A STUDY OF THE RELATIVE EFFECTIVENESS OF A HOMOEOPATHIC COMPLEX CONSISTING OF: SILICEA TERRA 30CH, NATRUM MURIATICUM 15CH, SULPHUR IODATUM 15CH, KALIUM BROMATUM 9CH AND SELENIUM 9CH, AND A HERBAL COMPLEX CONTAINING: ECHINACEA PURPUREA, ARCTIUM LAPPA, BERBERIS AQUIFOLIUM AND TARAXACUM OFFICINALIS IN THE TREATMENT OF ACNE VULGARIS IN TERMS OF ITS CLINICAL MANIFESTATIONS.

BY

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I, Tanya Barklie do declare that this dissertation represents my own work in both conception and execution.

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DEDICATION

This dissertation is dedicated to my mother, Josette MacIntyre whose emotional, financial and spiritual support has been invaluable.

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ABSTRACT

The purpose of this study was to compare the relative effectiveness of a homoeopathic complex consisting of: *Kalium Bromatum* 9CH, *Selenium* 9CH, *Sulphur Iodatum* 15CH, *Natrum Muriaticum* 15CH and *Silicea Terra* 30CH; and a herbal complex containing: *Echinacea purpurea, Arctium lappa, Berberis aquifolium* and *Taraxacum officinalis* in the treatment of acne vulgaris in terms of its clinical manifestations.

This study was a double blind, randomised study. Convenience sampling was employed to draw 30 patients, of both sexes, from the greater Durban area. Only patients suffering from acne vulgaris were accepted into this study and those suffering from acne fulminans, acne rosacea or sandpaper acne were excluded. Anyone undergoing any other form of treatment or medication for acne vulgaris was excluded as well as any pregnant person.

Of the 30 patients, 15 received the herbal complex and 15 received the homoeopathic complex. Both the herbal and homoeopathic complex were prepared by the Technikon Natal Homoeopathic Day Clinic.

The relative effectiveness of the homoeopathic and herbal complex was measured in terms of the reduction in the total number of acne lesions i.e. the Leeds Technique for assessing acne vulgaris - the counting technique.

The statistical techniques for non- parametric data used were the Mann- Whitney unpaired test and Wilcoxon's signed rank test.

The results showed no difference in the efficacy of the herbal or homoeopathic complex in the treatment of acne vulgaris.

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DEFINITION OF TERMS

Acne Vulgaris: A skin disease characterised by comedones, erythematous papules, pustules, nodules and cysts (Kaminer and Gilchrest 1995).

Comedo: A plug of keratin and sebum within the dilated orifice of a hair follicle (W.B. Saunders 1988: 363).

Law of Similars: The remedy prescribed should produce the same symptoms in healthy people as experienced by the ill patient (Jouanny 1993: 11-14).

Papule: A small circumscribed, superficial solid elevation of the skin (W.B. Saunders 1988: 1221).

Pustule: A visible collection of pus within or beneath the epidermis, often in a hair follicle or sweat pore (W.B. Saunders 1988: 1392).

Similimum: The substance which produces the same symptoms in healthy people as those symptoms experienced by the ill patient (Jouanny 1993: 11-14).

CHAPTER ONE – INTRODUCTION

Acne is a disfiguring dermatosis which may cause significant emotional distress. It can destroy self-confidence and may profoundly affect self-esteem and is most prevalent in adolescence. (Oakley 1996.)

According to Cotteril and Cunliffe (1997), the face is very important in body image and young men with severe acne scarring are prone to becoming depressed and are at risk of suicide.

Acne vulgaris is characterised by comedones, erythematous papules, pustules, nodules and cysts (Kaminer and Gilchrest 1995).

A variety of allopathic therapies are currently used to treat acne vulgaris. Topical agents include tretinoin, benzoyl peroxide, antibiotics and other anti-inflammatory agents. Systemic therapy makes use of antibiotics, oral isotretinoin, corticosteroids, anti-androgens and sex hormones. (Bergfield 1995.)

However, according to Rees and Willey (1993) side effects of these medicines include erythema, exfoliation, contact sensitisation, pruritis, photo-irritation, xerosis, cheilitis, vestibular toxicity, foetal malformation and miscarriage.

Propionibacteria acnes is the most important organism involved in the inflammatory aetiology of acne vulgaris and it is the aim of many acne therapies to reduce the amount and function of this organism. There are many clinical failures, however, as not all patients respond to such therapies. (Sommer et al. 1997.)

In today's health care environment, increasing emphasis is being placed on economic considerations in the treatment of certain diseases. Based on information obtained from Bergfield (1995) the average cost involved in a 20 week course of isotretinoin therapy for acne vulgaris is 2318,55 U.S. dollars.

From this literature review it can be seen that there are shortcomings in the allopathic treatment of acne vulgaris. Herbal and homoeopathic medicines have been used for many years in the treatment of acne vulgaris but they have only recently been clinically tested.

Jouanny (1993: 277-284) based on his clinical experience recommends symptomatic homoeopathic remedies for acne vulgaris as well as remedies for treating the patients terrain.

McDavid (1994) investigated the use of the similimum in the treatment of acne vulgaris. It was found that Homoeopathy improved the clinical manifestations of acne vulgaris. The results were statistically significant (P = 0.006). The remedies most frequently prescribed were *Sulphur Iodatum* 15CH (22 times) and *Kalium Bromatum* 9CH (18 times).

In another clinical trial, Lee (1997) investigated the role of a homoeopathic complex in the treatment of acne vulgaris. The treatment period was 2 months with 5 consultations. The results showed no significant improvement over the period of 5 consultations within both groups or between both groups.

Seki and Morohashi (1993) investigated the effects of alkaloids and flavanoids in Japanese Kampoh (traditional herbal) drugs; experientially known to be efficacious for the treatment of Acne Vulgaris, on lipogenesis in the sebaceous glands of the hamster ear. The hamster sebaceous gland was used, as it is an excellent animal model for the human sebaceous gland which is affected in acne vulgaris. They found that lipogenesis in hamster sebaceous glands was suppressed 63% and 54% by 10(-4)M Berberine (an alkaloid) and Wogonin (a flavanoid) respectively.

De Waard (personal communication 1998) recommends an herbal complex of mother tinctures of *Echinacea purpurea, Taraxacum officinalis, Arctium lappa* and *Berberis aquifolium* in the treatment of acne vulgaris. He recommends a dosage of 10 drops in a little water twice daily.

As there are many shortcomings in the allopathic treatment of acne vulgaris, other forms of treatment need to be investigated. It is thus important to compare the relative effectiveness of a herbal complex and a homoeopathic complex in the treatment of acne vulgaris in terms of it's clinical manifestations.

CHAPTER TWO - REVIEW OF THE RELATED LITERATURE

2.1 Definition and classification

Acne vulgaris is a skin disease characterised by comedones, erythematous papules, pustules, nodules and cysts.

The spectrum of acne:

Acne related to intrinsic causes: Acne vulgaris

Perioral dermatitis

Acne conglobata

Hydradenitis suppurativa

Acne fulminans

Pyoderma faciale

Acne related to extrinsic causes: Acne excoriee des jeunes filles

Acne mechanica

Acne tropicalis

Acne aestivalis

Favre-Racouchet syndrome

Drug-induced acne

Acne cosmetica

Pomade acne

Occupational acne

Chloracne

Childhood acne: Neonatal acne

Infantile acne

Acneiform eruptions: Rosacea

Acne keloidis nuchae

Gram-negative folliculitis

Steroid acne

(Kaminer and Gilchrest 1995.)

2.2 Psychosocial Effect of Acne

In a study by Girman et al. (1996) acne patients expressed concern about social interactions; particularly in meeting new people, socialising, going out in public or interactions with the opposite sex.

Cunliffe (1986) found that unemployment levels were significantly higher among acne patients than in a control group.

2.3 Aetiology

2.3.1 Genetics

It is often said that acne is an inherited disease, but although the circumstantial evidence is convincing, definitive proof is lacking. In an investigation of 95 pairs of identical twins with acne, in 97,9 percent of pairs, both twins were affected. Amongst dizygotic twin pairs, in 45,8 percent only one of each set had acne. (Cunliffe 1989:4-6.)

Identical twins have identical rates of sebum excretion, but although both may have acne, the severity is not identical (Walton et al. 1988).

2.3.2 Racial Studies

Acne in white Americans has been found to be more severe than in Japanese in Tokyo and Yokohama. These observations, and the previously reported higher incidence of male pattern baldness in Caucasoids than in Mongoloids, are in accord with the hypothesis that tendencies to pronounced development of secondary sex characteristics may merge with tendencies to certain sex-selective pathologic conditions. (Hamilton et al. 1964.)

2.3.3 Diet

Until two decades ago, the prevailing clinical impression among dermatologists was that of a relationship between acne and diet. Until around 1970, dermatologists told their patients to avoid certain foods, especially pork fat, chocolate, nuts etc. In a 1987 study investigating the relationship between acne severity and diet, one hundred acne subjects were interviewed by a dietician to establish their eating habits. No correlation was found between acne severity and types of food ingested. (Cunliffe 1989: 7.)

Fulton et al. (1969) in a study of 65 subjects with acne and 5 normal subjects found that the ingestion of large amounts of chocolate did not materially affect the course of acne vulgaris or the composition of sebum.

2.3.4 Stress

Kenyon (1960) investigated a group of adult women with acne and a group matched for sex, age and civil status but with a facial dematosis other than acne. It was concluded that acne was not purely a psychogenic condition but was intimately involved with endocrine factors. In the predisposed individual, however, exacerbations of acne could occur following emotional stress.

2.3.5 Sebum

The quantitative secretion of sebum was found to be very much greater in males with acne than in normal controls. Among acne subjects, the cases with minimal involvement showed less sebaceous gland activity than those with more severe acne. (Pochi and Strauss 1964.)

2.3.6 Hormones

Acne vulgaris is androgen dependent but the hormonal mechanisms are unclear (Ramsay et al. 1995).

The three major sources of androgens in women include the ovary, the adrenal gland and the skin. In abnormalities of ovarian secretion such as polycystic ovary syndrome, there is overproduction of ovarian androgen. It is a well-known clinical observation that women with polycystic ovary syndrome often have acne. (Lucky 1995.)

Lucky et al. (1983) found that more than half of a group of young adult women whose primary complaint was acne had elevated androgens or androgen precursors.

There is disagreement over whether or not men with acne have higher levels of androgens in their plasma. Lim and James (1974) found that in men with acne, there was no significant difference in androgen levels in the plasma to those of controls. Ramsay et al. (1995) found that in men with acne, the medians of androstenedione, testosterone and free androgen index were significantly higher than those of controls. In normal men the sources of androgens are the adrenal, testes and extra-glandular sites including the skin. As judged by sebum output, the sebaceous glands are overactive in acne and it is possible that the hyperactive sebaceous glands could be the sole source of excess androgen.

2.3.7 Menstrual cycle and pregnancy

Certain physiological factors such as the menstrual cycle are thought to modify acne. Sixty to seventy percent of female subjects noticed a deterioration of their acne in the week before menstruation (Cunliffe 1989:6.)

Adult premenstrual acne makes its appearance in adult women between the ages of 20 and menopause. The lesions are confined to the face and may make their appearance at any time during a two-week period preceding the onset of menstruation. Approximately 50% of the patients complain of menstrual disturbances in the form of irregular periods and premenstrual tension. (Newman and Feldman 1954.)

Ratzer (1964) found that in women with acne vulgaris, pregnancy had a markedly beneficial influence.

2.3.8 Other factors

Acne in women in their 20's, 30's and 40's is frequently caused by comedo-producing oil-based cosmetics and moisturisers. Mechanical factors such as rubbing, friction pressure and stretching of the skin rich in sebaceous glands can trigger acne. Among the more common mechanical causes are football helmets, surgical tape, shirt collars and wrestling. (Stawiski 1992:1006.)

2.4 Pathophysiology

The clinical expression of acne vulgaris ranges from non-inflamed open and closed comedones ("blackheads" and "whiteheads") to inflammatory papules, pustules and nodules (Webster et al. 1979).

The precursor lesion in the pathogenesis of acne is the microcomedo, which then develops into inflammatory or non-inflammatory lesions. The mechanism which controls whether a microcomedo will result in a mature comedo or an inflamed lesion is not yet understood. (Dolitsky and Shalita 1989.)

Comedo formation involves a significant change in the formation and desquamation of the keratinised cell layer inside the infundibulum of the pilosebaceous canal (Knutson 1974).

One or more components of sebum have a direct stimulating effect on the follicular epithelium causing it to produce an excessive quantity of horny cells (Kligman and Katz 1968).

The 'free fatty acid' theory of acne pathogenesis attributed the genesis of both comedones and inflammatory lesions to the free fatty acid portion of sebum. Kligman and Katz (1968) demonstrated that free fatty acids are comedogenic when applied to the external ear canal of rabbits.

Marked inflammation was induced clinically and histologically by the injection of sebum into human skin. The amount of inflammation was much reduced, however, when sebum was injected after prior removal of the free fatty acids. (Strauss and Pochi 1965.)

Kellum (1968) found that the topical application of fatty acids to human skin produced a primary irritant response. The C_8 to C_{14} acids, particularly the C_{12} acid, were found to be the most irritating.

Puhvel and Sakamoto (1977) questioned the free fatty acid theory of acne pathogenesis. They measured the quantities of fatty acids present in isolated pilosebaceous ducts and comedones by lipid analysis. Using these values, the effect of fatty acids on intracutaneous injection into human skin was investigated. No more than a very mild inflammatory reaction was produced.

Tucker et al. (1980) felt that the lack of inflammation caused by the experiments of Puhvel and Sakamoto may have been because they injected the free fatty acids into the dermis which would lead to a rapid decrease in concentration as the fatty acids diffused through the dermal space. Comedonal contents, by contrast, are isolated from the dermal space by epithelium. The concentration of free fatty acids at breaks in the comedonal wall would thus be less subject to rapid dilution because of the large reservoir of free fatty acids within the comedonal compartment.

Free fatty acids of skin surface lipids are derived from lipolysis of sebum triglycerides by esterases of bacterial origin (Marples et al. 1972).

All types of acne lesions (open and closed comedones, pustules and cysts) contain either a mixed population of *Corynebacterium acnes* (*Propionibacterium acnes*) and *Staphylococcus albus* (*Staphylococcus epidermis*) or pure cultures of either (Shehadeh and Kligman 1963).

Corynebacterium acnes is the organism which regulates the level of free fatty acids under ordinary circumstances. It's influence is much greater than the yeast Pityrosporum, since abolition of yeasts is without effect on free fatty acids, whereas suppression of *Corynebacterium acnes* leads to very low levels of free fatty acids. (Marples et al. 1972.)

Squalene is a free fatty acid derivative which has comedogenic properties. Squalene oxidation is a promoting factor in comedogenesis and may encourage the proliferation of micro-aerophilic flora due to the large amount of atmospheric oxygen bound during the oxidative process. (Saint-Leger et al. 1986.)

Inflammation in acne patients may be modulated by varying host response to inflammatory mediators (Dolitsky and Shalita 1989). Titres of antibodies to *Propionibacterium acnes* are significantly higher in patients with acne than in control groups (Puhvel et al. 1964).

Kirschbaum and Kligman (1963) hypothesised whether *Corynebacterium acnes* could proliferate in certain cysts and bring about their rupture; thereby precipitating an inflammatory lesion. When *Corynebaterium acnes* organisms were subsequently injected into non-inflamed cysts, severe inflammation was caused.

Propionibacterium acnes and its cellular constituents can propagate inflammation by the activation of complement by both the classical and alternative pathways, thereby generating C5 dependent chemotactic factors from human serum (Webster et al. 1978). The stimulation of the alternative pathway activation of complement might be responsible for the conversion of a non-inflamed lesion to an inflamed lesion. This activation generates products which increase vascular permeability with subsequent leakage of plasma to produce oedema. (Scott et al. 1970.)

Propionibacterium acnes can also stimulate inflammation by the production of small molecular weight, serum-independent chemotactic factors (Puhvel and Sakamoto 1978).

Vowels et al. (1995) demonstrated that intact cells of *Propionibacterium acnes* and *Propionibacterium acnes* culture supernatant are able to directly stimulate the production of proinflammatory cytokines by both the human monocytic cell lines and by peripheral blood mononuclear cells.

2.5 Treatment

2.5.1 Allopathic Treatment

For patients with noninflammatory, comedonal or mild-to-moderate papulopustular acne, the first approach to treatment is usually topical therapy.

When moderate-to-severe acne does not respond to topical therapy, systemic therapy with oral antibiotics is used. Oral isotretinoin is used for patients who do not respond to either topical or systemic therapy. (Bergfield 1995.)

2.5.1.1 Topical Treatment

Benzoyl peroxide is a broad-spectrum antibacterial agent which produces death via the interaction of oxidised intermediates with various constituents of microbial cells (Eady et al. 1994). Benzoyl peroxide was found to be a potent skin sensitiser in repeated insult patch tests (Poole et al. 1970).

Topical tretinoin is the most effective keratolytic agent (Bergfield 1995). Commercially available tretinoin use resulted in glazing with peeling and cracking, glazing with fissures, and erythema that was more severe and affected more sites than that associated with tretinoin containing polyolprepolymer-2 (Mills and Berger 1998).

The two most utilised topical antibiotic agents are erythromycin and clindamycin (Bergfield 1995). They have anti-inflammatory properties and reduce the pustular reaction (Esterly et al. 1978).

A gel containing 3% erythromycin with 5 % benzoyl peroxide has been shown to be more effective than either agent alone in reducing papules and pustules (Chalker et al. 1983).

In the treatment of acne vulgaris, 4% nicotinamide gel is of comparable efficacy to 1% clindamycin gel. Topical clindamycin, as with other antimicrobials, is associated with the emergence of resistant microorganisms and thus nicotiamide gel is a desirable alternative treatment for acne vulgaris. (Shalita et al. 1995.)

Topically used Silicol gel is a promising new treatment for patients with papulopustular acne of long duration (Lassus 1996).

In a large clinical trial comparing the efficacy and safety of 0.1% adapalene gel and the commercial 0.025% tretinoin gel, adapalene produced significantly greater reductions in acne lesion counts than the tretinoin gel. Mild irritation was reported in both groups. (Shalita et al. 1996.)

2.5.1.2 Systemic treatment

Minocycline is a derivative of tetracycline which is commonly used in the treatment of facial acne. Liver disease due to minocycline may be much more common than appreciated. With increasing minocycline usage for acne, hepatic injury due to minocycline may become increasingly more common. (Malcolm et al. 1996.)

Patients receiving minocycline therapy can develop pulmonary infiltrates and eosinophilia after a few days to a few weeks of treatment (Sitbon et el.1994).

Of 468 patients with acne attending the outpatient clinic at Leeds General Infirmary between 1 March 1991 and 29 February 1992, 178 patients carried propionibacterial strains resistant to one or more antibiotics (Eady et al. 1993).

Suitable oestrogen-progesterone combinations or low dose prednisolone may be given, alone or in combination, to suppress free circulating androgens in women with persistant acne vulgaris with a high probability of improving their acne (Darley et al. 1983).

It is possible that isotretinoin (13-cis-retinoic acid), which is effective clinically in the severe inflammatory forms of acne, acts as an anti-inflammatory agent by inhibiting lysosomal enzyme secretion from neutrophils (Camisa et al. 1982).

Isotretinoin appears to be clinically more effective in severe acne than oral antibiotics, and has the benefit of long remission periods, but it is associated with considerably more side effects. These side effects include cheilitis, facial dermatitis, epistaxis, desquamation, arthralgia, conjunctivitis and malaise. The drug causes a rise in the SGOT (serum γ glutamyl–o-transferase) which presumably reflects inflammatory changes in the liver. (Jones et al.1983.).

2.5.2 Homoeopathic Treatment

Jouanny (1993:277-284) based on his clinical experience recommends symptomatic remedies for acne vulgaris as well as remedies for treating the patient's terrain. Symptomatic remedies include *Selenium* 9CH, *Eugenia Jambosa* 5CH, *Ledum Palustre* 5CH, *Calcarea Picrata* 5CH *Kalium Bromatum*, 9CH, *Antimonium Tartaricum* 5CH and *Graphites* 9CH. Remedies for treating the terrain include *Sulphur*, *Thuja Occidentalis*, *Natrum Muriaticum*, *Sulphur Iodatum* and *Silicea Terra*.

Dr Med. Vassilis Ghegas recommends taking a complete history from the patient to see if there is an obvious constitutional remedy. After prescribing the constitutional remedy, the doctor should wait for 3 months, and then search for a specific remedy for the specific type of acne, which remains. A specific remedy can also be given when no constitutional remedy can be found. (Ghegas 1987.)

McDavid (1994) investigated the use of the similimum in the treatment of acne vulgaris. The author used an experimental group of 15 which received the similimum and a placebo group of 15. The treatment period was 4 months with 5 consultations. It was found that Homoeopathy improved the clinical manifestations of acne vulgaris ($p=0.006$). The remedies most frequently prescribed were *Sulphur Iodatum* 15CH (22 times) and *Kalium Bromatum* 9CH (18 times).

In another clinical trial, Lee (1997) investigated the role of a homoeopathic complex in the treatment of acne vulgaris. In the study, a control group of 16 patients received placebo and an experimental group of 18 patients received a homoeopathic acne complex consisting of *Silicea Terra* 30CH, *Selenium* 9CH, *Hepar Sulphuris Calcarea* 30CH, *Kalium Bromatum* 9CH, *Arctium Lappa* 3CH and *Pulsatilla Praetensis* 30CH. The treatment period was 2 months with 5 consultations. The results showed no significant improvement over the period of 5 consultations within or between both groups.

Homoeopathy is based on the law of similars and it is thus important to understand the symptom pictures (relating to acne) of the remedies used to compile the homoeopathic acne complex.

Kalium Bromatum: Acne of the face, pustules, itching acne, worse on chest, shoulders and face, scars remain after eruptions (Vermeulen 1997: 935).

Natrum Muriaticum: Comedones, small boils (Vermeulen 1997: 1182).

Selenium: Comedones, oily surface of skin, acne (Vermeulen 1997: 1451).

Silicea Terra: Painful pustular eruptions, acne, disposition to boils (Vermeulen 1997: 1483).

Sulphur Iodatum: Comedones, small boils (Vermeulen 1997: 1556)

2.5.3 Herbal Treatment

Seki and Morohashi (1993) investigated the effects of alkaloids and flavanoids in Japanese traditional herbal drugs that are experientially known to be efficacious for the treatment of acne vulgaris. They found that lipogenesis in hamster sebaceous glands was suppressed 63% and 54% by 10 (-4)M Berberine (an alkaloid) and Wogonin (a flavanoid) respectively.

Hoffman (1996: 215) mentions according to his clinical experience the use of herbs such as *Scrophularia nodosa, Galium aparine, Trifolium pratense, Mahonia* (*Berberis*) *aquifolium, Rumex crispus, Phytolacca decandra, Echinacea purpurea, Taraxacum officinalis, Iris versicolor* and *Arctium lappa* in a herbal approach to the treatment of acne and skin diseases.

De Waard (personal communication 1998) recommends an herbal complex of mother tinctures of *Echinacea purpurea, Taraxacum officinalis, Arctium lappa* and *Berberis aquifolium* in the treatment of acne vulgaris. He recommends a dosage of 10 drops in a little water twice daily.

2.3 Summary

Acne vulgaris is a very common skin disease that can cause severe emotional suffering in those who it affects. The allopathic drugs currently used in the treatment of acne have side effects severe enough to warrant a search for other forms of medication.

Homoeopathy is frequently used in the treatment of acne, however there have been conflicting results in studies done to assess the efficacy of Homoeopathy in the treatment of acne vulgaris. Herbal complexes are also frequently used in the treatment of acne vulgaris, but no studies have been conducted to assess the relative efficacy of herbal complexes in the treatment of acne.

A search of the indexes of the British Homoeopathic Journal 1982-1998 and Medline 1993-1998 reveals no research on the relative effectiveness of herbal and homoeopathic complexes in the treatment of acne vulgaris. There is thus a need to test the relative effectiveness of a herbal complex and a homoeopathic complex in the treatment of acne vulgaris.

CHAPTER 3 – MATERIALS AND METHODS

The objective of the research was to evaluate the relative effectiveness of an herbal and homoeopathic acne complex by measuring the reduction in the number of acne lesions on the patients' faces.

The study was a double blind clinical trial.

3.1 Advertising

Posters detailing the research and inviting participation were placed on notice boards at the Technikon Natal and in Health Shops and Pharmacies.

3.2 Selection

3.2.1 Selection criteria

Inclusion criteria: Patients had to have Acne Vulgaris lesions on the face as defined by Burke and Cunliffe (1984) to be included in the research.

Exclusion criteria: Any patient who was pregnant or undergoing any other form of treatment or medication for acne vulgaris was excluded. Patients suffering from acne fulminans, acne rosacea or sandpaper acne were excluded.

All patients had to be off acne treatment of any form for at least 4 weeks before the start of research treatment.

Ideally patients should be off treatment for at least 3 months before starting research but in practice this is normally impossible. This ensures that subjects are off treatment for a selected minimum period before a clinical trial in order to establish an adequate baseline. (Burke and Cunliffe 1984.)

3.2.2 Selection of patients by convenience sampling

30 patients were selected for the research. The selection was done by convenience sampling. The patients were of both sexes and from the greater Durban area. They were randomly divided into 2 groups (herbal complex and homoeopathic complex) in such a way that each patient had an equal chance of being selected for either group. A list of numbers ranging from 1 to 30 were made. Thirty pieces of paper were placed in an envelope of which 15 were marked herbal and 15 homoeopathic. An independent person (receptionist at Technikon Natal Homoeopathic Day Clinic) drew 1 piece of paper at a time and allocated either herbal or homoeopathic to the list of numbers from 1 to 30.

As each patient presented for treatment he was allocated a number sequentially from the list and in this way the dispenser knew whether to give the patient the herbal or homoeopathic complex.

3.3 Treatment

The herbal complex consisted of mother tinctures of *Taraxacum officinalis, Arctium lappa, Berberis aquifolium* and *Echinacea purpurea* mixed in an equal ratio.
The mother tinctures were supplied by Pharma Natura. Patients in the herbal complex group were each allocated two 25ml bottles of the herbal complex. They were instructed to take 10 drops of the complex in a little water twice daily 15 minutes before meals for 2 months.
The homoeopathic complex consisted of two number 2 vials of Saccharum lactus impregnated with: *Kalium Bromatum* 9CH, *Sulphur Iodatum* 15CH, *Silicea Terra* 30CH, *Selenium* 9CH and *Natrum Muriaticum* 15CH
The group allocated the homoeopathic complex was instructed to take a quarter capful of the complex half an hour after breakfast once every three days for 2 months.

In order for the research to be double blind, the researcher could not be aware of whether the patient received a homoeopathic or herbal complex. Therefore the patients were instructed not to mention to the researcher whether they were taking drops or granules or the dosage of their medicine. The independent clinician who administered the medicine placed the relevant instructions on the bottle or vial.

3.3 Assessment

At the first consultation each patient was assessed and the number and type of lesions tabulated. Only acne vulgaris lesions on the face were counted. Each patient participated in the research for 3 months. The patients took either the herbal or homoeopathic complex for 2 months, followed by a month during which they did not take the complex.

Each patient attended 3 follow-up consultations. After each month, the patient's acne lesions were observed by the researcher and any changes in number or type noted. Patients were observed by the same researcher under the same lighting conditions at each visit. Lighting was with an overhead flourescent light. Clinical manifestations of the Acne Vulgaris in the patients were measured by using the Leeds Technique (Burke and Cunliffe 1984).

3.3.1 The Leeds Technique for assessing acne – the counting technique

Lesions were divided into inflamed and non-inflamed as follows.

(a) *Non-inflamed lesions* were blackheads or whiteheads. Any intermediate lesions were counted according to their major component. Prominent follicles, small milia or trichostasis spinulosa must be rigorously excluded as they occur frequently and would badly skew the results.

(b) *Inflamed lesions* were either superficial (papules and pustules) or deep (nodules, cysts and deep pustules).

(i) *Superficial papules and pustules* varied in size from 0.1 cm (with minimal erythema) to 0.5 cm (with a marked macular flare). The smaller less inflammatory lesions were referred to as 'less active papules or pustules', the larger erythematous lesions as 'active papules or pustules'. Some 40% of lesions fell between these two types but in practice we assigned the lesion according to it's major component.

(ii) *Deep inflamed lesions* were predominantly nodules which were 0.5 cm or larger. Palpation was essential, since some nodules were almost invisible but easily palpable.

(iii) *Macules* represented the resolving phase of either superficial or deep lesions and were either large or small. They should be included in acne assessment as they contribute to the overall degree of inflammation. As they evolve they become brown and much less distinct. The counting of individual lesions may then be very difficult.

Lesion counting is not easy and perfection takes time. Attention to the following points will help to avoid errors.

(1) The patient should be sitting comfortably so that the observer can move around him easily to count each area.

(2) In addition to good background flourescent lighting, we recommend using a Brighton 1001 flourescent lamp, which can be easily moved to illuminate both sides of the patient during the examination.

(3) When counting, we divide the face into the right and left sides and count both sides. In some patients the lesions are clustered around the midline, making a right-left division difficult; we then count the forehead, the cheeks and chin seperately and combine the counts. Some authors count lesions from one area only. As acne affects several sites and may improve at one site as it deteriorates at another, we prefer to count the whole face.

(4) Palpation is necessary because some macules may look like a nodule, but on palpation show no depth at all. Conversely, a nodule may be hardly visible and yet it can be felt to lie deep to the skin.

(5) Stretching of the skin will increase the number of whiteheads and blackheads that are visible, but as the degree of stretching may vary, this is not permitted. For similar reasons we recommend that no lens be used. If a lesion is impalpable, and not obvious with good lighting, then such a vague lesion is best ignored.

Pitfalls for the unwary

Prominent follicles. Confusion of non-inflamed lesions with prominent follicles is a problem around the nose and on the chin, especially in mid-teenagers. In therapeutic trials, we recommend that non-inflamed lesions be not counted either on the nose or around the edge of the nose.

Sandpaper acne. Two percent of youngsters have the so-called 'sandpaper' acne. In these patients the forehead is covered with many (usually 100 or more) very superficial lesions, which are impossible to classify correctly. Such patients should be excluded from clinical trials.

Hair styles. Many young people change their hairstyle frequently. Long, uncut hair may mask non-inflamed lesions, and we avoid counting them around the hairline. However there is usually no difficulty in recognizing inflamed lesions in this area.

Shaving. Patients may grow a moustache or a beard during the trial and this will complicate the results. Patients may also develop low grade folliculitis on the chin and neck as a result of shaving trauma. However, the papules and pustules associated with a folliculitis are much less easily felt than acne lesions. Patients should shave daily, preferably at a constant time, as stubble can affect the interpretation of all lesions.

Cosmetics. Despite advice to the contrary, some females will use make-up. This must be removed and the patient observed 30 minutes later, when the erythema resulting from washing has settled.

Ultraviolet radiation. This will camouflage the non-inflamed lesions and make the inflamed lesions look less inflamed. For this reason, trials should not be performed in the summer.

Other dermatoses. Sycosis barbae may occur in association with acne and low grade seborrhoeic eczema may simulate a primary irritant dermatitis seen commonly with such treatments as benzoyl peroxide.

3.4 Statistical Analysis

The number and type of lesions were tabulated at each consultation in order for statistical analyses to be made.

Group 1 contained 15 patients that made the herbal group. Group 2 contained the remaining 15 patients that made the homoeopathic group. Since the sample size per group was small (n_1=15, n_2= 15), non-parametric methods were used for data analyses. Three variables of study were used: number of non-inflamed lesions, number of inflamed lesions and the total number of lesions. There were 4 consultations for each of the 3 variables of study.

Procedure 1: Comparison between Group 1 (herbal) and Group 2 (homoeopathic)

Mann-Whitney unpaired two-tailed tests were used to compare Groups 1 and 2 with respect to each variable of interest.

In each test, the null hypothesis states that there is no significant difference between Groups 1 and 2 with respect to the variable of interest, at the α=0.05 level of significance. The alternative hypothesis states that there is a significant difference.

Ho: $u_1 = u_2$

H_1: u_1 and u_2 are significantly different from each other.

$\alpha = 0.05$ = significance of test.

Decision rule:

The null hypothesis is rejected at the α level of significance if $p \leq \alpha/2$ where p is the observed significance level or P-value. Otherwise the null hypothesis is accepted at the same level:

Reject Ho if $p \leq \alpha/2 = 0.025$

Accept Ho if $p > \alpha = 0.025$

Procedure 2: Comparison between related samples within Group 1 (herbal)

Wilcoxon's sign ranked tests were used to compare results between related samples in Group 1 to find out whether there were any significant improvements between consultations 1 and 2, 1 and 3, 1 and 4, 2 and 3, 2 and 4 and 3 and 4, with respect to each variable of interest.

In each test, the null hypothesis states that there is no significant level of improvement between the 2 related samples being compared, at the α level of significance. The alternative hypothesis states that there is a significant improvement.

Ho: $u_1 = u_2$

H_1: u_1 and u_2 are significantly different from each other.

$\alpha = 0.05$ = significance of test.

Decision rule:

The null hypothesis is rejected at the α level of significance if $p \leq \alpha/2$ where p is the observed significance level or P-value. Otherwise the null hypothesis is accepted at the same level.

Reject Ho if $p \leq \alpha/2 = 0.025$

Accept Ho if $p > \alpha = 0.025$

Procedure 3: Comparison between related samples within Group 2 (homoeopathic)

Wilcoxon's sign ranked tests were used to compare results between related samples in Group 2 to find out whether there were any significant improvements between consultations 1 and 2, 1 and 3, 1 and 4, 2 and 3, 2 and 4 and 3 and 4, with respect to each variable of interest.

In each test, the null hypothesis states that there is no significant level of improvement between the 2 related samples being compared, at the α level of significance. The alternative hypothesis states that there is a significant improvement.

Ho: $u_1 = u_2$

H_1: u_1 and u_2 are significantly different from each other.

$\alpha = 0.05$ = significance of test.

Decision rule:

The null hypothesis is rejected at the α level of significance if $p \leq \alpha/2$ where p is the observed significance level or P-value. Otherwise the null hypothesis is accepted at the same level.

Reject Ho if $p > \alpha/2 = 0.025$
Accept Ho if $p > \alpha = 0.025$

(Van den Honert 1997.)

Statistical package:

The statistical package **Statgraphics** was used for data entry and analysis.

CHAPTER 4 - RESULTS

Table 1: Comparison of number of **non-inflamed lesions** in Group 1 (herbal) and Group 2 (homoeopathic).

(Mann-Whitney Test)

Consultation	S.L.	P-value	Ho
1	0.05	0.177	Accept
2	0.05	0.044	Accept
3	0.05	0.245	Accept
4	0.05	0.205	Accept

S.L.: significance level

Ho: there is no significant difference between Group 1 and Group 2.

Conclusion: there appears to be no significant difference in the number of non-inflamed lesions between the Herbal and Homoeopathic group over the four consultations at the $\alpha = 0.05$ level of significance.

Table 2: Comparison of number of **inflamed** lesions in Group 1 (herbal) and Group 2 (homoeopathic).

(Mann-Whitney Test)

Consultation	S.L.	P-value	Ho
1	0.05	0.228	Accept
2	0.05	0.114	Accept
3	0.05	0.191	Accept
4	0.05	0.361	Accept

S.L.: significance level

Ho: there is no significant difference between Group 1 and Group 2.

Conclusion: there appears to be no significant difference in the number of inflamed lesions between the Herbal and Homoeopathic group over the four consultations at the $\alpha = 0.05$ level of significance.

Table 3: Comparison of **total number of lesions** in Group 1 (herbal) and Group 2 (homoeopathic).

(Mann-Whitney Test)

Consultation	S.L.	P-value	Ho
1	0.05	0.836	Accept
2	0.05	1	Accept
3	0.05	0.967	Accept
4	0.05	0.507	Accept

S.L.: significance level

Ho: there is no significant difference between Group 1 and Group 2.

Conclusion: there appears to be no significant difference in the total number of lesions between the Herbal and Homoeopathic group over the four consultations at the $\alpha = 0.05$ level of significance.

Table 4: Comparison of samples within the Herbal group. (Number of **non-inflamed lesions**.)

(Wilcoxon's Signed Rank Test)

Samples	S.L.	P-value	Ho
Sample 1 t11 Sample 2 t21	0.05	0.789	Accept
Sample 1 t11 Sample 2 t31	0.05	0.579	Accept
Sample 1 t11 Sample 2 t41	0.05	0.039	Accept
Sample 1 t21 Sample 2 t31	0.05	0.610	Accept
Sample 1 t21 Sample 2 t41	0.05	0.121	Accept
Sample 1 t31 Sample 2 t41	0.05	0.546	Accept

S.L.: Significance level

t11: Consultation one

t21: Consultation two

t31: Consultation three

t41: Consultation four

Ho: There is no significant improvement between samples at the $\alpha = 0.05$ level of significance.

Conclusion: There is no significant improvement in the number of non-inflamed lesions in the Herbal group between the consultations.

Table 5: Comparison of samples within the Herbal group. (Number of **inflamed lesions**.)

(Wilcoxon's Signed Rank Test)

Samples	S.L.	P-value	Ho
Sample 1 t51 Sample 2 t61	0.05	0.002	Reject
Sample 1 t51 Sample 2 t71	0.05	0.000	Reject
Sample 1 t51 Sample 2 t81	0.05	0.002	Reject
Sample 1 t61 Sample 2 t71	0.05	0.606	Accept
Sample 1 t61 Sample 2 t81	0.05	0.096	Accept
Sample 1 t71 Sample 2 t81	0.05	0.546	Accept

S.L.: Significance level

t51: Consultation one

t61: Consultation two

t71: Consultation three

t81: Consultation four

Ho: There is no significant improvement between samples at the $\alpha = 0.05$ level of significance.

Conclusion: There was a significant improvement in the number of inflamed lesions in the Herbal group between the consultations 1 and 2, 1 and 3 and 1 and 4. There was no significant improvement in the number of inflamed lesion in the Herbal group between 2 and 3, 2 and 4 and 3 and 4.

Table 6: Comparison of samples within the Herbal group. (**Total number of lesions**.)

(Wilcoxon's Signed Rank Test)

Samples	S.L.	P-value	Ho
Sample 1 t91 Sample 2 t101	0.05	0.002	Reject
Sample 1 t91 Sample 2 t111	0.05	0.002	Reject
Sample 1 t91 Sample 2 t121	0.05	0.002	Reject
Sample 1 t101 Sample 2 t111	0.05	0.423	Accept
Sample 1 t101 Sample 2 t121	0.05	0.302	Accept
Sample 1 t111 Sample 2 t121	0.05	0.606	Accept

S.L.: Significance level

t91: Consultation one

t101: Consultation two

t111: Consultation three

t121: Consultation four

Ho: There is no significant improvement between samples at the $\alpha = 0.05$ level of significance.

Conclusion: There was a significant improvement in the total number of lesions in the Herbal group between the consultations 1 and 2, 1 and 3 and 1 and 4. There was no significant improvement in the total number of lesion in the Herbal group between 2 and 3, 2 and 4 and 3 and 4.

Table 7: Comparison of samples within the Homoeopathic group. (Number of **non-inflamed lesions.**)

(Wilcoxon's Signed Rank Test)

Samples	S.L.	P-value	Ho
Sample 1 t12 Sample 2 t22	0.05	0.610	Accept
Sample 1 t12 Sample 2 t32	0.05	1	Accept
Sample 1 t12 Sample 2 t42	0.05	1	Accept
Sample 1 t22 Sample 2 t32	0.05	0.423	Accept
Sample 1 t22 Sample 2 t42	0.05	0.789	Accept
Sample 1 t32 Sample 2 t42	0.05	0.302	Accept

S.L.: Significance level

t12: Consultation one

t22: Consultation two

t32: Consultation three

t42: Consultation four

Ho: There is no significant improvement between samples at the $\alpha = 0.05$ level of significance.

Conclusion: There was no significant improvement in the number of non-inflamed lesions in the Homoeopathic group between the consultations.

Table 8: Comparison of samples within the Homoeopathic group. (Number of **inflamed lesions**.)

(Wilcoxon's Signed Rank Test)

Samples	S.L.	P-value	Ho
Sample 1 t52 Sample 2 t62	0.05	0.010	Reject
Sample 1 t52 Sample 2 t72	0.05	0.002	Reject
Sample 1 t52 Sample 2 t82	0.05	0.04	Accept
Sample 1 t62 Sample 2 t72	0.05	0.610	Accept
Sample 1 t62 Sample 2 t82	0.05	0.040	Accept
Sample 1 t72 Sample 2 t82	0.05	0.182	Accept

S.L.: Significance level

t52: Consultation one

t62: Consultation two

t72: Consultation three

t82: Consultation four

Ho: There is no significant improvement between samples at the $\alpha = 0.05$ level of significance.

Conclusion: There was a significant improvement in the number of inflamed lesions in the Homoeopathic group between the consultations 1 and 2 and 1 and 3. There was no significant improvement in the number of inflamed lesion in the Homoeopathic group between 1 and 4, 2 and 3, 2 and 4 and 3 and 4.

Table 9: Comparison of samples within the Homoeopathic group. (**Total number of lesions**.)

(Wilcoxon's Signed Rank Test)

Samples	S.L.	P-value	Ho
Sample 1 t92 Sample 2 t102	0.05	0.010	Reject
Sample 1 t92 Sample 2 t112	0.05	0.010	Reject
Sample 1 t92 Sample 2 t122	0.05	0.010	Reject
Sample 1 t102 Sample 2 t112	0.05	0.610	Accept
Sample 1 t102 Sample 2 t122	0.05	0.302	Accept
Sample 1 112 Sample 2 t122	0.05	0.061	Accept

S.L.: Significance level

t92: Consultation one

t102: Consultation two

t112: Consultation three

t122: Consultation four

Ho: There is no significant improvement between samples at the $\alpha = 0.05$ level of significance.

Conclusion: There was a significant improvement in the total number of lesions in the Homoeopathic group between the consultations 1 and 2, 1 and 3 and 1 and 4. There was no significant improvement in the total number of lesion in the Homoeopathic group between 2 and 3, 2 and 4 and 3 and 4.

CHAPTER 5 – DISCUSSION

5.1 Interpretation

The 3 variables studied in this investigation were number of non-inflamed acne lesions, number of inflamed acne lesions and the total number of acne lesions.

It can be seen in Table 1, 2 and 3 that there was no significant difference with respect to any of the 3 variables between the herbal group (Group 1) and the homoeopathic group (Group 2).

This shows that no difference could be found in the relative effectiveness of the herbal and homoeopathic complex in the treatment of the clinical manifestations of acne vulgaris.

There was no significant difference in the number of non-inflamed lesions in the herbal group (Table 4).

However, with respect to the number of inflamed lesions in the herbal group, there was a statistically significant difference between consultations 1 and 2, 1 and 3 and 1 and 4.

There was no significant difference between consultations 2 and 3, 2 and 4 and 3 and 4 (Table 5).

With respect to the total number of lesions in the herbal group, there was a significant difference between consultations 1 and 2, 1 and 3 and 1 and 4. There was no significant difference between consultations 2 and 3, 2 and 4 and 3 and 4 (Table 6).

There was no significant difference in the number of non-inflamed lesions in the homoeopathic group (Table 7).

However, with respect to the number of inflamed lesions in the homoeopathic group, there was a significant difference between consultations 1 and 2 and 1 and 3. There was no significant difference between the number of lesions in the homoeopathic group between consultations 1 and 4,2 and 3,2 and 4 and 3 and 4 (Table 8).

With respect to the total number of lesions in the homoeopathic group, there was a significant difference between consultations 1 and 2, 1 and 3 and 1 and 4 (Table 9).

It can thus be seen that both the herbal complex and homoeopathic complex reduced the total number of acne lesions between the first and last consultations. It would seem that there was initially a large improvement which made a statistically significant difference, but that after the second consultation there was not a statistically significant improvement between consultations.

Similarly, the herbal complex reduced the number of inflamed lesions between the first and the last consultations.

The homoeopathic complex, however, only reduced the number of inflamed lesions between the first and third consultation.

5.2 Argument

Two possible explanations can be suggested for these results:

Homoeopathy is based on the Law of Similars. It should thus be the aim of the practitioner when prescribing a remedy to make sure that the remedy or remedies match the patient's symptoms. Herbalism works in a similar way in that different herbs may be prescribed for the same pathology in different people depending on the way the pathology manifests itself in the individual patient.

The herbal and homoeopathic complexes prescribed in this study were not matched exactly to the individual symptoms of each patient. Thus, while there was initially a significant improvement, the patients did not continue to improve as the complexes did not contain the individual remedies which they needed to sustain long term improvement.

The sample size per group was small (less than 30). Thus non-parametric statistical tests were used for data analysis. However non-parametric tests are usually unreliable and thus the results which they produce are unreliable. (Fischer and Van Belle 1993.)

5.3 Speculation

In future, studies should evaluate the relative effectiveness of the homoeopathic and herbal similimum in the clinical manifestations of acne vulgaris.

A consultation should be held in which a full case history is taken and the researcher decides on the correct homoeopathic and herbal remedy or remedies for the patient. An independent person should then administer either the herbal or homoeopathic remedy to the patient.

In this way the study would be double blind.

At least two researchers should count the patient's lesions at each consultation to ensure the accuracy of the data.

Sample sizes should consist of at least 30 patients and in this way parametric statistical tests could be used for data analysis. The results would thus be more reliable.

CHAPTER 6 – CONCLUSIONS AND RECOMMENDATIONS

6.1 Conclusions

In this study, the researcher attempted to investigate the relative effectiveness of a herbal and homoeopathic complex in the treatment of acne vulgaris in terms of its clinical manifestations.

No significant difference was found between the two complexes.

6.2 Recommendations

Future studies should concentrate on the relative effectiveness of the homoeopathic and herbal similimum in the treatment of acne vulgaris.

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APPENIDIX – DETAILED RESULTS

Variable:	t11
Average:	56.133
Median:	23
Mode:	18
Standard Error:	19.221
Range:	235
Coeff. of Variation:	132.616

Variable:	t12
Average:	27.2
Median:	17
Mode:	2
Standard Error:	9.225
Range:	140
Coeff. of Variation:	131.359

Variable:	t21
Average:	52.867
Median:	24
Mode:	24
Standard Error:	16.337
Range:	196
Coeff. of Variation:	119.681

Variable:	t22
Average:	22
Median:	15
Mode:	15
Standard Error:	5.686
Range:	89
Coeff. of Variation:	100.103

Variable:	t31
Average:	42.733
Median:	22
Mode:	12
Standard Error:	12.997
Range:	180
Coeff. of Variation:	117.792

Variable:	t32
Average:	21.933
Median:	17
Mode:	16
Standard Error:	3.901
Range:	53
Coeff. of Variation:	68.875

Variable:	t41
Average:	39.866
Median:	21
Mode:	13
Standard Error:	12.878
Range:	187
Coeff. of Variation:	125.112

Variable:	t42
Average:	17.933
Median:	18
Mode:	19
Standard Error:	2.325
Range:	33
Coeff. of Variation:	50.026

Variable:	t51
Average:	57.066
Median:	35
Mode:	27
Standard Error:	10.434
Range:	123
Coeff. of Variation:	70.811

Variable:	t52
Average:	75.8
Median:	60
Mode:	36
Standard Error:	14.0423
Range:	213
Coeff. of Variation:	73.695

Variable:	t61
Average:	33.533
Median:	21
Mode:	21
Standard Error:	6.332
Range:	73
Coeff. of Variation:	73.132

Variable:	t62
Average:	52.266
Median:	45
Mode:	54
Standard Error:	9.898
Range:	152
Coeff. of Variation:	73.350

Variable:	t71
Average:	31.933
Median:	26
Mode:	26
Standard Error:	5.101
Range:	57
Coeff. of Variation:	61.871

Variable:	t72
Average:	43.933
Median:	37
Mode:	37
Standard Error:	6.675
Range:	101
Coeff. of Variation:	58.851

Variable:	t81
Average:	28.8
Median:	20
Mode:	20
Standard Error:	5.300
Range:	55
Coeff. of Variation:	71.283

Variable:	t82
Average:	33.8
Median:	31
Mode:	43
Standard Error:	3.620
Range:	44
Coeff. of Variation:	41.483

Variable:	t91
Average:	113.2
Median:	67
Mode:	67
Standard Error:	24.152
Range:	280
Coeff. of Variation:	82.635

Variable:	t92
Average:	103
Median:	89
Mode:	89
Standard Error:	16.181
Range:	192
Coeff. of Variation:	60.842

Variable:	t101
Average:	87.133
Median:	53
Mode:	27
Standard Error:	18.162
Range:	213
Coeff. of Variation:	80.727

Variable:	t102
Average:	73.333
Median:	69
Mode:	69
Standard Error:	11.276
Range:	142
Coeff. of Variation:	59.550

Variable:	t111
Average:	74.666
Median:	65
Mode:	65
Standard Error:	14.597
Range:	197
Coeff. of Variation:	75.715

Variable:	t112
Average:	65.867
Median:	54
Mode:	53
Standard Error:	7.997
Range:	112
Coeff. of Variation:	47.022

Variable:	t121
Average:	69.133
Median:	54
Mode:	77
Standard Error:	14.022
Range:	205
Coeff. of Variation:	78.556

Variable:	t122
Average:	51.733
Median:	51
Mode:	63
Standard Error:	3.944
Range:	44
Coeff. of Variation:	29.528