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PHARMACOLOGICAL ASPECTS OF TEA TREE OIL (TTO) AND ITS ROLE IN DENTISTRY- A COMPREHENSIVE REVIEW

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ABSTRACT

Tea tree oil (TTO) is originated from ***Melaleuca alternifolia*** of the Myrtaceae family and is also known as ti-tree, ti-trol and melasol. TTO is one of the most used essential oils, and thousands of people swear by its wonderful healing properties.TTO is composed of terpene hydrocarbons, mainly monoterpenes, sesquiterpenes and their associated alcohols. Terpinen-4-ol is a major component of TTO and has been considered the main antimicrobial component of the oil. Tea tree oil is an antiseptic used to fight against the germs. It has also been used to treat cuts, minor burns, athlete's foot, and insect bites. Studies reveals that it can treat bacterial and fungal skin infections, wound infections, gum infections, acne, head lice, eczema, vaginal yeast infections, colds, pneumonia, and other respiratory illnesses. Hence the aim of the article is to compile the literature based upon its pharmacological aspects and its application in the field of dentistry for benefit of mankind.

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KEY WORDS

Tea tree oil, Essential oil, monoterpenes, terpinen-4-ol, antimicrobial, gum infections.

INTRODUCTION

Oral diseases such as Dental caries and Periodontal diseases are caused by micro organisms belonging to the resident micro flora rather than by classic microbial pathogens[1]. They are caused by the ecological imbalance in oral biofilms. Oral microbial flora is dominated by gram positive microorganisms and hence dental plaque which is formed on the tooth surface contains gram positive cocci and bacilli. When plaque community equilibrium is altered, the microbial flora shifts from aerobic to anaerobic side and these anaerobic organisms cause periodontal disease[2].

Dental plaque which forms on the tooth surface exists in a state of bio film which means the micro organisms present in the plaque live in communities and they are held together in a matrix. Hence mechanical disruption of plaque is necessary to prevent periodontal diseases. The mature and mineralized plaque may not be removed by brushing therefore professional intervention in the form of scaling is mandatory to remove the plaque. Microorganisms can hide in sites like dorsum of tongue, pocket epithelium; tonsillar regions and can recolonize the tooth surface. Use of antimicrobial agents along with mechanical plaque control is proved to be effective in preventing and treating periodontal diseases[3].

Absolute periodontal health can be achieved by maintaining a very high standard of plaque control. Such standards are attainable in the most highly motivated patients. However, all methods of mechanical plaque removal are time consuming both for the patient and the dental practioner .hence, for this reason many patients are unable to pursue with newly mastered techniques.

It is apparent therefore, that a need exists for means of plaque control adjunctive or alternative to the time honored mechanical methods. The adjunctive use of chemicals would therefore appear a way of overcoming deficiencies in mechanical tooth cleaning habits as practiced by many individuals[4].

Several products have been tried as mouth rinse but few are found to be effective. Those products that are effective in plaque control have side effects and hence the search for naturally derived mouth rinse with less side effects has been initiated. One of the natural products that show promising results is Tea tree oil.

Tea tree oil is extracted from the tree *Melaleuca alternifolia* that grows in Australia, and has been shown to have many beneficial medicinal uses as an antiseptic, antifungal and antibacterial agent[5]. Indigenous people of Australia have been used it to treat cough, cold, sore throat and skin ailments [6]. Studies indicate that *Melaleuca alternifolia* is extracted from the leaves and twigs by steam distillation and the yield is about 1.8% and that the main chemical component to have antimicrobial activity in tea tree oil is attributed to terpinen-4-ol[7].

***COMMON NAMES**:*

Australian tea tree oil, melaleuca oil.

SCIENTIFIC NAME:

Melaleuca alternifolia

BOTANICAL DESCRIPTION [8]:

It is a small tree from New South Wales in Australia, similar to Cypress, with needle-like leaves and heads of sessile yellow or purplish flowers and grows to about 7 meters (20 feet) high and thrives in marshy areas. The oil is only produced in Australia where the Aborigines used it for a long time for a variety of medicinal purposes. It has been cultivated in other parts of Australia successfully including Queensland and Western Australia. Other species of Melaleuca grow across Australia, New Zealand and Indonesia.

Tea Tree Oil (Melaleuca Alternifolia)

CHEMISTRY [9] :

TTO is composed of terpene hydrocarbons, like monoterpenes, sesquiterpenes and their associated Alcohols. There are several varieties, or chemotypes, of *M. alternifolia* and each produces oil with a distinct chemical composition. Six chemotypes have been described as follows: terpinen-4-ol chemotype (1), terpinolene chemotype (2), and four 1,8-cineole chemotypes (3-6) . The terpinen-4-ol chemotype typically contains levels of terpinen-4-ol of between 30-40% and is the chemotype used in commercial TTO production. There are several varieties, or chemotypes, of *M. alternifolia* and each produces oil with a distinct chemical composition. Six chemotypes have been described as follows: terpinen-4-ol chemotype (1), terpinolene chemotype (2), and four 1,8-cineole chemotypes (3-6) (Homer et al., 2000). The terpinen-4-ol chemotype typically contains levels of terpinen-4-ol of between 30-40% and is the chemotype used in commercial TTO production. TTO has a relative density of 0.885-0.906 (International Organisation for Standardisation, 1996), is only sparingly soluble in water and is miscible with non-polar solvents.

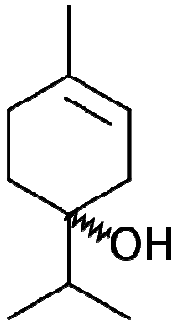

Fig 2
Structure of terpinen -4-ol

ACTIVE CONSTITUENT [10]

Tea tree oil contains 2.6% Cineole and 41.7 % Terpinen-4-ol. This tea tree oil is a uniquely defined combination of monoterpenes, sesquiterpenes and terpene alcohol with outstanding therapeutic properties. The main chemical components of tea tree oil (also referred to as ti-tree oil) are a-pinene, b-pinene, sabinene, myrcene, a-phellandrene, a-terpinene, limonene, 1,8-cineole, y-terpinene, p-cymene, terpinolene, linalool, terpinen-4-ol and a-terpineol.

OIL EXTRACTION [11]

The method of extracting Tea Tree Oil is by Steam Distillation. After harvest, the fine cut vegetation, consisting of chopped twigs and leaves, is transported to the distiller. Here the materials are subjected to steam and as the vapors rise from the steamed leaves, it passes through a cooling chamber. In the cooling chamber, the water and oil return to a liquid state, following which, the oil and water are separated leaving only the 100% tea tree oil. When the distillation is complete, the oil has been separated.

PHARMACOLOGICAL ACTIONS OF TEA TREE OIL
ANTI MICROBIAL ACTIVITY

Groppo FC *et al* conducted a study based upon the comparision of the Anti microbial activity of garlic,Tea tree oil,and chlorhexidine against oral micro organisms. the study revealed that garlic and chlorhexidine showed good anti microbial activity against *streptococcus mutans* than other oral micro organisms,whereas,TTO showed significant antimicrobial activity against *streptococcus mutans* and also with other oral microbes[12]. In conclusion Tea tree oil and Garlic have been reported as an effective agent to be used as an alternative to chlorhexidine.

Mary Fitzpatrick tested TTO abilities to control the growth of five bacteria. He also compared the antibacterial efficacy of fresh garlic (*Allium sativum*), an industrial cleaner and deodorizer, and mouthwash Listerine, a brand made by McNeil-PPC, Inc, contiguously with tea tree oil.[13] A bacterial lawn technique on agar plates for each tested bacterium have been carried out. In conclusion of his study, it was reported that tea tree oil possess potent antibacterial action of the strains tested due to the presence of significant zone of inhibition.

Hammer *et al* did a study to determine the antibacterial action of tea tree oil. A total of 162 bacterial isolates from the genera *Actinomyces, Branhamella, Capnocytophaga, Clostridium, Eikenella, Fusobacterium, Haemophilus,*

Lactobacillus, Neisseria, Peptostreptococcus, Porphyromonas, Prevotella, Stomatococcus, Streptococcus and *Veillonella* were tested for their susceptibility to tea tree oil [14]. All isolates were inhibited and killed by concentrations of tea tree oil 2%, and in fact most were inhibited or killed at concentrations below this. Isolates with the lowest MICs and MBCs were from the genera *Prevotella, Porphyromonas , Veillonella* and isolates with the highest MICs and MBCs were from the genera *Streptococcus, Fusobacterium , Lactobacillus.Streptococcus mutants* has been strongly associated with the development of dental caries. This suggests that tea tree oil used in a mouthwash formulation may be effective in reducing the numbers of *S. mutans, L. rhamnosus* or other bacteria within the mouth. The data from his study suggest that tea tree oil is of use in oral hygiene products.

ANTI FUNGAL ACTIVITY

Hammer *et al* investigated the mechanism of action of tea tree oil and its components against *Candida albicans*, *Candida glabrata* and *Saccharomyces cerevisiae*. Yeast cells were treated with tea tree oil or components, at one or more concentrations, for up to 6 h. During this time, alterations in permeability were assessed by measuring the leakage of 260 nm absorbing materials and by the uptake of Methylene Blue dye. Membrane fluidity was measured by 1,6-diphenyl-1,3,5-hexatriene fluorescence. The effects of tea tree oil on glucose-induced medium acidification were quantified by measuring the pH of cell suspensions in the presence of both tea tree oil and glucose. Result showed that the treatment of *C. albicans* with tea tree oil and components at concentrations of between 0.25 and 1.0% (v/v) altered both permeability and membrane fluidity. Membrane fluidity was also increased when *C. albicans* was cultured for 24 h with 0.016%–0.06% (v/v) tea tree oil, as compared with control cells. For all three organisms, glucose-induced acidification of the external medium was inhibited in a dose-dependent manner in the presence of 0.2%, 0.3% and 0.4% tea tree oil[15]. Data from his study support the hypothesis that tea tree oil and components exert their antifungal actions by altering membrane properties and compromising membrane-associated functions.

Weseler *et al* did a study to investigate the antifungal effect of tea tree oil. The lipophilic yeast *Malassezia pachydermatis* is part of the normal skin flora of most warm-blooded organisms. In a number of surveys it could be demonstrated that this yeast species might be involved in different skin diseases like seborrhoeic dermatitis, especially in dogs and cats. In order to look for an alternative therapeutic agent to the commonly used antimycotic and antiseptic synthetic substances the *in vitro* activity of Australian tea tree oil, the essential oil of *Melaleuca alternifolia*, against several strains of *Malassezia pachydermatis* was examined. All tested strains showed remarkably high susceptibility to tea tree oil. With these results the significant antibacterial activity of tea tree oil is extended to a new group of fungal pathogens colonizing mainly mammals' skin[16]. During the last ten years there was an increasing popularity of tea tree oil containing human health care products. The presented data open up new horizons for this essential oil as a promising alternative agent for topical use in veterinary medicine as well.

Carson *et al* conducted a study on the susceptibility of fungi to TTO; the early data was also largely limited to *Candida albicans*, which was a commonly chosen model test organism. Recent data shows that a range of yeasts, dermatophytes, and other filamentous fungi are susceptible to TTO. Although test methods differ, MICs generally range between 0.03 and 0.5%, and fungicidal concentrations generally range from 0.12 to 2%. The notable exception is

Aspergillus niger, with minimal fungicidal concentrations (MFCs) of as high as 8% reported for this organism. However, these assays were performed with fungal *conidia*, which are known to be relatively impervious to chemical agents. Subsequent assays have shown that germinated *conidia* are significantly more susceptible to TTO than nongerminated *conidia*, suggesting that the intact *conidial* wall confers considerable protection. TTO vapors have also been demonstrated to inhibit fungal growth and affect sporulation [17] .

In vitro activity of *Melaleuca alternifolia* (tea tree) oil against dermatophytes (n = 106) and filamentous fungi (n = 78) was conducted by K.A Hammer. In his study, Tea tree oil MICs for all fungi ranged from 0.004% to 0.25% and minimum fungicidal concentrations (MFCs) ranged from <0.03% to 8.0%. Time–kill experiments with 1–4 × MFC demonstrated that three of the four test organisms were still detected after 8 h of treatment, but not after 24 h. Comparison of the susceptibility to tea tree oil of germinated and non-germinated Aspergillus niger conidia showed germinated conidia to be more susceptible than non-germinated conidia [18]. These data revealed that tea tree oil has both inhibitory and fungicidal activity.

ANTI VIRAL ACTIVITY

The antiviral effect of Australian tea tree oil (TTO) and eucalyptus oil (EUO) against herpes simplex virus was examined by Schnitzler. In his study, Cytotoxicity of TTO and EUO was evaluated in a standard neutral red dye uptake assay. Antiviral activity of TTO and EUO against herpes simplex virus type 1 (HSV-1) and herpes simplex virus type 2 (HSV-2) was tested in vitro on RC-37 cells using a plaque reduction assay. Australian tea tree oil exhibited high levels of virucidal activity against HSV-1 and HSV-2 in viral suspension tests. At noncytotoxic concentrations of TTO plaque formation was reduced by 98.2% and 93.0% for HSV-1 and HSV-2, respectively. Virus titers were reduced significantly with TTO, whereas EUO exhibited distinct but less antiviral activity. In order to determine the mode of antiviral action of both essential oils, either cells were pretreated before viral infection or viruses were incubated with TTO or EUO before infection, during adsorption or after penetration into the host cells. Plaque formation was clearly reduced, when herpes simplex virus was pretreated with the essential oils prior to adsorption. These results indicate that TTO and EUO affect the virus before or during adsorption, but not after penetration into the host cell [19]. Thus TTO and EUO are capable to exert a direct antiviral effect on HSV.

December 2009 issue of "Letters in Applied Microbiology" published a study investigating the antiviral activity of TTO and its main component, terpinen-4-ol. These compounds were evaluated for their inactivating effects against several viruses; including, polio type 1, ECHO 9, Coxsackie B1, adeno type 2, and herpes simplex (HSV) type 1 and 2. The results of the study demonstrated that TTO and some of its constituents possess inhibitory effects on influenza virus subtype H1N1. However, all the compounds tested were ineffective against polio 1, adeno 2, ECHO 9, Coxsackie B1, HSV-1 and HSV-2 [20]. The authors further found that none of the tested compounds had the ability to inactivate viral particles individually. They concluded that TTO has an antiviral activity against influenza virus subtype H1N1 only, principally attributed to terpinen-4-ol, and TTO is a promising drug in the management of influenza infections.

A follow-up study was done by Garozzo *et al* published in the January 2011 issue of "Antiviral Research." they investigated the action of TTO and its active components against different steps of the replicative cycle of influenza virus subtype H1N1 in dog kidney cells at

different times after infection. These experiments showed that viral replication was significantly inhibited when TTO was added within two hours after infection of the cells, which indicated interference at the beginning of the viral replicative cycle during the adsorption step, or the actual entering of the virus into the host cell [21]. The results suggest that TTO did not interfere with attachment of the virus to the cell.

The November 2008 issue of "Complementary Therapies in Clinical Practice" summarized the first clinical study in which TTO was used for the successful treatment with of a pediatric patient with warts on her right middle finger. The clinicians applied TTO topically to the infection once daily for 12 days and found complete viral clearance of the infected areas [21]. This study emphasizes the potential use of TTO in the treatment of common warts due to human papilloma virus.

January 2004 issue of "Phytotherapy Research" published a study of essential oils from fresh leaves of several related species of the genus Melaleuca. The oils were distilled, analyzed and rated on efficacy as antimicrobials and antivirals against Herpes simplex virus type 1, HSV-1, the causive agent of oral and genital herpes in humans [22]. The antiviral properties of these oils were studied in African green monkey kidney cells infected with HSV-1 and found to be an effective treatment by inhibiting the replication of viral particles and preventing infection of surrounding cells.

ANTI HELMENTHIC ACTIVITY

TTO caused 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, respectively. Further investigation showed that terpinen-4-ol contributed significantly to this activity [23].

ANTI INFLAMMATORY ACTIVITY:

Numerous studies now support the anecdotal evidence attributing anti-inflammatory activity to TTO. *In vitro* work over the last decade has demonstrated that TTO affects a range of immune responses, both in vitro and in vivo. For example, the water-soluble components of TTO can inhibit the lipopolysaccharide-induced production of the inflammatory mediators tumor necrosis factor alpha (TNF-α), interleukin-1ß (IL-1ß), and IL-10 by human peripheral blood monocytes by approximately 50% and that of prostaglandin E_2 [24].

APPLICATION OF TEA TREE OIL IN DENTISTRY

Studies indicates that mouthwash containing tea tree oil reduces the swelling and gum infections. Tea Tree Oil is widely used in periodontal diseases as it helps in controlling bad breath, plaque formation, bleeding gums [25].

Tea Tree Oil is also applied on oral ulcers to aid in healing. This acts by reducing the growth of bacteria in the mouth. Some toothpaste also contains this as an ingredient.

Soukoulis conducted a double-blinded, longitudinal, non-crossover study in 49 medically fit non-smokers (24 males and 25 females) aged 18-60 years with severe chronic gingivitis. He assessed the effects of topically applied tea tree oil -containing gel on dental plaque and chronic gingivitis. Subjects were randomly assigned to three groups and given either tea tree oil –gel [26], chlorhexidine gel, or a placebo gel to apply with a tooth brush twice daily. Treatment effects were assessed using the Gingival Index , Papillary Bleeding Index and plaque staining score at four and eight weeks. No adverse reactions to any of the gels were reported. The data were separated into subsets by tooth (anterior and posterior) and tooth surface (buccal and lingual). The tea tree oil group had significant reduction in

PBI and GI scores. However, tea tree oil did not reduce plaque scores, which tended to increase over the latter weeks of the study period. Hence further studies are required, the anti-inflammatory properties of tea tree oil -containing gel applied topically to inflamed gingival tissues may prove to be a useful non-toxic adjunct to chemotherapeutic periodontal therapy.

SAFETY & TOXICITY

Despite the progress in characterizing the antimicrobial and anti-inflammatory properties of tea tree oil, less work has been done on the safety and toxicity of the oil [27]. The rationale for continued use of the oil rests largely on the apparently safe use of the oil for almost 80 years. Anecdotal evidence over this time suggests that topical use is safe and that adverse events are minor, self-limiting, and infrequent.

TTO can be toxic if ingested, as evidenced by studies with animals and from cases of human poisoning. 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.

CONCLUSION

Growing evidence substantiate the importance of non surgical periodontal therapy for treating gingivitis and periodontal diseases. Since plaque exists in a state of biofilm, it is essential to break the biofilm environment by professional scaling and root planing procedures. It is followed by anti microbial mouth rinse to eradicate the micro organisms from gingival sulcus. Various mouth rinses has been tried and few are found to be successful. But those mouth rinses that are effective have side effects. Hence a natural product like tea tree oil gains a lot of importance. Various studies substantiated the efficacy of tea tree oil against bacteria, fungi, virus, Helminths etc. More over tea tree oil possess anti inflammatory effect which is beneficial in treating gingivitis. Longitudinal studies are needed to evaluate the effectiveness of tea tree oil in treating gingival and periodontal diseases.

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CONFLICT OF INTEREST

No conflict of interest in the present article.

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