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# A Review on Efficacy of Tea Tree Oil in Treatment of Acne Vulgaris

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## Abstract

Tea tree oil (TTO) is an essential oil extracted from the leaves of *Melaleucaalternifolia* by steam distillation and its supercritical fluid extraction has found a broad range of antimicrobial activities as antifungal, antiviral, antibacterial, antimicrobial properties due to the presence of terpinen–4-ol as the major constituent. Tea tree oil is a natural product, non-toxic, biodegradable, and biocompatible. The several applications of tea tree oil make it one of the best medicated products having therapeutic effects. The present review is based on the application of tea tree oil, extraction process, constituents, and safety considerations in the treatment of Acne vulgaris. Acne is general problem acquired after puberty. It ranges from mild to moderate: papules, pustules, nodules to severe cyst. Various natural therapy can be employed for treatment of acne. 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. TTO is effective treatment option that can further be utilized in preparation of novel formulations like microemulsion based gels, liposome's, ethosomes, lipid nanoparticles along with other anti-microbial and antioxidant agents.

**Keywords**

Tea tree oil, Acne, efficacy, anti-microbial activity.

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## INTRODUCTION

Acne Vulgaris is one of the common skin conditions in adolescents. Acne Vulgaris effects more than 85% of adults, frequently starts in preadolescence and continue into adulthood [1,2]. If it is combined with negative impact on psychological health that shows increased prevalence or changes in mood, causes severe conditions like psychiatric problems, unemployment, and social intention [3]. The average annual burden of acne is $3000000000 in US [5]. Along with that, the existence of mental health diseases or disorders can cause schizophrenia depression that can lead to anxiety, alcohol use, adjustment, and many other disturbances. On the

circumstances of drastic development of antibiotics resistance around the world, there is a global movement that defines of away from the antibiotics monotherapy to reduce the use [4, 6]. Due to more prone ubiquitous feature of acne in the teenage, there will always be the need of new or novel treatments. In this present situation, Isotretinoin had become the drug of choice to scientists for mild to moderate to severe acne treatments [2,7]. It can cause distract in social life, mental life, emotional life and psychological disturbances can occur. Acne Vulgaris usually occurs due to development of body androgens. It may cause to anyone regardless to sex [4,8].

**CAUSES OF ACNE VULGARIS**

Acne Vulgaris is mainly caused due to the infectious bacteria known as staphylococcus aureus and propionic bacterium acne. These strains can be able to change is ability, activity, abnormal production of oil, changing in sloughing of acne pores and inflammation. Sometimes food is also one of the major factors to cause acne. Intake of glycolic diet may increase the problem. In some of the cases genetic and hormonal imbalance can also cause acne [9].

**Hormonal factors**

A range of factors triggers acne, but the main cause is thought to be a rise in androgen levels Androgen is a type of hormone, the levels of which rise when adolescence begins. In women, it gets converted into estrogen. Rising androgen levels cause the oil glands under the skin to grow. The enlarged gland produces more sebum. Excessive sebum can break down cellular walls in the pores, causing bacteria to grow [7-9].

**Other possible triggers**

Some studies suggest that genetic factors may increase the risk.

Other causes include.

some medications that contain androgen and lithium.

- Greasy Cosmetics
- Hormonal Changes
- Emotional Stress
- Menstruation

**General treatment for Acne vulgaris**

A variety of steroidal and non-steroidal creams and gels are available to treat acne, and many are effective. Mild acne can be treated with over the counter (OTC) medications, such as gels, soaps, pads, creams, and lotions that are applied to the skin. Creams and lotions are best for sensitive skin. Alcohol-based gels dry the skin and are better for oily skin [9,10].

OTC acne remedies may contain the following active ingredients:

- **Resorcinol**: Helps break down blackheads and whiteheads.
- **Benzoyl peroxide**: Kills bacteria, accelerates the replacement of skin, and slows the production of sebum.
- **Salicylic acid**: Assists the breakdown of blackheads and whiteheads and helps reduce inflammation and swelling.
- **Sulfur**: Exactly how this works is unknown.
- **Retin-A** helps unblock pores through cell turnover.
- **Azelaic acid:** strengthens cells that line the follicles, stops sebum eruptions, and reduces bacterial growth [10, 11].

**MEDICAL TREATMENT:** The treatment of cane can be done through topical, oral, or systemic routes. Patients with this problem suffer from mild to moderate and moderate to severity, inflammatory acne are given oral antibiotics as the first-line therapy isotretinoin is mainly recommended to avoid long term topical or oral antibiotic therapy. Although it is one of the powerful teratogens maintaining strict precautions for the use among women and during pregnancy. Patients with high risk of acne, both oral and topical treatments are usually prescribed after 6 to 8 weeks of usage the efficacy, adverse drug reactions and patient compliance is regulated and if any changes occurred the treatment regimen is changed, if necessary [11,12].

No regimen is free form side effects. A vast variety of treatment regimens are present for acne vulgaris include many ingredients. They are retinoids, isotretinoin, keratolytic soaps benzoyl peroxide, alpha hydroxy acids, azelaic acid, salicylic acid as well as hormonal, anti-seborrheic, anti-androgen treatments. There are some types of techniques used in the treatment like direct injection of steroids into inflamed cysts, chemical peels, radio frequencies, microderm abrasion, light or lasers have been shown a great relief on acne. Using of alternating methods for acne is using of herbal plant products [13].

**Evidence of selection of herbal oil**

Herbal oils are useful in prevention and treating variety of systemic manifestations such as carcinomas, cardiac related diseases, hormone related diseases as diabetes etc. Topical and oral antibiotic monotherapy is not actually recommended to be given worldwide as they cause bacterial resistance [14]. They should not be used as monotherapy as they are causing rapid resistance to antibiotics after weeks to months. Medicinal plants are also possessed to diminishing drug induced

adverse reactions. Topical antibiotics can be used as the choice of drugs for treating acne vulgaris and associated with anti-inflammatory effects [15].

**Medicinal plants with anti - acne activity.**

Ayurvedic extracts are composition that are incorporating phytonutrients from different varieties of plant sources showing the effects on skin functions and distributing nutrients which are beneficial for the smooth and glowing skin and beautiful hair [16,17]. These phytochemicals extracted from various sources are having two benefits:

- As they are treated as cosmetic products for skin care.
- The herbal components with biological activity to the skin and furnish nutrients beneficial for the healthy skin and hair [18, 20].

**Herbal medicines in treatment of acne**

Ayurvedic medicine is popular for is advantages as they are well tolerated by patients, gives better results on long use, show very minute reactions and are ridiculously cheap in cost [19,22]. Here is many evidence that Ayurveda had cured many difficult and noncured diseases [21,24]. Most prior other than consumption as prevention of treatment remedy, they may be associating with synthetic drugs to reduce their risk factors [24,25]. Acne vulgaris drugs have adverse effects whereas medicinal plants popularly known as herbal products are the combo in introducing newer drug regimens [23].

**ADVANTAGES OF HERBAL PRODUCTS:**

Advantages include.

- Using of herbal products like tea tree oil is highly nutrient rich. Our stratum corneum have the capacity to soak some substances. It acts as a preventive barrier for thew penetration of hazardous compounds. In some cases, cocoa butter acts as effective organic moisturizer having essential fatty acids, for the nourishment and healthy skin [24, 26].
- These herbal products are less expensive and economic when compared to chemical or conventional products. World Health Organization (WHO) has revealed that around 75-80 percent of the world population is depending on the herbal products in the antagonistic treatment on acne and to use the high cost manufactured products [22, 29].
- These herbal products are eco-friendly in nature and do not cause any side effects. Most of the conventional products contain aluminum in it which may cause Alzheimer's diseases and breast cancer. So, using of eco-friendly products is the better advice [26,27].
- Using of harsh chemicals is also one of the main reasons for not using conventional medicine and using herbal products. Using of chemicals may cause side effects which may lead to allergic reaction, irritation etc., in individual. Some of the chemicals can be poisonous for the endocrine system and may also cause Type II diabetes and cancer. So, use of herbal products without chemicals is the better way.
- These herbal products will increase the efficient nutrient safety, optimum entrapment efficacy and bioavailability.
- These are also used in heart and liver diseases.
- Used as anti-inflammatory, trophodermic, lipolytic, antioxidant and immunomodulatory agent [28,29].

**TEA TREE OIL**

Tea tree oil (TTO) is a volatile oil extracted from the leaves of Melaleucaalternifolia, a native plant from Australia. Tea tree oil (TTO) is used in the treatment like acne, tinea, dandruff, burns, vaginal thrush and arthritis due to its highly curable activity of anti-inflammatory, anti- microbial, anti- bacterial, antiseptic, and analgesic property [30, 32]. Clinical studies with tea tree oil products have shown efficacy for several superficial diseases including acne, oral candidiasis, tinea, onychomycosis and molluscumcontagiosum [31].

The volatility nature of TTO is only due to the presence of terpenes and about 90 percent. In recent years, the in vitro studies have proven that broad-spectrum anti-bacterial activity is against both gram positive and gram-negative bacteria [33,36]. One of the studies proved that TTO is powerful for mild to moderate to skin inflammation and for acne. The TTO composition is composed of terpene hydrocarbons, sesquiterpenes, monoterpenes and their associated alcohol. The primary active component is terpene-u-ol with ranging the concentration between 30-48 percent. The activity of terpinene-u-ol depends on retain of stability at a sufficient release rate [34, 35]. There are some other components like alpha terpenes, gamma terpinene and terpinolene. There can be oxidize in the existence of oxygen, light, humidity, high temperature. This degradation can cause skin irritation, odour and color changes and cause allergic reactions [37].

**Table 1: Summary of clinical studies evaluating tea tree oil (TTO) products for the treatment of acne.**

| S.NO | Treatment group | Trial design | Product application | Efficacy (mean reduction in total lesion count[a]) (%) | Tolerability (frequency of adverse events) | Outcomes | Reference |
|---|---|---|---|---|---|---|---|
| 1 | (1) TTO 5% gel (n = 58)<br>(2) BP 5% (n = 61) | Double-blind | Twice daily (left on) for 8 weeks | (1) 29.3<br>(2) 45.9 | (1) 44%<br>(2) 79% | Both treatments significantly reduced inflamed lesions, although BP better than TTO. Treatment's equivalent for reducing non-inflamed. Treatments equivalent for reducing non-inflamed lesions and erythema | 38 |
| 2 | (1) TTO 5% gel (n = 30)<br>(2) Erythromycin 2% gel (n = 30) | Investigator blind | Twice daily (left on) for 6 weeks | (1) 55<br>(2) 40 | Rates not stated; rates for groups not significantly different | TTO significantly better than 2% erythromycin at reducing lesion numbers | 39 |
| 3 | (1) TTO 5% gel (n = 30)(2) Placebo (n = 30) | Double-blind | Twice daily(washed off)for 6 weeks | (1) 43.6(2) 12.0 | (1) 10%(2) 6.7% | TTO significantly betterthan placebo at reducinglesion numbers. Significantdecrease in total lesioncount and acne severityindex after TTO treatmentbut not placebo | 40 |
| 4 | TTO 5% gel (n = 46)<br>(2) TTO 5% gel + Perfect tablet (n = 46)<br>(3) Perfect tablet alone (n = 48) | Open label | Gel applied once daily; tablets taken twice daily for 4 weeks | 1) 62.1<br>(2) 73.7<br>(3) 73.0 | No serious adverse events reported | All treatments significantly reduced lesion number compared with baseline. No statistics performed comparing all groups | 41 |
| 5 | TTO 5% extract (n = 34)<br>(2) LFCO 5% extract (n = 34) | Double-blind | Twice daily for 8 weeks | 1) 38.2c<br>(2) 65.3 | 1) 31.3%<br>(2) 12.6% | Inflammatory lesions significantly reduced by both treatments; LFCO better than TTO. LFCO also reduced non-inflammatory lesions | 42 |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| 6 | Baseline + mixture of TTO 3% and lavender oil 2% (n = 27) | Not stated | Oils applied twice daily (washed off) for 4 weeks. Baseline not stated | 1) 9.2<br>(2) 4.8 | 1) 3.7%<br>(2) 0% | Numbers of inflammatory lesions significantly reduced compared with baseline | 43 |
| 7 | TTO 0.1% + Ramulusmori extract 0.01% (n = 20) | Case controlled | 4 Weeks | 28.7 | Not stated inEnglishabstract | Numbers of inflammatorylesions significantlyreduced compared withbaseline | 44 |
| 8 | Pea-sized amount of **tea tree oil** medicated gel (containing 200mg/g **tea tree oil**) applied to the face twice daily for 12 weeks | Uncontrolled, Open-label, Phase II Pilot Study | Gel Applied Topically Twice Daily for the Treatment of Mild to Moderate Facial Acnefor 12 weeks. | NA | approximately 1.4%) | **Tea tree oil** gel will result in a significant improvement in acne | 45 |

Note: *BP, benzoyl peroxide; LFCO, Lactobacillus fermented Chamae cyparisobtusa. A. Data are from the end of the stated treatment period. B. The authors stated that the study was technically single blinded as patients were likely to be able to identify which product they had received. Inflammatory lesions only; reductions in total lesion count not state.*

**MECHANISM OF ACTION**

Terpinen-u-ol have the ability to decrease or reduce the development of tumor neurosis factor (TNF), interleukin -1(IL-1) , IL-8, IL-10 and prostaglandin E2 .In addition of this the water soluble property of TTO terpinene-u-ol and a-terpineol . Decrease the superoxide production by monocytes but not by neutrophils of oxy species. In additional to that, terpinene-u-ol but not 1,8-cineole or a-terpineole, modulates vasodilation and plasma extraction [33].

**EFFICACY OF TEA TREE OIL**

Tea tree oil is an olden days remedy it act as anti-fungal, anti-viral, acaricidal, wound healing, and antibacterial activity which reduce the irritation in turn can decrease skin inflammation [38]. It also act as a strong disinfectant and antiseptic property.it is a basic component in various sunscreen that mitigate sunburn by promoting blood circulation in vessels, conveying supplements to harming skin [46]. A study from the Skin Disease and Leishmaniasis Research Centre developed that tea tree oil was powerful from mild to moderate skin inflammation and acne. Tea tree oil is a popular Component in cosmetic remover [48].

Because of its acaricidal, anti-bacterial, anti-viral, anti-inflammatory, wound healing and immunomodulatory effects, TTO shows favourable results in managing human demodicosis. Terpinen-4-ol which is main component that may competitively block the neurotransmitter Terminating enzyme acetylcholinesterase (AchE) in parasites that may mediate to the arthropodicidal effect [47,49].It is a potent inhibitor of lipopolysaccharide (LPS)-induced cytokines, such as IL-1β, IL-6 and IL-10, Produced by mononuclear phagocytic macrophages upon activation of toll like receptors (TLR) 4 and TLR2/4; this Inhibition is mediated by interfering with the NF-κB, p38 or ERK MAPK metabolic pathways And thereby reducing inflammation [46,49].

TTO is a volatile essential oil obtained from the leaves of Melaleucaalternifolia, which is a olden plant from Australia. It is used as a treatment for a variety of Conditions like acne, arthritis, burns, vaginal thrush, tinea, and dandruff_ due to Its beneficial therapeutic properties such as antimicrobial, antiseptic, anti-Inflammatory, and analgesic [41,50]. Recent studies have suggested that several bacteria that had been exposed to tea tree oil subsequently were less susceptible to Antibiotics in vitro. Although reduction in antibiotic susceptibility were transient, this raises concerns that tea Tree oil hinders the effectiveness of conventional antibiotics by Either decreasing susceptibility or enhancing the development of Resistance [50, 51]. This is particularly important if tea tree oil is to become More widely used in hospital environments or in long-term care Facilities, such as for the decolonization of MRSA carrier. Tea tree oil or its main component, terpinen-4-ol (T4ol), effects the development of de novo antibiotic resistance in medically important bacteria [48,52].

Studies on efficacy of tea tree oil reported that TTO products decolonize the bacteria against the infections. In invited studies have resulted that broad spectrum of activity against the Gram-negative bacteria and Gram-positive bacteria. There is a disruption in the vital function of bacteria, as hydrocarbons can penetrate easily into the biological membrane, which may cause lysis, the loss of membrane integrity, leakage of ions, and an inhibition of respiration and ultimately death of bacteria [33, 53]. Tea tree oil is available globally and used for its antimicrobial activity. Its is used as topical applications for various infections but it is toxic when consumed orally. Studies have shown that TTO is not genotoxic in invitro mammalian cells. Active ingredients of TTO are incorporated in formulations for treating various skin infections and for reducing acne, dandruff, lice and various skin infections [52,54].

**Antimicrobial activity**

The main component of tea tree oil is terpinen–4-ol which is found to have anti-microbial activity. In recent studies have revealed that antimicrobial activity of TTO have high activity against the antibiotic resistant bacteria [55,62].Therefore various studies were performed on antimicrobial activity on number of strains but only less number of strains were Using specifically mupirocin-resistant and methicillin resistant strains of Staphylococcus aureus (MRSA) and of other bacteria [63].Most of the studies have reported the difference of TTO in sensitivity of antibiotic resistant and sensitive strains [56,58].Tea tree oil is an important alternatives as a topical antimicrobial for antibiotics. TTO shows low concentration in bacteriostatic but high concentration in bactericidal activity [59,60]. The TTO inhibit the more than 20 bacteria genara. susceptible bacteria have been reported the minimum inhibitor c0.003% (v/v) for Prevotellainter media and maximum >8% (v/v) For Enterococcus faecalis strain for Enterococcus faecalisstrains. A study on ATCC reference and clinical strains differ in bacteria (Pseudomonas Aeruginosa, Staphylococcus aureus, E. Faecalis, Salmonella Enteritidis S. Typhimurium, Escherichia coli, Klebsiellapneumoniae) reported MIC of TTO ≤0.5% (v/v) for all P. aeruginosa strains (4%, v/v). Terpinen-4-ol and terpineol components shows antibacterial and antifungal property with MICs, MBCs and MFCs

[61,65]. TTO may have Synergistic or opposing associations has been investigated in Vitro, however no critical connections were found [57, 61].

**Antiviral activity**

The present study have reported that the components of TTO includes terpinen-4-ol, α-terpinene, γ-terpinene, p-cymene, terpinolene and α-terpineol shows activity against some DNA and RNA viruses, including influenza A/PR8 virus subtype H1N1 in Madin-Darby Canine Kidney (MDCK) cells, Herpes simplex virus type 1 (HSV-1) and 2 (HSV-2) in VERO cells, Echovirus 9 (Hill strain) in LLC-MK2 cells, Poliovirus 1 (Sabin strain), Coxsackievirus B1 and Adenovirus 2 in Hep2cells [58,66].

Experiments were performed on TTO components by Australian botanical products. Terpinen-4-ol, αterpinene, γ-terpinene, p-cymene, terpinolene and α-terpineol were obtained from Sigma Chemical Company. TTO components were dissolved in dimethyl sulfoxide (DMSO; Sigma) to give a concentration of 10% (v/v) and diluted in maintenance medium at final concentrations ranging from 0·1% (v/v) to 0·0001% (v/v). Dilution test compounds containing low concentration of 0·01% DMSO (v/v) which was non-toxic to cells [65,67].

Stock solutions were prepared for testing viruses as cellular lysates using DMEM (or RPMI 1640 for MDCK cells) supplemented with 2% heat-inactivated foetal calf serum (FCS), 0·2 g l−1 of streptomycin and 200 U ml−1 of penicillin G [67].

TTO antiviral activity was tested on compounds against the polio 1, ECHO 9, Coxsackie B1, adeno 2, HSV1 and HSV-2 viruses by 50% plaque reduction assay. The concentration of compounds Required for inhibiting viral plaque formation and virus-induced cytopathogenicity by 50% was expressed as the 50% inhibitory dose (ID50) and calculated by dose–response curves and linear regression. Noninfected and infected cells in the absence of compounds served as cell and virus control. To test possible virucidal activity, equal volumes (0·5 ml) of virus suspension (containing 106 PFU $ml^{-1}$) and medium containing various concentrations of the compounds were mixed and incubated for 1 h at 37°C. Infectivity was evaluated by plaque assay after dilution of the virus below the inhibitory concentration.

The ID50 values were found to be 0·0025% (v/v), 0·0012% (v/v) and 0·025% (v/v) for terpinen-4-ol, terpinolene and α-terpineol, respectively. Finally, compounds α-terpinene, p-cymene and γ-terpinene were completely ineffective [6,67].

**Antiprotozoal activity**

TTO also have a antiprotozoal activity. TTO causes decreased development of the protozoa Leishmania major and Trypanosomabrucei at convergences of 403 mg/ml and 0.5 mg/ml separately. Therefore, examination have shown that terpinen-4-ol has activity. In Other examination, TTO at 300 mg/ml destroyed all cells of Trichomonasvaginalis [68].

**Anti- acne vulgaris**

TTO have revealed broad spectrum of activity in antimicrobial and anti-inflammatory properties. These effects help in reducing acne treatment. TO compounds are used to inhibit bacteria growth of Propionibacterium for treatment of acne vulgaris [67]. TTO active ingredients were used in topical preparations for treatment of bacterial infections involved in acne. Various studies have reported and suggested the use of 5% tea tree oil for the treatment of acne vulgaris and showing the efficacy of tea tree oil gel against Propionibacterium acnes. These basic facts prompted us to perform a double-blind placebo-controlled study to determine the efficacy of tea tree oil in the treatment of mild to moderate acne vulgaris. The study have demonstrated that both 5% TTO and 5% benzoyl peroxide remarkably ameliorate acne lesions by decreasing inflammatory and non-inflammatory elements (open and closed comedones), although the onset of effect in the case of TTO was slower. But fewer side effects were observed in patients treated with TTO [68].

Malhi et al., (2016) conducted clinical trials on mild to moderate acne; a 12-week Uncontrolled, open label phase II pilot study and reported the efficacy, tolerability, and Acceptability of a tea tree oil gel (200 mg/g) and face wash (7 mg/g) were significantly Improved mild to moderate acne and that the products were well tolerated.

Sinha et al., (2016) developed a novel Tea Tree Oil nanogel using response surface methodology (CCA). The optimized NE was developed into emulgel (EG) using pH sensitive polymer Carbopol 940 and triethanolamine as alkalizer and reported that TTO as conventional gel revealed broader zones of growth inhibitions against all the selected microbial strains.

Enshaieh et al., (2007) reported in randomized double-blind clinical trial performed in 60 patients with mild to moderate acne vulgaris as optical 5% tea tree oil is an effective Treatment for mild to moderate acne vulgaris.

The clinical preliminary examination was performed on acne vulgaris on 1of 60 patients (age from 15- 25 Years) with mild to moderate acne vulgaris.

The clinical preliminary test was performed on 60 patients, divided into two groups 30 patients in each group A and B. A group were treated with 5% tea tree oil gel and B group were treated with fake gel. Fake gel contains a carbomer gel which is not skin break out movement. As tea tree oil gel and fake gel are similar in colour, shading surface, packaging size and

unique in names. The patients were asked to apply the medication or fake gel twice a day. Apply medication or fake gel for 20minutes and wash with water. The treatment was Continued for 45 days. After 45days patients facial skin were observed by two specialists that any reactions or sore occurred or not. To decide the viability on skin breaks out seriousness We utilized both all-out sore checks (TLC) and the acne severity index (ASI).

The ASI was calculated as:

ASI = Papules + (2×pustules) + (comedones /4)

The TLC count was calculated as:

TLC = Papules + pustules + comedones + nodules

The primary results showed change in Mean TLC and ASI scores at the end of treatment compared to both the study and control groups. Secondary results showed a change in the mean numbers of Comedones, papules and pustules. The mean of these percentages of Improvement was calculated in each group of patients and Used for statistical analysis. At the end of the study, the data Were analysed by using SPSS (release 13) Program (student's t test) and then the labels were revealed [69,70].

**Anti-bacterial activity**:

Tea tree oil exhibits broad- spectrum of activity. Tea tree is an essential oil used in the development of antibiotic resistance in staphylococcus aureus and Escherichia colis. Meticillin-susceptible Staphylococcus aureus (MSSA), methicillin-resistant S. aureus (MRSA) and coagulase-negative staphylococci (CoNS) is effective against tea tree oil [35]. tea tree (Melaleucaalternifolia) oil (TTO) contains monoterpenes such as terpinen-4-ol (T4O), 1,8-cineole, limonene, p-cymene, and α-terpinene have been shown to be effective in controlling a wide range of parasitic infections [71]. The anti-parasitic effects of these compounds are mainly due to their antihistamine and anti-acetylcholinesterase activities as well as their ability to modulate host inflammatory responses. Tea tree oil and its monoterpenes are used to treat the parasitic infections in both humans and animals per American European combination of 0.5% TTO along with 5% solubilizer having 0.3% preservative found to have enhanced stability [72].

**Anti-inflammatory:**

Tea tree oil is one of the anti-inflammatory properties. In case of animal, terpinen-4-ol was found to suppress inflammatory activity in cases of mouth infection. In case of humans, tea tree oil is applied topically to reduce the swelling in histamine induced skin inflammation [73].

**Anti-fungal activity:**

tea tree oil is ability to kill the yeasts and fungi. TTO also inhibits respiration in C. albicans. TTO also inhibits glucose-induced medium acidification by C. albicans, C. glabrata, and Saccharomyces cerevisiae. Respiration was inhibited by approximately 95% after treatment with 1.0% TTO and by approximately 40% after treatment with 0.25% TTO. The respiration rate of Fusariumsolani is inhibited by 50% at a concentration of 0.023% TTO [74].

**Antioxidant activity**:

Antioxidant are derived from the crude TTO. Such as a-terpinene, a terpinolene, and c-terpinene. Their antioxidant action follows the order: a-terpinene> a-terpinolene> c-terpinen. Antioxidant activity of tea tree (Melaleucaalternifolia) oil (TTO) was determined using two different assays. In the 2,2-diphenyl-1-picrylhydrazyl assay, 10 micro-L/mL crude TTO in methanol had approximately 80% free radical scavenging activity, and in the hexanal/hexanoic acid assay, 200 micro L/mL crude TTO exhibited 60% inhibitory activity against the oxidation of hexanal to hexanoic acid over 30 days. These results were equivalent to the antioxidant activities of 30 mM butylated hydroxytoluene in both tests at the same experimental conditions. This indicated that the TTO could be a good alternative antioxidant. Inherent antioxidants, i.e., alpha-terpinene, alpha-terpinolene, and gamma-terpinene, in the crude TTO were separated and identified chromatographically using silica gel open chromatography, C-high-pressure liquid chromatography, and gas chromatography-mass spectrometry [75].

**TOLERABILITY OF TEA TREE OIL**

Basset et al conducted a single-blind randomised trial of benzoyl peroxide lotion versus Tea tree oil gel for treating mild acne to moderate acne.

1. 124 people suffering with acne are taken for test and asked to apply any one of above 2 for 3 months each day.
2. Number of inflamed and non - inflamed lesions has been predefined as primary endpoint of this study.
3. Lesions are counted before starting this and at monthly intervals.
4. The results were observed for 3 months.
5. In this study benzoyl peroxide was found more effective than TTO.
6. The effect of TTO Was slower however was clinically, apparent adverse effects with TTO was lower than control group than TTO was more effective [76].

Pearce et al conducted a study to find reduction of nickel induces contact hypersensitivity reaction by topical TTO in humans.

1. 1.A topical of 18 people having nickel hypersensitivity was taken into this study.
2. 2.100% TTO is taken and is used as test formulation.
3. The flare area and erythema were measured on 3,5,7 days.
4. The 5%TTO lotion, the placebo lotion and the100% macadamia oil were all do not have any significant effect.
5. No skin reaction is observed during study, but people exposed to oxidised degraded product of TTO show some adverse effects [77].
6. Joksimovic et al evaluation the efficacy and tolerability of hyaluronic acidity and methyl-sulfonyl metabe in a new gel medical device for treating haemorrhoids in a double-blind placebo controlled clinical trials.

1. This study is conducted on 36 people who are having haemorrhoid.
2. Author conducted 14 days with proctioal gel and found it is effective in reducing some symptoms of haemorrhoids.
3. The presence of TTO, Methyl - sulfonyl methane proctioal formulation provided a truly clear therapeutic efficacy.
4. TTO has 2 effects on eradication of bacteria which will produce hyaluronidase of hyaluronic acid and protect micro-environment in bleeding haemorrhoids.
5. This study also states that the proctioal treatment was safe and well tolerated.
6. This treatment is also effective in delaying and preventing haemorrhoidectomy [78].

The study on human volunteers using TTO has some allergic reactions, but rate of occurrence is less. But in reality TTO acne studies reported the tendency of having adverse effects in higher than patch test in evaluating function of TTO for non-acne lesion [76,78].

**SIDE EFFECTS OF TEA TREE OIL**

- At high temperature, light, and humidity the effect produced by TTO will worsen.
- Due to sensitivity TTO, its antioxidants present in it like Alpha-terpinene, Gamma-terpinene and terpinolene get converted to p-cymene.
- European cosmetic association allows only use of 1% of TTO and should be packed very carefully that it is exposed to minimal light.
- People sensitive to this oil usually develop Rashes.
- It causes erythema.
- It causes allergic reactions. These reactions make TTO to reduce its use in cosmetics.
- TTO has also shown to cause adverse effects with use of oxidised TTO preparation.
- And, at higher concentration TTO causes toxicity [79,80].

**Side effects from topical application**

Applying TTO on to skin can cause skin irritation, particularly when it is not diluted properly and also when used in high concentration. Symptoms of this include, Redness, dry or scaly skin, itching, burning, stinging. Some people may even develop allergic reactions by using this oil, and this type of reactions is called Allergic contact dermatitis [33,79].

In this case it causes a skin rash that may be red, swollen, and itchy.

- Use of improperly stored TTO or older ones is associated often with this type of reactions. But even fresh TTO can also cause skin reactions.
- In 2007 studies it was found that in some cases even abnormal chest growth is associated with TTO and lavender oil. This combination of oils is used by a young boy who is extensively using hair products with these oils had this problem. But this condition become normal when he stopped using these oils contained products [78,80].

**Side effects from inhalation**

TTO can be even used in aromatherapy. In this method oil is inhaled by using diffuser or even through stream inhalation. But when breathing is too much TTO or Inhaling this oil for so long may lead to headache, nausea, vertigo [81].

**Side effects for internal application**

This oil should not be used internally. As this oil can be toxic and can even be fatal when ingested. If swallowed then we see symptoms like Drowsiness, Confusion, Ataxia, Loss of consciousness [82,83].

**Conclusions:**

In the treatment of infectious diseases like Acne is necessary to prevent antibiotics becoming obsolete, and where appropriate, alternatives to antibiotics ought to be considered. Alternative therapies are viewed favourably by many patients because they are often not being helped by conventional therapy and they believe there are fewer detrimental side effects. In addition, many reports significant improvement while taking complementary and alternative medicines. A wealth of in vitro data now supports the long-held beliefs that TTO has antimicrobial and anti-inflammatory properties. Despite some progress, there is still a lack of clinical evidence demonstrating efficacy against bacterial, fungal, or viral infections. Large randomized clinical

trials are now required to cement a place for TTO as a topical medicinal agent.

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