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Review

A review of applications of tea tree oil in dermatology

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Abstract

Tea tree oil (TTO) is an essential oil, steam-distilled from the Australian native plant, Melaleuca alternifolia. It has a minimum content of terpinen-4-ol and a maximum content of 1, 8-cineole. Terpinen-4-ol is a major TTO component which exhibits strong antimicrobial and anti-inflammatory properties. Tea tree oil exerts antioxidant activity and has been reported to have broad-spectrum antimicrobial activity against bacterial, viral, fungal, and protozoal infections affecting skin and mucosa. Several studies have suggested the uses of TTO for the treatment of acne vulgaris, seborrheic dermatitis, and chronic gingivitis. It also accelerates the wound healing process and exhibits anti-skin cancer activity. This review opens up new horizons for dermatologists in the use of this herbal agent.

Introduction

Essential oils are distilled from vegetable materials and are considered to be alternative medicines. For thousands of years, these oils have been used to treat diseases.[1] Topical administration of essential oils is associated with rapid absorption from the skin into the bloodstream within 10–30 minutes.[2]

Tea tree oil (TTO) is an essential oil that is obtained by steam distillation of the leaves and terminal branches of *Melaleuca alternifolia* (Myrtales: Myrtaceae) in the states of New South Wales and Queensland in Australia.[3] Notably, TTO (melaleuca oil) has been demonstrated to be effective in a variety of skin infections and plays a role in the management of inflammatory/immune disorders affecting the skin. In addition, it is an antioxidant[4] and anti-skin cancer agent.[5]

The aim of this article is to gather and summarize the findings of *in vivo*, *in vitro*, and clinical studies on the use of TTO in dermatology. This article offers dermatologists valid and useful information about the use of TTO in clinical practice and will open the door to novel agents in dermatology.

Materials and methods

Extensive searches of the literature in two databases (PubMed and ISI Web of Knowledge) were carried out, following the methodology described by Liberati *et al.*[6] This produced a final total of 47 references. Searches were limited to articles published in English from 1990 to February 2011. The main search terms were "tea tree oil" and "dermatology" and equivalent expressions. Figure 1 presents a flow diagram of the search.

Results

Bioactive constituents and chemotypes

Tea tree oil contains almost 100 components, the majority of which are monoterpenes and related alcohols.[7] It has a minimum content of 30% of terpinen-4-ol and a maximum content of 15% of 1,8-cineole. Terpinen-4-ol is a major TTO component and exhibits strong antimicrobial and anti-inflammatory properties, whereas 1,8-cineole is probably an undesirable allergen in TTO products.[8] Storage of TTO changes its gradients; it increases the level of cymene and decreases the level of terpinene. Tea tree oil has six chemotypes, which are oils with different chemical compositions. These include a terpinen-4-ol chemotype, a terpinolene chemotype, and four 1,8-cineole chemotypes.[9] Adverse reactions to TTO diminish with minimization of 1,8-cineole content because the level of 1,8-cineole usually inverts the proportion of terpinen-4-ol. In commercial production, TTO is prepared as a terpinen-4-ol chemotype.[10]

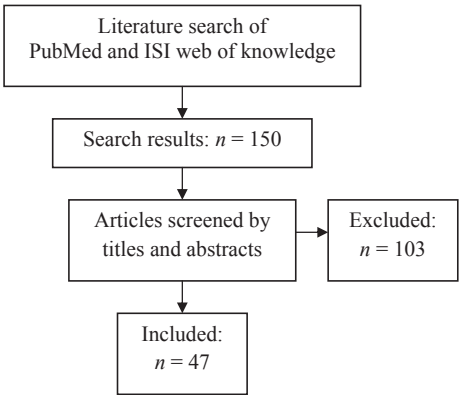

Figure 1 Flow diagram of study selection

Adverse effects

Tea tree oil can be potentially toxic if it is ingested at higher doses. Oral poisoning in children and adults has been observed, but patients respond to supportive therapy without apparent sequelae. No human deaths caused by TTO have been reported in the literature.[11] Topical application of TTO can cause adverse reactions at higher concentrations. Adverse effects including skin irritation, allergic contact dermatitis, systemic contact dermatitis, linear immunoglobulin A disease, erythema multiforme-like reactions, systemic hypersensitivity reactions, and idiopathic male prepubertal gynecomastia have been reported in parallel with increased use of TTO.[12,13] It is noteworthy that TTO and its components are not genotoxic.[11]

Mechanism of action

It is notable that terpinen-4-ol is able to reduce the production of tumor necrosis factor (TNF), interleukin-1 (IL-1), IL-8, IL-10, and prostaglandin E2. In addition, the water-soluble fractions of TTO, terpinen-4-ol and α-terpineol, suppress superoxide production by monocytes but not by neutrophils of oxygen species. Additionally, terpinen-4-ol, but not 1,8-cineole or α-terpineol, modulates vasodilation and plasma extravasation.[10]

Dermatologic applications of TTO

Antioxidant activity

Tea tree oil may be a good alternative antioxidant. Inherent antioxidants (i.e. α-terpinene, α-terpinolene, and γ-terpinene) in crude TTO have been separated. Their antioxidant activities can be ranked in the following order: α-terpinene > α-terpinolene > γ-terpinene.[14]

Regulation of wheal and flare

A study conducted by Khalil *et al.*[15] on rat skin indicated that 1,8-cineole, representing 2% of TTO, decreased vascular changes induced by sensory neuropeptides. Terpinen-4-ol (approximately 40% of TTO) reduced substance P-induced microvascular changes and protein extravasation by a direct nitric oxide-mediated effect on the microvasculature, without sensory nerve involvement. By contrast, topical application of TTO, particularly terpinen-4-ol, has been shown to regulate wheal and flare by reducing the histamine-induced edema often associated with type 1 allergic immediate hypersensitivities.[15–17]

Antibacterial activity

Terpinen-4-ol is a potent agent against methicillin-resistant *Staphylococcus aureus* (MRSA) and coagulase-negative staphylococcus (CoNS). A study showed that TTO used at a 10% concentration has effects comparable with those of topical mupirocin against the bacterium *S. aureus*. At this concentration, no resistance has been detected; however, it can occur at lower percentages.[18] In addition, washing with 5% TTO is effective in removing MRSA from the skin.[19]

The introduction of a solubilizer to a system containing TTO leads to a substantial increase in the bacteriostatic activity of the TTO. A combination of 0.5% TTO, 5% solubilizer, and 0.3% synthetic preservative ensures the microbiologic stability of soft body balm in accordance with American European Pharmacopoeia (AEP) criteria.[20] Tea tree oil is also effective against oral bacteria. Mouth washing with TTO reduces the amount of plaque that develops in the oral cavity.[21]

Antiviral activity

Schnitzler *et al.*[22] demonstrated that TTO has potent virucidal activity against herpes simplex virus 1 (HSV-1) and HSV-2 and affects the virus before or during adsorption, not after penetration into the host cell. Additionally, a randomized, placebo-controlled trial demonstrated that TTO may be a potentially cheaper alternative for the treatment of recurrent herpes labialis. It is acceptable to patients and possesses little threat of inducing resistance to systemic antiviral agents.[23] Tea tree oil has been shown to be efficient in the treatment of hand warts caused by human papillomavirus (HPV), facilitating the complete re-epithelialization of infected areas.[24]

Antifungal activity

Tea tree oil is able to kill candida *in vitro*.[25] A double-blinded randomized controlled trial (RCT) with 25% and 50% TTO showed a marked clinical response to TTO in the treatment of interdigital tinea pedis.[26] Additionally, it

has been demonstrated that 2% butenafine hydrochloride and 5% TTO cure 80% of patients with toenail onychomycosis with no occurrence of relapse.[27] In another multicenter RCT, patients with distal subungual onychomycosis were treated with 100% topical TTO for six months. This therapy resulted in improved nail appearance and symptomatology.[28] Tea tree oil is also active against *Madueralla mycetomatis in vitro* and can be a useful agent in the treatment of eumycetoma because the prime component of TTO can easily penetrate the skin.[29]

Antiprotozoal activity

Two studies revealed that the application of TTO causes a 50% reduction in the growth of *Leishmania major* and *Trypanosoma brucei*.[30] Additionally, TTO can be effective against *Trichomonas vaginalis*.[10]

A simple *in vitro* analysis indicated that no mites of *Sarcoptes scabiei* var. *hominis* survived three hours of exposure to 5% TTO.[31] A similar study showed the application of 5% TTO and the action of its active component, terpinen-4-ol, to be highly effective in reducing survival time in *Sa. scabiei* var. *hominis*.[32] Tea tree oil has been added to several preparations as an alternative treatment for head lice infestations. It is hypothesized that the insecticidal characteristic of TTO is attributable to its anticholinesterase activity.[33] One study demonstrated the high efficacy of TTO and lavender oil on subjects with live head lice and indicated that TTO can be used as an alternative to pyrethrin-based products.[34] Demodex is resistant to a wide range of antiseptic agents. A retrospective review of clinical studies demonstrated that an eyelid scrub with TTO can effectively eradicate eyelid demodex and improve demodicisosis.[35] Another study found that a weekly lid scrub with 50% TTO and a daily lid scrub with tea tree shampoo can be effective in eradicating eyelid demodex.[36]

Acne vulgaris

Antibiotics which inhibit the growth of *Propionibacterium* are the standard treatment for acne vulgaris, but the emergence of antibiotic-resistant strains is problematic. Tea tree oil has been shown to have broad-spectrum antimicrobial and anti-inflammatory properties *in vitro*. These effects have formed the basis of its use in acne treatment.[37] Tea tree oil preparations are extensively used as topical treatments for the control of skin bacteria involved in acne.[38] Various studies have suggested the use of 5% TTO in the treatment of acne vulgaris and have shown the efficacy of TTO gel against *P. acnes*. Bassett and colleagues conducted a single-blind RCT in 124 patients to evaluate the efficacy and tolerability of 5% TTO gel in the treatment of mild to moderate acne in comparison with 5% benzoyl peroxide lotion.[39] They demonstrated that both 5% TTO and 5% benzoyl peroxide significantly 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. Encouragingly, fewer side effects were observed in patients treated with TTO. Lesions markedly improved after three months with both preparations without differences between the two therapies.[39] Another double-blind RCT was performed in 60 patients (age range: 15–25 years) with mild to moderate facial acne vulgaris.[37] They were followed every 15 days for 45 days. Treatment responses were evaluated by total lesion counts (TLCs) and scores on the acne severity index (ASI). A significant difference was observed between TTO gel and placebo in outcomes based on TLCs and ASI scores. Tea tree oil gel proved to be 3.55 times and 5.75 times more effective than placebo in lowering TLCs and ASI scores, respectively. This study demonstrated that topical 5% TTO is effective in the treatment of mild to moderate acne vulgaris.[37]

Seborrheic dermatitis

Seborrheic dermatitis is a common clinical conundrum of the skin, affecting 3–5% of the population. It is considered a superficial fungal skin disorder, occurring in areas rich in sebaceous glands. The exact etiopathogenesis of seborrheic dermatitis is unclear; however, colonization by *Malassezia furfur* and an inflammatory response to this lipophilic yeast may play a role in its etiology. Several studies have revealed that TTO exerts antifungal activity against *Malassezia* species, which may be of benefit in the treatment of seborrheic dermatitis.[40,41] Satchell *et al.*[42] performed a randomized, single-blind, parallel-group study in 126 patients aged $\geq$ 14 years to investigate the efficacy and tolerability of 5% TTO and placebo, respectively, in mild to moderate dandruff. Patients were randomized to receive either 5% TTO shampoo or placebo, each of which was used daily for four weeks. The group using 5% TTO shampoo showed a 41% improvement, whereas the placebo group showed an improvement of 11%. There were no adverse effects. This study illustrated that 5% TTO appears to be useful and is well tolerated in the treatment of dandruff.[42]

Wound healing

There is evidence for the influence of essential oils in wound healing and their potential application in clinical practice.[43] Tea tree oil hydrogel seems to be effective in cooling burn wounds and increasing the rate of wound healing in both immediate and delayed applications.[44]

Anti-tumor activity

It has been proposed that the effect of TTO on tumor cells is mediated by its induction of a reorganization of the lipid architecture of plasma membrane.[45] Topical 10% TTO/dimethyl sulfoxide (DMSO) has been shown to significantly retard the growth of subcutaneous melanomas.[5] Bozzuto *et al.*[46] demonstrated that TTO is capable of inhibiting the growth of melanoma cells and overcoming multidrug resistance. Tea tree oil and its main active component, terpinen-4-ol, can also interfere with the migration and invasion processes of drug-sensitive and drug-resistant melanoma cells.

Chronic gingivitis

The anti-inflammatory properties of TTO can be exploited in the topical application of gel containing TTO to inflamed gingival tissues. Interestingly, TTO may be a useful non-toxic adjunct to chemotherapeutic periodontal therapy.[47]

Discussion

A review of the medical literature demonstrates growing interest in the use of non-conventional, non-prescription natural medicine. There is also an acknowledged necessity to find new approaches to the therapy of skin diseases. Tea tree oil could play an important role in the treatment of dermatologic diseases if dermatologists realize the valuable applications of this herbal agent. This is the first review of the medical literature to summarize the various applications of TTO in dermatology (Fig. 2).

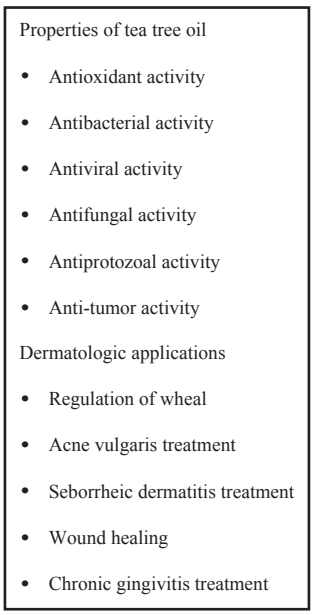

Figure 2 Properties and dermatologic applications of tea tree oil

In some conditions, various TTO compounds have different efficacy profiles. For example, terpinen-4-ol is a major TTO component and exhibits strong anti-inflammatory, antimicrobial, and anti-tumor properties, whereas 1, 8-cineole is probably an undesirable allergen in TTO products. The anti-inflammatory activity of TTO is mediated through the reduction of TNF, IL-1, IL-8, prostaglandin E, and monocyte superoxidase.[10] Topical TTO may regulate wheal and flare by reducing histamine-induced edema.

Tea tree oil may be a good alternative antioxidant. Its antioxidant activity reflects the properties of α-terpinene, α-terpinolene, and γ-terpinene.[14]

A paradigm shift in the therapy of infectious diseases is required to prevent antibiotic prescription. Alternative therapies are viewed favorably by many patients because their conditions are often not resolved by conventional therapy and because patients perceive alternative therapies as having less detrimental side effects.

Tea tree oil products have been proven to be as effective as conventional treatments in the control of cutaneous bacterial infections in MRSA.[18,19] Additionally, the efficacy of the TTO component terpinen-4-ol in the treatment of viral, fungal, and protozoal infections has been identified.

Tea tree oil is noteworthy in the treatment of acne vulgaris[37–39] and acts in anti-inflammatory and antibacterial capacities simultaneously. The broad-spectrum antibacterial activity of TTO means that it can be evaluated in cases of acne vulgaris that are resistant to conventional treatments. In addition, TTO can be considered to be safe in pregnancy as there are, to date, no reports of its teratogenicity.

Interestingly, seborrheic dermatitis responds well to TTO because the oil's antifungal properties are effective against *Malassezia* yeasts, the underlying factor in dandruff.[40–42]

The anti-tumor activity of TTO can mainly be attributed to its active component, terpinen-4-ol, which interferes with the growth, migration, and invasion processes of drug-sensitive and drug-resistant melanoma cells.[5,45,46]

In conditions for which TTO treatment is of benefit, further research is necessary to establish guidelines for its application, preparations, and therapeutic indices.

Questions (answers on page 790)

1. How is tea tree oil obtained?
   a) Steam distillation of the leaves
   b) Soaking dry leaves in alcohol
   c) Soaking dry roots in alcohol

d) Boiling the roots

2. The major ingredient of tea tree oil is:
   a) Terpene
   b) Polyphenole
   c) Starch
   d) Cineol
3. How does the storage of tea tree oil change its ingredients?
   a) It increases terpinene
   b) It decreases cymene
   c) It decreases terpinene and increases cymene
   d) It increases cymene and terpinene
4. Which of the following actions is not a mechanism of tea tree oil?
   a) Inhibition of tumor necrosis factor-α
   b) Inhibition of interleukin-1, IL-8 and IL-10
   c) Inhibition of prostaglandin E2
   d) Inhibition of leukoterin D
5. The following statements on the effect of TTO are correct except?
   a) It is genotoxic
   b) It has anti-inflammatory properties
   c) It supports wound healing
   d) It has anti-melanoma properties
6. Which of the following diseases is not considered to respond to tea tree oil?
   a) Skin melanoma
   b) Atopic dermatitis
   c) Seborrheic dermatitis
   d) Acne vulgaris
7. Tea tree oil does not have which of these properties?
   a) Antioxidant
   b) Anti-acne
   c) Anti-keloid
   d) Anti-tumoral
8. In which stage can tea tree oil interfere with melanoma cells?
   a) Migration
   b) Growth
   c) Invasion
   d) All of the above
9. Which of the following is not an antimicrobial effect of tea tree oil?
   a) Antifungal
   b) Antibacterial
   c) Antiviral
   d) Antimycobacterial
10. Which of the following is not a sign of an adverse reaction to tea tree oil?
   a) Skin irritation
   b) Stevens–Johnson syndrome
   c) Id reaction
   d) Erythema multiforme-like reaction

References

1 Teissedre PL, Waterhouse AL. Inhibition of oxidation of human low-density lipoproteins by phenolic substances in different essential oils varieties. *J Agric Food Chem* 2000; **48**: 3801–3805.

2 Halm MA. Essential oils for management of symptoms in critically ill patients. *Am J Crit Care* 2008; **17**: 160–163.

3 Pazyar N, Yaghoobi R. Tea tree oil as a novel antipsoriasis weapon. *Skin Pharmacol Physiol* 2012; **25**: 162–163.

4 Mantle D, Gok MA, Lennard TW. Adverse and beneficial effects of plant extracts on skin and skin disorders. *Adverse Drug React Toxicol Rev* 2001; **20**: 89–103.

5 Greay SJ, Ireland DJ, Kissick HT, *et al.* Inhibition of established subcutaneous murine tumor growth with topical *Melaleuca alternifolia* (tea tree) oil. *Cancer Chemother Pharmacol* 2010; **66**: 1095–1102.

6 Liberati A, Altman DG, Tetzlaff J, *et al.* The PRISMA statement for reporting systematic reviews and meta-analysis of studies that evaluate health care interventions: explanation and elaboration. *Ital J Public Health* 2009; **6**: 354–391.

7 Papadopoulos CJ, Carson CF, Chang BJ, Riley TV. Role of the MexAB-OprM efflux pump of *Pseudomonas aeruginosa* in tolerance to tea tree (*Melaleuca alternifolia*) oil and its monoterpene components terpinen-4-ol, 1,8-cineole, and alpha-terpineol. *Appl Environ Microbiol* 2008; **74**: 1932–1935.

8 Mondello F, De Bernardis F, Girolamo A, *et al. In vivo* activity of terpinen-4-ol, the main bioactive component of *Melaleuca alternifolia* Cheel (tea tree) oil against azole-susceptible and -resistant human pathogenic *Candida* species. *BMC Infect Dis* 2006; **6**: 158.

9 Homer LE, Leach DN, Lea D, *et al.* Natural variation in the essential oil content of *Melaleuca alternifolia* Cheel (Myrtaceae). *Biochem Syst Ecol* 2000; **28**: 367–382.

10 Carson CF, Hammer KA, Riley TV. *Melaleuca alternifolia* (tea tree) oil: a review of antimicrobial and other medicinal properties. *Clin Microbiol Rev* 2006; **19**: 50–62.

11 Hammer KA, Carson CF, Riley TV, Nielsen JB. A review of the toxicity of *Melaleuca alternifolia* (tea tree) oil. *Food Chem Toxicol* 2006; **44**: 616–625.

12 Crawford GH, Sciacca JR, James WD. Tea tree oil: cutaneous effects of the extracted oil of *Melaleuca alternifolia*. *Dermatitis* 2004; **15**: 59–66.

13 Henley DV, Korach KS. Physiological effects and mechanisms of action of endocrine disrupting chemicals that alter estrogen signaling. *Hormones* 2010; **9**: 191–205.

14 Kim HJ, Chen F, Wu C, *et al.* Evaluation of antioxidant activity of Australian tea tree (*Melaleuca alternifolia*) oil and its components. *J Agric Food Chem* 2004; **52**: 2849–2854.

15 Khalil Z, Pearce AL, Satkunanathan N, *et al.* Regulation of wheal and flare by tea tree oil: complementary human

and rodent studies. *J Invest Dermatol* 2004; **123**: 6836–6890.
16 Brand C, Townley SL, Finlay-Jones JJ, Hart PH. Tea tree oil reduces histamine-induced edema in murine ears. *Inflamm Res* 2002; **51**: 283–289.
17 Koh KJ, Pearce AL, Marshman G, *et al.* Tea tree oil reduces histamine-induced skin inflammation. *Br J Dermatol* 2002; **147**: 1212–1227.
18 Loughlin R, Gilmore BF, McCarron PA, Tunney MM. Comparison of the cidal activity of tea tree oil and terpinen-4-ol against clinical bacterial skin isolates and human fibroblast cells. *Lett Appl Microbiol* 2008; **46**: 428–433.
19 Thompson G, Blackwood B, McMullan R, *et al.* A randomized controlled trial of tea tree oil (5%) body wash versus standard body wash to prevent colonization with methicillin-resistant *Staphylococcus aureus* (MRSA) in critically ill adults: research protocol. *BMC Infect Dis* 2008; **8**: 161.
20 Kunicka-Styczyska A, Sikora M, Kalemba D. Lavender, tea tree and lemon oils as antimicrobials in washing liquids and soft body balms. *Int J Cosmet Sci* 2011; **33**: 53–61.
21 Soukoulis S, Hirsch R. The effects of a tea tree oil-containing gel on plaque and chronic gingivitis. *Aust Dent J* 2004; **49**: 78–83.
22 Schnitzler P, Sch—n K, Reichling J. Antiviral activity of Australian tea tree oil and eucalyptus oil against herpes simplex virus in cell culture. *Pharmazie* 2001; **56**: 343–347.
23 Carson CF, Ashton L, Dry L, *et al. Melaleuca alternifolia* (tea tree) oil gel (6%) for the treatment of recurrent herpes labialis. *J Antimicrob Chemother* 2001; **48**: 450–451.
24 Millar BC, Moore JE. Successful topical treatment of hand warts in a pediatric patient with tea tree oil (*Melaleuca alternifolia*). *Complement Ther Clin Pract* 2008; **14**: 225–227.
25 Hammer K, Carson C, Riley T. *In vitro* activity of essential oils, in particular *Melaleuca alternifolia* (tea tree) oil and tea tree oil products, against *Candida* spp. *J Antimicrob Chemother* 1998; **42**: 591–595.
26 Satchell AC, Saurajen A, Bell C, Barnetson RS. Treatment of interdigital tinea pedis with 25% and 50% tea tree oil solution: a randomized, placebo-controlled, blinded study. *Australas J Dermatol* 2002; **43**: 175–178.
27 Syed TA, Qureshi ZA, Ali SM, *et al.* Treatment of toenail with 2% butenafine and 5% *Melaleuca alternifolia* (tea tree) oil in cream. *Trop Med Int Health* 1999; **4**: 284–287.
28 Buck DS, Nidorf DM, Addino JG. Comparison of two topical preparations for the treatment of onychomycosis: *Melaleuca alternifolia* (tea tree) oil and clotrimazole. *J Fam Pract* 1994; **38**: 601–605.
29 Van de Sande WW, Fahal AH, *et al. In vitro* susceptibility of *Madurella mycetomatis*, prime agent of Madura foot, to tea tree oil and artemisinin. *J Antimicrob Chemother* 2007; **59**: 553–555.
30 Mikus J, Harkenthal M, Steverding D, Reichling J. *In vitro* effect of essential oils and isolated mono- and sesquiterpenes on *Leishmania major* and *Trypanosoma brucei*. *Planta Med* 2000; **66**: 366–368.
31 Walton SF, Myerscough MR, Currie BJ. Studies *in vitro* on the relative efficacy of current acaricides for *Sarcoptes scabiei* var. *hominis*. *Trans R Soc Trop Med Hyg* 2000; **94**: 92–96.
32 Walton SF, McKinnon M, Pizzutto S, *et al.* Acaricidal activity of *Melaleuca alternifolia* (tea tree) oil: *in vitro* sensitivity of *Sarcoptes scabiei* var. *hominis* to terpinen-4-ol. *Arch Dermatol* 2004; **140**: 563–566.
33 Mills C, Cleary BJ, Gilmer JF, Walsh JJ. Inhibition of acetylcholinesterase by tea tree oil. *J Pharm Pharmacol* 2004; **56**: 375–379.
34 Barker SC, Altman PM. A randomized, assessor blind, parallel group comparative efficacy trial of three products for the treatment of head lice in children – melaleuca oil and lavender oil, pyrethrins and piperonyl butoxide, and a suffocation product. *BMC Dermatol* 2010; **10**: 6.
35 Gao YY, Di Pascuale MA, Li W, *et al. In vitro* and *in vivo* killing of ocular Demodex by tea tree oil. *Br J Ophthalmol* 2005; **89**: 1468–1473.
36 Gao YY, Di Pascuale MA, Elizondo A, Tseng SC. Clinical treatment of ocular demodecosis by lid scrub with tea tree oil. *Cornea* 2007; **26**: 136–143.
37 Enshaieh S, Jooya A, Siadat AH, Iraji F. The efficacy of 5% topical tea tree oil gel in mild to moderate acne vulgaris: a randomized, double-blind placebo-controlled study. *Indian J Dermatol Venereol Leprol* 2007; **73**: 22–25.
38 Martin KW, Ernst E. Herbal medicines for treatment of bacterial infections: a review of controlled clinical trials. *J Antimicrob Chemother* 2003; **51**: 241–246.
39 Bassett IB, Pannowitz DL, Barnetson RS. A comparative study of tea tree oil versus benzoylperoxide in the treatment of acne. *Med J Aust* 1990; **153**: 455–458.
40 Gupta AK, Nicol K, Batra R. Role of antifungal agents in the treatment of seborrheic dermatitis. *Am J Clin Dermatol* 2004; **5**: 417–422.
41 Waldroup W, Scheinfeld N. Medicated shampoos for the treatment of seborrheic dermatitis. *J Drugs Dermatol* 2008; **7**: 699–703.
42 Satchell AC, Saurajen A, Bell C, Barnetson RS. Treatment of dandruff with 5% tea tree oil shampoo. *J Am Acad Dermatol* 2002; **47**: 852–855.
43 Woollard AC, Tatham KC, Barker S. The influence of essential oils on the process of wound healing: a review of the current evidence. *J Wound Care* 2007; **16**: 255–257.
44 Jandera V, Hudson DA, de Wet PM, *et al.* Cooling the burn wound: evaluation of different modalities. *Burns* 2000; **26**: 265–270.
45 Giordani C, Molinari A, Toccacieli L, Calcabrini A, *et al.* Interaction of tea tree oil with model and cellular membranes. *J Med Chem* 2006; **49**: 4581–4588.
46 Bozzuto G, Colone M, Toccacieli L, *et al.* Tea tree oil might combat melanoma. *Planta Med* 2011; **77**: 54–56.

47 Saxer UP, Stðuble A, Szabo SH, Menghini G. Effect of mouthwashing with tea tree oil on plaque and inflammation. *Schweiz Monatsschr Zahnmed* 2003; 113: 985–986.

Answer key

1. a
2. a
3. c
4. d
5. a
6. b
7. c
8. d
9. d
10. b