazil tea, Houx Mate`, Go`n gouha and South American holly (Centers, 1995).

2.7.1.1 Medicinal action and uses

The tea is very sustaining, and sometimes the only refreshment carried for a journey of several days. It is also a tonic, diuretic, diaphoretic, and powerful stimulant. In large doses it causes purging and even vomiting (Grieves, 2002).

2.7.1.2 Chemical composition

Caffeine, theophylline, and theobromine are natural components of the leaves. These are also found in coffee, guarana and cocoa beans. According to Saldana et al. (1999), these alkaloids act as stimulants on the human body, affecting the central nervous system, muscles and cardiovascular system. Estimates of caffeine intake due to mate tea consumption far exceed intakes recorded in the literature from other beverages containing this alkaloid (Saldana et al. 1993). According to Cortina (1994:221), the active constituent in the treatment of enuresis is a stimulating alkaloid called mateine, which in large doses causes marked nocturnal diuresis with deep sleep and unresponsiveness. This leads to its homoeopathic indication in this condition.

In this study a potency of 6x was used. This indicates that the base substance (*Ilex paraguensis* tincture) has been diluted 6 times in a decimal ratio (1: 9). This

potency is what is termed a low potency. At this level of dilution the remedy still contains traces of the chemical constituents of the original crude substance. The action of the remedy is thus partially a result of these chemical constituents.

2.7.1.3 Clinical trial using *Ilex paraguensis*

A trial conducted by Cortina (1994:220) involved twenty enuretic children treated over two months with *Ilex paraguensis* administered in a herbal tea form. The results were complete disappearance of enuresis and improvement of concomitant psychological symptoms in 50% of the children. The trial contained the following short falls, providing an opportunity for further research.

- The trial was not placebo controlled
- There was no observation period prior to the treatment period
- There was no follow up period after the treatment period
- The trial was based on a clinical rather than an experimental model
- Methodology employed in measuring wet or dry nights was not mentioned
- Statistical analysis was insufficient
- References were incomplete

2.8 Placebo

A placebo is an intervention designed to simulate medical therapy but not believed to have a specific effect on the condition to which it is being applied (Ellis S.J., Adams R.F., 1997).

In this study the placebo group were given identical powders to the experimental groups. A common placebo group was used to compare the effects of homoeopathic simillimum (Bloch,2002), homoeopathic complex (Lockyear,2002) and homoeopathic Ilex paraguensis, in the treatment of nocturnal enuresis.

The debate on the applicability of the double-blinded, placebo-controlled randomised clinical trial to homoeopathic research (Harris, 1970) is beyond the scope of this discussion.

2.9 Conclusion

From the literature reviewed in this chapter it is evident that:

- A large number of children suffer from enuresis (both relatively and absolutely). It thus has a significant social footprint in terms of its effects on a general population.

- Enuresis significantly affects the quality of life of the sufferer with possible long-term effects on the self- image and confidence of the individual.
- Current treatment options remain less than optimal, both in terms of side effects and in terms of efficacy (short, medium and long term).
- Homoeopathic alternatives to medical treatment do exist, but need to be explored further.
- *Ilex paraguensis* is a potentially promising remedy for the clinical treatment of nocturnal enuresis, but the results derived by Cortina (1994) need to be tested as a prerequisite for wider acceptance and use.

CHAPTER 3

MATERIALS AND METHODS

3.1 The Data

Primary and secondary data were utilised in this study. The primary data were represented by the number of wet nights the subjects presented with, as well as the medical records of each subject.

Secondary data were obtained from the available literature on enuresis, as well as information sourced from the Internet.

3.2 The research methodology

3.2.1 Subjects

The sample group was obtained by approaching children's homes in the local Durban area. The sample comprised twenty-six children between five and eighteen years old; five received placebo, and twenty-one received *Ilex paraguensis* 6x. All participants had to meet inclusion criteria (Pg 21, 3.2.2).

This study was part of a larger group research, which comprised of sixty-eight children divided into four groups: three treatment groups of fifteen, sixteen and twenty-one children each, and one placebo group of sixteen children. Of the other two trial groups, one received simillimum (Bloch, 2002) and the other a homoeopathic complex consisting of *Cantharis vesicatoria* 12ch, *Equisetum hymenale* 12ch, *Sarsaparilla* 12ch, *Staphysagria* 12ch and *Uva ursi* 12ch (Lockyear, 2002). The trials for all three groups ran simultaneously and shared a placebo group. Results for each trial were documented separately.

3.2.2 Inclusion criteria

All the participants had to meet the following inclusion criteria.

- Age falling between five and eighteen years.
- Satisfying the DSM 4-R (307.6) criteria which states:
 - " A. Repeated voiding of urine into bed or clothes (whether intentional or involuntary).
 - B. The behaviour is significant as manifest by either a frequency of twice a week for at least three consecutive months or the presence of clinically significant distress or impairment in social, academic (occupationally), or other important areas of functioning.
 - C. Chronological age is at least five years (or equivalent developmental level).

D. The behaviour is not due exclusively to the direct physiological effect of a substance (e.g., a diuretic) or a general medical condition (e.g., spina bifida, a seizure disorder, diabetes). " (DSM-4, 1995:109).

- Completion and signing of the assent form, by the subject.
- Completion and signing of the consent form by the subject's guardian.
- Subjects had to reside at the various homes.

3.2.3 Exclusion criteria

- Use of other enuresis-related treatment.
- Relevant anatomical, neurological or structural abnormalities.
- Presence of any other illness that may, clinically, have contributed to their enuretic condition.
- Lactose intolerance.

3.3 Experimental design

Children's homes were contacted and asked if they are interested in participating in the research study. They were then asked to provide an estimate of the number of children who bedwet and the number of incidences per child. At this stage no names were mentioned, ensuring confidentiality of the subjects.

Following this, a meeting with the guardians and caregivers was conducted. The objectives and methods, including homoeopathic consultation, treatment and physical examination, were explained in detail. (The homes are divided into cottages, each with a group of children and a full time house parent.) The input of house parents was included in the design methodology in order to ensure their co-operation in the research programme.

Once they understood the procedure the guardians were required to sign the guardian consent form. (Appendix 1) In addition each participant was asked to sign an assent form (Appendix 2) if they agreed to participate in the study.

3.3.1 Initial assessment

At the beginning of the initial assessment, the homoeopathic consultation, treatment and physical exam procedures were explained to each subject. The subjects, who agreed to participate, were then asked to sign an assent form. (Appendix 2) The assent form is the equivalent of a consent form but worded in such a way as to make it child friendly.

The initial consultation included a physical examination (Appendix 5) and a medical case history (Appendix 1) aimed at establishing any known causes of nocturnal enuresis e.g. urinary tract infection. The subject's medical files, which are kept at the homes, were examined with the guardian's consent. The purpose

of this consultation was to ensure that participants met the inclusion criteria (pg 14). The subjects were screened for infrequent or day time wetting, recurrent urinary tract infections, anatomical and neurological abnormalities that might have resulted in nocturnal enuresis, and systemic or metabolic causes of enuresis e.g. hyperglycaemia. A urine sample was taken for dipstick analysis to exclude any possible urinary infections or glucosuria.

All examinations, special tests and treatment administered to the subjects during this study were free of charge.

3.4 The Process of Randomisation

The study was placebo controlled, double blind and randomised. The sixty-eight subjects were randomly divided into three groups (homoeopathic simillimum - project 1, homoeopathic complex –project 2, and Ilex paraguensis – project 3); in addition each group was randomly subdivided into a placebo and treatment group. The purpose of the randomisation was to ensure the double blind nature of this trial; and was performed by the supervisor. Subject's names were written on a piece of paper and placed in a hat. The supervisor then allocated, in sequential order, a name to each group, thereby dividing the original group of sixty-eight into two groups of twenty-three and one of twenty two. The same process was then followed for each sub-group, with the exception that every fourth name was allocated to the placebo group thereby dividing the original

group of twenty-two into two sub-groups of sixteen (treatment group) and six (placebo group). Thus the researchers had effective treatment groups of fifteen, sixteen, and twenty-one and a shared placebo group of sixteen (two groups of five and one of six). It was possible to share the same placebo group as the criteria for the research was the same for each of the three research projects.

Upon completion of randomisation the supervisor assessed the groups for reasonable uniformity in terms of gender and age distribution. At this point the process of randomisation could have been repeated in order to assure uniformity of all groups.

All the names and their corresponding treatments were noted on a sheet and referred to for dispensing purposes and statistical analysis once the study was complete. The gender and age distribution of the treatment and placebo groups for this study were as follows.

Table 3.1 Table of gender and age distributions between treatment and placebo groups for *Ilex paraguensis* trial

	Treatment Group	Placebo Group
No of Male	13	9
No of Female	8	7
Age 5-12	20	14
Age 13-18	1	2

3.5 Homoeopathic consultation

A homeopathic consultation was conducted with each subject. (Appendix 4).

A physical examination was performed and the subject's medical records examined with permission. Upon completion of this stage the simillimum was established for each child. The homeopathic scripts were forwarded to the supervisor who then modified them according to the randomisation schedule (i.e. placebo vs. treatment).

3.6 Medicine preparation

An appointed member at the Durban Institute of Technology Homoeopathic Clinic prepared the scripts. The homoeopathic remedies were prepared in granules, which were then dispensed in lactose powders. The *Ilex paraguensis* was obtained from Natura laboratories in tincture form. This was then taken up to a 6x potency using 96% ethanol. The process involved taking one drop of the tincture and adding it to ninety-nine drops of ethanol and then succussing the bottle one hundred times. The resultant mixture was labelled *Ilex paraguensis* 1x. The same procedure as above was carried out using the 1x potency, to make a 2x potency.

This was repeated until the 6x potency was reached. Lactose granules were then triple impregnated with the *Ilex paraguensis* 6x, which were then dispensed in lactose powders.

The placebo group received lactose powders containing un-medicated granules.

The granules were triple impregnated with 96% ethanol.

Each child received fourteen numbered powders, in two packs of seven. All 14 powders in the treatment group contained medicated granules. The appearance, presentation and administration of powders were identical for all three treatment groups, and the placebo group.

3.7 Treatment and measurement

3.7.1 Observation Period

After the homeopathic consultation the subjects were observed for two weeks to determine the baseline number of wet nights per week. To facilitate this process each subject was provided with a weekly diary (Appendix 6) that was ticked off each morning by the resident house parent. The diary was collected at the end of each week by the researcher, and a new one provided. This allowed the house parent to communicate any problems with diary keeping to the researchers.

3.7.2 Treatment Period

The treatment period lasted for two weeks. At the beginning of each week, each subject received powders numbered 1 to 7 along with a 7-day diary. The powders were taken one daily before bed. At the end of each week diaries were collected and the following week's 7 powders and diaries provided. This provided an opportunity for house parents to communicate any difficulties with diaries or medication. This also provided an opportunity to ensure compliance and hence more reliable data.

3.7.3 Follow-up Period

The follow-up observation period lasted for four weeks. This was again achieved by the use of weekly diaries. There was a final consultation at the end of this period. Children who had shown improvement were referred to the homoeopathic day clinic and placebo group members were identified and offered free treatment.

3.8 Data Analysis

The body of data obtained was processed using the following statistical methods. Summary Statistics were applied to the raw data to see if any obvious trends were apparent. These included the gender ratio, average no. of wet nights for each week of the study, and age ranges of the subjects.

Wilcoxon's Signed Rank test was used to evaluate the significance of any changes within each of the groups (statistical procedure 1 and 2). This was done with respect to objectives 1 and 2 (see 4.4.1 and 4.4.2). The results within each group were compared from week to week and between the different periods of the study.

The Mann-Whitney U test used to compare treatment and placebo groups (inter-group), was used to assess the significance of the differences between the average numbers of wet nights in each of the groups for the relevant periods in the trial (trial and post-trial observation). This inter-group comparison formed objective 3 (see 4.4.3; Statistical procedure 3).

3.8.1 Interpretation Of Data

The results obtained in Chapter 4 (as described in 3.9) were used to draw the conclusions reached.

3.9 Ethical considerations

3.9.1 Use of Placebo

This was a double blind placebo study. Enuresis is not a life threatening condition, nor were the children in the homes being treated for enuresis prior to

the study. Bearing this in mind the researchers considered it ethically acceptable to give placebo. Thus by administering placebo, the subjects were not being denied any other treatment. At the completion of the study those that received placebo were informed and offered treatment free of charge.

All subjects were informed about the possibility of receiving placebo and entered the research willingly, with this knowledge.

3.9.2 Confidentiality

Confidentiality was ensured as all subjects were only referred to in terms of numbers and percentages, as opposed to names.

Confidential data was retained until the completion of the research. The confidential information was then handed over to the respective children's homes for their medical records.

3.9.3 Language Considerations

Most subjects were familiar with English. Zulu translations of the subject information letter (Appendix 3), and consent form (Appendix 2), were made for those requiring it.

3.9.4 Side Effects of Treatment

Only homoeopathic remedies were used. All remedies have been clinically proven and have no known side effects.

3.9.5 Consent and Assent

Written consent was obtained from the management of each home and assent was obtained from each subject taking part in the research. In this research project 'minors' were considered persons younger than eighteen years.

CHAPTER 4

RESULTS

4.1 Introduction

The data from the wet night diaries were used to derive the results. After the initial consultation the exclusion criteria were applied and the randomisation procedure conducted on the remaining subjects.

Both descriptive and non-parametric procedures were performed to obtain the results. These tables and figures are summarised in Fig 4.1.

Fig 4.1 Summary of Results

Chapter 4: Results		
<p>Demographic Data</p> <p>Figure 4.2 Gender Distribution</p> <p>Figure 4.3 Age Distribution of Subjects</p> <p>Fig 4.4 Age Distribution of Subjects</p>	<p>Average No. of Wet Nights per Week</p> <p>Table 4.2 Comparison based on the percentage differences between baseline period and trial period</p> <p>Table 4.3 Comparison based on the percentage differences between baseline period and post-trial period</p> <p>Figure 4.4 Comparison of average number of wet nights in placebo and treatment groups</p>	<p>Non-Parametric Tests</p> <p>Procedures 1 and 2 Wilcoxon's Signed Rank tests Tables 4.4 – 4.5</p> <p>Procedure 3 Mann-Whitney U Test Tables 4.6 – 4.9</p>

4.1.1 Problem statement

This study aimed to evaluate the efficacy of homoeopathic *Ilex paraguensis* 6x in the treatment of primary nocturnal enuresis, in terms of the number of wet nights experienced by a child in a week. Improvement was measured as the decrease in the average number of wet nights in a week. From this evaluation, an understanding of the role this method of treatment plays in the management of primary nocturnal enuresis can be gained.

In order to statistically evaluate the effect of the homoeopathic *Ilex paraguensis* three objectives were identified. These allow hypothesis testing to be applied using the relevant statistical procedures.

4.1.1.1 First objective

The first objective proposed to evaluate the response of the treatment group to homoeopathic *Ilex paraguensis* 6x, in order to evaluate the role this played in the management of nocturnal enuresis. Wilcoxon's Signed Rank test was used to compare the intra-group data from this group (Statistical procedure 1).

4.1.1.2 Second objective

The second objective proposed to evaluate the response of the placebo group to placebo treatment, in order to evaluate the role placebo played in the management of nocturnal enuresis. Wilcoxon's Signed Rank test was used to compare the intra group data from this group (Statistical procedure 2).

4.1.1.3 Third objective

The third objective proposed to compare the responses of the treatment and placebo groups in order to evaluate the efficacy of homoeopathic *Ilex paraguensis* 6x in the treatment of nocturnal enuresis. The Mann-Whitney U test was used for the necessary inter-group comparisons performed (Statistical procedure 3).

4.1.2 Abbreviations

The following terms and abbreviations were used:

p = probability of equalling or exceeding $\alpha/2$

n/s = no significant difference in the medians

s = significant difference in the medians

H_0 = Null hypothesis

H1 = Alternative hypothesis

Wk = week

If $P < 0.05$ then no significant difference was concluded (5% level of significance)

If $P \geq 0.05$ then no significant difference was concluded (5% level of significance)

Success= a 50% or greater reduction in the average number of wet nights.

Treatment group= the group of children receiving *Ilex paraguensis*.

Placebo group= the group of children receiving placebo.

Baseline period= the 2 week period of observation prior to treatment.

Trial period= the 2 week period during which the children received treatment.

Post-trial observation period= the 4 week period following the treatment period.

Table 4.1 Illustration of the different periods during the study.

Baseline Period		Trial Period		Post-trial Observation Period			
Wk 1	Wk2	Wk 3	Wk 4	Wk 5	Wk 6	Wk 7	Wk 8

4.2 Criteria for Admissibility of Data

- Data was accepted only from subjects satisfying the inclusion criteria. This included informed consent of the subjects as well as the legal guardian.

- Only data collected from the Wet Night Diaries completed for each child, was used or admissible.
- The data was admissible only if the diaries were correctly completed.

4.3 Descriptive statistics

Fig 4.2 Gender distribution of the subjects.

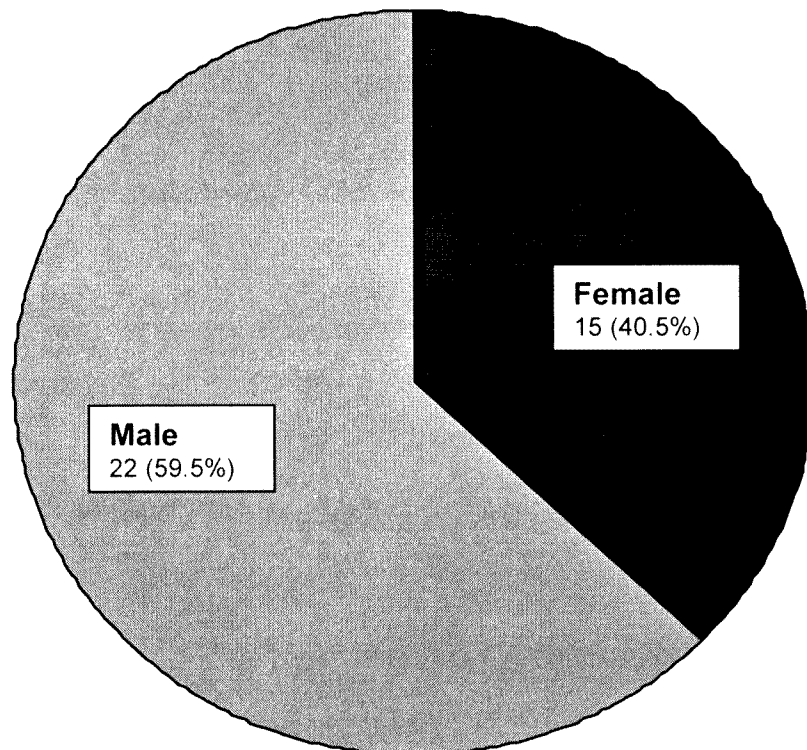


Fig 4.3 Age Distribution of Subjects (5-8 yrs, 9-12 yrs, 13-18 yrs)

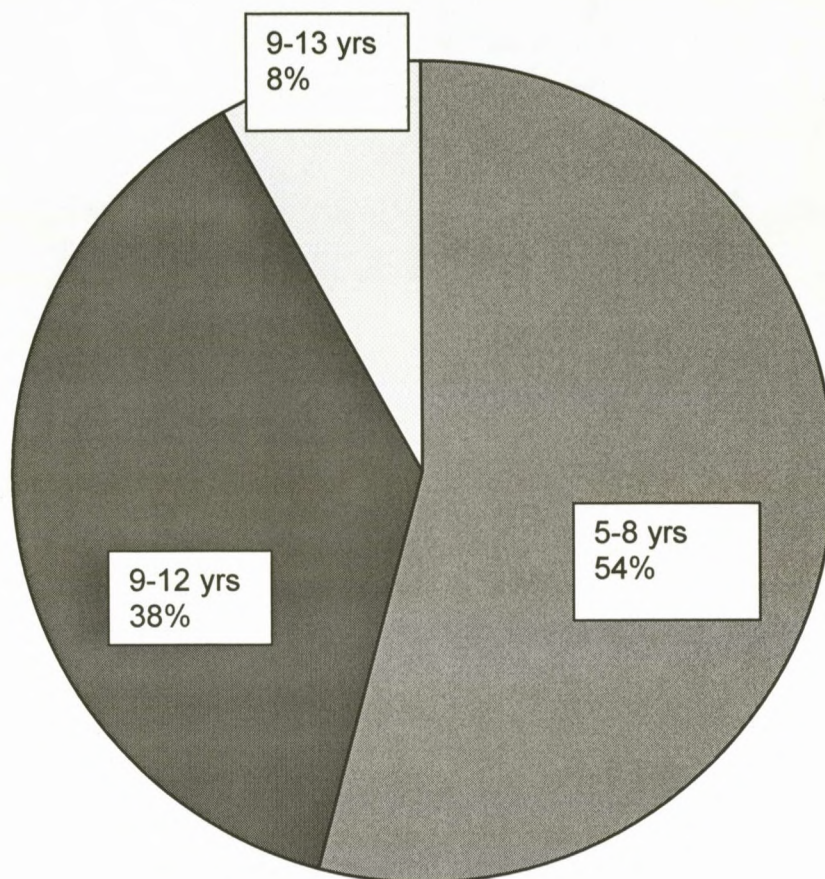


Fig 4.4 Age Distribution of the subjects

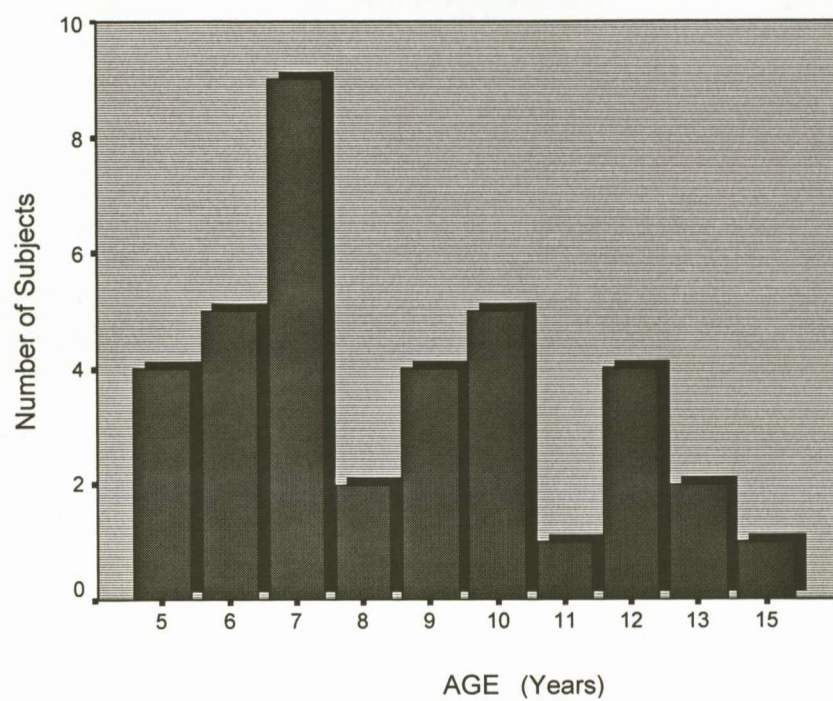
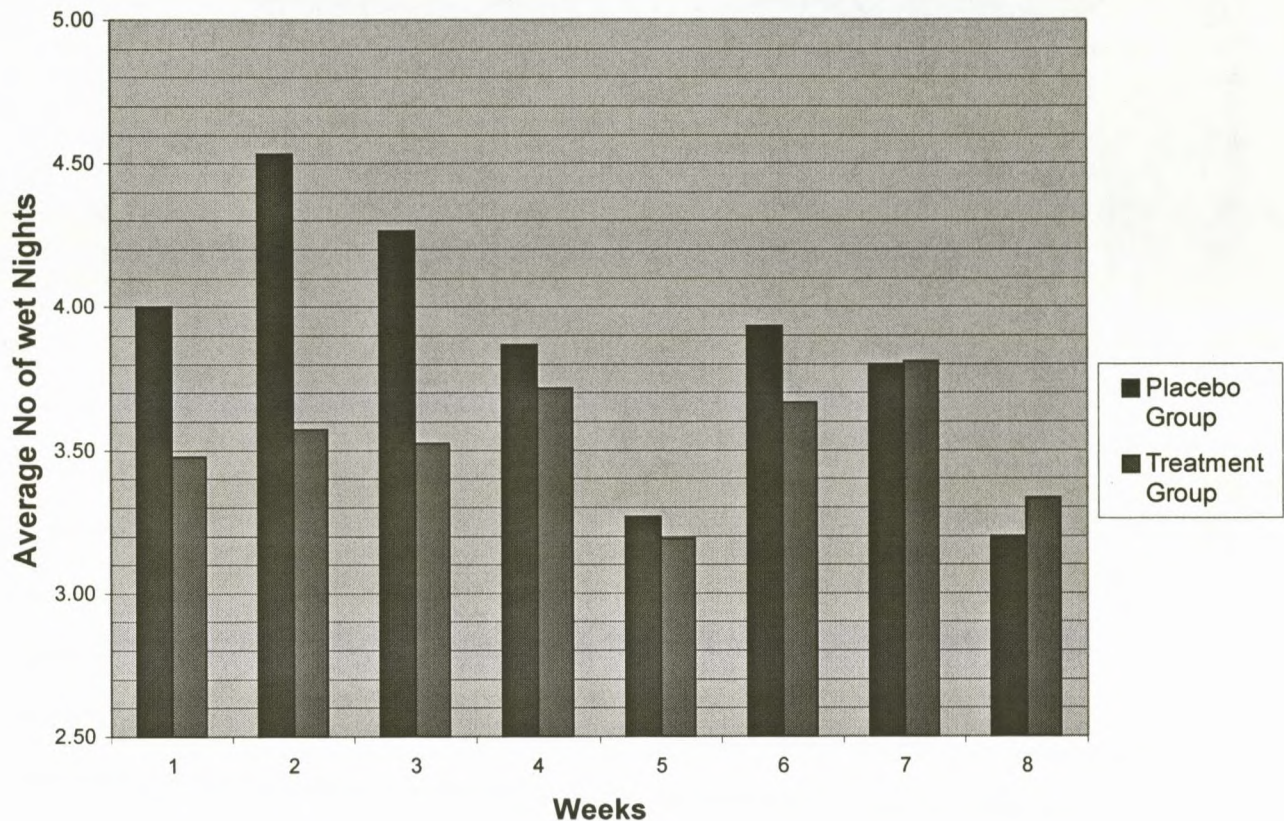


Fig 4.5 Comparison of the average number of wet nights in the placebo and the treatment group.



In Fig 4.3 it is apparent that both the treatment and placebo group experienced very low average wet nights in the week immediately following the treatment period (week 5). This could have been due to a placebo effect after having completed the course of treatment. It is also possible that the treatment group could have experienced a cumulative benefit from the *Ilex paraguensis* that wore off as the post- trial period progressed.

Table 4.2 Comparison based on the percentage differences between the baseline period and the trial period for the treatment and placebo groups.

(Note the shaded area indicates the threshold level of success).

	Neg Results	0-24% Impr.	25-49% Impr	50-74% Impr	75-100% Impr	Sample Size
Placebo	6	2	5	3	0	16
Treatment	9	4	4	3	1	21

The four cases of success in the treatment group demonstrated a positive effect of the *Ilex paraguensis*, however the placebo group also showed a few successes (three). This indicates that the response to the trial may not be attributable to the effects of the *Ilex paraguensis*. This is supported by the absence of statistical significance for the improvements noted. The fact that the improvement occurred during the trial period, but disappeared in the post-trial observation period supports the argument for a cumulative effect of *Ilex paraguensis*, which wore off as the post-trial observation period progressed. This could also have been due to a placebo effect, as there was no statistically significant difference in the placebo and treatment group for the trial period.

Table 4.3 Comparison based on the percentage differences between the baseline period and the post-trial period for the treatment and placebo groups. (Note the shaded area indicates the threshold level of success).

	Neg Results	0-24% Impr.	25-49% Impr	50-74% Impr	75-100% Impr	Sample Size
Placebo	5	3	5	3	0	16
Treatment	11	6	2	2	0	21

Both groups had some successes in the post trial observation period, however the gains were not statistically significant in either case. The apparent deterioration in the number of wet nights in the treatment group during the post trial observation period, supports the argument for the effect of *Ilex paraguensis* wearing off over the duration of the post-trial observation period.

4.4 The analysed data

4.4.1 Non- parametric Hypothesis Testing

4.4.1.1 Statistical procedures 1 and 2: Intra group comparisons using Wilcoxon's Signed Rank test

H₀: It was hypothesised that there would be no significant difference between average number of wet nights during the pre- trial and trial and post trial periods on analysing the intra group data, for placebo and treatment groups at a confidence level of 5%. This was an indication that there was no improvement in the condition.

H₁: It was hypothesised that there would be a significant difference between the pre- trial and trial and post trial results on analysing the intra group data for placebo and treatment groups at a confidence level of 5% This was an indication that there was an improvement in the condition, attributable to the treatment.

A 95% confidence interval was required to reject the null hypothesis. Thus H₀ was accepted if $p \geq 0.05$, and H₀ was rejected if $p \leq 0.05$. i.e. a 5% level of significance was used.

Table 4.4 Sample analysis of the placebo group comparing the average number of wet nights of the baseline period to the average number of wet nights of each week of the study using Wilcoxon's Signed Rank test.

Placebo	Baseline vs Wk 3	Baseline vs Wk 4	Baseline vs Wk 5	Baseline vs Wk 6	Baseline vs Wk 7	Baseline vs Wk 8
p Value	.388	.660	.031	.528	.222	.024
	n/s	n/s	S	n/s	n/s	S

The null hypothesis was accepted for weeks 3,4,6,7 because at a 5% level of significance there was no significant difference between these weeks and the baseline period. There was therefore no significant improvement in the subject's condition during these weeks of the study. During week 5 and week 8, however, there were significantly fewer wet nights than other weeks. This could be due to the end of the treatment period, and end of trial placebo effects.

Table 4.5 Sample analysis of the treatment group comparing the average number of wet nights of the baseline period to the average number of wet nights in each week of the study, using Wilcoxon's Signed Rank test.

Treatment	Baseline vs Wk 3	Baseline vs Wk 4	Baseline vs Wk 5	Baseline vs Wk 6	Baseline vs Wk 7	Baseline vs Wk 8
p Value	.207	.470	.509	.843	.418	.259
	n/s	n/s	n/s	n/s	n/s	n/s

The null hypothesis was accepted for week 3-8 because at a 5% level of significance there was no significant difference between these weeks and the baseline period. There was therefore no significant improvement in the subject's condition during the study.

4.5.1.2 Statistical procedure 3: Inter-group analysis using the Mann-Whitney U test

H_0 : It was hypothesised that there would be no significant difference between the placebo and the treatment group with regard to the average number of wet nights per week.

H_1 : It was hypothesised that there would be a significant difference between the placebo and the treatment group with regard to the average number of wet nights per week.

A 95% confidence interval was required to reject the null hypothesis. Thus H_0 was accepted if $p \geq 0.05$, and H_0 was rejected if $p \leq 0.05$. i.e. a 5% level of significance was used.

Further, both one-tailed and two tailed p-values were obtained. The reason for this lies in the unknown action of *Ilex paraguensis* in 6x potency. The one tailed p value was used to determine if there was any significant *decrease* in the average number of wet nights between the placebo and the treatment group. The two tailed p value was used to determine if there was any significant *difference* in the average number of wet nights in the placebo and treatment group. Theoretically *Ilex paraguensis* could contribute to an increase in the average number of wet

nights. This is in accordance with the homoeopathicity of a substance i.e. a substance will cure that which it will cause in a healthy subject.

Table 4.6 Statistical comparison between the placebo and treatment groups for the baseline period using the Mann- Whitney U test.

Baseline Period	p Value (two tailed)	p value (one tailed)
	0.450	0.229
	n/s	n/s

The null hypothesis was accepted. At the 5% level of significance there was no significant difference between the placebo and the experiment for the baseline period. This forms a check that the sampling was not erroneous, as the difference in the average number of wet nights between the two groups, for the baseline period is not significant.

Table 4.7 Statistical comparison between the placebo and treatment groups for the trial period using the Mann- Whitney U test.

Trial Period	p Value (two tailed)	p value (one tailed)
	0.758	0.387
	n/s	n/s

The null hypothesis was accepted. At the 5% level of significance there was no significant difference between the placebo and the treatment group for the trial period.

Table 4.8 Statistical comparison between the placebo and treatment groups for the post-trial observation period using the Mann- Whitney U test.

Post trial Observation Period	p Value (two tailed)	p value (one tailed)
	0.840	0.422
	n/s	n/s

The null hypothesis was accepted. At the 5% level of significance there was no significant difference between the placebo and the treatment for the post trial observation period.

Table 4.9 Statistical comparison between the placebo and treatment groups for each week of the trial using the Mann- Whitney U test.

	Week 3	Week 4	Week 5	Week 6	Week 7	Week 8
p Value (two tailed)	0.698 n/s	0.951 n/s	0.988 n/s	0.988 n/s	0.827 n/s	.707 n/s
p value (one tailed)	0.452 n/s	0.353 n/s	0.452 n/s	0.494 n/s	0.422 n/s	0.364 n/s

The null hypothesis was accepted. At the 5% level of significance there was no significant difference between the placebo and the experiment for weeks 3-8.

There was thus neither a significant decrease, nor a significant increase in the average number of wet nights in the treatment group as compared to the placebo group, for any of the weeks of the trial.

CHAPTER 5

DISCUSSION

This research was designed to evaluate the efficacy of homeopathic *Ilex paraguensis* 6x in the treatment of nocturnal enuresis. Results were assessed in terms of the number of wet nights recorded in wet/dry night diaries.

Numerous treatment modalities for nocturnal enuresis have been introduced, including pharmacological and non-pharmacological approaches. The most popular allopathic drug used is Imipramine hydrochloride (Tofranil ®) with a reported cure rate of 25% to 40%, but relapses usually occur when the drug is stopped – in up to 90% of the cases (Rushton, 1989; Warady et al., 1991). Side effects (Appendix 6), are relatively frequent and often lead to discontinuation of the medication. Desmopressin acetate has been found to have a success rate of 41%. Although the pharmacological effect of the drug ceases immediately on withdrawal, it appears to be a reasonable agent to use in those children needing fast results on specific occasions. Side effects (Appendix 6) are usually mild and limited to mucosal irritation, epistaxis, headaches, nasal congestion and occasional gastrointestinal upset (Toffler et al., 1991). While on a continuum of medically acknowledged side effects, these are mild, for enuresis sufferers and

their parents they can be debilitating and occasionally more uncomfortable than the original condition.

The results of this research showed no significant statistical improvement in either the treatment or placebo group. There are several factors, which could have contributed to this result:

5.1 Indication for the remedy

There has been no proving done on *Ilex paraguensis* making the information available on the remedy very scanty. A proving of this substance would provide more mental symptoms allowing for accurate prescription based on the law of similars. The efficacy of homoeopathic treatment is in large part due to rigorous individualisation of the remedy. Without a detailed knowledge of the symptomatology of *Ilex paraguensis*, it is difficult to assess the level to which the results reflect a lack of action of *Ilex paraguensis* as opposed to a fundamental error in applicability of *Ilex paraguensis* to a particular case.

5.2 Posology

In the trial carried out by Cortina (1999), the participants were treated with *Ilex paraguensis* 6x for one month, followed by the 6c for another fortnight. The dose

was ten pillules one hour before meals i.e. three times a day. This comprised a total treatment period of 6 weeks, with a total of one hundred and twenty-six doses, in ascending potency. In this research the treatment period was two weeks, using a low potency (6x) in a single daily dose, with total number of fourteen doses. The number of doses could have had an effect on the results obtained and further research could incorporate a longer treatment period to clarify this issue.

A further posology consideration was the low potency used in this research i.e. 6x. Some of the participants may have responded more positively to a higher potency, or to a potency matched to their level of susceptibility. In a homoeopathic context the higher potencies generally have a more lasting and more profound effect. The use of a 6x potency, could have contributed to the transient decrease in the average number of wet nights recorded at the conclusion of the trial period. (see Fig 4.3).

5.3 Observation period

The post treatment observation period in this research was two weeks. Homeopathic remedies are known to have varying times of action. Some remedies can still be active sixty days after being taken. (Information regarding activity of a remedy is obtained from provings.) Therefore the *Ilex paraguensis*

may have had an effect on the participants that was not observed due to the short observation period.

5.4 Measurement of improvement

A consideration in terms of judging the efficacy of *Ilex paraguensis* was the use of wet nights as a measure of improvement. Frequency of occurrence is a standard indicator in evaluating the efficacy of a treatment (Rushton, 1989). From a homoeopathic perspective however, other more subjective symptoms may provide a skilled clinician with an indication of improvement. In a normal family setting the mother, may note improvement in less quantitative symptoms of enuresis e.g. amount of urine passed, number of times urine passed per night, whether the child wakes on voiding, characteristic times of voiding etc. In the children's home setting these parameters are less easy to record. They could, however, give a significant indication of improvement, over and above whether the bed is wet in the morning or not.

A further consideration was the measurement of concomitant symptoms. The efficacy of the remedy was measured in terms of decrease in the average number of wet nights. Homeopathic remedies are holistic in their action; therefore there may have been improvement in concomitant symptoms, which would not have been noted and often cannot be measured statistically. Although beyond

the definition of this study, improvement in well being, behaviour, concentration, socialisation and energy levels could be experienced by the subjects.

5.5 Clinical homeopathy

This research was based on the concept of clinical homeopathy, i.e. treating a local symptom (enuresis), with a remedy specifically indicated for that condition. This application is useful in acute conditions that have a clear aetiology (Castro, 1990). However in chronic conditions, such as enuresis, a deeper acting remedy is often needed as psychosocial issues play an important role. In chronic case taking, emphasis is on the mental and emotional symptoms presented by the child and behaviours noted by care givers. (De Schepper, 2001). The effectiveness of homoeopathic treatment is based on the accuracy of case taking and the degree of similitude between the remedy picture and the patient's symptomatology. In a clinical mode of prescribing, the remedy picture is not based on the totality of the symptoms but on the pure pathological presentation. Clinical treatment is thus recognised as less effective than individualised prescription of a specific remedy (Das, 1998).

CHAPTER 6

CONCLUSIONS AND RECOMMENDATIONS

Based on the statistical analysis of the data, homoeopathic *Ilex paraguensis* 6x had no clinical effect on the average number of wet nights in nocturnal enuresis sufferers. There was no statistically significant improvement in either the treatment or the placebo group; nor was there any significant difference between the average number of wet nights in the treatment vs. placebo groups. It can be concluded that this study demonstrated no benefit to the subjects in the reduction of the average number of wet nights they suffered.

Given the results of Cortina's trial (1994) however, the use of *Ilex paraguensis* in the treatment of enuresis should not be discounted by the results of this trial. Further research is needed to test the effectiveness of homoeopathic *Ilex paraguensis* in the treatment of nocturnal enuresis.

It is recommended that the following areas should be explored in trying to further establish a role for *Ilex paraguensis* in the treatment of primary nocturnal enuresis:

- Conduct a homoeopathic proving of the substance: A proving is a single blind research protocol in which healthy volunteers take homoeopathic potencies of a particular substance. These volunteers (provers) keep extensive journals recording their subjective symptoms over the course of the trial. These journals are collated by the supervisor or researcher at the conclusion of the trial, and a composite picture of the substance's remedial action is formulated. These proving symptoms form the basis for the prescription of the drug in clinical situations. A proving of *Ilex paraguensis* will thus give researchers more indication as to the applicability of this treatment in individual cases.
- Use different potencies of *Ilex paraguensis*: A different potency may have different physiochemical effects to the 6x potency. Higher potencies e.g. 1M could be used if the totality of the symptoms fitted the remedy picture of *Ilex paraguensis*. Use of the tincture can be considered.
- Increase the number of doses depending on potency: Cortina (1994) used multiple daily doses over an extended period of time. This may account in part for the results of that trial. *Ilex paraguensis* could be repeated up to three times a day in a low potency (6x).

- Increase the treatment period, post treatment observation, observation period, number of doses and size of the sample group: This may contribute to increasing the dose as well as giving enough time to observe longer term change in the symptoms. While the statistical methods used in this study are useful in deriving significance from small samples, a larger sample group would add weight to the results and help to eliminate sampling error, which can obscure meaningful outcomes. Increasing the number of children participating in the study would increase the reliability and validity of the conclusions reached and help to establish different options for the treatment of enuresis.
- Observation in a more controlled environment: The measurement system could somehow be expanded to take into account the more subjective aspects of enuresis (amount of urine voided, frequency in one night, time of voiding etc). A measure that includes other factors such as behaviour, energy levels, mood and socialisation could also contribute to deeper understanding of the role of *Ilex paraguensis* in the treatment of nocturnal enuresis.
- Focus on other subjects for research: Children in the homes have a history of emotional trauma and face social pressures that could influence the results of the research. Further research could involve children from a "normal" environment.

LIST OF REFERENCES

- Butler, N.R. and Golding, J. 1986. From Birth To Five. Oxford, England: Pergamon Press. ISBN 0-08-033372-9
- Castro, M. 1990. The Complete Homeopathy Handbook. London, UK: MacMillan Publishers. 257p. ISBN 0-333-55581-3
- Cendron, M. 1999. Primary Nocturnal Enuresis: Current Concepts. American Family Physician, 1-11
- Cendron, M. and Klauber, G. 1998. Combination therapy in the treatment of Persistent nocturnal enuresis. British Journal of Urology, 81: 26-28
- Centers, F.D.C. 1995. Anticholinergic poisoning associated with herbal tea. Centers for Disease Control (U.S.) Morbidity and mortality weekly report, 44(11):193-195.
- Cortina, J. 1994. Enuresis and it's homoeopathic treatment: Study of 20 cases treated with *Ilex Paraguensis*. British journal of Homoeopathy, 83: 220-222

Das A.K.1998. A Treatise On The Organon Of Medicine. Calcutta, India:

Souvik Homoeo Publications. 114p.

De Schepper, L. 2001. Hahnemann Revisited. Santa Fe, USA: Full of Life

Publications. 572 p. ISBN 0-942501-12-8

Dorland's Medical Dictionary, 1989. 24th ed. Philadelphia: W.B. Saunders

Company. 471p. ISBN: 0721631274

Ellis SJ, Adams RF.1997. The cult of the double-blind placebo-controlled trial.

Br J Clin Pract, 51(1): 36-39.)

Lackgren, G., Lilja, B., Neveus, T. and Stenberg, A. 1998. Desmopressin in

the treatment of severe nocturnal enuresis in adolescents- a 7 year follow

up study. British Journal of Urology, 81: 17-23

Farrington, E.A. 1992. Clinical Materia Medica (reprint edition) New Delhi,

India: B. Jain Publishers Pvt. Ltd. 826p. ISBN 81-7021-029-1

Glazener, C.M.A., Evans, J.H.C.2001. Desmopressin and nocturnal enuresis

in children Cochrane Review. The Cochrane Library, 3: 1-2.

Glicklich, L.B. 1951. An historical account of Enuresis. Paediatrics, 8:859-876.

Harris, E.L. and Fitzgerald, J.D. 1970. The Principles and Practice of Clinical Trials. Based on a Symposium Organized by the Association of Medical Advisers in the Pharmaceutical Industry. Edinburgh and London: E. and S. Livingstone, 1970.

Gemmell, Jacobson. 1989. Chiropractic Management of Enuresis. Journal of Manipulative and Physiological Therapeutics, 12(5): 2-3.

Grieve, M.1998. Paraguay Tea. A Modern Herbal. Great Britain, United Kingdom: Mackays of Chatham Plc. 609p. ISBN1-85501-249-9.

Grobler, N. 1996. A Study Of The Efficacy Of Chiropractic Treatment In The Management Of Functional Nocturnal Enuresis. Durban Institute of Technology.

Leboeuf, C., Brown, P., Herman, A., Leembruggen, K., Walton, D. and Crisp, T.C.1991. Chiropractic care of children with nocturnal enuresis: a prospective outcome study. Journal of Manipulative and Physiological Therapeutics, 14 (2): 110-115.

Jalswal, G.D. 1989. Nocturnal Enuresis-A perplexing problem. Indian Journal of Homoeopathy, 332-334

- Medel, R., Ruarte, A.C., Castera, R. and Poesta, M.L. 1998. Primary enuresis: a urodynamic evaluation. British Journal of Urology, 81: 50-52
- Moore, K.L. 1992. Clinically Oriented Anatomy (third edition) Baltimore, U.S.A: Williams and Wilkins Ltd. ISBN 0-683-09485-8
- Norgaard, J.P., van Gool, J.D., Hjalmas, K., Djurhuus, J.C. and Hellstrom, A.L. 1998. Standardization and definitions in lower urinary tract dysfunction in children. British Journal of urology, 81: 1-16
- Saldana, M., Mohammed, R. 1999. Extraction of purine alkaloids from mate (*Ilex paraguensis*) using supercritical carbon dioxide. American Chemical Society, Books and Journals Division, 97(9): 3804-3808.
- Rushton, H.G. 1989. Nocturnal Enuresis: epidemiology, evaluation and currently available treatment options. Journal of Paediatrics, 114: 691-696.
- Sere, T.A, Perk, H., Koyuncuoglu, H.R., Kosar, A., Celik, K., Deniz, N. 2001. Acupuncture therapy in the management of persistent primary nocturnal enuresis –preliminary results. Scandinavian Journal of Urology and Nephrology, 35(1):43.

Toffler, W.L. and Weingatren, F. 1991. Epitomes – General and family practice. California Medical Association, 154 (3): 326.

Ullom-Minnich, M.R. 1996. Diagnosis and Management of Nocturnal Enuresis. American Family Physician, 54: 2259-2266

Van Gool, J.D., Niewenhuis, E., Doeschate, I., Messer, T.P., De Jong, P.V. 2001. Subtypes in Monosymptomatic Nocturnal Enuresis. Scandinavian Journal of Urology and Nephrology, 33 (6): 8-11.

Vithoulkas, G. 1980. The Science of Homoeopathy (first edition) New York, U.S.A.: Grove Press, Inc. 331p. ISBN 0-394-17560-3

Warady, B.A., Alon, U. AND Hellerstein, S. 1991. Primary Nocturnal Enuresis: current concepts about an old problem. Pediatric Annals, 20 (5): 246-255.

APPENDIX 1

CASE TAKING FORM FOR ENURESIS RESEARCH

PATIENT DETAILS:

Name _____ Date _____

Address _____

Code: _____

Date of Birth: _____ Age: _____

Sex: Male/Female: _____ Consultation: Initial/Follow Up _____

PARENT DETAILS:

Name of Parent/Guardian: _____

Telephone: (H) _____ (W) _____

MAIN COMPLAINT: _____

PAST MEDICAL HISTORY AND TREATMENT: (including childhood diseases)

Medication: _____

Vaccinations: _____

Allergies: _____

FAMILY HISTORY: _____

BIRTH HISTORY: Pregnancy _____

Labour _____

MILESTONES: _____

GENERALS:

Sleep: (patterns and positions) _____

Weather preference: _____

SYSTEMS REVIEW:

HEAD: _____

ENT: _____

RESPIRATORY: _____

CARDIOVASCULAR: _____

GIT: Feeding / diet _____

Cravings and aversions _____

Appetite _____

Thirst _____

Stool (colour, consistency, frequency) _____

GENITO-URINARY: _____

Urine _____

Discharges _____

MUSCULOSKELETAL AND CNS: _____

SKIN: _____

Perspiration _____

PERSONALITY: Temperament _____

Relations with others _____

Fears

PHYSICAL EXAMINATION

VITAL SIGNS:

Temperature_____Pulse rate_____

Respiratory rate_____BP_____

Height_____Weight_____

GENERAL EXAMINATION:

Jaundice/ anaemia/ cyanosis/ dehydration/ oedema/ lymphadenopathy_____

ENT: _____

CHEST EXAMINATION: _____

ABDOMINAL EXAMINATION: Abdominal masses, distension, sphincter tone

NEUROLOGICAL EXAMINATION: Gait, reflexes, observation of spinal cord,
dermatomes and myotomes L2, L3, L4, L5

TESTS: Urine dipstick

APPENDIX 2

Minor assent form

My name is.....

- I wish to take part in your research project.
- The project has been carefully explained to me.
- I am not being forced to take part.
- I understand that I can decide to not take part at any time.

.....

Signature

Date.....

Igama lami lingu.....

- Ngginaso isifiso sokubamba ocwaningweni lakho.
- Lolw cwaningo luchaziwe kabanzi kimina.
- Angiphoqeletwanga ukubamba kimina.
- Ngiyazi ukuthi ngingawushintsha noma inini umqondo mayelana nokubamba iqhaza.

.....

Sayina

Usuku.....

Appendix 3

Patient Information Sheet

The purpose of this study is to determine the efficacy of a homoeopathic complex, *Ilex paraguensis* and the homoeopathic simillimum in the treatment of nocturnal enuresis.

Homoeopathy: According to the World Health Organisation homoeopathy is the second most widely used form of therapy worldwide. Homoeopathic remedies produce no side effects and thus bring about cure in a gentle manner and are safe for use in children. Homoeopathy was founded by S Hahnemann two hundred years ago and is based on the law of Similars. This implies that a homoeopathic remedy will cure a disease state similar to that which it can cause when administered to a healthy person.

Homoeopathic complex: A homoeopathic complex comprises a number of remedies that are known to have an effect on a particular condition. For the purposes of this research the complex will be specially formulated for bed-wetting.

Homoeopathic simillimum: The simillimum is a single remedy that most accurately reflects the state of the patient. Rather than being specific for a given complaint it reflects the state of the patient on the mental, emotional and physical plane. For this reason there are a number of remedies that can be used for bedwetting, each with an entirely different symptom picture.

Ilex paraguensis: *Ilex paraguensis* is a herb which is used for a tea in Paraguay. This herb when homoeopathically prepared is reputed to be effective in the treatment of bed-wetting.

Double blind study: A double blind study is one in which neither the researchers nor the patients know the nature of the medication. For the purpose of this study this implies that neither patient nor researcher will know who is receiving placebo, complex, simillimum or *Ilex paraguensis*.

Placebo: Fifteen patients out of seventy will receive placebo. For the purposes of this study the placebo will be non-medicated powder that have an identical appearance and taste to medicated powder. The use of placebo or a control in clinical trials is considered to be in keeping with the scientific method. Its main purpose is to provide a base line against which results can be measured.

Patients who received placebo will be offered treatment free of charge after completion of the study.

Powders: The medication to be used will be dispensed in lactose powders. (see example provided) These powders are sweet tasting and easy to use.

The powders are to be administered in numerical order prior to going to sleep.

The child should not eat, drink nor brush teeth fifteen minutes before or after administration.

Nocturnal enuresis: (bed-wetting) Nocturnal enuresis is the inability to maintain bladder control during sleep. It is a common disorder that is thought to be 80% psychogenic. Other causes of enuresis include chronic bladder infection, delayed maturation and neurological abnormalities. It is divided into primary and secondary types. Subjects who have never achieved voluntary bladder control are considered to fall into the primary type. Those who have had bladder control and then develop enuresis at a latter stage are considered to fall within the secondary type. Both categories will be considered with children under the age of five, those with chronic infections and those with anatomical causes being excluded.

Outline of study: The study will comprise of seventy children. The supervisor will randomly divide them into four groups (simillimum, complex, I. Paraguensis and control). Each child will receive a physical examination as well as have their case taken by the students. Part of the case taking will include interviewing the

caregivers, particularly for the very young children. Once the case taking is complete there will be a two-week observation period in which the incidence of bedwetting will be noted. Thereafter the treatment period of two weeks will commence with each child receiving a single powder each evening before bed. Once this period is complete, post treatment observation of four weeks will commence with completion of enuresis diaries. Once the study is over children on placebo will be offered free treatment.

Enuresis diary: This will comprise a simple calendar which will be filled in with a yes/no answer each day by either the caregivers or the students.

Contact: The student researchers will be in regular contact with the caregivers and children. In addition they will be telephonically available, as will their supervisors.

Dr C Hall 2042041

Michael Bloch 2050111

Heather Lockyear 3128402

Paddy Rielly 4641025

Confidentiality: All data collected will be confidentially handled. The final thesis will be presented in such a way that the confidentiality of participants will be ensured.

Follow up: The aim of this project is to evaluate the use of homoeopathy in treatment of enuresis, with the well being of the participants being of foremost importance. For this reason children who have had improvement or who wish to will be encouraged to attend our day clinic after the trial. The clinic offers a free service (consultation and medicine) to those willing to be observed.

isiZulu:

Siyakwamukela kulolucwaningo. Lelikhasi lichaza esikwenzayo kulolucwingo. Kubalulekile ukuba wazi ukuthi ungenela lolucwaningo ngokuthanda kwakho, nokuthi ulwazi ukuthi lusebenza kanjani.

Homeopathy: Uhlobo lwemithi yemvelo olusiza umzimba ukuba uzelaphe ngokwawao. Uphephile kubantwana.

Homeopathic complex: Uhlobo oluthile lomuthi olwnzile ngengxube yemithi emihlanu. Lusetshenziswa ukwelapha ukuchama uma ulele.

Homeopathic Simillimum: Uhlobo lomuthi olukhethelwa lowo muntu oluqondene naye, okusho ukuthi umntwana ngamunye uthola lowo muthi oqondene nesimo akuso.

Ilex Paraguensis: Isitshalo esitholakala e South America eselapha ukuchama ume ulele.

Placebo: Abanye abantwana bazonikezwa I placebo. I placebo into ebukeka umuthi, kodwa kungesiwo. Abantwana ukudingeka banikezwe I placebo bayonikezwa ekupheleni kocwaningo.

Double Blind Study: Loku kusho ukuthi wena kanye nomcwaningi wophenyo angeke naziswe ukuthi unikezwe I placebo. Loku kwenzelwa ukuba ucwaningo lube lula kwezesayensi (scientific).

Medicine: Imithi enizoyinikezwa iyoba izimpushana. Inambitheka ngokusashukela, kulula futhi nokuyisebenzisa. Imithi lena kumele ithathwe zonke izinsuku ebusuku ngaphambi kokuba ulale. Imithi lena inezinombolo futhi kumele ithathwe ngokulandelana kwezinombolo e.g. 1,2,3...etc,. Akumele udle, uphuze noma uwashe amazinyo imizuzu engu 15 ngaphambili noma ngemuva kokusebenzisa lempushana. Umlomo kumele uhlanzeke. Umuthi kumele umnyungwe ngolimi, asikho isidingo sokuwuxuba namanzi.

Bedwetting: Ukuchama ebusuku uma ulele.

The study: Amasonto amabili okuqala sibala izikathi umntwana azichamela ngazo ebusuku uma elele. Amasonto amabili alandelayo abantwana bazonikwezwa imithi (impushana). Amasonto alandelayo amane (4 weeks), siphinde sibaleizikathi umntwana azichamele ngazo ebusuku uma ulele. Sizohlangana nomntwana kanye nomzali ukuze sithole ukwazana nabo.

Assent Form: Ifomu okumele umntwana ngamunye alisayine. Lelifomu lenzela ukuqinisekisa ukuthi akekho umntwana ophoqiwe ukuba angenele lolucwaningo.

Diary: Zonke izinsuku umzali kumele abeke uphawu kwikhalenda oluchaza ukuba umntwana uchamile yini ngenkathi elele nome cha.

Izinombolo zocingo: Sitholakala kulezizinombolo ezilandelayo:

- Dr C Hall – 204 2041(Supervisor)
- Michael Bloch – 205 0111
- Heather Lockyear – 312 8402
- Paddy Rielly – 464 1025

Sizonivakashela wonke amasonto

Confidentiality: Lonke ulwazi oluzotholakala kulolucwaningo luyobe luyimfihlo, azekho omunye umuntu ozolwazi. Akukho muntu ozokwazi ukuthu ubungomunye wabangenile kulolucwaningo.

APPENDIX 4

Parent / Guardian Consent Form

Title of research project: A double blind study to determine the efficacy of a homoeopathic complex, *Ilex paraguensis* 3x and the homoeopathic simillimum in the treatment of nocturnal enuresis in children.

Name of supervisor: Dr C Hall.

Name of research students: M Bloch, H Lockyear and P Rielly.

(Please circle the appropriate answer)

Have you read the information form? Yes/No

Have you had the opportunity to discuss this study with the
Above research students? Yes/No

Have you had the opportunity to ask questions regard this study? Yes/No

Have you received satisfactory answers to your questions? Yes/No

Do you understand that participants are free to withdraw from the study at any time? Yes/No

Do you understand the nature of this research project and its structure? Yes/No

Do you agree to allow your child or children under your care to participate in this study ? Yes/No

Do you agree to provide access to the children’s medical records in your possession? Yes/No

Ithe undersigned, as parent/ guardian hereby give consent forto participate in the above mentioned study.

.....
Signature parent/ guardian

.....

.....

Witness name

Witness signature

Date:.....

Appendix 5:Diary.

Childs name	Monday	Tuesday	Wednesday	Thursday	Friday	Saturday	Sunday

Appendix 6

Side effects of allopathic drugs commonly used in the treatment of nocturnal enuresis

Imipramine hydrochloride (Tofranil ®):

Insomnia

Personality changes

Nervousness

Danger of overdose

Oxybutin chloride (Ditropan ®):

Constipation

Dizziness

Tremors

Desmopressin acetate (DDVAP):

Weight gain

Convulsions

Coma

Headaches

Allergic skin reactions

Serum sodium loss if there is restricted water intake

APPENDIX 7 Summary of Research Design

