A Random Controlled Trial To Compare The Effects Of Two Home Treatments: Melaleuca Alternifolia (Tea Tree) Oil And Salicylic Acid (Salactol) On The Resolution Rates Of Verrucae Pedis.

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Abstract

A random controlled trial was conducted to compare the effectiveness of two home treatments: Melaleuca alternifolia (tea tree oil) and Salicylic acid (salactol) on the resolution rates of verrucae pedis and pain levels experienced when using a visual analogue scale. Ten subjects, (age range 16-45), with single plantar warts were randomly assigned to one of the two experimental treatment groups. Subjects received once-daily applications of either Salicylic acid (16.7%) or Melaleuca alternifolia (100%) for 12 weeks. Debridement and clinical assessment were performed at 0, 4, 8 and 12 weeks. Statistical analysis using a parametric unrelated t test revealed that no significant difference could be identified ($p>0.05$) when using Salicylic acid or Melaleuca alternifolia for the treatment of verrucae pedis. Therefore the null hypothesis was accepted. Statistical analysis using a non-parametric Mann-Whitney U test identified that there was a significant difference ($p>0.05$) when comparing the pain levels experienced when using a visual analogue scale. This concluded that there was an overall significant pain reduction when treating verrucae pedis with Melaleuca alternifolia.

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Chapter One

INTRODUCTION

Verrucae (warts) on the feet are very common problems which the podiatrist sees and treats regularly. Several over-the-counter preparations are available for the self treatment of verrucae. One of these clinically employed treatments is the use of salicylic acid which if correctly applied will cure 70-80% of common warts (Bunney 1986). However, the application of the acid can have adverse effects including local irritation. Salicylic acid acts by a corrosive action on the epithelium by destroying intercellular cohesiveness in the upper part of the stratum corneum, facilitating the removal of squames containing the active virus (Huber and Christopher 1977).

As consumer awareness of the side effects of synthetic drugs grows, people are seeking natural alternatives such as tea tree oil (Melaleuca alternifolia) for minor ailments. Tea tree oil has both antibacterial and antifungal properties and is non-corrosive (Atkinson 1949). It is recommended as a non-poisonous, non-irritant antiseptic of unusual strength even to sensitive tissues (Olsen 1999). No clinical trials have been carried out to assess the effectiveness of tea tree oil on verruca pedis. However, Hitchen in 1993 reported that "Verrucae treated with the neat oil have been found to shrink and disappear within a very short time after this oil has been applied".

Although using tea tree oil for treatment of verruca pedis is not a new concept much of the evidence appears to be anecdotal, whereas salicylic acid is one of the common treatment

modalities used for verruca pedis (Barbosa 1998). Justification for this research project is the need for investigation of the comparative efficacy of tea tree oil (Melaleuca alternifolia) as a non-invasive treatment of verruca pedis.

Aims of Study

1. The study aimed to assess the effectiveness of the topical application of 16.7% Salicylic acid 'Salactol" compared with that of 100% Melaleuca alternifola "Tea Tree" oil for the treatment of single plantar warts (verrucae), using a recommended course of treatment.

Objectives of Study

1. To measure and record the surface area of a number of verrucae on voluntary subjects at 0, 4, 8, and 12 weeks.
2. Subjects were randomly allocated to one of two experimental groups to receive salicylic acid or melaleuca alternifolia.
3. To analyse the data to establish if melaleuca alternifolia has a value, or not, as a treatment for verruca pedis.
4. The study also adds to the body of knowledge on verruca treatments.
5. A visual analogue scale has been incorporated into the experimental design, to record pain levels experienced by subjects during the clinical trial. These findings may indicate a decrease in pain levels that may support claims that melaleuca alternifolia has an analgesic effect and is also a non-poisonous, non-irritant antiseptic (Price 1995, Altman 1988).

Significance of the Study

Verrucas or warts represent one of the most common viral infections of the skin and the management of these infections is usually undertaken by podiatrists (Lorimer, *et al* 1998). Therefore, it is of utmost importance for the Podiatric Profession to have a clear understanding and knowledge of the aetiology, transmission of the wart virus and various treatment options available, so informed choices can be made by patients.

The current general policy in the U.K. for the treatment of verrucae is to treat if symptomatic and pain is usually the main justification for treatment. Therefore, is it of significance to investigate home treatments in an attempt to provide information for the profession and patients on possible alternative treatment options (Melaleuca alternifolia) compared to mainstay treatments such as salicylic acid preparations, when treating either symptomatic or asymptomatic lesions.

Null Hypothesis (H_o)

There will be no significant difference in the effects of the application of Melaleuca alternifolia compared to Salicylic acid on the resolution rates of verruca pedis.

Alternative Hypothesis (H_1)

There will be a significant difference in the effects of the application of Melaleuca Alternifola compared to Salicylic acid on the resolution rates of verruca pedis. (two tailed).

Null Hypothesis (H_0)

There will be no significant difference in the effect of the application of Melaleuca alternifolia compared to Salicylic acid on the pain experienced by the visual analogue scale.

Alternative Hypothesis (H_2)

There will be a significantly greater reduction in pain levels with the application Melaleuca alternifolia compare to Salicylic acid when using a visual analogue scale. (one tailed).

Level of Significance

(α)=0.05. If the results are significant at this set level the null hypotheses will be rejected.

Chapter Two

Literature Review

Data Sources

- Medline search 1966 to 1999. Selective to: English Language, meta-analysis, journal articles, review academic and tutorial
- Cinhal & Bids Search

Key Words: Warts, Tea Tree oil, Salicylic Acid, Verruca Pedis, Aromatherapy, Melaleuca alternifolia, Skin, Human Papilloma Virus

Other sources:

- Pharmaceutical Companies
- Internet
- References from textbooks and journals
- Newspapers

The literature search revealed no evidence of a previous study or research comparing the effectiveness of two home treatments: Melaleuca alternifolia (Tea Tree) oil and Salicylic acid (Salactol) on the resolution rates of verrucae pedis.

History of Warts

The wart virus has plagued human beings for many centuries. As far back as the first century AD, Celsius described in his "De Medicina" three types of warts; *acrochordon*, which occurred in children and often disappeared spontaneously; *thymion*, a vascular papillomatous lesion which occurred on the palms, soles and genitalia and *myrmecia* which resembled plantar warts (Bunney, *et al* 1992). The term verruca which means a steep place or height was first introduced by Sennertus (Bunney et al 1992). Until the last century the infectious nature of the wart virus was not fully appreciated. In 1891, Joseph Payne wrote 'On the Contagious Rise of Common Warts' which described how he developed a wart on his thumb after using it to scrape a wart off a patient. Licht and Variot in 1894 injected ground up wart preparations to induce warts in volunteers. Other experiments were repeated at this time showing the infectious nature of the common wart. In 1907 Ciuffo postulated that a viral aetiology existed and this theory was substained by Strauss in the 1950's by identifying viral particles by electron microscopy (Glover 1990).

Until recently, warts were classified by their morphological features and attributed to a single virus, but newer techniques led to the discovery of many different types. The human papilloma virus (HPV) is the virus responsible for all human wart conditions and is a member of the family Papovaviridae (Barbosa 1998). The papilloma virus contains a double-stranded, circular, supercoiled DNA, enclosed in 72 capsomes that contain no envelope (Cobb 1990). To date, 77 types of human papilloma viruses (HPV) have been cloned and fully characterised; with types I, II and IV positively linked to the different types of verruca pedis (Rook, Wilkinson and Ebling 1998).

It is important to note that the HPV I has the largest particle density of all types of the virus and therefore is the most infectious (Cobb 1990, Ordoukhanian and Lane 1997).

Currently the HPV cannot be reproduced in the laboratory setting, therefore experimental research is limited, focusing mainly on the aetiology and transmission of the virus. Most of the experimental research investigating common warts and verrucae pedis was conducted during the 1950's up to the 1980's and this is discussed throughout the review.

Transmission

It has been postulated that the HPV can be transmitted between individuals and is spread via microtrauma to the skin, commonly affecting the plantar surface of the feet. Successful transmission results if there is a breach in the skin whereby inoculation can occur (Bunney *et al* 1992). Infected scales (stratum corneum) which are detached from the skin (epidermis) either by minor damage or friction are partly responsible for the spread of the virus (Bunney *et al* 1971). The length of time the scales remain infective is unknown. The viability of the virus and the susceptibility of the individual is also important (Bunney *et al 1992*).

If the skin is macerated through water or sweat, the transmission of the virus will occur more easily, therefore, public communal areas such as swimming pools are common transmission sites. This may explain why those people who use these facilities appear to be more susceptible to verrucae (Gentles and Evans 1973). It has been suggested that all individuals who develop warts have a reduction in their immune responsiveness and it is well

established that individuals who are immuno-deficient and/or on immunosuppressive drugs often develop resistant warts (Bunney *et al* 1992).

It has been assumed that once detached from the active wart, infectivity does not last. In this context the proximity of warts is important. Massing and Epstein (1963), showed that new warts occurred three times more often in those patients with existing warts and it is a common observation that patients with warts on both hands always have more on one. Further evidence that viral infectively might be short lived is provided by the fact that the incidence of plantar warts is higher in group swimming than it is in populations using the same pool individually (Gentles and Evans 1973).

Massing and Epstein (1963), reported that new warts occurred three times as frequently in infected children as in uninfected. Occupational handlers of meat, and poultry seem to have high incidences of hand warts as not only are they subject to trauma but also their skin is subjected to prolonged states of maceration by immersion in water and tissue fluids (Bunney *et al* 1992).

Immunology

It has long been recognised that warts undergo spontaneous regression. Massing and Epstein (1963), illustrated in their 1963 study, that 67% of patients involved, experienced resolution of their warts within a two year period without any treatment used. It is not certain whether cell mediated immunity is wholly responsible for the regression, or whether destruction of wart-infected cells releases the virus, inducing the immune response. The

presence of immunoglobins IgM and IgG antibodies to the human papilloma virus have been recognised as of crucial importance for the regression as they have been identified in patients experiencing resolution and are absent in patients with active verrucae. It has been shown that warts present for less than one year will usually regress within two months if the wart-specific IgGb antibodies develop (Cobb 1990). This suggests that the presence of these antibodies prevent infection and help resolution to occur. However, permanent protection is not guaranteed, as individuals may experience subsequent attacks of the virus.

Clinical features of the regression include the characteristic appearance of black dots, which are due to thrombosed capillaries in the stratum corneum (Rook and Mailbach 1983). In addition the wart has a tendency to liquefy or desiccate (shrink). Within a two month period, restoration of normal epidermal skin ridges should be observed (Bunney *et al* 1986, Cobb 1990 and Rook, Wilikinson and Ebling 1998).

Epidemiology

The epidemiology of the study of warts is limited, mainly focusing on a few studies of school and institutionalized children (Glover 1990). Information gathered is specific to the population studied and therefore difficult to generalise to the whole population. The prevalence of verrucae is worldwide (Robinson and Heath 1983), and the referral rates of warts to dermatology clinics have increased in the last four decades (Champion *et al*, 1992). However, the increase in frequency of attendance, may be due to an increase in the demand for treatment, rather than an increased number of verrucae. Generally, warts are unusual in infancy and early childhood, but prevalence increases to 10-20% at aged 11-14

years (Keefe 1991). This may be due to increased sporting/communal activities in this particular age group.

Warts become less common over the age of 25 years except in certain occupations. For example, the prevalence of hand warts in butchers can be as high as 50%. It has been suggested the incidence in male and females is probably equal, but seem to be more persistent in females (Massing and Epstein 1963).

Clinical Features of Verrucae Pedis

Verrucae are defined as benign, epidermal neoplasms produced after an HPV infection of epidermal keratinocytes (Barbosa 1998). The appearance of the plantar verrucae can be determined by the type of HPV infecting the tissue, as well as by physical characteristics including location of infection, weightbearing of the lesion, and the wetness of the area (Brooks 1991, Fields 1990 & Jenkin, 1994).

Classification of verrucae pedis is usually based on clinical appearance (Glover 1990). Verrucae pedis can be identified into three main clinical types:

Verrucae Plantaris (Myrmecia): usually deep, singular lesions situated in the epidermis. They are often located beneath pressure points such as metatarsals and the heel, causing pain on weightbearing. These lesions are caused by HPV Type I (Cobb 1990 and Barbosa 1998).

Mosaic warts: identified by a collection of multiple, superficial warts which form a mosaic pattern and tend to be symptomless. Research has indicated that these lesions are most resistant to treatment (Barr and Coles 1968). These warts are associated with the HPV Type II virus (Barbosa 1998).

Punctuate Verrucae (Marked with points, differentiated from surrounding skin by elevation or texture): generally smaller in size and superficial compared to verrucae plantaris. They appear to be more keratotic compared to the other two viruses and lack characteristic bleeding. The lesions are distinctly separate but multiple in numbers with a punctuate appearance and are associated with infection by HPV type IV virus (Barbosa 1998).

Some features can be observed in all three types, such as acanthosis (thickening of the stratum spinosum), papillomatosis ('cauliflower' or textured appearance), thrombosed capillaries (punctuate black dots), and hyperkeratosis (increase in the stratum corneum) (Barbosa 1998 and Cobb 1990).

Diagnosis

Diagnosis is usually made on clinical examination using 10x magnification to identify disruption of skin lines (interrupted dermatoglyphics), and whether sharp pain is experienced on lateral palpation (Lorimer, *et al* 1998)

In cases where diagnosis is in question, biopsy can usually establish the diagnosis of a wart (Glover 1990).

Differential Diagnosis

Warts are usually accurately diagnosed in general practice (Keefe 1991). However, even the trained practitioner may find it difficult to differentiate between certain lesions which possess similar characteristics. For instance, heloma dura (hard corns) and warts do possess common features such as being raised lesions, having hyperkeratotic tops, pain being elicited upon pressure and being predominately over weightbearing sites. Factors which distinguish warts from heloma dura are as follows: the onset of warts is much more rapid compared to heloma dura which are associated with chronicity. Warts are usually associated with young people whereas heloma dura are more commonly seen in middle-aged and older people. When warts are abraded, bleeding will occur quite freely from dilated capillaries compared to most classifications of corns such as hard (heloma dura) and soft (heloma molle) when hyperkeratotic tissue is removed (Lorimer, *et al* 1998). Vascular corns which show intrusions of vascularised dermal tissue into the epidermis can bleed quite profusely if cut. These features must be taken into account when diagnosing and may suggest that a lesion is a vascular corn rather than a wart (Merriman and Tollafield 1995).

Other lesions which should be considered as differential diagnoses for warts include:

Molluscum Contagiosum - smooth, round papule with characteristic pearl centre caused by the pox virus (Hunter *et al* 1995).

Granuloma Annulare - lesion are dermal and have a smooth surface outline often is annular (ring-shaped) (Hunter *et al* 1995).

Seborrhoeic Warts - benign, epidermal tumour, may be flat, raised or pedunculated (stalk-like). These warts are unrelated to sebaceous glands and are not classified as true warts. (Hunter *et al* 1995, Keefe 1991).

Treatments Modalities

Various methods for the treatment of warts exist. In the past many treatments revolved around the application of juices of plants or wart cures based on the idea of transference to another person or object. Today, the treatment of warts remains controversial, giving rise to debate for and against treatments. One school of thought suggests that viral warts are self-limiting and therefore should be left alone to spontaneously resolve with no preventative measures against the spread of infection. Others suggest that some can persist for many years and resolution cannot be predicted. The response rate of wart treatments decreases as their duration increases and the older the patient, therefore earlier treatment is likely to be more effective (Bunney *et al* 1992).

Generally warts are disliked by patients, causing distress and may have a psychosocial stigma that can lead to fear of uncontrolled spread to other sites and people (Ordoukhanian, Lane 1997). Many warts cause discomfort, pain and disability - especially on the feet where weightbearing occurs. Secondary infection can occur with fissuring and hyperkeratosis. Painful plantar warts can also lead to postural defects and incorrect walking in children (Bunney *et al* 1992).

The management of plantar verrucae includes many different treatment modalities. Problems are associated with different treatments; for instance, Bunney *et al* (1982) states that all treatments work in some cases, but no treatment works in all cases. Another problem is that one cannot reproduce the wart treatment results of another investigator (Rulison 1942). Treatments are difficult to assess, as the virus is difficult to reproduce in the laboratory and has a variable natural history, tending to disappear spontaneously.

Therefore selection of the most suitable treatment modality is difficult and certain factors must be considered including size, number, location, presence of pain, previous treatments and the immunologic status of the patient (Barbosa 1998). Most of the studies focusing on the treatment of warts seem to classify all types of warts together and do not report treatment success rates separately. There is evidence that plantar warts respond at a different rate to treatment than other types of warts (Glover 1990).

Classification of treatment modalities generally fall into four main categorises. These are home treatments, special topical applications, cryotherapy and surgical intervention, although newer treatments such as laser therapy and old remedies such as hypnosis are still practised. For the purpose of this study, home treatments will be described in detail, especially salicylic acid as a treatment modality for verruca pedis, a review of the other main categories will be summarised focusing on contemporary treatments used.

Home Treatments

Of all the treatments reviewed in the literature, salicylic acid is the most commonly used agent prescribed for plantar verucae (Steele, 1988). It is one of the first recorded treatments for warts and has been suggested to be highly effective (Bunney 1986). Other popular treatments are gluteraldehyde and homeopathic preparations such as thuja occidentalis. Salicylic acid can be present in three preparations: liquid, gel and rubber-based patches which are manufactured for over-the-counter dispensing in various strengths from 11-25% in proprietary preparation such as Cuplex®, Duofilm®, Salactol® and

Posalfilin®. Other concentrations of salicylic acid range from 25% up to 60% but are classified as prescription-only-medications. It seems to represent the first line of approach by patients before consulting a general practitioner or a podiatrist (Barbosa 1998).

Salicylic acid acts by destroying the intercellular cohesiveness in the stratum corneum (upper part of the epidermis) which assists in the removal of squames containing the active virus (Huber and Christopher 1977). These changes appear to increase dermal vascularity and provoke an inflammatory action that renders the virus more accessible to an immune response. (Bunney, *et al* 1992, Bunney ,1971).

SalactolÒ

Salactol contains 16.7% salicylic acid and 16.7% lactic acid in a flexible collodion. Salicylic acid is combined in a flexible collodion to assist localisation, so when applied in a solution, it dries to form an adhesive film that minimises the spread of the formulation from the site. The lactic acid component improves the release for the salicylic acid into the underlying skin (Dermal Laboratories, 1999). Salicylic acid has both bacteriostatic and fungicidal actions as well as keratolytic properties. The combination of salicylic acid and lactic acid in the flexible collodion has shown to be particularly efficacious in treating warts, verrucae, corns and calluses (Dermal Laboratories, 1999).

Few side effects have been reported although hypersensitivity reactions do cause irritation to the skin. Possible adverse effects from high doses include reduced blood pressure and alterations in kidney and liver function (Dermal Laboratories Ltd, 1999). If excessive acid is

applied, maceration of the skin surrounding the lesion will occur (Barbosa 1998). Continued use of salicylic acid may lead to local dermatitis (Lorimer, *et al* 1998).

Advantages of salicylic acid include minimum disability, no anaesthesia is needed, minimal discomfort and low risk of scarring. Obvious disadvantages include the need for multiple treatments, varying cure rates and recurrences (Landsman *et al* 1996).

Several studies have been conducted using Salactol alone or combination with other preparations to observe cure rates for warts.

Between 1969 and 1976 extensive research investigating comparative wart treatment trials were undertaken by Bunney, *et al* (1976). One of these trials investigated 12 week cure rates for simple plantar warts using topical preparations of salicylic acid "Salactol" (salicylic acid 1 part; lactic acid 1 part in flexible collodion), compared to podophyllin. Results showed an 84% cure rate when using salicylic acid, which favourably compared with an 81% success rate using podophyllin. There was one recurrence by 6 months. Although the results appear to be significant and advocates the treatment to be very beneficial, no results were reported for continued therapy treatment failures at 3 months. In addition, there was only a difference of 3%, therefore an 81% success rate should also be highly regarded. This may have been interpreted by the researcher in this way because salicylic acid has a higher speed of cure and fewer side effects compared to podophyllin (Bunney *et al*, 1976).

Steele and Irwin (1988), investigated the use of liquid nitrogen and salicylic acid as "Salactol" (salicylic acid 1 part; lactic acid 1 part; collodion 4 parts) for the treatment of

common hand and simple plantar warts over a 12 week period. Combination therapy cured 87% of common hand warts over a 6 week period, and was significantly more effective than either treatment used separately. The results for simple plantar warts were disappointing with no one treatment proving to be particularly successful.

The only other published study which assessed the treatment of common hand warts using salicylic/lactic acid paint and liquid nitrogen together and separately was conducted in a 12 week trial in two hospital centres by Bunney *et al* in 1976. Results gathered from the two centres indicated very different success rates and were combined for the purpose of statistical analysis. It was claimed that liquid nitrogen and wart paints resulted in a higher cure rate than either agent used separately, though the results failed to reach statistical significance. The trial suffered from several drawbacks such as a 35% withdrawal rate owing to non-compliance and patients being drawn from older age groups than those normally associated with common warts. In addition, the treatment of simple plantar warts was not studied and the side effects of the treatments were not assessed. Mosaic warts were used which are notorious for their longevity and resistance to treatment (Bunney *et al*, 1992). Furthermore, there was a failure to standardise the size of lesions on entry to the study.

More recently, Berth-Jones and Hutchinson in 1992, observed lower cure rates when treating plantar and hand warts compared to previous research conducted by Bunney *et al*, 1976. Subjects were randomly allocated to receive a combination of liquid nitrogen, salactol and paring. Findings suggested a 52% cure rate after 12 weeks when using salactol

and liquid nitrogen. Possible explanations for lower cure rates compared to Bunney *et al* (1976) who investigated 3 month cure rates using wart paints, cryotherapy at 3 -week intervals and a combination of both treatments, could be partial due to the lack of paring in 50% of the individuals, however the overall cure rate was still lower. Furthermore, differences were observed in the wart virus strains and the patient population understudy. It was concluded that the chance of cure was related both to the length of history and to the diameter of the largest wart (Berth-Jones and Hutchinson, 1992).

Hence there have been several studies of salicylic acid for the treatment of plantar warts, with most achieving high cure rates.

Special Topical Applications

Acids, such as (25% to 60 %) salicylic, mono or trichloroacetic acids have been a popular method of treating skin warts. Steele *et al* (1988), investigated the use of monochloroacetic acid and 60% salicylic acid for the treatment of single plantar warts. Findings suggested that 66% of 57 participants were cured after 6 weeks. This research supports previous studies by Dutta (1983), concluding that monochloroacetic acid/60% salicylic acid is an effective treatment for simple plantar warts. Wright (1955), reported that by paring plantar warts in 56 patients, followed by weekly treatments with trichloracetic acid and 40% salicylic acid plaster, 65.3% cure rate could be achieved, 31 of these patients required four more treatments and five required five more treatments. There was a 14% recurrence rate by the end of 5 months. The author reported that lesions were tender after treatment and it was difficult to persuade patients to return for more treatments (Glover 1990). The effects of

these agents is to topically elicit localised hydrolysis, inflammation and eventual destruction of the verruca. Occlusive dressing are often used to promote absorption. Their effectiveness is no greater than that of gentler treatments and the likelihood and degree of discomfort and complications are greater. Extreme care must be taken when treating diabetic patients because of an increased danger of ulceration. Caustics such as monochloracetic acid are often mixed with keratolyitcs to create delamination of keratin. Monochloroacetic acid is sometimes applied as an acid crystal that can cause localised inflammation and even cellultis. (Tollafield, 1979) cited in Merriman and Tollafield, (1995).

Cryotherapy

Cryotherapy, which is the therapeutic use of cold is widely used for the treatment of warts. One of the most commonly utilised procedures is the use of liquid nitrogen (-195.8°C) which has shown to have a 91% cure rate (Lemont, 1989). Carbon dioxide snow (-79°C) and nitrous oxide gas (-70°) are also employed. "Histofreezer" (Pedinol) is commonly utilised by practitioners which is composed of dimethylether and propane. The human papilloma virus is resistant to the effects of freezing, therefore the action of cryotherapy is to freeze and thaw the cells which leads to histological changes and destruction. The exact techniques and the freezing times vary depending on the agent and on the nature of the lesions (Landsman *et al*, 1996). One or more applications may be necessary, and individual application times range from 40 to 60 seconds. Treatment should be repeated weekly. The main advantages of cryotherapy is that no anaesthesia is needed, both patient discomfort and scarring is minimal. Histofreezer has been reported to have that added

advantage of alleviating pain and discomfort which is often associated with the forementioned therapies.

Disadvantages included localised burning, pain and oedema following cryosurgery. There is also the possibility of decreased effectiveness when treating large or mosaic lesions (Landsman *et al*, 1992). Other complications of cryotherapy include blistering, throbbing and hypopigmentation (especially in patients with darker skin). Longer freezing times can cause damage to peripheral nerves resulting in anaesthesia which can last for several months. It has also been suggested that the treatment of digital warts can result in damage to joints and tendons after extended freezing times (Barbosa, 1990).

Surgical Intervention

Curettage is a common surgical intervention employed for the management of plantar verrucae (Barbosa, 1998). It is frequently used when topical agents and cryosurgery have failed. This procedure involves debriding the verruca until bleeding occurs and then a surgical dermal curette is employed to excochleate the lesion. Some patients see it as the ultimate cure, being that if the wart is cut out it will not return (Bunney *et al*, 1992). Even if all infected tissue is removed, eradication of the virus it not guaranteed, and recurrence following surgical removal is high. Vickers (1961) stated a recurrence rate of 30 per cent.

The procedure requires the use of local anaesthesia and the aim of the treatment is to remove all of the infected viral tissue, including the basal cells of the epidermis that contains genomic material of the HPV (Barbosa, 1998).

Curettage is expensive and requires careful planning by the physician. The immediate side-effects involve pain associated with the injection of the anaesthetic, aswell as pain associated with the after-effects of the surgery. Potential complications of the surgical procedure include post-operative infections, prolonged healing, nonhealing, poor or painful scar formation and recurrence of lesions (Barbosa, 1998).

Electrosurgery

Electrosurgery is the use of electricity in the performance of surgery (Lorimer *et al* 1998). It is usually used for the treatment of cutaneous lesions, such as verrucae and heloma dura (corns). There are several methods of administration including fulguration, dessication and electrosection which all slightly differ but deliver high frequencies of electrical current. The administration of local anaesthesia is required before electrosurgery can be performed. An electrical current is emitted through a small electrode. This produces a intense current which is dispersed through a larger electrode to prevent undue damage to the tissues. Several studies have various success rates using electrosurgery as a treatment modality. Hortwitz and Marker (1960) reported a success rate of 65%, Wright (1955) found 64% of patients with plantar warts were cured, but all complained of pain (Glover 1990).

The major benefit of electrosurgery is that one treatment is usually effective, and it is a simple way of treating some of the most intractable podiatric lesions (Lorimer, *et al* 1998). The use of electrosurgery is contra-indicated in patients who have cardiac pacemakers and those individuals who have extensive scar tissue or replacement joints where the two electrodes could intensify the current and cause tissue damage. Possible side effects include

moderate-to-severe pain, difficulty in controlling depth, and recurrence of larger or recalcitrant warts (Landsman *et al*, 1996).

Laser Emission

Laser can be defined as light amplification stimulated by emission of radiation and is considered to be an alternative to electrosurgery (Lorimer, *et al* 1998. The most popular types are carbon dioxide or pulsed-dye for recalcitrant lesions (Tan, 1993 and Webster, 1995). Surgical laser is a method which is very versatile and allows more accurate localisation of tissue destruction than the previous techniques. Surgery is conducted under local anaesthesia. The laser emission is directed on the lesion and tissue destruction is controlled by visual monitoring. The advantages of laser therapy is that emissions can be controlled, so little damage occurs to the surrounding healthy tissue. After treatment rapid healing will occur due to immediate haemostasis and postoperative pain and risk of infection will be minimised. In contrast, the disadvantages are a variation of penetration resulting from electrical wattage and focal distance, and the possibility of tissue damage because of excessive exposure leading to permanent scarring.

Part Two

Aromatherapy and Essential Oils

The art and science of aromatherapy is not new. Its origins can be traced back 5,000 years when aromatic plants were used for medicinal purposes in Persia, Egypt and India (Baker 1999). Aromatherapy is suggested to be the art of using essential oils which when extracted from plants can help the body to heal itself on mental, physical and emotional levels (Armstrong 1991). Aromatherapy and herbal remedies are widely available over-the-counter and are used for physical and psychological means. Various methods of treatments exist including ingestion, inhalation, massage, vaporisation and neat application to the skin.

Essential oils are complex chemical components of esters, aldehydes and other organic compounds which can be distilled from flowers, leaves, twigs, resin and roots of plants (Which? Way To Health, 1991). Essential oils are volatile substances that can easily evaporate and do not dissolve in water. Tea tree oil (Melaleuca alternifolia) is one of the well known essential oils. It is either a pale yellow or colourless substance with a distinctive, pungent odour and is a member of the Myrtaceae family (Melaleuca and Leptospermum), (Price 1995).

History of Tea Tree Oil

Tea tree oil (Melaleuca alternifolia) originated from a place called Bungawalbyn meaning "Healing Ground". Indigenous to the low-lying northern coast of New South Wales in Australia, the healing power of the Tea Tree plant has been used for centuries by the Aboriginal Bundfjabung Tribe. First reported by Captain Cook in 1777, it was used to

treat minor ailments like stings, burns and cuts by aborigines. After white settlement, the leaves of the tea tree were steam-distilled and the first oil was produced.

Since the early 20th century, tea tree oil has been used for a wide variety of bacterial and fungal infections of the skin and mucosa (Nenoff 1996). In the late 1920's Dr A.R. Penfold, an Australian Governmental Scientist, illustrated its uses as an antiseptic bactericidal agent, stronger than carbolic acid, which in the early 1900's was considered to be the universal standard. It was also noted to be a non-toxic, non-irritative and active in the presence of organic matter (Mayo 1992).

Numerous studies followed, and by the 1930's its popularity had grown both in medicine and the home. In 1933, it was noted in the British Medical Journal as being useful as a wound cleansing agent (Walker 1972), and also listed in the British Pharmaceutical Codex in 1949.

Tea tree oil reached a zenith during the Second World War, becoming standard issue in first-aid army kits of Australian troops used as a antifungal in combating foot rot. However, demand outstripped supply and synthetic germicides such as antibiotics were manufactured as part of the war effort by large pharmaceutical and chemical companies which swept aside many natural remedies.

During the post-war years the tea tree oil industry stagnated for more than 30 years. By the 1970's the first plantation had been developed, until then it had been harvested exclusively in the bush. With sophisticated marketing and large-scale production, tea tree oil has now gained world-wide popularity.

Previous Research Documenting The Uses of Tea Tree Oil

Tea tree oil has been reported to be effective in a number of infectious conditions, including acne, gum disease, gingivitis, vaginal infection, paronychia, furunculosis, tinea and thrush. However, the majority of these reports are based on anecdotal evidence or case studies. For the oil to be universally accepted, published clinical studies need to be reviewed as proof of efficacy. A search of the Medline database back to 1966 revealed eighteen mentions of tea tree oil, three of these related to controlled clinical studies on onychomycosis, acne and tinea pedis; other studies focused on the antibacterial and antifungal properties of the oil. Buck *et al* (1994) assessed the efficacy and tolerability of topical application of 1% Clotrimazole solution, compared with that of 100% Melaleuca alternifolia (tea tree) oil for the treatment of distal subungual onychomycosis. Findings suggested that both preparations provided significant improvements in nail appearance and symptomology for over one half of all subjects. This study also demonstrated the need to use a potent (in this study 100%) concentration of tea tree oil to produce both short-term and long term efficacy. Tong *et al* (1992), compared tea tree oil 10% with that of tolnaftate 1% cream for the treatment of tinea pedis in 104 patients. Findings concluded that although a reduction in symptomology of tinea pedis was experienced when using tea tree oil, it was not effective in achieving a mycological cure. However, improved results were obtained when using a higher concentration.

Barnetson (1990), demonstrated its significant efficacy in treating acne, with fewer side-effects than a standard topical agent. Bartneson (1990), suggested that the study may have been improved if the preparation had been applied more frequently or if the concentration of the gel had been increased to 10%. In none of the studies was the chemical composition of the oil defined.

Most of the published research cited centres on the antibacterial and antifungal properties of tea tree oil both in vitro and vivo, demonstrating its activity against various life-threatening resistant organisms, especially Pseudomonas aeruginosa, Staphylococcus aureus and Escherichia coli as demonstrated by Smith *et al* (1997). Belaiche (1985), showed it to have a powerful action against Candida albicans. Shapiro, Meier and Guggenheim's (1994), findings showed potency against anaerobic oral bacteria.

The Relevance of Tea Tree Oil to Podiatry

Podiatric uses of tea tree oil have been illustrated by Walker (1972) using it for various common foot problems, such as onychomycosis, tinea pedis, bromidrosis (and associated fissures) post-surgical sutured wounds and inflamed corns. Fogarty (1990), investigated its combination with an emollient for rehydration of the skin, as a preventative measure in reducing superficial bacterial flora and assisting in maintaining skin tissue patency. Perry (1994), has incorporated its uses into successful pressure ulcer and wound management.

Carson and Riley (1993), conclude that the full therapeutic potential of tea tree oil has yet to be elucidated, further research and development will generate products specifically

formulated for particular uses, and that successful promotion will require further development of appropriate medical research regarding its potential applications.

A Treatment For Verrucae

Melaleuca alternifolia has been cited as a treatment for verrucae (Drury, 1994, Lawless, 1994, Kippen, 1996, Mayo 1992). Without support from published clinical trials and quantitative data for the efficacy against viruses these claims remain anecdotal. Unpublished research comparing the efficacy of tea tree oil against arachis oil on verrucae resolution rates in adults concluded that although no statistically significant difference was achieved, a marked reduction in lesion size was noted compared to a placebo group. Melaleuca alternifolia appears to become more effective when it is used over a period of time and seems to produce an analgesic effect whereby the verrucae became less painful (Lock 1995). Further unpublished research investigated the application of tea tree oil on the resolution rates of verrucae in children compared to a placebo. Results indicated no significant difference in the resolution rates of both groups, but in both groups the lesions decreased in size, and a high resolution rate occurred (Weaver 1996).

If effective, tea tree oil may suggest a treatment modality for verrucae pedis, providing a non-invasive, painless source of treatment aimed at certain client groups such as individuals with diabetes mellitus, the immunosuppressed and young children.

Percutaneous Absorption Of Tea Tree Oil On The Skin

The skin has many functions. One of these is to keep out potentially harmful chemicals. The application of bioactive substances to the skin and the pharmacolgic consequences has

gained much interest through the years (Shaw, 1991). Human beings are exposed to many chemicals during the course of a normal day such as toiletries, detergents etc. Some chemicals evaporate or will be washed off, whereas others will be absorbed and become systemically available (percutaneous absorption) (Hotchkiss, 1994). Mechanical damage and hydration of the outer layer of the skin (stratum corneum) by using water impermeable coverings seems to increase percutaneous absorption (Foreman, 1988). Watt (1995), states that tea tree oil contains highly volatile chemicals that will quickly evaporate with body heat therefore, an occlusive adhesive plaster is necessary to maximise absorption.

According to Carson and Riley (1993), the lipophilic nature of tea tree oil enables it to penetrate skin and potentiate its antiseptic action. Altman (1988), also suggests that tea tree oil may have good skin penetration due to its oily nature but this requires further investigation. Furthermore, Altman (1989) has shown tea tree oil to have relatively low skin sensitivity, therefore being a suitable candidate for use in topical preparations. Other supportive evidence shows it to have low toxicity, being virtually non irritant even to sensitive skin (Mayo 1992). The chemical composition of tea tree oil (Melaleuca alternifolia) consists of a mixture of active ingredients including terpinen-4-ol, alph-terpineol, and alpha-pinene, 1,8-Cineole (Williams, 1988). Investigations of terpenes present in essential oils have been shown to enhance skin penetration by altering the barrier function of the stratum corneum. 1,8-Cineole which is present in tea tree oil has been suggested to promote the percutaneous absorption of several drugs (Barry and Williams, 1993). However, it has been known to cause some skin irritation depending on the concentration of oil used (Tisserand 1995).

Further claims have suggested tea tree oil to be effective against viral infections, to be a powerful immuno-stimulant and have an analgesic effect. (Lawless, 1994, Franchomme & Penoel, 1991). Again, these claims are only supported by anecdotal and empirical evidence.

Chapter Three

METHODOLOGY

DEFINITION AND OPERATIONAL TERMS

AROMATHERAPY: The therapeutic use of essential oils that have been distilled from plants.

COMPARE: To examine in order to observe differences or resemblance.

CURE: Restoration of skin dermatoglyphics when viewed at x10 magnification.

EFFECTIVENESS: The extent to which a drug or other agent achieves its intended therapeutic purpose.

POPULATION: A collection of people or objects who have at least one characteristic in common.

RESOLUTION: Subsidence of the symptoms of a disease.

SAMPLE: A small section of the population understudy.

VERRUCA PEDIS: A viral, epidermal tumour located on the foot which disrupts the dermatoglyphics of the skin and may elicit pain on lateral pressure.

VISUAL ANALOGUE SCALE: Assessment of severity of pain.

SPONTANEOUS REGRESSION: The spontaneous disappearance of verrucae, without the influence of any treatment or medical intervention. It is associated with the cell-mediated immune response and with the presence of complement-fixing IgG class antibodies.

TREATMENT: A way of attempting to cure the verrucae by a variety of different methods.

HOME TREATMENT: A treatment carried out, usually daily, by the patient themselves in their own home.

CURED VERRUCAE: Where the verrucae (and virus) disappears completely and the normal epidermal dermatoglyphics are restored.

EFFECTIVENESS OF THE TREATMENT: Whether the treatment cures the verrucae, or has any effect upon its size/pain level.

Ethical Committee Approval

The study involved twelve subjects and gave rise to certain ethical issues. Request of ethical committee approval was granted on the 14th October 1999 by the Northampton Medical Research/Ethics Committee.

Letter of approval is enclosed - refer to appendix (A)

Research Design

The research project conducted used inferential statistics. Therefore, information derived from the project could be inferred to be representative of the parent population, allowing the opportunity to generalise and make wider inferences with regard to the data obtained (Hicks 1990).

An experimental design was employed to test the hypotheses, therefore by manipulating the independant variable (IV) any effects on the dependant variable (DV) could be monitored (Hicks 1990). The variables were as follows:

To test Experimental Hypothesis (H_1)

Independant variable: Topical treatments

Dependant variable: Resolution rates of verruca pedis

To test Experimental Hypothesis (H_2)

Independant variable : Topical treatments

Dependant variable: Pain measured on a visual analogue scale.

The data collected to test hypothesis 1 was ratio level measurement, this allowed statistical analysis to be conducted using the following parametric test:

1) The t-test

The experimental design uses two (separate) groups of subjects. Each group produces a set of data. The t-test for unrelated data will predict whether the results from the two experimental groups were significantly different or whether the results were due to random error (Hicks 1990).

Certain assumptions need to be satisfied before proceeding with a parametric test:

- Level of measurement must be from at least an interval or ratio scale.
- The design must be either related or unrelated.
- The sample must be drawn from a normally distributed population.
- The variance of the two samples are not significantly different - homogeneity of variance.

The data collected to test hypothesis 2 was ordinal (ranked) level of measurement, this allowed statistical analysis to be conducted using the following non-parametric test:

2) The Mann-Whitney U test

The Mann-Whitney U test indicates whether the scores obtained from two (unrelated) groups of subjects differ significantly from each other (Coolican 1992, Hicks 1990).

Sources of Error

Experimenter Bias / Inter / Intra Observer Errors

To exclude the possibility of experimenter bias two investigators were involved in the collection of data.

The principal investigator performed assessments including identification of verruca, reduction of overlying callus. Clinical inspection of continuation of skin striae was assessed

by an independant observer to see if full healing had occurred. This obtained the maximum level of test reliability and intra-observer reliability.

An independent observer recorded all measurements of verruca lesion size at 0, 4, 8 and 12 weeks.

Inter-observer error was excluded, as only one principal investigator was responsible for performing the assessments.

Random Errors

Random errors can never be entirely eradicated from any research project. However, by using a random and incidental sampling technique this minimised the extent of errors and influence they would have on the research.

Participants

The research project was designed to recruit thirty subjects. However only twelve subjects were recruited. Once fulfilling the patient criteria, subjects were randomly allocated to one of the two experimental conditions.

Definition of Population

The population in this research can be defined as patients attending Northampton School of Podiatry (clinicians and students were asked to refer anyone with verrucas who fulfilled the selection criteria and who was willing to participate).

Recruitment's were also gathered by patients referrals from State Registered Podiatrists working in Northampton National Health Clinics.

From this a target population was drawn which satisfied the specified inclusion/exclusion criteria.

INCLUSION CRITERIA

1) Informed written consent

2) Patients aged between 16 and 45 years old

(Response to treatment for warts decrease with increasing age of the subject Bunney 1986)

3) Male and female gender

4) Healthy

5) One single or several discrete plantar warts (verrucae)

6) Alert and able to follow simple instructions in English

7) Able to reach feet comfortably in order to apply substances

EXCLUSION CRITERIA

Certain medical conditions and social habits, which could adversely influence the outcome of the research, project by distorting the data in a constant and predictable way (Hicks 1990). Subjects who had been diagnosed or showed clinical symptoms of the following conditions/habits were excluded from project:

1) Taking certain prescribed medication which may have adverse effects (with exception of oral contraceptives)

2) Smokers of cigarettes/cigars

3) Certain systemic illnesses

4) Mosaic warts and warts located on any other part of the body

5) Verrucae previously treated within 4 weeks of the controlled trial

6) Suffer from known allergies or other skin conditions

Justifications for exclusion criteria:

1) Certain medications if used for a prolonged time can impair or prolong healing. Steroid therapy can increase skin fragility and increase the likelihood of ulceration in response to 'relatively normal stresses'. Steroids can also interfere with the immune system and depress the inflammatory response, so signs of infection are reduced (Merriman and Tollafield 1995). Other medications such as cytotoxics, immunosuppressants, penicillamine and other non-steroidal anti-inflammatory drugs (NSAIDS) may also prolong or impair healing.

2) Cigarette smoke contains two components; nicotine and carbon monoxide which appears to play an important role in inhibiting wound healing. Nicotine inhibits epithelization, its vasoconstricting properties reduce blood flow to the extremities. This in turn delays wound healing (Sherwin and Gastwirth 1990). This factor may have a potential effect on resolution rates of verruca pedis.

3) Individuals suffering from diabetes mellitus or with impaired peripheral blood circulation should avoid the use of salicylic acid as this may cause prolonged or depressed healing to occur (Dermal Laboratories 1999).

4) Immunosuppressed patient including those undergoing chemotherapy, steroid therapy or anti-rejection therapy, and those with leukaemia or HIV are not only more susceptible to HPV, but also find verrucae more resistant to treatment (Ordoukhanian and Lane 1997). Research suggests that individuals who are immunocompromised are less likely to experience spontaneous resolution of HPV than their immunocompetent counterparts. They may experience malignant changes of warts (Beutner *et al* 1991).

5) Mosaic warts are notorious for their longevity and resistance to treatment (Bunney 1992).

6) Past treatment modalities including cryotherapy, strong acids, home treatments such as 'Salactol' used on the verruca four weeks prior to the commence of the trial. These were excluded to rule out the possibility of regression of the lesion being due to something other than the treatments being used in the trial.

7) Salicylic acid can cause sensitivity, excessive drying and local irritation to the skin in some patients (British National Formulary 1998).

Sample Selection

The principle sampling methods used for the purposes of this research project were random and incidental sampling (Polgar and Thomas 1992). True random sampling would have been selection by using a sampling frame and computer-generated figures. However, due to time constraints, a selection of 12 subjects from the parent population were randomly allocated to experimental groups by using a standard table of random numbers.

Individuals meeting inclusion/exclusion criteria were approached with regards to the possibility of participating in the research project.

Materials

All treatments distilled into 10ml dark glass bottles with droppers:

6 bottles: 100% undiluted Melaleuca alternifolia "Tea Tree oil" (Thursday Plantation®)

6 bottles: 16.5% salicylic acid, 16.5% lactic acid in flexible collodion (Salactol®)

Example of treatment label - refer to appendix F

1 emery board (per subject)

Occlusive dressings :

Hapla-Band Strapping (Cuxson Gerrard), varying widths

Sleek Waterproof Strapping, (Smith & Nephew) 2.5 cm width

Semi-compressed felt (5mm)

Graph acetate sheets

Fine permanent acetate marker pen

Resource Funding

All materials were supplied free of charge by the principal investigator.

Computer Software

Microsoft Word Version 3.1 (1995)

Statistical Analysis of data: SPSS 7.5 for Windows Student Version

Graphs:

Microsoft Excel Version 6.0 (1997)

Pilot Study

A pilot study, involving three subjects (without verruca pedis) were selected from the student population attending Northampton School of podiatry to evaluate the methodology. No problems were identified.

Experimental Procedure

All of the controlled trials were performed at Northampton School of Podiatry.

Subjects meeting the inclusion criteria were invited to participate in the research project. Appropriate project information (see appendix B) and instruction sheets were verbally explained by the principal investigator. Informed written consent was required (see appendix C). A full medical history was also documented.

Randomisation of allocation to the two experimental treatments was performed by using a standard table of random numbers.

Allocation to experimental groups was conducted an independent person. Treatments were allocated blind, the key was held by a member of staff at the School of Podiatry.

A patient questionnaire, which also served as a data sheet was documented by the principal investigator with the subject at entry (see appendix D). This recorded information concerning the sex and age of the subject, the history of the verruca, duration, implementation of past treatments and any history of previous verrucas and their duration, allergies, pain and itching caused. A pain scale was also implemented to record details such as pain, which presented at 0, 4, 8 and 12 weeks of the controlled trial. There are several charts available to measure pain. A visual analogue scale (VAS) was used, this is a 10 cm line with end values of ‘no pain’ and ‘pain could not be worse’ (as illustrated on patients

questionnaire/data sheet in appendix D). It was adopted because it is quick to administrate and easy to interpret (Herr and Mobily 1991).

Clinical Diagnosis of Verrucae Pedis

Verrucae Pedis was positively diagnosed by clinical appearance and when meeting the following criteria: -

- The lesion being a single and sharply circumscribed tumour with a hyperkeratotic covering.
- Sharp pain experienced on lateral pressure.
- Interrupted dermatoglyphics was identified (using 10x magnification).

The above methods are commonly recognised for clinical diagnosis (Lorimer, *et al* 1998,)

Data Collection

Verruca lesion size was measured at weeks 0,4, 8 and 12. Measurements were taken by lesion tracing on acetate grid mm^2 squared. An independent observer carried out this procedure to eliminate intra observer error. There were no risks involved in carrying out this procedure. Any overlying callus was reduced with a sterile scalpel blade to facilitate penetration of the substances used a) "Salactol" b) "Tea Tree" oil.

Treatment Application

On entry, participants were instructed on the application of treatments. Subjects were supplied with the following materials:

10 ml bottle either Salactol or Tea Tree oil

1 emery board

Occlusive dressing:

Sleek Waterproof Strapping

Hapla-Band Strapping

Semi-compressed felt

Skin surrounding the plantar wart was protected by masking with a pre-cut aperture pad of semi-compressed felt (5mm). Two drops of one of the substances was inserted into the aperture. The area was then occluded by securing a pre-cut amount of waterproof strapping to the lesion site.

To standardise treatments both experimental groups followed manufacturers instructions for the "Salactol" - refer to appendix E

Method of application directed participants to apply nightly, one of the two substances refer to appendix follows: E

Estimated risks involved the possibility of skin irritation. Patients were advised to adhere to the guidelines as shown on enclosed instruction sheet (see appendix E). If skin irritation did occur patients were informed to discontinue use and contact principal investigator.

Assessment:

Effectiveness of treatments were determined by resolution rates (reduction in size) of the verruca. Clinical inspection for continuation of skin striae was performed by an independant observer. Identification of treatment occurred at the end of the controlled trial. The criteria for cure was complete restoration of the skin ridges in the area of the wart on examination with a magnifying glass (Bunney 1975). Once resolution occurred, participants were not required to attend subsequent appointment for treatments but were continued to be

monitored. If the verruca was still present at the end of the trial, usual podiatric treatment was offered.

Duration: Each patient was treated for twelve weeks, those not cured by the end of the period were deemed as treatment failures. Patients who failed to keep their monthly appointments were given an extra 72 hours in which to be seen by the principal observer. If they failed to do this, they were excluded from the trial but offered conventional podiatric treatment for their verrucae.

Chapter Four

Results

Introduction

Twelve patients entered the study, two males and eight females, aged from 16 to 45 years old.

Two males withdrew from the trial after failing to attend their fourth weekly appointments. Consequently, five subjects participated in each experimental group and satisfied the inclusion/exclusion criteria. Mean ages of subjects participating in the Salicylic acid group were 38 years (range 24-45), compared to the Melaleuca alternifolia group showing a mean age of 27 years (range 16-42).

Treatments were randomly allocated to the numbered bottles as follows:

Melaleuca alternifolia (Tea Tree oil)	**Salicylic acid (Salactol)**
2,5,6,8,10	**1,3,4,7,9**

The raw data collected has been illustrated in tables 1.1 & 1.2 (see Appendix G). Tables 1 and 2 summarises the percentage change of lesion size in both treatment groups.

Table 1: Percentage change of lesion size - Melaleuca alternifolia (Tea Tree oil) group

Patient Number	Measurement	0 Weeks	4 Weeks	8 Weeks	12 Weeks
2	Area in mm^2 % Change	8.0mm^2 -	6.0mm^2 -25.0%	21.0mm^2 +162.5%	16.5mm^2 +106.25%
5	Area in mm^2 % Change	68.5mm^2 -	41.5mm^2 -39.4%	73.0mm^2 +6.6%	36.0mm^2 -47.4%
6	Area in mm^2 % Change	61.0mm^2 -	42.0 mm^2 -31.1%	35.0mm^2 -42.6%	57.0mm^2 +6.6%
8	Area in mm^2 % Change	1.5mm^2 -	1.5mm^2 0%	1.0mm^2 -33.3%	0.5mm^2 -66.6%
10	Area in mm^2 % Change	78.5mm^2 -	67.0mm^2 -14.6%	56.0mm^2 -28.6%	38.0mm^2 -51.6%

% Change has been calculated from the original verruca size therefore it is not accumalative.

Table 2: Percentage change of lesion size - Salicylic acid (Salactol) group

Patient Number	Measurement	Time (in weeks)			
		0 weeks	4 weeks	8 weeks	12 weeks
1	Area in mm % change	12.5mm^2 –	11.5mm -8.0%	6.0mm^2 -52.0%	0.0mm^2 -- 100.0%
3	Area in mm^2 % change	21.0mm^2 -	15.0mm^2 -28.6%	13.0mm^2 -38.0%	13.0mm^2 -38.0%
4	Area in mm^2 % change	26.0mm^2 -	13.5mm^2 -48.0%	21.0mm^2 -19.2%	18.0mm^2 -30.76%
7	Area in mm^2 % change	11.0mm^2 -	4.0mm^2 -63.6%	15.0mm^2 +36.3%	8.0mm^2 -27.27%
9	Area in mm^2	71.0mm^2	64.0mm^2	54.0mm^2	40.0mm^2

	% change	**-**	**-9.8%**	**-23.9%**	**-43.66%**

% Change has been calculated from the original verruca size therefore it is not accumulative.

Table 3. Analysis of the percentage mean change of lesion size at weeks 4, 8, 12 for Melaleuca alternifolia (Tea tree oil) treatment group

Time	Mean	Standard Deviation
Week 4	-22.0200	15.2752
Week 8	12.9200	85.6691
Week 12	-10.5500	70.9242

Table 4 Analysis of the mean percentage change of lesion size at weeks 4, 8 and 12 for Salicylic acid (Salactol) treatment group

Time	Mean	Standard Deviation
Week 4	-31.600	24.1566
Week 8	-19.3600	33.6582
Week 12	-47.9380	29.7900

The mean difference in percentage change of lesions sizes for both groups at weeks 4, 8, and 12 are illustrated above in tables 3 and 4. The means (averages) shown in table 4 indicates that overall a larger decrease in lesion size occurred when treated with Salicylic acid (salactol) compared to lesions treated with Melaleuca alternifolia (tea tree oil).

In order to establish whether there was a significant difference in the percentage change of lesion size between the two treatment groups, an unrelated t test was performed. The following results were obtained:

4 weeks (t=.750 n=10, p <0.05) sign (2 tailed) .475

8 weeks (t=.784. n= 10, p< 0.05) sign (2 tailed) .456

12 weeks (t=.1.087 n=10, p<0.05) sign (2 tailed) .309

The unrelated t tests illustrated that the results were not significant (when P>0.05) and therefore the null hypothesis could not be rejected.

The raw data collected from the visual analogue scale has been illustrated in tables (See appendix H).

Table 5: Mean change in Pain levels for the Melaleuca alternifolia (Tea Tree oil) treatment group

Time	Mean	Standard Deviation
Weeks 0	6.2	3.5637
Weeks 4	3.4	2.0736
Weeks 8	0.8	. 8367
Weeks 12	0.2	.4472

Table 6: Mean change in pain levels for the Salicylic acid (Salactol) treatment group

Time	Mean	Standard Deviation
Week 0	7.2	1.7889
Week 4	6.8	1.6432
Week 8	4.6	.8944
Week12	3.8	2.3875

The mean difference in pain levels for both treatment groups at weeks 0, 4, 8, and 12 are illustrated in tables 5 and 6. Table 5 illustrates that at week 0, pain levels when using a visual analogue scale was comparable. However, analysis at week 4, 8 and 12 shows a significantly greater mean reduction in pain levels when treated with Melaleuca alternifolia compared to Salicylic acid.

Figure 1 demonstrates a graphical representation of the mean percentage change in lesion size between the two treatment groups at week 4, 8 and 12.

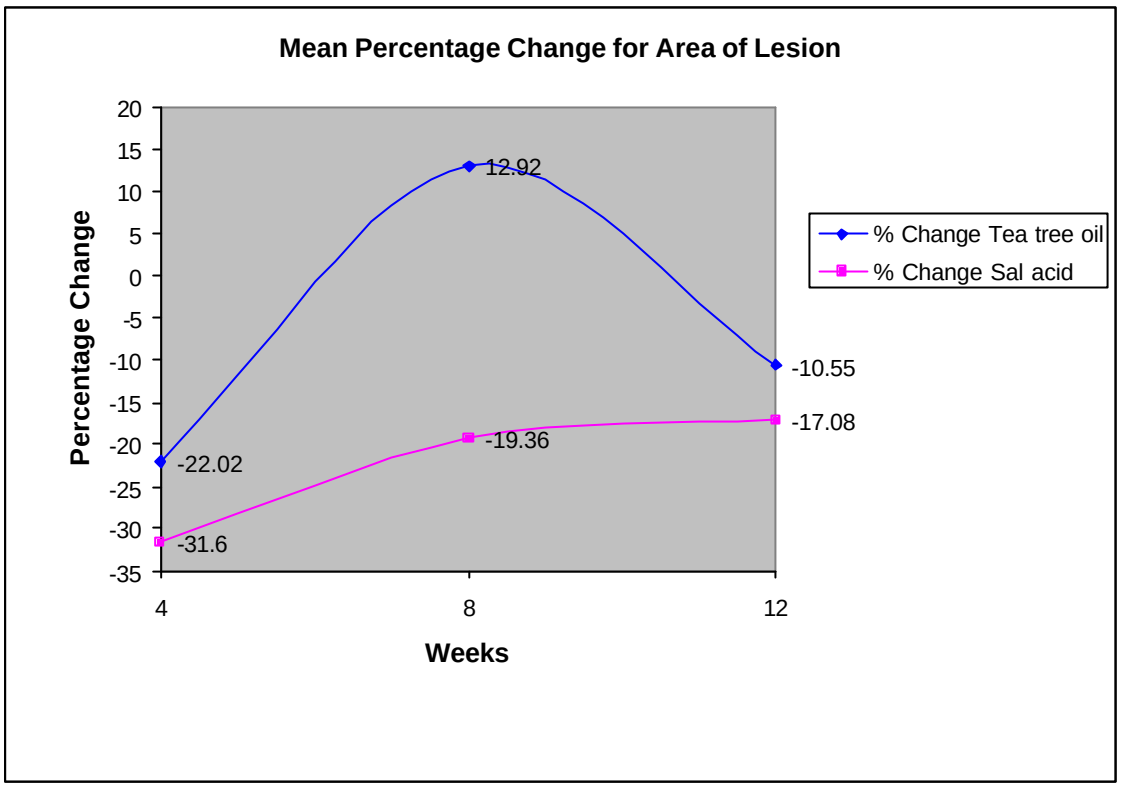
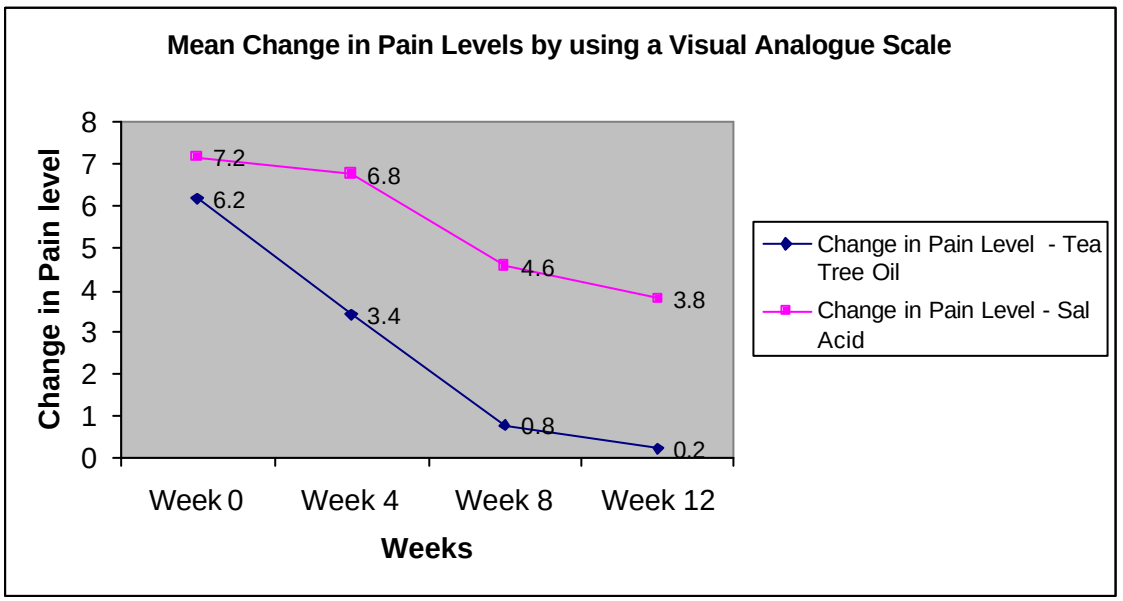
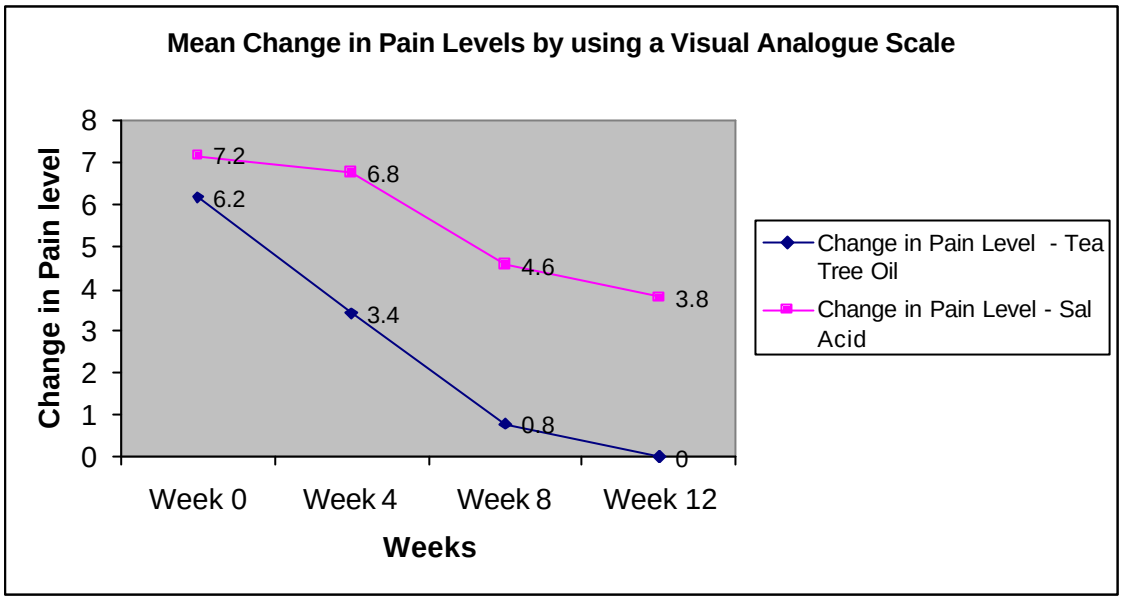


Figure 2 demonstrates a graphical representation of the mean change in pain levels at weeks 0, 4, 8 & 12 of both treatment groups when using a visual analogue scale.





To establish if there was a significant difference in the pain experienced between the two treatment groups when using the visual analogue scale, three Mann Whitney U test were performed. The following results were obtained:

0 Weeks

U = 12.000, n = 10, P< 0.05, sign (1 tailed) .1.000

4 Weeks

U = 2.500, n = 10, P<0.05, sign (1 tailed) .032

8 Weeks

U = 0.000, n = 10, P<0.05 sign (1 tailed) .008

12 Weeks

U = 2.500, n = 10, P<0.05, sign (1 tailed) .032

The Mann Whitney U tests showed that the results at weeks 4, 8 and 12 weeks were significant (when P>0.05), therefore the null hypothesis can be rejected.

Chapter Five

Discussion

The aims and the objectives were successfully achieved as outlined in chapter one.

Significance of the Results

Parametric t tests for unrelated data were used to statistical analyse hypothesis 1(H_1). No significant difference when ($P > 0.05$) was identified when comparing the effects of Melaleuca alternifolia (tea tree oil) to Salicylic acid on the resolution rates of verrucae pedis (two tailed). Therefore, the null hypothesis was accepted.

Non-parametric Mann Whitney U tests was used to statistically analyse hypothesis 2 (H_2). A significant difference was identified, concluding that pain experienced when using a visual analogue scale at weeks 4, 8 and 12 was significantly reduced when treated with Melaleuca alternifolia (one-tailed). The data offered support to the experimental hypothesis (when $P>0.05$) and therefore the null hypothesis was rejected.

The results from this study are not comparable to the findings of Bunney *et al* (1976), who reported a 70-80% cure rate when using Salicylic acid for the treatment of simple plantar warts. The vast majority of subjects were deemed as treatment failures, as only one subject showed complete resolution when treated with Salicylic acid. Subjects 4 and 9 from the salicylic acid group and subjects 2, 8 and 10 from the Melaleuca alternifolia group demonstrated signs of clinical regression occurring; thrombosed capillaries, inflammation and pruritus (itching) (Bender 1986, Cobb 1990, Rook, Wilkinson and Ebling 1998).

Verrucae treated with salicylic acid at 4, 8 and 12 weeks, showed a greater reduction in percentage mean change when compared to lesions treated with Melaleuca alternifolia, as illustrated in figure 1. However, a mean increase (12.9200) in lesion size was observed at week 8 when treated with Melaleuca alternifolia. The increase in lesion sizes and low cure rates could be due to the poor response to previous treatments modalities especially 'over-the-counter' preparations. This could explain why resolution did not occur, thus allowing the virus to become established, and reduce the host's immune response (Lelliot and Robinson 1999).

Subjects ages ranged from 16-45 years old. The mean age for the Salicylic acid group was 38 and 27 for the Melaleuca alternifolia group. Factors such as age, duration of the lesions (range 1-4 years), (see Appendix I), resistance of the warts and the immunologic status of the patient may have also influenced the response to treatment and resolution (Bunney *et al* 1976, Barbosa 1998). The response of warts to treatment decreases as their duration increases, as it does with the advancing age of the patient (Bunney, *et al* 1992).

Massing and Epstein in 1963 reported 67% warts will spontaneously resolve within a two year period. Therefore the assessment of any wart treatment must consider the phenomenon of spontaneous resolution when analysing these results. It is also worthwhile to remember mechanical factors or cell mediated immune responses, (or both), play a part in the cure of these lesions (Steele *et al* 1988).

Pain and the visual analogue scale

Ninety percent of the subjects complained that their plantar warts were painful prior to entry. These were equally distributed between the two treatment groups. As demonstrated in figure 2, significantly more subjects in the Melaleuca alternifolia group reported an overall mean reduction in pain at weeks 4,8 and 12 compared to the other group when using a visual analogue scale. The visual analogue scale is suggested to be simple, economical and can be used with minimal instructions (Chapman, Casey and Duber 1985). Measurement of pain only demonstrates one dimension of the pain experience and therefore is subjective. It also relies on the visual and motor co-ordination of the user (Weir and Burrow 1998).

The results from this study offers support to anecdotal evidence, claiming that Melaleuca alternifolia has analgesic effects (Price 1995, Atlman 1988). The researcher noted that no skin irritation was reported by subjects in the Melaleuca alternifolia group. This could be viewed as supportive to claims that Melaleuca alternifolia is sensitive to skin (Mayo 1992). Similar results were reported by Lock (1995) suggesting that Melaleuca alternifolia appears to produce an analgesic effect, causing plantar warts to become less painful. These finding are subject to criticism, since decrease in pain levels were reported in both the experimental and placebo groups.

Pain is proportional to the degree of hyperkeratosis present (Glover 1990). Subjects 8 and 10 from the Melaleuca alternifolia group and subjects 3, 4 and 7 from the other group reported pain relief on weightbearing after debridement of the hyperkeratotic lesions. The researcher also noted patients reported pain reduction when applying the felt aperture pads,

this may have been attributed to the material re-distributing pressure away from the site. Furthermore, Rook *et al* (1983), suggested that prior to spontaneous regression, verrucae become more painful, therefore this must not be overlooked.

Critique of the Methodology

A double blind procedure would have been desirable to eliminate any bias that may occur through the expectations of the subjects and the researcher (experimenter bias) towards the treatments carried out. This was considered but not adopted as both treatments used have very different properties and distinctive odours.

Because this research was structured around a sample of ten subjects recruited by means of incidental sampling, any interpretation or inferences taken from the data may be questionable (Hicks 1990).

It should be noted that this study relied heavily on the clinical judgement and diagnostic skills of the principal investigator and the independant observer, whose knowledge and experience was limited. Errors could have occurred in the diagnosis of single plantar warts as they could have been perceived as being mosaic lesions. (Bunney *et al* 1992) postulated that mosaic warts are notorious for their longevity and resistance to treatment and this may have accounted for the low cure rates observed.

As illustrated in table 1 and 2 the original diameter of warts varied in both experimental groups. Failure to standardise the size of lesions on entry could have had some influence when statistically analysing the results, as regression could have occurred at different rates.

Berth-Jones and Hutchinson (1992) suggests that the larger the maximum wart diameter, the less likely a patient will be cured.

Recruitment of subjects

Difficulties were encountered in identifying and recruiting subjects that met the inclusion criteria of the study. Several methods of recruitment were employed as indicated in the methodology. Originally, an optimum number of 30 subjects were envisaged, being representative of the parent population however, only 12 subjects were recruited. The small sample size is open to criticism as this is less representative and subject to sampling bias (Coolican 1999, Hicks 1990).

The failure to recruit a larger sample population was due to several reasons:

1) There were a limited number of patients with plantar warts attending the School of Podiatry for treatment.
2) Students and lecturers selecting patients with plantar warts for their own research projects.
3) Many of the patients with verrucas referred to and seen at the School of Podiatry have long-standing lesions that have proved resistant to less invasive treatments modalities.
4) General Practitioner's surgeries incorporate wart clinics into their practices and provide treatment such as cryosurgery.
5) Reduced funding for podiatric services have led to discharge of large number of patients, subsequently this may influence GP's to only refer when absolutely necessary.

Subject Compliance

Patient compliance is a complex issue and a formidable medical problem, which can be influenced by many factors such as, the extent of the patients knowledge, health beliefs, illness behaviour and practitioner-patient communication (Henderson 1998). No subjects within the treatment groups reported non-compliant behaviour. It was attempted to encourage compliance by the inclusion of a chart in the instruction sheet, in which the subject could 'tick' boxes daily which would act as a mnemonic. Written instructions were reinforced with verbal explanations, and any queries were addressed. Compliance, however was not measured quantitatively. Attempts to measure compliance could have been incorporated into the design of this study, for instance, subjects could have been required to return the instruction sheets (with chart) at each appointment.

In addition, it was observed that several of the patients expected instant 'cures' for their plantar warts. This could explain why two of the patients originally recruited withdrew from the trial, as they felt that treatment was insufficiently 'aggressive' and would have no effect.

Measurement of Verrucae

Visual estimations, as adopted in this study, are subjective and can be unreliable (Polgar and Thomas 1992). Discrepancies in the measurement of the verrucae taken at weeks 0,4,8 and 12 may have been attributed to errors made by the investigator in measuring the size of lesions. In future research, test-retest methods of reliability should be employed as part of the pilot study to measure the size of lesions by an independent observer. The test-retest method would show the same result upon was obtained upon repeated administration

(Polgar S, Thomas S 1990). The independant observer may have shown improved accuracy in measuring lesion size as the trial progressed, this is known as practice effect (Hicks 1990).

Difficulties occurred when drawing around the lesions, especially when trying to define the borders. Techniques also relied heavily on the investigator's vision, which was often impaired due to poor lighting. It may have been beneficial to photograph the lesion at each appointment, to record the size, monitor pathological changes and evaluate the effects of the treatments (Merriman and Tollafield 1995).

The acetate sheets used were quite inflexible, and problems were encountered predominantly with raised lesions. It was found to mould poorly around the lesion, therefore the accuracy of measurement is questionable. Opsite® flexigrids were considered as alternative mediums as they are thin, transparent and flexible, however they are costly and measure 1 cm, which is less accurate than the medium used.

Occulsion of the verrucae

Although sleek waterproof strapping was applied universally, it would have been expected from the nature of the material, that maceration would have occurred in both experimental groups. Patients in the salicylic acid experimental group showed whitening of the skin (induced by the salicylic acid) whereas in the melaleuca alternifolia experimental group, the skin surrounding the verrucae was soft and oily without skin maceration this was probably due to the properties of the tea tree oil (Altman 1988).

Further Recommendations for Future Research

No large-scale controlled studies have yet been conducted in this area. It is recommended that future research should take into consideration the problems and issues encountered during this study which have been raised in the discussion. Recruitment of subjects from wart or dermatology clinics within the National Health Service would probably be most conducive to obtaining a larger sample. It is also recommended that research should be divided into separate studies focusing not only adult subjects but also paediatrics.

The trial was restricted to studying single plantar warts because 85% of patients possess this type (Steele, 1988). In future research it may be of interest to investigate other types such as mosaic warts.

A matched pairs design could be incorporated, so groups are matched for age, size, type, number and duration of warts. Treatments groups could be randomised, therefore eliminating factors that may distort the results.

The trial lasted 12 weeks to keep in line with other verruca trials conducted on conventional treatments (Bunney *et al*, 1976). It would be useful for a similar study to be conducted over a longer period of time, in order to learn if the affects of melaleuca alternifolia are enhanced, lost or maintained.

Conclusion

The findings from this study demonstrated that there was no significant difference when comparing the effectiveness of Melaleuca alternifolia (Tea Tree oil) to Salicylic acid (Salactol) for the treatment of single plantar warts. These findings however, should be viewed with caution due to the limitations as outlined in the discussion.

A significant difference was demonstrated, illustrating that Melaleuca Alternifolia significantly reduced pain levels when using a visual analogue scale at week 4, 8 and 12 of the clinical trial. This suggests that Melaleuca alternifolia may have a value for the treatment of verrucae pedis and could be a potential treatment modality for the management of pain relief as part of podiatric practice.

Little evidence based research has been conducted into the therapeutic uses of Melaleuca alternifolia and therefore further investigations are warranted.

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Appendix B

PATIENT INFORMATION SHEET

Verrucae or warts on the feet are a very common problem which we see and treat regularly. They are caused by the same virus which is responsible for warts. Many different treatments are available, some of which are available as home treatments which can be purchased over-the-counter from Pharmacists. Most verrucae will disappear without treatment but this could take 1 or 2 years to happen.

A study is being carried out at Northampton School of Podiatry to investigate the effectiveness of the use home treatments for verrucae. The study will involve applying a treatment of Melaleuca Alternifolia (tea tree) oil, "Salactol" (Salicylic acid) or a placebo (a dummy treatment which contains no active ingredient) to the verrucae.

The student will initially need to measure your verruca and record any pain or discomfort it may be causing. Your first treatment will be given in clinic. Removal of hard skin over the verruca will also be necessary before applying one of the home treatments. You will receive a bottle of one of the substances to use daily at home for the next 12 weeks together with written instructions and a chart for you to complete. It will also be necessary for you to return to the clinic after **4, 8 and 12 weeks** for the assessment and monitoring of your verruca. Each visit should last no longer than 30 minutes.

It is unlikely that you will have any adverse reactions to the substances used. They are widely used. If you find that you are having a any reactions such as if the area becomes red and swollen or undue pain or discomfort, please discontinue. Please keep the substance in a safe place out of the reach of children. Under no circumstances should the substance be taken internally and contact with eyes should be avoided.

All personal information gained is **strictly confidential** and will only be used for the purposes of this study At any time you may withdraw from the study and this will not prejudice further treatment.

Thankyou for agreeing to participate in this study.

Leisa James
Final Year Podiatry Student

Appendix C

Centre Number:
Study Number:
Patient Identification Number for this trial:

CONSENT FORM

Title of Project: "A random controlled trial to compare the effects of two home treatments: Melaleuca alternifolia and Salicylic acid on the resolution rates of verrucae"

Name of Researcher: Leisa James

Please initial

1. I confirm that I have read and understand the information sheet dated ……..... ☐

(version…….) for the above study and have had the opportunity to ask questions.

2. I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason, without my medical care or legal rights being affected. ☐

3. I understand that sections of any of my chiropody notes may be looked at by responsible individuals from the School of Podiatry or from regulatory authorities where it is relevant to my taking part in research. I give permission for these individuals to have access to my records. ☐

4. I agree to take part in the above study. ☐

Name of Patient	**Date**	**Signature**
Name of Person taking consent (if different from researcher)	**Date**	**Signature**
Researcher	**Date**	**Signature**

1 for patient; 1 for researcher; 1 to be kept with clinical

Appendix D

DATA FROM PATIENTS QUESTIONNAIRE / DATA SHEETS

STRICTLY CONFIDENTIAL

MEDICAL HISTORY QUESTIONNAIRE

Name:..... Age:.....
Sex:.....

1. How long has the verruca been present?.....

Howmany are there?.....

Have they increased/decreased in number?.....

2. Has the verruca been treated previously? Please give details of the treatment(s), with their length of duration, and by whom they were undertaken.....
.....

3. Have you any known allergies?.....
(Including skin allergies)

4. Does the verruca cause pain, discomfort, itching or prevent you from performing any usual activities? (please give details) .....
.....

- -

Date Record

(I) Size of lesion (diameter)

Week 0 _____ Week 4 _____

Week 8 _____ Week 12 _____

(ii) Pain scale (0-10) or alteration in discomfort level:

Week 0

|——————————|

(Scale 5cm)

Week 4

|——————————|

(Scale 5cm)

Week 8

|——————————|

(Scale 5cm)

Week 12

|——————————|

(Scale 5cm)

(iii) Description of appearance of verruca e.g. hard skin present, black dots present, bleeding caused at site.

Appendix E

(Manufacturer Instructions)

TREATMENT OF YOUR VERRUCA

Your verruca must be treated regularly everyday, usually in the evening. If you have more than one verruca, only treat the one indicated by the investigator for the duration of this study, and do not use any other treatments than those supplied.

1. Remove plaster over the verruca.
2. Soak the foot in warm water for 2 to 3 minutes.
3 Dry thoroughly with your own towel (to avoid cross-infection).
4. Gently rub away any loose hard skin which is present on the surface of the verruca with the manicure emery board provided (please do not let anyone else use the manicure emery board, to avoid cross-infection).
5. Cut a hole in the felt to fit the size of your verruca and apply it over the verruca (supplied)
6. Unscrew the cap of the bottle, using the dropper /applicator inside, carefully apply two drops inside the felt aperture. Take care to avoid spreading onto surrounding healthy skin, as this may cause inflammation (redness).
7. Cover immediately with another plaster (supplied).
8. Tick and date the chart below as a daily reminder.

WEEK	MON	TUES	WEDS	THURS	FRI	SAT	SUN
1							
2							
3							
4							
5							
6							
7							
8							
9							
10							
11							
12							

During your treatment you may feel a slight tingling sensation and/or some mild tenderness. This is normal and only temporary. However, if you experience undue pain or irritation please discontinue with the treatment. Please only use the substance on the area indicated, do not use on the face, armpits, breasts, bottom or genital regions. Not to be used on moles, birthmarks, hairy warts or any other skin lesions. If accidentally you apply the substance to normal skin, wipe it off straight away, with a tissue, and, if necessary, wash the area.

Appendix F

EXAMPLE OF TREATMENT LABEL

Verrucae Trial Medication

Avoid contact with eyes

Apply Two Drops To the Verruca

APPLY ONCE DAILY

Date of issue:

Name:

No:

_____

Keep out of the reach of Children

Northampton School of Podiatry

Cliftonville Road, Northampton

EXTERNAL USE ONLY

Appendix G

Table 1.1

Patient Number	Measurement	0 Weeks	4 Weeks	8 Weeks	12 Weeks
2	Area in mm^2	$8.0mm^2$	$6.0mm^2$	$21.0mm^2$	$16.5mm^2$
5	Area in mm^2	$68.5mm^2$	$41.5mm^2$	$73.0mm^2$	$36.0mm^2$
6	Area in mm^2	$61.0mm^2$	$42.0\ mm^2$	$35.0mm^2$	$57.0mm^2$
8	Area in mm^2	$1.5mm^2$	$1.5mm^2$	$1.0mm^2$	$0.5mm^2$
10	Area in mm^2	$78.5mm^2$	$67.0mm^2$	$56.0mm^2$	$38.0mm^2$

Table 1.2.

Patient Number	Measurement	Time (in weeks)			
		0 weeks	4 weeks	8 weeks	12 weeks
1	Area in mm	$12.5mm^2$	11.5mm	$6.0mm^2$	$0.0mm^2$ --
3	Area in mm^2	$21.0mm^2$	$15.0mm^2$	$13.0mm^2$	$13.0mm^2$
4	Area in mm^2	$26.0mm^2$	$13.5mm^2$	$21.0mm^2$	$18.0mm^2$
7	Area in mm^2	$11.0mm^2$	$4.0mm^2$	$15.0mm^2$	$8.0mm^2$
9	Area in mm^2	$71.0mm^2$	$64.0mm^2$	$54.0mm^2$	$40.0mm^2$

Appendix H

APPEARANCE/SYMPTOMOLOGY INCLUDING PAIN SCALE

SALACTOL GROUP								
Subject	**Week 0**	**Pain Scale 0-10**	**Week 4**	**Pain Scale 0 - 10**	**Week 8**	**Pain Scale 0 - 10**	**Week 12**	**Pain Scale 0 - 10**
1	Macerated with overlying callus. No bleeding/ black dots present.	5	Macerated with less callus. No bleeding but itchy	7	Dry, hard callus. Itchy	4	Dry, superficial callus. Restoration of normal epidermal skin ridges	0
3	Slight callus; small hard lump. Painful on lateral compression	9	Macerated and white. Painful on palpation/ no bleeding present	8	Macerated and white. No pain. No bleeding.	4	Hard, macerated tissue with dry skin surrounding the lesion. No itching	3
4	Hard raised callus. Painful on lateral compression.	7	Macerated and white. No bleeding. Itchy. Less painful	4	White hard callus present. No bleeding. No itching	4	Hard, raised callus. Itching intermittently. No bleeding present	5
7	Very callused and hard. Black dots present	9	White macerated tissue. Heavy callus surrounding the lesion. No bleeding	8	White macerated tissue. Slight callus surrounding the lesion. No bleeding. Intermittent pain	6	White, macerated tissue. Intermittent pain	5
9	Soft callus. Black dots present. No bleeding	7	White macerated tissue. Thrombus formation.	7	White macerated tissue. Slight callus around lesion. Throbosed capillaries	5	Superficial callus. Occasional itching. Thrombosed capillaries.	6

APPEARANCE/SYMPTOMOLOGY INCLUDING PAIN SCALE

TEA TREE OIL GROUP								
Subjects	**Week 0**	**Pain Scale 0-10**	**Week 4**	**Pain Scale 0-10**	**Week 8**	**Pain Scale 0-10**	**Week 12**	**Pain Scale 0-10**
2	Superficial callus. No itching present.	4	Soft superficial callus. Itchy. No bleeding	3	Soft superficial callus. Bled when filed. Still itchy.	0	Hard callus. Thrombosed Capillaries. Itchy	0
5	Hard callus present. No itching. Painful on lateral compression.	6	Soft callus present. Less painful. No itching. No bleeding but tender	5	Soft callus. present. No itching. Less discomfort	1	Soft callus. present. No itching	1
6	Hard callus present. No itching or bleeding.	0	Callus not as hard. No bleeding. No itching	0	Soft callus.	0	Raised lesion with soft callus. No itching	0
8	Dry callus over site. No itching painful on compression	5	Superficial dry callus. Itchy when removing dressings	4	Soft callus present. Decrease in pain and increase in itching. No bleeding	2	Soft callus. Black dots present. No bleeding. Quite itchy	0

Appendix I

SALACTOL GROUP						
SUBJECT	**SEX**	**AGE**	**NO OF VPS**	**VP SITE TREATED**	**DURATION**	**PAST TREATMENTS**
1	F	24	2	R/F medial plantar aspect of heel	1 year	No Treatment
3	M	42	1	Right foot 5th MTPJ	1 year	Scholl Verruca Pads
4	F	45	1	Right foot Medial aspect of heel	4 years	Cuplex, Bazuka, Sal acid, Monchloracetic acid
7	M	39	3	Right foot 2nd MTPJ	2 years	Bazuka
9	F	40	1	Left Foot Proximal phalanx of hallux	2 years	Bazuka Liquid Nitrogen

TEA TREE OIL GROUP						
SUBJECT	SEX	AGE	NO OF VPS	VP SITE TREATED	DURATION	PAST TREATMENT
2	F	25	2	R/F medial plantar aspect of the heel	R 2 yrs L 6 years	Bazukka & Laser Therapy
5	F	34	1	Right foot Lateral plantar aspect of styloid process	2 years	Liquid Nitrogen
6	F	42	2	Right foot proximal to 2nd MTPJ	4 years	Salicylic Acid
8	F	16	2	L/F medial plantar aspect of heel	4 years	Bazuka
10	F	19	9	Right foot dorsal aspect of 5th MTPJ	4 yrs	Liquid Nitrogen/ Silver Nitrate