The efficacy of R53 (Comedonin®) acne drops in the treatment of acne vulgaris

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by

Neeha Shard Jivan

(Student number: 802052470)

Supervisor:_____ Date:_____

Dr. R. Razlog

M. Tech Hom; BMDP (TWR)

Co-Supervisor:_____ Date:_____

Dr. M. Caminsky

M. Tech Hom (TWR)

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DECLARATION

I declare that this dissertation is my own, unaided work. It is being submitted for the Degree of Masters of Technology: Homoeopathy at the University of Johannesburg, Johannesburg. It has not been submitted previously to this or any other institution for the purpose of obtaining a degree or a Masters qualification.

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(Signature of candidate)

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ABSTRACT

Acne vulgaris is a dermatological condition, pathologically characterized by the inflammation of the sebaceous glands and hair follices and is most prominent among adolescents (Holmes, 2001). Symptoms include the formation of inflammatory and non-inflammatory lesions, which can lead to the formation of scars (Boon *et al*., 2006). These eruptions occur on the chest, face, back and arms (Martini *et al*., 2001). The aetiology of acne vulgaris is multifactorial and hence there are a large variety of treatment options which range from topical applications to systemic drug treatment (Docrat, 2008).

The homoeopathic complex remedy R53 (Comedonin) ® acne drops is a product which contains a combination of homoeopathic remedies that are used to treat the symptoms of acne vulgaris such as inflammatory and non inflammatory eruptions. The remedy R53 (Comedonin) ® is an over-the-counter remedy that is readily available and is indicated in the treatment of acne vulgaris (Dr.Reckeweg, 2010). No research has been conducted on its efficacy.

The aim of this study was to determine the efficacy of R53 (Comedonin) ® acne drops in the treatment of mild to moderate acne vulgaris that presents on the face, chest and / or back in males. The evaluation of symptoms was done by using scales and the Digermizer software to calculate the surface area of the affected areas.

This research study was a double blind placebo-control study that was conducted on thirty male participants between the age of fifteen to twenty years old with mild to moderate acne vulgaris on the face, back or chest. Participants who agreed to the procedure of the study were randomly divided into the treatment and placebo groups respectively. These groups consisted of fifteen participants each. The treatment group received the R53 (Comedonin) ® acne drops whereas the placebo group received the placebo drops.

This research was conducted over an eight week period at the University of Johannesburg Health Centre. All the participants were instructed to take ten drops of the medication three times a day. Evaluations were conducted at week zero, week four and week eight according to APPENDIX B. As part of the evaluation, photographs of the affected areas were taken at week zero and week eight, in order to attain the surface area affected before and after the treatment period (Appendix B).

The results acquired from this study were statistically analysed by Statcon at the University of Johannesburg by means of descriptive statistics and non-parametric tests, which included the

Wilcoxon Signed Rank Test and the Mann-Whitney U Test.

This research study has determined that the homoeopathic complex, R53 (Comedonin) ® acne drops, did not show a statistically significant improvement or effect in the treatment of the severity of the symptoms of mild to moderate acne vulgaris on the face and associated symptoms of peeling, oiliness and burning related to the skin.

However, the p-value (<0.016), regarding the lesions count scores of the non-inflammatory lesion and total lesions over the 8 week period overall, showed that there was a significant improvement in the severity of symptoms of mild to moderate acne vulgaris according to the Wilcoxon Signed Rank Test and Mann Whitney Test within the treatment group.

DEDICATION

I dedicate this dissertation to the founder acarya of ISKCON A.C. Bhaktivedanta swami Prabhupada, my spiritual master HH Bhakti Caitanya Swami, my loving parents, Shard and Prabha Jivan for all of their unconditional love, guidance, motivation and support as they remove the darkness of my ignorance with the light of true knowledge.

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God and His devotees	Sri Sri Radha Syamasundara and Sri Sri Nitai Gaura-Hari for all of their love, guidance, inspiration, tolerance and mercy.

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1. INTRODUCTION

Acne vulgaris is a condition that occurs mainly among the adolescent population and can be viewed as a normal variant of life (Docrat, 2008). This condition causes the occlusion of the pilosebaceous units forming comedones. These blocked follicles become infected and form characteristic pustules which may rupture and lead to the formation of scars (Boon *et al*., 2006).

Acne usually affects the face, chest, back and arms (Tan *et al*., 2008). Studies have found that males have a greater risk of developing acne than females as acne is dependent on circulating testosterone (White, 1998). Therapeutic options may range from topical applications to superficial chemical peels, although these medications can have numerous side effects (Docrat, 2008).

R53 (Comedonin ®) acne drops is a product which contains a combination of homoeopathic remedies that are used to treat symptoms of acne vulgaris such as pustules and comedones. As a Homoeopathic complex, over-the-counter remedy it is readily used for the treatment of acne vulgaris (Dr. Reckeweg, 2010). No research has been conducted on its efficacy.

1.1 Purpose of the study

The aim of this study is to determine the efficacy of R53 (Comedonin ®) acne drops in the treatment of mild to moderate acne vulgaris that presents on the face, chest and / or back in males. The evaluation of symptoms was done by using scales and the Digermizer software to calculate the surface area of the affected areas.

1.2 Hypothesis

It is hypothesised that the homoeopathic complex preparation R53 (Comedonin ®) acne drops will have a positive effect in the treatment of acne vulgaris when compared to the placebo group

1.3 Null Hypothesis

It is hypothesised that the homoeopathic complex preparation R53 (Comedonin ®) acne drops will have no effect in the treatment of acne vulgaris when compared to the placebo.

1.4 Assumptions

During the course of the study, the following assumption were presumed:

- All participants had good compliancy with administration of the treatments in both the active medication and placebo groups.

1.5 The need for the study

The results of the study will determine:

- The efficacy of R53 (Comedonin ®) acne drops on the amelioration of acne symptoms, in males suffering from acne vulgaris.
- The extent to which associated symptoms are ameliorated by R53 (Comedonin ®) acne drops.
- The effect of R53 (Comedonin ®) acne drops in reducing the size of the skin surface area affected.

2. LITERATURE REVIEW

2.1 Acne Vulgaris

Acne vulgaris is an inflammatory skin condition of the sebaceous glands and hair follicles (Holmes, 2001). It is an exceedingly common dermatological condition, which is seen by many primary health care practitioners and other complementary practitioners throughout the world (Docrat, 2008). It is estimated that 80% of the world's population is affected by acne at some point in their lives (Nakatsuji *et al*., 2009).

This condition generally develops at the age of puberty due to the increase in sensitivity of sebaceous glands and hair follicles to the changes in hormone concentrations (Martini *et al.*, 2001). Studies have shown that males are at a greater risk of developing acne than females (White, 1998).

The characteristic symptoms of acne vulgaris includes the formation of inflammatory and non-inflammatory lesions, which generally appear on the face, chest and back (Boon *et al*., 2006). Symptoms may range from mild to severe (Tan, 2008).

2.2 Structure of the Skin

The skin is the largest organ of the body and covers a surface area of about two square metres in an average adult. The main functions of the skin are to protect underlying tissues or organs, allowing for excretion of waste, maintain normal body temperature, synthesise vitamin D, store nutrients and detect pressure, pain, touch and temperature. The skin consists of three layers namely the epidermis, dermis and subcutaneous tissue (Martini *et al*., 2001).

2.2.1 The Epidermis

The epidermis is the most superficial layer and provides protection from microorganisms. It consists of stratified keratinised squamous epithelium, which is constantly being shed and is replaced by cells originating in the germinating layer of the epidermis (Silverthorn, 2010).

The epidermis does not contain any blood vessels or nerve endings, as it obtains its nutrients and oxygen from the interstitial fluid of the dermis (Silverthorn, 2010).

2.2.2 The Dermis

Beneath the epidermis lies the dermis which consists of blood vessels, lymph vessels, sensory (somatic) nerve endings, sweat glands with their ducts, sebaceous glands and hair follicles. The dermis is also interlaced with collagen fibres and elastin, which gives skin its tensile strength and elasticity (Silverthorn, 2010).

2.2.3 The Subcutaneous Tissue

The subcutaneous tissue is composed of adipose tissue (fat cells) and blood vessels. Many other large structures are found within this subcutaneous tissue which will be explained below (Kansal & Kaushal, 2004).

2.2.4 The Sweat Glands

Sweat glands are found throughout the skin and are more numerous in certain regions of the body. The bodies of the sweat glands lie coiled in the subcutaneous tissue. Some of the sweat gland ducts open onto the skin's surface and some open onto hair follicles. Sweat glands are activated at the time of puberty (Martini *et al*., 2001).

2.2.5 The Hair Follicles

The growth of hair starts at the hair root or hair bulb and extends upward through the epidermis as the hair shaft. The shaft consists of dead keratinized cells which make up the outer cortex and soft keratin which make up the medulla or the core of the hair shaft (Silverthorn, 2010).

2.2.6 The Sebaceous Glands

Sebaceous glands are halocrine glands that can communicate or connect with a single hair follicle. When the errector pili muscle contracts, it erects the hair and squeezes the gland. In this way an oily substance, known as sebum, is secreted onto the hair shaft and surrounding tissue (Beers *et al*., 2003).

Sebum is a mixture of proteins, triglycerides, cholesterol and electrolytes. Sebum functions as a lubricant that protects the keratin of the hair shaft and conditions the surrounding tissue (Martini *et al*., 2001).

Large sebaceous glands or follicles, which are not associated with hair follicles can also be found on the chest, back and face. It is important to note that these glands are very sensitive to the change in sex hormone levels at puberty (Silverthorn, 2010).

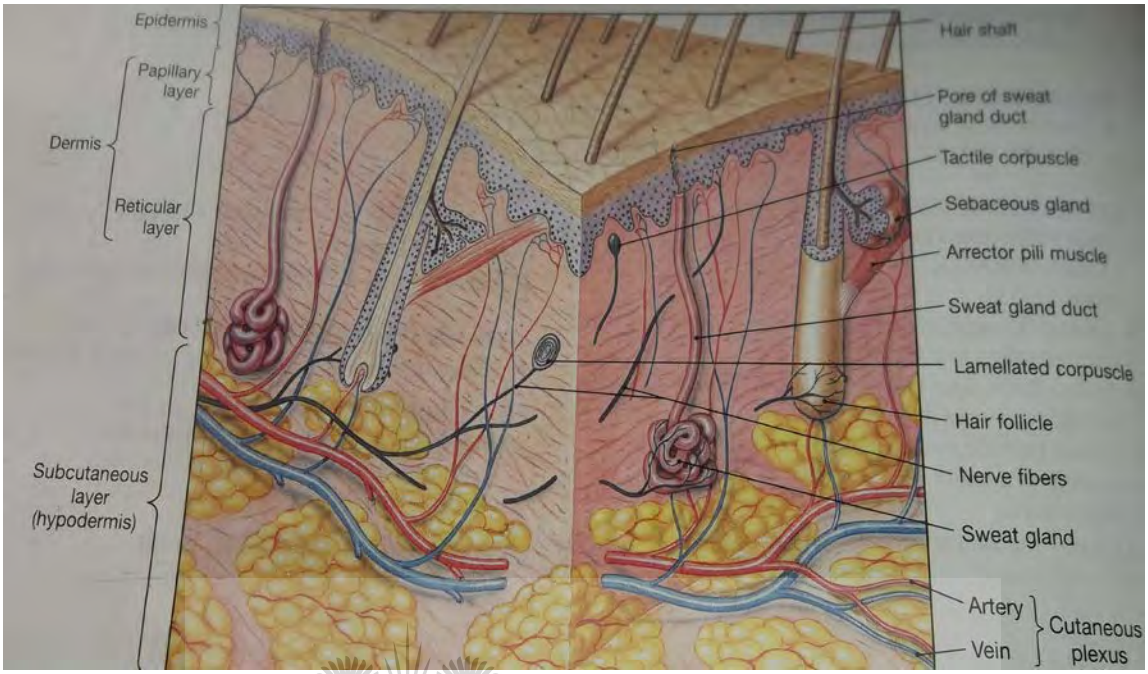


Figure 2.1: Anatomy of the Skin (Martini *et al*., 2001)

2.3 Types of Acne

There are many different types of acne which are classified based on the severity of the symptom presentation of inflammatory and non-inflammatory lesions (Burge & Wallis, 2011).

2.3.1 Acne Vulgaris

Mild to moderate acne vulgaris is characterised by the appearance of inflammatory and non-inflammatory lesions on the affected areas. It is caused by an increase in sensitivity of sebaceous glands to the changes in hormone concentration at the time of puberty (Beers *et al*., 2003).

2.3.2 Keloidalis Nuchae

Keloidalis nuchae is a chronic form of folliculits, which occurs mostly in people of African origin. It characteristically presents with the formation of cysts, pustules and papules, which are obscured in shape and contain broken shafts of hair or ingrown hairs (Letada, 2011).

Systemically symptoms such as myalgia, arthralgia, weight loss and synovitis may also arise (Burge & Wallis, 2011).

Pathologically this condition is caused by the growth of curly hair and ingrowths of hair. This condition is aggravated by shaving and rubbing (Letada, 2011).

2.3.3 Acne Fulminans

Acne fulminans characteristically presents with fever and polyarthritis with the appearance of inflammatory and non-inflammatory lesions. This condition occurs when *Propionibacterium acnes* triggers a type III or type IV immunological reaction, and when there is an increase in testosterone. Genetic factors can also play a role (Zaba, 2011). This condition is chronic and severe scaring can occur (Brown *et al*., 2008).

2.3.4 Acne Conglobata

Acne conglobata is the one of the most severe forms of acne. It presents on the back, chest, buttocks and groins. This condition is characterised by the formation of clustered blackheads and cysts which may interconnect with each other. It may lead to large hypertrophic scar formation. This condition is treated with isotretinoin, steroids and surgical drainage of cysts (Burge & Wallis, 2011).

2.3.5 Acne Rosacea

This condition is most common among middle aged people, with the formation of papules and pustules, overgrowth of soft tissue of the nose (deformation of the nose) and sebaceous gland hyperplasia. A characteristic feature of acne rosacea is intermittent blushing which leads to fixed erythema and telangiectasia. The aetiology of acne rosacea is unknown. Oral antibiotics are used for the treatment of this condition (Boon *et al*., 2006).

2.4 Classification and Grading of Acne

Acne can be graded or classified according to the severity of the symptoms (Tan, 2008).

2.4.1 Grade One / Mild Acne

Grade one acne is characterized by the presence of non-inflammatory lesions (Lavers, 2011) with:

- Fewer than 20 comedones (non-inflammatory lesions) in the affected area;
- Fewer than 15 inflammatory lesions in the affected area; and /or
- A total count of fewer than 30 lesions in the affected area (Tan, 2008).

2.4.2 Grade Two / Moderate Acne

Moderate acne is characterized by the formation of inflammatory and non-inflammatory lesions (Lavers, 2011) with:

- Fewer than 100 comedones (non-inflammatory lesions) in the affected area;
- Fewer than 50 inflammatory lesions in the affected area; and / or
- A total count of fewer than 50 lesions in the affected (Tan, 2008).

2.4.3 Grade Three / Severe Acne

Grade three acne is characterized by the formation of many inflammatory papules, nodules and cysts; which lead to the formation of severe scars (Lavers, 2011) with:

- Greater than 100 comedones (non-inflammatory lesions) in the affected area;
- Greater than 50 inflammatory lesions in the affected area;
- Greater than 5 cysts; and / or
- Total lesion count in excess of 125 the affected area (Tan, 2008).

2.4.4 Grade Four Acne / Cystic Acne

This is the most severe form of acne and it is characterized by the formation of numerous cysts and pronounced amounts of inflammatory lesions. This condition must be treated by a specialist within the field (Palmer, 2012).

2.5 Aetiology and Epidemiology of Acne

Acne appears mostly during adolescence and affects both males and females in their teens and early twenties. It can also affect adults older than twenty five years of age (Docrat, 2008). Studies have shown that males are more frequently affected than females (White, 1998). White males have a greater tendency to develop more severe types of acne as compared to males of other races (Aly & Maibach, 1999).

Studies show that *Propionibacterium acnes* and *Propionibacterium granulosum* are the main causative bacterial organisms in the pathology of acne as they promote inflammation of the comedones. However, the presence of these bacteria is not diagnostically significant (Ward *et al*., 2009).

2.5.1 Risk of Developing Acne

Genetic factors may increase the risk of developing acne and this includes the XYY chromosomal phenotype. People suffering from endocrine disorders such as polycystic ovarian syndrome, hyperandroginism, hypercortisolism and precocious puberty have a tendency to develop more severe types of acne (Bolognia *et al*., 2003).

2.5.2 Contributing Factors

The aetiology of acne is multi-factorial. Daily simple cosmetics, emollients and sunscreens may physically obstruct follicles; thus aiding in the formation of lesions. Some hormonal drugs, including progestins and corticosteroids, may exacerbate acne. Non-hormonal drugs have been shown to have the same effect (Rajagopalan *et al*., 1998). `

2.6 Symptoms of Acne Vulgaris

The most common areas of the skin affected by acne vulgaris are the face, back, chest, buttocks and arms. The presentation of acne vulgaris ranges from mild to severe, and may include the formation of inflammatory papules, nodules, comedones, abscesses or cysts (Tan, 2008).

2.6.1 Comedones

Comedones are cavities filled with keratinous material and numerous bacteria in the opening of a hair follicle. There are two types of comedones: white heads and black heads. White heads or closed comedones are firm nodules with a small white head (Weedon, 2002). Black heads or open comedones which are caused by the process of oxidation that takes place when oil from the plugged hair follicle comes into contact with air on the surface of the skin (Tan, 2008). Comedones are usually non-inflammatory lesions (Bolognia *et al*., 2003).

2.6.2 Inflammatory Lesions

Inflammatory lesions are caused by an immune response which causes an influx of T-helper lymphocytes, giant cells and neutrophils. This initiates inflammation of the sebaceous glands or hair follicles leading to the formation of papules (< 5mm), nodules (< 5mm), pustules (< 5mm) and cysts > 5mm (Bolognia *et al*., 2003).

2.6.3 Other Lesions

Inflammatory and non-inflammatory lesions are known as primary lesions (Boon *et al*., 2006). Lesions like scarring, excoriations and hyperpigmentation are known as secondary lesions, since they develop from the primary lesion or from manipulation of the primary lesion (Tan, 2008).

2.7 Pathology of Acne Vulgaris

There are three main causes of the pathological development acne vulgaris (Boon *et al*., 2006).

- Increased production of sebum

There is a link between increased sebum production and severity of acne. Although increased sebum production alone cannot cause acne, in combination with other causative factors, the production of sebum can exacerbate the symptoms of acne. Androgenic hormones are the main

cause of increased sebum production, and therefore, teens and young adolescents are greatly affected by acne (Bolognia *et al*., 2003).

- Infection with *Propionibacterium acnes*

The growth of the anaerobic microorganism *Propionibacterium acnes*, within the pilosebaceous unit, is one of the most important pathological causes of acne (Bolognia *et al*., 2003). These bacteria secrete exoenzymes like hyaluronidase, proteases, lipases and chemotactic factors that attract neutrophils, lymphocytes and macrophages. This simulates an inflammatory response, which in turn brings about the formation of inflammatory lesions, pustules and cysts. *Propionibacterium acnes* is also linked to the formation of comedones. These bacterial secretions are dependent on changeable factors, like pH and oxygen (Burkhart *et al*., 1999)

- Occlusion of pilosebaceous unit

The occlusion of the pilosebaceous unit occurs when the cells of the wall of the sebaceous glands are shed; this is known as follicular hyperkeratosis. When these units become blocked, the sebum accumulates beneath the blockage and this causes the formation of inflammatory and non-inflammatory lesions (Holmes, 2002).

2.8 Hormones and Acne

Hormones, in particular androgens, also play an important role in the pathogenesis of acne vulgaris. Increased androgens cause the sebaceous glands to enlarge and increase sebum production, which in turn predisposes one to the formation of acne (White, 1998). Clinically, hormone-related acne generally presents with lesions that appear along the jaw line or chin. These patients generally have a history of acne and have an increased risk of developing adult acne (Junkins-Hopkins, 2010).

The development of hormonal acne is largely dependent on circulating testosterone, which is converted to the active hormone by enzymes contained within the pilosebaceous unit itself. Thus males are at greater risk of developing acne than females (White, 1998).

2.8.1 Dihydrotestosterone and Acne

Dihydrotestosterone or DHT (a steroid derivative of testosterone) is directly linked to causing of acne as it causes production of fats that become sebum. It also produces proteins in the keratinocytes that become the keratin in beard hair. It is important to note that this keratin is contained within comedones (Danby, 2010).

Male patients with hormone-responsive acne do not have a measurable increase in circulating testosterone, as this hormone tends to enter and leave the blood stream very rapidly. Hence the total level of testosterone in the blood does not help in the understanding of its pharmacokinetic action on the body (Danby, 2010). Despite this evidence, studies have found that free testosterone does have an effect on peripheral tissues. The effect of androgenic hormones on the skin have been discussed above (Junkins-Hopkins, 2010).

DHT is directly linked to the formation of acne in females and it has been linked to hirsutism, polycystic ovarian syndrome, Cushing's syndrome and ovarian cancer. This is the main cause of adult acne (Longmore *et al*., 2008).

2.8.2 Formation of DHT

When testosterone reacts with the enzyme 5-α reductase, it is converted into 5-α dihydrotestosterone or DHT which is a direct cause of acne as stated above (Junkins-Hopkins, 2010).

2.8.3 Non-Reproductive Hormones and Acne

Non-reproductive hormones, such as growth hormone, can also stimulate the formation of acne as they also increase sebum secretions in an indirect way. Growth hormone is secreted from the anterior pituitary gland and it stimulates the production of insulin–like growth factor (IGF–1) within the liver. Studies have found that increased IGF–1 coincides with increased testosterone production, since IGF–1 stimulates steroid genesis in the testes (Danby, 2010).

Insulin and IGF–1 simulate sterol-response element–binding protein-1 (SREBP–1). In turn, SREBP-1 increases androgen production and increases sebaceous lipogenesis, resulting in increased sebum output. SREBP-1 also affects the germinating epithelium and the basal layer of

the skin; therefore, stimulating keratinocyte production which can cause occlusion of pilosebaceous units (Danby, 2010).

2.8.4 Hormones, Milk and Acne

The link between diet and acne is controversial, although studies have indicated that cow milk proteins can cause an exacerbation of acne in young men (Danby, 2010). Milk or dairy products have high levels of hormones, and contain over 60 molecules that consist of reproductive hormones, non-reproductive hormones and proteins (Balch, 2006).

Milk has many hormonal components and hormonal derivatives that are about two or three enzymatic reactions away from the formation of DHT. The required converting enzymes are naturally found within the pilosebaceous units of the skin. Therefore, when these components are absorbed and circulated within the blood stream, they can affect the skin (Danby, 2010).

The amount of testosterone found within milk can range from about 0.02 to 0.15µg/L, and the amount of androstenedione (a precursor of testosterone) ranges from 0.1 to 3.5µg/L. The processing of food, such as cheese, that contains precursors like androstenedione and estrone can increase the concentration of testosterone as well. Other studies have shown that milk intake can also increase IGF-1 (Adebamowo *et al*., 2005).

2.9 Treatment of Acne

Contrary to popular belief, frequent washing of the affected areas with soaps, abrasive agents, alcohol pads and heavy frequent scrubbing does not help to alleviate symptoms of acne vulgaris, but can cause further acute irritation to the skin (Beers *et al.*, 2003). Drug treatment is greatly dependent on the severity of the symptoms, but the first line of therapy generally involves topical applications (Docrat, 2008).

2.9.1. Antibiotics

These drugs work by attempting to kill acne causing bacteria (*Propionibacterium acnes)* and preventing the formation of new acne eruptions. Examples of antibiotics used for the treatment of acne include clindamycin and erythromycin. Antibiotics can be used systemically or topically (Snyman, 2010).

2.9.1.1 Systemic Use of Antibiotics in Acne

Oral antibiotics have to be taken for weeks or even months to notice a therapeutic effect. General examples of side effects include nausea, diarrhoea and headache (Patel *et al.,* 2010).

Commonly used antibiotics and side effects:

- Doxycycline is a broad-spectrum antibiotic that can be used to treat acne. Its mechanism of action is to inhibit the growth cycle of the gram-positive or gram-negative bacteria. Specific side effects include increased photosensitivity, erosive oesophagitis, and increased fungal growth (Woodard, 2002). It is also known to be hepatotoxic (Snyman, 2010).

- Minocycline is a broad-spectrum antibiotic that is generally used in the treatment of gonorrhoea, but it can be used to treat some skin conditions, including acne (Field, 1982). A specific side effect of minocycline is the bluish staining of teeth, nails and skin (Beers *et al.*, 2003).

- Erythromycin kills gram-positive bacteria and is used to treat patients that are allergic to penicillin. Erythromycin is a general antibiotic that can be used for moderate skin infections. This drug causes increased photosensitivity (Beers *et al.*, 2003).

- Cindamycin is used for severe infections and is effective in killing anaerobic bacteria (Field, 1982). The most specific side effect of this drug is gastro-intestinal disturbances (Woodard, 2002).

- Tetracycline is the most commonly used antibiotic as it is lipophilic and has an anti-inflammatory action. Tetracycline cannot be taken with foods containing calcium and iron

as they bind with the medication and inhibit absorption. Side effects include photosensitizing of the skin (Woodard, 2002).

Studies on the use of systemic antibiotics have found an increasing number of drug resistant bacteria cases. Furthermore, these antibiotics kill both target and non-target bacteria, increasing the susceptibility to opportunistic infections. Therefore it is advisable to take antibiotics only when needed, for short periods of time, as they lose their effectiveness by developing drug resistant bacteria (Holmes, 2002).

Even with the use of therapeutic drugs and topical agents, acne vulgaris may remain persistent. These drugs may have many side effects and continual use thereof promotes the formation of drug resistant organisms. It is therefore becoming increasingly important to look for complementary and alternative forms of therapy (Patel *et al*., 2010).

2.9.1.2 Topical Antibiotics

Topical antibiotics have anti-inflammatory properties and also help in reducing perifollicular lymphocytes, which aid in the formation of comedones. Antibiotic creams have a concentration of between 1%- 4% of active ingredient. Studies have shown that tetracycline cream is less effective than erythromycin, while clindamycin cream has shown to be as effective as benzoyl peroxide (Savage and Layton, 2010).

Topical antibiotics increase the resistance of *Propionibacterium acnes*. Worldwide studies have shown that 47% of patients on topical erythromycin, 41% of patients on clindamycin and 18% of patients on tetracycline have antibiotic–resistant strains of *Propionibacterium acnes.* Furthermore, there is also development of resistance in non-target bacteria (Savage and Layton, 2010).

2.9.2 Benzoyl Peroxide

Benzoyl peroxide is a unique antibiotic as its bactericidal action is through the process of oxidation. It is most effective when used in the form of a cream or lotion (Holmes, 2002). It may, however, take months before any effects can be noticed on the affected area of skin (Snyman, 2010). The common side-effects of this drug include contact dermatitis, type I hypersensitivity reactions, abdominal pain, pruritis, desquamation of skin and it can even promote cross-resistant organism growth. Its use is contra-indicated in pregnancy and in children (Snyman, 2010).

2.9.3 Drying Agents

Drying agents work by drying out pimples and pustules. Examples of these include creams that contain salicylic acid, sulphur and resorcinol (Beers *et al.*, 2003). They work by removing dead skin and cells, and reducing the rate of flaking skin which helps to prevent occlusion of the pilosebaceous unit (Holmes, 2002). The common side-effects of these drugs include skin irritation and dermatitis (Snyman, 2010).

2.9.4 Retinoids

Retinoids are derivatives of vitamin A. Therefore, in order to understand their function and role in the treatment of acne, it is also important to look at the function of vitamin A within the body (Snyman, 2000).

2.9.4.1 Vitamin A

The main function of vitamin A is to regulate growth and differentiation of cells (Woodard, 2002). It also strengthens the protective epithelial skin tissue (Balch, 2006). Sources of vitamin A include animal liver, eggs, carrots and milk (Safeliz, 2008a).

Among other signs, a deficiency of vitamin A leads to the formation of dry and fissured skin (Griffith, 1988). Studies have found that acne patients have decreased levels of plasma vitamin A, and that these levels correlate with the severity of acne (Woodard, 2002).

2.9.4.2 Provitamin A

Provitamin A is a precursor to vitamin A. It contains substances known as carotenoids, of which the beta-carotene is the most important, as it is transformed into vitamin A within the intestine (Archbold & Cherne, 2004). These carotenoids have strong antioxidant properties (Safeliz, 2008a).

It is important to note that plant-based sources contain more vitamin A than animal based sources of vitamin A. Vitamin A derived from plant-based sources can be taken in large quantities without the risk of developing any toxicity (Archbold & Cherne, 2004).

2.9.4.3 Retinoid Drugs

Roaccutane is an example of a retinoid drug. It contains an active ingredient known as isotretinoin. This drug can be taken orally or applied topically as a cream (Bolognia *et al*., 2003).

When applied topically, retinoids prevents the occlusion of pores (Beers *et al.*, 2003) and have anti-inflammatory properties (Savage & Layton, 2010).

When taken systemically, it reduces the production of sebum and inhibits the formation of *Propionibacterium acne* (Marqueling & Zane, 2007). Histological studies show that it decreases the size of the sebaceous glands themselves (Snyman, 2000)

Systemically, these drugs are effective and bring about a visible change within four to eight weeks, but they have many potential side-effects including: dryness of the skin, photophobia, depression, suicide, psychosis, glomerulonephritis, increased blood pressure, increased blood glucose, joint pain, irritable bowel syndrome, lymphadenopathy and eye diseases (Snyman, 2010). Increased levels of triglycerides can trigger pancreatitis, and can cause hypercalcaemia with loss of bone mass (Woodard, 2002).

Due to the occurrence of these side effects, patients on isotretinoin must go for monthly blood tests to monitor the following:

- Liver function, as isotretinoin can induce hepatitis in 15% of patients (Snyman, 2000).
- Plasma cholesterol levels, as 25% of patients on isotretinoin have increased plasma cholesterol. This is due to an increase in plasma triglycerides and a decrease in high density lipoproteins (HDL). HDL helps to remove plasma cholesterol and stores fat within the liver. Increased cholesterol levels also increase the bioavailability of isotretinoin, thus testing of cholesterol levels helps the practitioner to control the treatment dose (Snyman, 2000**).**
- Females that are on isotretinoin and sexually active must conduct regular pregnancy tests and contraception should be used for as long as one month after completion of treatment. As isotretinoin is teratogenic, it can cause abnormalities within the central nervous system and cardiovascular system of the growing foetus. Nursing mothers are also advised not to

breastfeed their infants, as there will be transmission of the drug from mother to child in this way (Henry, 2001).

Studies have found that teenagers are more susceptible to the development of depression when using isotretinoin (Rajagopalan et al., 1998) and it is very important to closely monitor these patients (Marqueling & Zane, 2007).

Patients on isotretinoin should not take vitamin A supplements, as this can increase the risk of developing side effects. Tetracycline antibiotics should be avoided as drug interaction with isotretinon may cause increased intracranial pressure (Henry, 2001).

2.9.5 Hormonal Treatment

Hormonal treatment is mostly used for treating females with acne. The oral contraceptive pill is the most common form of hormonal treatment for females with acne (Gawkrodger, 2008). Studies have found that oral contraceptives are very effective in the treatment of acne, since they reduce inflammatory and non-inflammatory lesions. The main active ingredients of an oral contraceptive pill are oestrogen and progestin. These two hormones prevent the secretion of follicle-stimulating hormone and lutenizing hormone (Junkins-Hopkins, 2010), which are secreted from the anterior pituitary gland. These hormones stimulate follicular development in females. Oral contraceptives increase the synthesis of sex hormone binding globulin (SHBG). Therefore, they decrease the levels of androgens within the blood. Furthermore, they block androgen receptors and inhibit the activity of 5-α reductase, which is the enzyme that converts testosterone into 5-α dihydrotestosterone (DHT) (Junkins-Hopkins, 2010).

Oral contraceptives have many potential side effects including: myocardial infarctions, malignant breast cancer and strokes (Snyman, 2010).

Cyproterone is an example of a hormonal drug that helps to control the effects of testosterone on the skin by reducing the production of sebum (Holmes, 2002). Side effects of this drug include: gynaecomastia, tiredness, weight gain, nausea, vomiting, diarrhoea, constipation, headaches and depression (Snyman, 2010).

2.9.6 Other Forms of Hormonal Treatment

Spironolactone is a potassium-sparing diuretic which is also used in the treatment of hormonal acne. There are four mechanisms of action for this drug (Bergstrom, 2010).

- It competes for dihydrotestosterone (DHT) or androgen receptors on the skin; thereby it prevents the effects of these hormones and suppresses the secretion of sebum (Bergstrom, 2010).
- It increases the levels of sex hormone binding globulin (SHBG), which attaches itself to free androgen hormones, namely testosterone, within the blood (Bergstrom, 2010).
- It increases liver hydroxylase activity, which allows the liver to break down excessive hormones within the blood, thus decreasing the effect of excess hormones and toxins on the skin in this way (Bergstrom, 2010).
- It decreases 5-α reductase activity (Woodard, 2002).

Reports show that spironolactone decreases sebum production in acne and general improvement is reported to be between 35% - 100%. Spironolactone is commonly used with oral contraceptives as this improves the response of both medications (Strauss *et al*., 2007).

Side effects include decreased libido, gynaecomastia, headaches, dizziness, hypotension and hyperkalemia (Strauss *et al*., 2007).

2.10 Homoeopathy

Homoeopathy is a system of healing that simulates the body's own healing energy, the vital force, to bring about a cure. The word homoeopathy is a Greek word that is made up of two parts *"Homeos"* meaning similar, and *"Pathos"* meaning suffering. This word alone gives a clear indication that homoeopathy is based on the principle of "*like cures like"*; which explains that a crude substance can bring about cure in a ill person if it can produce similar symptoms in a healthy person (Marks, 2002).

Dr Samuel Hahnemann (1755-1843), the founder of homoeopathy, became inspired by this law after experimenting on himself with quinine. He found that the intake of quinine in a healthy

person created the symptoms similar to that of malaria. Thus he proved the law of similars (De Schepper, 2007).

Today, there are over two thousand homoeopathic remedies, which are sourced from the plant, mineral and animal kingdoms (De Schepper, 2007).

2.10.1 The History of Homoeopathy

Homoeopathy was discovered about 200 years ago in the eighteenth century. Hahnemann found that because allopathic medication was given in high concentrations and doses, they produced many side effects and where even very toxic. He produced a system of dilution, but found that these diluted substances where not so effective. He then developed the process of "*potentisation"*. Herewith the diluted substances are shaken vigorously in order to release the natural healing properties of the substance. This vigorous shaking is known as "*succussion"* (Stibbe, 1999).

Hahnemann used the ratio of one part crude substance to 99 parts of inert substance (such as distilled water or alcohol), which produces a substance that has one percent of the original concentration. This is known as the CH scale: C stands for centesimal and H stands for Hahnemann. This same process is used for a decimal dilution, which has a ratio of 1:10. Decimal dilutions are represented by a D or an X. This decimal dilution process produces a substance that is one tenth the strength of the original substance (De Schepper, 2007).

Homoeopathic remedies can be prescribed as a "*simplex"* which contains a single homoeopathic remedy or as a "*complex"* which contains two or more homoeopathic remedies that work well together for a specific condition or disease (De Schepper, 2007).

2.10.2 Homoeopathy and Acne

Homoeopathy may provide a more gentle form of therapy with fewer side effects for the treatment of acne. A homoeopathic study in Japan, dealing with chronic skin conditions, has shown that there was a 50% improvement in 88.3% of the total sample group using individualized homoeopathic treatment (Itamura, 2006).

A homoeopathic study was conducted by using individualized homoeopathic treatment to treat adults and children on a variety of dermatological conditions, including acne; for a minimal

period of three months. Results showed that 59% of the study group had a significant physical and psychological improvement in their condition (Priven *et al*., 2009).

Previous research conducted by Bekker (2004) on mild to moderate acne vulgaris of the face, investigated the use of the homoeopathic complex preparation *Testis Compositum*®, which was administered twice a week by subcutaneous injection into the acupuncture point Large Intestine 11. The study was conducted over a six week period. Statistical analysis showed reduction in inflammatory and non-inflammatory lesions. Bekker recommended that the frequency of the dose should be increased for oral administration and that the treatment period of six weeks was too short to see the full effect of *Testis Compositum*® (Bekker, 2004).

2.10.3 R53 (Comedonin) ® Acne Drops

R53 (Comedonin) ® is manufactured by Dr. Reckeweg & Co (2010) and contains a combination of homoeopathic remedies that are used to treat symptoms such as pustules and comedones. This product is a homoeopathic complex that consists of the following remedies: *Bromium* (D12), *Hepar sulphuris calcareum* (D30), *Juglans regia* (D30), *Kalium bromatum* (D12) and *Natrium chloratum* (D200). All of these remedies are clinically indicated in the treatment of acne vulgaris (Dr. Reckeweg, 2010).

2.10.3.1 Bromium

The clinical presentation of *Bromium* is well indicated for the treatment of acne vulgaris where the affected area of skin presents with the formation of acne pimples, pustules and boils on arms and face with the formation of red inflamed eruptions on the chest (Boericke, 2005). The patient may experience an itching, prickling and stitching sensation on the affected area of the skin (Vermeulen, 1997).

2.10.3.2 Hepar sulphuris calcareum

The clinical presentation of *Hepar sulphuris calcareum* is well-indicated for acne vulgaris with skin that is unhealthy looking with eruptions that are prone to suppurate. Discharge from these eruptions is thick, mucopurulent and cheese-like. These eruptions bleed easily and are very sensitive to touch. The patient may experience a burning or an itching sensation of the skin (Vermeulen, 1997).

2.10.3.3 Juglans regia

The clinical presentation of *Juglans regia* is well indicated for acne eruptions that appear on the face with formation of prominent red pustules and comedones (Boericke, 2005). The patients may experience an itching sensation on the affected area of skin (Vermeulen, 1997).

2.10.3.4 Kalium bromatum

The clinical presentation of *Kalium bromatum* is suited to a patient that presents with acne on the face and chest. There may be eruptions of boils and the patient may experience a sensation of itching and burning on the affected area of skin. This remedy is well indicated in acne that is caused by a hormonal imbalance (Clarke, 1994).

2.10.3.5 Natrium chloratum

The clinical presentation of *Natrium chloratum* or *Natrium hypochlorosum* includes a patient presenting with eruptions of pimples and pustules on the face that are red and angry looking. Moist eruptions may appear around the mouth (Clarke, 1994).

2.11 Laser and Light Therapy for Acne

Light therapy is used when the desired results is not acquired or when one does not want to, or cannot, take any long-term medications for the treatment of acne vulgaris. Infrared lasers, low-energy pulsed lasers and radiofrequency devices are used. Special types of cream can also be applied to the affected area to allow for better absorption. Light therapy is used as a complementary therapy with systemic drugs (Hamilton *et al*., 2009).

Light-based therapy has two mechanisms of action:

- Light therapy can work by selectively damaging sebaceous glands with the use of lasers, which cause coagulation of sebaceous glands and associated hair follicle. This decreases sebum secretion (Hamilton *et al*., 2009).

- Light therapy kills *Propionibacterium acnes* directly. Porphyrins in the skin absorbs light at the middle of the UV- blue light spectrum to form single oxygen radicals which are highly reactive. These reactive oxygen radicals attack the bacteria and destroy them

in this way (Kim & Del Rosso, 2010).

2.12 Psychology and Acne

Acne has a strong psychological and social impact on adolescents. Studies have found that there are general increased feelings of insecurity, inferiority and anger in these patients. The psychological and emotional impact of acne is shown to be as prominent as those reported by patients with arthritis, epilepsy, asthma and diabetes. It is important to note that the psychological impact does not correlate to the severity of acne (Zip, 2008).

In severe cases, acne sufferers may become depressed, and due to embarrassment they withdraw from social activity. Other studies have found that acne sufferers have a increased unemployment rate (Docrat, 2008).

2.13 Nutrition and Acne

Nutrition and diet play an important role in the treatment of any medical condition. Studies have found that a diet high in carbohydrates or a high glycaemic load provokes hyperinsulinemia, which initiates a hormonal cascade that favours unregulated tissue growth. It increases sebum production and also has an androgenic effect, which in turn cause increased sebum production as well (Bowe *et al*., 2009). A study done on males with acne, on a low glycaemic diet with decreased carbohydrates, showed a significant decrease in total lesion count after twelve weeks (Werbach, 2008).

Drinking lots of water helps to improves lymphatic drainage. Fibre intake, like apples and other fruit and vegetables, helps to remove toxins and strengthens the immune system which is very helpful in the treatment of acne (Holford, 2003).

The skin in particular is very sensitive to nutritional deficiencies, as the skin cells are continually being replaced by new ones. Therefore, there is a continual need for essential fatty acids and vitamins to maintain healthy skin. Generally, the most important vitamins needed for healthy skin include, vitamins A, B, C, E, selenium and essential fatty acids (Holford, 2003).

2.13.1 Vitamin B Complex

Many B vitamins help with acne as they prevent the formation of blackheads and help to control sebum production. Vitamin B_6 helps to balance hormones (Werbach, 2008). Vitamin B_{12} and folic acid help with the growth of cells, aid the healing processes, improve circulation and help to fight infections, thereby promoting healthy skin and hair (Archbold & Cherne, 2004).

A deficiency of vitamin B complex is associated with acne. Sources of B-complex vitamins include brewers yeast, deep green leafy vegetables and wheat germ (Safeliz, 2008a).

2.13.2 Vitamin C

Vitamin C or ascorbic acid is naturally found in raw fruit and vegetables (Safeliz, 2008a), including oranges, lemons and black currants (Griffith, 1988). Vitamin C is a good antioxidant, and helps to removes toxins . It strengthens the immune system; promotes wound healing and aids in the formation of collagen and thereby, preventing the formation of scars and inflammatory lesions (Balch, 2006).

2.13.3 Vitamin E

Vitamin E is an important antioxidant that promotes healing, increases circulation and prevents the formation of scar tissue. Studies have found that acne patients have decreased amounts of both cellular antioxidants and plasma levels of vitamin E. Furthermore, vitamin E works in conjunction with vitamin A to maintain healthy skin (Archbold & Cherne, 2004).

2.13.4 Zinc

Zinc is an essential mineral needed for the proper development and functioning of skin (Bowe *et al*., 2009). Natural sources of zinc include nuts, whole grains and legumes. Studies have found that teenage males have decreased levels of zinc (Werbach, 2008). Other studies have found zinc to be almost as effective as tetracycline antibiotics in treating acne vulgaris. The best results are obtained when zinc is taken in conjunction with a good diet (Murray *et al*., 2006).

2.13.5 Selenium

Selenium regulates the formation of prostaglandins, which are part of the inflammatory process. It stimulates the immune system by aiding in the production of antibodies (Safeliz, 2008a). It plays a role in the production of hormones; maintains healthy skin; maintains the elasticity of the skin and it is also required for normal liver function. The liver breaks down excess hormones that can aggravate the symptoms of acne (Balch, 2006).

Studies have found that selenium taken with vitamin E may be effective in the treatment of severe pustular acne in males (Werbach, 2008).

2.13.6 Essential Fatty Acids and Healthy Skin

Essential fatty acids (EFA's) are good fats (unsaturated fats) that are needed for the development and maintenance of many important bodily functions. The two most prominent EFA are omega 3 and omega 6 essential fatty acids (Archbold and Cherne, 2004).

Essential fatty acids have numerous functions, but in this context are important for the maintenance of health skin (Archbold and Cherne, 2004). Studies have found that a diet rich in omega 3 oils can help with the treatment of acne, as increased omega 3 consumption helps to decrease inflammatory cytokine production. By decreasing the production of leukotriene B_4, a decrease in the formation of inflammatory lesions occurs.

Other studies have found that omega 3 oil also decreases the hormone Insulin–like growth factor (IGF-1), which can aggravate acne (Bowe *et al*., 2010).

Good sources of omega 3 oil is fish, like tuna and salmon, and flaxseed and walnut oil. Sources of omega 6 include raw nuts, seeds, legumes and unsaturated vegetable oils such as grape seed oil and primrose oil (Archbold and Cherne, 2004).

2.14 Herbs Used in the Treatment of Acne

There are quite a number of herbs that can be used in the treatment of acne (Barnes *et* al., 2007).

2.14.1 *Echinacea angustifolia* and *Echinacea purpurea* (Echinacea)

Echinacea angustifolia and *Echinacea purpurea* can be used to stimulate the immune system. They have antimicrobial, anti-inflammatory and wound-healing properties. Thus, they are used to treat skin symptoms such as recurring boils, carbuncles and enlarged lymphatic glands (Van Wyk and Wink, 2009).

2.14.2 *Taraxacum officinale* (Dandelion)

Dandelion is used to detoxify the liver. This helps to break down excess hormones and purify blood. In this way it helps in the treatment of acne vulgaris (Barnes *et al.*, 2007)

2.14.3 *Calendula officinalis* (Calendula)

Calendula treats a variety of skin conditions, as it has anti-inflammatory, anti-microbial and wound healing properties. It is very useful in the treatment of acne (Van Wyk & Wink, 2009).

2.14.4 *Arctium-Lappa* (Burdock)

Burdock can be used to treat a variety of skin conditions, as it has anti-bacterial and anti-microbial qualities, while it remove toxins (Barnes *et al.*, 2007).

3. METHODOLOGY

3.1 Sample Group

Participants were recruited via advertisements (Appendix D) at schools, general practitioner's offices, high schools, the University of Johannesburg campus, pharmacies and somatology clinics with relevant permission. The study group consisted of 30 male participants between the ages of 15 to 25 years, that presented with acne vulgaris which predominated over the face, chest or back.

3.1.1 Inclusion Criteria for the Study:

The participant needed to present with mild to moderate acne vulgaris, on the chest, back or face. The following acne count criteria was used to grade the acne:

- Fewer than 100 comedones (non-inflammatory lesions) in the affected area
- Fewer than 50 inflammatory lesions in the affected area
- Total lesion count was fewer than 125 lesions (Tan, 2008).

Only male participants between the ages of 15 to 25 years where recruited.

3.1.2 Exclusion Criteria for the Study:

Participant where excluded from the study if they:

- Were on any form of long-term or chronic medication, or commenced any other forms of chronic long-term treatment during the study.

3.2 Research Procedure

A randomized, double-blind, placebo-controlled study was conducted at University of Johannesburg Health Centre Doornfontein campus. All participants were informed about the nature of the study and the requirements needed in order to participate in the study. Qualified participants were then requested to sign an information consent form (APPENDIX A) and a photograph permission form (APPENDIX C). All participants under the age of 18 years where required to obtain consent from a parent or guardian (APPENDIX C).

The study was conducted over an eight-week period with a full evaluation being conducted on the first day of the study, then at four weeks and at the end of eight weeks. At each evaluation the following procedure were followed (APPENDIX B):

- Photographs of the affected areas where taken by the researcher at week 0 and week 8 of the study. To maintain confidentiality and consistency the consultations where conducted in the same consulting room within the UJ Health Centre with the light on. A piece of paper with the measurement of one to six centimetres was placed on the affected area as this was required to help ascertain the surface area affected in centimetres when using the Digermizer to calculated surface area affected at week 0 and week 8. The affected areas where adequately exposed and participants where requested to stand under the light. For the facial acne, frontal and bilateral photos were taken. For acne that presented on the chest, frontal photos were taken. For acne that presented on the back, posterior central photos were taken. Photographs were taken in a way to keep the dignity and privacy of the participants. A 14 Mega pixel Kodak easyshare KLIC-7006 digital camera with the flash on was used to take all the required photographs.

- Response to treatment was assessed by the researcher at week four and week eight by comparing the baseline photographs to the participant's current condition. This showed subjective improvement on researcher's perception as seen on the appearance of the photographs, by using the following scale:

  0 - Completely cleared

  1 - Approximately 90% improved

  2 - Approximately 75% improved

  3 - Approximately 50% improved

  4 - Approximately 25% improved

  5 - No change

  6 – Exacerbation (Bekker, 2004).

- The number of lesions on the affected areas were counted and compared. The lesion where divided into inflammatory lesions (papules, pustules and cyst that were greater than 4mm) and non inflammatory lesions (comedones). The lesions where palpated and inspected under good light (Bekker, 2004).

- Evaluation of associated symptoms such as peeling, burning, itching (pruritus), redness (erythema), oiliness and dryness of the skin was assessed by interview and examination. Participants where requested to record the symptoms and report any changes in symptoms in week four and week eight by using the following scale:

  0 - None

  1 - Very mild

  2 - Mild

  3 - Moderate

4 - Severe

5 - Extreme (Bekker, 2004).

3.3 Medication Administration

The product R53 (Comedonin ®) contains 36% ethanol, aqua pur as well as the remedies *Bromium* (D12), *Hepar sulphuris calcareum* (D30), *Juglans regia* (D30), *Kalium bromatum* (D12) and *Natrium chloratum* (D200). The placebo / control medication was packaged and labelled identically and contained 36% ethanol. Randomisation was conducted by the German based company Dr. Reckeweg & Co. Dr (Dr. Reckeweg, 2010).

Participants were instructed to take 10 drops of the medication in a little water three times daily before meals for the duration of the study. Each participant received two 50ml amber glass bottles of the medication, one at beginning of the study and the other at week four of the study.

3.4 ETHICS

All participation during the study was voluntary and each participant had the freedom to withdraw their consent at any time during the study. All participants had the full right to confidentiality and the outcome of the study was made available at their request. Participants under the age of 18 were required to obtain consent from a parent or guardian.

All information regarding the study was explained at the beginning of the study and all information obtained was kept with strict confidentiality. In all photographs, the participant's identity will remain anonymous and unidentifiable as far as possible.

3.5. DATA ANALYSIS

Data was analysed by Statcon at the University of Johannesburg. The data showed that there was a lack of normality and equal variances, therefore non-parametric tests were conducted, namely the Mann Whitney U-Test, and the Wilcoxon Signed Rank test was used for intra- group analysis (Van Staden, 2010).

4. RESULTS

4.1 Introduction

This double-blind, placebo-controlled study consisted of a total sample group of 30 participants, which was divided into two equal groups of 15. All of the participants consisted of males, between the ages of 15 – 25 years. The participants presented with mild to moderate acne vulgaris on the face, back or chest. Symptoms were measured by scales, lesion counts and surface area calculations, using the Digermizer programme. The results of this study were statistically analysed by Statcon at the University of Johannesburg; using non-parametric tests which included the Friedman test, Wilcoxon Signed Rank test and the Mann-Whitney U test. These non-parametric tests were conducted as there was lack of normality across the distribution of variables. The presentation of some extreme values in the study caused the skewness in the data to occur (Van Staden, 2012).

4.1.1 Kolmogorov-Smirnov

The Kolmogorov-Smirnov is a statistical test for normality of the distribution of data. A p-value greater than 0.05 indicates that parametric tests should be used, and a p-value less than 0.05 indicates that there is lack of normality, which indicates the use of non-parametric tests (Pallant, 2007).

4.1.2 Friedman Test

The Friedman test is a non-parametric test that indicates change over time, and evaluates normality between two groups. Where there are three or more periods of time, a p-value of < 0.05 indicates that there is a statistically significant change over time. This test helps with intergroup analysis and is used to determine if there is a statistically significant difference in the severity of symptoms over different time periods, for the placebo and the treatment groups. The Friedman test generally follows the Wilcoxon Signed Rank Test and indicates where the changes have occurred over time (Pallant, 2007).

4.1.3 Wilcoxon Signed Rank Test

The Wilcoxon Signed Rank test is a non-parametric test that is used when there are repeated measures assessed at two different occasions. This test converts the scores into ranks across the groups. The test gives an indication of a statistically significant difference existing between the two groups. A p-value < 0.05 shows a statistically significant difference between the two groups. However, when there is a comparison of more than one set of two points (comparisons), the Bonferroni Adjustment must be taken into account. Therefore, this adjustment is used to keep the rate of experiment wise error to 5%, when using multiple comparisons. As seen in this study, where there are three comparisons, i.e. week 0 to week 4; week 4 to week 8, and week 0 to week 8, the p-value of 0.05 is divided by the number of comparisons. Thus, the p-value, when divided by three (0.05/3), equals a p-value of 0.0167. For this study, where there is intergroup analysis with three comparisons, a p-value < 0.0167 will indicate that there is a statistically significant change or difference between the groups (Pallant, 2007).

4.1.4 Mann-Whitney U Test

The Mann-Whitney U test is a non-parametric test for an independent sample group that indicates the difference between the placebo and treatment groups. On a consistent variable, a p-value of < 0.05 shows a statistical significant change between the groups. The scores are converted across ranks between the two groups and as such, the distribution of scores was unimportant (Pallant, 2007).

4.1.5 Leven's Test for Equality

Leven's Test for Equality is used to determine comparability between groups. A p-value greater than 0.05, indicates that a statistically significant change has occurred regarding comparability between two groups (Pallant, 2007).

4.2 Hypothesis

It was hypothesised that the homoeopathic complex preparation R53 (Comedonin ®) acne drops will be effective in the symptomatic treatment of acne vulgaris when compared to the placebo.

4.3 Null Hypothesis

It is hypothesised that the homoeopathic complex preparation R53 (Comedonin ®) acne drops would not be effective in the treatment of acne vulgaris when compared to the placebo.

4.4 Sample Group

Table 4.1 Subdivisions of race within the study group.

Race	Number of participants (n)	Percentage of the group affected
African	17	56.7%
Caucasian	2	6.7%
India	11	36.7%

The study group consisted of 30 male participants, between the ages of 15 to 25 years. Figure 4.6.1 shows that the total sample group consisted of a frequency of 56.7% (n=17) African participants, 36.7% (n=11) Indian participants, and 6.7% (n=2) Caucasian participants.

Table 4.2 Area affected by acne vulgaris

Area affected	Number of participants (n)	Percentage of participants affected within the total sample group
Face	21	70%
Back and Chest	3	10%
Face and Back	1	3.3%
Face, Back and Chest	4	13.3%
Back	1	3.3%

Table 4.2 shows that 70% of the participants had acne on their face, 10% of the participants had acne on their back and chest, and 13.3% of the participants had acne on their face, chest and back.

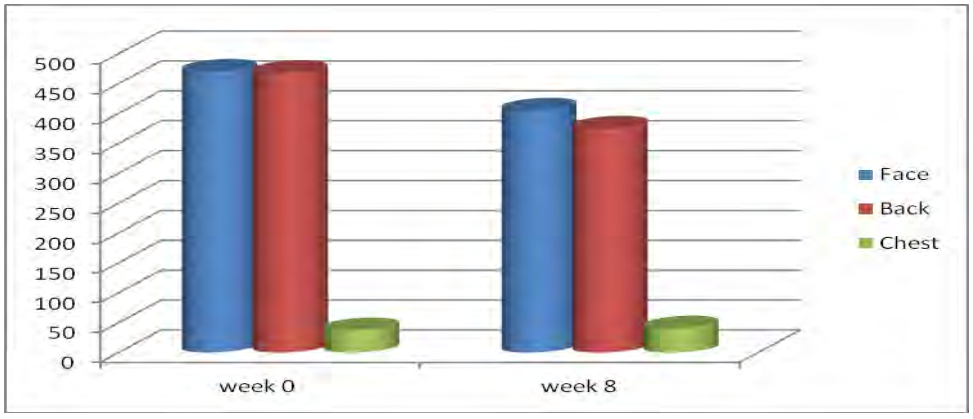
In the treatment group, 13 participants were affected by acne on their face, 2 participants were affected by acne on their chest and 4 participants had acne on the back.

In the placebo group, 13 participants were affected by acne on their face, 4 participants were affected by acne on their chest and 5 participants were affected by acne on their back.

4.5 Surface Area Affected

The surface area was calculated by using the Digermizer programme. Each area affected was calculated to determine if there was a change in the size of the surface area affected over the 8 week period. For this reason, the total surface area was added together for the face, chest and back respectively, for both treatment and the placebo groups.

Figure 4.1 Total surface area affected for the Treatment Group



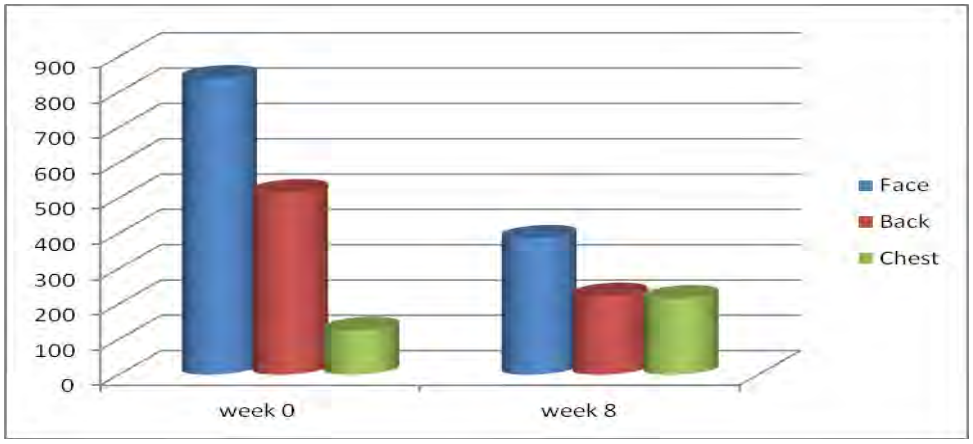
Participants in the treatment group : surface area				
	Face	**Back**	**Chest**	**Total surface area**
Week 0	469.74cm^2	467.7cm^2	37.2cm^2	974.64cm^2
Week 8	404.8cm^2	374.7cm^2	40.4cm^2	819.9 cm^2

Figure 4.1 shows the total surface area affected on the face, chest and back for week 0, week 4 and week 8 for the treatment group.

This figure shows that there was a decrease in the surface area affected on the face from week 0 to week 8. The surface area affected on the back decreased from week 0 to week 8. However, the surface area affected on the chest showed an increase from week 0 to week 8 for the treatment group. In total there was a 15% improvement in the total surface area from week 0 to week 8 in the treatment group.

Of the total sample group, 86.7% (n=13) where affected by facial acne. The surface area that affected the face for the treatment group at week 0 ranged from 0-70cm^2, and at week 8, the surface area ranged from 0-60cm^2. Of the total sample group, 13.3% (n=2) in the treatment group were affected by acne on the chest. At week 0, the surface area on the chest ranged from 0-20cm^2 and at week 8 the surface area ranged from 0- 30cm^2. In the treatment group, 26.7% (n=4) of the participants were affected by acne on the back. At week 0 the surface area affected ranged from 0-250cm^2 and at week 8 the surface area affected ranged from 0- 250cm

Figure 4.2 Total Surface area for the Placebo Group



Participants in the placebo group : surface area				
	Face	**Back**	**Chest**	**Total surface area**
Week 0	838.3cm^2	515.5cm^2	125.5cm^2	1479.3 cm^2
Week 8	385.8cm^2	222.4cm^2	215.4cm^2	823.6 cm^2

Figure 4.2 shows the total surface area affected on the face, chest and back for week 0, week 4 and week 8, for the placebo group. There was a decrease in the surface area affected on the face and back from week 0 to week 8. However, the surface area affected on the chest increased. In total, there was a 55% improvement in surface area for the placebo group.

Of the sample group, 86.7% (n=13) within the placebo group were affected by acne on the face. The surface area affected on the face at week 0 ranged from 0-400cm^2, and at week 8, the surface area ranged from 0-100cm^2. 26.7% (n=4) of the placebo group where affected by acne on the chest. At week 0, the surface area affected on the chest ranged from 10-70cm^2 and at week 8, the surface area ranged from 0-120cm^2. 33.3% (n=5) of the placebo group where affected by acne on the back. At week 0, the surface area ranged from 0-400cm^2 and at week 8, the surface area ranged from 0-80cm^2.

Table 4.3 Friedman Test for surface area affected

Group	**Week 0**	**Week 8**
Treatment Group (p-value)	0.2	0.2
Placebo Group (p-value)	0.003	0.016

From the table above, it can be seen that in the treatment group, the p-value is > 0.05, which indicates that there was a lack of normality at week 0 (p=0.2) (total surface area 819.9cm^2) and at week 8 (p=0.2) (total surface area 974.64 cm^2). However, the p-value of the placebo group is < 0.05 at week 0 (p=0.003) (total surface area 1479.3 cm^2) and at week 8 (p=0.016) (Total surface area 823.6 cm^2), which indicates that there is a normality within the placebo group.

Table 4.4 Comparison of the Mann-Whitney U Test related to the surface area of the affected areas from week 0 to week 8.

Group		**Face week 0**	**Face week 8**	**Chest week 0**	**Chest week 8**	**Back week 0**	**Back week 8**
Mean	Treatment	36.1cm^2	31.18cm^2	18.6cm^2	20.2 cm^2	129.6cm^2	93cm^2
	Placebo	64.5cm^2	29.7cm^2	31.38cm^2	53.85cm^2	103cm^2	44cm^2
Standard Deviation	Treatment	19.7cm^2	18.6cm^2	1.273cm^2	7.637cm^2	98.05cm^2	96.5cm^2
	Placebo	101.7cm^2	27.5cm^2	25.49cm^2	45.27cm^2	117.74cm^2	29.6cm^2
Mann-Whitney U Tests p-value		0.939	0.457	0.643	0.355	0.806	0.806

The mean value in Table 4.4 is an indication of the average surface area affected at week 0 and week 8, for the treatment and the placebo groups.

For the treatment group, the participants with acne on the face had a mean value of 36.1cm^2, at week 0 and at week 8 the mean was 31.8cm^2. This indicates that there is a slight decrease in the surface area affected on the face.

Table 4.6 shows the p-value regarding the Mann-Whitney U Test for the treatment group and the placebo group at week 0 and week 8 for the surface areas affected on the face, chest and back. All of the p-values regarding the face, chest and back at week 0 compared to week 8 were not < 0.05. This indicates that there was no statistically significant change in the surface area affected over the 8 week period.

Table 4.5 Wilcoxon Signed Rank Test for the surface area affected

Group		**Face**	**Back**	**Chest**
p-value	Treatment Group	0.064	0.144	0.655
	Placebo Group	0.028	0.043	0.465

In Table 4.5, the p-value for the treatment group is 0.064, 0.144 and 0.655 for the face, chest and back respectively. This indicates a lack of statistically significant change in the treatment group. For the placebo group, the p-values for the same areas are p=0.028, p=0.043 and p=0.465 respectively. The p-values in the placebo group were < 0.05 for the participants with acne on the face and back. This indicates that there was a statistically significant improvement regarding the surface area affected in the placebo group.

4.6 Inflammatory Lesions

Table 4.6 Comparison of Mean and Standard Deviation for Inflammatory Lesions

Time		Mean Face	Standard Deviation Face	Mean Chest	Standard Deviation Chest	Mean Back	Standard Deviation Back
Week 0	Treatment	23.85	20.9	8.5	2.121	23.25	37.924
	Placebo	18	16.8	11.75	18.839	22.4	32.715
Week 4	Treatment	18	18.3	15	1,414	23.5	37.864
	Placebo	14.46	14.06	10.5	19.689	23.8	37.104
Week 8	Treatment	15.54	17.64	15	28.28	19.4	20.293
	Placebo	12	12.5	5.25	9.845	18	28.19

The above table shows that there was a decrease in the mean value of inflammatory lesions over time in both the treatment and placebo groups. However, participants in the treatment group with acne on the chest, showed an increase in inflammatory lesions over the 8 week period (week 0=8.5 inflammatory lesions and week 8=15 inflammatory lesions).

Table 4.7 Mann-Whitney Test for Inflammatory Lesions: p-values

Time	**Face**	**Chest**	**Back**
Week 0	0.342	0.348	0.537
Week 4	0.425	0.348	0.621
Week 8	0.504	0.348	0.618

Table 4.7 shows the p-values regarding the Mann-Whitney U test for the treatment group and the placebo group, at week 0 and week 8, for inflammatory lesions on the face, chest and back. All the p-values were greater than 0.05, therefore indicating that there was no statistically significant change in the number of inflammatory lesions over the 8 week period on the face, chest and back.

Table 4.8 Wilcoxon Signed Ranks Test for Inflammatory Lesions

Value	Group		Week 0-4	Week 4-8	Week 0-8
p-value	Treatment	Face	0.03	0.05	0.01
	Placebo		0.019	0.002	0.016
	Treatment	Chest	0.180	1.000	0.180
	Placebo		0.102	0.180	0.059

For this particular section, the p value < 0.016 is statistically significant as the Bonferroni Adjustment was taken into account. This test was not conducted on areas affected with acne vulgaris on the back as the sample group was too small with insufficient data (Table 4.2) (Pallant, 2007).

The p-values for the treatment group for the face (p=0.03, p=0.05 and p=0.01) and chest (p=0.180, 1.000 and 0.180) are not < 0.016; therefore, there was no statistically significant change in the treatment group. In the placebo group however, for the face, the p-value (0.002) is < 0.016 between weeks 4 - 8. No other significant changes were noted.

4.7 Non Inflammatory Lesions

Table 4.9 Comparison of Mean and Standard Deviation for Non-Inflammatory Lesions

Time		Mean Face	Standard Deviation Face	Mean Chest	Standard Deviation Chest	Mean Back	Standard Deviation Back
Week 0	Treatment	56.77	21.28	20	14.14	59.75	34.93
	Placebo	49.46	20.46	31.25	14.36	50	30.82
Week 4	Treatment	50.38	21.3	20	14.14	55.50	31.69
	Placebo	44.31	19.94	24	9.52	55	28.06
Week 8	Treatment	38.92	16.60	22.5	17.62	50	29.43
	Placebo	42.31	19.91	28	13.64	53	27.29

This table shows that there was a decrease in the mean values of non-inflammatory lesions over time in both the treatment and placebo groups. However, the participants affected with acne on the chest for the treatment group show an increase in non-inflammatory lesions at week 8 (week 4= 20 lesions and week 8=22, 5 lesions).

The participants affected by acne on the back showed a steady improvement for the treatment group (week 0=59.75 lesions and week 8=50 lesions) and the placebo (week 0=50 lesions; week 4=55 lesions and week 8=53 lesions) showed an increase in the average number of lesions at

week 4 and week 8.

Table 4.10 Mann-Whitney Test for Non-Inflammatory Lesions, p-values

Time	Face	Chest	Back
Week 0	0.451	0.335	0.901
Week 4	0.456	0.803	0.806
Week 8	0.700	0.481	0.712

Table 4.10 shows that all the p-values at week 0, week 4 and week 8 are > than 0.05. This indicates that there is a lack of statistical evidence of improvement in the treatment and the placebo groups.

Table 4.11 Wilcoxon Signed Ranks test for Non-inflammatory Lesions

For this particular section, the p-value < 0.016 is statistically significant as the Bonferroni Adjustment was taken into account. This test was not conducted on areas affecting the chest and back as the sample group was too small (Table 4.2).

Value	Group		Week 0-4	Week 4-8	Week 0-8
p-value	Treatment	Face	0.004	0.003	0.001
	Placebo		0.024	0.008	0.005

The treatment group shows p-values of 0.004, 0.003 and 0.001 respectively compared to the placebo group with p-values of 0.024, 0.008 and 0.005. This indicates that there was a statistically significant difference between the treatment and the placebo groups. There was a greater statistical improvement in the number of non-inflammatory lesions within the treatment group when compared to the placebo group.

4.8 Total Lesion Count

Table 4.12 Comparison of Mean and Standard Deviation for Total Lesions Count

Time		Mean Face	Std. Deviation Face	Mean Chest	Std. Deviation Chest	Mean Back	Std. Deviation Back
Week 0	Treatment	80.62	37.49	28.50	16.26	83	64.25
	Placebo	66	30.68	43.5	31.98	75.40	60.56
Week 4	Treatment	68.62	35.22	35.5	12.02	79	61.80
	Placebo	58.72	37.92	29.75	16.58	90.20	66.30
Week 8	Treatment	57.92	32.54	37.50	14.85	68	48.7
	Placebo	53	25.22	40.75	20.68	66.40	47.72

Table 4.10 shows a decrease in mean values and a decrease in standard deviation of total lesions on the face, over the 8 week period, for the treatment and placebo groups. Within the treatment group, the participants affected by acne on the chest show an increase in standard deviation and a decrease in mean over the 8 week period. On the back, the standard deviation is relatively high and the mean within the placebo group increased at week 4, and then decreased at week 8.

Table 4.13 Mann-Whitney U Test for Total Lesion Count: p-values

Time	Face	Chest	Back
Week 0	0.240	0.814	1.000
Week 4	0.382	0.643	0.806
Week 8	0.817	1.000	0.624

Table 4.13 shows that the p-value for total lesions count is not < 0.05, showing lack of statistical significance in the improvement of total lesion count over the 8 week period between the treatment and the placebo groups.

Table 4.14 Wilcoxon Signed Ranks Test for Total Lesion Count

Value	Group		Week 0-4	Week 4-8	Week 0-8
p-value	Treatment	Face	0.002	0.002	0.001
	Placebo		0.086	0.030	0.023

For this particular section, the p-value of < 0.016 is statistically significant, as the Bonferroni Adjustment was taken into account. This test was not conducted on areas affected on the chest and back as the sample group was too small (Table 4.2).

Table 4.16 shows that the p-values for the treatment group (p=0,002; p=0.002 and p=0.001) are < 0.016 and the p-values for the placebo group (p=0.086;p=0.030 and p=0,023) are not < 0.016. These p-values show a statistically significant improvement in the total number of lesions on the face for the treatment group only.

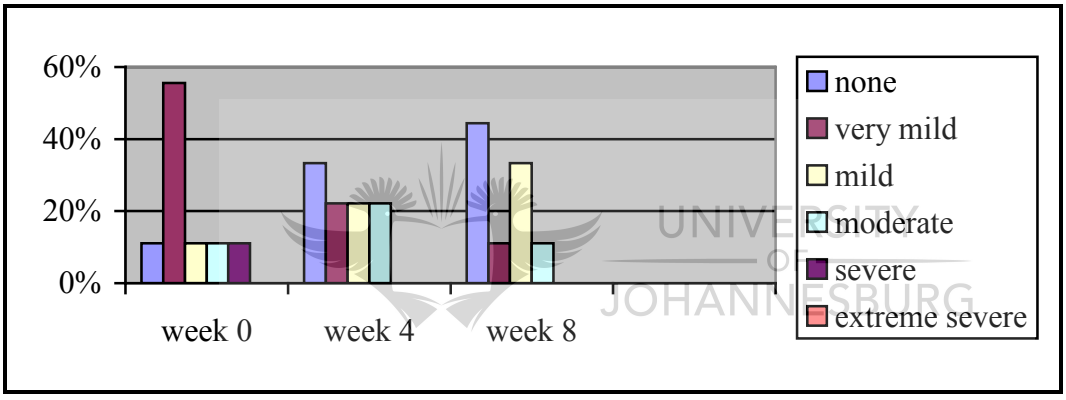
4.9 Associated Symptoms

Associated symptoms were assessed by the participants using a scale from 1-5 (Appendix B), at week 0, week 4 and week 8. For the purpose of this description, associated symptoms at week 0 will be compared to the associated symptoms at week 8.

The percentage of participants is relative to the amount of participants affected by that particular symptom. Only substantial findings are discussed as in some instances only a very few or none of the participants displayed the associated symptom of dryness of skin and pruritus.

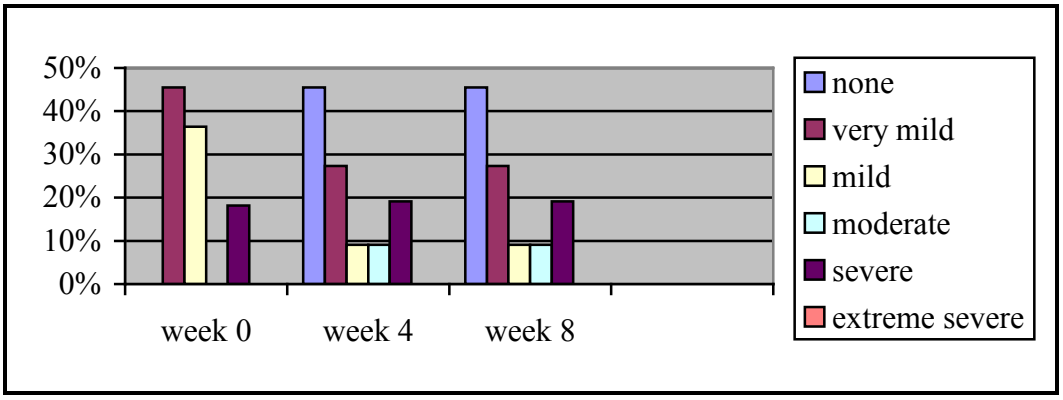
4.9.1 Peeling

Figure 4.3 The Percentage of Participants Affected by Peeling for the Treatment Group



In the treatment group, a total number of 9 participants were affected by peeling. Figure 4.3 shows an increase in the symptom of mild peeling from week 0 (11.1%, n=1), to week 4 (22.1%, n=2) and week 8 (33.3%, n=3). The symptom of severe peeling also decreased to 0% at week 8. This shows that there has been a decrease in the severity of the symptom of peeling for the treatment group.

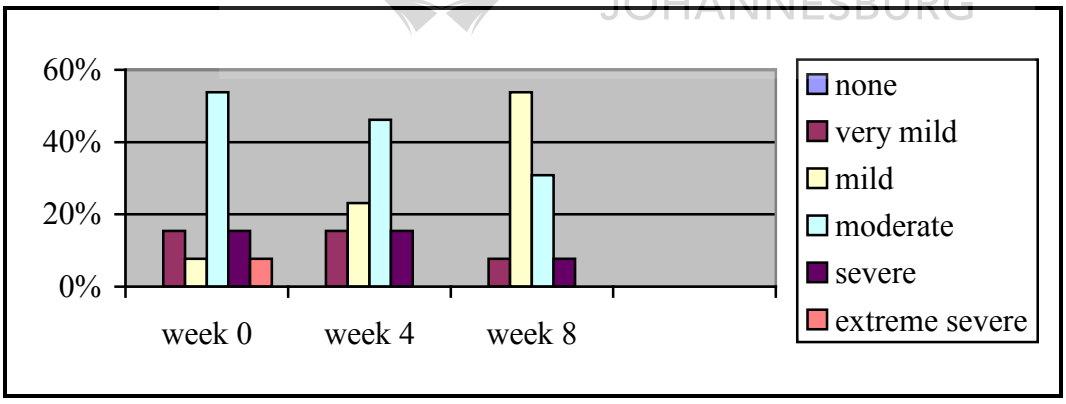
Figure 4.4 The Percentage of Participants Affected by Peeling for The Placebo Group



Eleven participants were affected by peeling within the placebo group. In the placebo group at the beginning of week 0, 45.5% (n=5) of the participants experienced very mild peeling. At the end of week 8, 45.5% (n=5) showed no symptoms of peeling. The graph above indicates that there was an improvement in the symptom of peeling.

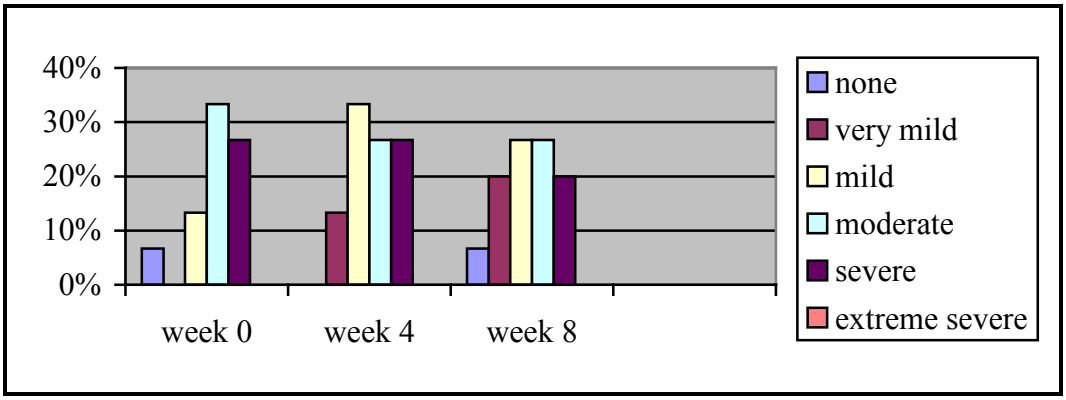
4.9.2 Oiliness

Figure 4.5 The Percentage of Participants Affected by Oiliness in The Treatment Group



A total of 13 participants were affected by the associated symptom of oiliness. At the end of week 8, 53.8% (n=7) had mild oiliness.

Figure 4.6 The Percentage of Participants Affected by Oiliness in The Placebo Group

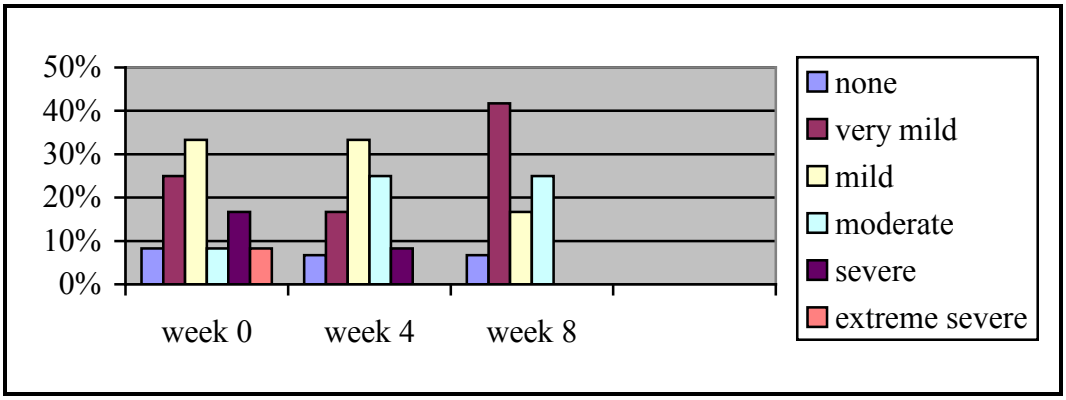


All of the affected participants with oiliness within the placebo group showed that the percentage of participants with severe oiliness decreased from week 0, 26.7% (n=4) to week 8 20% (n=3). The percentage of participants affected with moderate oiliness at the beginning of week 0 is 33.3% (n=5) in week 8 and at the end of week 8 is 26.7% (n=4).

This indicates that within the treatment group the severity of oiliness decreased by 8%. There was a greater improvement in the symptom of oiliness within the treatment group when compared to the placebo group.

4.9.3 Redness / Erythema

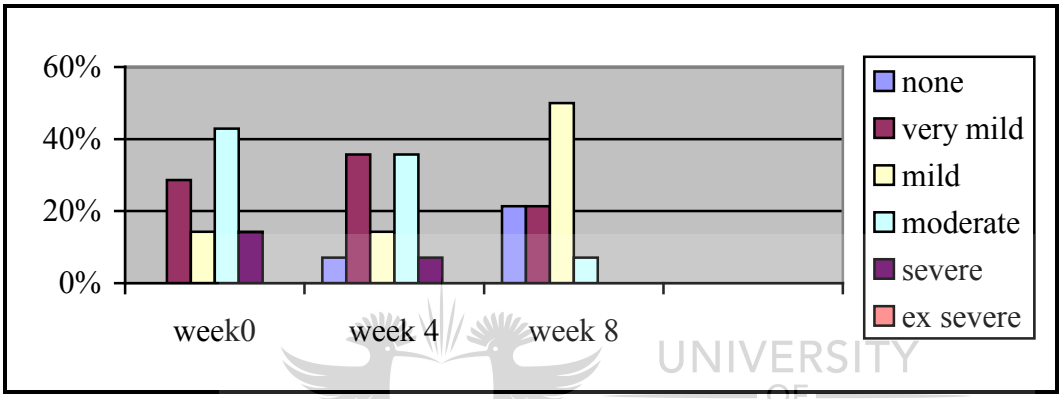
Figure 4.7 The Percentage of Participants Affected by Redness / Erythema in the Treatment Group



Twelve participants within this group were affected by the associated symptom of erythema. The

percentage of participants affected by severe erythema at the beginning of week 0 was 16.7% (n=2), and at the end of week 8, was 0% (n=1) of the participants were affected by severe erythema. The participants affected with moderate erythema showed a decrease in the severity of erythema from at the beginning of week 0 to the end of week 8, 25% (n=3). The number of participants affected by mild erythema also decreased in severity from the beginning of week 0, 33.3% (n=4) to the end of week 8, 16.7% (n=2).

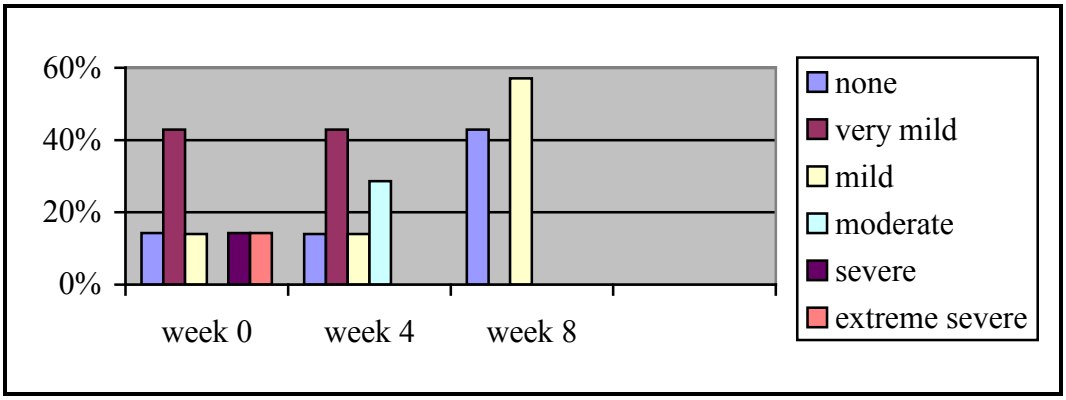
Figure 4.8 The Percentage of Participants Affected by Redness / Erythema in the Placebo Group



Fourteen of the participants within this group were affected by erythema. Within the placebo group, 28.6% (n=4) had very mild erythema, 42.9% (n=6) had moderate erythema, and 14.3% (n=2) had severe erythema at the beginning of week 0. At the end of week 8, 21.4% (n=3) had very mild erythema.

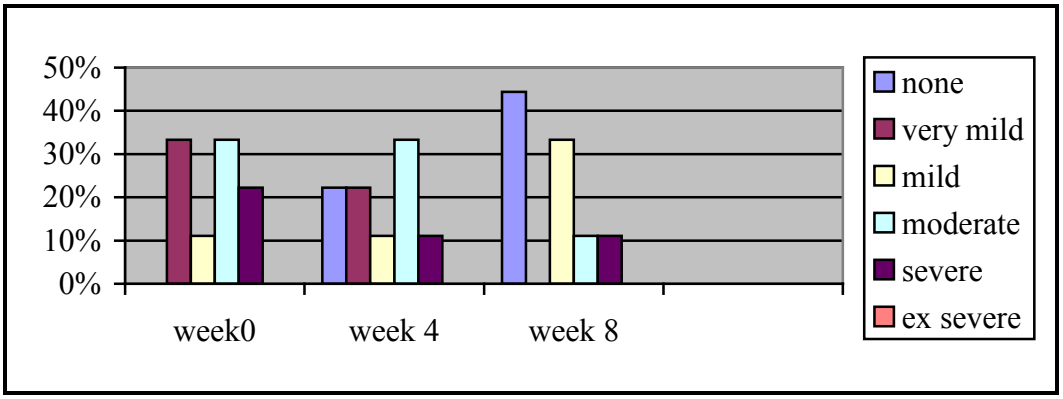
4.9.4 Burning

Figure 4.9 The Percentage of Participants Affected by Burning in the Treatment Group



A total of seven participants were affected by burning within the treatment group. At the end of week 8, 42.9% (n=3) of the participants had no symptoms of burning. At the beginning of week 0, 42.9% (n=3) and 57% (n=4) at week 8 had mild burning. The participants affected with severe burning showed an improvement from week 0 to week 8. None of the participants were affected with moderate burning at week 0 or week 8. However, at the end of week 8, 42.9% (n=3) of the participants had no symptoms of burning and 57.1% (n=4) of the participants had mild burning.

Figure 4.10 The Percentage of Participants Affected by Burning in the Placebo Group

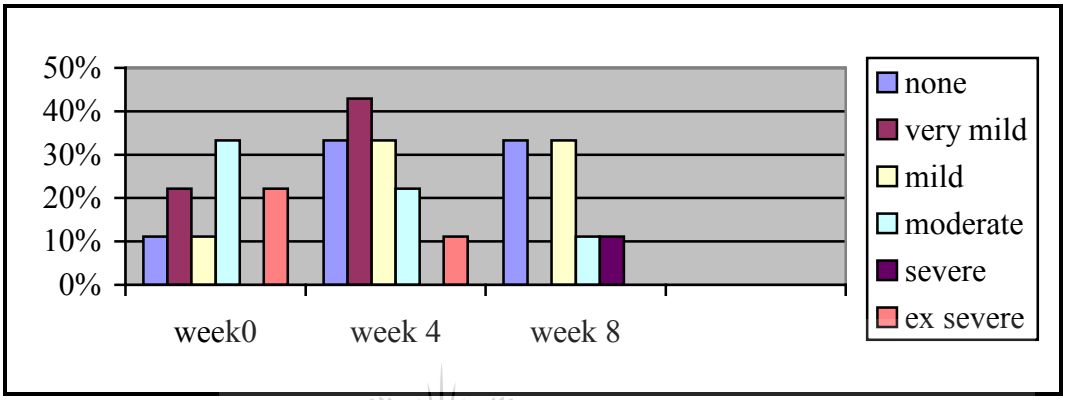


A total of nine participants within the placebo group where affected by burning. Figure 4.10 indicates a decrease in the percentage of participants affected with moderate burning from the beginning of week 0 33.3% (n=3), to the end of week 8, 11.1% (n=1). The percentage of participants that were not affected with the symptom of burning increased from week 0, 0%

(n=0) to week 4, 22.2% (n=2) and at the end of week 8, 44.4% (n=4). There was a marked difference or improvement within the treatment group, regarding the associated symptom of burning.

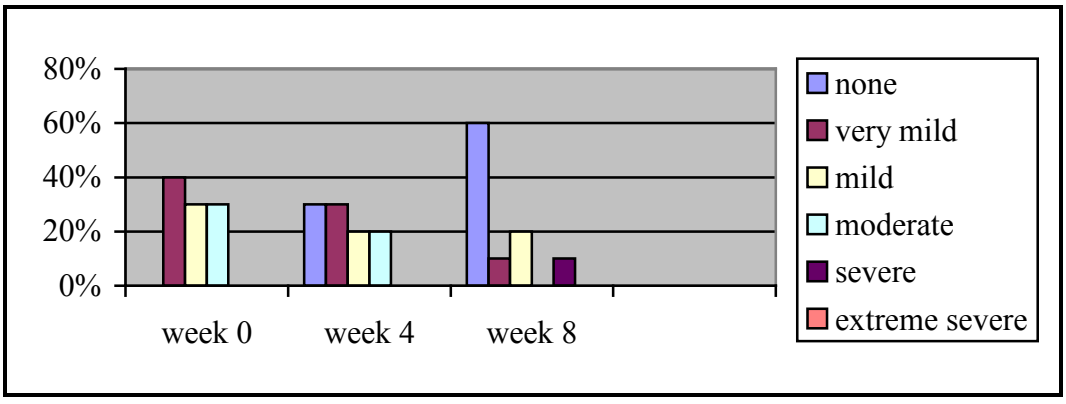
4.9.5 Pruritus / Itching

Figure 4.11 The Percentage of Participants Affected by Pruritus / Itching in The Treatment Group



A total of nine participants were affected by pruritus within this group. At the end of week 8, 33.3% (n=3) of the participants had no pruritus and 66.7% (n= 7) had a decrease in the severity of pruritus.

Figure 4.12 The Percentage of Participants Affected by Pruritus in the Placebo Group



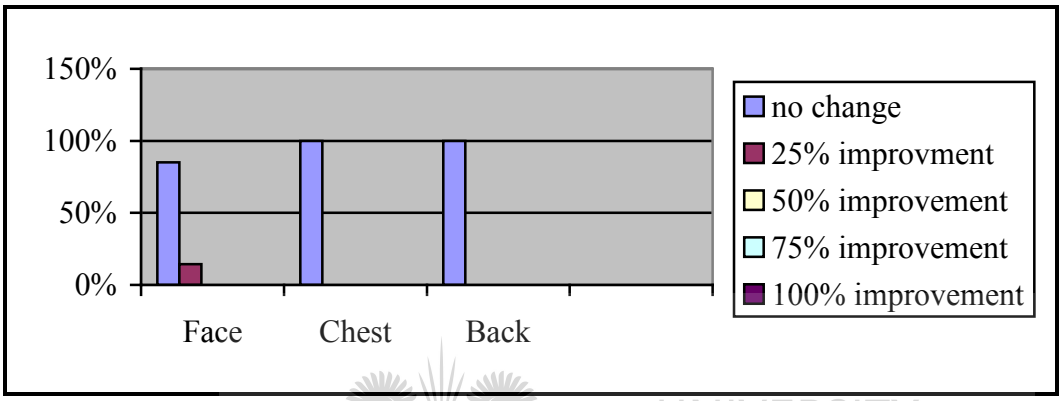
Ten participants within this group were affected by the associated symptom of pruritus. In the placebo group, 40% (n=4) had very mild pruritus and 30% (n=3) had mild pruritus at week 0. At

week 8, 60% (n=6) of the participants had no pruritus. This indicates that there was a greater improvement within the placebo group than in the treatment group.

4.10 Response to Treatment

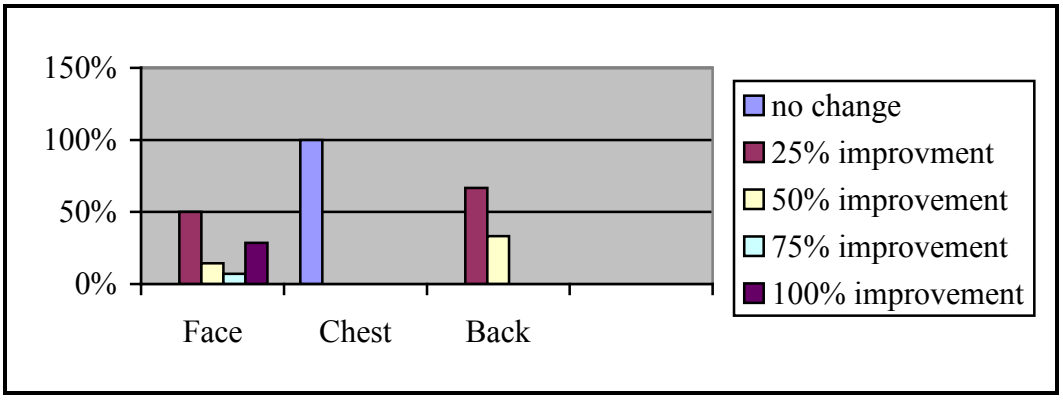
The response to treatment was assessed by the researcher at week 4 and week 8 by using the baseline photographs that were taken at week 0 (APPENDIX B).

Figure 4.13 Response to Treatment of the Treatment Group at Week 4



Within the treatment group, 14.3% (n= 2) of the participants affected with acne on the face showed a 25% improvement and 85% (n= 11) of the participants showed no change in their condition at week 4. All participants in the treatment group with acne on their chest and back showed no improvement at week 4.

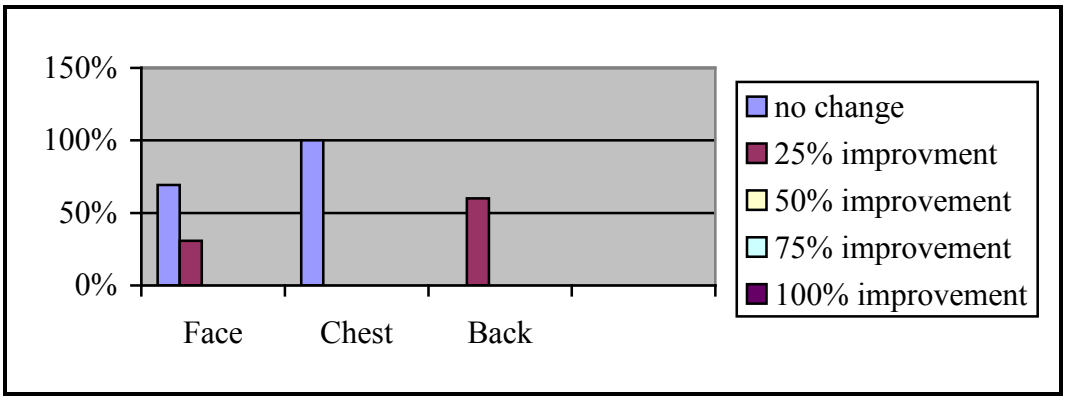
Figure 4.14 Response to Treatment of The Treatment Group at Week 8



At week 8, 50% (n=6) of participants with acne on the face and 66.7% (n=2) with acne on the

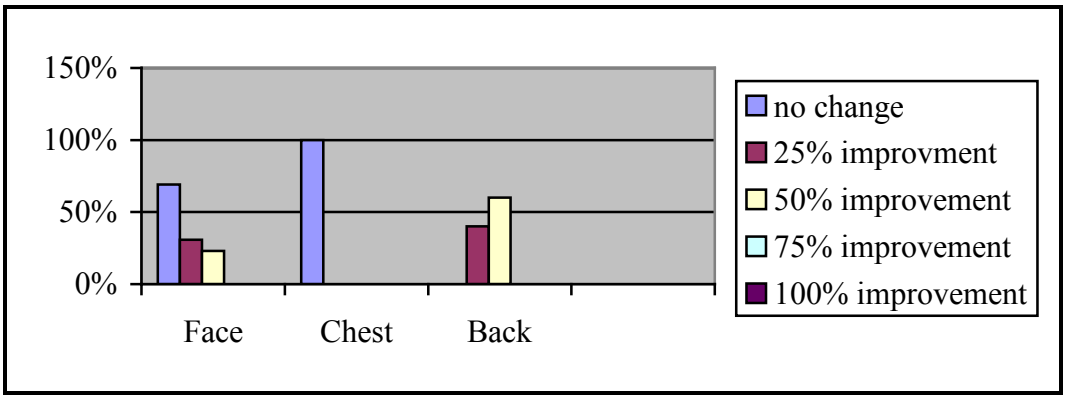
back showed a 25% improvement in their condition. 14.3% (n=2) of the participants with acne on the face and 33% (n=1) of participants with acne on the back showed a 50% improvement whereas the all the participants affected by acne on the chest within this group 28.6% (n= 4) showed no change in their condition.

Figure 4.15 Response to Treatment of the Placebo Group at Week 4



Within the placebo group, 30.8% (n=7) of the participants affected with acne on the face showed a 25% improvement and 69.2% (n= 9) of the participants showed no change to their condition. 60% (n=3) of the participants affected with acne on the back showed a 25% improvement in their condition at the end of week 4. All the participants affected with acne on the chest showed no change in their condition at week 4.

Figure 4.16 Responses to Treatment for the Placebo Group at Week 8



At week 8, 46.2% (n= 6) of the participants with acne on the face showed a 25% improvement in their condition, 23.1% (n= 3) of the participants showed a 50% improvement, and 30.8% (n=4)

of the participants within this group showed no change in their condition. Of the participants affected with acne on the back, 60% (n=3) of the participants showed a 50% improvement in their condition. Participants affected with acne on the chest showed a improvement in their condition only at week 8.

5. DISCUSSION

The sample group consisted of a total of 30 male participants, between the ages of 15-25 years, presenting with mild to moderate acne vulgaris. This group was then divided into two equal groups of 15 each, where one group was given the placebo and the other group was given the treatment R53 (Comedonin ®) acne drops. All of the participants were requested to take ten drops in water, three times a day. Evaluation took place at week zero, week four and week eight (APPENDIX B).

5.1 Surface Area

The surface area affected by acne vulgaris was calculated with the use of the Digermizer programmer using photographs of the affected areas taken by the researcher at week zero and week eight. This assessment was conducted in order to see the effect of R53 (Comedonin ®) acne drops on the surface area of the affected parts. In the treatment group, there was a 15% decrease in the surface area affected over the 8 week period (refer to Figure 4.1). This equates to a 15% improvement in total surface area affected. The placebo group showed a decrease in the surface area on the face and back and an increase in the surface area of the chest (Figure 4.2). The placebo group showed a total of 55% improvement in the total surface area affected on the face, chest and back. This could be due to increased awareness of the condition, hormonal changes or influences, changes in diet and the fact that acne vulgaris is a self-limiting condition that generally improves over time (Beers *et al.*, 2003).

The Friedman test indicated that there was no statistically significant change within the treatment group, however the placebo group showed a statistically significant change or improvement in the surface area affected over time (table 4.3). This could be possibly due to the fact that there is a strong psychological impact or influence in persons that are affected with acne, which is not linked with the severity of acne, but can possibly contribute to the placebo effect (Zip, 2008).

The p-value of the Mann-Whitney U Test showed that there was a lack of statistically significant difference between the treatment and the placebo group The p-value at week 8 for the face, chest and back was p=0.457,p= 0.355 and p=0.806 respectively (Table 4.4). The p-value of the Wilcoxon Signed rank test showed a lack of statistically significant change in the treatment

group (p=0.064, p=0.144, p=0.655) and the p-value in the placebo (p=0.028, p=0.043,p=0.465) showed a significant statistical change (Table 4.5). The p-values show that there was a greater improvement in the size of the surface area affected within the placebo group.

These findings could be due to the fact that in order for the total surface area affected to decrease, both the number of inflammatory lesions and non-inflammatory lesions have to decrease dramatically (Tan, 2008). The lack of a significant decrease in the number of lesion or decrease in affected surface area of the treatment group can be attributed to the fact that acne vulgaris has a multifactorial aetiology. Therefore, stress, hormones and diet can have an effect on the improvement or lack of improvement in this condition (Bolognia *et al*., 2003). A further possibility that there was a lack of compliance, and that the participants did not administer the medication as required.

5.2 Inflammatory Lesions

The Mann-Whitney U tests shows all p-value are not < 0.05 (Table 4.7), which indicated that there was no significant change between the groups for the number of inflammatory lesions to show a statistically significant result. This could possibly be due to the fact that many factors can contribute to the formation of inflammatory lesions, and thus it may take a long time to heal (Rajagopalan *et al*., 1998). The treatment plan of this study was possibly too short for an oral form of treatment, and a period of three months or longer may have yielded better results (Docrat, 2008).

The p-value in Table 4.8 shows that there was a lack of statistical significance for the number of inflammatory lesions. However, the p-value in the placebo group at week 4-8 (p=0.002) shows a statistically significant change, whereas the p-value at week 0-8 (p=0.016) showed that there was a lack of a statistically significant change. Overall, Table 4.8 shows that there was no statistically significant change over time between the treatment and placebo groups.

According to Woodard (2002), these results could possibly be due to the fact that the treatment period was too short to see the full effect of the treatment, as oral treatment should generally be given for three to six months. There is also a possibility that the D-potency used in the complex R53 (Comedonin ®) acne drops is too low (*Bromium* (D12) and *Kalium bromatum* (D12)) to

show the homoeopathic effect of the remedies as they still contain some traceable amount of active substance and therefore they are not working fully on homoeopathic principle alone. It is possible that if the potency of the remedies are increased, and the frequency of administration of the remedy decreased, that this could possibly improve the compliance of the participants and therapeutic effect (De Schepper, 2007).

Another possibility is that the study group was too small to show a statistically significant change. Furthermore, the deviation of more than one particular area affected namely face, chest and back, caused a greater subdivision of the small sample group as the smallest sample group should not be less then 15 (Pallant, 2007).

The remedies *Juglans* D30 and *Natrium chloratum* D200 may cause an undesired proving of the remedy and can considerably aggravate the presenting symptoms with frequent administration. This could also contribute to the initial aggravation of symptoms, again suggesting that the treatment period may have been too short (De Schepper, 2007).

Therefore it may be advantageous to use remedies that are all in the same potency instead of using different potencies.

5.3 Non-Inflammatory Lesions

Table 4.11 shows the mean and standard deviation of the non-inflammatory lesions within the treatment and placebo groups. The Mann-Whitney U test shows that all the p-values are not < 0.05. This shows that there was a lack of a statistically significant change between the two groups (Table 4.12). Again this could be due to the fact that acne is a multifactorial disease and therefore the appearance of these lesions are dependent on a variety of conditions, pathogens and even diet (Bolognia *et al*., 2003).

The p-value for the Wilcoxon Signed Rank test for participants affected with acne on the face shows that there is a p-value < 0.016 (according to the Bonferroni adjustment) for the treatment and placebo groups. Table 4.11 indicates that a statistical significance can be presumed. It was also noted that the treatment group had greater statistically significant change than the placebo group. This could be due to the fact that non-inflammatory lesions take a shorter time to heal as

there is less tissue damage caused by inflammation, and the fact that a decrease in the pathological factors like sebum production can play an important role (Boon *et al*., 2006).

The statistically significant p-values (0.004, 0.003 and 0.001) in Table 4.11 could be largely attributed to the fact that there was a larger number of participants in the sample group affected by facial acne (Table 4.2). The number of participants affected by acne on the back (in the treatment group n=4 and in the placebo group n=5) or chest (in the treatment group n=2 and in the placebo group n=4) was low, and therefore this made statistical validity of such a small sample group very difficult (Pallant, 2007).

5.4 Total Lesion Count

The evaluation of total lesion count was conducted by adding the lesion count scores of the inflammatory lesions and non-inflammatory lesions together.

The Mann-Whitney U test shows a p-value of the face, chest and back of > 0.05, which indicates that there was no significant change between the groups (Table 4.13). This could be due to the fact that there needs to be a relatively large improvement in both the inflammatory and non-inflammatory lesions in order to see a significant improvement or change between the placebo and the treatment groups as this will influence total lesion count (Tan, 2008).

The p-value for the Wilcoxon Signed Rank test was < 0.016 (according to the Bonferroni adjustment) for the treatment group. This indicates that a statistical significance can be presumed.

It was also noted that the p-values (0.002, 0.002, 0.001) for the treatment group had a greater statistically significant change than the placebo group (0.086, 0.030, 0.023) affected with acne vulgaris on the face (Table 4.14). This result could be due to the fact that there was a large percentage of the sample group affected by facial acne, and therefore, there was sufficient data to show a statistically significant change. Due to lack of data, this test was not conducted on participants affected by acne on the back and chest (Table 4.2). This result can also be due to the fact that there was a statistically significant decrease in the number of non-inflammatory lesions (Table 4.13), and therefore there is also a decrease in total lesion count. The presence of a large

sample group of participants is the most important possibility that should be considered (Pallant, 2007).

5.5 Associated Symptoms

Associated symptoms were assessed by grading the symptoms on a scale (APPENDIX B), which were recorded at the beginning of week 0, and at the end of week 4 and week 8.

5.5.1 Associated Symptom of Peeling

Figure 4.3 and Figure 4.4 show that the treatment group showed a greater improvement in the percentage of participants affected with the symptom of peeling, as compared to the placebo group. As participants affected with severe peeling within the treatment group decreased to 0% at the end off week 8.

5.5.2 Associated Symptom of Dryness

In the treatment group there was an aggravation in the symptom of dryness. These results were not statistically significant as there was insufficient data for analysis. This could be due to the remedies *Juglans regia* D30 and *Natrium chloratum* D200, which could cause an aggravation of the symptoms with frequent use (Dr. Reckeweg, 2010).

Within the placebo group, there was a decrease in the severity of dryness over the 8 week period. However, the data was not statistically significant as the sample group was too small to collect sufficient data for conclusive findings.

5.5.3 Associated Symptom of Oiliness

Oiliness of the skin within the treatment group at the end of week 8 decreased by 8%. There was a greater improvement in oiliness in the treatment group (Figure 4.5 and 4.6). This could be possible as the symptom of oiliness is dependent or sensitive to changes in hormones, stress levels and diet (Woodard, 2002).

5.5.4 Associated Symptom of Redness / Erythema

Figure 4.7 and 4.8 indicates that within the treatment group there was an improvement of the symptom of erythema at week 8. The remedies indicated for this symptom of redness/erythema *Juglans regia, Kalium bromatum*, *Natrium chloratum* and *Hepar Sulphuris Calcareum* (Clarke, 1994).

The placebo group also showed an improvement in symptom of redness however this can be due to the fact that the symptoms of acne vulgaris are very changeable and can be affected by diet, hormones, stress and (Bolognia *et al*., 2003).

5.5.5 Associated Symptom of Burning

Figure 4.9 and 4.10 shows that there was an improvement within the treatment group, regarding burning of the skin (Woodard, 2002). The remedies indicated for the symptom of burning are *Hepar sulphuris calcareum*, *Bromium* and *Kalium bromatum* (Vermeulen, 1997).

5.5.6 Associated Symptom of Pruritus / Itching

Figure 4.11 and 4.12 indicates that there was a greater improvement within the placebo group than in the treatment group for the symptom of pruritus. This could be due to the placebo effect (Zip, 2008).

The results from the scale overall show an improvement in the associated symptoms over the 8 week period. In some cases, it seems that due to the placebo effect, certain symptoms within the placebo group have shown to have a greater improvement than in the treatment group. This could be due to the very small samples and the fact that the associated symptoms of acne are very changeable and are dependent on many factors, like hormones and diet, as this can affect the sensitivity of the skin (Bolognia *et al*., 2003). The validity of this measurement can be questioned as it is subjective. The remedies indicated for the symptom of pruritus / itching are *Juglans regia*, *Bromium* and *Hepar sulphuris calcareum* (Clarke, 1994).

5.6 Response to Treatment

Response to treatment was assessed by comparing the base line-photographs of each participant at the beginning of week 0 to the participants' condition at week 4 and at the end of week 8 (APPENDIX B).

In the treatment group, the participants affected by acne on the chest showed a greater improvement than the participants affected with acne on the chest within the placebo group, which showed no improvement in their condition at the end of week 8 (Figure 4.14 and 4.16). However, within the treatment group, there were only two participants affected with acne on the chest and four participants with acne on the chest within the placebo group. Therefore there is a lack of statistical significance due to the fact that the sample group was very small (Pallant, 2007).

Of the participants affected by acne on the back, the placebo group showed a greater improvement than the treatment group (Figure 4.14 and 4.16). This can be due to the placebo effect (Zip, 2008). Table 4.2 again shows that there was a small number of participants affected with acne on the back and therefore there is a lack of statistical significance and evidence due to the small sample size (Pallant, 2007).

Of the participants affected by acne on the face, 85% of the participants in the treatment group and 69.2% of the participants in the placebo group showed no improvement at the end of week 4 (Figure 4.13 and 4.15). Figure 4.14 shows that 28.6% of the participants in the treatment group with acne vulgaris on the face showed no improvement in their condition at the end of week 8. However, the treatment group showed a greater improvement than the placebo group.

6. CONCLUSION AND RECOMMENDATIONS

6.1 Conclusion

This research study has determined that the homoeopathic complex, R53 (Comedonin ®) acne drops, did not show a statistically significant improvement or effect in the treatment of the severity of the symptoms of mild to moderate acne vulgaris on the face and associated symptoms of peeling, oiliness and burning related to the skin.

Evaluation of response to treatment showed a greater improvement within the treatment group than within the placebo group.

The p-value (<0.016) for the Wilcoxon Signed Rank Test, regarding the lesions count scores of the non-inflammatory lesion and total lesions over the 8 week period overall, showed that there was a significant improvement in the severity of symptoms of mild to moderate acne vulgaris according to the Wilcoxon Signed Rank Test and Mann-Whitney U Test within the treatment group.

6.2 Recommendations

The following recommendations should be considered in order to improve the research study:

- A larger sample group should be considered to produce reliable statistical data.
- A single affected area should be taken into account in order to produce reliable statistical data.
- The study should be extended over a three month period, in order to establish the effect that the treatment will have over a longer period of time.
- The potency of the remedies within the complex could possibly be evaluated, as the frequent use of high potencies can bring about an aggravation of symptoms, as proving of the remedies can occur.
- Compliance regarding of administration of medication should be monitored.

- Acne vulgaris is a multifactorial condition, and therefore dietary intake should also be considered as this can influence the skin in different ways and can increase the hormonal effect on the skin.
- The use of oral medication with a combination of a topical cream should also be considered as this has shown to be effective in the treatment of mild to moderate acne vulgaris (Beers *et al.*, 2003).

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APPENDIX A: INFORMATION AND CONSENT FORM

The efficacy of R53 (comedonin ®) acne drops in the treatment of acne vulgaris

Dear participant,

I am a 5th year homoeopathic student and I am currently completing my Masters degree within the field. I will be conducting a research study on "The efficacy R53 (comedonin ®) acne drops in the treatment of acne vulgaris."

Acne is a very common skin disorder with a wide range of treatment options. These therapies may also have side effects. Homoeopathy may possibly provide a more gentle form of therapy with fewer side effects. I will be conducting a study in the treatment of acne in males using a homeopathic complex called R53 (comedonin ®) acne drops.

I am inviting you to participate in this 8 week study on the homoeopathic treatment for acne. The total study group will be divided into two groups; one group will be given R53 (comedonin ®) acne drops and the second group will be given a placebo. A placebo is a substance that contains no medicinal properties. Each participant will be instructed to take the medication orally by putting ten drops in a little water three times a day before meals.

A full evaluation will be conducted on the first day of the study with follow up evaluations that will take place at week 4 and week 8. Treatment will be assessed by using different criteria. At each evaluation photographs of the affected area will be taken by me to be used for comparisons. The number of lesions on the affected area will be counted; evaluation of symptoms will be conducted using a five point scale and response to treatment will be graded by using a six point scale.

To be included in the study you must be a male between the ages of 15-25 years, with moderate to mild acne vulgaris. If however you are on any form of long term medication prior to the study, you will be unable to participate. You are requested not to take any long term medication during the study.

There are no anticipated risks for this study. This study can be beneficial as the treatment may reduce your acne and it will help to increase our knowledge on the use of homoeopathic treatment for acne vulgaris.

All participation in the study will be voluntary. You will be free to withdraw your consent at any time. You will have full right to confidentiality and privacy. You may ask questions related to

the study at any time. A copy of the results will be made available at your request. In all photographs the participant's identity will remain anonymous and unidentifiable as far as possible. All information obtained will be kept with strict confidentiality .

I hereby give my consent to participate in this study. I understand the benefits and risk of the study and I agree to the method of treatment. I understand my right to confidentiality and to withdraw my consent at any time.

Participant Name_____ Date _____

Parent / Guardian Name _____ Date _____

I have fully explained the nature and purpose of this study to the best of my ability. I will address all questions that will arise during the cause of this study.

Researcher _____ Date _____

Neeha Jivan Contact number: 0762024606

Dr.R. Razlog Contact number: (011) 559 - 6218/ 33

Dr.M. Caminsky Contact number: (011) 640 - 6260

APPENDIX B: ASSESSMENT SHEET

Participant name: _____ Date:_____

Number of bottle: _____

1. Lesion counts:

Area affected	Comedones (Non inflammatory lesions)			Inflammatory lesions			Total lesion count		
Week Date	O _____	4 _____	8 _____	0 _____	4 _____	8 _____	0 _____	4 _____	8 _____
Face									
Back									
Chest									

2. Associated symptoms

0 - None
1 - Very mild
2 - Mild
3 - Moderate
4 - Severe
5 - Extreme (Bekker, 2004).

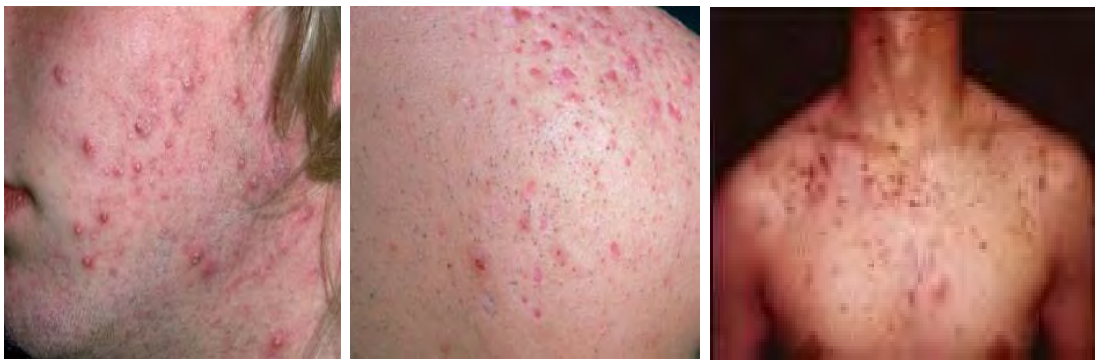
Signs and Symptoms	Participant's Score		
Week Date	0 _____	4 _____	8 _____
Peeling			
Dryness/ Oiliness			
Redness (erythema)			
Burning			
Itching (pruritis)			

2. Response to treatment:

	Face		Back		Chest	
Week Date	4 ____	8 ____	4 ____	8 ____	4 ____	8 ____
0 - Completely cleared						
1- 90% Improved						
2 - 75% Improved						
3 - 50% Improved						
4 - 25% Improved						
5 - No change						
6-Exacerbation (Bekker, 2004).						

Surface area	Face	Chest	Back
Week 0			
Week 8			

DO YOU SUFFER FROM ACNE ON YOUR FACE, CHEST OR BACK? (APPENDIX D)



If you are male and between the ages of 15 – 25 years, you may qualify to participate in a research study conducted by the Department of Homoeopathy on:

"The efficacy of Homoeopathic, acne drops in the treatment of Acne Vulgaris"

Ethical clearance number: AEC85/02-2010

This study will be conducted at the University of Johannesburg's Homoeopathic Health Centre.
All participation in the study is voluntary and strict confidentiality will be maintained throughout the study.

Qualified participants will receive **FREE** consultation and treatment.

For more information call: Neeha Jivan
O762024606