CHAPTER I

INTRODUCTION

Tea tree oil, or melaleuca oil, is the essential oil produced by steam distillation of the leaves of the Australian native plant *Melaleuca alternifolia* or tea tree. It has been used medicinally for almost 70 years and many claims have been made regarding its antimicrobial activity. There is no accurate documentation of specific medicinal applications of *M. alternifolia* or the oil by Aboriginals prior to white colonization of Australia. Due to the distillation process required to extract the oil from the leaves of *M. alternifolia*, it is unlikely that this part of the plant was used by Aborigines. However, the medicinal properties may have been known to the Bundjabung Aboriginals of northern New South Wales who told of the healing properties of water into which tea tree leaves had fallen and decayed. It is thought that crushed leaves were also used to make poultices. Regardless of the authenticity of these observations, the highly aromatic nature of the leaves of *M. alternifolia* would probably have led to their use by Aboriginals. *M. alternifolia* is in family Myrtaceae, which has single leaves, regular and bisexual flower with 4-5 petals. Several closely related species, *M. cajuputi, M. leucadendron, M. linariifolia* and *M. quinquenervia* were used medicinally by the Aboriginals for the treatment of headaches, aches and pains, colds and as an insect repellant. The tea tree is a paperbark tree with small narrow leaves arranged on fine branchlets. The oil is found in the leaves. Flowering occurs during spring with fluffy white flowers arranged in clusters. In most cases leaves and small branches were

crushed and the vapor inhaled. Sometimes bruised leaves were soaked in water, which was then swallowed or poured over the body. The early settlers soon came to learn about the healing power of the tea tree and used it on wounds and bites. When Captain James Cook landed at Botany Bay in 1770, Sir Joseph Banks, the botanist, collected samples of leaf from several species of Melaleuca and brewed up a native tea, giving them their common name "Tea Trees". However, extensive use of tea tree oil did not begin until its antiseptic and disinfectant properties were reported early this century. The scientific discovery of tea tree oil was first make by Arthur Penfold, curator and chemist at the Technological Museum, Sydney, in 1922. His studies determined that tea tree oil had a Ridealwalker coefficient of between 11 and 13. This means the oil is 11 to 13 times more powerful than Carbolic acid (phenol) for killing bacteria and fungi yet non-caustic the skin. Subsequent studies revealed tea tree oil as a broad spectrum antibacterial and anti-fungal with a wide range of applications.

In 1930's, commercial production began when Mr. H James, managing director, Australian Essential Oils Limited, arranged for important fundamental research by leading medical and dental practitioners. The raw product his company produced was call "Ti-Trol", and in soluble form of "Melasol". The results of these investigations showed its highest germicidal value was far greater than anticipated. The use of Melasol as a disinfectant and inhalant was advocated in reviews of Preparations and Appliances in the British Medical Journal 1933. The Journal indicated that a wide range of

conditions had responded to the application of tea tree including pediculosis, ringworm, tinea, throat and mouth conditions (Acute nasopharyngitis, catarrh, thrush, "apthous" stomatitis, tonsillitis, mouth ulcers and sore throat), pyorrhea and gingivitis. Melasol was used to treat a large diabetic ulcer, which healed without further infection.

During World War II, all supplies of tea tree oil were commandeered by the Australian Defense Force and people working in the tea tree oil industry were exempt from military service. Tea tree oil became standard first aid issue and was known as the "medicine kit in a bottle". Tea tree oil was also added to machine cutting oils in munitions factories during the war to reduce the infection rate from cuts and injuries to the skin.

During the post World War II years, the tea tree oil industry fell into decline due to a number of factors such as unreliable supply and variable quality. These factors, coupled with a lack of promotion and the advent of antibiotics, led to a decrease in demand for this natural antiseptic. At this point, Australian interest in tea tree oil all but ceased.

Since the reduction in demand for commercial tea tree oil preparations as an antimicrobial agent have enjoyed only sporadic use, primarily by alternative health practitioners. These preparations have consisted mostly of non-commercial formulations made for small-scale use.

Since the 1960's, however, tea tree oil has been experiencing a revival in popularity. The "flower power" generation of the 1960's

and 1970's created a renewed awareness worldwide of natural products and medicines. This brought about the resurgence of tea tree oil and scientists again undertook expansive testing of tea tree oil both in Australia and overseas, in particular the USA and France. The natural product renaissance seen in recent years has resulted in a large range of products containing tea tree oil becoming available in Australia and overseas. Today, tea tree oil has many commercial and personal applications. Many households retain a bottle of tea tree oil for treating common ailments such as acne, minor cuts, dandruff, boils and fungal infections. Moreover, tea tree oil is also used commercially in medicated shampoos, soaps, antiseptic cream, cosmetics, in air conditioning ducting to kill bacteria, in insecticides and in many other ways. New uses are currently in the process of development. (Carson and Riley, 1993:49-55)

Tea tree oil has been examined and found to have a pH-ideal for using on human and animal skin. The pure tea tree oil is non-toxic and does not damage healthy skin around the area treated. Tea tree oil is a complex mixture of hydrocarbons and terpenes consisting of approximately 100 components. There are eight major components, which Terpinen-4-ol is regarded as the main antimicrobial component. Other major components included *p*-cymene, linalool, α- and γ-terpinene, α-terpineol, terpinolene and 1,8-cineole. These components constitute approximately 80-90% of tea tree oil. (Carson and Riley, 1995:264-269) The concentration of each component can vary widely depending on the oil sample and the combination of oil components, which optimizes antimicrobial activity, has yet to be determined. The

oil has gained considerable popularity as a topical antimicrobial agent in recent years. It is reputed to have several medicinal properties including antibacterial, antifungal, antiviral, anti-inflammatory and analgesic properties but the need for appropriate clinical data on the efficacy of tea tree oil products, data on safety are also required. (Carson, Riley and Cookson, 1998:175-178) However, some components responsible for adverse reactions to tea tree oil have been identified, including 1,8-cineole, D-limonene, α-terpinene, *p*-cymene, aromadendrene, α-phellandrene, α-pinene, terpinolene and α-terpinene. For many years, 1,8-cineole was regarded as an undesirable constituent in tea tree oil due to its reputation as a skin and mucous membrane irritant.

Tea tree oil is produced by steam distillation of freshly harvested leaves and terminal branches with water. The oil is then separated from the condensed aqueous distillate and varies from clear to pale yellow in colour. The yield of oil is relatively low, as it occurs at a concentration of approximately 1-2% of the wet plant material weight. (Carson and Riley, 1993:49-55) Today, most tea tree oil is produced on large-scale, mechanized plantations. Quality assurance practices have evolved also. Although a number of national and international standards for tea tree oil have been developed and implemented over the years. These have been largely superceded by the most recent international standard for tea tree oil. For tea tree to be sold commercially for medicinal purposes in Australia, it must meet the Australian Standard for "Oil of Melaleuca Terpinen-4-ol type" (AS2782-1985), which requires the terpinen-4-ol content to exceed

30% and the 1,8-cineole content to be less than 15%. Terpinen-4-ol is the active antimicrobial constituent and that 1,8-cineole is potentially a skin irritant. A recent survey on the use of alternative and complementary medicines in Australia has reported tea tree oil as the most frequently used. Now, tea tree oil products are marketed widely throughout Australia and there is an increasing export market. This increasingly popular nostrum is widely available in North America and Europe in an extensive range of cosmetic and medicinal products through health food stores, alternative health practitioners and some pharmacies. These products include antiseptic creams, hair care products, acne treatments, mouthwashes, and tea tree oil-impregnated toothpicks. In addition, a wide variety of soaps and skin washes claiming antiseptic properties are also available. (Carson and Riley, 1995:264-269)

The present study attempts to formulate suitable hydrogels of tea tree oil using as topical antiviral preparation, particularly for Herpes simplex treatment. However, tea tree oil is not soluble by itself in a hydrogel due to its lipophilicity. Several surfactant systems will, therefore, be evaluated to optimize the gel formulation with respect to the physical stability of the gel and the extent of skin permeation of terpinen-4-ol, the main component of tea tree oil.

Objectives of this study :

1. To develop antiviral gel formulations of tea tree oil for herpes simplex by using four different emulsifiers with three different concentrations.
2. To determine the release characteristic of main component (terpinen-4-ol) of tea tree oil gel formulations.