

**THE EFFECTIVENESS OF AN ORAL HOMOEOPATHIC
PREPARATION OF SELENIUM SULPHIDE 12X
IN THE MANAGEMENT OF DANDRUFF
(SEBORRHEIC DERMATITIS OF THE SCALP)**

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Mini-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, Keri Kent, declare that this mini-dissertation represents my own work, both in conception and execution.

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DEDICATIONS

This dissertation is dedicated to:

Mark Kent: My wonderful husband who patiently gives me endless love, support and encouragement.

Jeff and Anne Judge: My loving parents, for supporting me throughout this degree and making it all possible.

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ABSTRACT

This double-blind, placebo controlled study evaluated the effectiveness of Selenium sulphide 12X in the management of dandruff, as measured by a Visual Analogue Scale. The sample group of thirty-three consisted of participants between the ages of 18 and 50 who resided in the greater Durban area.

Dandruff can be defined as an abnormality of the desquamative process which is strictly confined to the scalp (Pierard-Franchimont, Hermanns, Degreeef, and Pierard, 2000). It is often confused with a disorder known as seborrhoeic dermatitis, which is defined as a chronic, superficial, scaling, inflammatory disease of the skin, in which the skin is often red and irritated (Smith, Baker, and Williams, 2002). For the purpose of this study, dandruff and seborrhoeic dermatitis were considered to be part of the same disease process, yet at opposite ends of the spectrum.

The study design required a minimum of thirty participants in order for the trial to be statistically viable. Thirty eight participants were however accepted into the trial in order to account for the possibility of drop outs. Through a process of randomisation, eighteen participants were selected for the treatment group, and twenty for the placebo group. In total five participants withdrew from the trial, all of whom were in the placebo group. Statistical analysis used the measurements from all who completed the trial; hence the treatment group numbered eighteen and the placebo group numbered fifteen.

The clinical trial commenced once the participant had refrained from using an anti-dandruff shampoo for a week and once the initial consultation was performed. The trial was conducted over a four week period and consultations took place on day 1, day 14, and day 28. At each consultation the participant's dandruff was assessed by three individuals – the participant themselves, the researcher, and an independent party (a qualified homoeopathic clinician or the concomitant researcher, Teleman) - through the use of the Visual Analogue Scale (VAS). The variables assessed were 'scaling', 'irritation', 'greasiness', 'global impression', 'percentage of scalp affected', and 'itchiness'. Each consultation ended with a physical examination. If the participant was found to be pregnant, using antimycotics or antibiotics, or suffering from immunodeficiency, psoriasis, atopic or irritant contact dermatitis, tinea capitis or Parkinsons Disease they were excluded from the trial.

The results were analysed at a 95% confidence rating with $p = 0.05$ as follows:

- The scores for each variable (taken by the researcher, participant, and independent third party) were added together and averaged for each consultation.
- Using these averages, intra-group analysis then took place through performing The Friedman's Test and Wilcoxon's Signed Rank Test (i.e. independent analysis for both treatment group and placebo group).
- Inter-group analysis was then conducted through the Mann Whitney U Test in order to see if there was a significant difference between the treatment group and placebo group.

On statistical analysis a significant improvement was demonstrated within both the treatment and placebo groups when analysed independently (i.e. intra-group analysis) through use of the Friedman's Test and the Wilcoxon's Signed Rank Test.

The treatment group showed a significant improvement in all of the six variables assessed, and by the end of the trial the P-values were as follows: 0.000 for 'scaling'; 0.002 for 'irritation'; 0.013 for 'greasiness'; 0.000 for 'global impression'; 0.000 for 'percentage of scalp affected'; and 0.003 for 'itching'.

The placebo group only showed a significant improvement for three of the six variables. These variables were 'scaling', 'global impression' and 'itching' with P-values at the end of the trial of 0.005, 0.012, and 0.018 respectively.

When results from the treatment group were compared to those from the placebo group (i.e. inter-group analysis) through the Mann-Whitney U Test, there proved to be a significant difference in only one of the variables, namely 'irritation' with a P-value of 0.015. All the other variables showed no significant improvement and therefore Selenium sulphide 12X did not prove to be effective in the management of dandruff.

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DEFINITION OF TERMS

Allopathy

A therapeutic system based on the Law of Opposites. The treatment of disease uses medicines whose effects are different from those of the disease being treated and which have no relationship to the disease symptoms (Yasgur, 1998:9).

Androgen

Substance producing or stimulating masculine characteristics, such as testosterone (Tortora and Grabowski, 1996:G9).

Andropause

A decline in androgen levels in males in their late forties or early fifties (Anderson, *et al.*, 2002:92).

Corneocyte

A product of maturation of a keratinocyte which differentiates into a dead, anucleate plate of keratin and can be found on the outermost layer of the epidermis, where they are eventually shed (Graham-Brown and Bourke, 1998:1).

Dandruff

A dry, flaky, branny desquamation, beginning in small patches and rapidly involving the entire scalp, with profuse amount of fine powdery scales (Odom, James and Berger, 2000:214).

Dendrocyte

Bone-marrow derived cells found in different parts of the dermis. They have a possible role in tissue repair and haemostasis (Weedon, 2003:34).

Desmosome

A well defined plaque-like area of point contact, for cell-to-cell adhesion (Weedon, 2002:130).

Desquamation

A normal process in which the cornified layer of the epidermis is sloughed in fine scales (Kumar, Cotran, and Robbins, 1997:701).

Erythema

Redness of skin usually due to vasodilation (Gawkrodger, 2002:66).

Flora

Micro-organisms that live on or within a body to compete with disease-producing micro-organisms and provide a natural immunity against certain infections (Anderson, Keith, Novak and Elliot, 2002:688).

Fluxion

A method of manufacture of liquid potencies without succussion strokes. The potentising effect is produced by the turbulence of flowing or injected water (Swayne, 2000:87).

Hair follicle

Structure composed of epithelium surrounding the root of a hair from which hair develops (Tortora and Grabowski, 1996:G27).

Hawthorne effect

The Hawthorne effect is a phenomenon which occurs when people are singled out for a study of any kind. Their performance or behavior improves not because of any specific condition being tested, but simply because of all the attention they receive (Rice, 2004).

Homoeopathy

A therapeutic system based on the Law of Similars. Disease is treated with substances that produce, in a healthy person, symptoms similar to those displayed by the person who is ill (British Homoeopathic Association, 1992:1).

Hyperproliferation

An increase in keratinocyte migration (from the basal layer to the surface of the skin) or in other words, an increase in cell turnover (Sinclair, 2000).

Keratin

Insoluble protein found in the hair, nails, and other keratinised tissues of the epidermis (Tortora and Grabowski, 1996:G32).

Keratinocyte

The most numerous of the epidermal cells that function in the production of keratin (Tortora and Grabowski, 1996:G32).

Langerhans cell

Epidermal dendritic cell that functions as an antigen presenting cell during an immune response (Tortora and Grabowski, 1996:G32).

Lymphocyte

A type of white blood cell, found in lymph nodes, associated with the immune system (Tortora and Grabowski, 1996:G34).

Macrophage

Phagocytic cell derived from monocyte (Tortora and Grabowski, 1996:G34).

Mast cell

A cell found in areolar connective tissue along blood vessels that produces histamine, a dilator of small blood vessels during inflammation (Tortora and Grabowski, 1996:G34).

Melanocyte

A pigmented cell located between or beneath cells of the deepest layer of the epidermis that synthesise melanin (Tortora and Grabowski, 1996:G35).

Merkel cell

Type of cell in the epidermis of hairless skin which functions in touch (Tortora and Grabowski, 1996:G35).

Onycholysis

A painless separation of the nail plate from the nail bed (Bickley and Hoekelman, 1999:158).

Papule

A circumscribed, solid elevation of the skin up to 1cm in diameter (Canizares, 1993:13).

Pharmacopoeia

The supreme authoritative book, published by an authority, government of any country that deals with the rules and regulations of standardization of drug substances (Goel, 2002:14).

Placebo

A non-medicated substance, that is relatively inert pharmacodynamically to contrast the effects of relative non-medication in controlled experiments with those of medication in two comparable groups of patients (Gaier, 1991:426).

Plaque

An elevated, flat, 'plateau-like' lesion greater than 2cm with moderate depth (Canizares, 1993:13).

Potentisation

The preparation of a homoeopathic remedy through the process of serial dilution and succussion (Ullman and Reichenberg-Ullman, 1997:101).

Proving

The investigation of the effects of a drug, at different physiological strengths, on healthy human volunteers who note the signs and symptoms that develop during the trial. This information is augmented by the known toxic effects of the homoeopathic medicinal agent and the observed clinical cures. The sum of all this information provides the drug effects for that homoeopathic agent (Gaier, 1991:390).

Pruritus

The symptom of itching (Longmore, Wilkinson, and Torok, 2001:62).

Scale

Dry, horny, plate like excrescence; usually the result of imperfect cornification (Kumar, Cotran, and Robbins, 2001:698).

Sebaceous gland

An exocrine gland in the dermis of the skin, almost always associated with a hair follicle, which secretes sebum (Tortora and Grabowski, 1996:G47).

Seborrhoeic dermatitis

A chronic, superficial, inflammatory disease of the skin characterised by scant, loose, dry, moist, or greasy scales, and by crusted pink or yellow patches of various shapes and sizes (Odom, James, and Berger, 2000:214).

Sebum

Lipid rich secretion from a sebaceous gland (Graham-Brown and Burns, 1996:7).

Stratum corneum

The outermost dead layer of skin (Ackerman, Chongchitnant, Sanchez, Guo, Bennin, Reichel and Randall, 1997:14).

Succussion

The action of shaking up, or the condition of being shaken up, vigorously of a liquid dilution of a homoeopathic medicine in its phial or bottle, where each stroke ends with a

jolt, usually by pounding the hand engaged in the shaking action against the other palm (Gaier, 1991:532).

Suppression

Holding back, putting down, curtailing or repressing symptomatic responses through the 'principle of contradiction' also known as 'contraria contrariis' (Gaier, 1991:533).

Trituration

One of the processes of homoeopathic drug preparation. It is the act of prolonged grinding with a pestle and mortar to reduce homoeopathic drug to a fine powder while amalgamating it thoroughly with the sugar of milk by rubbing the two together under the pestle in the mortar (Gaier, 1991:559).

CHAPTER 1

1.1 Introduction

This study has been based upon a few of the concepts utilised by Smith, Baker and Williams (2002) who conducted homoeopathic research on the treatment of dandruff. They evaluated the efficacy of a low potency, oral homeopathic medication consisting of Potassium bromide 1X, Sodium bromide 2X, Nickel sulphate 3X, and Sodium chloride 6X. It was found to have significant improvement in the management of seborrhoeic dermatitis and dandruff when compared to placebo ($p < 0.04$). Smith, Baker, and Williams (2002) state that Nickel and Bromide were chosen for homoeopathic investigation because they are effective at improving and eventually clearing dandruff when taken in an allopathic, oral, low dose.

In the same light, this study chose to investigate the effectiveness of Selenium sulphide in a low, oral homoeopathic potency due to its allopathic success in managing dandruff. Selenium sulphide has been shown to be highly effective in treating dandruff (Wyndham, 2004:28) and functions by decreasing epidermal turnover rates (Katzung, 2001:1082). However, it leads to many side effects in the process (Danby, Maddin, Margesson and Rosenthal, 1993). As homoeopathic remedies are free from toxic side effects (Ullman and Reichenberg-Ullman, 1995:35), it would be of great benefit if Selenium sulphide was found to be effective in homoeopathic potency for the treatment of dandruff. Hence, this study proposed to evaluate the effectiveness of Selenium sulphide 12X in the

management of dandruff. It focused on participants between the ages of eighteen and fifty-five and obtained measurements, over a four week period, through the use of the Visual Analogue Scale (VAS) with regard to scaling, itchiness, greasiness, irritation, percentage of scalp effected, and global impression.

Dandruff, as stated by Baran and Maibach (1994:102), is a near physiological scaling condition of the scalp, whereby the normal physiological shedding of dead scalp cells is increased (Saranow, 2003:3). It has been regarded as a mild expression of seborrhoeic dermatitis by some and by others as a completely separate disorder. Seborrhoeic dermatitis is defined as a chronic dermatosis with erythematous, scaling papules and plaques, sometimes with a greasy yellow appearance (Weedon, 2003:107-108). For the purposes of this study, dandruff will be considered as a scaling condition of the scalp that ranges from a dry scalp to seborrhoeic dermatitis.

Statistics regarding the prevalence of dandruff vary quite substantially. Schwanke (2002) and Harding, Moore, Rogers, Meldrum, Scott, and McGlone (2002) state that dandruff is a relatively common condition that affects as much as half of the global population. This means that large numbers of people are affected by dandruff, and although dandruff isn't a life threatening disease, the unsightly scales do cause considerable social concern (Bulmer and Bulmer, 2000). Wyndham (2004:28) states that the social manifestations of skin disease should never be underestimated, and McLean (1999:1) says that up to 57% of dandruff sufferers feel self conscious about their condition.

Despite the large sums of money spent worldwide to eliminate the problem (Bulmer and Bulmer, 2000), no product yet is actually able to cure dandruff. Many products effectively suppress the condition, but as soon as treatment is stopped, the symptoms return (Rook, Wilkinson and Ebling, 1992:551).

The pharmacological drugs available have various modes of action through which they suppress the symptoms of dandruff. Some are antifungal in action, some anti-inflammatory, and others act primarily through their keratolytic properties (Gupta, Madzia, and Batra, 2004). Many of the products have undesirable side effects (Wyndham, 2004:28).

Non-pharmacological treatments are also available, a few examples include lime juice, cider vinegar, dead sea mud, and scalp exercises, but none have been documented to effectively and permanently cure dandruff (Saranow, 2003).

1.2 Objective

To determine the effectiveness of Selenium sulphide 12X compared to placebo in the management of dandruff in terms of assessing the degree of scaling, itchiness, greasiness, irritation, percentage of scalp effected, and global impression using the VAS.

1.3 Statement of Hypothesis

It is hypothesised that Selenium sulphide 12X will not be effective when compared to placebo in reducing dandruff symptoms as measured by the VAS.

1.4 Conclusion

Dandruff is extremely prevalent and although it isn't a life threatening disease it does cause considerable social concern and large sums of money are spent worldwide to eliminate the problem (Bulmer and Bulmer, 2000).

Allopathic treatment can be effective at suppressing dandruff, but there is a high rate of recurrence (Rook, Wilkinson and Ebling, 1992:551). Baroni, *et al.*, (2000) therefore suggest that this provides an opportunity for alternative treatment.

Smith, Baker and Williams (2002) have demonstrated that homoeopathy can be effective in the management of dandruff. Their research is a good beginning, but more homoeopathic investigation is needed.

CHAPTER 2

REVIEW OF RELATED LITRATURE

2.1 Introduction

The following chapter is a discussion about dandruff and includes the recent understanding pertaining to its epidemiology, aetiology, physiology, and management. This information has been sourced from the current literature available on dandruff.

Dandruff is extremely prevalent, some texts say as much as 50% to 80% of the population are affected (Procter and Gamble Company, 2002:11), and although it isn't a life threatening disease it causes considerable social concern (Bulmer and Bulmer, 2000). Pirkhammer, Seeber, Honigsmann and Tanew (2000) state that it leads to cosmetic disfigurement and the associated itching may considerably impair daily life. Dupuy, Maurette, Amoris and Chosidow (2001) agree and say that dandruff has functional and aesthetic consequences. Also, research shows that just a little scratching damages the hair at the root, which only recovers once the hair has totally grown out (Reiman, 2003).

Added to this, large sums of money are spent worldwide to eliminate dandruff (Bulmer and Bulmer, 2000), but no treatment yet is actually able to permanently cure it (Rook, Wilkinson and Ebling, 1992:551).

Although dandruff seems to be a relatively simple disease, it is actually subject to quite a few conflicts regarding its aetiology and nomenclature. Early conflicts have been documented between Celsus and Galen in the eighteenth century and still exist today (Saint-Leger, 1990).

2.2 Definition

Dandruff can be defined as an abnormality of the desquamative process which is strictly confined to the scalp (Pierard-Franchimont, Hermanns, Degreef, and Pierard, 2000), or as Baran and Maibach (1994:102) suggest, it is a near physiological scaling condition of the scalp. Pityriasis simplex, furfuracea or capitis are synonyms for the popular term 'dandruff' (Pierard-Franchimont, *et al.*, 2000).

'The condition is generally characterized by the presence of flakes on the scalp and in the hair, and by itch'. The symptoms do vary however depending upon the severity of the dandruff (Harding, *et al.*, 2002), and it can be episodic, recurrent or constant (Pierard-Franchimont, *et al.*, 2000).

The scales are usually mild, dry and greyish-white, similar to dry skin. With increasing severity the scales become more numerous, larger and oily, accompanied by excessive sebum production, erythema, and an accumulation of thick crusts. Itching is inconsistently present in both dry and oily types (Odom, James and Berger, 2000: 214).

This range in severity has caused a lot of semantic ambiguity as to whether the term dandruff can be used to define this broad spectrum of symptoms, or, whether it is more appropriate to use the term seborrhoeic dermatitis. Seborrhoeic dermatitis is a chronic, superficial, scaling, inflammatory disease of the skin. It is characterized by pruritic, oily, red patches of various sizes and shapes covering inflamed areas of the scalp, and other areas of skin that are rich in sebaceous glands (Smith, Baker and Williams, 2002).

Although there are varying opinions, authors tend to agree that dandruff represents a mild form of seborrhoeic dermatitis (Wyndham, 2004: 28) and both conditions are considered to be an expression of the same disorder (Pierard-Franchimont, Pierard, Arrese, and Doncker, 2001). Dawber and Grey (2002) say that dandruff and seborrhoeic dermatitis represent different ends of a spectrum of disordered desquamation. They suggest that dandruff has minimal pruritus and no erythema, while seborrhoeic dermatitis has very considerable symptomatology and visible erythema. This opinion is echoed by Harding, *et al.*, (2002) when they state that 'It is generally accepted, although the data are equivocal, that the presentation of dandruff ranges from dry scalp to seborrhoeic dermatitis'.

Therefore, for the purposes of this research dandruff will be considered as a scaling condition of the scalp that ranges from a dry scalp to seborrhoeic dermatitis.

2.3 Epidemiology

The literature varies quite substantially when it speaks about the prevalence of dandruff and seborrhoeic dermatitis. A South African publication states that the prevalence of seborrhoeic dermatitis in the normal population is 5% (Holm, 1999), and an article by Pirkhammer, *et al.*, (2000) gives seborrhoeic dermatitis a prevalence rating of 2-10%. Articles however that use the term 'dandruff' as opposed to 'seborrhoeic dermatitis', state that it is a relatively common condition that affects as much as half of the global population (Harding, *et al.*, 2002). An article in Health & Medicine Week stated that 50% of Caucasians and 80% of people with African decent are affected by dandruff (Procter and Gamble Company, 2002:11), and in a recent seminar for the Royal Society of Pathologists in London dandruff was said to be the most widespread condition apart from the common cold (Procter and Gamble Company, 2003). This large variation in the statistics seems to be caused by the confusion surrounding the nomenclature of dandruff and seborrhoeic dermatitis. From the researcher's experience in doing this research, it does seem that the latter statistics are more accurate.

Age, gender and seasonal epidemiological factors are statistics that do however correlate between the varying literatures.

Baran and Maibach (1994:133) say that the peak incidence is reached at the age of eighteen and becomes less frequent after fifty years of age. This is repeated frequently

in most of the literature, although some say that there is no upper age limit and say that dandruff can continue throughout life (Schwanke, 2000).

The prevalence and severity of dandruff is greatest in young men, and wintertime exacerbates the condition (Pierard-Franchimont, *et al.*, 2000). Sunlight seems to improve its clinical appearance (Gupta, *et al.*, 2004).

Although the literature supports the fact that dandruff is more prevalent in males (Harding, *et al.*, 2002), it was interesting to see that most of the participants in this research were female. This may be because dandruff is largely a cosmetic condition (Pierard-Franchimont, *et al.*, 2000), something that may concern women more than men.

Prevalence also seems to be increased in certain conditions such as Parkinson's disease and HIV (Wyndham, 2004:28).

2.4 Aetiology

Dandruff is a common problem that has been subject to a large amount of research. Despite this, little is known about its aetiology and little progress has been made towards its understanding (Harding, *et al.*, 2002).

For the past century *Malassezia*, a type of yeast, has been the suspected cause of dandruff (Pierard-Franchimont, *et al.*, 2001). It is part of the normal scalp flora (Procter and Gamble Company, 2002:11). In one study the yeast was found to comprise 46% of the scalp flora in healthy individuals and 74% in those with dandruff (Peter and Richarz-Barthauer, 1995).

Malassezia furfur was the initial suspected culprit (Schwanke, 2002), and over the years it has also been referred to as *Pityrosporum orbiculare*, *Pityrosporum ovale*, or simply *Malassezia* (Gemmer, DeAngelis, Theelen, Boekhout and Dawson, 2002). However, research conducted in 2002 at The Procter & Gamble Company has shown that *Malassezia* is an organism composed of seven separate species. *Malassezia furfur* has now been found not to occur on dandruff scalps at all (Schwanke, 2002). Two newly discovered species of *Malassezia* are now thought to be involved: *Malassezia globosa* and *Malassezia restricta*, which were found on 70% and 45% of dandruff scalps respectively (Gemmer, *et al.*, 2002).

The exact role of *Malassezia* in dandruff formation is uncertain and it is a topic under constant dispute (Pierard-Franchimont, *et al.*, 2001). Some researchers suggest that dandruff is the result of an altered immune response to *Malassezia* and say that even a normal amount of the yeast can trigger an inflammatory reaction. Other researchers believe that dandruff occurs solely as a result of hyperproliferation of corneocytes, some say it is due to toxins that are released by the yeast, while others say that it is simply due to an overgrowth of the *Malassezia* yeast. The latest research however seems to

indicate that dandruff actually results from the lipase activity of *Malassezia* (Gupta, *et al.*, 2004).

Research conducted in 2002 by the Procter & Gamble Company found that *M. globosa* and *M. restricta* are lipophilic, in other words, they require lipids to live. Essentially they 'eat' the lipids on the skin surface (there are more lipids on the scalp than anywhere else on the body surface). In the process of doing this, they release free fatty acids (oleic acid in particular) that linger on the skin surface and act as an irritant (Schwanke, 2002). These fatty acids seem to penetrate the stratum corneum and break down its barrier function. The body responds by trying to rebuild the barrier, but this leads to hyperproliferation with an increased production of sebum. This increases the nutritional material available, and the problem is perpetuated (Dawber and Gray, 2002).

The theory that dandruff is caused by the 'lipid waste' of *M. globosa* and *M. restricta* (Procter and Gamble Company, 2002:11) is not however complete yet. Kaczinsky, one of the initial researchers investigating this theory, believes that they have solved one part of the puzzle, but there is still more to dandruff's aetiology to discover (Jesitus, 2003).

A question that many researchers are asking is: If *Malassezia* is present on all scalps, then what makes the difference between a healthy scalp and a dandruff scalp? (Schwanke, 2002). 'No pathogenic mechanism has been associated with deterioration from a healthy scalp to a dandruff scalp' (Harding, *et al.*, 2002). There are many

possible aggravating factors as is found in the literature. Saranow (2003:3) suggests that climate, hormonal fluctuations (especially androgenic influences), stress and genes can trigger *Malassezia* to multiply. Rochester (1998) adds that an increase in oil production, illness, neurological disorders such as Parkinson's disease, a suppressed immune system, infrequent shampooing, and extra sensitivity to the *Malassezia* fungus may also contribute. Cosmetic hair products may also be responsible as well as air-borne substances in the environment (Pierard-Franchimont, *et al.*, 2000).

In research conducted by Harding, *et al.*, (2002) researchers have perhaps identified another predetermining factor to dandruff formation. The research showed that dandruff sufferers seem to have a decreased level of scalp lipids and intercellular lipids. These are critical components of the epidermal water barrier, and, with the water holding capacity of the tissue perturbed, there is a reduction in the corneodesmosomal degradation (i.e. increased attachment between corneocytes and their desmosomes). This leads to the characteristic scaling. If this is an important factor in predetermining whether an individual is predisposed to dandruff, it may explain why 'everybody has *Malassezia* but not everybody has dandruff'.

Harding, *et al.*, (2002) propose that an impaired barrier makes dandruff sufferers more prone to the irritant effects of microbial activity on scalp skin, and to environmental factors such as styling products, surfactants and pollutants.

2.5 Pathophysiology

No matter what the trigger is, the end result is the same. The normal physiological shedding of dead scalp cells is increased (Saranow, 2003:3). This shedding, also referred to as keratinocyte migration (from the basal layer to the surface), is shortened from 24 days to as little as 3 to 4 days and is also associated with hyperproliferation (Sinclair, 2000). It results in keratinocytes that do not completely mature and which also become irregularly arranged (Baran and Maibach, 1994:134). Their adhesion to surrounding cells is therefore reduced, which leads to easy detachment from the scalp - this forms the gross flakes of dandruff. Normally the horny layer consists of twenty-five to thirty-five layers of fully keratinised cells, but with dandruff, it is reduced to fewer than ten layers (Orfanos and Happle, 1990:990).

It is likely that both perturbed stratum corneum maturation and *Malassezia* contribute to the incidence and severity of dandruff, although the question as to whether impaired epithelial differentiation is a predisposing cause of dandruff or a consequence of *Malassezia* interaction with the scalp is uncertain (Harding, *et al.*, 2002).

2.6 Anatomy and physiology of the skin

The skin is the largest organ in the body (Gawkrodger, 2002:2). It may seem simple in structure, but it is in fact a complex organ which governs the body's response to the external environment (Kumar, *et al.*, 2001:698).

2.6.1 Skin structure

The skin is conventionally divided into three main functional areas: the epidermis, the dermis, and the subcutaneous layer as shown in figure 2.1 (Haslett, Chilvers, Hunter, and Boon, 2000:878).

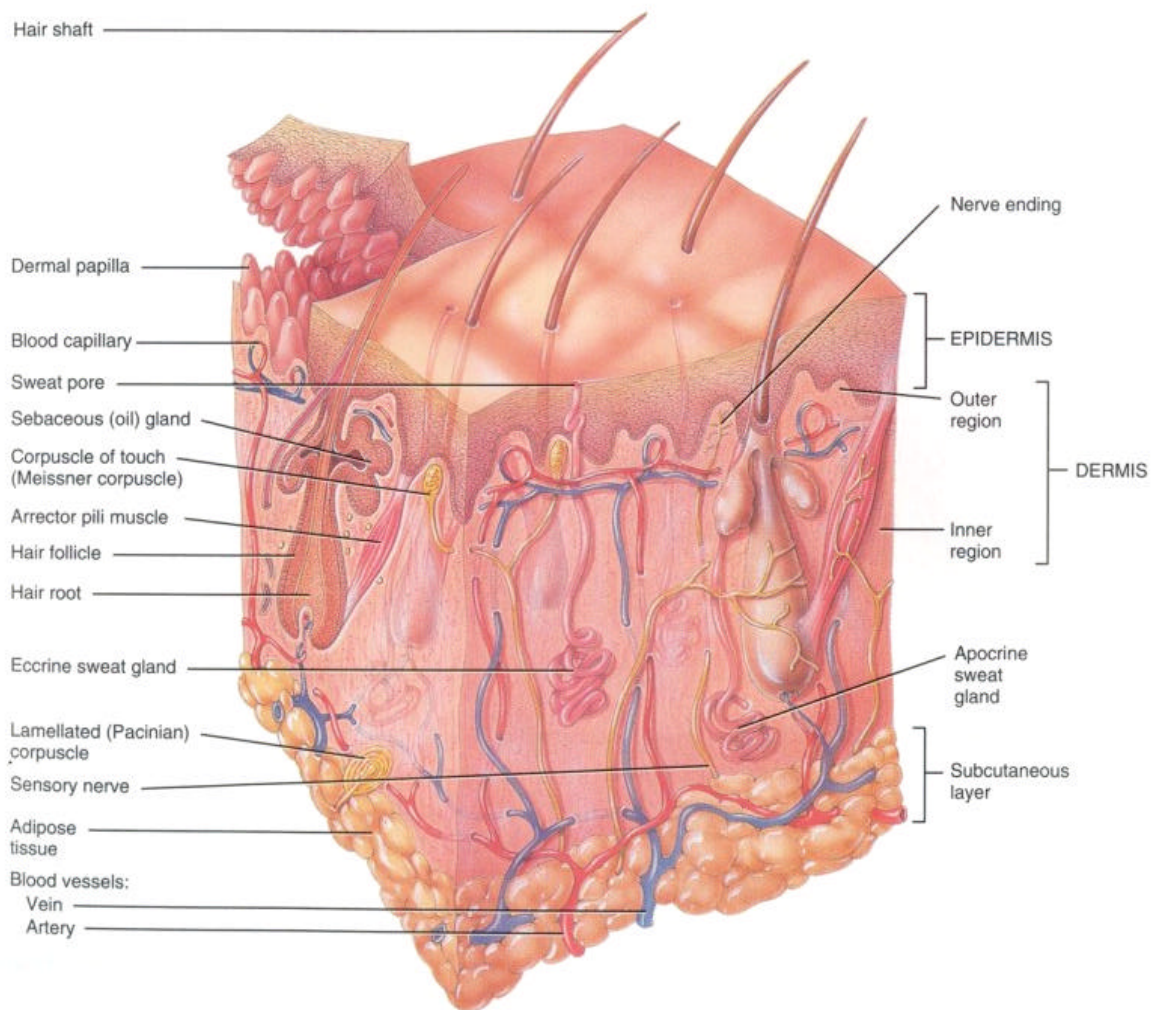


Figure 2.1 Structure of the skin (Tortora and Grabowski, 2001:101).

2.6.1.1 The Epidermis

The epidermis is the outermost part of the skin and is divided into four layers. (The stratum lucidum, as seen in Figure 2.2, is only found in thick skin, i.e. the palms and soles). Beginning at the outer surface and working inwards these four layers are: the stratum corneum or the horny layer (composed of dead cornified cells); the granular layer also known as stratum granulosum (the zone where epidermal nuclei disintegrate); the germinative or prickle cell layer known as stratum spinosum (where the bulk of the living cells are found); and the basal layer or stratum basale (where undifferentiated cells undergo cell division), (Mackie, 1991:16-17).

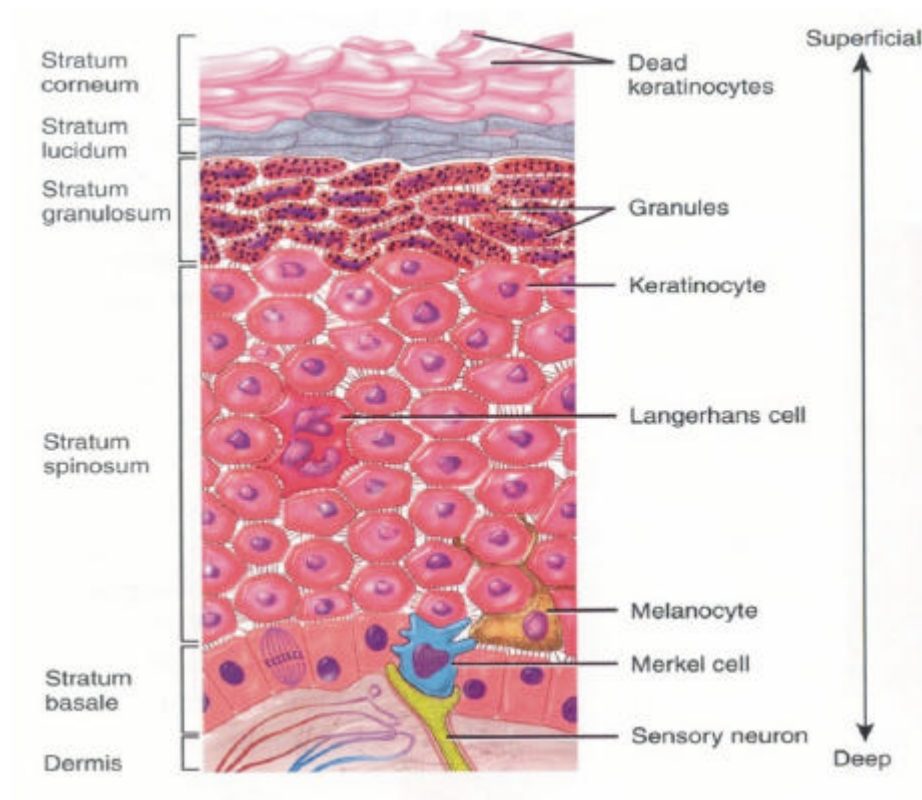


Figure 2.2 Layers of the epidermis (Tortora and Grabowski, 2001:102).

The main cells of the epidermis are the keratinocytes, they produce the protein keratin. The four layers of the epidermis represent the stages of maturation of keratinocytes, from their differentiation in the basal layer, into dead, but functionally important corneocytes that make up the horny layer. The corneocytes are eventually shed from the skin surface. Studies show that the total cell turnover time from the basal layer to shedding at the surface, on average, is twenty-four days (Gawkrodger, 2002:2, 6).

The cellular connections within the epidermis are important as they provide strength to the skin, and enable it to function as a barrier. Corneocytes are bonded together by tonofilaments, these are aggregations of keratin produced by the keratinocytes (MacKie, 1991:22). Lipid glue, produced by the underlying granular layer, also 'sticks' the corneocytes together. Within the prickle layer, intercellular bridges called desmosomes are responsible for connecting the keratinocytes (Gawkrodger, 2002:2, 6).

Other cell types that can be found in the epidermis are pigment producing cells called melanocytes, Langerhans cells that are immunologically active, and Merkel cells that have a role in sensation (MacKie, 1991:18).

The basement membrane divides the epidermis from the dermis and literally holds the skin together by anchoring down the basal layer (MacKie, 1991:28). It also allows free movement of cells and nutrients between dermis and epidermis (Haslett, *et al.*, 2000:878).

2.6.1.2 The Dermis

The dermis is a tough, supportive connective tissue matrix composed mainly of collagen fibres and a few fibres of elastin. It is found just below the epidermis and contains many specialised structures, including lymphocytes (white blood cells), macrophages (phagocytic cells), mast cells (cells of the connective tissue involved in immune and inflammatory responses), dermal dendrocytes (bone-marrow derived cells), and fibroblasts (cells within the connective tissue) (Gawkrodger, 2002: 3). Embedded within the dermis are the nerves, lymphatics and vasculature (MacKie, 1991: 29). It is both a structural and nutritional support to the epidermis (Haslett, *et al.*, 2000:880).

2.6.1.3 The Subcutaneous layer

The subcutaneous layer, also known as the hypodermis, lies immediately below the dermis. It mainly consists of fat traversed by nerves and blood vessels (Graham-Brown and Bourke, 1998:5).

2.6.1.4 The skin appendages

There are three important appendages of the skin, all of which are derived from the epidermis: the nails, the sweat glands, and the hair follicles.

There are over 100 000 hairs on the average human scalp. A hair is a filament of keratin consisting of a root and a shaft, situated within a hair follicle within the epidermis (Graham-Brown and Bourke, 1998:6). Each hair follicle has an attached sebaceous gland which secretes sebum into the follicle by means of a duct. This sebum is then discharged onto the surface of the skin for the purposes of a waterproofing mechanism (Haslett, *et al.*, 2000:880). The sebum carries with it a flora of bacteria, yeasts and mites as well as desquamated corneocytes (Ackerman, *et al.*, 1997:46). Sebaceous glands are mainly found on the face, scalp, chest, and upper back (MacKie, 1991: 34).

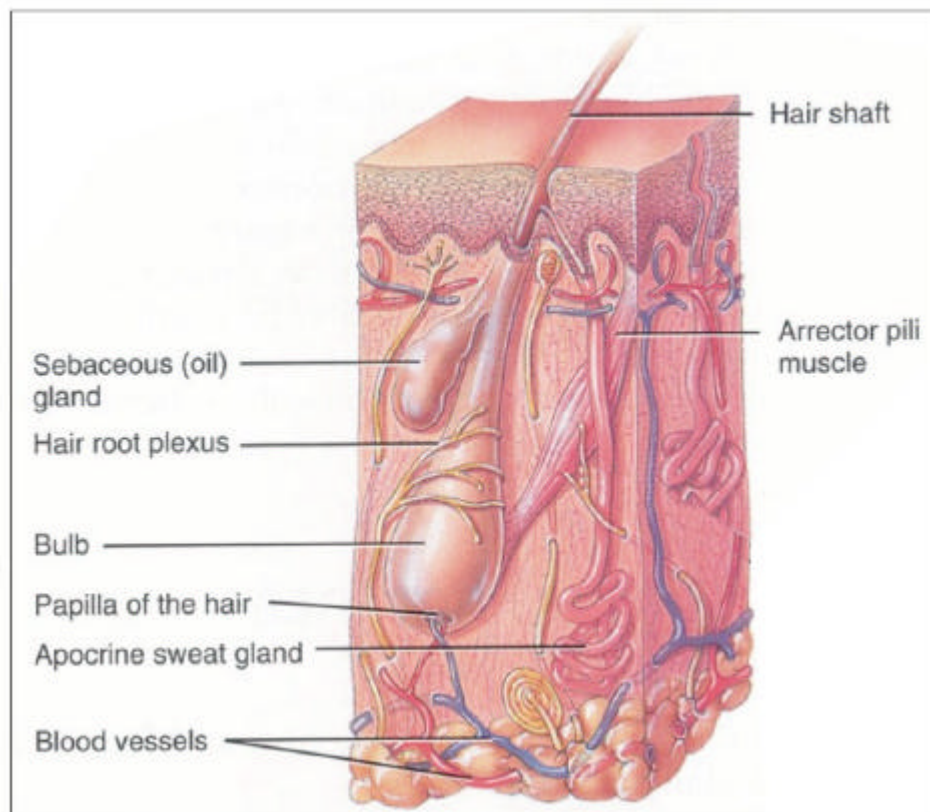


Figure 2.3 Hair and its surrounding structures (Tortora and Grabowski, 2001:104).

Sebaceous glands are however undifferentiated epithelial cells until puberty. At puberty endogenous androgens are produced by the body and cause the undifferentiated cells to form sebaceous lobules and ducts. The lobules then begin to fill with lipids. At menopause and andropause the effects of androgens diminish and the sebaceous lobules begin to regress again (Ackerman *et al.*, 1997:46).

2.6.2 Functions of the skin

Graham-Brown and Burns (1996:10) list the following functions of the skin:

- Prevents loss of essential body fluids.
- Protects against entry of toxic environmental chemicals and micro organisms.
- Protects against damage from UV radiation.
- Regulates body temperature.
- Synthesis of vitamin D.
- Important in sexual attraction and psychosocial interaction.

Haslett, *et al.*, (2000:880) also include the following functions:

- Sensation.
- Calorie Reserve.
- Shock absorber.
- Lubrication and waterproofing.

2.7 Differential Diagnosis

There are a number of conditions which have similar symptoms to dandruff and which may be wrongly diagnosed as dandruff, or vice versa. The literature concerning the differential diagnosis is mostly unanimous and includes psoriasis; irritant contact dermatitis; atopic dermatitis; head lice; fungal infections and dry scalp.

Psoriasis is a scaling condition which may occur on the scalp. The scales however are usually well demarcated and more prominent than those in dandruff (Ackerman, *et al.*, 1997:722). Wyndham (2004:28) adds that the thick scales of psoriasis may 'grow' along the hair shaft and may sometimes form plaques. Wolverton (2001:647-648) goes on to say that purple-red plaques with white scaling can be found on other sites of the body as well, i.e. knees, elbows. The nails too are sometimes affected with pitting, dystrophy and onycholysis.

Both irritant contact dermatitis and atopic dermatitis can mimic dandruff. The central part of both of these diseases is extreme itching, rubbing and scratching. Irritant contact dermatitis of the scalp may occur due to sensitiveness of certain hair care products (Wolverton, 2001:648), and due to its artificial nature, may be sharply delimited (Ackerman, *et al.*, 1997:722). Atopic dermatitis occurs in allergy prone individuals who have a hypersensitive reaction to common environmental antigens (i.e. pollen). This reaction can cause patches of dry, pruritic, thickened skin and it is often associated with asthma, hay fever and urticaria (Haslett, *et al.*, 2000:897).

The nits of head lice may look like dandruff scales, the key to differentiation however, is that a dandruff scale is easily dislodged, but a nit stays tightly attached to the hair shaft (Wyndham, 2004:28).

Fungal infections, including *Tinea capitis*, may mimic dandruff by causing red scaling of the scalp. They also however, produce an area of alopecia, unlike in dandruff (Wyndham, 2004:28). Wolverton (2001:648) includes that fungal infections leave marginated, vesicular borders.

A dry scalp caused by infrequent showering or from cold winter months may be confused with dandruff (Saranow, 2003:3), but the associated scales are usually smaller and less oily (Spelhaug, 2004).

Finally, scaling may be a sign of serious disease elsewhere in the body (Wolverton, 2001:648). Lupus erythematosus is one example, and forms discrete plaques, indurated adherent scales, and follicular plugs (Ackerman, *et al.*, 1997:722). Cutaneous T-cell lymphomas are another example, although they are very rare. They begin with a plaque stage that resembles psoriasis, but after this they develop a skin tumour (Haslett, *et al.*, 2000:916). Lastly, Pityriasis rubra pilaris, a chronic inflammatory scaling skin disease that resembles psoriasis, could also be confused with dandruff (Haslett, *et al.*, 2000:916).

Ackerman, *et al.*, (1997:722) say that no laboratory confirmation exists for the diagnosis of dandruff.

2.8 Treatment

2.8.1 Introduction

The modern approach to the treatment of dandruff is not an ideal one. Many products are available that effectively suppress dandruff, yet none are able to actually cure the condition. As soon as treatment is stopped, the symptoms return (Rook, Wilkinson and Ebling, 1992:551). Pierard (2003) mirrors this view by stating that 'treatments are helpful but not curative', as does Baroni, De Rosa, De Rosa, Donnarumma, and Catalanotti (2000) when they say that dandruff 'represents a therapeutic problem due to the high rate of recurrence'. Reiman (2003) goes as far to say that dandruff is 'a life long condition'.

2.8.2 Pharmacological treatment

There are roughly 300 over-the-counter antidandruff products available on the market (Saranow, 2003). Not all of them are equal in efficacy (Pierard-Franchimont, *et al.*, 2000), and it is difficult to conduct and interpret comparative studies between them (Pierard, 2003). They are either topical in their application, including shampoos, creams, ointments and lotions, or they are taken orally (Gupta, *et al.*, 2004). It seems

that topical treatment is associated with poor patient compliance while oral treatment has better compliance and also a decreased rate of relapse (Baroni, *et al.*, 2000).

The mode of pharmacological action varies among the treatments; this highlights the confusion surrounding the aetiology of dandruff. Some directly target the *Malassezia* species with their antifungal properties, some are anti-inflammatory in action, and others act primarily by breaking down dead skin cells (keratolytic properties). Gupta, *et al.*, (2004) believe that these differences are of little importance and all the treatments are in fact compatible.

2.8.2.1 Antifungal agents

The modern therapeutic approach to control dandruff acts by targeting the *Malassezia* species (Pierard, 2003), and hence decreases colonization of the yeast (Johnson and Nunley, 2000).

Specific antifungal agents include Zinc pyrithione, Selenium sulphide, Ciclopirox olamine, Terbinafine (topical and oral), Butenafine, Tacrolimus, Pimercrolimus, Lithium gluconate, Climbazole and a few Imidazoles (Gupta, *et al.*, 2004). Of the Imidazoles, Ketoconazole (topical and oral) is the leading representative (Pierard-Franchimont, *et al.*, 2000) and it is believed to be one of the most effective agents active against dandruff (Pierard, 2003). Other Imidazoles include Bifonazole, Metronidazole, Fluconazole (topical and oral), Climbazole, Miconazole, and Itraconazole (topical and

oral). The Imidazoles are the largest group of antifungals used in the treatment of dandruff (Gupta, *et al.*, 2004).

Most of these antifungals are safe to use as over-the-counter medications and are effective at killing the yeast responsible for dandruff (Bulmer and Bulmer, 1999).

Table 2.1 A list of the most popular over-the-counter products (Bulmer and Bulmer, 1999).

Product	Active Ingredient
Head and Shoulders ®	Zinc pyrithione
Gard Violet ®	Climbazole
Nizoral ®	Ketoconazole
Selsun Blue ®	Selenium sulphide

2.8.2.2 Keratolytic agents

Keratolytic products are 'the older antidandruff agents' and were the popular mode of treatment before *Malassezia* was discovered as the probable cause. They are active topically and include Propylene glycol, sulphur and tar containing compounds and Salicylic acid. Both Selenium sulphide and Zinc pyrithione, though classed as antifungals, also show some keratolytic properties (Gupta, *et al.*, 2004).

Keratolytic agents actively loosen the bonds between the corneocytes; this releases the adherent scales from the scalp and washes them away. The stratum corneum is thus thinned, leading to less dandruff (Wolverton, 2001:650). Coal tar additionally inhibits cell division and slows down the build up of flakes on the scalp (Wyndham, 2004:28).

2.8.2.3 Anti-inflammatory agents

Topical treatment with weak corticosteroids is useful episodically when treatment with therapeutic shampoo alone is ineffective (Pierard, 2003). 'Corticosteroids have potent anti-inflammatory and antipruritic effects' (Wolverton, 2001: 650) and are available in solutions, lotions, creams and ointments (Johnson and Nunley, 2000). However, recurrence is prompt and relapse rates are high (Wolverton, 2001: 650), so corticosteroids use should be restricted to treating the inflammatory component only, and should be combined with other therapies (Dupuy, *et al.*, 2001).

The Imidazoles, along with their antifungal properties, are also believed to have global anti-inflammatory effects (Pierard-Franchimont, *et al.*, 2000), as is Terbinafine (Scaparro, Quadri, Virno, Orifici, and Milani, 2001).

2.8.3 Selenium sulphide

As mentioned above, Selenium sulphide is both antifungal and keratolytic in its action. This means that it acts by decreasing the colonization of *Malassezi* and also breaks

down the build up of dead skin cells (Gupta, *et al.*, 2004). Katzung (2001:1082) adds that Selenium sulphide also acts as a cytostatic agent and therefore decreases epidermal turnover rates.

Unfortunately there are a number of side effects that can result from the use of Selenium sulphide shampoo. These side effects include pruritis; burning sensations; skin eruptions; psoriasis; and bleaching of hair colour (Danby, *et al.*, 1993). It may also stain the scalp orange and increase sebum production – thus worsening the disease (Wyndham, 2004:28). When a bioassay of oral Selenium sulphide (ranging from 20-100 mg/kg/day) was performed on rats and mice, hepatocellular carcinomas and adenomas resulted. Following this, a further bioassay of topical Selenium sulphide was conducted on rats and mice in which equivocal carcinogenic effects were produced (National Toxicology Program, 1980). As a result of these reports, Selenium sulphide has been classified as a 'probable human carcinogen' (RPS Group Plc, 2002:7).

According to a report by Wolverton (2001:652), systemic absorption of Selenium sulphide is possible if one washes one's hair with the shampoo in a bath and then soaks in the water. He also reports of an isolated case where damaged scalp skin lead to Selenium sulphide absorption followed by intoxication (tremors, perspiration, garlicky breath, weakness, vomiting, and abdominal pain).

Selenium sulphide is highly effective in the treatment of dandruff. As a result, despite the harmful side effects it produces, it is still a popular ingredient in antidandruff

shampoos (Wyndham, 2004:28). It is for this reason that this trial investigated a homoeopathic alternative for Selenium sulphide in the management of dandruff. Due to the minute dilutions utilised, homoeopathic prescriptions are free from toxic side effects (Ullman and Reichenberg-Ullman, 1995:35).

2.8.4 Side effects of other antidandruff products

Some of the other treatments mentioned have recorded side effects and are listed as follows:

Ketoconazole, oral dose: nausea, vomiting, dizziness, sensitivity to light, skin rashes, decrease in liver function, adjustment of adrenal and testicular steroid metabolism, cardiac arrhythmias if co-administered with terfenadine or astemizole (Ellis, 1996).

Ketoconazole, topical application: itching and burning (Wyndham, 2004:28), no systemic adverse effects have been reported (Wolverton, 2001: 651).

Fluconazole, oral dose: nausea and vomiting, but generally well tolerated with very few drug interactions (Ellis, 1996), may be immunotoxic (Baroni, *et al.*, 2000).

Itraconazole, oral dose: Generally well tolerated with minor adverse effects of nausea, headache and abdominal pain (Ellis, 1996).

Tar shampoo: green staining of hair, increased risk of sunburn (Saranow, 2003), potential carcinogenic risks (Pierard-Franchimont, *et al.*, 2000).

Salicylic acid ointment: salicylate intoxication (Wolverton, 2001: 651).

Topical corticosteroid shampoo: folliculitis, skin atrophy, secondary infection, telangiectasias, hypertrichosis, hypopigmentation, and striae. Use may also suppress the hypothalamus-pituitary-adrenal axis (Wolverton, 2001: 651, 653). Chronic use of strong steroids may lead to steroid dermatitis and rosacea-like lesions (Pierard, 2003).

None of the products have been adequately tested in pregnancy or on children (Wolverton, 2001: 651).

2.8.5 Therapeutic guidelines

2.8.5.1 Oral Antifungals

Ketoconazole is the oldest oral antifungal agent, which, due to the side effects it produces, has largely been replaced by newer oral antifungal agents (namely Fluconazole and Itraconazole). In third world countries however, it is still widely used. Dosage is normally 200 mg/day, which is usually prescribed for a period of five to ten days. If the patient is non-responsive, the dosage is increased to 400 mg/day. It is best

to take Ketoconazole with food and at regular time intervals. It must not be taken more often than directed and it is important to finish the full course prescribed (Ellis, 1996).

Itraconazole, one of the newer oral antifungal agents, is most effective when 200 mg/day is taken over a period of five to seven days. Absorption from the gastrointestinal tract is improved if the drug is given with food (Ellis, 1996).

Fluconazole is unaffected by food intake and can either be prescribed as a single 400mg dose, or a weekly dose of 150 mg over a period of four weeks (Ellis, 1996).

2.8.5.2 Antidandruff shampoos

Generally, shampoos are applied to a wet scalp and should be kept in contact with the scalp for five minutes before rinsing (Wolverton, 2001: 653). Initially the shampoo can be used daily, but once the dandruff is under control, the frequency can be reduced to twice weekly (Johnson and Nunley, 2000).

A trial by Danby, *et al.*, (1993) tested the safety and effectiveness of 2% ketoconazole shampoo versus 2.5% Selenium sulphide shampoo. The trial took place over a four week period during which time visual assessments for scaling, irritation, global improvement and itching were made (the severity ratings were the same as those used for this trial). The presence of yeast on the scalp was also determined at each visit through the use of oil immersion microscopy. The results of the trial showed that both

shampoos were significantly more effective than placebo in the management of dandruff. However, all nine adverse effects that were reported during the trial occurred in the group treated with Selenium sulphide shampoo.

Antidandruff shampoos seem to lose their effectiveness as the body adapts to them (Saranow, 2003) and patients often benefit more by using several shampoos from different classes in a rotational manner (Wolverton, 2001: 653).

2.8.6 Topical Treatment Verses Oral Treatment

The current mainstays in the treatment of dandruff are topical antifungal agents; shampoos in particular (Pirkhammer, *et al.*, 2000). Interestingly, a number of reports indicate that topical treatment is associated with poor patient compliance, while oral treatment on the other hand has better compliance, and also a decreased rate of relapse (Baroni, *et al.*, 2000).

Topical treatments seem to be more popular however for a number of reasons. Firstly, they are relatively inexpensive; secondly, they provide an immediate reduction in infectivity; and thirdly, they are mainly free of systemic adverse effects. On the other hand, oral antifungal agents are more costly and have potential harmful systemic effects (Ellis, 1996).

The problem remains however, that with topical treatment, patient compliance is generally poor (Ellis, 1996).

Based on the above information, this trial chose to use an oral homoeopathic preparation. The advantage is not only the hope for better patient compliance, but unlike current allopathic oral medication, homoeopathy is inexpensive and free from toxic side effects (Ullman and Reichenberg-Ullman, 1995:35).

2.8.7 Non-pharmacological treatment

There are several natural treatment suggestions, some which people swear by, but none which the dermatologists feel are adequate enough to replace current conventional treatment. These include suggestions such as lime juice, cider vinegar, dead sea mud, scalp exercises (Saranow, 2003), and a healthy diet. The most common nutritive suggestions include limiting sugar and yeast and adding plenty of B vitamins, zinc, and omega-3 fatty acids to the diet (Spelhaug, 2004). Hygiene is another frequent suggestion and includes frequent washing (which removes excess oil and improves seborrhoea) (Johnson and Nunley, 2000); regular brushing (to remove scales and debris); and avoidance of sticky cosmetic agents for the hair, i.e. mousse and hair spray (Wyndham, 2004:28).

An alternative to antimycotic shampoo is a buffered acidic shampoo which decreases the pH and increases the ionic strength on the scalp surface resulting in a drastic inhibition of the growth of *M. ovalis* (Baroni, *et al.*, 2000).

Lastly, narrow-band ultra violet light is considered an effective alternative especially in those patients unresponsive to conventional treatment (Pirkhammer, *et al.*, 2000). It appears however, due to the lack of references available in the current literature, that few dermatologists have as yet incorporated this into their treatment regime. This may be due to the fact that it is relatively recent research.

2.9 Homoeopathy

2.9.1 Definition and laws

Homoeopathy is a safe, gentle, and effective system of medicine that powerfully stimulates the body's vital force to cure illness (Vithoukas, 1987:15). It was founded by Samuel Hahnemann and is based on a number of fundamental principles including 'Like Cures Like'; 'Infinitesimal dose'; and 'Individualisation' (De Schepper, 2001:26-43).

2.9.1.1 Like Cures Like

The defining principle of homoeopathy can be found in its name which, when translated, means 'similar suffering' (Vithoukas, 1987:15). *Similia Similibus Curentur*, or in other

words “let likes be cured by likes”, simply means that ‘substances capable of causing disorder in healthy subjects can be used as medicines to remedy similar patterns of disorder experienced by people when they are ill’. These patterns of disorder are obtained through ‘provings’ in which healthy volunteers undergo a drug trial (Swayne, 1998:17).

2.9.1.2 Infinitesimal dose

The second principle is that of the infinitesimal potentised dose, or in other words ‘the minimal dose’. Hahnemann showed that only minute doses of drugs are required to bring about a curative reaction (De Schepper, 2001:38-42). Homoeopathic remedies have very little, if in fact any original substance left in them (Ullman and Reichenberg-Ullman, 1995:35). These minute potencies are prepared through a series of dilution and succussion, trituration, or fluxion (Swayne, 2000:169). This step-by-step process makes the remedy powerful, but at the same time harmless. The remedies are extremely dilute, have no side effects and are very safe to use (Ullman and Reichenberg-Ullman, 1995:35).

2.9.1.3 Individualisation

The third principle is based on individualisation. ‘Homoeopaths do not treat diseases, but rather they treat sick individuals, no two persons with the same disease are ill in exactly the same way’ (De Schepper, 2001:42). Bodman (1990:5) reiterates this law by

saying 'the prescriptions of homoeopathic remedies do not depend on the pathological or bacteriological report' but rather as Swayne (1998:22) states 'the correct homoeopathic medicine must accurately reflect the experience of the illness in the individual patient'.

2.9.2 Homoeopathic treatment of dandruff

Smith, Baker, and Williams (2002) conducted homoeopathic research for the possible management of dandruff. The treatment was a low potency, oral homoeopathic preparation of Potassium Bromide 1X, Sodium Bromide 2X, Nickel Sulfate 3X, and Sodium chloride 6X. It was a double-blind, placebo controlled trial which made use of the cross-over design. Forty-one participants with a mean age of 53 were accepted into the ten week trial and assessments took place on week 0, 5, and 10. The medication (placebo or active) was self administered once daily at the beginning of each day on an eight hour fasted stomach. At the end of the ten week period all participants crossed over to active medication for an additional 10 weeks. Assessment used two different visual scales; the first scale (on a rating of 0 to 6) rated the percentage of skin involved; the second rated erythema and flaking on a scale of 0 to 4. It was found that the treated patients improved significantly when compared to patients that were on placebo with $P < 0.004$, and when placebo patients crossed over to treatment $P < 0.01$. The treatment was found to be essentially side effect free.

Research by Teleman (2005) was conducted simultaneously, yet independently to this trial, at the Durban Institute of Technology. A preparation of Selenium sulphide 8X was added to a neutral shampoo base and researched for its possible effectiveness in the management of dandruff. Thirty-three participants were accepted into a four week trial in which the shampoo had to be used twice weekly. The assessment process was identical to that of this trial. The results showed an improvement within the treatment group with $P < 0.01$, but inter-group analysis showed no significant improvement.

Treatment for dandruff is listed in the homoeopathic repertory, there are thirty-six remedies listed under the heading 'Head – dandruff' of which *Cantharis vesicatoria*, *Carboneum sulphuratum*, *Graphites*, *Natrum muriaticum*, *Phosphorus*, and *Sulphur* are the most commonly indicated remedies (Schroyens, 1998: 254). It is interesting that neither Nickel nor Bromide are mentioned in this list, yet Smith, Baker, and Williams (2002) showed that they are in fact both effective in the management of dandruff. This shows us that the repertory is not complete and remedies outside of this list could be found effective in the treatment of dandruff.

Other homoeopathic remedies useful for the management of dandruff are mentioned by Master, Wig, Bharucha and Shah (1999:16) and include *Ceanothus*, *Cochlearia armoracia* (local application), *Gratiola*, *Kali sulph*, *Lycopodium*, *Petroleum*, *Pilocarpus*, *Quillaya*, *Saponaria*, and *Rosemarinus*.

The remedies listed above (i.e. by Master, *et al.*, 1999 and Schroyens, 1998) are prescribed by means of a clinical prescription – as opposed to a classical prescription. A clinical prescription simply means that a remedy is prescribed based on the pathological and physiological presentation of the disease – that which can be seen physically. This approach believes that certain remedies almost always work when given in similar circumstances, in other words there are specific remedies for specific diseases (Master, *et al.*, 1999:2). The classical approach, on the other hand, is one which is strictly based on conventional Hahnemannian principles, in other words, the Law of Similars, the Infinitesimal dose, and Individualisation. This approach does not believe that there are specific remedies for each disease, but rather that there are specific remedies for each individual (De Schepper, 2001:42). Classical homoeopaths prescribe on the totality of symptoms - from physical, emotional, and mental levels (Kayne, 1997:88).

This trial is therefore based on the concepts of the clinical approach. The prescription was not based upon the Law of Similars or upon Individualisation. It was based purely on the physical, pathological symptoms and took no account of any emotional or mental symptoms.

2.9.3 Remedy selection

A homoeopathic preparation of Selenium sulphide 12X was the choice of treatment for this trial. It was made from the crude substance according to homoeopathic principles.

It is not a remedy that is listed in any *Materia Medica*, and there is no documentation to suggest it has been used homoeopathically before. It must be noted therefore that this research is not based on the homoeopathic principle of 'the Law of Similars'. For this to be the case there would have to be a proving performed. A proving would provide us with a 'drug picture' and hence a template to which ailments Selenium sulphide could cure. In other words, if dandruff became a symptom in a prover, then it could be used homoeopathically to cure dandruff in one who suffers with the disease, this would then be based on the Law of Similars (Kayne, 1997:25-26).

The justification, therefore, for the selection of Selenium sulphide is based on previous research conducted by Smith, Baker, and Williams (2002) who chose to study the homoeopathic effect of Nickel, Bromide and Sodium chloride in the treatment of dandruff. The treatment choice of nickel and bromide was based purely on their allopathic success. Literature reports that these elements are effective in clearing dandruff when given orally in a low systemic dose (Smith, Baker, and Williams, 2002).

Likewise, Selenium sulphide has proven to be effective, allopathically, in the treatment of dandruff (Wyndham, 2004:28).

Selenium sulphide was also chosen due to the many side effects that the allopathic preparation causes (Danby, *et al.*, 1993). Homoeopathic treatment is side effect free (Ullman and Reichenberg-Ullman, 1995:35).

'In some cases the whole drug picture may be derived from toxicological or clinical observations and not from a true proving' (Kayne, 1997:26). Unfortunately, according to the U.S. Environmental Protection Agency (2004), there is inadequate data to support the toxicological effects of Selenium sulphide from human studies, but there is sufficient evidence from animal studies. Amongst many other symptoms, skin irritation was found to occur in mice and rats on exposure to Selenium sulphide. Interestingly, hyperkeratosis and acanthosis are specifically mentioned as the types of skin irritation that occurred. Hyperkeratosis is overgrowth of the horny layer of the epidermis, and acanthosis is overgrowth of the prickle cell layer of the epidermis (Anderson, *et al.*, 2002:11, 845). In dandruff, there is an overgrowth of the cells within the epidermis from the basal layer to the surface (Sinclair, 2000). This hyperproliferation therefore includes the cells of the horny layer and the prickle cell layer. An article by Heyl and Swart (1990:97) in fact describe dandruff as hyperkeratosis of the scalp. Although this information alone is not enough to justify the study of Selenium sulphide in the management of dandruff, it does however add to the validity of the trial.

Both Selenium metallicum and Sulphur, independently, are homoeopathic remedies recorded in the Materia Medica and they both have skin ailments within their proving picture. According to Springer (1997) 'in cases where both components of the salt are well known as homoeopathic remedies, the Materia Medica of the correspondent salt will contain elements of both its constituents'. In other words, the homoeopathic preparation of Selenium sulphide will contain curative elements that are characteristic in both Sulphur and Selenium metallicum.

The following is a list of the skin symptoms found in Sulphur and Selenium which could be compared with the symptoms of dandruff:

Sulphur: dry, scaly, and unhealthy skin. Pruritis as if there was life beneath the skin.

Burning sensations, scratching makes the condition worse and leads to bleeding. Every little injury suppurates (Vermeulen, 2000:1504). Morrison (1993:371-372) adds that the eruptions are tremendously itchy and even specifically names dandruff as one of Sulphur's common ailments. Sulphur is also listed in the repertory under the heading 'head-dandruff' (Schroyens, 1998:254). It is given a rating of 'three' out of a possible 'four', this means that dandruff occurred in many of the provers during the proving of Sulphur, it also means that it has led to repeated cures (Schroyens, 1998:vii).

Selenium metallicum: Dry scaly eruptions with itching. Seborrhoea oleosa (an oily form of dandruff). Frequent tingling in a small spot of skin, and great irritation to scratch. Itch suppressed by Sulphur (Vermeulen, 2000:1405). Murphy (2001:1583) adds that 'the parallelism with Sulphur is seen all through the pathogenesis of Selenium and perhaps more especially in the skin'. He goes on to say that an itch checked by Sulphur often requires Selenium. The itching is often accompanied by tingling, and the scalp is sometimes affected with an eczematous eruption.

2.9.4 Potency selection

The potency (drug strength) of Selenium sulphide for this trial was chosen to be 12X.

Potentisation refers to a process that is both mathematical and mechanical. The process reduces a crude, inert, or poisonous medicinal substance, according to a definite scale, into a substance which becomes soluble, therapeutically active, harmless, and physiologically assimilable, for use as a homoeopathic remedy (Goel, 2002:219).

The 'mathematics' of potentisation refers to the scale under which the drug is diluted and occurs in a definite ratio (Goel, 2002:219). The Hahnemannian method of potentisation uses two scales for dilution, the decimal scale, and the centesimal scale (Kayne, 1997:49). The decimal scale (denoted as X) uses a scale with the ratio of 1:9. This means that the first potency (1X) contains one-tenth of the original drug, and each succeeding potency contains one-tenth part of the potency preceding it (Gaier, 1991:446). The centesimal scale (denoted as 'CH') uses the same principle but uses a scale with a ratio of 1:99. The remaining $9/10^{\text{ths}}$ in the decimal dilution and $99/100^{\text{ths}}$ in the centesimal dilution comprise of an inert alcoholic vehicle (Goel, 2002:219-222).

The 'mechanics' of potentisation refers to the actual physical (frictional) process of potentisation. This includes both trituration and succussion (Goel, 2002:219).

Trituration, as defined by Gaier (1991:559), is the act of prolonged grinding with a pestle and mortar to reduce a homoeopathic drug to a fine powder. Succussion is defined as 'the systematic and repeated shaking of a homoeopathic medicine after each serial dilution' (Ullman and Reichenberg-Ullman, 1997:102).

Therefore, through a series of dilution, according to scale, and friction, by means of succussion or trituration, the drug base is potentised. With each dilution, the homoeopathic strength is increased (Kayne, 1997:48-49) and the curative properties of materials are released (Goel, 2002:224).

Therefore, the potency of choice for this trial, '12X', means that the original drug was subjected to the process of dilution and friction 12 times through use of the decimal scale. Mathematically, therefore, 12X denotes that the strength of the drug is 10^{-12} (Goel, 2002:225, 222).

The first reason for potentising Selenium sulphide was based on the Arndt-Schulz law which states that 'minute stimuli encourage life activity, medium to strong stimuli tend to impede it, and very strong stimuli stop or destroy it' (Gaier, 1991:265). In other words, the larger the physiological dose, the more of a damaging effect it will have on the body. Through potentisation, the physiological dose is reduced so greatly (to 10^{-12} in this case) that its stimuli will be minute enough to 'encourage life activity' – or in other words, encourage the body to heal itself.

According to Gaier (1997:433), once substances are potentised there is an optimal potency for each case, and extensive investigation found that low potencies are best suited to organic disease, medium potencies are best for influencing function, and high potencies produce the best response with mental symptoms. In terms of Hahnemannian potencies, Wheeler (1948:22) explains that low potencies are classified

as those from tincture to 6X, medium potencies as those from 7X to 24X, high potencies from 25X to 60X, and 'very high' potencies as anything beyond 60X. To add to this, Kohler (1987:145) states that the lowest useful homoeopathic potency for highly toxic drugs (i.e. Selenium sulphide) is 10X, because potencies less than this are still considered to be in their 'aggressive range'.

In light of the above information, this trial chose to use a 12X preparation of Selenium sulphide because theoretically it will be out of its 'aggressive range' and would be optimal for influencing function (in other words, altering the bodily functions that encourage the overgrowth of *Malassezia* and hence dandruff formation).

2.10 Placebo

The word placebo comes from the Latin verb "placere", which means "to please" (Rocha do Amaral, Renato, and Sabbatini, 1999). The earliest entry where placebo is defined can be found in a medical dictionary written in 1785 in which placebo is defined as 'calculated to amuse for a time', and then in 1811 as 'given more to please than to benefit the patient' (Peters, 2001:18). A relatively recent definition, as defined by Allen (1990:909), hasn't changed much and it is said to be 'a pill, medicine, etc. prescribed for psychological reasons but having no physiological effect'. However, contrary to this, current research has led to changes in opinion and it is now suggested that placebo is 'any therapy or component of therapy that is used for its non-specific psychological or psychophysiological effect'. The difference between the first three definitions and the

latter is that now therapeutic benefit is attributed to placebo treatment. In a recent meeting, the National Health Institute agreed that a placebo does in fact have a therapeutic effect, all be it a non-specific one (Peters, 2001:18). In fact the healing power of an inert tablet is now considered a well proven scientific fact and is demonstrable in about one-third or more of all patients in a variety of diseases (Peters, 2001:46). Ernst and Resch (1995) state that those who equate 'placebo' with 'untreated' distort the perception of what placebo effect is now perceived to be.

The extent of the therapeutic outcome for those on placebo will however vary due to vulnerability from bias. Firstly, a patient's attitude can affect the outcome. They are usually very optimistic because they think the trial can provide something from which they can benefit. This makes them highly compliant with a desire not to disappoint the investigators who have taken so much interest in them. This can therefore produce an enhanced placebo effect on the part of the participant (Cleophas, 1995). Peters (2001:4, 40,181) adds that a patient may also give positive feedback to be polite, show gratitude, please the doctor, or because they think that it is expected of them. Bouchet, Guillemin, and Briancon (1996) state that the outcome is also influenced by the credibility of the treatment (whether it is generally considered effective), its perceptual characteristics (size, colour... etc), the credibility of the physician, and the patient-physician relationship.

The Hawthorne effect may also add to the variation of results within a placebo group. This effect is noted in someone who changes their behaviour positively because they

are the object of special interest (Peters, 2001:20). In other words, the subject, by just knowing that he/she is being experimented on and consequently observed will change their behaviour, be it to that which is more socially desirable, restrained, subdued, or defiant. No matter what the subject's response, it produces results that are inaccurate (Burns, 2000:149).

Interesting insight can be drawn from the above information, that is, that all active medicines, besides from their actual pharmacological effect, also have a placebo effect. The two effects cannot be easily separated from each other (Rocha do Amaral, Renato and Sabbatini, 1999).

The importance of this discussion, however, is to note that placebo treatment is not neutral and at least 30% of the group should show some therapeutic benefit. Cadesky (2001) states however that despite this, placebo groups are still a useful tool for comparison in clinical trials.

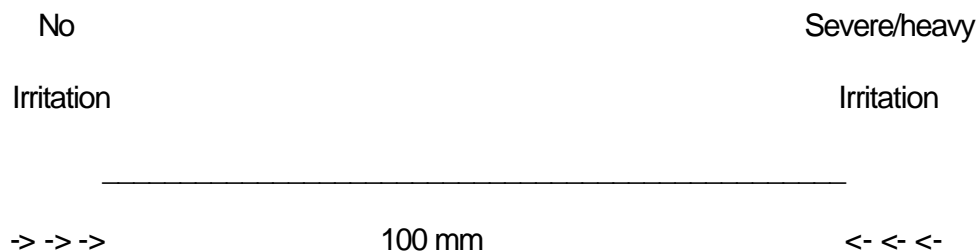
Finally it is of interest to note that not all placebo effects are curative. It is possible to get negative effects, called nocebo effects, which normally mimic the side effects of the active treatment (Peters, 2001:23).

2.11 Measurement Tool

The Visual analogue scale (VAS) was the measurement tool of choice for this trial. It is one of the most frequently used measurement scales in health care research (Johnson, 1997) and exhibits a good degree of within-participant reliability and validity (Stubbs, Hughes, Johnstone, Rowley, Reid, Elia, Stratton, Delargy, King, and Blundell, 2000).

It is a self-report device which is used extensively to measure subjective experiences (Gift, 1989). It is most commonly known and used to measure pain but can be used to measure the perception of a variety of stimuli including sensations, attitudes and opinions (Johnson, 1997). It has previously been used in the assessment of dandruff (Journal of the American Academy of Dermatology, 1992).

The scale consists of a straight line that is usually 100mm in length with descriptions at each end to indicate the extremes of the sensation under study (Gift, 1989). The line may be horizontal or vertical, although linear horizontal scales are preferred by participants and are more reliable in general (Johnson, 1997). An example is shown below, and Appendix D and E are samples of the VASs used for this trial.



Participants are instructed to place a mark on the line in order to reflect the intensity of the sensation being experienced. It is important to tell the participants that the measurement refers to their perception at that particular time; it is not a measurement drawing a comparison to the way they felt before. Although not all researchers agree, it is generally accepted that results are less accurate if subjects are allowed to see previous scores before rating their perception on a second occasion (Johnson, 1997).

The intensity of the sensation is scored by measuring the millimeters from the low end of the scale to the subjects mark. This method has been shown to have high inter-subject repeatability (Gift, 1989).

The VAS has a number of advantages. It is quick and easy to use, simple to interpret, it does not require the participants to use their own descriptive terms, it allows for considerable discrimination, and it is presented in a standardized format that can be compared under a variety of different experimental manipulations (Stubbs, *et al.*, 2000).

There are also a number of disadvantages. Firstly, some people find it difficult to represent a subjective sensation on a straight line. This difficulty can be overcome however if researchers explain beforehand how the scale is used. Secondly, the scale is unidimensional. This means that multiple VASs are needed in order to measure the different aspects or dimensions of a sensation. Finally, due to the subjective nature of the scale, the participants' expectations of the treatment can influence the scores (Gift, 1989).

It appears that the VAS is most effective in trials which test the effects of different treatments under similar circumstances in which the participants are able to take repeated measurements within the trial period (Stubbs, *et al.*, 2000).

'When used properly, the VAS is a reliable, valid, and sensitive self-report measure for studying subjective patient experiences' (Gift, 1989), and according to Stubbs, *et al.*, (2000) it is one of the most productive systems.

CHAPTER 3

MATERIALS AND METHODS

3.1 The problem statement

This study evaluated the effectiveness of an oral homoeopathic preparation of Selenium sulphide 12X on the management of dandruff. The effectiveness was measured by the participant (Appendix D), by the researcher and by an independent third party (the qualified homoeopathic clinician or the concomitant-researcher, Teleman) (Appendix E) using the Visual Analogue Scale (VAS).

3.2 The Data

Primary and secondary data were used in this study. The primary data was obtained through the use of the VAS from the perspectives of the participant, researcher and an independent third party. This third perspective was included in this study due to the subjective nature of the assessment. A third clinical observation gives more validity to the readings obtained.

The secondary data represents information obtained from the available literature on dandruff, as well as information sourced from the Internet.

3.3 The Research Methodology

3.3.1 Participants

The participants for this research were obtained from the Durban area and were between the ages of eighteen and fifty-five years old. They were all screened against the inclusion and exclusion criteria (See 3.3.3 and 3.3.4).

3.3.2 Sample

The minimum number of participants required was thirty. The objective therefore, in this trial, was to have two groups with fifteen participants in each, one group receiving the homoeopathic preparation of Selenium sulphide 12X and the other group receiving placebo. In total, thirty-eight participants were recruited into this study, eighteen received treatment and twenty received placebo. The reason for recruiting thirty-eight as opposed to thirty participants was to allow for those who may withdraw. In total three participants withdrew and two were non compliant and were hence excluded, all five were in the placebo group. All those who completed the trial properly were used in the statistical analysis. Hence the placebo group eventually had fifteen participants and the treatment group had eighteen participants.

3.3.3 Inclusion Criteria

- i. Participants were considered for the study if they met the following criteria (Journal of the American Academy of Dermatology, 1992).
 - o Noticeable scaling of the scalp.
 - o Irritation of the scalp.
 - o Itchiness of the scalp.
 - o Greasiness of the scalp.

- ii. Participants were included into the study once they had read an information letter (Appendix A) and signed a consent form (Appendix B).

3.3.4 Exclusion Criteria

- i. If any of the participants suffered from the following they were excluded:
 - o Psoriasis.
 - o Atopic or irritant contact dermatitis.
 - o Tinea capitis.
 - o Parkinsons Disease.
 - o Immunodeficiency.

- ii. If a female was pregnant or lactating she was excluded.

- iii. If the participant was currently using antibiotics or antimycotics the participant was excluded.

3.4 Experiment design and procedure

3.4.1 Obtaining the Sample

The participants were recruited into the research through convenience sampling. Advertisements were placed on the Durban Institute of Technology (DIT) notice boards, in local hairdressers, gyms, libraries, health shops, pharmacies, and in local newspapers. Pamphlets were also handed out in shopping centres and around DIT (Appendix C).

On response to the advertisements, the participants were asked to come into the clinic for an initial assessment. This comprised of investigating the inclusion and exclusion criteria, followed by a detailed discussion about the objectives and methods of the research. If they met the criteria and were willing to participate, they were asked to read a subject information letter (Appendix A) and, once they had understood and agreed to the trial, they were asked to sign a consent form (Appendix B).

3.4.2 The Process of Randomisation

This trial was a double-blind placebo controlled trial. Double blind means that neither the participants nor the assessors were aware as to who was in the placebo group or treatment group. The placebo group was incorporated into this trial to be used as a measure against which treatment could be compared. The placebo group also helped to eliminate bias from the results as the VAS is a subjective assessment tool.

Randomisation was carried out to ensure that the trial was double-blind in nature. The supervisor for this trial drew up a list and randomly allocated equal numbers into placebo and treatment group. On entering the trial each participant was randomly placed into either the placebo group or the treatment group depending upon what number participant they were. This was controlled by the laboratory technician at the Homoeopathic Day Clinic, and as a result, the assessors and the participants were unaware as to who was in either group. The participants were informed that there was a possibility of being randomised into the placebo group.

Both groups underwent the same consultation and examination procedures, and also received their treatment in the same form and at the same time intervals. Those participants in the treatment group received a homoeopathic preparation of Selenium sulphide 12X, and those in the placebo group received placebo treatment, both were in granule form. The treatment and placebo granules were identical in appearance, taste and smell.

At the completion of the study, those that received placebo were informed and offered treatment free of charge.

3.4.3 Interview and consultation

The first consultation began after the pre-trial assessment described above. If the participant was using an anti-dandruff shampoo they were asked to stop using it and return after one week. The participant's dandruff was then assessed. The assessment comprised of three sets of VAS readings, taken by the participant (Appendix D), the researcher and an independent third party (Appendix E). Participants and independent third parties were instructed that the measurement was to refer to their perception at that particular time, and that they were not to draw a comparison to the way the dandruff symptoms were before.

The participant's assessment was based upon the following categories:

- Scaling (The extent of flaking on the scalp).
- Irritation (The extent to which their dandruff disturbed their day).
- Greasiness (Oiliness of the scalp and hair).
- Itchiness (How much they felt compelled to scratch their scalp).
- Global impression (Overall feeling towards the severity of their dandruff).

The researcher and an independent third party made an assessment based on the following categories:

- Scaling (The extent of flaking on the scalp).
- Percentage of scalp affected (This was assessed to the nearest 10%).
- Greasiness (Oiliness of the scalp and hair).
- Irritation (Visual confirmation of irritation, i.e. redness and scratch marks).
- Global impression (Overall impression about the severity of the dandruff).

Each category was given a severity rating between 0-10, 0 representing none, and 10 representing very severe. The participant marked the rating on the VAS according to their subjective assessment, (Appendix D). The researcher and independent third party marked the rating on the VAS according to their observation (Appendix E).

The consultation was then concluded with a general physical examination of the participant (Appendix F).

It was assumed on acceptance of the trial that participants would follow all the agreed upon terms for the entire duration of the trial.

3.4.4 Medicine preparation

Both placebo and treatment granules were prepared by Natura (a homoeopathic laboratory in Pretoria, South Africa) according to the methods and regulations in the German Homoeopathic Pharmacopoeia (British Homoeopathic Association, 1991).

Selenium sulphide was obtained in its crude form from Sigma-Aldrich (Pty) LTD, Johannesburg, Batch number 105 19HA.

3.4.4.1 Preparation of Selenium sulphide 12X

Homoeopathic remedies are prepared through a series of dilution and friction (by means of succussion or trituration), by a process known as potentisation (Kayne, 1997:49).

3.4.4.1.1 Trituration

When potentiating insoluble chemicals, such as Selenium sulphide (Kerr, 2004), dilution must first take place in a base of lactose powder (sugar of milk) and friction is provided through a process known as trituration (Kayne, 1997:48).

This method is a precise one and is documented in The German Homoeopathic Pharmacopoeia (GHP) under Method 6 as follows (British Homoeopathic Association. 1991:36-37):

??The lactose is divided into three parts.

??The first part is placed in a porcelain mortar and triturated for a short period. The basic drug is then added and triturated for 6 minutes, scraped down for 4 minutes, triturated for a further 6 minutes and scraped down again for 4 minutes.

??The second part of the lactose is then added and the process of trituration followed by scraping is repeated.

?? Finally the third part is added and the procedure is repeated.

In this trial, the triturations of Selenium sulphide were prepared in the above manner using the decimal scale in a ratio of 1:10 up to and including the 4th dilution. Triturations 5X and 6X were then prepared in the ratio 1:9 as stipulated by the GHP (British Homoeopathic Association, 1991:36-37).

3.4.4.1.2 Succussion

Once the 6th potency (6X) is reached the preparation becomes soluble, meaning it can be converted into a liquid preparation (Kayne, 1997:48). Liquid preparations are potentised by a process known as succussion (British Homoeopathic Association, 1991:38).

Therefore, according to Method 8a in the GHP, 1 part of the Selenium sulphide 6X trituration was dissolved in 9 parts of water and succussed ten times. One part of this was then combined with 9 parts of 30% ethanol. In this way, the 6X trituration of Selenium sulphide was converted into an 8X liquid preparation (British Homoeopathic Association, 1991:38). This is called the 'jumping potency' because the 6X trituration 'jumps' directly to an 8X liquid preparation. It is not possible to make a 7X preparation because there would not be enough water to dissolve the solute adequately (Goel, 2002:249-250).

The 8x liquid preparation of Selenium sulphide was then converted systematically to a 12X liquid preparation through a series of dilution, according to the decimal scale, followed by succussion. This was in accordance to Method 5a in the GHP (British Homoeopathic Association, 1991:35). Therefore, at each stage (i.e. from 8X to 9X), 1 part of the previous potency (in this example 8X) was added to 9 parts of 30% alcohol in a vial. It was then corked and succussed with ten powerful down strokes striking the palm of the hand. The next potency was thus produced (in this example 9X) (Goel, 2002:244). This process was repeated until 12X was reached, however, in the last stage, 30% ethanol was replaced with 96% ethanol, and hence Selenium sulphide 12X at 96% ethanol concentration was produced.

3.4.4.1.3 Impregnation of Granules

The final stage in the remedy preparation was to dispense Selenium sulphide 12X in its chosen vehicle. For this trial, it was decided that granules would be the preferred choice of dispensing vehicle.

In accordance with Method 10 in the GHP, the granules were impregnated with the 12X dilution at 1% (v/v) by means of triple impregnation. This means that 100 parts of sucrose granules were evenly moistened with 1 part of the Selenium sulphide 12X dilution (British Homoeopathic Association, 1991:35). The GHP states that the ethanol content of the dilution should not be less than 60%, but as Kayne (1997:72) points out, if the alcohol content is actually less than 95% the lactose granules will dissolve due to the

higher water content. It was for this reason that the alcohol concentration of the 12X dilution was chosen to be 96%.

3.4.4.2 Preparation of placebo

Placebo granules were prepared through triple impregnation at 1% (v/v) with 96% ethanol. This was done in order for there to be no detectable difference, in taste, sight, or smell, between placebo and treatment granules.

3.4.4.3 Final product

All participants received an eight millilitre bottle containing either placebo granules or treatment granules. The appearance of the granules, presentation of the bottles, and the instructions for administration of the granules were identical for both groups.

3.5 The Protocol

A one-week washout period prior to the beginning of the study was required for those who were using an anti-dandruff shampoo. During this period, and throughout the trial, all participants had to refrain from using all brands of anti-dandruff shampoo.

Once the washout period was completed the participant returned to the clinic for their initial consultation. If no washout period was necessary, this consultation took place

immediately after the pre-trial assessment. On completion of the consultation, the Homoeopathic Day Clinic laboratory technician randomised the participant into one of two possible groups and dispensed the treatment accordingly. Day one of the trial began once treatment commenced.

The clinical trial was conducted over a four-week period. During this period, participants were required to take a quarter of a capful of their granules each morning on waking. Follow-up consultations took place on day fourteen (mid-trial), and on day twenty-eight (end of trial).

At each consultation the participants' dandruff was assessed by themselves, the researcher, and an independent third party. Each assessment took place using clean, unmarked VAS sheets (Appendix D and E), meaning that participant, researcher, and independent third party had no reference to previous assessment scores and no reference to each others scores. Each consultation was concluded with a general physical examination.

3.6 Measurements

At the completion of the trial, the data from each of the participants was correlated, analysed, and assessed according to statistical methods. The final analysis was made from the results of thirty-three participants, eighteen of whom were in the treatment group and fifteen in the placebo group.

Data was obtained from the VAS assessment scores of the participant, researcher and an independent third party from each of the three consultations.

3.7 Data Analysis

3.7.1 Statistical methods

There were six continuous variables of interest in this study: itchiness, scaling, irritation, greasiness, global impression, and percentage of scalp affected. The researcher and independent third party obtained results using the latter five variables, and the participant obtained results using the first five variables. The VAS was the tool used to obtain the results which was used on three different occasions, day 1 (beginning of trial), day 14 (mid-trial), and day 28 (end of trial).

3.7.2 Statistical Analysis

SPSS Software Suite, version 12.1, (manufactured by SPSS Inc, 444n. Michigan Avenue, Chicago, Illinois, USA) is the statistical software program which was used to analyse the data.

Non-parametric methods of data analysis were used due to the size of the sample groups, namely fifteen and eighteen respectively. Type 1 error was set at 5% for all

tests, meaning $\alpha = 0.05$. If the P value was found to be less than 0.05, then the result was deemed significant, and the null hypothesis was to be rejected.

Statistical analysis took place descriptively through the use of graphs and tables (including but not limited to means, percentages and proportions), and inferentially using various hypothesis-testing techniques. Unless otherwise stated, all statistics given are the average of the sum of the three assessments taken (i.e. participant, researcher and independent third party) for each variable for the time period specified.

3.7.2.1 Procedure 1 (Intra-group test)

The Friedman Test

The Friedman's ANOVA method was used to compare three related samples taken on day 1(baseline), 14 (follow-up consultation 1), and 28 (follow-up consultation 2) within both the treatment and placebo group. These samples are the VAS readings for itchiness, scaling, irritation, greasiness, global impression, and percentage of scalp affected.

i. Hypothesis testing

The null H_0 , states that there is no significant difference between the visits being compared at the $\alpha = 0.05$ level of significance. The alternative hypothesis H_1 , states that at least two of the visits will differ significantly at the same level of significance.

ii. Decision rule

At the $\alpha = 0.05$ level of significance, the null hypothesis is rejected if $p = \alpha$ where p is the observed significance level. Otherwise, the null hypothesis is accepted at the same significance.

3.7.2.2 Procedure 2 (Intra-group test)

Wilcoxon's Signed Rank Test

If there were any significant differences between the visits, the Wilcoxon's Signed Rank Test was used to determine between which two visits the difference lay.

i. Hypothesis testing

The null hypothesis H_0 , states that there is no significant difference between the two visits being compared at the $\alpha = 0.05$ level of significance. The alternative hypothesis H_1 , states that there is a significant difference between the two visits being compared.

ii. Decision rule

At the $\alpha = 0.05$ level of significance, the null hypothesis is rejected if $p = \alpha$ where p is the observed significance level. Otherwise, the null hypothesis is accepted at the same level of significance.

3.7.2.3 Procedure 3 (Inter-group test)

The Mann-Whitney U-Test

The Mann-Whitney U-Test was used to determine if there was a significant difference between the placebo and treatment group with regards to the six variables of the study.

i. Hypothesis testing

In each test the null hypothesis H_0 , states that there is no significant difference between the groups being compared at the $\alpha = 0.05$ level of significance. The alternative hypothesis H_1 , states that the groups will differ significantly at the same level of significance.

ii. Decision rule

At the $\alpha = 0.05$ level of significance, the null hypothesis is rejected if $p = \alpha$ where p is the observed significance level. Otherwise, the null hypothesis is accepted at the same level of significance.

CHAPTER 4

RESULTS

4.1 Introduction

This chapter covers the demographic and statistical non-parametric analysis of the results gathered from the placebo group and treatment group during this trial.

The first set of results presents the demographic data and includes average age, gender, and race.

The second set of results shows diagrammatically the comparisons between the mean Visual Analogue Scale (VAS) readings for all six variables.

The third set of results present the non-parametric tests which seek to determine the efficacy of the supposed treatment regime, firstly by evaluating intra-group and then inter-group data.

Intra-group analysis looks at both the treatment and placebo group independently, making comparisons of the results within each group and without reference to the other.

These tests were conducted through use of The Friedman's Test and The Wilcoxon's Signed Rank Test.

The Friedman Test was used to determine if there was a difference between the three visits on day 1 (baseline), 14 (follow-up consultation 1), and 28 (follow-up consultation 2) within both the treatment and placebo group.

H_0 (null hypothesis): There is no significant difference between the visits.

H_1 (alternative hypothesis): There is a significant difference between the visits.

In each case α was set at 0.05 (specified level of significance). H_0 was rejected if $p < \alpha$, and accepted if $p > \alpha$, where p is the observed significance level.

If there was found to be a significant difference between the visits, the Wilcoxon's Signed Rank Test was used to determine between which two visits the difference lay.

H_0 : There is no significant difference between the two visits.

H_1 : There is a significant difference between the two visits.

In each case α was set at 0.05 (specified level of significance). H_0 was rejected if $p = \alpha$, and accepted if $p = \alpha$, where p is the observed significance level.

The inter-group analysis refers to comparisons made between both groups, i.e. treatment and placebo groups are compared using the same time intervals. This analysis was conducted through the use of the Mann-Whitney U Test. It was used to determine if there was a significant difference between the placebo and treatment group with regards to the six variables of the study.

H_0 : There is no significant difference between the groups.

H_1 : There is a significant difference between the groups.

In each case α was set at 0.05 (specified level of significance). H_0 was rejected if $p < \alpha$, and accepted if $p \geq \alpha$, where p is the observed significance level.

4.2 Criteria governing the admissibility of the data

- ?? The statistical analysis in this chapter uses data obtained from this trial only, through the use of the VAS.
- ?? All data was collected in the manner described in Chapter Three, and it was assumed that all participants, on acceptance of the trial, followed the instructions accurately.
- ?? Data was only admissible if the participants attended all three consultations and all forms were completed correctly.
- ?? All participants gave consent for their data to be used.

4.3 Demographic data

The following charts and tables show the demographics in this trial. Figure 4.1 shows that more females took part in the trial than males, which is broken down further in Table 4.1 to show how many males and females were in each group. This table also includes the average age within each of the groups. Figure 4.2 then goes on to show that more Black participants took part than Asian or White participants.

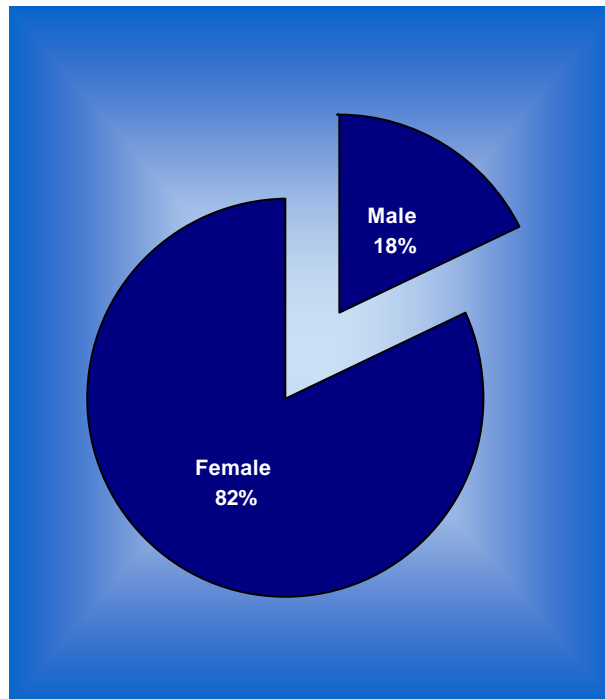


Figure 4.1 Pie Chart showing the percentage of male and female participants (Female participants n=27, male participants n=6).

Table 4.1 Age and sex distribution of participants within treatment and placebo groups.

	Total number	Average age	Number males	Number females
Treatment	18	25.4	2	16
Placebo	15	26.0	4	11

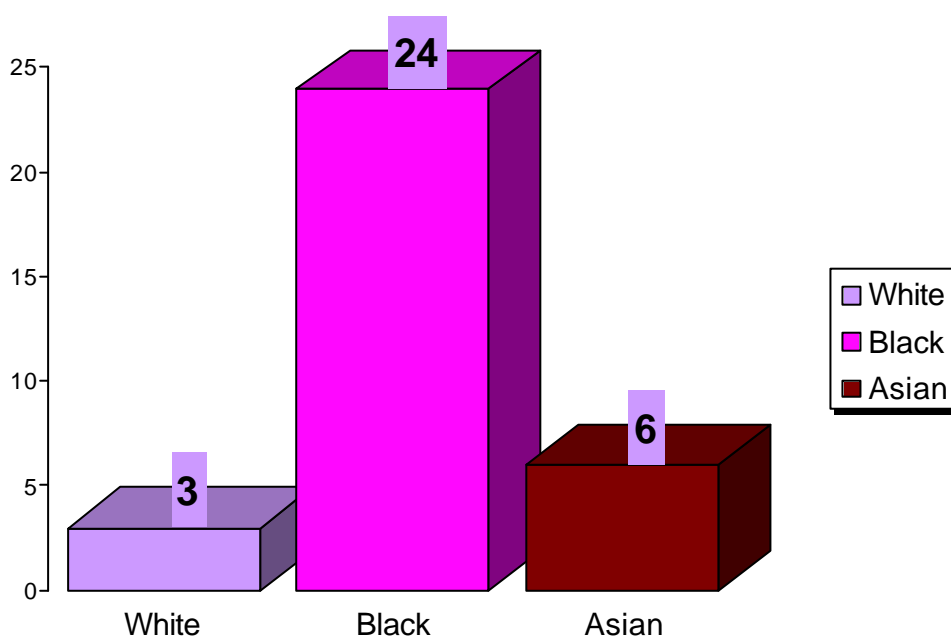


Figure 4.2 Bar chart showing the ethnicity of participants in the trial.

4.4 Graphic comparisons between the treatment group and the placebo group.

Section 4.4 graphically represents the data obtained from the VASs. Each variable that was assessed is represented independently on its own graph. The scores represented on the graphs are an average of the severity ratings taken by the three assessors (i.e. participant, researcher, and third party).

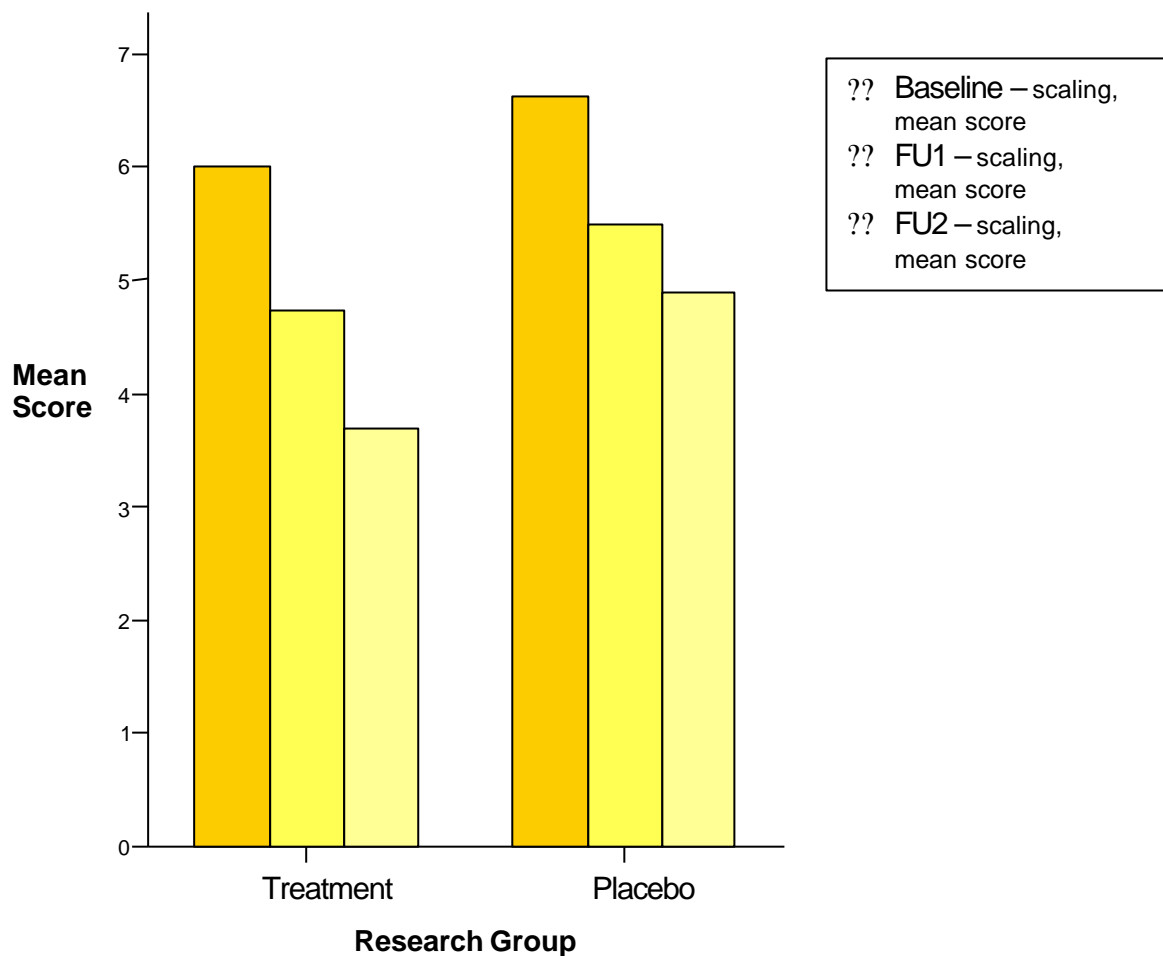


Figure 4.3 Bar chart showing mean scores for ‘scaling’ as measured by the patient, researcher, and independent third party using the VAS at baseline, follow-up consultation one (FU1), and follow-up consultation two (FU2).

As Figure 4.3 shows, ‘scaling’ decreased for those participants in the treatment group, from an average reading of ‘6’ at baseline to ‘4.7’ at FU1 and finally to ‘3.7’ at FU2. The placebo group began at baseline with an average reading of ‘6.6’, decreasing to ‘5.5’ at FU1, and ‘4.9’ at FU2.

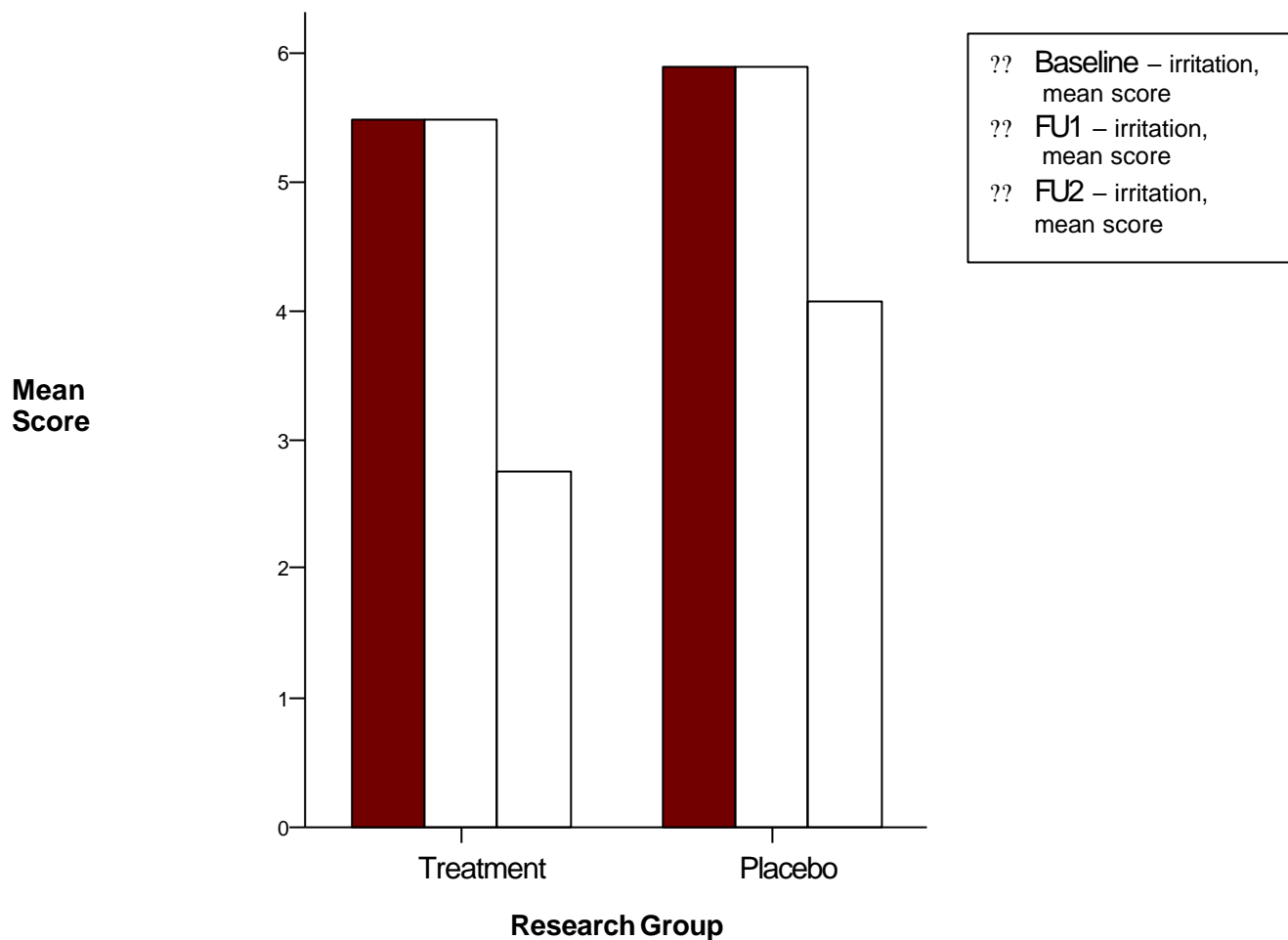


Figure 4.4 Bar chart showing mean scores for ‘irritation’ as measured by the patient, researcher, and independent third party using the VAS at baseline, follow-up consultation one (FU1), and follow-up consultation two (FU2).

As Figure 4.4 shows, there was no change in the average score for ‘irritation’ between baseline and FU1 in both the treatment group and the placebo group, remaining at ‘5.5’ and ‘5.9’ respectively. There was a decrease however for both groups between FU1

and FU2, with the treatment group average decreasing to '2.8', and the placebo group to '4.0'.

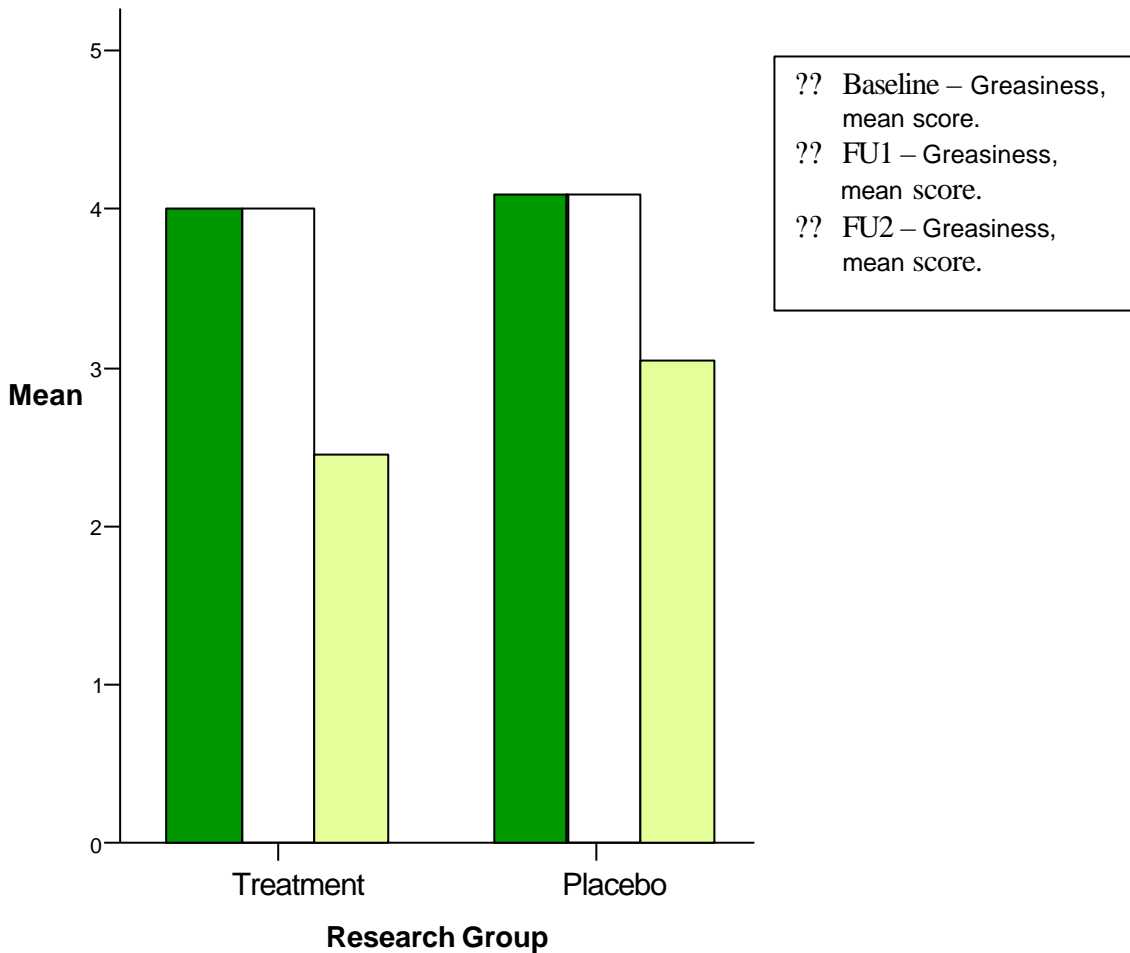


Figure 4.5 Bar chart showing mean scores for 'greasiness of scalp' as measured by the patient, researcher, and independent third party using the VAS at baseline, follow-up consultation one (FU1), and follow-up consultation two (FU2).

As Figure 4.5 shows, there was no change in the average score for 'greasiness of the scalp' between baseline and FU1 in both the treatment group and the placebo group, remaining at '4.0' and '4.1' respectively. There was a decrease however for both groups

between FU1 and FU2, with the treatment group average decreasing to '2.4', and the placebo group decreasing to '3.0'.

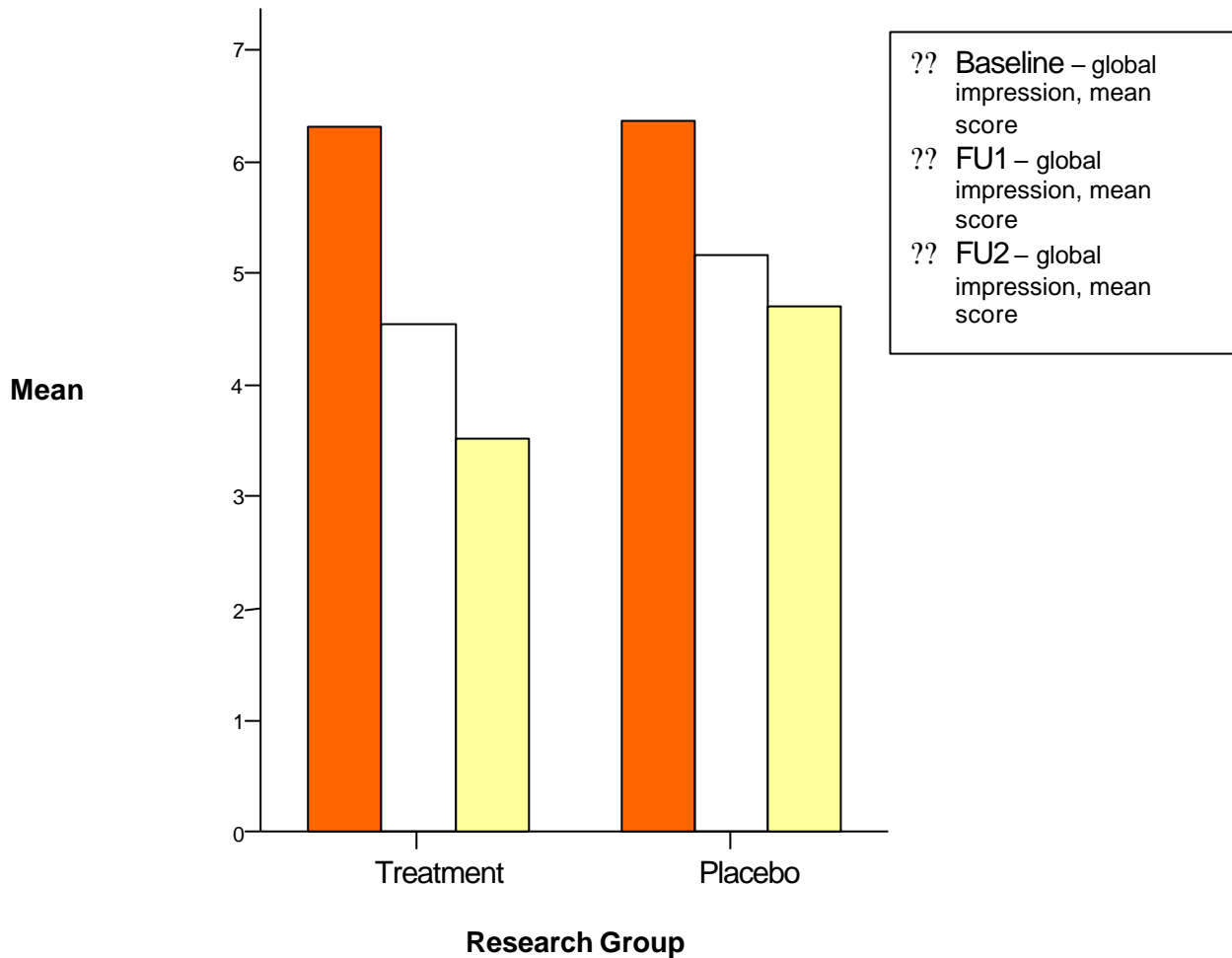


Figure 4.6 Bar chart of mean scores for 'global impression' as measured by the patient, researcher, and independent third party using the VAS at baseline, follow-up consultation one (FU1), and follow-up consultation two (FU2).

As Figure 4.6 shows, for those participants in the treatment group, 'global impression' decreased from an average reading of '6.3' at baseline, to '4.5' at FU1 and finally to '3.5'

at FU2. The placebo group began at baseline with an average reading of '6.4', decreasing to '5.2' at FU1, and '4.7' at FU2.

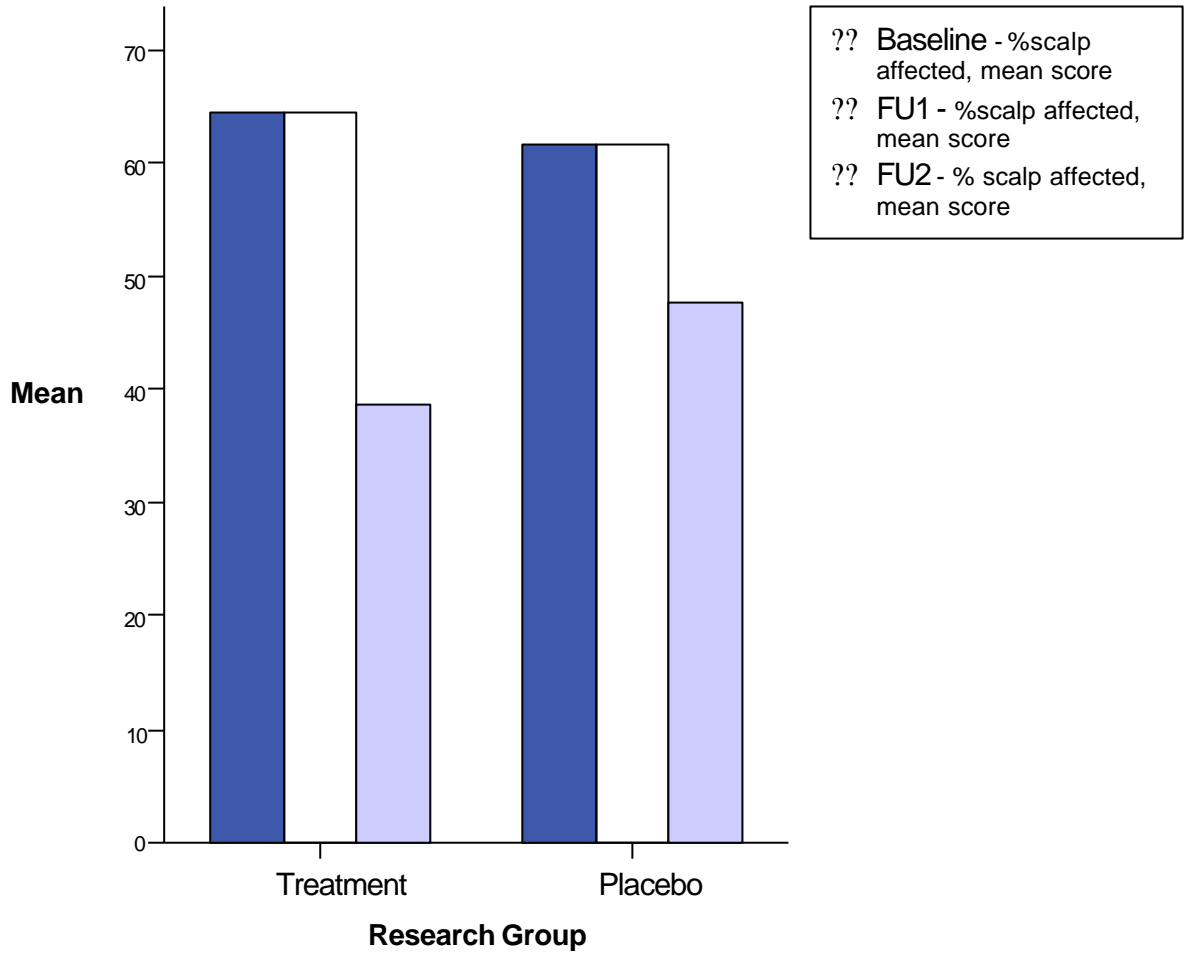


Figure 4.7 Bar chart showing mean scores for 'percentage of scalp affected' as measured by the researcher and independent third party using the VAS at baseline, follow-up consultation one (FU1), and follow-up consultation two (FU2).

As Figure 4.7 shows, there was no change in the average score for 'percentage of scalp affected' between baseline and FU1 in both the treatment group and the placebo group, with the average scores remaining at '6.4' and '6.2' respectively. There was a decrease however for both groups between FU1 and FU2, with the treatment group average decreasing to '3.9', and the placebo group decreasing to '4.8'.

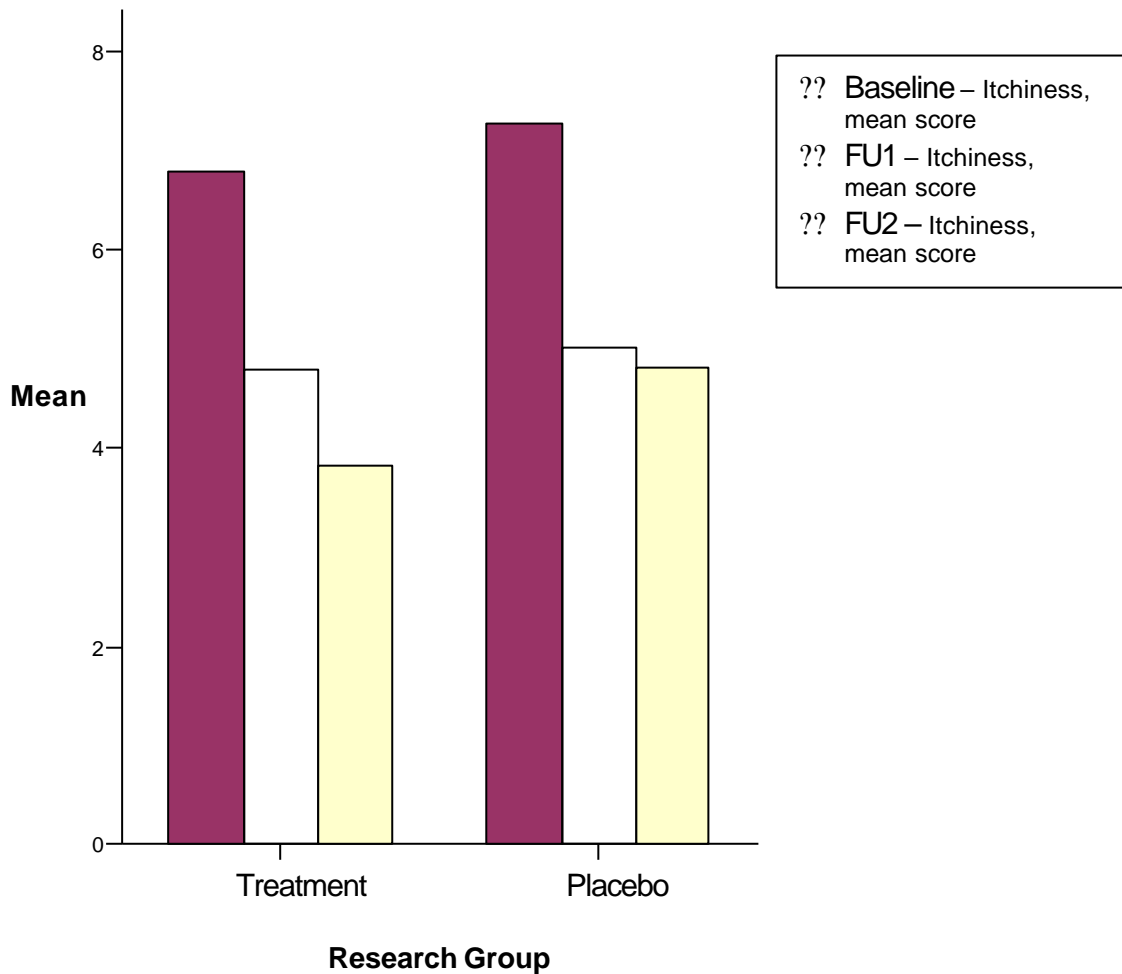


Figure 4.8 Bar chart of mean scores for 'itchiness' as measured by the patient using the VAS at baseline, follow-up consultation one (FU1), and follow-up consultation two (FU2).

As Figure 4.8 shows, 'itchiness' decreased, for those participants in the treatment group, from an average reading of '6.8' at baseline, to '4.8' at FU1 and finally to '3.8' at FU2. The placebo group began at baseline with an average reading of '7.3', decreasing to '5.0' at FU1, and '4.8' at FU2.

Table 4.2 and Figure 4.9 below are a summary of all of the above six variables added together. By reflecting the 'total score' at each consultation, they draw a comparison between the assessments made by the participant, researcher, and independent third party.

Table 4.2 Comparison of the total scores made by the three assessors at baseline, follow-up consultation one and follow-up consultation two, for both treatment and placebo groups.

	Treatment	Placebo
Participants' mean score		
Baseline	29.78	33.53
Follow up 1	23.17	24.67
Follow up 2	17.33	22.27
Researchers mean score		
Baseline	83.11	79.33
Follow up 1	67.22	71.27

Follow up 2	51.39	64.80
Independent third party's mean score		
Baseline	88.11	86.67
Follow up 1	56.56	69.67
Follow up 2	49.56	63.13

Figure 4.9 below diagrammatically reflects Table 4.2.

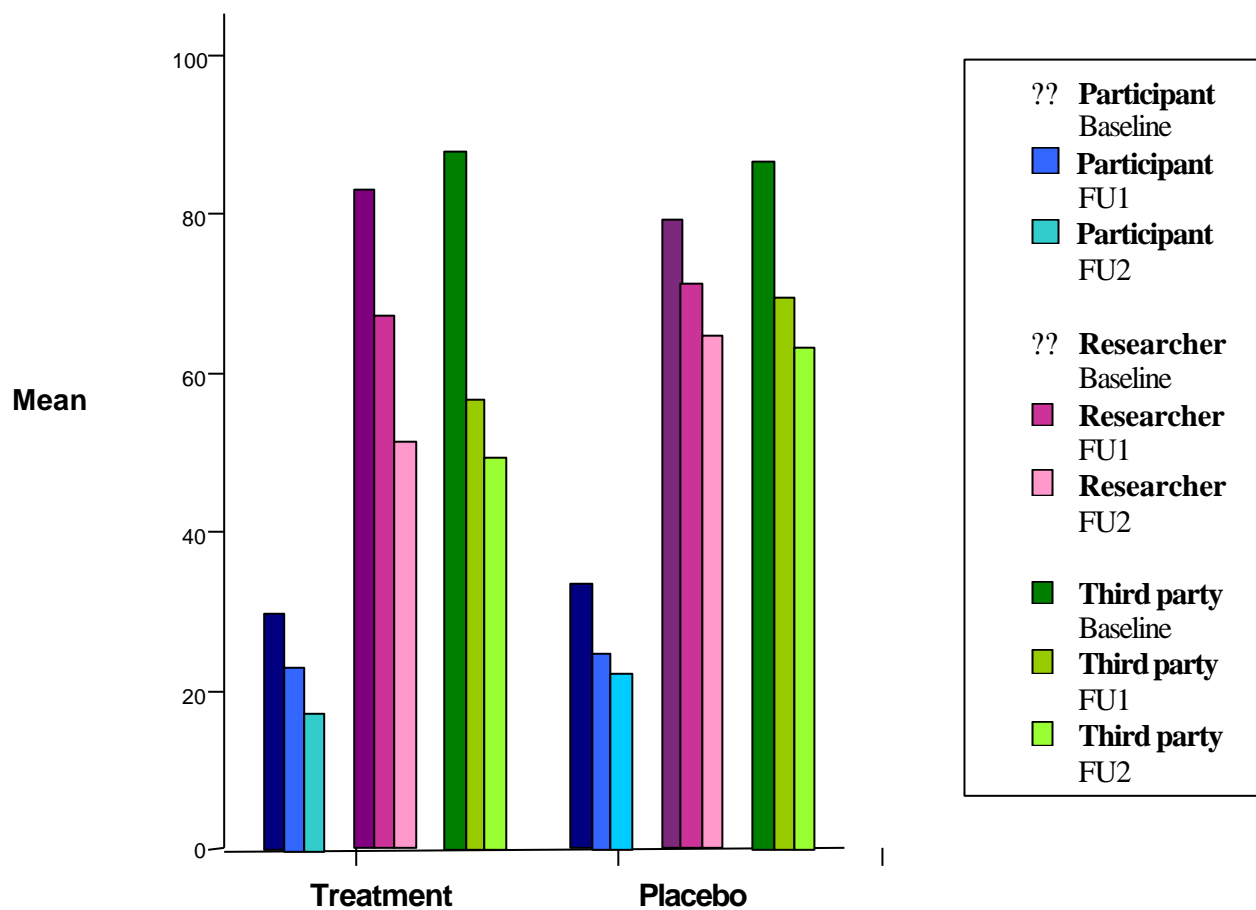


Figure 4.9 A comparison of the total scores - at baseline, follow-up consultation one (FU1) and follow-up consultation two (FU2), as taken by patient, researcher, and independent third party.

Figure 4.9 reflects two interesting features. Firstly, it is clear that the independent third party and researcher assessed the participants' dandruff similarly, as being severe. However, the participants assessed their symptoms as being much less severe. This was true for all three consultations. Secondly, although there was a decline in symptom severity in both placebo and treatment groups, the decline is most obvious in the treatment group, as documented by all the three assessors. While it is interesting that Figure 4.9 graphically shows more of an improvement in the treatment group, this information only becomes important if the improvement is statistically significant, which, as section 4.5 shows, it is not.

4.5 Statistical analysis through non-parametric tests

This section represents the non-parametric analysis of the data obtained from the VAS sheets. The Friedman's Test, Wilcoxon's Signed Rank Test, and Mann-Whitney U Test were utilised for the analysis through the use of SPSS Software Suite, version 12.1.

4.5.1 Intra-group analysis

4.5.1.1 Group 1 (Treatment Group)

Friedman's Test

Table 4.3 Friedman's Test. Comparison of mean scores for each of the six variables obtained via the VAS, to see if there is a significant difference (P value) between baseline, follow-up consultation one (FU1), and follow-up consultation two (FU2).

Variables	Means			P-value
	Baseline	FU 1	FU 2	
Scaling	6.00	4.47	3.69	0.000
Irritation	5.48	5.48	2.76	0.004
Greasiness	4.00	4.00	2.44	0.001
Global impression	6.30	4.54	3.52	0.000
% of scalp affected	6.44	6.44	3.86	0.000
Itching	6.78	4.78	3.83	0.004

The Friedman's Test was utilised to determine if there was a significant difference between the consultations at baseline, follow-up consultation one (FU1) and follow-up consultation two (FU2). All the tests revealed that the P-value < 0.05. Hence, at the $\alpha = 0.05$ level of significance, the alternative hypothesis was accepted and the null

hypothesis was rejected. In other words, there was a significant difference between the consultations for all the variables tested.

Since the P value < 0.05 for all variables, further analysis was done using the Wilcoxon's Signed Rank Test to establish at which consultation the significant difference occurred.

Wilcoxon's Signed Rank Test

Table 4.4 Wilcoxon's Signed Rank Test. A comparison of the mean scores (average of participants', researchers, and independent third party's results) between baseline, follow-up consultation one (FU1), and follow-up consultation two (FU2) to see between which consultation the significant difference lies.

Variables	Comparison of mean scores between baseline and FU1; FU1 and FU2; baseline and FU2.			P-values
	Baseline	FU1	FU2	
Scaling	6.00	4.74	-	0.011
	-	4.74	3.69	0.004
	6.00	-	3.69	0.000
Irritation	5.48	5.48	-	1.000
	-	5.48	2.76	0.002
	5.48	-	2.76	0.002
Greasiness	4.00	4.00	-	1.000
	-	4.00	2.44	0.013
	4.00	-	2.44	0.013
Global impression	6.30	4.54	-	0.001
	-	4.54	3.52	0.002
	6.30	-	3.52	0.000
% of scalp affected	6.44	6.44	-	1.000
	-	6.44	3.86	0.000
	6.44	-	3.86	0.000
Itching	6.78	4.78	-	0.008
	-	4.78	3.83	0.024
	6.78	-	3.83	0.003

The Wilcoxon's Signed Rank Test was used to determine between which visits the significant difference lies. At the $\alpha = 0.05$ level of significance, where H_0 was rejected if $p = \alpha$, and accepted if $p > \alpha$, the tests revealed the following:

For scaling: There was a significant difference between baseline and FU1, FU1 and FU2, and baseline and FU2 respectively, meaning for all three readings, $P < 0.05$. Hence the alternative hypothesis was accepted and the null hypothesis rejected for all three visits.

For irritation: There was no significant difference between baseline and FU1 because $P = 1.000$, meaning $P > 0.05$. However, there was a significant difference between FU1 and FU2, and baseline and FU2 respectively as $P < 0.05$. This means that between baseline and FU1 the null hypothesis was accepted and the alternative hypothesis rejected, and between FU1 and FU2, and baseline and FU2, the alternative hypothesis was accepted and the null hypothesis was rejected.

For greasiness: There was no significant difference between baseline and FU1 because $P = 1.000$, meaning $P > 0.05$. However, there was a significant difference between FU1 and FU2, and baseline and FU2 respectively as $P < 0.05$. This means that between baseline and FU1 the null hypothesis was accepted and the alternative hypothesis rejected, and between FU1 and FU2, and baseline and FU2, the alternative hypothesis was accepted and the null hypothesis was rejected.

For global impression: There was a significant difference between baseline and FU1, FU1 and FU2, and baseline and FU2 respectively meaning, for all three readings, $P < 0.05$. Hence the alternative hypothesis was accepted and the null hypothesis rejected for all three visits.

For percentage of scalp affected: There was no significant difference between baseline and FU1 because $P = 1.000$, meaning $P > 0.05$. However, there was a significant difference between FU1 and FU2, and baseline and FU2 respectively as $P < 0.05$. This means that between baseline and FU1 the null hypothesis was accepted and the alternative hypothesis rejected, and between FU1 and FU2, and baseline and FU2, the alternative hypothesis was accepted and the null hypothesis was rejected.

For itching: There was a significant difference between baseline and FU1, FU1 and FU2, and baseline and FU2 respectively meaning, for all three readings, $P < 0.05$. Hence the alternative hypothesis was accepted and the null hypothesis rejected for all three visits.

4.5.1.2 Group 2 (Placebo group)

Friedman's Test

Table 4.5 Friedman's Test. Comparison of mean scores (as measured by the participants, researcher, and independent third party) for each of the six variables

obtained via the VAS, to see if there is a significant difference (P value) between baseline, follow-up consultation one (FU1) and follow-up consultation two (FU2).

Variable	Means			P-value
	Baseline	FU 1	FU 2	
Scaling	6.62	5.49	4.89	0.010
Irritation	5.89	5.89	4.07	1.103
Greasiness	4.09	4.09	3.04	0.549
Global impression	6.38	5.16	4.69	0.004
% of scalp affected	6.17	6.17	4.77	0.076
Itching	7.27	5.00	4.8	0.021

The Friedman's Test was utilised to determine if there was a significant difference between the consultations at baseline, follow-up consultation one, and follow-up consultation two. At the $\alpha = 0.05$ level of significance, the tests revealed the following:

'Scaling', 'global impression', and 'itching' had P-values of 0.010, 0.004, and 0.021 respectively; meaning all had P-values < 0.05 . Hence for these three variables, at the $\alpha = 0.05$ level of significance, the alternative hypothesis was accepted and the null hypothesis was rejected. In other words, there was a significant difference found between the consultations.

'Irritation', 'greasiness', and 'percentage of scalp affected' had P-values of 0.103, 0.549, and 0.076 respectively, meaning all had P-values > 0.05 . Hence for these three variables, at the $\alpha = 0.05$ level of significance, the null hypothesis was accepted and the alternative hypothesis was rejected. In other words, there was no significant difference found between the consultations.

Since 'scaling', 'global impression', and 'itching' had P-values < 0.05 further analysis was done using the Wilcoxon's Signed Rank Test to establish at which consultation the significant difference occurred.

Wilcoxon's Signed Rank Test

Table 4.6 Wilcoxon's Signed Rank Test. A comparison of the mean scores (average of participants', researchers, and independent third party's) between baseline, follow-up consultation one (FU1) and follow-up consultation (FU2) to see between which consultation the significant difference lies.

Variables	Comparison of mean scores between baseline and FU1; FU1 and FU2; baseline and FU2			P-values
	Baseline	FU1	FU2	
Scaling	6.62	5.49	-	0.029
	-	5.49	4.89	0.059
	6.62	-	4.89	0.005
Global impression	6.38	5.16	-	0.023
	-	5.16	4.69	0.045
	6.38	-	4.69	0.012
Itching	7.27	5.00	-	0.032
	-	5.00	4.80	0.607
	7.27	-	4.80	0.018

The Wilcoxon's Signed Rank Test was used to determine between which visits the significant difference lies. At the $\alpha = 0.05$ level of significance, where H_0 was rejected if $p < \alpha$, and accepted if $p > \alpha$, the tests revealed the following:

For scaling: The P-values between baseline and FU1, and baseline and FU2 were 0.029 and 0.005 respectively, meaning there was a significant difference between these visits because $P < 0.05$. The P-value between FU1 and FU2 was 0.059, in other words $P > 0.05$, and therefore there was no significant difference between these visits. Hence, between baseline and FU1, and baseline and FU2 the alternative hypothesis was

accepted and the null hypothesis rejected and between FU1 and FU2 the null hypothesis was accepted and the alternative hypothesis rejected.

For global Impression: There was a significant difference between baseline and FU1, FU1 and FU2, and baseline and FU2 respectively meaning, for all three readings, $P < 0.05$. Hence the alternative hypothesis was accepted and the null hypothesis rejected for all three visits.

For itching: The P-values between baseline and FU1, and baseline and FU2 were 0.032 and 0.018 respectively, meaning there was a significant difference between these visits because $P < 0.05$. The P-value between FU1 and FU2 was 0.607, in other words $P > 0.05$, and therefore there was no significant difference between these visits. Hence, between baseline and FU1, and baseline and FU2 the alternative hypothesis was accepted and the null hypothesis rejected and between FU1 and FU2 the null hypothesis was accepted and the alternative hypothesis rejected.

4.5.2 Inter-group analysis

Mann-Whitney U Test

Table 4.7 Mann-Whitney U Test. Comparison of treatment and placebo group at baseline, follow-up consultation one (FU1) and follow-up consultation two (FU2) for each of the six variables.

Variables	Consultation	Means		P-values
		Treatment group	Placebo group	
Scaling	Baseline	6.00	6.62	0.292
	FU1	4.74	5.49	0.126
	FU2	3.69	4.89	0.088
Irritation	Baseline	5.48	5.89	0.703
	FU1	5.48	5.89	0.703
	FU2	2.76	4.07	0.015
Greasiness	Baseline	4.00	4.09	0.828
	FU1	4.00	4.09	0.828
	FU2	2.44	3.04	0.217
Global impression	Baseline	6.30	6.38	1.000
	FU1	4.54	5.16	0.121
	FU2	3.52	4.69	0.037
% of scalp affected	Baseline	6.44	6.17	0.390
	FU1	6.44	6.17	0.390
	FU2	3.86	4.77	0.230
Itching	Baseline	6.78	7.27	0.443
	FU1	4.78	5.00	0.884
	FU2	3.83	4.80	0.411

The inter-group analysis by means of the Mann-Whitney U Test was conducted in order to see if there was a significant difference between the results of those in the treatment group and those in the placebo group, with regard to the six variables of the study.

For this test $\alpha = 0.05$ (level of significance), where H_0 was rejected if $P = \alpha$, and accepted if $P < \alpha$, hence P needed to be < 0.05 for there to be a significant difference. Therefore, there was only one variable that was found to significantly differ when treatment was compared to placebo. This variable, 'irritation', was found to significantly differ with a P-value of 0.015, but this difference is only noted at the end of the trial (follow-up consultation two). For all the other variables there was no significant difference noted. Therefore, the alternative hypothesis was accepted and the null hypothesis was rejected for the variable 'irritation'. For all the other variables, the null hypothesis was accepted and the alternative hypothesis was rejected.

CHAPTER 5

DISCUSSION

5.1 Results

A statistically significant improvement was demonstrated within the treatment group and the placebo group when analysed independently (i.e. intra-group analysis) through use of the Friedman's Test and the Wilcoxon's Signed Rank Test.

The treatment group showed a significant improvement in all of the six variables tested, and by the end of the trial the P-values were as follows: 0.000 for 'scaling'; 0.002 for 'irritation'; 0.013 for 'greasiness'; 0.000 for 'global impression'; 0.000 for 'percentage of scalp affected'; and 0.003 for 'itching' (Table 4.4). Interestingly, by day 14 (follow-up consultation one) three of these variables, namely 'scaling', 'global impression', and 'itching' had already shown a significant improvement and continued to improve between day 14 and day 28 (follow-up consultation two). The other three variables however ('irritation', 'greasiness', and 'percentage of scalp affected') showed no improvement at all on day 14, but by day 28 they all showed a significant improvement.

The placebo group only showed a significant improvement in three of the six variables. These variables were 'scaling', 'global impression' and 'itching' with P-values at the end of the trial of 0.005, 0.012, and 0.018 respectively (table 4.6). These improvements were

found to be significant on day 14. 'Global impression' continued to improve between day 14 and day 28, whereas there was no further improvement after day 14 for 'scaling' and 'itching'. The severity of 'scaling' and 'itching' did not however regress, and maintained its improvement until the end of the trial (day 28). The three variables that statistically showed no improvement in the placebo group had P-values on completion of the trial as follows: 0.103 for 'irritation', 0.549 for 'greasiness', and 0.076 for 'percentage of scalp affected'. Interestingly, these latter three variables correspond to those in the treatment group that only showed improvement on day 28.

When results from the treatment group were compared to those from the placebo group (i.e. inter-group analysis) through the Mann-Whitney U Test, there showed to be a significant difference in only one of the variables. This variable, 'irritation', only showed a significant difference on day 28 of the trial with a P-value of 0.015 (Table 4.7). All the other variables showed no significant improvement and therefore Selenium sulphide 12X did not prove to be effective in the management of dandruff.

5.2 Comparison of placebo and treatment

Figure 4.9 illustrates that the baseline scores for participants in the placebo group and treatment group were very similar. The statistics are available in Table 4.2 and state the baseline average scores as follows:

??Participants' baseline assessment - 29.8% severity in treatment group; 33.5% severity in placebo group.

??Researcher's baseline assessment - 83.1 % severity in treatment group; 79.3% severity in placebo group.

??Independent third party's baseline assessment - 88.1% severity in treatment group; 86.7% severity in placebo group.

The results above indicate two things. Firstly, that the participants in both groups began with similar dandruff severity ratings. This is of importance because the significance of the final results would be negatively influenced if the starting point for both groups were not similar. Secondly, the results show that participants viewed their symptoms far less severely than both the researcher and independent third party. This is of little significance however because, as can be seen in Figure 4.9, the difference in opinion remains proportionate and consistent throughout the trial.

As stated earlier, the placebo group significantly improved with regards to three of the variables, 'scaling', 'global impression' and 'itching'. These improvements were found to be significant on day 14. Likewise, the treatment group also showed significant improvement for these same three variables on day 14. The three variables in the placebo group which did not significantly improve at all were 'irritation', 'greasiness', and 'percentage of scalp affected'. These latter variables did however significantly improve in the treatment group, although no improvement was noted until day 28 of the trial.

This may have some significance, possibly indicating that the initial improvement in both groups was due to influences other than those of the medicated or un-medicated granules. The fact that the improvement in the placebo group did not regress supports

this statement. The overall improvement in the treatment group may then have resulted once the medicated granules had time to take effect. This is all speculation however, and more research would have to be conducted for confirmation.

The Hawthorne effect could have some part to play in this initial improvement. It states that people tend to change their behaviour when they are the target of special interest and attention (Peters, 2001:21), as for example in a research trial. This change of behaviour may simply have included increasing the frequency with which they washed their hair or brushed it. Johnson and Nunley (2000) state that hygiene plays a key role in controlling dandruff, saying that frequent cleansing with soap removes oils from the affected area and hence improves seborrhoea. Pierard-Franchimont, *et al.*, (2000) add that surfactants in shampoos are in fact therapeutic agents themselves and can detach superficial corneocytes and the micro-organisms inhabiting them. Regular brushing also helps as it removes the excess scales and debris (Wyndham, 2004:28).

Further comparison between the treatment group and placebo group shows that placebo participants did not improve to the same degree as treatment participants. This is evident from Figure 4.3 through to Figure 4.8 where each variable is displayed independently, and also on Figure 4.9 where the overall response (all variables added together) is diagrammatically represented; however this difference is not statistically significant.

5.3 Demographic results

The demographic results are of interest as firstly it is evident that more females took part in the trial than males. This contradicts the literature which states that, due to androgenic influences, more males are affected with dandruff than females (Pierard-Franchimont, *et al.*, 2000). This could be due to cosmetic reasons as more women would have been inclined to seek help than men.

The second set of demographics that are of interest is that in this trial 72% of the participants were of African descent. Statistics mentioned in Health & Medicine Week (Procter and Gamble Company, 2002:11) state that dandruff is more prevalent in people that are of African descent. This trial therefore corroborates with the literature.

The last set of demographic information pertains to the age of the participants. The average age within the treatment group and placebo group were very similar, being 25.4 and 26.0 years respectively. This similarity adds to the validity of the results.

5.4 Comparison to other dandruff trials

There are many trials that have been conducted in order to find an effective solution to dandruff.

The first trial the researcher would like to draw a comparison to is that of Teleman (2005) where a homoeopathic preparation of Selenium sulphide 8X was added to a neutral shampoo base. The participants in the trial were assessed over a four week period within which they were asked to use the shampoo twice a week. The Visual Analogue Scale (VAS) was used for the assessment and incorporated the variables 'scaling', 'irritation', 'greasiness', 'global impression', 'percentage of scalp affected', and 'itching' on a severity rating of 1 to 10. The research design used in Teleman's trial (2005) was in fact the same design used in this trial. The two trials were run at the same time, but independently of each other. Both trials showed significant improvement within both the treatment and placebo groups when the groups were analysed independently. However, when the treatment and placebo groups were compared, both trials found that there was no significant improvement in the overall management of dandruff.

Another homoeopathic trial of interest is that conducted by Smith, Baker, and Williams (2002) in which a preparation of Potassium bromide 1X, Sodium bromide 2X, Nickel sulphate 3X, and Sodium chloride 6X was given daily in oral dose over a ten week period. The assessment utilised several different scales in which the severity of 'percentage of skin involved', 'erythema', and 'scaling' were assessed. The trial was placebo controlled using the cross-over design. Unlike in this trial, the treatment by Smith, Baker, and Williams was found to be effective when compared to placebo with $P < 0.004$, and when placebo patients crossed over to treatment $P < 0.01$. When drawing a comparison between these two trials (namely that by Smith, Baker, and Williams, to

that of this trial), there are noticeably a few differences in the research designs.

Although it is impossible to say exactly why the trial by Smith, Baker, and Williams was successful and why this trial was not, it is possibly due to the fact that the potency of the treatment used by Smith, Baker, and Williams was lower than that used in this trial. This could imply that it was the physiological, crude dose still present in the treatment (which has been proven to be effective allopathically) that acted in that trial.

Allopathic trials can also be useful for comparative purposes. A trial by Danby, *et al.*, (1993) tested the safety and effectiveness of 2% ketoconazole shampoo versus 2.5% Selenium sulphide shampoo. The trial took place over a four week period during which time visual assessments for scaling, irritation, global improvement and itching were made (the severity ratings were the same as those used for this trial). The presence of yeast on the scalp was also determined at each visit through the use of oil immersion microscopy. The results of the trial showed that both shampoos were significantly more effective than placebo in the management of dandruff. However, all nine adverse effects that were reported during the trial occurred in the group treated with Selenium sulphide shampoo. A couple of comparisons can be drawn from this information.

Firstly, over a four week period, when compared to placebo, Selenium sulphide in crude dosage (namely 2.5%) was significantly effective, while Selenium sulphide in homoeopathic potency (namely 12X) was not effective. In fact, after only one week Selenium sulphide 2.5% showed a significant improvement. It is possible, that with more time Selenium sulphide 12X could show a significant improvement. Secondly, it is

of interest to see that Selenium sulphide 2.5% produces quite a few side effects, whereas there were no side effects reported in the trial with Selenium sulphide 12X.

5.5 Difficulty in evaluating dandruff trials

Pierard-Franchimont, *et al.*, (2001) suggest that there are difficulties with the methods involved in the clinical screening of dandruff. They say that overall, there is a lack of sensitivity in the screening methods. Pierard (2003) also voices this by stating that comparative studies between dandruff products are difficult to conduct and the interpretation of the results proves to be a problem.

This trial was also faced with the difficulty of finding a way to obtain results accurately. The method of choice, the VAS, is a measurement tool which takes readings based on the human perception. Gift (1989) says that when the VAS is used properly, it is a reliable, valid, and sensitive measure of subjective experiences. However, Pierard-Franchimont, *et al.*, (2001) point out that there is an overall lack of sensitivity, and human error, bias, differences in opinion about severity and untruthfulness can result in inaccuracies.

A report by Pierard (2003) indicates that, for the assessment of dandruff, human measurement tools (for example the VAS) may be just as good as bioinstrumentation readings, although the latter may provide less numeric variation. Even though instrumental objective assessment would be less variable, the literature reflects that the

majority of dandruff trials use measurements based on human readings. Some examples include research conducted by Smith, Baker, and Williams (2002) who used two different scales; the first scale (on a rating of 0 to 6) rated the percentage of skin involved; the second rated erythema and flaking on a scale of 0 to 4. Other examples include Peter and Richarz-Barthauer (1995) who used a four point scale system (0 = absent, 1 = mild, 2 = moderate, 3 = severe) which assessed erythema, desquamation, and pruritus. This method seems quite popular and has been used by a number of other researchers including Dupuy, *et al.*, (2001), Scaparro, *et al.*, (2001), and Pirkhammer, *et al.*, (2000). Another measurement tool frequently used is the VAS which measures dandruff symptoms on a scale of 1 to 10 (Journal of the American Academy of Dermatology, 1992).

In light of the short falls of taking human readings, this trial was designed for the assessment to be taken by three different individuals – the participant, researcher, and an independent third party. In this way, a more accurate assessment was hoped for.

5.6 Problems encountered in the trial

Viewing the results from this trial it is evident that the time period of four weeks was not a long enough assessment period. Three of the variables in the treatment group only began to show improvement on day 28 of the trial, in other words improvement only began in the latter phase of the trial. If the time period was increased, improvement may have continued further.

The literature speaks about all current dandruff products being suppressive in their action, meaning as soon as treatment is stopped, the symptoms return (Rook, Wilkinson and Ebling, 1992:551). In light of this, it would have been of benefit to have a month's follow-up period in which no treatment was given. This would then reveal if treatment was suppressive or curative.

The way in which treatment and placebo groups were compared in this trial was perhaps not the most effective method. The cross-over design which Smith, Baker, and Williams (2002) utilised seems to be a more accurate assessment when comparing placebo and treatment groups. In this design the participants are used as their own control. In other words participants are randomly assigned into either placebo or treatment group, and after a certain time period they are swapped over into the other group. The theory is that placebo participants now placed into the treatment group start to show improvement, and participants going from treatment to placebo show signs of deterioration. This method is especially useful with chronic conditions (Monsen, 1992:18).

CHAPTER 6

CONCLUSION AND RECOMMENDATIONS

6.1 Conclusion

It is concluded that oral homoeopathic preparation of Selenium sulphide 12X is ineffective in the management of dandruff (seborrheic dermatitis of the scalp).

6.2 Recommendations

1. The trial period should be extended in order to ascertain if any further improvement will occur after day 28.
2. The trial should be conducted by means of the cross-over design.
3. A follow-up assessment should be performed after the trial in order to determine if the treatment has a lasting curative effect, or if symptoms revert back to the way they were before the trial.
4. 12X may not be the optimum dose for Selenium sulphide in the treatment of dandruff. A trial could be performed experimenting with different ranges in potency levels.

5. A proving can be performed on Selenium sulphide in order to note the symptoms it can cure through the law of similars, and to see if dandruff is part of the symptom picture.

6. The results could be analysed more accurately through use of a combined approach, in other words through human readings and bioinstrumentation methods. Possibilities for bioinstrumentation include a method which collects dandruff flakes using strippings of adhesive-coated discs and another is via squamometry X assessments. (Pierard Franchimont, *et al.*, 2001).

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APPENDICES

Appendix A: Subject Information Letter

Title of Research Project: The effectiveness of oral Homoeopathic preparation of Selenium Sulphide 12X in the management of dandruff (Seborrhoeic dermatitis of the scalp).

Name of Supervisor: Dr Madhu Maharaj

Name of co-supervisor: Dr Ingrid Couchman

Name of Researcher: Keri Kent

Date:

Dear Participant

Thank you for the time and effort you are taking to read this letter.

I am a fifth year homoeopathy student at the Durban Institute of Technology. In order to complete my Masters degree I am required to complete a mini dissertation. In this research I will be investigating the effect of selenium sulphide in an oral homoeopathic dose on the symptoms of dandruff.

The clinical trials will be conducted in the Homoeopathy Day Clinic during the afternoons. All information provided by the participants will remain confidential and will be destroyed on completion of the research, in which the anonymity of the patients will be assured.

The trial will run for four weeks and you will be required to attend four consultations, all of which will be supervised by a qualified homoeopath. The consultations will be conducted firstly on inclusion into the study and then on day one, fourteen, and twenty-eight of the trial. Each participant must comply with certain criteria in order to enter the study; this will be ascertained in the first consultation.

If you fulfil the criteria and are willing to participate, you will be accepted into the trial and we appeal for your full co-operation and assistance.

This is a double-blind, randomised, placebo-controlled trial. This means you will have a 50% chance of being randomised into the placebo group. Both groups will be given a set of powders. You will be required take one powder each morning on a fasted

stomach. "Double-blind" refers to the fact that neither the patient nor the researcher will be aware of what treatment the patient is receiving. Only at the end of the data collection phase will the patient's group be revealed. If you are placed in the placebo group, at the end of the trial you will receive a course of the active powders free of charge.

It is possible that you may, during the course of the trial, experience an aggravation of your original symptoms. Homoeopathically this is considered a step towards cure and hence a good sign. Should anything concern you however, please do not hesitate to phone.

One week prior to the beginning of the trial, and for the duration of the trial, no other treatment for dandruff will be permitted.

Your participation in this study is completely voluntary and if, at any point during this study, you decide to withdraw, no reason need be given.

All consultation and treatment costs will be covered by the Durban Institute of Technology.

If you have any questions or experience any problems during this study please do not hesitate to contact my supervisor or myself on the following numbers:

Dr Maharaj: 031 204 2041

Keri Kent: 083 331 9394

Thank you for your assistance.

Keri Kent
Department of Homoeopathy
Durban Institute of Technology

Appendix B: Informed Consent Form

Title of Research Project: The effectiveness of oral Homoeopathic preparation of Selenium Sulphide 12X in the management of dandruff (Seborrhoeic dermatitis of the scalp).

Name of Supervisor: Dr Madhu Maharaj

Name of co-supervisor: Dr Ingrid Couchman

Name of Researcher: Keri Kent

PLEASE CIRCLE THE APPROPRIATE ANSWER:

- | | |
|---|--------|
| 1) Have you read the subject information letter? | YES/NO |
| 2) Have you had an opportunity to ask questions regarding this study? | YES/NO |
| 3) Have you received satisfactory answers to your questions? | YES/NO |
| 4) Have you had an opportunity to discuss this study? | YES/NO |
| 5) Have you received enough information regarding this study? | YES/NO |
| 6) Who have you spoken to? _____ | |
| 7) Do you understand the implications of your involvement in this study? | YES/NO |
| 8) Do you understand that you are free to withdraw from this study at any time without having to give a reason? | YES/NO |
| 9) Do you agree to voluntarily participate in this study? | YES/NO |

If you have answered NO to any of the above, please obtain the information before signing.

Participant name: _____

Signature: _____

Witness name: _____

Signature: _____

Researcher's name: _____

Signature: _____

Appendix C: Advertisement placed on notice boards and handed out as pamphlets.

Are you sick and tired of your dandruff?

**Free treatment is being offered at the
Homoeopathic Day Clinic
Durban Institute of Technology**

If you are between the ages of 18 – 50 and you meet the research criteria you could take part in the homoeopathic study.

If you are interested please phone one of the following:

Keri Kent: 083 331 9394
Silvana Teleman: 072 474 2324

Appendix D:

**Visual Analogue Scale
Participant's Assessment**

Participant name: _____

Date: _____

<u>Severity Rating</u>	
0:	none
1 - 2:	almost none/very slight
3 - 4:	mild
5 - 6:	moderate
7 - 8:	marked
9 - 10:	severe/heavy

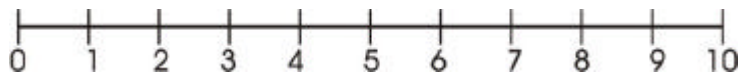
1) Scaling:



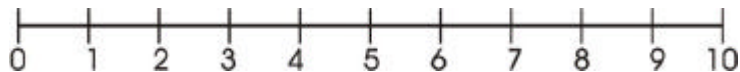
2) Irritation:



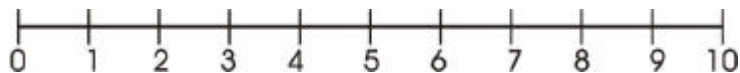
3) Greasiness:



4) Itchiness:



5) Global impression:



Appendix E:

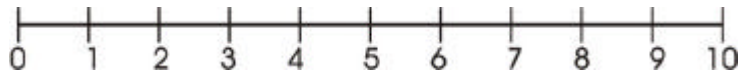
**Visual Analogue Scale
Researcher's and Third Party's Assessment**

Name of assessor: _____

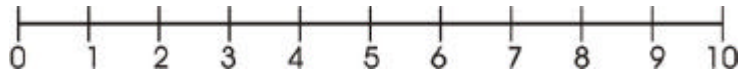
Date:

<u>Severity Rating</u>	
0:	none
1- 2:	almost none/very slight
3 - 4:	mild
5 - 6:	moderate
7 - 8:	marked
9 - 10:	severe/heavy

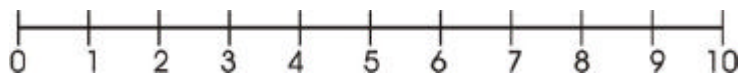
1) Scaling:



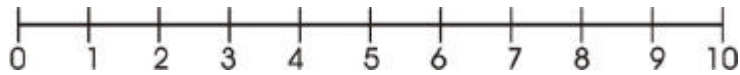
2) Irritation:



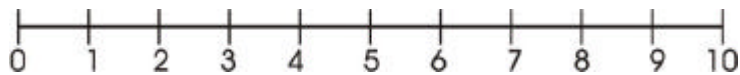
3) Greasiness:



4) Percentage of scalp affected:



5) Global impression:



Appendix F: Physical examination

VITAL SIGNS:

Temperature _____

Respiratory rate _____

Height _____

Pulse rate _____

Blood Pressure _____

Weight _____

GENERAL EXAMINATION:

Jaundice/ anaemia/ cyanosis/ clubbing/ dehydration/ oedema/ lymphadenopathy?
