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Review article

TEA TREE OIL - ITS USES AND APPLICATIONS

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ABSTRACT: Tea tree oil (TTO) is an essential oil which has been used in cosmetology since decades. Its phytotherapeutic properties make it useful in several dermatological conditions like acne, dandruff, atheletes foot, etc. TTO is antibiotic, antifungal, antiviral, and anti-inflammatory. Its main chemical constituent is terpenen 4-ol which comprises 40% along with other terpenes. There is toxicity concern associated with TTO. The oil needs more extensive extraction for the isolation of constituents.

Keywords: TTO, antifungal, anti-inflammatory, antitumor, toxicity concern.

INTRODUCTION:

Herbal medicine has been used since thousands of years for treatment of various diseases specially skin disorders. India has been witness of using ayurvedic medicine since 3000 BC. Essential oils (EOs) are volatile, natural, aromatic oily liquids obtained from several parts of the plants like leaves and flowers. It is recommended not to expose EOs directly on to skin because of allergic reactions. The allergenic activity, mainly the contact reactions is produced by the oxidation products of terpenes, terpenoids and other plant metabolites. Hence it needs to use a small quantity on cosmetic formulations, to protect the site of application, and also the integrity of the oil. EOs cannot be used without a pharmaceutical vehicle due to high volatility of its components. Also the possible routes of administration are limited because of the low aqueous solubility. (Pedro et.al. 2013)

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Tea Tree Oil (TTO) is an essential oil containing 40% terpinen-4-ol as a chief constituent determined by gas chromatography (Faiyazuddin et.al. 2009). It is obtained from leaves of *Melaleuca alternifolia* (Myrtaceae) species by a steam distillation process. TTO has been used from decades for its antimicrobial and anti inflammatory properties. It is used topically for its antibacterial and antifungal activities. Sometimes used for its antiviral properties (Carson et.al. 2006). *Melaleuca alternifolia* (tea tree) essential oil has subinhibitory effect on the development of antibiotic resistance in *Staphylococcus aureus* and *Escherichia coli* (Hammer et.al. 2012).

There are three different species of Myrtaceae growing in Australia and New Zealand are known as 'Tea-tree': the Australian Tea tree (Melaleuca alternifolia), the New Zealand Manuka (Leptospermum scoparium) and Kanuka (Kunzea ericoides). All three essential oils are used by aromatherapists, although only Melaleuca has been tested for toxicity, and its antimicrobial effects studied. Differences are between the three essential

oils in their action on smooth muscle: Manuka had a spasmolytic action, while Kanuka and Melaleuca had an initial spasmogenic action. On the uterus,they caused a decrease in the force of the spontaneous contractions. This action suggests caution in the use of these essential oils during childbirth, as cessation of contractions could put the baby, and mother, at risk. Kanuka has strong antibacterial activity than antifungal activity, whilst Manuka displayes a stronger antifungal effect, though not as potent as Melaleuca. The antioxidant activity of Manuka samples was more consistent than that of Kanuka, while Melaleuca showed no activity (Lis-Balchin et.al. 2000).

According to a study by Santos and coworkers nanoparticle of tea tree oil represent antimicrobial activity against American and European foulbrood diseases (AFB and EFB respectively) agents where nanoparticle showed advantages such as slow, gradual and controlled release, increased bioavailability, and reduced side-effects. While evaluating *in vitro* antimicrobial activity of Tea Tree Oil (TTO) nanoparticles against *Paenibacillus* species, including *P. larvae* and *M. plutonius,* it was found that TTO nanoparticle in comparison to TTO presented higher activity and showed no toxic effect even after 7 days of observation. TTO nanoencapsulation resulted in an alternative approach to effectively treat AFB and EFB (Santos et.al. 2014).

Activity of TTO formulations like microemulsions, liposomal dispersions, multiple emulsions and a colloidal bed of sterile clay is affected by change in pH (5.0, 5.5, 6.0, 6.5, and 7.0). Biju et.al. 2005, found that maximum effect of formulation containing 5%w/w TTO was at pH 5.5.

To analyse the terpinen-4-ol concentration in TTO, a validated HPTLC method was used in which the linear calibration curve of terpinen-4-ol was in the range of 100-900 ng. The minimum detectable amount was found to be 60 ng. The tea tree oil recovery was greater than 99% (Biju et.al. 2005).

Though TTO is very promising for topical application but it has been reported by Ernst et.al. 2000 that study on TTO provide no evidence for its efficacy in dermatological condition.

Properties of TTO (WHO 1999)

- Physical appearance: white and transparent oil
- Refractive index: 1.475–1.482
- Optical rotation: +5° to +15°
- Relative density: 0.885–0.906
- Solubility in alcohol: soluble in two volumes of 85% ethanol at 20°C

Chemical Constituents

Tea Tree Oil obtained from *Melaleuca alternifolia* has various mono- and sesquiterpenes along with aromatic compounds. The monoterpenes are terpinen-4-ol, α-terpinene, α-terpinene, 1, 8-cineole, p-cymene, α-terpineol, α-pinene, terpinolenes, limonene and sabinene which account for 80 - 90% of the oil (Table 1).

Table 1: Chemical Constituents present in Tea Tree Oil

Constituent	Minimum %	Maximum %
Terpinolene	1.5	5
1,8Cineole(eucalyptol)	Trace	15
α- Terpinene	5	13
Y- Terpinene	10	28
p- Cymene	0.5	8
Terpinen-4-ol	30	48
α- Terpineol	1.5	8
Limonene	0.5	1.5
Sabinene	Trace	3.5
Aromadendrene	Trace	3
δ- Cadinen	Trace	3
Globulol	Trace	1
Viridiflorol	Trace	1
α- Pinene	1	6
Ledene	Trace	3

Commercially available preparations of TTO (Lahkar et.al. 2013).

Toners- the Bodyshop Tea Tree skin clearing toner
Face cream- Alkeme Gesichtscream Face cream
Mouthwashes- Desert Essence Tea Tree Oil Mouthwash
Shampoos- Patanjali Kesh Kanti Shampoo with Rosemary and Tea Tree Oil
Facewash- Ayur Tea Tree Face Wash for Acne-Prone & Oily Skin

TTO in acne

If 5% tea-tree oil gel in the treatment of mild to moderate acne is compared with 5% benzoyl peroxide lotion. Then both 5% tea-tree oil and 5%

benzoyl peroxide show significant effect in ameliorating the patients' acne by reducing the number of inflamed and non-inflamed lesions (open and closed comedones), although the onset of action in the case of tea-tree oil was slower (Bassett et.al. 1990).

TTO as Antifungal

TTO is active against different varieties of fungus like *Fusarium graminearum*, *F. verticillioides*, *F. subglutinans, F. oxysporum, F. avenaceum, Diaporthe helianthi, Diaporthe phaseolorum var. caulivora, Phomopsis longicolla, P. viticola, Helminthosporium sativum, Colletotrichum coccodes, Thanatephorus cucumeris*, *Candida ablicans* and also *Trichophyton rubrum*, *Trichophyton mentagrophytes*, *Trichophyton tonsurans*, *Aspergillus niger* spices when tested *in vitro* (Lahkar et.al. 2013).

The antifungal efficacy of nanocapsules and nanoemulsions containing *Melaleuca alternifolia* essential oil (tea tree oil) for Onychomycosis has been studied by Flores et.al., 2013. The study demonstrated that the oil containing nanocapsule is most efficient as it reduce the growth of *T. rubrum* on nail infection model, to great extent.

Study demonstrate that the in vivo effect of tea tree oil ointment in the therapy of fungal infections of the skin and mucous membranes as well as in the treatment of dandruff, a mild form of seborrheic dermatitis, may be partly due to an antifungal activity of tea tree oil (Neonoff et.al. 1996).

Hammer et.al., 1998 examined *invitro* activity of essential oil including *Melaleuca alternifolia* and TTO products against candidal species. The tests indicate that TTO containing products retain their activity against *C. albicans*. So they suggested that essential oils are good for treatment of topical superficial infections by candidal species.

For the management of toe nail infection 2% butenafine hydrochloride and 5% *Melaleuca alternifolia* oil is prepared in form of cream (Syed et.al. 1999).

Encapsulating silver ion and TTO in liposome as a combination can enhance its efficacy and can be effective against *Pseudomonas aeruginosa*, *Staphylococcus aureus* and *Candida albicans* at smaller concentration and can also reduce toxicity related problems was reported by (Low et.al. 2013)

For investigation of topical Clotrimazole solution 1% when compared with 100% TTO for its effect against toe nail infection reported symptomatic relief in onychomychosis. (Buck et.al. 1994)

Antifungal effect of TTO has been investigated by Hammer et.al. 2003 which concluded that except β-myrcene, all other components of TTO had antifungal activity. Where they found that some components had lesser antifungal activity during micro dilution as they were absorbed into the polystyrene of microtitre tray. So they sugesseted that TTO should not be stored in plastic containers.

TTO in Tumor

Cutaneous melanoma is invasive, metastatic and resistant to chemotherapeutics. So for innovation in clinical oncology anti-tumoral activity of TTO was studied by Calcabrini et.al. 2004. The study suggested that tea tree oil having terpinen-4-ol as main constituent are able to impair the growth of human M14 melanoma cells and effective on their resistant variants, which express high levels of P-glycoprotein in the plasma membrane, overcome resistance to caspase-dependent apoptosis exerted by P-glycoprotein-positive tumor cells.

TTO as Anti-inflammatory

Inflammatory reactions release various cells like macrophages; nuetrophils which also damage tissues.TTO possess anti-inflammatory properties along with antibacterial properties. Terpinen-4-ol suppress inflammatory mediator production like Intraleukin(IL)-1β, IL-8, IL-10,(Tumor necrosis factor) TNFα, Prostaglandin E_2 (PG-E_2) was determined by examining activated human peripheral blood monocytes and suggested that water soluble component of TTO can suppress production of pro inflammatory mediators by activated human monocytes. TTO when applied to skin may reduce inflammatory responses produced by skin and also produce less toxicity while the water soluble component of TTO may regulate the inflammatory processes (reduce the inflammatory cells and mediators) by penetration into the dermis (Hart et.al. 2000).

Water soluble component of TTO has its effect on superoxides produced by monocytes but not neutrophils. TTO is very toxic it needs to be diluted to prevent toxicity of cells.The water soluble component of TTO is terpinen-4-ol, α-terpineol and

1,8-cineole whose uptake by monocytes and neutrophills is determined by gas chromatography-mass spectroscopy analysis.The cineole and other components of TTO impart percutaneous penetration properties.So they penetrate beyond *startum corneum*. Human peripheral blood monocytes produce TNFα, IL-1, IL-8, IL-10 and PGE2 which is suppressed by terpinen-4-ol of TTO. TTO suppress superoxide produced by monocyte thereby prevent oxidative tissue damage due to chronic inflammatory reactions.

Mechanism

Hammer et.al. 2004 had studied mechanism of action of TTO on *Candida albicans*, *Candida glabrata* and *Saccharomyces cerevisiae*. Permeability and membrane fluidity was assessed that reported that antifungal activity was due to alteration in membrane properties and its functions.

Table 2: Mechanism of TTO (Carson et.al. 2006)

Action	Mechanism
Antibacterial	Disrupt bacterial membrane structural functionality and also inhibit glucose dependent respiration
Antifungal	Inhibit formation of germ tube
Antiviral	TTO application at virus replicative cycle shows greater effect
Antiprotozoal	A 50% reduction in growth (compared to controls) of the protozoa *Leishmania major* and *Trypanosoma brucei* at concentrations of 403 mg/ml and 0.5 mg/ml of TTO respectively.

Table 3: Dose of TTO for different purposes (Carson et.al. 2006)

Dose	Dosage form
5% TTO	Acne
0.2% TTO	Mouthwash
10% TTO	Nasal ointment
5% TTO	Antidandruff shampoo
6% TTO	Antiviral gel
5% TTO	Body wash and hand wash

Toxicity

It is also reviewed that TTO is toxic if ingested orally. It has been reported by The American Cancer Society that tea tree oil when swallowed causing drowsiness, confusion, hallucinations, coma, unsteadiness, weakness, vomiting, diarrhoea, stomach upset, blood cell abnormalities, and severe rashes. It should be kept away from the reach of pets and children. There could arise dermatitis on contact with TTO in air due various oxidation products formation. Correct concentration of TTO is needed to put emphasis on as it can lead to endocrine disturbance which can cause gyanaecomastia (Lahkar et.al. 2013).

In case of oral toxicity the 50% lethal dose for TTO in a rat model is 1.9 to 2.6 ml/kg, and rats dosed with ≤1.5 g/kg TTO appeared lethargic and ataxic. Whereas no death has been reported yet.Dermal prepation with 10% TTO found no irritation. The allergic reactions caused by TTO suggested to avoid the use of neat TTO instead well formulated preparations should be used. Storage of TTO is a major issue due to its volatilization and also that it get absorbed into plastics need a suitable glass container in cool and dry place. Shelf life is around two to three years (Carson et.al. 2006).

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