Efficacy and safety of tea tree oil as a topical antimicrobial agent

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Introduction

The Australian native plant Melaleuca alternifolia has been used medicinally by Aborigines for several millennia. European colonists soon recognized the therapeutic properties of the plant and furthered its applications by distilling oil from the leaves. The oil, known colloquially as tea tree oil, has gained considerable popularity as a topical antimicrobial agent in recent years, initially on the basis of anecdotal evidence. A recent survey on the use of alternative and complementary medicines in Australia reported tea tree oil as the most frequently used. Tea tree oil is reputed to have several medicinal properties including antibacterial, antifungal, antiviral, anti-inflammatory and analgesic properties. However, it is the antibacterial activity which has attracted the most attention and there are now considerable data available concerning the in-vitro activity.

The colonization of healthcare workers and patients with methicillin-resistant Staphylococcus aureus (MRSA) poses significant challenges to infection control and antibiotic prescribing practices. The emergence of mupirocin-resistant MRSA confounds the situation further. As MRSA, including strains resistant to mupirocin have been recently shown to be susceptible to tea tree oil, tea tree oil is being considered as a potential MRSA de-colonization agent. In addition to the need for appropriate clinical data on the efficacy of tea tree oil products, data on safety are also required. While some work has been conducted for industry purposes, little has been published. In addition, there is some confusion about the concentrations and amount of oil that may elicit an adverse reaction, either topically or systemically.

Production and quality assurance

Historically, tea tree oil was produced by manual harvesting of natural bush stands of M. alternifolia. Today, most tea tree oil is produced on large-scale, mechanized plantations. Quality assurance practices, which contribute to the
provision of a consistent product, have evolved also. Although a number of national and international standards for tea tree oil have been developed and implemented over the years, these have been largely superseded by the most recent international standard for tea tree oil, ISO 4730. This standard is the most comprehensive to date and defines the physical and chemical parameters which tea tree oil samples must fulfil. Tea tree oil contains approximately 100 components with less than 10 components, including terpinen-4-ol, 1,8-cineole, α-terpineol, terpinolene and α- and γ-terpinene, comprising up to 90% of the whole oil. This standard provides ranges within which 14 components must fall, including several of the major antimicrobial components such as terpinen-4-ol and α-terpineol.

Antimicrobial activity

Early work examining the antimicrobial activity of tea tree oil provided largely qualitative information about the broad spectrum of organisms susceptible to the oil, including Gram-positive and Gram-negative bacteria, acid-fast bacilli, yeasts and fungi. More recently, and with more discriminating, quantitative methods, the antimicrobial activity has been characterized in detail. Minimum inhibitory concentrations (MICs) have been determined for many organisms including coagulase-negative staphylococci (0.06–3% v/v), Staphylococcus aureus (including MRSA) (0.12–0.5%), Streptococcus spp. (0.03–0.12%), vancomycin-resistant enterococci (0.5–1%), Acinetobacter baumannii (0.06–1%), Escherichia coli (0.12–0.25%), Klebsiella pneumoniae (0.12–0.5%), Candida albicans (0.12–0.25%), other Candida spp. (0.12–0.5%) and Malassezia furfur (0.12–0.25%). The wide range of organisms susceptible to tea tree oil suggests that this agent may be useful for skin antiseptic. Furthermore, many organisms that colonize skin transiently have been shown to be more susceptible to tea tree oil than commensal organisms. This differential susceptibility may provide further impetus for the application of tea tree oil in situations where eradication of commensal flora is not desirable, particularly where maintenance of the commensal flora supports the continuity of a barrier against colonization by transient flora. This would include settings in wound management, MRSA decolonization and hygienic hand disinfection.

Toxicity

Much work has been performed in animals but the generalizability of these data is unclear.

Cutaneous toxicity

The acute dermal LD₅₀ in rabbits was recorded as in excess of 5.0 g/kg since this dose resulted in 2/10 deaths in rabbits. Furthermore, it was observed at necropsy that neat tea tree oil produced irritant effects and skin abnormalities in rabbits patch tested at this dose for 24 h with occlusion. Although some irritation was observed, undiluted tea tree oil did not produce phototoxic effects on the skin of hairless mice.

Clinical reports of adverse cutaneous events involving tea tree oil and humans have consisted mainly of individual case reports of cutaneous sensitivity to tea tree oil. While these reports have served to alert users and the medical professional to the existence of tea tree oil sensitivity, they have not provided data on either incidence rates or the basis of sensitivity. Although some experimental work has been conducted, this has generally been with a small number of subjects. A 48-h occlusive patch test with 1% tea tree oil on 22 volunteers produced no irritation and a maximization test also produced no sensitization reactions. In 13 subjects patch-tested with 5% tea tree oil, no adverse reactions were elicited. More recently, 50 participants were patch-tested with 1 and 5% tea tree oil and no adverse reactions were seen. In another study, repeated challenge over 21 days with 25% tea tree oil did not result in any sensitivity in 23 of 28 subjects. However, the remaining three subjects were removed from the trial because of a severe allergic (as distinct from irritant) response to tea tree oil. The influence
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of compromised skin on the incidence and severity of sensitivity reactions is unknown also.

Tea tree oil is a complex mixture of terpenes and related alcohols. Some components responsible for adverse reactions to tea tree oil have been identified, including 1,8-cineole, D-limonene, α-terpinene, aromadendrene, terpinen-4-ol, α-phellandrene, p-cymene, α-pinene, terpinolene and α-terpinene. For many years, 1,8-cineole was regarded as an undesirable constituent in tea tree oil due to its reputation as a skin and mucous membrane irritant. However, the latter two studies suggest that this component is not responsible for a large proportion of sensitivity reactions.

There are no data documenting the safety of tea tree oil for application to granulation tissue. This is an important area as many patients are colonized with MRSA in wounds, varicose ulcers and pressure sores.

Systemic toxicity

Most of the work on the systemic toxicity of tea tree oil in animals has been performed for commercial purposes and has not been published in the public domain. The acute LD₅₀ in rats has been reported as 1-9 g/kg (1.4-2.7 g/kg), similar to the acute oral LD₅₀ of eucalyptus oil (2.5 g/kg).

Several cases of human tea tree oil poisoning have been reported, mostly involving the ingestion of modest volumes (~10-25 mL) of oil. In two cases, ingestion of tea tree oil resulted in what appeared to be systemic contact dermatitis. Seawright reported that a patient was comatose for 12 h and then semi-conscious for 36 h after ingestion of approximately half a cup of tea tree oil. In separate cases, two children who ingested less than 10 mL tea tree oil became ataxic and drowsy or disoriented. Both were treated supportively and recovered fully without further complications.

Discussion

A broad range of properties attributed to tea tree oil is corroborated, in particular the antimicrobial activity in vitro, it seems likely that the oil will find application in a diverse range of conditions. Already, tea tree oil has been 'grandfathered' into several markets largely on the basis of its 'long history of use'. To be considered for therapeutic use in humans, further information regarding the safety of its application must be sought. Since many of the potential applications of tea tree oil involve mucous membranes, such as nasal, oral or vaginal mucosa, this work must include mucosal as well as skin toxicity. In the first instance, the incidence of sensitivity to tea tree oil must be determined.

Hopefully, the components or fractions responsible for sensitivity will be identified also and this may assist in the development of oils with a lower propensity to cause sensitivity. Elimination of allergenic components may be achieved by manipulating the distillation process, rectification or by the genetic selection of plants which contain lower quantities of these components.

Due to its systemic toxicity, tea tree oil should only be used as a topical agent. Most product manufacturers, distributors and retailers support this qualification, although a few continue to advocate systemic use. In the absence of data supporting its safety in this context and in the presence of clinical experience clearly indicating its toxicity, any recommendations of systemic use appear injudicious. Furthermore, while current interest seems centred around the safety of acute exposure, whether topical or systemic, the question of chronic exposure remains neglected.

Tea tree oil contains several compounds known to penetrate skin and to enhance the penetration of other compounds. While this may augment the action of its medicinal properties, it may also potentiate the opportunities for toxicity.

Tea tree oil has exhibited some promising antimicrobial properties in vitro and it remains for these properties to be evaluated suitably in vivo. Before it can be introduced widely for therapeutic use, randomized, controlled, preferably double-blind clinical trials must be performed and comprehensive safety data obtained.

References