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A review on efficacy and tolerability of tea tree oil for acne

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ABSTRACT

Acne is common problem acquired generally after puberty. It ranges from mild to moderate: papules, pustules, nodules to severe cyst. Various natural therapy can be employed for treatment of acne including Tea tree oil (TTO). Tea tree oil has wide spectrum anti-microbial agent showing in treatment of acne. Usually it is utilized in various topical preparations. It contains more than 80-90% monoterpenes namely terpinen-4-ol, -cymene, α-terpinene, limonene 1,8-cineol, α-terpineol, terpinolene, 1,8-cineol, sabinene and α-pinene, The European cosmetic Association recommended not more than 1% use of tea tree oil in cosmetic preparations. In this review, we listed various efficacy and tolerability studies along with challenges in application of tea tree oil in cosmetics and dermatological preparations. TTO is a moderate sensitizer and upon oxidation it increases in its allergenic potency. This is a comprehensive review of using Tea tree oil against various microbial species. Various studies revealed the use of TTO as anti-bacterial, anti-fungal, anti- oxidant agent. TTO is effective treatment option that can further be utilized in preparation of novel formulations like liposomes, ethosomes along with combination with other anti-microbial and anti-oxidant agents.

Keywords: Acne, Tea-tree oil, Application, Antioxidant, Nano particles.

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1. INTRODUCTION

1.1 Acne Vulgaris

Acne is produced by bacterium *Propionibacterium acne*. It is a chronic inflammatory skin disorder caused by a combination of factors, including excessive sebum production, abnormal desquamation of the follicular epithelium **[Kurokawa et al., 2009].** Up to 95% of the population suffers from acne vulgaris **[Ho et al., 1995].** Usually acne is classified on the basis of its severity in to mild, moderate and severe. Generally acne are characterized by the existence of small pimples as well as whiteheads and blackheads comedones with the absence of inflammation. Patient having moderate acne developed larger blackheads, pustules and papules along with having inflammation. Mild acne are of closed and open comedones which are generally less than 20 whereas inflammatory lesion are generally less than 15. In moderate acne abundant papules and pustules were observed along with comedones **(Layton 2005; Truter 2009)**. Severe acne forms painful pustules comedones and cyst nodules that often leave scars on skin. The total cyst observed is less than 5, total comedones in severe acne are observed greater than 100 whereas total number of lesions were found to be more than 125. **(Taher et al., 2017; Jacob et al., 2001).**

The incidence of acne vulgaris starts at the age of 17 **(Raap et al., 2006**) as at late adolescents age **(Tasoula et al., 2012)** the appearance develops to change. Even it may persist after age of 25 years. In a study done by France and USA, the activity of acne persists during 30-40 years **(Layton, 2010**). Topical agents are mostly used for the treatment of acne. These are generally alpha- hydroxyl acid, azelaic acid, retinoids, keratolytics etc. **(Ross et al., 2003; Humphrey 2012).**

Essentials oils and medicinal plant extracts have been extensively studied as another option to overcome the problem of antibiotics resistance. Herbs are known as safe, effective as well as multifunctional. Ingredients used in topical acne treatments, especially herbs and naturally derived compounds have fewer adverse effects in comparison with synthetic agents **(Daud et al., 2013).**

1.2 Tea Tree Oil

Essential oil of Melaleuca alternifolia i.e tea tree oil consists largely of cyclic monoterpenes comprising of 50% are oxygenated and 50% are hydrocarbons. The active ingredient of tea tree oil is terpinen-4-ol that attenuates to broad- spectrum antimicrobial activity **(Southwell et al., 1993).** TTO has a wide range of pharmacological action including antibacterial **(Low et al., 2013**), anti-fungal **(Bakkali et al., 2008**), anti-inflammation **(Hart et al., 2000**, antioxidant, anti-tumorial, and immune regulational effects **(Ramage et al., 2012**). Various clinical studies of tea tree oil

suggested better efficacy in multiple diseases like oral candidiasis, molluscum contagiosum, tinea, acne and onychomycosis **(carson et al., 2013; Markum et al., 2013).**

In many OTC product tea tree oil are used including those are targeted at treating acne. Products are included body washes, soaps, toners, face wash, mask and blemish sticks. Many OTC topical combination products are available containing TTO with another acne treatment agents like salicylic acid, benzoyl peroxide, azelaic acid and glycolic acid are available (**Hammer, 2015).**

1.3 Mechanism of action

Terpinen-4-ol is known to reduce the production of interleukin-1 (IL-1), IL-8, IL-10, prostaglandin E2, and tumor necrosis factor (TNF). The water-soluble fractions of TTO, terpinen-4-ol and a-terpineol, suppress superoxide production by monocytes but not by neutrophils of oxygen species. Additionally, terpinen-4-ol, modulates vasodilation and plasma extrava- sation **(Carson et al., 2006).**

2. COSMETO-DERMATO APPLICATION OF TTO

2.1 Antioxidant activity

Tea tree oil serves as an antioxidant. a-terpinene, a-terpinolene, and c-terpinene are the antioxidants derived from crude TTO. Their antioxidant action follows the order: a-terpinene > a-terpinolene > c-terpinene **(Kim et al., 2004).**

2.2 Antibacterial activity

Terpinen-4-ol is very effective against agents coagulase-negative staphylococcus (CONS) and methicilline-resistance staphylococcus aureus(MRSA). At 10% concentration TTO effect was comparable with those of topical mupirocin against the bacterium s. aureus **(Thompson et al., 2008).**

An addition of solubilizer to formulation containing TTO increases the anti-bacterial activity of TTO. As per American European combination of 0.5% TTO along with 5% solubilizer having 0.3% preservative found to have enhanced stability of soft body balm **(Soukoulis et al., 2004).**

2.3 Antifungal activity

TTO is also found to kill candida species in vitro **(Hammer et al., 1998).** In a double blinded randomized control study with 25% and 50% TTO demonstrated influential response in tinea pedis **(Satchell et al., 2002).** It is also showed that a formulation with 2% butenafine hydrochloride and 5% TTO resulted is 80% reduction in toenail onvchomycosis without any relapse **(Syed et al., 1999).**

Due to easy penetration action TTO it is also found to be effective against madueralla mycetomatis and hence it is efficience treatment option for eumycetoma- a chronic fungal disease **(Sande et al., 2009).**

3. EFFICACY OF TEA TREE OIL IN TREATMENT OF ACNE

Earlier study on melaleuca plant reveals strong antimicrobial, antifungal and anti-infective property which accelerate its used in dermatological and cosmetological preparation. It has been extensively employed in toothpaste, soaps, gels, lotions and creams **(Julie, 2006; Cox et al., 2000).** The plant of genus melaleuca became common in second and third decade of 20th century during Second World War **(Carson et al., 2006; Julie, 2006)**.

In a study by Feinblatt, 35 patients in which 10 were untreated controls and 25 were tea tree oil treated were subjected for the treatment of furunculosis. The scientist used TTO and reported that the incidence of incision on the infected site was reduced (**Feinblatt, 1960).**). 5% TTO gel observed to improve acne lesions however the onset of action in the case of TTO was slower **(Enshaieh et al., 2007**).

In a single-blind randomly comparative therapeutic clinical trial, effectiveness of 2% tea tree lotion was compared with 5% zinc sulphate. 47 patients with acne vulgaris were randomly divided in a group of two. Group A used TTO lotion and group B used 5% zinc sulphate solution. Patients with papulopustular lesions were involved in the study, while patients with severe acne were excluded. 2% TTO lotion was found to be better remedy in treatment of acne vulgaris and was much beneficial than 5% zinc sulphate **(Sharique et al., 2008).**

In a study by Mazzarello et al., a combination of propolis, tea tree oil and aloevera compared to erythromycin cream. Two double blind investigation were carried on 60 patient suffering from mild to moderate acne. Patients were divided in to 3 groups: first treatment with cream containing 20% propolis, 3% TTO and 10% aloe vera, second with 3% erythromycin cream and third with placebo. In comparison to placebo group patient treated with TTO, aloevera, propolis and erythromycin cream significantly showed high reduction in papules and scar lesion after 15 and 30 days (**Mazzarello et al., 2018).**

In a eight week double blind randomized controlled split-face study clinical efficacy and histological effect between lactobacillus fermented chamaecyparis obtusa and TTO for the treatment of acne was compared. A total of 34 patient were advised to apply 5% LFCO on one side of face and 5% TTO extract on other side for 8 weeks. It was found that, inflammatory acne lesion were reduced by 65.3% on using LFCO while 38.2% reduction was seen with TTO. LFCO also showed quicker onset efficacy time without any side effect. The compound LFCO found to be more effective and safer way of treatment as compare to TTO **(Kwon et al., 2014).**

Malhi et al., conducted on open label control study evaluation of TTO gel and face wash for the treatment of mild to moderate facial acne. 18 participants enroll for the study and the effect of formulation was determined after 4,8 and 12weeks. The author found means total lesion count were23.7 at baseline, 17.2 at 4, 15.1 at 8 and 10.7 at 12 weeks. The product was found to be well tolerated with no serious adverse effect **(Malhi et al., 2016)**

4. TOLERABILTY

Yadav et al evaluated efficacy of tea tree oil for acne an open-label comparative study among 5% tea tree oil gel, 5% tea tree oil gel along with polyherbal tablet (neem, turmeric and black pepper) and polyherbal tablet alone has been performed. The gel to be applied once in a day and the tablet were taken twice a day for 4 weeks. 62.1% total reduction in lesion count was observed in case of tea tree oil gel 73.7% in along with tablet and 73.0% for tea tree oil alone. Acne was found to be improved but no side effects have been reported **(Yadav et al., 2011).**

Basset et al conducted a single – blind randomised trial of benzoyl peroxide lotion versus TTO gel for the treatment of mild to moderate acne. 124 patient enroll for the study were asked to apply either one or the other treatment each day for 3 month. The number of inflamed and non-inflamed lesions had been pre-defined as the primary endpoint of the study. Lesions were counted at baseline and at monthly intervals. The result were analysed for 1, 2 and 3 months. Benzoyl

peroxide was found to be more effective than TTO. The effect of TTO was slower however was clinically, apparent adverse effect with TTO was lower than control group than TTO was more effective **(Ernst and Huntley 2000).**

Pearce et al conducted one study to find reduction of nickel induces contact hypersensitivity reaction by topical TTO in humans. A topical of 18 patients with nickle hypersensitivity was induced in the study. 100% TTO was taken used as a test formulation. The flare area and erythema was measured on 3, 5 and 7 days. The 5% TTO lotion, the placebo lotion and the 100% macadamia oil were all without significant effect. No skin reaction was observed during the study, however population expose to oxidized degraded product of TTO show adverse reaction **(Pearce et al., 2005).**

Joksimovic et al evaluated the efficacy and tolerability of hyaluronic acid, TTO and methyl- sulfonyl methane in a new gel medical device for treatment of haemorrhoids in a double blind placebo controlled clinical trial. The study was conducted on 36 haemorroidal patients. Author reported 14 day treatment with proctioal gel and found its efficacy decreasing some symptom of haemorrhoids. The presence of hyaluronic acid, TTO and methyl – sulfonyl methane proctioal formulation provided a crystal clear therapeutic efficacy. TTO exerted dual effect on eradication of bacteria that produce hyaluronidase of hyaluronic acid and also protect micro- envoirment in bleeding haemorrhoids. This clinical trial also reveal that the proctioal treatment was safe and well tolerated. This topical treatment was also effective to delay and prevent hemorrhoidectomy **(Joksimovic et al., 2012).**

The study on human volunteers using TTO has experienced allergic reactions but the rate of occurance is low. In reality TTO acne studies reported the tendency of having adverse reaction is higher than patch test in evaluating function of TTO for non acne lesion **(Aspres et al.,2003; Toholka et al., 2014).**

5. CHALLENGES WITH TEA TREE OIL

In presence of high temperature, light and humidity, the effect of tea tree oil worsen up.

Due to sensitivity tea tree oil, its antioxidant compound α-terpinene, ɣ-terpinene and terpinolene get converted to p-cymene. European Cosmetics Association allowed any only 1% use of TTO and should be packed to provide minimal light exposure **(Sarkic and Stappen, 2018).** People sensitive to TTO develop rashes, erythema and allergic reaction reducing its effect in use of cosmetics. It has also shown to cause adverse effect with the use of oxidized tea tree oil preparation. At high concentration, TTO causes toxicity.

6. COMMERCIALIZATION OF TEA TREE OIL

As the demand of natural product are increasing effectively the sales of TTO is also increase. TTO has multiple natural advantages yet some of them are being used by industry. In the previous study of revival it is used “cure all” agent. This oil has a good clean to aforementioned description but market is limited for such prod To cover wide range of advantage, various clinical evidence is required that prove for its efficacy **(Southwell A and Lowe R; 2005).**

7. Future prospects

Tea tree oil however at lower concentration is effective against candida albicans, E.coli, Propionibacterium acne and many more disease. Various novel formulations like nanoparticles, liposomes, ethosomes can be prepared using various anti-microbial agents like Tritinoin, salicylic acid, benzoyl peroxide, lemon oil, *Azadirachta* so *indica* extract etc. Various formulations should be prepared with variation in their strategies that it should be stable and not degraded with oxidation. Various anti-oxidants can also be included so that no degradation of product can take place.

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