THE EFFECT OF *TESTIS COMPOSITUM* IN THE TREATMENT OF ACNE VULGARIS

A research report submitted to the Faculty of Health Sciences, Technikon Witwatersrand, in partial fulfilment of the requirements for the degree of

Master of Technology: Homoeopathy

by

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Johannesburg 2004
DECLARATION

I declare that this research report is my own, unaided work. It is being submitted for the degree of Master of Technology: Homoeopathy at the Technikon Witwatersrand, Johannesburg. It has not been submitted before for any degree or examination in any other Technikon or University.

___________________________
Marelize Bekker

_________ day of ________________
ABSTRACT

Acne vulgaris is a common skin condition, affecting mostly adolescents. This study attempts to demonstrate the effect of the homoeopathically prepared remedy *Testis compositum* in the treatment of acne vulgaris.

Thirty participants were selected for the study, but only 28 completed the study. The study was conducted over a period of 8 weeks. All the participants formed the control group during the first two weeks of the study, and then formed the experimental group for the next six weeks. During the control period, the participants received placebo medication. At the start of the control period, and at two week intervals through the duration of the study, the participants were assessed by counting the acne lesions – only facial Acne vulgaris was assessed during the trial. At the start of the control period, the start of the experimental period, and after completion of all treatment, frontal and bilateral facial photographs were taken to enable visualisation of the changes that occurred during the study.

The results were statistically analysed using the t-test, the Wilcoxon test and descriptive statistics. The results show that treatment with *Testis compositum* had a significant effect in improving acne vulgaris.
I would like to dedicate this research to
Brett, Miles and my parents
for their love, support and encouragement throughout this process
ACKNOWLEDGEMENTS

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CHAPTER ONE

INTRODUCTION

1.1.1 Statement of the Problem

Acne vulgaris is a common skin condition, affecting mostly adolescents. Conventional treatments have many associated side effects that are not seen with the homoeopathic treatment of acne vulgaris. This study aimed to prove that a homoeopathic remedy, Testis compositum, could be used successfully to treat acne vulgaris.

1.1.2 Importance of the Problem

Acne vulgaris is an extremely common skin condition, affecting eighty to ninety five percent of male and seventy nine to eighty two percent of female adolescents (Lello et al., 1995 and Goulden et al., 1999). Acne vulgaris is not confined to adolescents (Lookingbill and Marks, 1993), affecting three percent of male and twelve percent of female adults (Goulden et al., 1999). It may persist for many years, even into the sixth decade and beyond (Goulden et al., 1997).

Improved treatment has modified the prevalence and severity of acne vulgaris, but it is still a matter of great concern for many practitioners, especially when seen in conjunction with the psychological impact that it has on sufferers (Aktan et al., 2000).

1.2 Hypotheses

Hypothesis one is that Testis compositum will have a positive effect in the treatment of acne vulgaris.
The null hypothesis is that *Testis compositum* will have no effect in the treatment of acne vulgaris.

### 1.3 Aim of the Study

The aim of the study is to determine the efficacy of *Testis compositum*, prepared according to homoeopathic principles, in the treatment of acne vulgaris. This study aims to prove that *Testis compositum* reduces the severity of acne vulgaris. *Testis compositum* therefore has significant therapeutic value in treating acne vulgaris, without the side effects.
CHAPTER TWO

LITERATURE REVIEW

2.1 Acne Vulgaris

Acne vulgaris is the most common skin disease treated by physicians. It affects between seventeen million (Krowchuk, 2000) and forty five million (White, 1999) people in the United States of America, with many more affected throughout the world.

Acne vulgaris is a chronic inflammatory disease of the pilosebaceous unit, characterised by comedones, papules, pustules, cysts, nodules and scars. It occurs primarily on the oily (seborrheic) areas of the skin (Odom et al., 2000), affecting the face, chest and upper back (Usatine and Quan, 2000 and Aktan et al., 2000). On the scalp, forehead, cheeks and chin there are between four hundred and nine hundred sebaceous glands per square centimetre, compared to fewer than one hundred per square centimetre on other parts of the body (Champion et al., 1992). The ears are frequently involved with large comedones in the concha and cysts in the ear lobes (Odom et al., 2000). The lower trunk is less often involved and the lower extremities are always spared (Lookingbill and Marks, 1993).

2.1.1 Pathogenesis of Acne Vulgaris

Acne is caused by the interaction of four factors:

- Increased sebum production
- Outlet obstruction of the sebaceous follicle (Usatine and Quan, 2000)
- Proliferation of bacteria (Russell, 2000)
- Inflammation (Johnson and Nunley, 2000)
2.1.1.1 Increased Sebum Production

Sebum production increases due to androgenic stimulation of the sebaceous glands (Usatine and Quan, 2000). The process of acne starts between seven and ten years of age when hormonal surges cause enlargement of the sebaceous glands (White, 1999). In general, the severity of acne correlates with the rate of sebum secretion (Rothman and Lucky, 1993). Sebum from acne patients is deficient in linoleic acid, which may cause changes in keratinization and follicular obstruction (Krowchuk, 2000).

2.1.1.2 Outlet Obstruction of the Sebaceous Follicle

The outlet of the sebaceous follicle becomes obstructed due to an abnormal keratinisation process with increased cohesiveness and turnover of follicular epithelial cells (Usatine and Quan, 2000). Blocking of the follicle allows sebum to collect. The sebum solidifies and becomes pigmented, giving rise to comedones (Cunningham, 1998). The obstruction of the pilosebaceous canal is the primary cause of acne (Russell, 2000).

2.1.1.3 Proliferation of Bacteria

The combination of sebum and desquamated epithelial cells provides a perfect environment for the proliferation of bacteria, especially *Propionibacterium acnes* (Russell, 2000). *Propionibacterium acnes* is an anaerobic diptheroid that resides in the pilosebaceous follicle (Odom *et al*., 2000). It has been suggested that *Propionibacterium acnes* enhances immune responses and may provide some protection against haematological malignancies (Sheehan-Dare *et al*., 1988), but not against solid tumours (Rampen, 1989). The ratio of *Propionibacterium acnes* levels in patients with acne, compared to those without acne, is very high. Between ages eleven to fifteen the ratio is 15 000:0, and between ages sixteen to twenty, the ratio is 85 000:590 (Odom *et al*., 2000).
Propionibacterium acnes contributes to the formation of acne in two ways (Krowchuk, 2000):

- Firstly, bacterial lipase acts on the sebum to produce free fatty acids (Odom et al., 2000) causing irritation of the follicular wall (Usatine and Quan, 2000). This stimulates an immune response, leading to the development of inflammatory lesions (Russell, 2000).

- Secondly, Propionibacterium acnes produces chemotactic factors that cause polymorphonuclear neutrophils to enter the pilosebaceous follicles. As the polymorphonuclear neutrophils ingest Propionibacterium acnes, hydrolytic enzymes are released that damage the follicular wall. As the contents of the follicle leak into the dermis, inflammatory reactions take place, manifesting as erythematous papules, pustules or nodules (Krowchuk, 2000). Propionibacterium acnes also induces follicular keratinocytes to release interleukin-I (Leyden, 2003), which causes the proliferation of keratinocytes and contributes to the formation of microcomedones (Guy et al., 1996).

2.1.1.4 Inflammation

Inflammation is mediated by the irritation of sebum leaking into the dermis and the chemotactic factors, promediators and free fatty acids generated by Propionibacterium acnes (Johnson and Nunley, 2000 and Usatine and Quan, 2000).

2.1.1.5 Other Contributing Factors

Many other factors play a role in the pathogenesis of acne vulgaris including genetics, androgenic hormones, stress, occupational exposure to oils and chemicals, comedogenic cosmetics and medications (Usatine and Quan, 2000 and Fitzpatrick and Aeling, 1996).

Familial studies have shown that hereditary factors play an important role in an individuals’ susceptibility to develop acne vulgaris (Goulden and McGeown et al., 1999). The tendency to develop acne, the size and activity of sebaceous glands, seborrhoea and
large skin pores are all inherited. If both parents had acne, the probability of their child developing acne at puberty is about fifty percent (Braun-Falco et al., 1991), but it is not possible to accurately predict acne severity for an individual based on family history (Krowchuk, 2000). Genetic and environmental factors also cause differences between the formation and appearance of acne vulgaris in white skin and skin of colour (Berardesca and Maibach, 2003). Twin studies showed that while genetics control sebum production, environmental factors modify the development of clinical lesions (Walton et al., 1989). Evidence suggests that acne vulgaris is more prevalent in westernised populations than in non-industrialised societies (Cordain et al., 2002).

The frequency and severity of acne, as well as the tendency to scar, is greater in adolescent males than females (Bershad, 2001). A male dominance of infantile acne has also been proven (Cunliffe et al., 2001).

Sebum secretion at birth is similar to that in adults (Agache et al., 1980). The sebaceous glands regress to become minute during the pre-pubescent period, but then enlarge at puberty when the sebum output of males increases more than five times (Pochi et al., 1979).

The role of hormones in the pathogenesis of acne is evident by the onset of acne at puberty (Canizares, 1993). Androgenic hormones control the development of the sebaceous glands and sebum excretion (Braun-Falco et al., 1991). Testosterone increases the thickness of the skin and the ruggedness of the subcutaneous tissues (Guyton, 1991). These androgens are mainly testicular or adrenal in origin. Testosterone synthesis in the testis is controlled by serum luteinizing hormone (Farrell et al., 1999). The finding of luteinizing hormone receptors in the sebaceous glands (Pabin et al., 1996) also shows the importance of this hormone in the pathogenesis of acne. In a study conducted by Farrell et al. a sub-group of men with acne had shown raised levels of serum luteinizing hormone (LH). They also found that while serum LH levels decrease with age, the decrease in LH occurred slower in men with acne vulgaris. Testosterone, dehydroepiandrosterone sulfate (DHEAS), androstenedione and 5α-dihydrotestosterone
have all been shown to stimulate sebum production (Champion et al., 1992), with the serum levels of dehydroepiandrosterone sulfate showing the best correlation to acne (White, 1999). At age eight to ten, before the appearance of secondary sexual characteristics, the adrenal glands start producing increasing amounts of DHEAS (Pochi, 1990). Increased levels of DHEAS cause sebaceous glands to enlarge and produce more sebum (Stewart et al., 1992). Despite the importance of hormones in causing acne, most acne patients have normal hormone levels (Lucky et al., 1994 and Lucky et al., 1997), but may have decreased sex-hormone-binding globulin (Marynick, 1983). Although increased serum androgen levels correlate with the presence of severe nodular acne in men and women, these levels are often within the normal range with mild to moderate acne (Thiboutot et al., 1999).

Acne in women may be associated with higher serum androgen levels (Thiboutot et al., 1999), and may be accompanied by hirsutism or menstrual irregularities (Lucky, 1995). Acne vulgaris may be the only clinical symptom of androgen excess in men (Degitz et al., 2003). Androgenic anabolic steroids used to enhance athletic performance and for bodybuilding can cause acne or aggravate existing acne (Braun-Falco et al., 1991 and Lookingbill and Marks, 1993). Bagatell et al showed that serum levels of testosterone produced by the administration of two hundred milligrams of testosterone every week, lead to suppressed levels of plasma high-density lipoprotein (HDL) cholesterol, changes in calcium metabolism, increased body weight, and mild acne.

Certain drugs, including phenytoin, lithium, bromides and iodides can cause acne when administered systemically (Orkin et al., 1991). Topical or systemic corticosteroids can cause an acneiform eruption (Lookingbill and Marks, 1993). Corticosteroids are the most common cause of drug-induced acne. The acne in these cases is usually monomorphic, consisting of uniform papulopustular lesions and the absence of comedones (Orkin et al., 1991).

Dietary factors used to be considered important, but there is no proof that diet plays a significant role in the development of acne (Orkin et al., 1991). Hygiene and diet have
been shown to have little or no influence on acne (Bershad, 2001). However, Canizares (1993) states that in some individuals, eating excess sugar or fatty foods may aggravate acne.

Comedogenic materials in cosmetics can cause acne. It may also occur from physical trauma such as rubbing (Orkin et al., 1991). Picking or squeezing the lesions also aggravates acne, causing additional tissue damage and sometimes resulting in scars (Canizares, 1993 and Lookingbill and Marks, 1993). Other factors such as menstruation, nervous tension, insufficient sleep and chronic illness may also aggravate acne (Canizares, 1993). It is unlikely that stress alone can induce the formation of acne lesions (Kenyon, 1966), although acne itself may induce stress (Champion et al., 1992). Up to fifteen percent of acne patients notice that sweating causes an aggravation in their acne, especially if they live or work in a hot, humid environment (Champion et al., 1992).

Smoking is a clinically important factor contributing to acne prevalence and severity. There is also a dose dependant relationship between smoking and the severity of acne (Shäfer, et al., 2001). Smoking has been associated with several skin disorders, including skin carcinomas (Grodstein, et al., 1991). Specific skin changes are associated with smoking: wrinkles, atrophy, grey appearance of skin or a red complexion (Shäfer, et al., 2001). Many studies have shown impaired wound healing in smokers that seems to be caused mainly by vasoconstriction (Goldminz and Bennet, 1991).

Acne vulgaris tends to show seasonal variations, generally improving in summertime and aggravating in wintertime (Gfesser and Worret, 1996). Moderate exposure to sunlight is usually beneficial, while extreme heat and humidity often aggravate (Canizares, 1993). Sunbathing is thought to improve inflammatory lesions by increasing blood flow to the effected areas. Because of the negative effects of ultraviolet radiation on the skin, acne cannot be treated with ultraviolet radiation (Gfesser and Worret, 1996). Ultraviolet radiation may also enhance the comedogenicity of sebum (Mills et al., 1978).
2.1.2 **Clinical Features of Acne Vulgaris:**

Acne vulgaris is a polymorphic disease that occurs predominantly on the face (ninety-nine percent), and to a lesser extent on the back (sixty percent) and chest (fifteen percent). In young men the face is mostly affected and in older males the back (Taaffe et al., 1983).

Acne lesions can be divided into:
- Primary non-inflammatory lesions
- Secondary inflammatory lesions
- Post-inflammatory lesions (Usatine and Quan, 2000 and Braun-Falco et al., 1991).

### 2.1.2.1 Primary Non-inflammatory Lesions

Primary non-inflammatory lesions are closed comedones (whiteheads) and open comedones (blackheads). In the secondary inflammatory stage, inflammation occurs in the comedones, leading to the formation of papules, pustules, indurated nodules and nodular abscesses. If the inflammatory lesions were severe, post-inflammatory lesions may be visible, such as fistulated comedones, cysts and scars (Usatine and Quan, 2000 and Braun-Falco et al., 1991).

A comedo is a plug of sebum and keratin lodged in the follicular duct (Bershad, 2001). Initially, obstruction in the follicles is microscopic, giving rise to microcomedones. As these comedones enlarge, they give rise to open comedones (blackheads) and closed comedones (whiteheads) (Krowchuk, 2000). Comedones are also caused by some medications, such as lithium and corticosteroids, and by topical occlusion, such as pomades and other hair products (Rassner, 1992).

Open comedones are the basic lesions in acne (Odom et al., 2000). They are flat or slightly raised, brownish or black and up to five millimetres in diameter (Usatine and Quan, 2000). The open comedone is produced by hyperkeratosis of the lining of these
follicles, associated with retention of keratin and sebum. The plugging produced by the comedone dilates the mouth of the follicle. Papules are formed by inflammation around the comedones (Odom et al., 2000). The black colour of open comedones is caused by oxidation of melanin, a change in the transmission of light by compacted epithelial cells or the presence of certain lipids within the sebum.

Closed comedones are flesh-coloured or whitish, slightly palpable, approximately one to three millimetres in diameter (Usatine and Quan, 2000), and without surrounding erythema. They consist of follicles with a microscopic opening to the skin surface, dilated with cellular and lipid debris (Krowchuk, 2000). When a comedone causes the follicular wall to rupture, an inflammatory reaction follows, resulting in clinically evident papules, pustules, nodules and cysts (Bershad, 2001).

2.1.2.2 Inflammatory Lesions

Inflammatory lesions include papules and pustules, indurated nodules and nodular abscesses (Graham-Brown and Bourke, 1998 and Braun-Falco et al., 1991). Inflammatory lesions may be shallow or deep (Champion et al., 1992). Superficial lesions become papules and pustules that are less than five millimetres in diameter, and deep lesions become deep pustules and nodules (Orkin et al., 1991 and Champion et al., 1992). Acne papules are pink or reddish lesions that range from two to five millimetres in diameter. Pustules are superficial papules that contain grossly purulent material. Acne nodules are solid, raised lesions that are bigger than five millimetres in diameter and are situated deeper in the dermis than papules (Usatine and Quan, 2000). In some cases, instead of developing an open comedo, the wall of the closed comedo may rupture, spilling the follicular contents into the dermis and lead to the development of inflammatory lesions (Orkin et al., 1991). Nodules, especially if they are exudative or haemorrhagic, are particularly disfiguring. Epithelial-lined sinus tracts may form between nodules (Champion et al., 1992 and Odom et al., 2000).
2.1.2.3  **Post-inflammatory Lesions**

Fistulated comedones, cysts and scars are typical of previous severe acne (Braun-Falco *et al*., 1991).

Acne cysts are pus-filled acne lesions greater than five millimetres in diameter, with a wall composed of inflammatory cells and scar tissue (Bershad, 2001). The acne cyst is usually a large nodule that has suppurated and has become fluctuant (Usatine and Quan, 2000). The formation of cysts involves the partial or complete destruction of the sebaceous gland (Odom *et al*., 2000). Cysts may rupture and give rise to abscesses (Braun-Falco *et al*., 1991).

Scars do not occur in all patients, but are the result of the healing process (Graham-Brown and Bourke, 1998 and Rassner, 1992). Scarring is most likely to occur in adolescents who develop large nodules and cysts (Rothman and Lucky, 1993, Champion *et al*., 1992 and Odom *et al*., 2000), but even small inflammatory lesions may give rise to scars (Krowchuk, 2000). The scars that may result from acne are usually small, punched out pits called ice-pick scars (Orkin *et al*., 1991 and Usatine and Quan, 2000). Hypertrophic keloid scars are common with acne lesions on the chest and back, and beneath the chin line (Graham-Brown and Bourke, 1998 and Rassner, 1992).

The severity of the disease depends on:

- The appearance of the lesions
- The psychological impact of the disease
- The potential for scarring
- The failure of previous therapy
- Occupational disability (Cunliffe, 2000 and Allison *et al*., 1997).

It is important to take the total impact of the disease into account. The possible complications of lesions, such as drainage, haemorrhage and pain, should also be taken into account. (Allison *et al*., 1997).
2.1.2 Acne Vulgaris in Skin of Colour:

Eighty percent of the world’s population consists of individuals with pigmented skin (Halder and Nootheti, 2003). Common skin diseases, such as acne vulgaris, display clinical and histological differences in people with skin of colour compared with white skin (Caucasians). The response to therapeutic agents may also be different in people with skin of colour (Taylor et al., 2002).

In a study conducted by Halder et al. (1983) the diagnoses of five hundred and fifty white and two thousand black patients were compared. Acne vulgaris was the most common diagnosis in both groups, presenting almost twenty eight percent of the black patients and thirty percent of the white patients (Halder et al., 1983). Among two hundred and seventy four black patients, Child et al. found the most common diagnosis to be acne vulgaris, presenting almost fourteen percent of the patients.

In South Africa, dermatologists found higher rates of acne among white patients (Findlay, 1967) than among black patients (Park, 1968). In white adolescents the incidence of acne was forty five percent, while the incidence in black adolescents was sixteen percent. In entire population samples across all ages, the overall occurrence of acne in white patients was ten percent, compared to two percent in black patients (Findlay, 1967 and Parks, 1968).

There is not enough evidence to conclude that the pathogenesis of acne vulgaris differs between white and black skin. The pathogenesis of acne in skin of colour most likely involves the same factors as in white skin (Taylor et al., 2002). These factors are the formation of a follicle plug, increased sebum production, the proliferation of Propionibacterium acnes, and inflammation (Freedberg et al., 1999).

In the only study comparing facial bacterial colonisation by Propionibacterium acnes in black and white skin, there was a trend towards greater overall density of Propionibacterium acnes in black skin (Warrier et al., 1996). In black males, sebaceous
glands are significantly larger and they have higher skin sebum levels than in white males (Taylor et al., 2002).

Taylor et al. (2002) noticed histological differences in the manifestation of acne vulgaris in black patients compared to white patients. It has been assumed for a long time that inflammation is more common in white patients than in black patients. Comedonal lesions in black patients showed marked inflammation with infiltrates of polymorphonuclear leukocytes. This contrasts with comedones in white skin that is non-inflammatory (Taylor et al., 2002). Black patients have especially dark open comedones while albinos have white ones (Braun-Falco et al., 1991). Inflammation seems uncommon in black patients because it is well hidden by the darker colour of their skin (White, 1999). In a study on acne vulgaris in darker skin conducted by Halder et al. (1996), acne lesions that did not show marked clinical inflammation showed a high degree of histological inflammation. Acne vulgaris in skin of colour differs from acne in Caucasian skin on both clinical and histopathological level (Halder et al., 1996). Papular and pustular lesions also demonstrate inflammatory infiltrates. These infiltrates are dense and distributed beyond the actual papule or pustule (Taylor et al., 2002).

The presence of inflammation in comedones and the marked inflammation of classic inflammatory lesions account for the tendency of darkly pigmented skin to develop significant post-inflammatory hyper-pigmentation, known as the acne hyper-pigmented macule. In the study conducted by Taylor, et al. (2002) over thirty seven percent of the patients had dark marks that lasted four months or longer. This pigmentation is often the main complaint in dark skinned patients with acne, being both disfiguring and long lasting (Taylor, 2002). Much of the melanin in post-inflammatory hyper-pigmented macule is found in the epidermis, and not in the dermis as previously believed. This means that these dark spots are accessible to topical therapy (White, 1999).

There seems to be a lower incidence of nodulocystic acne in black patients, but a higher incidence of keloidal scarring (Taylor, 2002).
2.1.4 Psychological Impact of Acne Vulgaris:

Acne can be both physically and psychologically painful (Usatine and Quan, 2000). Studies have shown that many acne patients experience shame, embarrassment, anxiety, lack of self-confidence, impaired social contact and problems with unemployment (Cunliffe, 1986 and Jowett and Ryan, 1985). Severe acne may also be associated with increased anger and anxiety (Wu et al., 1988).

Acne, like most skin diseases, has a major psychological effect, especially when it affects the face (Graham-Brown and Bourke, 1998). Patients with severe acne report psychological and social problems similar to patients with chronic asthma, epilepsy, diabetes or arthritis (Mallon et al., 1999). Patients with acne often have low self-esteem and feelings of inferiority, depression, anger, frustration and embarrassment (Mallon et al., 1999 and Aktan et al., 2000). Studies have shown poor academic performance in students with severe acne (Fitzpatrick and Aeling, 1996), and that acne may even precipitate suicide (Cotterill and Cunliffe, 1997).

2.1.5 Differential Diagnosis of Acne Vulgaris:

The diagnosis of acne vulgaris is made on the clinical features (Rassner, 1994) and is rarely difficult to make, especially in teenagers (Lookingbill and Marks, 1993). Differentiation of various special forms of acne depends on adequate history (Orkin, 1991). Occasionally, bacterial cultures may be indicated to rule out infection, but biopsy is not indicated (Lookingbill and Marks, 1993).

A variety of diseases that resemble acne, but have a different pathogenesis, must be differentiated, such as warts, acne conglobata, acne rosacea, bacterial folliculitis, steroid folliculitis, adenoma sebaceum and periorificial dermatitis (White, 1999, Lookingbill and Marks, 1993 and Fitzpatrick and Aeling, 1996).
Comedones may be confused with flat warts, which are small flesh-coloured papules, usually located on the face (Lookingbill and Marks, 1993).

Acne conglobata is the most severe form of acne and affects males more often than females. The comedones, papules, pustules and nodules have a tendency to bleed. This leads to the formation of large atrophic and keloidal scars. There are typically groups of fistulated comedones with dark-pigmented plugs, especially on the back. Giant comedones give rise to cysts that persist for many years and do not heal spontaneously. Acne conglobata occurs on parts of the skin not usually affected by acne vulgaris, such as the gluteal area, stomach, upper arms, neck, ear lobes and scalp (Rassner, 1992).

Pustular acne can be confused with acne rosacea or bacterial folliculitis. Acne rosacea usually occurs later in life than acne vulgaris. Rosacea has a background erythema and telangiectasia in the absence of comedones. In bacterial folliculitis, hairs can be seen in some of the pustules and a bacterial culture will be positive, usually for *Staphylococcus aureus* (Lookingbill and Marks, 1993).

Steroid acne is caused by the use of corticosteroids. It is distinguished from acne vulgaris by its sudden onset and appearance. All the lesions are in the same stage of development, and comedones are absent. The papules and pustules are uniform, two to three millimetres in diameter, red and firm. With systemic steroids the eruption occurs primarily on the upper trunk, while eruptions due to topically applied agents occur mostly on the face. The eruption clears when the drug is withdrawn (Fitzpatrick and Aeling, 1996 and Lookingbill and Marks, 1993).

Papular acne may be confused with adenoma sebaceum. It is a skin manifestation of tuberous sclerosis, characterised by firm, pink papules that are clustered mostly in the centre of the face. The lesions are persistent and resistant to acne therapy (Lookingbill and Marks, 1993).
2.2 Conventional Treatment:

The treatment of acne has six goals:

- To improve the patient’s appearance
- To treat the lesions that do occur
- To lessen the physical discomfort from the inflamed lesions
- To prevent or minimise scarring
- To prevent the formation of new lesions
- To avoid the psychological impact of the disease on the patient (Usatine and Quan, 2000).

The treatment of acne is aimed at one or more of its pathogenic precipitants. These precipitants include androgenic stimulation of the sebaceous gland, excess sebum secretion, faulty occlusion of the follicular orifice by altered keratinisation, colonisation of the follicle by Propionibacterium acnes and inflammation (Bershad, 2001 and Orkin et al., 1991).

The usual approach in conventional medicine is “combination therapy”, with the oral retinoid isotretinoin being the notable exception. "Combination therapy" comprises the use of two or more agents that are applied at different times during the day. Usually a topical antibiotic is applied in the morning and a keratolytic agent is applied at night (Bershad, 2001). When the predominant lesion type is inflammatory papules or pustules, the conventional treatment is topical and systemic antibiotics. Since comedones are the primary lesion of acne, most patients will benefit from using keratolytic agents at the same time (Bershad, 2001). Due to the antibiotic resistance of Propionibacterium acnes (Eady et al., 1996), it may be better to use antibiotics twice a day, followed by a keratolytic agent at night (Bershad, 2001). Non-steroidal anti-inflammatory drugs can be used together with antibiotics to help improve the inflammatory component (Berger et al., 1990).
Conventional medications for acne therapy can be topical and/or systemic (Usatine and Quan, 2000). In some instances physical therapies, such as acne surgery and intralesional therapy, are also used. Acne surgery removes open comedones, closed comedones and small pustules by using a comedo extractor. The comedo extractor exerts uniform pressure around the lesion and the contents of the lesion are expressed. Intralesional therapy involves the direct injection of corticosteroids into the acne lesions. This treatment has an anti-inflammatory effect and is of great benefit in the treatment of nodulocystic lesions. No more than 0.1 millilitre of fluid should be injected at a time to avoid tissue atrophy and scar formation. Intralesional therapy should only be used for the treatment of large cysts, and not for the treatment of papules or pustules (Orkin et al., 1991). The treatment of acne depends on the severity and the extent of involvement (Odom et al., 2000).

2.2.1 Topical Applications:

Topical applications for acne include retinoids such as azelaic acid and alpha-hydroxy acid, benzoyl peroxide, topical antibiotics or synergistic combinations of these therapeutic agents (Usatine and Quan, 2000). The treatment of acne prevents the formation of new lesions; therefore topical applications must be applied to the whole affected area, not just individual lesions (Berger et al., 1990). When choosing a topical agent, the vehicle (substance in which the active ingredient is dispersed) is very important. By determining the rate at which the active ingredient is absorbed through the skin, the vehicle affects the potency of the active agent. The choice of vehicle is affected by many factors, including skin characteristics, the site of acne involvement, the climate and humidity, and patient preferences. The most commonly used vehicles are creams, ointments, gels, lotions and solutions (Habif, 1996).

Comedonal acne is treated with keratolytic agents that target faulty occlusion of the follicular orifice. These agents include retinoids, azelaic acid and alpha-hydroxy acids (AHAs). Immediate results can be achieved with acne surgery, which involves the
manual extraction of impacted comedones (Bershad, 2001). Vitamin A acid (retinoids) softens comedones, enhancing their removal (Berger et al., 1990).

### 2.2.1.1 Topical Retinoids:

Virtually all patients benefit from the use of a retinoid (Kligman, 1997). Retinoids are topical vitamin A acid applications which are the most potent keratolytic agents. Medications in this group include topical tretinoin, adapalene, tazarotene, azelaic acid and alpha-hydroxy acid (Bershad, 2001).

Topical tretinoin normalises keratinisation by increasing the turnover of follicular epithelial cells (Bershad, 2001). This leads to the extrusion of comedones and inhibits comedo formation (Oh and Myung, 1996). The onset of improvement is relatively delayed and variable and may take one to three months (Shalita, 1983). The use of tretinoin is limited by local skin irritation and it may cause increased sun sensitivity. Retinoids are often combined with oral or topical antibiotics to inhibit the inflammatory process (Bershad, 2001). Tretinoin may also cause clinical worsening after two to four weeks of treatment (Gibson, 1996) when the extrusion of comedones may elicit a pustular reaction (Bershad, 2001).

Adapalene and tazarotene are selective for nuclear retinoic acid receptors, thereby affecting keratinocyte differentiation and blocking inflammation (Bernard, 1993 and Chandraratna, 1996). Adapalene inhibits comedo formation by binding to retinoic acid receptors and modulating cell differentiation, and it has a direct anti-inflammatory effect (Brogden and Goa, 1997). Compared to tretinoin, adapalene produces much greater lesion reduction and less skin irritation (Shalita et al., 1996). Adapalene may cause an inflammatory acne flare towards the end of the first month of therapy (Bershad, 2001). Adapalene reduces both inflammatory and non-inflammatory lesions and may be used as an effective monotherapy for mild forms of acne (Dunlap et al., 1998). Tazarotene also has erythema and irritation as common side effects (Bershad, 2001).
Azelaic acid inhibits comedogenesis by preventing follicular hyperkeratosis (Oh and Myung, 1996). It also has antimicrobial properties against Propionibacterium acnes (Bojar et al., 1991) and it does not induce resistant Propionibacterium acnes (Graupe et al., 1996). Azelaic acid is very safe, but may cause slight burning, pruritis, stinging and tingling (White, 1999). Mild skin irritation is only seen in five to ten percent of patients using azelaic acid (Fitton and Goa, 1991 and Sykes and Webster, 1994). It is a good alternative for moderate acne in patients with sensitive skin, for acne of the neck and for patients with post-inflammatory hyperpigmentation (White, 1999). Azelaic acid is as effective as five percent benzoyl peroxide, 0.05 percent tretinoin or two percent erythromycin (Nguyen and Bui, 1995). Azelaic acid and tretinoin are particularly useful in treating post-inflammatory hyper-pigmentation in dark skinned patients (Bulengo-Ransby et al., 1993).

Alpha-hydroxy acids facilitate the desquamation of the stratum corneum (Van Scott and Yu, 1984), making it useful in the treatment of comedonal acne, especially glycolic acid and gluconolactone (Hunt and Barnetson, 1992 and Wang et al., 1997). Lower concentrations of alpha-hydroxy acids cause less skin irritation, making it useful as a non-prescription way of treating mild acne (Bershad, 2001).

2.2.1.2 Benzoyl Peroxide:

Benzoyl peroxide is a potent bactericidal agent that is widely available in prescription and non-prescription products. It reduces Propionibacterium acnes and free fatty acids in sebum (Bershad, 2001). It has been shown that five percent benzoyl peroxide applied daily can reduce follicular Propionibacterium acnes counts one hundred fold within just two days (Bojar et al., 1995). Benzoyl peroxide reduces comedones (Chu et al., 1997) and improves inflammatory acne (Burke et al., 1983).

Common side effects of benzoyl peroxide include dry skin with redness and peeling, and bleaching of skin and fabrics (Bershad, 2001). These side effects can often be reduced by using an emollient or a water-based gel, or by reducing the benzoyl peroxide.
concentration (Rothman and Lucky, 1993). Some studies raised concerns that benzoyl peroxide enhances carcinogenesis in laboratory animals (O’Connell, et al., 1986).

2.2.1.3 Topical Antibiotics:

The topical antibiotics clindamycin and erythromycin have been available as hydro-alcoholic solutions for about twenty years. Newer hydrophilic gels and lotions have been formulated to try and reduce skin irritation. Clindamycin and erythromycin reduce the colonisation of *Propionibacterium acnes* and have a direct anti-inflammatory effect by suppressing neutrophil chemotaxis (Bershad, 2001).

Fixed combination gels, containing erythromycin or clindamycin in combination with benzoyl peroxide, have been found to be superior to their individual components for acne treatment (Chu et al., 1997 and Chalker et al., 1983 and Lookingbill et al., 1997). A further advantage of these combinations may be a reduction in drug-resistant *Propionibacterium acnes* (Eady et al., 1996).

Erythromycin can also be combined with zinc, a suppresser of inflammation, by adding zinc to the topical application. Zinc may also act to inhibit penetration, which leaves the antibiotic on the surface of the skin. This extends the effect of the antibiotic on the skin surface (Van Hoogdalen et al., 1996).

Other topical antibiotics that are used to treat acne are metronidazole, sulphur and sulphur compounds (Bershad, 2001), although sulphur may be both comedogenic (Mills and Kligman, 1972) and comedolytic (Strauss et al., 1978).

Topical therapies can be used as maintenance therapy after cessation of systemic therapies (Olsen, 1982).
2.2.2 Systemic Treatment:

Systemic treatments include oral antibiotics, hormone-related therapies and isotretinoin (Usatine and Quan, 2000).

2.2.2.1 Systemic Oral Antibiotics:

Systemic oral antibiotics are indicated for moderate to severe acne, especially if there is potential for scarring (Bershad, 2001). Oral therapies are usually prescribed for a period of four to six months (Cunliffe, 2000).

Effective systemic antibiotics for acne include tetracycline, minocycline, doxycycline, erythromycin (White, 1999), lymecycline (Cunliffe et al., 2003), azithromycin and trimethoprim alone or combined with sulfamethoxazole (White, 1999).

The tetracyclines and erythromycin are the most commonly used oral anti-bacterial agents (Cunliffe et al., 2003). The most notable side effects of oral antibiotics are phototoxicity from the tetracycline group, vertigo-like dizziness from minocycline, gastro-intestinal problems from erythromycin, and drug eruptions from a trimethoprim-sulfamethoxazole combination. All oral antibiotics predispose to Candida albicans infections, especially vaginitis (Bershad, 2001).

Patients on minocycline should be warned of the potential development of blue skin, nails and teeth (White, 1999). A recent study showed that minocycline has a greater tendency than tetracycline to cause rare side effects, such as hypersensitivity reactions, serum-sickness-like reactions and single organ failure (Shapiro et al., 1997). The symptoms of hypersensitivity reactions include fever, lymphadenopathy, eosinophilia, lymphocytosis, hepatitis and dermatitis (Knowles et al., 1996). Other rare side effects include pustular drug eruptions, black discoloration of breast milk and acute hepatic failure (Min et al., 1992). Minocycline is also associated with many pulmonary complications (Oddo et al., 2003) including pneumonitis (Sitbon et al., 1994), pulmonary lupus (Oddo et al., 2003).
and pleural effusion (Clayton et al., 1999). Despite these rare but serious side effects, minocycline is still considered safe for long-term use, but should only be used for treatment resistant acne (Goulden et al., 1996 and Cunliffe, 1996 and Gottlieb, 1997).

Lymecycline is a tetracycline antibiotic with better oral absorption, improved tissue penetration and slower elimination than tetracycline (Cunliffe et al., 1998). It is converted into tetracycline in the gastrointestinal tract before it is absorbed (Sjölin-Foersberg and Hermansson, 1984). Blair (1968) showed that lymecycline is a well-tolerated and effective treatment for acne vulgaris. Compared to minocycline, lymecycline is as effective in reducing lesion counts and acne severity, with no significant safety differences between the two drugs (Cunliffe et al., 1998). Lymecycline can be regarded as a suitable first-line oral treatment for acne vulgaris (Cunliffe et al., 2003).

The excessive use of systemic antibiotics has led to the detection of increasing numbers of antibiotic-resistant bacteria on the skins of acne patients (Coates, et al., 1997). The bacterial resistance of Propionibacterium acnes to antibiotics is a problem of growing clinical significance (Odom et al., 2000). The use of tetracyclines and erythromycin leads to the resistance of Propionibacterium acnes to these antibiotics. This may result in therapeutic failure of these antibiotics and in the propagation of resistance of the bacteria in the skin and gastrointestinal tracts of the patient and close contacts to these antibiotics (Ross, Huang et al., 2003). Although acne vulgaris is not an infectious disease, resistant strains of Propionibacterium acnes may be transmissible between susceptible individuals (Ross, Snelling et al., 2003). Antibiotic therapy for acne vulgaris also causes a three-fold increase in the prevalence of Streptococcus pyogenes in the oropharynx of patients compared to those not using any antibiotics (Ross, Huang et al., 2003). This resistance can be addressed by prescribing antibiotic therapy only when non-antibiotic therapy did not work, stopping antibiotics during maintenance, using benzoyl peroxide in combination with antibiotics, and by avoiding the use of different oral and topical antibiotics at the same time (Odom et al., 2000). Oral isotretinoin has been reported to
reduce the number of antibiotic-resistant bacteria on the skin of patients with acne (Layton et al., 1997).

### 2.2.2.2 Hormone-Related Therapies:

Hormonal therapy has previously been used mostly for women with acne. Many studies have shown a direct relationship between serum androgen levels and acne (Bershad, 2001). It may also be possible that the sebaceous glands of patients with acne are hyper-responsive to normal serum androgen levels (Lever and Marks, 1990).

Topical and systemic treatments can be used to treat severe nodulocystic acne, especially oral antibiotics combined with a topical keratolytic agent, as well as hormonal therapy in women (Bershad, 2001). Oral administration or intralesional injections of corticosteroids can be used to help control severe outbreaks (Levine and Rasmussen, 1983), but chronic corticosteroid use is contra-indicated in acne (Bershad, 2001). Intralesional corticosteroids such as triamcinolone acetonide are helpful in treating large inflammatory lesions. Only large lesions with significant elevation over the surrounding skin should be treated in this way, due to the risk of atrophic scarring associated with this procedure. The corticosteroid should be injected into the centre of the lesion until the redness blanches (White, 1999). Some larger lesions persist because they represent sinus tracts. These lesions are usually oblong or linear in shape (Leyden, 1997) and have to be surgically removed (White, 1999).

### 2.2.2.3 Isotretinoin:

Isotretinoin (13-cis-retinoic acid), trading as Accutane or Roaccutane (McLane, 2001), remains the treatment of choice for recalcitrant nodulocystic acne and acne conglobata (Ott et al., 1996). From 1992 to 2000, the number of dispensed prescriptions for isotretinoin in the United States of America has increased by two-hundred and fifty percent to nearly twenty million (Wysowski et al., 2002).
Isotretinoin is used for moderate to severe acne that is resistant to conventional therapy (White, 1999). The Food and Drug Administration (FDA) labels it only for the treatment of severe recalcitrant nodular acne (Accutane Prescribing Information, 1998). Data shows that an increasing proportion of isotretinoin is used for mild to moderate acne (Wysowski et al., 2002). The indications for isotretinoin include:

- Acne that is resistant to oral antibiotics
- Severe scarring acne
- Acne that has persisted for many years that quickly relapses when oral antibiotic therapy is discontinued (White, 1999).

Isotretinoin causes dedifferentiation of the sebaceous gland, leading to suppressed sebum production (Orfanos et al., 1997). It promotes shedding of keratinocytes and decreases colonisation with *Propionibacterium acnes* due to the decrease in sebum (Bershad, 2001). Isotretinoin often reduces lesion counts by ninety percent or more within three months. These results are prolonged - a single twenty-week course produces significant improvement for three years or longer in about eighty percent of patients (White et al., 1998).

The usual dose range of isotretinoin is 0.5-2.0 milligrams per kilogram of body weight per day (Bershad, 2001). Doses as low as 0.1 milligram per kilogram of body weight per day are effective, but have relapse rates of about fifty percent (Jones et al., 1983). Researchers have observed that the cumulative dose over the twenty-week period is more important than the daily dose in ensuring success. Guidelines recommend a cumulative dose of one hundred and twenty milligrams per kilogram of body weight over a single twenty-week course of therapy (Bershad, 2001).

Adverse effects are reported in nearly one hundred percent of isotretinoin users (Bershad, 2001). Patients should be evaluated every four weeks during treatment for side effects and to ensure compliance (Orfanos and Zouboulis, 1998). These effects subside one to three weeks after therapy is stopped. Dryness of the skin and mucous membranes and chapped lips (retinoid chelitis) are universal at therapeutic doses. Eczematous patches
(retinoid dermatitis) occur commonly, especially on the dorsum of the hands and forearms. These side effects are managed with moisturisers, greasy topical corticosteroids and dosage adjustments, if necessary. Skin fragility and susceptibility to sunburn are frequently reported. Dry eyes, nosebleeds, shedding of hair, arthralgias and myalgias are also common (Bershad, 2001). Patients may complain of fatigue or mood changes or even depression. There have also been reports of patients committing suicide while on isotretinoin (Johnson and Nunley, 2000).

A rare side effect of isotretinoin is the onset of acne fulminans, a severe and painful exacerbation of cystic acne with exuberant granulation tissue and scarring (Tan et al., 1997). Acne fulminans can be managed by temporarily decreasing the isotretinoin dose and using a short course of systemic corticosteroids (Allison et al., 1997).

The use of the antibiotic tetracycline and its derivatives and vitamin preparations containing vitamin A should be avoided during isotretinoin therapy. These medications may increase the risk of pseudomotor cerebri (Goulden et al., 1996).

Other less common to rare side effects include hair loss, urticaria, erythema nodosum, tendinitis, paronychia, reversible myopathy, oesophagitis, renal impairment, dysphonia, exacerbation of asthma due to drying of mucous membranes, spontaneous bruising, vasculitis and loss of taste (Bigby and Stern, 1988).

The FDA ranks isotretinoin fourth, fifth and tenth with regard to the number of reports which link this drug to depression, serious depression and suicide attempts respectively. It is also the only non-psychotropic medicine which is ranked among the top ten drugs with relation to suicide attempts. The manufacturer of Accutane / Roaccutane changed the product warnings in 1998 to include that isotretinoin may cause depression, psychosis and rarely suicide ideation, suicide attempts and suicide (Hong Ng and Schweitzer, 2003).
The most important systemic effects of isotretinoin are its teratogenicity and its effect on serum lipids (Bershad, 2001). Major foetal malformations may occur in up to thirty percent of foetuses exposed to tretinoin. The most common developmental defects involve the structures of the craniofacial, cardiac, thymic and central nervous systems (Lammer, 1985). Two negative pregnancy tests are required before initiating isotretinoin treatment, and monthly pregnancy testing is mandatory for sexually active females during treatment. Patients may also not donate blood during isotretinoin therapy (Bershad, 2001). Changes in serum lipid and lipoprotein are common, especially elevation of triglycerides (Bershad et al., 1985). Isotretinoin may also cause hepatotoxicity, with about fifteen percent of individuals in clinical trials experiencing mild to moderate elevations in liver enzyme levels. All patients need a baseline fasting triglyceride and at least one liver enzyme test (White, 1999). Mean triglycerides increase by about fifty percent and cholesterol by about fifteen percent within two to three months on isotretinoin. Overweight patients have an increased risk of developing isotretinoin-induced hypertriglyceridaemia. Fasting triglyceride and cholesterol levels should be performed at baseline and at two to four week intervals during treatment (Orfanos et al., 1997). Homocysteine, a sulphur-containing amino acid, is metabolised in the liver requiring folate, vitamin B6 and B12, and the activity of the enzyme cystathionine-β-synthase. Homocysteine levels were significantly increased in a group of patients after forty-five days of isotretinoin therapy (Schulpis et al., 2001). This can be easily reversed with a relatively low daily dose of vitamins (Ubbink, et al., 1981). Increased homocysteine levels are an independent risk factor for the onset of coronary artery disease (Pancharutini et al., 1994).

Isotretinoin has been linked to the premature closure of the epiphyses of long bones in laboratory animals (Newton et al., 1997). It is therefore best to reserve its use for patients past their growth spurt. The level of adolescent bone growth can be assessed with a baseline serum alkaline phosphatase level (Bershad, 2001).

Some degree of acne relapse occurs in perhaps as many as sixty percent of patients within three years (White et al., 1998). Patients at risk for recurrence are adolescents under
eighteen years of age, women with hormonal acne (Leyden, 1997) and patients whose cumulative dose is less than one hundred milligrams per kilogram of body weight (White et al., 1998). These relapses are usually minor and can be managed with conservative topical therapy. About twenty percent of patients have acne relapses that are severe enough to warrant a second course of isotretinoin. This second course may only be started after a drug-free interval of at least eight weeks (Bershad, 2001).

It is much easier to prevent scars than to fix them (White, 1999). Many approaches are available, including excision, resurfacing with pulsed carbon dioxide laser (Alster et al. 1996) and intradermal collagen injections (White, 1999). Scar revision should be reserved for patients with severe scarring, whose acne is well controlled. Revision of scars should also be delayed for at least one year, allowing the scars to evolve to their final appearance (Usatine and Quan, 2000).

2.3 Homoeopathy

Homoeopathy is widely used throughout the world (D’Huyvetter and Cohrssen, 2002) and about one billion dollars is spent on homoeopathic medications every year (Jonas and Jacobs, 1996). It is estimated that in 1997, nearly two and a half million patients in the United States of America used complimentary alternative medicine modalities (D’Huyvetter and Cohrssen, 2002). In Europe between thirty and fifty percent of patients are using complimentary medicine modalities, of which approximately three and a half percent is using homoeopathy (Eisenberg et al. 1998). More than ten thousand French and German physicians practice homoeopathy (Vickers and Zollman, 1999). About thirty percent of referrals made to homoeopathic hospitals in the United Kingdom come directly from oncologists (Thompson and Kassab, 2000).

Physicians use homoeopathy for the treatment of several disease conditions, such as acute pain, coryza, asthma (D’Huyvetter and Cohrssen, 2002), hay fever (Reilly et al., 1986), migraine (Straumsheim et al., 2000) and diarrhoea (Jacobs et al., 1994).
Homoeopathy dates back about 2400 years to Hippocrates (Widakowich, 2000). Hippocrates was the first physician to treat patients by means of similars or by means of contras. The medical profession followed the law of contras (Jouanny, 1994). Modern homoeopathy dates back to the 1800’s, when Samuel Hahnemann used the principle of similars in his practice of medicine (Eizayaga, 1991). Hahnemann studied the principle of similars and conducted experiments to prove the theory. He discovered that the theory was valid, but only when infinitesimal doses were used. Hahnemann then created the law of similars (Jouanny, 1994), which is the guiding principle of homoeopathy (D’Huyvetter and Cohrssen, 2002).

The law of similars, *Similia Similibus Curentur* or like cures like (Hughes, 1991), states that any substance that produces symptoms in a healthy person will cure those same symptoms when they appear in a sick person. It is also necessary to consider the totality of symptoms when prescribing a homoeopathic remedy. The mental, emotional and physical symptoms of the patient must be matched to the remedy (D’Huyvetter and Cohrssen, 2002).

Homoeopathic remedies are prepared using the process of potentisation. Potentisation is a combination of ultra-dilution of a substance (even beyond Avogadro’s number) and succussion (vigorous shaking of the substance). Hahnemann started the process of potentisation after observing that it increased the therapeutic effectiveness of the remedies (D’Huyvetter and Cohrssen, 2002 and Resch and Gutmann, 1987). In modern homoeopathy, substances are generally diluted in the centissimal (C or 1:100) or decimal (D or X, or 1:10) potencies (D’Huyvetter and Cohrssen, 2002).

Based on the decimal system, the procedure of dilution consists of mixing one part of the original, undiluted medicine with nine parts of the solvent, so that the drug is reduced to one tenth of its original concentration. The result of this first step of dilution is called D1. The diluted remedy must then be succussed to enhance the energy and reactivity of the remedy (Resch and Gutmann, 1987). Mixing one part of the D1 dilution with nine parts of solvent, followed by succussion makes the next dilution, called D2. This process is
repeated as many times as needed to get to the required potency (D’Huyvetter and Cohrsen, 2002).

Patients may experience a homoeopathic aggravation after taking a homoeopathic remedy. This involves an initial worsening of the patients’ clinical symptoms. The symptoms that are aggravated are usually the symptoms that the patient complains of during the consultation. In a recent trial it was found that patients who reported an initial aggravation were the ones who had the best outcome after treatment (Eizayaga, 1991 and Taylor et al., 2000).

There are two basic types of homoeopathic prescribing. The first type is acute prescribing, which is short acting and treats a single symptom or condition. The second type is constitutional prescribing, which treats the patient in totality and considers mental, emotional and physical manifestations of the condition in order to bring about long-term changes in the individual (D’Huyvetter and Cohrsen, 2002).

Homoeopathic treatment of acne usually includes symptomatic and constitutional remedies, and should include a remedy that acts on the emotional plane (Jouanny et al., 1994). Most patients who seek homoeopathic treatment are already using some form of allopathic treatment. It is important that new patients understand the law of cure - the importance of detoxification through the skin, which could result in the worsening of the acne before it starts to improve (Morrison, 1998).

2.3.1 Homotoxicology:

*Testis compositum*, the medication used in this study, is prepared in accordance with the principles of homotoxicology. Homotoxicological therapy aims to stimulate and regulate the body’s self-healing power. Homotoxins are substances that are poisonous to humans, including metabolic products that are not broken down and eliminated quickly enough (Reckeweg, 1991).
Illnesses are agent-determined reactive processes in which homotoxins can bring about inflammation. During the course of a disease these toxins are then rendered harmless and eliminated by the body. Illnesses are symptoms and processes that show that the body is fighting these toxins with the intention of making them harmless and then eliminating them (Reckeweg, 1991).

This view of the concept of disease leads to a corresponding change in the methods of treating disease. Treatment should introduce the absolute minimum of noxious side effects into the body, since the body is already damaged, but at the same time it should also achieve optimum healing or alleviation of the symptoms. Therapies such as corrective surgery, chemotherapy or radiotherapy may be employed depending on the state of the disease, and after careful consideration of the patient as a whole being. Inhibiting or suppressing an illness will prevent the body from eliminating homotoxins in a physiological way (Reckeweg, 1991).

In the body’s fight against homotoxins, there are six separate antitoxic defence phases of disease. Phases one to three are known as the "humoral phases" and the phases four to six as the "cellular phases" (Reckeweg, 1991).

The humoral phases include:

- The excretion phase
- The reaction phase
- The deposition phase

During the humoral phases, the body can deal with detoxified toxins through elimination or deposition. There is no damage to cells or organs. Excretion is adequate, enzymes remain in tact and the body can continue to heal itself. The humoral phases are separated from the cellular phases by the "biological section" (Reckeweg, 1991).

The cellular phases include:

- The cellular impregnation phase
• The degeneration phase
• The neoplasm phase with neoplastic change or proliferation

During the cellular phases, the body succumbs increasingly to the destructive action of homotoxins. Enzymatic damage occurs and the body’s equilibrium is upset. There is a tendency towards deterioration and recovery becomes impossible (Reckeweg, 1991).

The body’s counter measure to homotoxins is called the "greater defensive system". This system consists of five parts that are linked and render homotoxins harmless. If the “greater defensive system” is affected by drugs, such as antibiotics, the immediate effects may be beneficial, but it may lead to the continued progression of the disease and the deterioration of the patient’s condition. This is called "progressive vicariation". However, if the greater defensive system can be stimulated, the progress of the disease can be reversed, with a change of phase in the direction of recovery. This is called "regressive vicariation" (Reckeweg, 1991).

When treating patients with antihomotoxic therapy, single or combination homoeopathic remedies can be used. All of these remedies are prepared according to homoeopathic principles and include preparations from plants, organs and tissues, nosodes, trace elements, potentised allopathic drugs, and attenuations of toxins and chemical compounds of all kinds. Great care should be taken to administer remedies in the correct potency in order to prevent reinforcing the body’s toxic state and to avoid exerting a negative influence on the body (Reckeweg, 1991).

2.3.2 Testis compositum:

*Testis compositum* is a complex preparation, developed to be highly effective, yet low in side effects. It is a combination of various single homoeopathic remedies, potentised allopathic medicines, suis organ preparations and a catalyst. Through the combination of these constituents, a broad and in-depth therapeutic effect is achieved, providing great promise in the treatment of various chronic diseases, including acne (-Heel, 2000).
There are sixteen single homoeopathic remedies in *Testis compositum*:

1. *Selenium metallicum* (D10) for oily skin, comedones and acne
2. *Lycopodium clavatum* (D28) for acne, pustules on the face, large clusters of pimples on the back and the neck, and many disorders of the male urogenital system
3. *Conium maculatum* (D28) for itching pimples and acne on the face
4. *Ferrum phosphoricum* (D10) for inflammatory symptoms, acne and erysipelas as well as frequent mood changes
5. *Zincum metallicum* (D10) for red eruptions on the chin, small pimpl es between the scapulae and testicular atrophy
6. *Phosphorus* (D8) for small boils on the neck and chest and wounds that keep on reappearing
7. *Curare* (D8) for dirty looking skin with boils and tubercles on the nose and scrofulous eruptions behind the ears and on the face
8. *Caladium seguinum* (D6) has a marked action on the genital organs and treats rough, dry skin with white, suppurating pimpl es
9. *Cantharis* (D8) targets the sexual organs, and is indicated for severe, destructive inflammation
10. *Agnus castus* (D6) for sexual weakness and mental depression
11. *Damiana* (*Turnera aphrodisiaca*) (D8) for impotence and neurasthenia
12. *Panax ginseng* (D4) for pimples on the neck and chest, to stimulate secretory glands, and for exhaustion
13. *Kalium picrinicum* (D6) for severe exhaustion where the patient cannot rouse himself to even slight mental or physical achievement
14. *Strychnium phosphoricum* (D6) for exhaustion
15. *Magnesium phosphoricum* (D10) for exhaustion

*Testis compositum* contains five suis organ preparations:

1. *Testis suis* (D4) is prepared from animal testicles and used for male impotence and sterility, spermatic cord neuralgia and exhaustion
2. *Embryo suis* (D8) is used for revitalisation
3. *Diencephalon suis* (D10) regulates most of the autonomic nervous system
4. *Cor suis* (D8) is indicated for a variety of cardiovascular disorders, including hypertension and angina pectoris
5. *Glandula suprarenalis suis* (D13) is indicated for adrenal insufficiency and exhaustion (Reckeweg, 1991).

*Testis compositum* contains *Acidum ascorbicum* and *Cortisonum aceticum*:
1. *Acidum ascorbicum* (D6) is potentised vitamin C. It acts as a co-factor for enzyme functions
2. *Cortisonum aceticum* (D13) is a potentised allopathic compound prepared from cortisone-21-acetate. It is indicated for damage and impaired function of the adrenal cortex, pituitary gland and connective tissue (-Heel, 2000 and Reckeweg, 1991).

*Testis compositum* is prepared as an injection solution in 2.2 millilitre ampoules that can be administered subcutaneously, one to three times per week. The remedies are all present in equal parts (-Heel, 2000).

Research has shown that remedies for skin conditions, such as *Testis compositum*, works best when it is administered by subcutaneous injection into the Large Intestine 11 (LI. 11) acupuncture point. This point is located at the lateral end of the transverse crease when the elbow is flexed to a right angle. This point is a homoeostatic and immune enhancing point. Large Intestine 11 is often used for the treatment of allergic and infectious disorders, skin disorders, endocrine disturbances and depression (Stux and Pomeranz, 1998). This acupuncture point is a specialised point for skin disease (MacPherson and Kaptchuk, 1997) and is used, together with other points, to treat acne vulgaris of the face and back (Stux and Pomeranz, 1998).
2.3.3 Natural Approach to Treating Acne Vulgaris:

When treating acne vulgaris, good diet, nutritional supplements and herbal treatments may contribute to the treatment and the general health of the patient.

2.3.3.1 Diet

High protein diets are beneficial to acne sufferers. About forty four percent of daily dietary intakes should consist of protein, thirty five percent carbohydrates and twenty one percent fats. Concentrated or refined carbohydrates should be eliminated from the diet. Trans-fatty acids and foods with high fat content should be avoided. Foods high in iodine (found in cough mixtures, kelp and salt) and milk should be limited. Acne patients have impaired glucose tolerance. High chromium yeast supplements improve glucose tolerance and may improve acne (Pizzorno et al., 2002 and Lockie and Geddes, 1995).

2.3.3.2 Nutritional Supplements

Vitamin A (retinol) reduces the production of sebum and hyperkeratinisation of sebaceous follicles. One of the symptoms of a vitamin A deficiency is rough, dry, scaly or blemished skin. One hundred thousand International Units (100 000 IU) must be taken four times per day for three months (Pizzorno et al., 2002 and Scott and Scott, 1998).

Zinc is an antioxidant and essential to normal skin functioning. It is involved in the production of local hormones, wound healing, tissue regeneration and immune function. Symptoms of a zinc deficiency include infertility, slow growth and delayed sexual maturity, hair loss, dandruff, white spots on nails, frequent infections, slow wound healing, skin problems, and behavioural and psychiatric problems. Serum zinc levels are lower in thirteen to fourteen year old males than in any other male age group. Between fifteen and fifty milligrams (15-50 mg) of zinc picolinate or zinc monomethionine must be taken four times per day for at least twelve weeks to show good results (Pizzorno et al., 2002 and Scott and Scott, 1998).
Vitamin E is a fat-soluble antioxidant and regulates retinol levels in humans. Male acne patients have decreased levels of glutathione peroxidase in their red blood cells. These levels normalise with the administration of vitamin E and selenium. Selenium acts as an anti-oxidant and should always be taken in conjunction with vitamin E. Patients should take one hundred International Units (100 IU) of vitamin E and fifty micrograms (50 mcg) of selenium, four times per day (Pizzorno et al., 2002 and Scott and Scott, 1998).

Additional supplements include ten milligrams of betacarotene, two hundred milligrams of vitamin C (twice a day) and a vitamin B complex (once a day).

The guiding symptoms of a vitamin C deficiency are depression, red pimples, easy bleeding and bruising, slow wound healing and frequent infections (Pizzorno et al., 2002 and Scott and Scott, 1998).

Deficiency symptoms for the vitamin B group include fatigue, depression, personality changes, red greasy skin with scaly patches (combination skin) and cracks at the corners of the mouth. Pantothenic acid (vitamin B5) is involved in the synthesis of cholesterol and steroids. At high doses (ten grams four times per day in divided doses for one to two weeks) it induces the regression of lesion without any side effects (Pizzorno et al., 2002 and Scott and Scott, 1998).

2.3.3.3 Herbal Treatments

Many plants are used all over the world to treat bacterial infections (Martin and Ernst, 2003). Topical treatments are used to reduce bacteria and inflammation (Pizzorno et al., 2002).

Natural topical applications include tea tree oil (Melaleuca alterniflora) in a five to fifteen percent preparation or daily cleansing with soap containing calendula (Pizzorno et al., 2002). Calendula (Calendula officinalis) has healing and antimicrobial properties. It can be used for cuts, grazes, infected sores, fungal infections, dry skin or inflammatory
skin conditions. Tea tree oil has antibacterial, antifungal, antiviral and decongestant properties. It is indicated for use in bronchitis and sinusitis, acne, ringworm, dandruff, cold sores, wounds, cuts and insect bites and stings (Scott and Scott, 1998). Bassett et al. (1990) compared the use of five percent tea tree oil gel with five percent benzoyl peroxide lotion for the treatment of mild to moderate acne. Both treatments were effective in reducing the number of lesions. The tea tree oil had a slower onset of action, but also produced significantly less skin irritation (Bassett et al., 1990). Orafidiya et al. (2002) compared a range of concentrations of bushy basil (Ocimum gratissimum) oil with ten percent benzoyl peroxide and a placebo on acne lesions. At a concentration of two to five percent, the Ocimum gratissimum oil was significantly more effective in reducing acne lesions than benzoyl peroxide (Orafidiya et al., 2002).
CHAPTER THREE

METHODOLOGY

3.1 Materials:

See Appendix B.

3.1.1 *Testis compositum:*

–Heel (Germany) supplied the *Testis compositum* used in this trial. Mister Surge supplied the alcohol swabs, needles, syringes and rubber gloves.

3.2 Methods:

3.2.1 Sampling of Participants:

A randomised sample of thirty male participants, with a history of acne vulgaris, predominantly of the face, was recruited for this study. All participants were volunteers recruited via advertising posters and pamphlets posted and distributed, with the necessary permission, at various healthcare facilities such as the Technikon Witwatersrand, the University of the Witwatersrand Medical School, doctors’ rooms, Helen Joseph Hospital, Hillbrow Hospital, health stores and high schools.

Inclusion criteria required participants to have mild to moderate acne vulgaris of the face. This is defined as:

- Ten to two hundred comedones (open and closed) and / or
- Ten to sixty inflammatory lesions (papules and pustules) and / or
- Fewer than three nodulocystic lesions (Bershad *et al.*, 2002).
Once the study had been explained, participants and parents/legal guardians of those younger than eighteen years completed consent forms (Appendix D). Each participant also completed a patient information form outlining personal data (Appendix C).

3.2.2 Procedure:

Due to the possible psychological impact of acne vulgaris on participants, all participants formed part of the control and experimental groups during the course of the study.

Participants were assessed on the first day of the control period. This period lasted fourteen days. Participants were assessed again on the day that treatment was initiated, and again after two, four and six weeks of treatment. Frontal and bilateral facial photographs (Appendix A) were taken at the first, second and final assessments (Bershad et al., 2002).

At each visit, the efficacy of the treatment was assessed in three ways (Appendix E):

1. Facial lesion counts were performed of individual acne lesions, divided into non-inflammatory lesions (comedones), inflammatory lesions (papules and pustules) and nodulocystic lesions (bigger than four millimetres). Good light, palpitation and inspection were required for assessments (Champion et al., 1992).

2. Response to treatment was assessed by comparing each participants’ condition with their baseline photographs. The response was graded from zero to six as follows:
   - 0 – completely cleared
   - 1 – ninety percent improved
   - 2 – seventy five percent improved
   - 3 – fifty percent improved
   - 4 – twenty five percent improved
   - 5 – no change
   - 6 – exacerbation (Bershad et al., 2002).
3. Facial skin signs and symptoms, including peeling, dryness or oiliness, redness (erythema), burning and itching (pruritus), were assessed by interviewing and physical examination. Participants were asked to report the occurrence and severity of these signs and symptoms, even if these have resolved by the time of the visit. Signs and symptoms were graded from zero to five as follows:

- 0 – none
- 1 – very mild (localised, awareness without discomfort)
- 2 – mild (diffuse, occasional discomfort)
- 3 – moderate (diffuse, constant discomfort)
- 4 – severe (dense, constant discomfort, may interfere with normal activities)
- 5 – extreme (prominent, dense, constant discomfort, often interferes with normal activities) (Bershad et al., 2002).

Injections were performed by the researcher under supervision of the research supervisor. During the control period, saline solution (placebo) was injected twice per week, subcutaneously into the Large Intestine 11-acupuncture point. Testis compositum solution was administered twice a week, for six weeks, as a subcutaneous injection into the Large Intestine 11 (LI. 11) acupuncture point (-Heel, 2000).

3.2.3 Data Collection and Analysis:

All data from all the assessments (Appendix F) was statistically analysed. The data were categorical in nature and statistical techniques for analysing such data sets were used, e.g. Wilcoxon tests, one-sample t-tests and paired sample t-tests. Numbers were analysed using ANOVA (Analysis of Variance) techniques to determine whether there has been an improvement in the condition. Improvement in the appearance of facial acne vulgaris of each participant, compared with baseline photographs, was assessed. Treatment success was based on achievement of a response to treatment score of zero to three, with three showing a fifty percent improvement and zero showing a one hundred percent improvement in the severity of the signs and symptoms of acne vulgaris (Bershad et al., 2002).
CHAPTER FOUR

RESULTS

4.1 Statistics Utilised:

The total number of participants in the study was twenty eight. All twenty eight participants were in the control group that received saline injections for two weeks, and then in the experimental group for six weeks. During the experimental period they received *Testis compositum* injections.

All the results from the study were statistically analysed by making use of the Wilcoxon test, the one-sample t-test and the paired-samples t-test.

The Wilcoxon test is a nonparametric procedure used with two related variables. It tests the hypothesis that the two variables have the same distribution, but makes no assumptions about the shapes of the distributions of the two variables. This test takes information about the magnitude of differences within pairs into account, and gives more weight to pairs that show large differences than to pairs that show small differences. The Wilcoxon test statistic is based on the ranks of the absolute values of the differences between the two variables.

The one-sample t-test procedure tests whether the mean of a single variable differs from a specified constant. In this study the specified constant is zero. The paired-samples t-test compares the means of two variables for a single group. It calculates the differences between values of the two variables for each case and tests whether the average differs from zero.

Two different analyses were used:

- The first used values directly from the readings and working with them as such
- The second analyses involved calculating the percentages and working with them
Percentage changes were calculated as \((\text{old} - \text{new}) / \text{old}\). This ensured that an improvement in the participant’s condition would show a positive percentage. By using these two methods a middle point can be attained.

4.2 Testing of the Hypothesis:

The null hypothesis stated that the mean of the trial group for the control period equals the mean of the trial group for the experimental period.

The alternative hypothesis states that the mean for the trial group for the control period does not equal to the mean for the trial group for the experimental period.

4.2.1 The p-value:

The null hypothesis would be rejected if the p-value was less than 0.05. If the p-value was equal to or greater than 0.05 the null hypothesis would be accepted.

4.3 Statistical Results:

Because the experimental group was relatively small, the individual lesion counts were added together to create workable numbers (Appendix G). The different types of lesion were numbered as follows (Appendix F):

- A: Non-inflammatory lesions
- B: Inflammatory lesions
- C: Nodulocystic lesions

The different assessments were numbered as follows (Appendix F):

- 1: First assessment at the start of the control period
- 2: Assessment at the end of the control period and the start of the experimental period (after 2 weeks)
- 3: Assessment after 4 weeks
• 4: Assessment after 6 weeks
• 5: Final assessment at the end of the trial

For the nodulocystic group the function \( Y = X + 1 \) was created to make the readings more accurate. This means that instead of using zero as the base, the base was one.
TABLE 4.1: T-TEST FOR DEPENDANT SAMPLES (NON-INFLAMMATORY LESIONS)

<table>
<thead>
<tr>
<th></th>
<th>Mean</th>
<th>Std.Dv.</th>
<th>N</th>
<th>Diff.</th>
<th>Std.Dv. Diff.</th>
<th>t</th>
<th>df</th>
<th>p</th>
</tr>
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<tbody>
<tr>
<td>1a: ASSESMENT 1</td>
<td>14.0000</td>
<td>17.5161</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2a: ASSESMENT 2</td>
<td>15.2500</td>
<td>18.1590</td>
<td>28</td>
<td>-1.2500</td>
<td>4.1777</td>
<td>-1.58</td>
<td>27</td>
<td>0.125013</td>
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<tr>
<td>3a: ASSESMENT 3</td>
<td>14.9643</td>
<td>19.4880</td>
<td>28</td>
<td>0.2857</td>
<td>6.0115</td>
<td>0.251</td>
<td>27</td>
<td>0.803335</td>
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<tr>
<td>4a: ASSESMENT 4</td>
<td>8.0714</td>
<td>14.3318</td>
<td>28</td>
<td>7.1786</td>
<td>9.9109</td>
<td>3.832</td>
<td>27</td>
<td>0.000688</td>
</tr>
<tr>
<td>5a: ASSESMENT 5</td>
<td>3.5714</td>
<td>7.2949</td>
<td>28</td>
<td>11.6785</td>
<td>12.8035</td>
<td>4.826</td>
<td>27</td>
<td>0.000049</td>
</tr>
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</table>

The first row in table 4.1 shows the difference between the number of lesions from the baseline count at the start of the control period, and then two weeks later at the end of the control period. The second, third and fourth rows compare the number of lesions at the start of the experimental period with the number of lesions after two, four and six weeks of treatment respectively.

Table 4.1 shows the results of the t-test for non-inflammatory lesions, using the values directly from the readings and using them as such. The table also indicates the changes in the mean that occurred from the beginning of the study. The standard deviation indicates
the difference between the patients with the smallest and largest number of lesions. During the experimental period and the first two weeks of treatment, the p-value is greater than 0.05, indicating little change during this period. The p-value for the last four weeks of treatment is less than 0.05, indicating a significant improvement during this period.
### TABLE 4.2: T-TEST FOR DEPENDANT SAMPLES USING PERCENTAGE VALUES (NON-INFLAMMATORY LESIONS)

<table>
<thead>
<tr>
<th></th>
<th>Mean</th>
<th>Std.Dv.</th>
<th>N</th>
<th>Diff.</th>
<th>Std.Dv. Diff.</th>
<th>t</th>
<th>df</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>1a vs 2a</td>
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<td>61.98515</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>2a vs 3a</td>
<td>5.9179</td>
<td>43.58090</td>
<td>28</td>
<td>-23.4271</td>
<td>82.31598</td>
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<td>1a vs 2a</td>
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<tr>
<td>3a vs 4a</td>
<td>42.3382</td>
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<td>4a vs 5a</td>
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<td>35.64605</td>
<td>28</td>
<td>-62.5461</td>
<td>60.00464</td>
<td>-5.51562</td>
<td>27</td>
<td>0.000008</td>
</tr>
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</table>

Table 4.2 indicates the percentage values for the non-inflammatory lesions. These values show the same trends as the direct values taken from the research results.
**TABLE 4.3: T-TEST FOR DEPENDANT SAMPLES (INFLAMMATORY LESIONS)**

Marked differences are significant at $p < .05000$

<table>
<thead>
<tr>
<th></th>
<th>Mean</th>
<th>Std.Dv.</th>
<th>N</th>
<th>Diff.</th>
<th>Std.Dv. Diff.</th>
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<td>23.92014</td>
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<td>5.560157</td>
<td>-2.65111</td>
<td>27</td>
<td>0.013258</td>
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<td>23.92014</td>
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</tr>
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<td>3b: ASSESMENT 3</td>
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<th>Mean</th>
<th>Std.Dv.</th>
<th>N</th>
<th>Diff.</th>
<th>Std.Dv. Diff.</th>
<th>t</th>
<th>df</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>2b: ASSESMENT 2</td>
<td>38.39286</td>
<td>23.92014</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4b: ASSESMENT 4</td>
<td>20.71429</td>
<td>13.33016</td>
<td>28</td>
<td>17.67857</td>
<td>13.74922</td>
<td>6.803747</td>
<td>27</td>
<td>0.000000</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>Mean</th>
<th>Std.Dv.</th>
<th>N</th>
<th>Diff.</th>
<th>Std.Dv. Diff.</th>
<th>t</th>
<th>df</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>2b: ASSESMENT 2</td>
<td>38.39286</td>
<td>23.92014</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5b: ASSESMENT 5</td>
<td>10.71429</td>
<td>8.23208</td>
<td>28</td>
<td>27.67857</td>
<td>18.19453</td>
<td>8.049739</td>
<td>27</td>
<td>0.000000</td>
</tr>
</tbody>
</table>

Table 4.3 shows the results of the t-test for inflammatory lesions, using the values directly from the readings and using them as such. The p-value for the control period (first row), as well as the experimental period, is less than 0.05, indicating a significant change. The inflammatory lesion counts increased during the control period, and then started to decrease after the first two weeks of treatment.
**TABLE 4.4: T-TEST FOR DEPENDANT SAMPLES USING PERCENTAGE VALUES (INFLAMMATORY LESIONS)**

<table>
<thead>
<tr>
<th></th>
<th>Mean</th>
<th>Std.Dv.</th>
<th>N</th>
<th>Diff.</th>
<th>Std.Dv. Diff.</th>
<th>t</th>
<th>df</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>1b vs 2b</td>
<td>-20.0736</td>
<td>40.10332</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2b vs 3b</td>
<td>10.3929</td>
<td>25.61700</td>
<td>28</td>
<td>-30.4664</td>
<td>55.88250</td>
<td>-2.88486</td>
<td>27</td>
<td>0.007605</td>
</tr>
<tr>
<td>1b vs 2b</td>
<td>-20.0736</td>
<td>40.10332</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3b vs 4b</td>
<td>35.0332</td>
<td>21.44081</td>
<td>28</td>
<td>-55.1068</td>
<td>41.22223</td>
<td>-7.07380</td>
<td>27</td>
<td>0.000000</td>
</tr>
<tr>
<td>1b vs 2b</td>
<td>-20.0736</td>
<td>40.10332</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4b vs 5b</td>
<td>48.9457</td>
<td>21.96108</td>
<td>28</td>
<td>-69.0193</td>
<td>50.63904</td>
<td>-7.21214</td>
<td>27</td>
<td>0.000000</td>
</tr>
</tbody>
</table>

Table 4.4 shows the percentage values for the inflammatory lesions. This confirms the trends seen in the direct values for the inflammatory lesions used in Table 4.3. The p-value for the entire research period, including the control period (first row) is less than 0.05, indicating a significant change.
Table 4.5 shows the results of the t-test for nodulocystic lesions, using the values directly from the readings and using them as such. The p-value for the control period (first row) is greater than 0.05, indicating that no significant changes took place during this period. The p-values for the experimental period (second to fourth row) indicate a significant improvement.
Table 4.6 shows the percentage values for the nodulocystic lesions. The p-value for the control period (first row) is greater than 0.05, indicating that no significant changes took place during this period. The p-values for the experimental period (second to fourth row) indicate a significant improvement.
Figure 4.1 shows the results for each individual participant for non-inflammatory lesions as well as the general trend for the group (thick brown line). Although some of the participants showed an aggravation at the start of the experimental period, all twenty-eight participants showed an improvement at the end of the experimental period.
Figure 4.2 summarises the results for the inflammatory lesions per individual participant and the general trend for the group. The group in general showed an aggravation during the control period, but improved dramatically at the end of the experimental period.
Figure 4.3 shows the trend and individual results for the nodulocystic lesions. Although only ten participants had nodulocystic lesions at the start of the trial, it is still clear that these lesions showed a marked reduction in numbers at the end of the trial.
**Table 4.7: One-Sample T-Test**

<table>
<thead>
<tr>
<th></th>
<th>Mean</th>
<th>Std.Dv.</th>
<th>N</th>
<th>Reference Constant</th>
<th>t-value</th>
<th>df</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>1a vs 2a: % Difference Between 1a and 2a</td>
<td>-17.5093</td>
<td>61.98515</td>
<td>28</td>
<td>0.00</td>
<td>-1.49472</td>
<td>27</td>
<td>0.146584</td>
</tr>
<tr>
<td>2a vs 3a: % Difference Between 2a and 3a</td>
<td>5.9179</td>
<td>43.58090</td>
<td>28</td>
<td>0.00</td>
<td>0.71853</td>
<td>27</td>
<td>0.478601</td>
</tr>
<tr>
<td>3a vs 4a: % Difference Between 3a and 4a</td>
<td>42.3382</td>
<td>32.07756</td>
<td>28</td>
<td>0.00</td>
<td>6.98410</td>
<td>27</td>
<td>0.000000</td>
</tr>
<tr>
<td>4a vs 5a: % Difference Between 4a and 5a</td>
<td>45.0368</td>
<td>35.64605</td>
<td>28</td>
<td>0.00</td>
<td>6.68552</td>
<td>27</td>
<td>0.000000</td>
</tr>
<tr>
<td>1b vs 2b: % Difference Between 1b and 2b</td>
<td>-20.0736</td>
<td>40.10332</td>
<td>28</td>
<td>0.00</td>
<td>-2.64864</td>
<td>27</td>
<td>0.013335</td>
</tr>
<tr>
<td>2b vs 3b: % Difference Between 2b and 3b</td>
<td>10.3929</td>
<td>25.61700</td>
<td>28</td>
<td>0.00</td>
<td>2.14677</td>
<td>27</td>
<td>0.040952</td>
</tr>
<tr>
<td>3b vs 4b: % Difference Between 3b and 4b</td>
<td>35.0332</td>
<td>21.44081</td>
<td>28</td>
<td>0.00</td>
<td>8.64605</td>
<td>27</td>
<td>0.000000</td>
</tr>
<tr>
<td>4b vs 5b: % Difference Between 4b and 5b</td>
<td>48.9457</td>
<td>21.96108</td>
<td>28</td>
<td>0.00</td>
<td>11.79343</td>
<td>27</td>
<td>0.000000</td>
</tr>
<tr>
<td>1c vs 2c: % Difference Between 1c and 2c</td>
<td>-16.9104</td>
<td>46.32766</td>
<td>28</td>
<td>0.00</td>
<td>-1.93149</td>
<td>27</td>
<td>0.063982</td>
</tr>
<tr>
<td>2c vs 3c: % Difference Between 2c and 3c</td>
<td>17.2218</td>
<td>23.07145</td>
<td>28</td>
<td>0.00</td>
<td>3.94987</td>
<td>27</td>
<td>0.000505</td>
</tr>
<tr>
<td>3c vs 4c: % Difference Between 3c and 4c</td>
<td>13.4661</td>
<td>33.14120</td>
<td>28</td>
<td>0.00</td>
<td>2.15007</td>
<td>27</td>
<td>0.040666</td>
</tr>
<tr>
<td>4c vs 5c: % Difference Between 4c and 5c</td>
<td>4.2857</td>
<td>13.45185</td>
<td>28</td>
<td>0.00</td>
<td>1.68585</td>
<td>27</td>
<td>0.103348</td>
</tr>
</tbody>
</table>

Table 4.7 compares the percentage values from one assessment period to the next. The non-inflammatory lesions (1A to 5A) showed significant improvement from the second week of treatment. The inflammatory lesions (1B to 5B) showed a significant change from the experimental period, while the nodulocystic lesions (1C to 5C) showed an improvement from the first week of treatment.

### 4.4 Descriptive Statistics:

Questionnaires (Appendix C) were completed at the start of the study to determine whether any of the participants have been diagnosed by a professional health practitioner as having acne vulgaris. Only six of the participants were previously diagnosed by a professional as having acne vulgaris, but all of them fitted the criteria to be included in the study. The majority of the participants used over-the-counter preparations such as creams and face wash before, with varying degrees of success. All the participants felt that having acne vulgaris had a negative impact on their self esteem and general daily activities.
4.5 **Box-and-Whisker Plots:**

The box-and-whisker plots are used to make visualisation of the data easier by representing the range of data received. Box-and-whisker plots allow for representation of where most of the numbers lie that apply to the study. It is a summary plot based on the median, quartiles and extreme values.

The median is represented by the small box inside the bigger box. The big box shows where the majority of the cases lie (25-75%). The borders of the big box are the upper quartile and the lower quartile.

The lower quartile is in the middle between the mean and the lower extreme. The lower extreme is the lowest possible number. The upper quartile is between the mean and the upper extreme. The upper extreme is the highest possible number. The numbers that lie outside the big box indicate cases that either significantly improved or worsened. The numbers above the big block are in the upper quartile. These numbers would normally be discarded to get a truer reflection of the trends, but because of the small number of participants in this study, they remained part of the research.
Figure 4.4 shows the results for the non-inflammatory lesions over the eight week period of the study. The median stays constant during the control period, and then starts declining, showing a decrease in the number of lesions and an improvement of the acne vulgaris. The bigger box (25%-75%) also becomes smaller, showing improvement in the group.
Figure 4.5 shows the results for the inflammatory lesions. It confirms that a degree of improvement has already occurred during the control period.
Figure 4.6 represents the results for the nodulocystic lesions during the trial. Because this was a relatively small number to work with, the improvement is not that clear when represented on the box-and-whisker plot.
CHAPTER FIVE

DISCUSSION

Acne vulgaris is a common skin condition, but it is becoming increasingly resistant to conventional treatment. Although it is a skin condition, it also has a marked effect on the overall health of the patient, including the mental status and social interactions of the individual. Finding alternative ways of treating and managing acne vulgaris is becoming vital. The homoeopathic remedy *Testis compositum* provides a valuable alternative to conventional treatments.

5.1 Questionnaires:

The questionnaires were completed to establish whether the participants had acne vulgaris (prediagnosed or other) and to assess the effects that the acne has on their daily activities. The previous or current use of medication or topical treatments was also assessed.

5.2 Control Period:

During the control period of two weeks at the beginning of the study, twenty-eight participants formed the control group. During this period they received saline injections only.

Although the non-inflammatory and nodulocystic lesions showed no significant change during the control period, the inflammatory lesions improved significantly. This could be due to the anti-inflammatory properties of the saline (sodium chloride) used during the control period (Budavari et al., 1989).

5.3 Experimental Period:

Twenty-eight participants formed the experimental group and received *Testis compositum* for a period of six weeks. In all cases the acne vulgaris improved significantly and every participant’s skin cleared up considerably.
5.4 Homoeopathy:

This study has proved that the homoeopathic complex remedy *Testis compositum* is effective in the treatment of acne vulgaris. This study also showed that an external disease such as acne vulgaris can be treated successfully with the correct internal homoeopathic treatment. In homoeopathy, it is believed that all diseases, even external skin disorders, originate from an internal disturbance and are cured by the internal administration of the correct remedy. For this reason homoeopathic medicines are usually given internally, and not as topical applications (Sankaran, 1996).

The results can be summarised as follows:

- The condition of the twenty-eight participants improved to some extent or cleared completely, without any exceptions.
- During the control period, ten participants improved on inflammatory lesions, but the majority of this group got worse or stayed the same.
- The participants that improved for inflammatory lesions during the control period represent only thirty six percent of the control group.
- The general trend for the group was that the inflammatory lesions showed no change or aggravated during the control period.
- During the control period, the non-inflammatory and nodulocystic lesions got worse or stayed the same, with the exception of two participants.

These results prove beyond any doubt that *Testis compositum* significantly inhibits the development of acne vulgaris and that it can effectively treat this disease.
CHAPTER SIX

CONCLUSION AND RECOMMENDATIONS

6.1 Conclusion:

This study has proved that homoeopathically prepared *Testis compositum* definitely has a positive and inhibitory effect in the treatment of acne vulgaris. All the participants benefited greatly from the treatment they received during the course of the study. The number of acne lesions decreased substantially or cleared up completely. Although the quality of the photographs was not consistent throughout the study period, they provide ample evidence that the appearance of the skin of the participants has generally improved. Participants themselves also reported enhanced self-confidence which led to better social interaction.

None of the participants reported any side effects, discomfort or irritation during the treatment period. This study has clearly established that *Testis compositum* is a safe, effective treatment for acne vulgaris. *Testis compositum* gives practitioners a new way to treat acne vulgaris, making it unnecessary to constantly revert to allopathic drugs and their associated side effects.

*Testis compositum* can therefore be recommended without hesitation as a gentle, yet very effective, treatment for acne vulgaris.

6.2 Recommendations:

This study proved that *Testis compositum* has a positive effect in the treatment of acne vulgaris. At the end of this study, the following recommendations have to be made:

- *Testis compositum* has not been tested for use in the treatment of acne vulgaris before. Attention should be given to promoting this additional application.
- Many potential participants did not take part in the study because of an aversion to injections.
- Participants also found it difficult to comply with the required frequency of injections for the full period of eight weeks.
Further studies could be conducted to determine the effect of *Testis compositum* when administered orally by the participants themselves. The frequency of the dosage may have to be increased for oral administration.

The use of photographs provides an efficient and easy way to determine the rate of improvement over the course of the trial. Although the participants showed marked improvement, it is not clear enough on the photographs. In any follow-up or similar studies, more attention should be given to adequate and consistent lighting and other aspects of taking high quality photographs, and thus also the accuracy of photographs as an assessment tool.

The treatment period of six weeks was too short to see the full effect of *Testis compositum*. When looking at other clinical trials for the treatment of acne vulgaris, the treatment period is seldom shorter than twelve weeks.
REFERENCES:


of the Efficacy and Safety of Adapalene gel 0.1% and Tretinoin gel 0.025% in the Treatment of Acne Vulgaris: A Multicentre Trial, *Journal of the American Journal of Dermatology*, 34: 482-485.


APPENDIX A: PHOTOGRAPHS:

A1: Patient number 22 – Left-sided view:

Patient number 22 at the beginning (above) and at the end (below) of the study
Patient number 22 at the beginning (above) and at the end (below) of the study.
A3: Patient Number 21 – Left-sided view:

Patient number 21 at the beginning (above) and at the end (below) of the study
A4: Patient number 21 – Right-sided view:

Patient number 21 at the beginning (above) and at the end (below) of the study
A5: Patient number 20 – Frontal view:

Patient number 20 at the beginning (above) and at the end (below) of the study.
A6: Patient number 20 – Left-sided view:

Patient number 20 at the beginning (above) and at the end (below) of the study
A7: Patient number 20 – Right-sided view:

Patient number 20 at the beginning (above) and at the end (below) of the study
A8: Patient number 18 – Frontal view:

Patient number 18 at the beginning (above) and at the end (below) of the study
A9: Patient number 13 – Left-sided view:

Patient number 13 at the beginning (above) and at the end (below) of the study
A10: Patient number 13 – Frontal view:

Patient number 13 at the beginning (above) and at the end (below) of the study.
A11: Patient number 15 – Frontal view:

Patient number 15 at the beginning (above) and at the end (below) of the study.
A12: Patient number 3 – Left-sided view:

Patient number 3 at the beginning (above) and at the end (below) of the study.
A13: Patient number 3 – Right-sided view:

Patient number 3 at the beginning (above) and at the end (below) of the study
A14: Patient number 7 – Frontal view:

Patient number 7 at the beginning (above) and at the end (below) of the study.
### APPENDIX B: MATERIALS USED:

<table>
<thead>
<tr>
<th>Item</th>
<th>Supplier</th>
</tr>
</thead>
<tbody>
<tr>
<td>Testis compositum ampoules</td>
<td>Heel, Germany</td>
</tr>
<tr>
<td>Saline ampoules</td>
<td>Heel, Germany</td>
</tr>
<tr>
<td>70% alcohol swabs</td>
<td>Mista Surge</td>
</tr>
<tr>
<td>26G X 1/2” needles</td>
<td>Mista Surge</td>
</tr>
<tr>
<td>5 ml syringes</td>
<td>Mista Surge</td>
</tr>
<tr>
<td>Surgical gloves</td>
<td>Mista Surge</td>
</tr>
</tbody>
</table>
APPENDIX C: QUESTIONNAIRE:

Do you suffer from facial acne?  Yes  No
Have you previously been diagnosed as having facial acne?  Yes  No

Does the acne have any effect on your daily activities? In which way does it affect you?

________________________________________________________________________________
________________________________________________________________________________
________________________________________________________________________________

Are you currently using any medication and / or ointment for the acne?  Yes  No
What medication and / or ointment are you using and for how long have you been using it?

________________________________________________________________________________
________________________________________________________________________________
________________________________________________________________________________

What effect has your current treatment had on the acne?

________________________________________________________________________________
________________________________________________________________________________
________________________________________________________________________________

What other medication and / or ointment have you tried previously? What was the effect?

________________________________________________________________________________
________________________________________________________________________________
________________________________________________________________________________
APPENDIX D: INFORMATION AND CONSENT FORM

The effect of *Testis compositum* in the treatment of acne vulgaris

Dear participant,

Acne is one of the most common conditions of our society, affecting almost one hundred percent of all males at some point in their lives, usually in their teens and twenties. Despite the advances and development of drugs and other treatments, the treatment of acne remains a big problem. The purpose of this study is to determine the effect of the complex remedy, *Testis compositum*, as a treatment for acne vulgaris.

You have been selected to participate in this study. The study will run over eight weeks. *Testis compositum* is a homoeopathic remedy. The *Testis compositum* will be injected twice a week for the duration of the study. The injections are given subcutaneously (just under the skin) at the elbow crease on the arm. At the start of the research period, and every two weeks thereafter, the acne will be assessed on different criteria. On three occasions, photographs will be taken and used for comparisons.

The potential benefit for those participating in the study is that this treatment may reduce or completely cure your acne. Irrespective of the outcome of this study, all participants will contribute to medical knowledge, resulting in greater efficacy in the therapeutic management of people who suffer from acne.

Participation in this study is voluntary. You are free to refuse to participate or to withdraw your consent and discontinue participation at any time. Such refusal or discontinuance will not affect your regular treatments or medical care in any way. A signed copy of this consent form will be made available to you.

_____________________________________________________________________

I have been fully informed about the procedures to be followed, including those that are investigational. I have been given a description of the attended discomforts, risks and benefits to be expected and the appropriate procedures. In signing this consent form I agree to this method of treatment and I understand that I am free to withdraw my consent and discontinue my participation in this study at any time. I understand that if I have any questions at any time, they will be answered.

Participant: ____________________________ Date:______________________

Parent / Guardian:_______________________ Date:______________________

I have fully explained the procedures to be followed, identifying those that are investigational, and have fully explained their purpose. I have asked if any questions have arisen regarding the procedures and have answered these questions to the best of my ability.

Researcher:____________________________ Date:______________________
### APPENDIX E: ASSESSMENT SHEET

Patient Name: ___________________________  Date: ______________________

#### 1. LESION COUNTS:

<table>
<thead>
<tr>
<th>Location</th>
<th>Non-inflammatory Lesions (comedones)</th>
<th>Inflammatory Lesions (papules and pustules)</th>
<th>Nodulocystic Lesions (&gt;4mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Left Cheek</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Right Cheek</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Forehead</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nose</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chin</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

#### 2. RESPONSE TO TREATMENT:

- 0 – completely cleared
- 1 – 90% improved
- 2 – 75% improved
- 3 – 50% improved
- 4 – 25% improved
- 5 – no change
- 6 – exacerbation

<table>
<thead>
<tr>
<th>Location</th>
<th>Left Cheek</th>
<th>Right Cheek</th>
<th>Forehead</th>
<th>Nose</th>
<th>Chin</th>
</tr>
</thead>
<tbody>
<tr>
<td>Participants’ Score</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

#### 3. SKIN SIGNS AND SYMPTOMS:

- 0 – none
- 1 – very mild (localised, awareness without discomfort)
- 2 – mild (diffuse, occasional discomfort)
- 3 – moderate (diffuse, constant discomfort)
- 4 – severe (dense, constant discomfort, may interfere with normal activities)
- 5 – extreme (prominent, dense, constant discomfort, often interferes with normal activities)

<table>
<thead>
<tr>
<th>Signs and Symptoms</th>
<th>Participants’ Score</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peeling</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dryness / Oiliness</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Redness (erythema)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Burning</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Itching (pruritis)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
APPENDIX F: SUMMARY OF LESION COUNTS DIVIDED INTO LESION TYPES

ASSESSMENT 1 (start of control period)

<table>
<thead>
<tr>
<th></th>
<th>1A</th>
<th>1B</th>
<th>1C</th>
</tr>
</thead>
<tbody>
<tr>
<td>1A</td>
<td>Non-inflammatory lesions (comedones)</td>
<td>Inflammatory lesions (papules and pustules)</td>
<td>Nodulocystic lesions (&gt;4mm)</td>
</tr>
<tr>
<td>TOTAL</td>
<td>392</td>
<td>997</td>
<td>41</td>
</tr>
</tbody>
</table>

ASSESSMENT 2 (start of experimental period)

<table>
<thead>
<tr>
<th></th>
<th>2A</th>
<th>2B</th>
<th>2C</th>
</tr>
</thead>
<tbody>
<tr>
<td>2A</td>
<td>Non-inflammatory lesions (comedones)</td>
<td>Inflammatory lesions (papules and pustules)</td>
<td>Nodulocystic lesions (&gt;4mm)</td>
</tr>
<tr>
<td>TOTAL</td>
<td>427</td>
<td>1075</td>
<td>48</td>
</tr>
</tbody>
</table>

ASSESSMENT 3

<table>
<thead>
<tr>
<th></th>
<th>3A</th>
<th>3B</th>
<th>3C</th>
</tr>
</thead>
<tbody>
<tr>
<td>3A</td>
<td>Non-inflammatory lesions (comedones)</td>
<td>Inflammatory lesions (papules and pustules)</td>
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ASSESSMENT 5 (end of treatment)

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### APPENDIX G: SUMMARY OF LESION COUNTS PER PARTICIPANT

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