

**A REVIEW ON *MELALEUCA ALTERNIFOLIA* (TEA TREE) OIL****MANJULA RAMADASS AND PADMA THIAGARAJAN****School of Biosciences and Technology, VIT University, Vellore, India, 632014***ABSTRACT**

Melaleuca alternifolia (tea tree) originates from Australia and belongs to the family *Myrtaceae*. Tea tree oil is known to have a wide range of medicinal properties that include antimicrobial, antiseptic, analgesic, anti-inflammatory, insecticidal and repellent activities. Recent research has suggested that tea tree oil may have a specific role to play in topical applications, for example, in the treatment of acne, rashes, hotspots and other cutaneous infections. Hence its wider function in pharmaceutical and cosmeceutical fields is envisaged in the near future. This review highlights the history, ecology, chemical composition and formulations of tea tree oil that may be important for its potential applications.

KEYWORDS: *Melaleuca alternifolia*, Tea tree oil, Natural product, Pharmaceuticals, Cosmeceutics**PADMA THIAGARAJAN**School of Biosciences and Technology, VIT University, Vellore, India, 632014
padmadk4@gmail.com

INTRODUCTION

Melaleuca alternifolia is commonly known as tea tree. It belongs to the *Myrtaceae* family and is an Australian native plant comprising of more than 150 species. Australian soldiers used its essential oil as a local antiseptic during the II world war. Due to increased applications of *Penicillium* in 1940's, this oil had lost its importance as a potential product for research¹. Tea tree oil exhibits a broad spectrum of antimicrobial activity^{2,3}. It is active against both Gram positive and Gram negative bacteria and other pathogenic yeast. It is also known for its potent cidal properties⁴. It is one of the primary essential oils used in phytotherapy^{5, 6}. It is also used as a vapour decontaminant in health care units⁷. Tea tree oil is one of the very active ingredients in topical formulations. Based on the Scientific Committee on Consumer Products (SCCP), this oil is used in 0.2% of oral hygiene products, 1.25% of skin care products, about 2% of hair care and personal hygiene products and in upto 20% of nail care products⁸.

HISTORY AND ECOLOGY OF TEA TREE

Since several years, the property of tea tree was well known to the Australian Bundjabung

aborigines in the north of New South Wales. The healing potency of tea tree was represented at the end of 18th century by the members of the crew of James Cook⁸. Tea trees are also known as "paperbark trees" and the term specifically refers to the species *Melaleuca* or *Leptospermum* genera⁹. By the nomenclature, the tea tree oil is known as "Melaleuca oil" and "ti tree oil". This oil is extracted by distillation of *Melaleuca* species and is turbid due to the presence of complex mixture of many chemicals. The *Melaleuca* genus (*Myrtaceae* family) involves 230 species that are generally native to Australia. Most of the commercial tea tree oil is produced from *Melaleuca alternifolia*². Generally, tea tree grows naturally, to a maximum of 5-8 meters in height and has a shrub like appearance. During the months of October and November, white to creamy coloured flowers bloom in this tree with terminal spikes that are 6-28m long. Australian tea trees are cultured in plantations and proliferated from seeds^{3,8}.

COMPONENTS OF TEA TREE OIL

As per ISO 4730 (International organization for standardization standard number 4730) the tea tree oil components and their concentrations are given in Table 1^{1,8}:

Table 1
Tea tree oil components and their concentrations

COMPOUNDS	CONCENTRATION as per ISO 4730 (%)	AVERAGE COMPOSITION
Terpinen-4-ol	30-48	40.1
γ-terpinene	10-28	23
α-terpinene	5-13	10.4
1,8-Cineole	0-15	5.1
Terpinolene	1.5-5	3.1
α-terpineol	1.5-8	2.4
α-pinene	1-6	2.6
p-Cymene	0.5-12	2.9
Limonene	0.5-4	1
Aromadendrene	Trace-7	1.5
δ-Cadinene	Trace-8	1.3
Sabinene	Trace-3.5	0.2
Viridiflorol	Trace-1.5	0.1
Globulol	Trace-3	0.2

The tea tree oil is obtained by steam distillation of the leaves. It contains a mixture of 100 components approximately with terpinen-4-ol being the major one and being present in the oil to an extent of about 40%⁸. Based on the chemical composition the tea tree oil is classified into six types. A terpinen-

4-ol type, a terpinolene type and four 1,8-cineole types. Terpinen-4-ol (monocyclicterpene alcohol) is a major active component present in tea tree oil and has anti inflammatory and antimicrobial properties^{9,10}. A terpinolene, that is a monocyclic terpene, and 1,8-cineole that is monocyclic terpene

alcohol, are second major components present in tea tree oil. These sometimes produce allergenic reactions to the tea tree oil products¹¹. However, recent reports have suggested that 1,8-cineole may not be an irritant. In spite of this, reducing the content of 1,8-cineole would help in increasing the levels of terpinen-4-ol which is an important antimicrobial component of tea tree oil¹².

MEDICAL APPLICATIONS OF TEA TREE OIL

Tea tree oil is known for its medical potency that includes its efficacy as an antibacterial¹³, antifungal, antiviral¹⁴, antiprotozoan¹⁵, anti-inflammatory and antiseptic agent^{16,17}. The hydrophobic nature of its most important constituent, *ie.*, terpenes may be responsible for these properties. However the mechanism of action has not been clearly elucidated in most cases. It has been reported that tea tree oil has the ability to activate monocytes and this may play a role in its antimicrobial action^{18, 19}. 20% of pure tea tree oil can penetrate into the human epidermis. Terpinen-4-ol is the single largest compound that can penetrate into the skin^{20, 21}. Tea tree oil is used as a face and body cleaner, toner, healer, scar remover and itch reliever. It is also employed for treating other minor irritations and rashes, as a topical formulation²². Many tea tree oil product are available in market as self treating ones and it has been reported that tea tree oil is one of the essential oil that has shown progressive improvement in its usage for topical applications^{23, 24}.

TREATMENT OF ACNE

Acne is a chronic inflammatory disorder of the skin that affects the young adults and adolescents. It is caused by the bacteria *Propionibacterium acnes*. Certain other factors like abnormal desquamation of follicular epithelium and excessive sebum production may also be responsible for its occurrence²⁵. Acne results in psychological stress and also other physical disturbances such as scar production²⁶. Tea tree oil is one of the best known topical agents to treat acne²⁷. It can be effectively employed to reduce the intensity of lesions (mild to moderate acnes). It has been reported that 5% tea tree oil shows an equivalent effect as

2%erythromycin and 5%benzoyl peroxide. Due to its moderate potency, a combination therapy of tea tree oil with other antibiotics may also be highly effective²⁸.

TREATMENT OF METHICILLIN - RESISTANT STAPHYLOCOCCUS AUREUS

Methicillin-resistant *Staphylococcus aureus* (MRSA) and Methicillin-sensitive *Staphylococcus aureus* (MSSA) are susceptible to tea tree oil²⁹. The oil is applied topically to control MRSA colonized wounds due to its medicinal property. Several *in vitro* studies have revealed the effective activity of tea tree oil against MRSA. 10% of this oil was found to eradicate 87.5% MRSA infections within 28days without any side effects when applied topically. It also promotes fast healing of chronic wound infections³⁰. The efficacy of tea tree oil has been compared with the standard treatment adopted for decolonization of MRSA. About 63% MRSA was isolated from the skin of patients. The infected patient was treated with 5% tea tree oil body wash and 4% tea tree oil nasal ointment with vancomycin (IV)³¹. Mild burning and swelling was reported with the tea tree oil nasal ointment. It was observed that tea tree oil promotes better improvement when compare to standard treatment^{32, 33,34}. *In vitro* studies have been carried out to determine the susceptibility of MRSA to this oil with 1024 mg/L of tea tree oil, 0.5 mg/L of mupirocin and 0.125 mg/L of lysostaphin. It was observed that tea tree oil and lysostaphin can offer additional treatment for decolonization³⁵.

ACARICIDAL AND OVINE LOUSICIDAL ACTIVITIES OF TEA TREE OIL

Ixodes ricinus is an important vector for pathogenic agents that are responsible for causing Lyme disease (*Borrelia burgdorferi*), human granulocytic ehrlichiosis (*Anaplasma phagocytophilum*) and *Rickettsia helvetica*. *Melaleuca alternifolia* is effective lethal agent against the nymphs of *ixodes ricinus*. A study, carried out using different doses of this oil at different time intervals, for treatment of *ixodes ricinus* revealed that at least 90minutes is required to treat the ticks. 8µl of the oil was found to be lethal to 70% of the ticks and 10µl was needed to treat 80% of them³⁶. Due to its acaricidal effects, the tea tree oil is intensely useful in controlling these pathogenic vectors.

Its active component terpinen-4-ol is also used to control *Lucilia cuprina*, which is an Australian sheep blowfly. 1% tea tree oil killed the eggs of *Lucilia cuprina* to an extent of 100%³⁷. *Bovicola ovis* is a sheep infesting louse and its presence affects the quality of wool to a large extent. This can be controlled by a tea tree oil formulation and in turn the nature of wool can be improved³⁸. 1% and 2% tea tree oil have been used to eradicate the lice by soaking and jetting them with the tea tree oil formulation. 100% mortality of eggs and adult lice has been observed upon their treatment with 1% tea tree oil formulation (dipping the wool for 60sec). It is hence inferred that tea tree oil is highly toxic to *Bovicola ovis*³⁹.

TREATMENT OF TINEA PEDIS

Dermatophytes can be controlled by tea tree oil. A randomized double-blinded study to regulate the safety and potency of 25% and 50% tea tree oil for the treatment of interdigital tinea pedis has been reported. Infected patients were randomly treated for 4 weeks with either 25%, 50% tea tree oil or the placebo. A 72% clinical response was reported in patients treated with 25% tea tree oil, 68% response was seen in those treated with 50% tea tree oil and 39% was observed in the placebo group. Severe to moderate dermatitis was reported in 3.8% (four patients) who were treated with tea tree oil⁴⁰.

TREATMENT OF TOE NAIL ONYCHOMYCOSIS

Dermatophytes are responsible for most of these infections⁴¹. 90% of nail infections are caused by *Trichophyton rubrum*. Onychomycosis is a superficial fungal infection that affects the nail bed and total nail plate⁴². A controlled double-blind study was carried out to determine the ability of 5% tea tree oil and 2% butenafine hydrochloride integrated into a cream to treat onychomycosis. The study concluded that the incorporated cream is potent, tolerable, safe and sufficient to cure toenail infections as compared to the placebo⁴³. 80% of the patients were found to be cured of the infections⁴⁴.

EFFECTS ON PLAQUE AND CHRONIC GINGIVITIS

A tea tree oil containing gel is used to control dental plaque and chronic gingivitis⁴⁵. In a double blinded, non cross over, longitudinal study that involved medically fit non-smokers in the age group of 18-60 years with chronic gingivitis, the subjects were treated twice daily with either 2.5% tea tree gel, 0.2% chlorhexidine gel or a placebo gel. It was observed that the 2.5% tea tree gel showed good response in improving gingival and papillary bleeding index⁴⁶. The tea tree group showed high response towards buccal surfaces, all teeth (anterior and posterior) and no response was seen in with respect to plaque staining score. Further responses in periodontal therapy are envisaged^{25, 46}. The role of tea tree oil *Melaleuca alternifolia* against dentistry has been reviewed⁴⁷.

ANTICANCER PROPERTY

Melaleuca alternifolia showed anti-tumor activity against human melanoma M14 wild type cells and M14 adriamycin-resistant cells. Both the resistant and sensitive cells were cultivated in 0.005-0.03% tea tree oil⁴⁸. The terpinen-4-ol, which is the major component present in the oil has the ability to induce apoptosis of melanoma cells (caspase-dependent) mediated by restructuring of membrane lipids and interaction with plasma membrane⁴⁹. The study reported that both the tea tree oil and terpinen-4-ol have the ability to inhibit the proliferation of M14 human melanoma cells and are active against their resistant variants⁵⁰. Terpinene is reported for cytotoxicity and antioxidant property against mouse leukemia p388 cells and cytotoxic activity against tumor cell B16-F10. It was observed that 10% tea tree oil can directly promote cytotoxicity on subcutaneous AE17 tumor cells that activates the specific local immune response⁵¹.

ANTI HELMENTIC PROPERTY

The protozoa *Trypanosoma brucei* and promastigotes of *Leishmania major* were controlled at the concentration of 0.5mg/ml and 403mg/ml respectively and shows 50% reduction. It was suggested that terpinen-4-ol was the major component of tea tree oil responsible for the toxic effects on *Trypanosome brucei*^{47,52}.

CONCLUSION

Tea tree oil, with its versatile medicinal properties can be exploited for pharmaceutical and cosmeceutical applications. It also evokes good response in terms of combination therapy. However, more comprehensive

studies are warranted with respect to the pharmacological aspects.

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