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Cutaneous implications of essential oils

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surge in the popularity of natural products, these oils have garnered increased attention. EOs are complex natural mixtures obtained plant materials, and have demonstrated potent biological effects *in vitro*. They have commercial value in the food, cosmetics, and fragrance industries, and also have also experienced a steady rise in personal and home use as part of aromatherapy. Currently, widespread acceptance and use of EOs is limited by a lack of large-scale clinical trials in humans. In addition, they are associated with notable side effects such as contact and allergic dermatitis, among a myriad of rare but serious systemic side effects. This review is intended to provide the clinician with key background information and biology of essentials oils, identify key trials demonstrating benefits, and describe adverse effects, with a focus on cutaneous presentations.

Key words: Essential oils; Photosensitization; Contact dermatitis; Aromatherapy

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Core tip: Essential oils (EOs) have been used as home remedies for millennia. Currently, widespread acceptance and use of EOs is limited by a lack of large-scale clinical trials in humans. In addition, EOs are associated with notable side effects such as contact and allergic dermatitis, among a myriad of rare but serious systemic side effects. We review the current usage of EOs and identify pertinent cutaneous manifestations.

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Abstract

Essential oils (EOs) as home remedies and for health benefits have been used for millennia, but with the recent

INTRODUCTION

Essential oils (EOs) are complex volatile substances extracted from plants, and used in food, cosmetic, and

Table 1 Commonly used essential oils (botanical origin)

Tea tree oil (<i>Melaleuca alternifolia</i>)
Jasmine absolute (<i>Jasminum officinale</i>)
Sweet bay (Laurel) oil (<i>Laurus nobilis</i>)
Cedarwood oil (<i>Juniperus virginiana</i>)
Patchouli oil (<i>Pogostemon cablin</i>)
Ylang-ylang oil (<i>Cananga odorata</i>)
Lemongrass oil (<i>Cymbopogon spp.</i>)
Clove oils (<i>Eugenia caryophyllus</i>)
Jasmine absolute (<i>Jasminum officinale</i>)
Sweet bay (Laurel) oil (<i>Laurus nobilis</i>)
Neroli oil (<i>Citrus aurantium</i> flower)
Peppermint oil (<i>Mentha piperita</i>)
Narcissus absolute (<i>Narcissus poeticus</i> Flower Extract)
Lemon oil (<i>Citrus medica limonum</i>)
Eucalyptus oil (<i>Eucalyptus globulus</i>)
Orange oil (<i>Citrus aurantium dulcis</i>)

fragrance industries. They have gained the attention of the medical community for their biologically active effects and therapeutic potential for many illnesses. In addition, EOs are also experiencing a tremendous growth in aromatherapy and home use for their reported health benefits^[1]. EOs are well-known allergens and photosensitizers; however, there is a paucity of data on the dermal exposure of essential oil use in the United States. In addition, the production and use of EOs is not currently standardized or regulated and may pose an occupational hazard for those with close and repeated contact with EOs. With increasing popularity of essential oil consumption, clinicians can expect to come across more cases of cutaneous and systemic reactions to these complex substances. This review provides the most updated and relevant scientific information related essential oil use, primarily pertaining to cutaneous involvement.

BACKGROUND

EOs are secondary metabolites found in plants^[1]. They are derived from plant material, such as leaves, stems, flowers, bark, and roots^[1]. Common methods used to extract the components include steam distillation, or mechanical expression; oils produced with the aid of chemical solvents are not considered true EOs^[1]. The major chemical composition of EOs includes terpenes, esters, aldehydes, ketones, alcohols, phenols, and oxides^[2]. A given essential oil contains varying amounts of each of these compounds, which imparts a particular fragrance and determines its therapeutic characteristics^[2]. In contrast, a fragrance is chemically made to mimic the smell of a plant or flower.

EOs can be divided into two main distinct biosynthetic origins: The terpenes and terpenoids, and the aromatic and aliphatic components^[3]. There is great interest in the main biologically active component of EOs - terpenes and terpenoids. Terpenes are a large and diverse class of organic compounds that consist of five-carbon bases^[4]. Some terpenes, such as the diterpenes, are the building

blocks for biologically active compounds such as retinol, retinal, and taxol^[1]. Diterpenoids have antioxidant, antimicrobial, anticancer, anti-inflammatory, wound healing, antihypertensive, analgesic, and anxiolytic activities^[5-7].

APPLICATIONS OF EOS

Currently, of the approximately 3000 EOs that have been described, 300 are commercially important^[8,9]. The use of EOs is common in food flavoring, fragrance, and cosmetic industries. The United States Food and Drug administration has classified most EOs as "generally recognized as safe" at specified concentration limits^[3].

EOs comprise the key ingredient in aromatherapy, which is rapidly growing in popularity worldwide^[10-13]. Many spas, massage therapists, and practitioners of alternative medicine provide aromatherapy. The most commonly used EOs in aromatherapy include patchouli, cedarwood, lavender, tea tree oil, along with citrus-scented oils such as bergamot, lemon, and orange oils (Table 1). The oils are usually applied to the skin, but can also be given orally, by inhalation, or by diffusion through the air. Currently, aromatherapy products do not need approval by the FDA^[13].

Little is known about consumption habits and exposure to EOs, especially in the United States. The most comprehensive study of usage patterns was a 2014 study, which focused on the 12 most types of EOs among 1507 participants in France^[14]. Information about types of EOs used, skin areas exposed, frequencies and quantities were collected. Lavender (*Lavanda*) species are the most used EOs among both females and males, followed by *Eucalyptus* oil (Table 2)^[14]. The study notably pointed out the increased prevalence of female users for almost all types of Eos^[14]. In addition, females tend to apply EOs on their face and neck, while males applied the products on the chest^[14].

MEDICINAL USES

EOs are composed of many biologically active molecules, which may have promising therapeutic benefits in many diseases and ailments. EOs have been recognized for their antibacterial, antiviral, antifungal, and insecticidal properties, which led to their acceptance and wide-spread use in the food industry^[15-19]. Pre-clinical studies have shown that in addition to aforementioned properties, EOs also demonstrate potent anti-inflammatory, and antioxidant activity^[20-22]. Because of the great number and variety of constituents, EOs do not have specific cellular targets. They exert their cytotoxic effects through disruptions in the structure and functions of key intracellular lipids and proteins^[2]. In eukaryotic cells, EOs can change the fluidity of membranes, which become abnormally permeable resulting in leakage of radicals, cytochrome C, calcium ions and proteins^[2]. Permeabilization of outer and inner mitochondrial membranes leads to cell death through apoptosis and

Table 2 Usage patterns of essential oils by gender (percentage of use)

	Females	Males
Essential oils	Lavender (60%)	Lavender (50%)
	Eucalyptus (35%)	Eucalyptus (42%)
	Menthol (28%)	Ylang ylang (21)
	Ylang ylang (28%)	Tea Tree (19%)
	Tea Tree (24%)	Citrus (19%)
	Citrus (24%)	Menthol (18%)
	Vanilla (17%)	Vanilla (16%)
	Rosemary (16%)	Pine (15%)
	Ravintsara (16%)	Rosemary (14%)
	Pine (11%)	Neroli (9%)

necrosis^[2]. Similar cytotoxic effects were observed *in vitro* in many gram positive and gram negative bacteria of relevance to the food industry including *S. aureus* and *E. coli*^[2].

Bottom of form

Of all the EOs, tea tree oil (TTO) is arguably the most recognized and investigated compound in dermatology. Numerous studies have demonstrated its tolerability and efficacy and against *P. acnes*^[22-24]. A 1990 single-blind randomized controlled trial (RCT) in 124 patients showed that 5% TTO gel has a comparable efficacy to that 5% benzoyl peroxide lotion^[22]. In 2007, a double-blind RCT was performed in 60 patients with mild to moderate facial acne vulgaris^[23]. A significant difference between TTO gel and placebo was observed based on decreases in total lesion counts and acne severity index scores^[23]. Most recently, the results of a 2016 phase II pilot study assessing tea tree oil for the treatment of mild to moderate acne further demonstrated its efficacy, and favorable side-effect profile^[24]. No serious adverse events were reported in this study and side effects were limited to self-resolving peeling, dryness and scaling^[24]. In addition, tea tree oil has shown promising results for other common dermatologic ailments such as seborrheic dermatitis^[25-27]. A 2002 single-blind parallel controlled trial of 126 patients with mild to moderate dandruff showed that the use of 5% TTO shampoo showed 41% improvement in dandruff, as measured by quadrant-area-severity score, compared with 11% in the placebo group ($P < 0.001$)^[27].

EOs have also been studied for the treatment of alopecia areata. A double-blind RCT involving 86 patients showed that a mixture of thyme, rosemary, lavender, and cedarwood EOs massaged into patients' scalps produced significant improvement when compared with the carrier oils alone (improvement in 54% and 21% of patients, respectively, $P = 0.08$)^[28]. The efficacy of the treatment was evaluated at initial assessment and 3 and 7 mo after treatment by dermatologists' visual scoring of photographs and a computerized analysis of traced areas of alopecia^[28]. However, the study had limited external validity, as the extent and severity of the alopecia areata in the subjects were not mentioned. At this time, there

are no further clinical trials using EOs for alopecia areata.

There is little doubt that EOs may have great relevance to the field of dermatology, and more studies should be performed given all of their *in vitro* findings. Further work on the antimicrobial, antiviral and antifungal effects of EOs may have immense potential in the treatment of dermatological diseases. Indeed, a 2012 study showed that a combination of TTO with iodine was superior to iodine alone in the treatment of molluscum contagiosum virus in 53 children^[29]. Moreover, EOs may have benefits in other cutaneous maladies, such as hyperpigmentation. The efficacy of α -bisabolol, a terpene derivative of the essential oil of *Matricaria chamomilla*, exerts an inhibitory effect on melanogenesis^[30]. In a 2010 study, α -bisabolol was evaluated in an 8-wk clinical trial of 28 Asian females, and led to a significant decrease in hyperpigmentation^[31].

ADVERSE EFFECTS

While safety testing on EOs has shown minimal adverse effects, the use of EOs still poses risks and allergic responses that clinicians should be aware of. Under normal conditions of established use, most oils appear to have a good safety profile^[12]. The majority of adverse events are mild, but serious toxic reactions from some EOs have been observed, including abortions or abnormalities in pregnancy, neurotoxicity manifesting as seizures or retardation of infant development, bronchial hyperreactivity, and hepatotoxicity^[12]. Accidental ingestion by young children has occasionally proved fatal^[32]. Repeated exposure to topical lavender and tea tree oils was associated with the development of prepubertal gynecomastia in a case-series of 3 subjects^[33]. This outcome was reversible upon discontinuation of the oils, and was attributed to the mild estrogenic and anti-androgenic activities of lavender and tea tree oils^[33].

Notably, the majority of adverse effects of EOs are cutaneous in nature. The field of dermatology has encountered an increase in the frequency of allergic reactions to EOs, likely secondary to the growing popularity of topical use of EOs^[12]. EOs are known sensitizers, and there is extensive evidence linking them to cases of contact allergy and allergic contact dermatitis^[34,35]. One case of airborne contact dermatitis secondary to sensitization after inhaled aromatherapy has also been described^[36]. As EOs age, they are often oxidized so their chemical composition changes, and may become more allergenic or prone to irritation^[13]. The most common allergens are ylang-ylang oils, lemongrass oil, jasmine absolute, sandalwood oil, and clove oil^[13]. However, in clinical practice, it may be difficult to identify specific EOs in many cases. For example, in aromatherapy, the practitioner commonly uses undefined mixtures of EOs without specifying the plant sources.

In addition, many EOs contain chemicals prone to causing sensitization, including limonene, linalool, citral, and cinnamyl alcohol (Table 3)^[14]. This is most commonly seen with citrus oils, such as bergamot, lemon, lime, and orange, which contain furocoumarins, in addition

Table 3 List of commonly used essential oils (botanical origin) and allergenic ingredients

Ylang-ylang oil (<i>Cananga odorata</i>)	Linalool, Benzyl benzoate, Benzyl salicylate, Geraniol, Isoeugenol, Eugenol
Lemongrass oil (<i>Cymbopogon</i> spp.)	Citral, Geraniol, Limonene, Trans-isocitral, Eugenol, Linalool
Clove oils (<i>Eugenia caryophyllus</i>)	Eugenol, Isoeugenol
Jasmine absolute (<i>Jasminum officinale</i>)	Benzyl benzoate, Linalool, Eugenol, Benzyl salicylate, Isoeugenol
Sweet bay (Laurel) oil (<i>Laurus nobilis</i>)	Linalool, Limonene, Eugenol, Geraniol
Neroli oil (<i>Citrus aurantium</i> flower)	Linalool, Limonene, Geraniol, Citral
Peppermint oil (<i>Mentha piperita</i>)	Menthol, Limonene, Linalool
Narcissus absolute (<i>Narcissus poeticus</i> Flower Extract)	Benzyl benzoate, Cinnamyl alcohol, Isoeugenol
Lemon oil (<i>Citrus medica limonum</i>)	Limonene, Citral, Linalool, Geraniol
Eucalyptus oil (<i>Eucalyptus globulus</i>)	Limonene
Orange oil (<i>Citrus aurantium dulcis</i>)	Limonene, Linalool, Citral
Patchouli oil (<i>Pogostemon cablin</i>)	Cinnamyl alcohol

to limonene, linalool, and citral. Linalool, a terpene derivative found in many EOs, is the most sensitizing components in many EOs^[36]. It is a fragrant chemical also found in lavender, ylang-ylang, and jasmine oils^[36]. Cinnamyl alcohol is found in patchouli oil^[15]. Factors influencing risk of photo-sensitization also include the amount of product applied and the area of exposure. This is important as the major study determining exposure patterns of topical essential oil use found that females tend to apply to areas such as the face and neck, thus placing themselves at greater risk of photosensitive reactions^[14].

NEED FOR FURTHER RESEARCH

Although it is well established that allergic contact dermatitis can result from essential oil use, the allergens in EOs are largely unknown. Moreover, patch testing currently does not provide accurate or particularly reliable information on EOs, as many EOs lack standardization in manufacturing and production^[37]. Finally, larger scale studies on exposure patterns are needed to reliably estimate the use of EOs. Many patients struggle with chronic cutaneous diseases and often wish to try to "natural" or "alternative" therapies, without being aware of the potential allergenic side effects.

CONCLUSION

The use of EOs, which are complex volatile substances with strong odors, has long been established in the fragrance and cosmetic industries. In addition, EOs have notable effects as antimicrobial agents, and are widely used in food industries. In recent times, EOs in the form of aromatherapy have experienced a resurgence in their popularity. They are notable for causing allergic and photosensitivity reactions, along with serious but rarely occurring side effects. More controlled clinical studies are needed to determine the benefits and risks of plant-derived products, especially EOs, in dermatology. This review describes historical and current results from scientific studies of essential oil components and highlights the areas in need of further research.

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