

Letter to the Editor

Eucalyptus oil and tea tree oil

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Dear Sir,

We read the excellent short review article of Higgins et al. (1) on contact allergy to and the safety of eucalyptus oil with great interest. Having recently finished writing a full literature review of contact allergy to and the chemical composition of essential oils (2), we would like to give some additional information on eucalyptus oil. Also, we will address the question raised by these authors of why there is a low rate of allergic contact dermatitis caused by eucalyptus oils, but there are multiple reports of allergic contact dermatitis caused by tea tree oil, although this oil has constituents in common with eucalyptus oil (1).

What is eucalyptus oil?

Eucalyptus oil is the essential oil obtained by steam-distillation of the leaves and terminal branches of *Eucalyptus* species. Most commercial 'eucalyptus oils' are probably produced from the (southern, Victorian) blue gum, *Eucalyptus globulus* Labill (ISO 770:2002). For the production of Australian-type eucalyptus oil (ISO 3065:2011), *Eucalyptus polybractea* R. Baker is mainly used. Eucalyptus oils from China are mostly obtained from *Cinnamomum longipaniculatum* (Gamble) N. Chao ex H. W. Li. This means that they are not, strictly speaking, eucalyptus oils according to ISO criteria, but their composition generally conforms to the standard. Other species of the genus *Eucalyptus* from which essential oils are mentioned in the European Commission database with information on cosmetic substances and ingredients CosIng (3) include *Eucalyptus dives*, *Eucalyptus radiata*, and *Eucalyptus Smithii*. Finally, there is eucalyptus citriodora oil, but this is a misnomer. This oil is obtained from the citron-scent gum (lemon-scent gum) *Corymbia citriodora* (Hook) K. D. Hill & L. A. S. Johnson, which was formerly (and is still often today) incorrectly termed *Eucalyptus citriodora* Hook. This oil has a composition that is completely different (main components 75–98%

citronellal and up to 10% neoisopulegol + isoisopulegol in the commercial chemotype oil) from that of oils obtained from *Eucalyptus* species [main component 60–80% 1,8-cineole (eucalyptol)] (2).

Contact allergy to eucalyptus oil

We have found 17 publications on contact allergy to/allergic contact dermatitis caused by eucalyptus oil (2); a number of these have already been mentioned by Higgins et al. (1). In all but one [(4); essential oil from *E. globulus*], the botanical origin of the eucalyptus oil was not specified. In two studies, consecutive patients suspected of having contact dermatitis were tested with eucalyptus oil 2% pet., which yielded 0.6% (5) and 1.5% (6) positive patch test reactions. The latter study was conducted in Poland nearly 40 years ago on only 200 patients (6). There are seven studies in which eucalyptus oils have been patch tested in groups of selected patients, for example, patients with dermatitis suspected of being caused by exposure to fragrances, patients using consumer products containing eucalyptus oil, or patients previously reacting to the fragrance mix (6–12). In one study (9), eucalyptus oil was tested 10% in pet., in all others 2% in pet. The number of patients tested ranged from 51 to 6680 (median $n = 96$). Prevalence rates of positive patch test reactions varied from 0.2% in 6680 patients from the Information Network of Departments of Dermatology (Germany, Austria, and Switzerland) (7) to 5.9% (3 of 51) in patients tested in Poland before 1976, who were allergic to *Myroxylon pereirae* resin and/or turpentine and/or wood tar and/or colophony (6). The median percentage of positive reactions to eucalyptus oils in these seven groups of selected patients was 1.8%. In seven of these nine studies (two with consecutive patients; seven with selected patients), no data on relevance were provided. In one investigation with four positive reactions in 679 consecutive patients (0.6%), all were considered to be relevant. However, this study had certain flaws, and 'relevant' also included 'questionable relevance' and 'past relevance' (5). In another study, in which 96 patients using consumer products containing eucalyptus oil were

tested, the 3 (3.1%) positive reactions were considered to be 'at least possibly relevant' (8).

There have also been a number of case reports of allergic contact dermatitis caused by eucalyptus oils, including positive patch test reactions considered to be relevant by the authors (4,13–19). An aromatherapist had chronic hand dermatitis, and had positive patch test reactions to 17 of 20 oils used at her work (tested 1% pet. and 5% pet.), including eucalyptus oil (13). Another aromatherapist had non-occupational contact dermatitis with allergies to multiple essential oils used at work, including eucalyptus oil (14). Occupational allergic contact dermatitis caused by eucalyptus oil (ex *E. globulus*) was observed in 1 patient with hand dermatitis working in the food industry (4). Two patients had positive patch test reactions to eucalyptus oil, which was present in cosmetics that had given a positive patch test result or had been positive in a usage test, seen in a 9-year period in one clinic in Belgium (15). In a group of 70 patients with proven allergic cosmetic dermatitis, eucalyptus oil was the allergen in 1 (16). One patient had allergic contact dermatitis caused by eucalyptus oil in Vicks Vaporub (17), and another had allergic contact dermatitis caused by eucalyptus oil present in an anti-inflammatory cream (18). Two more cases of contact sensitization to eucalyptus oil in topical pharmaceutical products have been reported (19). Finally, a positive patch test reaction to eucalyptus oil was observed in a patient with airborne allergic contact dermatitis resulting from aromatherapy, but this was caused by other essential oils (20).

Thus, we have found eight reports of allergic contact dermatitis caused by eucalyptus oil, comprising 10 patients, which we feel is neither common nor rare. In addition, testing in groups of consecutive patients and selected patients yields low to fairly low rates of sensitization (routine testing, 0.6% and 1.5%; testing in selected patients, 0.2–5.9%; median, 1.8%). Moreover, in these groups, relevance data are largely if not totally lacking (2).

Contact allergy to tea tree oil

Higgins et al. (1) compared eucalyptus oil with tea tree oil. Therefore, we provide some data on contact allergy to tea tree oil, but only briefly, as this will be fully reviewed in a separate article. Of all essential oils, tea tree oil appears to have caused most (reported) allergic reactions since the first case reports were published in 1991 from Australia, where tea tree oil is produced. The oil has been extensively investigated. Neat tea tree oil is a moderate sensitizer in humans. Contact allergy to/allergic contact dermatitis caused by tea tree oil has been reported frequently. We have found 18 patch test studies in consecutive patients [tea tree oil 5% was added to the screening

series of the North American Contact Dermatitis Group (NACDG) in 2003], six patch test studies in groups of selected patients, 30 case reports and numerous publications with positive patch test reactions to tea tree oil of unknown relevance. In groups of consecutive patients suspected of having contact dermatitis (range of number of patients tested: 221–5137), prevalence rates of positive patch test reactions varied from 0.1% to 2.5%, with a median value of 0.95%. In six studies in selected groups of patients, rates ranged from 1.6% to 41% (median 3.2%). The very high positivity rate of 41% was seen in a small group of 17 patients suspected of having cosmetic dermatitis and tested with the undiluted oil, which may give rise to irritant reactions (although 6 of 7 reactions were considered to be relevant). In two well-documented studies, current relevance was found for 41% and 56% of the positive patch tests. In the NACDG studies, 'definite' + 'probable' relevance ranged from 20% to 56%. We have found 30 case reports of allergic contact dermatitis caused by tea tree oil in at least 85 patients. Exposure to light and air leads to the formation of allergenic chemicals and increases the allergenicity of tea tree oils (the allergens are discussed below).

It can be concluded that there is extensive literature on contact allergy to and allergic contact dermatitis caused by tea tree oil. However, prevalence rates of sensitization in consecutive patients of > 1.5% have been observed in five studies only, of which three were performed in Australia, the 'homeland' of tea tree oil (which may reflect the percentage of people using it or of products containing it), one in the United States (2.1%; a weak study; a high rate of macular erythema counted as allergic), and one in the United Kingdom (2.4%; patients were tested with pure oxidized tea tree oil, which may result in irritant reactions). In 10 of 18 consecutive patient studies (56%), prevalence rates were < 1%. Thus, in most countries other than Australia where it has been routinely tested, tea tree oil does not appear to be a frequent allergen (2).

Do eucalyptus oils and tea tree oils have constituents in common?

Do eucalyptus oils and tea tree oils indeed have constituents in common, as stated by Higgins et al.? As will be shown below, the answer is a definite yes. However, before exploring this, we want to stress that this is the case for many essential oils. We have reviewed the (possible) chemical compositions of 91 essential oils and two absolutes (*Jasminum grandiflorum* and *Jasminum sambac*) (2). Approximately 4350 constituents have been identified by chemical analysis and been reported in literature; these are listed alphabetically in our book, with > 900

synonyms, mentioning all oils/absolutes in which they have been found (2). The majority of the chemicals were found in a few oils or even in one oil only. However, many chemicals may be present in more than one-third of all oils, and certain compounds, such as limonene and β -caryophyllene, are present in nearly all essential oils. This may be an explanation for the observation that patients usually react to more than one oil or even multiple essential oils, if tested. 1,8-Cineole, for example, the main ingredient of eucalyptus oil (see below), has been found in 78 of the 93 oils/absolutes. Terpinolene, α -terpinene and α -phellandrene, which are known allergens in tea tree oil, have also been identified in 77, 76 and 76 other oils, respectively. This phenomenon has also been well illustrated by the investigations of Dharmagunawardena et al (14). These authors investigated one sample each of 27 essential oils, and two samples each of 11 other essential oils, used by one or two aromatherapists, who reacted to many of these oils, by gas chromatography–mass spectrometry (14). One of the patients was also allergic to geraniol, linalool, linalyl acetate, and α -pinene, and the other was also allergic to geraniol, α -pinene, and caryophyllene. α -Pinene was found in 42 oil samples, 13 of which had concentrations of 1–10% (vol/vol), and five of which had concentrations of > 10%. Linalool was found in 22 samples, nine of which had concentrations of 1–10% (vol/vol), and 11 of which had concentrations of > 10%. Geraniol was found in 16 oil samples, seven of which had concentrations of 1–10% (vol/vol), and eight of which had concentrations of > 10%. Linalool was found in 22 samples, nine of which had concentrations of 1–10% (vol/vol), and 11 of which had concentrations of > 10%. Caryophyllene was found in 37 samples, 20 of which had concentrations of 1–10% (vol/vol), and nine of which had concentrations of > 10% (5).

It can thus be stated that many essential oils share common constituents with many other essential oils.

Regarding the chemicals found in both eucalyptus oils and tea tree oils, one of us (E.S.) has analysed nearly 6400 commercial samples of the essential oils and absolutes discussed in ref. (2). These include 185 samples of eucalyptus oils (ex *E. globulus*) and 97 samples of tea tree oil. The 10 components of both oils found in the highest concentrations, together with their concentration ranges, are shown in Table 1. As can be seen, eucalyptus oils are always dominated by 1,8-cineole (eucalyptol), which constitutes 61.6–88.7% of the oil. Other important components are limonene (4.5–12.9%) and, possibly, α -pinene, β -pinene, γ -terpinene, and terpinolene, but these may also be present in very low concentrations. In tea tree oils, there is much more variability. The highest

concentrations may be reached by terpinolene (45.7%) and terpinen-4-ol (44.9%), but they can also be present in far lower concentrations. 1,8-Cineole (eucalyptol) is always present in the tea tree oils investigated, in concentrations ranging from 0.5% to 18.3%. It should be mentioned that a so-called 'chemotype' of tea tree oils exists that is dominated by 1,8-cineole, but commercial tea tree oils are always of the terpinen-4-ol chemotype.

Of the 10 major compounds found in the oils, 6 are found in both eucalyptus oil and tea tree oil (Table 1). α -Pinene and α -terpineol have approximately the same concentration ranges in both oils, but the others have a very different concentration profile, with a far higher concentration of 1,8-cineole in eucalyptus oil and higher (possible) concentrations of γ -terpinene, terpinolene and *p*-cymene in tea tree oils. However, the high concentration of 45.7% for terpinolene in tea tree oil was found in one Chinese sample only. The concentration range of terpinolene in the other 96 tea tree oil samples was 0.04–7.6%, with an average of 3.0% and a median of 3.3%. Thus, in fact, the concentration ranges of terpinolene in eucalyptus and tea tree oils do not appear to differ greatly, although the concentrations are probably slightly higher in tea tree oils.

Why is there a low rate of allergic contact dermatitis caused by eucalyptus oils, whereas there are multiple reports of allergic contact dermatitis caused by tea tree oil, which has constituents in common with eucalyptus oil?

This is the question that the authors of the article to which we are responding (1) asked themselves. Several possible explanations need to be considered:

- 1 'Seek and thou shalt find'. Tea tree oil (currently oxidized 5% in pet.) is routinely tested in the United States (and possibly elsewhere, as it is part of the international comprehensive baseline series of the major producer of commercial patch test materials), whereas eucalyptus oil is not. Were eucalyptus oil to be tested routinely, more cases of contact allergy would be detected (although, admittedly, possibly at low rates).
- 2 On the same note, tea tree oil allergy has been widely reported and the oil has been investigated extensively, which makes dermatologists more alert to this possibility in their patients with contact dermatitis. This does not apply to eucalyptus oil contact allergy.
- 3 Tea tree oil reaches the market in larger quantities than eucalyptus oils. This is not a likely explanation. In 2007, eucalyptus oil was fourth among the

Table 1. The 10 major components in commercial eucalyptus oils and tea tree oils (2), and a comparison of the ingredients present in both

Eucalyptus oils (ex <i>Eucalyptus globulus</i>) (n = 185)	Minimum–maximum concentration (%)	Tea tree oils (n = 97)	Minimum–maximum concentration (%)
1,8-Cineole	61.6–88.7	Terpinolene	0.04–45.7
Limonene	4.5–12.9	Terpinen-4-ol	6.2–44.9
α -Pinene	0.3–8.2	γ -Terpinene	3.1–23.0
β -Pinene	0.3–5.8	cis-Sabinene hydrate	tr–19.4
γ -Terpinene	0.2–4.9	p-Cymene	0.3–19.4
Terpinolene	0.02–3.6	1,8-Cineole	0.5–18.3
p-Cymene	1.1–3.1	α -Terpinene	2.3–11.7
α -Terpineol	0.02–1.9	α -Pinene	1.8–9.2
Aromadendrene	0.01–1.8	β -Phellandrene	tr–5.2
trans-Pinocarveol	0.01–1.7	α -Terpineol	1.9–4.2
Constituents found in both oils			
1,8-Cineole	61.6–88.7		0.5–18.3
α -Pinene	0.3–8.2		1.8–9.2
γ -Terpinene	0.2–4.9		3.1–23.0
Terpinolene	0.02–3.6		0.04–45.7
p-Cymene	1.1–3.1		0.3–19.4
α -Terpineol	0.02–1.9		1.9–4.2

tr, trace.

essential oils with the highest estimated trade volumes, with 4000 tons, whereas the estimated production of tea tree oil was 544 tons (21).

- 4 Tea tree oil products are used in higher concentrations than eucalyptus oils, thereby increasing the risk of sensitization. Tea tree oil is often used for its alleged pharmaceutical activities on diseased skin, and in many cases undiluted. Among the 85 patients described in 30 case reports of tea tree oil contact allergy collected by us (2), nearly two-thirds of cases were caused by the application of pure tea tree oil for a variety of skin conditions, including acne, eczema, sunburn, wounds (of any cause), warts, herpes, and fungal infections. Although eucalyptus oil is widely used in pharmaceutical preparations and also in aromatherapy, we were not aware of any use of undiluted oil for such or other purposes, so we considered this to be a distinct possibility.

However, when we showed this letter to the authors of the article to which we are responding, they kindly informed us of the following: 'In Australia, there is a long tradition of using eucalyptus oil (undiluted) in the domestic setting for cleaning purposes in particular. It is commonly used undiluted for removing sticky substances/labels/glue, removing crayon/pastels from surfaces/walls, added neat to the washing cycle, as a stain remover (e.g., carpets), and for cleaning/disinfecting surfaces. Some apply it neat to insect bites, to the neck region when they have a cold or to their handkerchief. So, there appear

to be numerous opportunities for direct skin contact with undiluted eucalyptus oil in the Australian community, particularly the "older generation"' (Claire Higgins and Rosemary Nixon, E-mail communication, 2 June 2015). This excludes the possibility of the use of undiluted oil being responsible for the difference.

- 5 The allergenic ingredients of tea tree oil [terpinolene, ascaridole, α -terpinene (and its oxidation products), 1,2,4-trihydroxymenthane, α -phellandrene, and limonene (2)] are not the chemicals that are also present in eucalyptus oil. This may indeed be the case for ascaridole and 1,2,4-trihydroxymenthane (which are formed by autoxidation of tea tree oil and should not be present in fresh samples), but the other chemicals are also possible constituents of eucalyptus oils.
- 6 The main sensitizers in tea tree oil are present in lower concentrations in eucalyptus oils. This is indeed the case for α -terpinene (maximum 11.7% in tea tree oil and 0.1% in eucalyptus oil). For terpinolene, the concentration ranges are similar, and the maximum concentrations of α -phellandrene and limonene are even higher in eucalyptus oil (1.6% and 12.9%, respectively) than in tea tree oil (0.6% and 3.0%, respectively).
- 7 The allergens in eucalyptus oils differ from those in tea tree oil. As the oil consists of 60–90% 1,8-cineole, this chemical would be a prime candidate. However, it has never caused positive reactions in patients reacting to eucalyptus oil, and has, in

fact, rarely been reported as an allergen (22). In this case, it was the allergen in oil labelled as tea tree oil, but with an atypical composition. In one case where a patient reacted to eucalyptus oil, α -pinene may have been an allergen (14).

- 8 The test substance of 2% fresh eucalyptus oil is inadequate for detecting contact allergy. The concentration may be too low or – as with tea tree oil – the oil should be oxidized before being prepared as a test substance, for instance to detect sensitization to oxidation products of 1,8-cineole (this is obviously highly speculative; autooxidation is probably unlikely to happen) or limonene. On the same note, it might be worthwhile investigating whether oxidizing oils with high concentrations of geraniol (geranium oil and rose oil), linalool and linalyl acetate (lavender and lavandin oils) and limonene (citrus oils) would result in increased rates of positive patch test reactions, as it has been shown that these chemicals, when oxidized, are far stronger contact allergens (23–29).

We realize that we have not answered the question 'Why is there a low rate of allergic contact dermatitis caused by eucalyptus oils, whereas there are multiple reports of allergic contact dermatitis caused by tea tree oil, which has constituents in common with eucalyptus oil', but suggest that there are so many possible explanations that the discrepancy between the frequency of eucalyptus oil allergy and that of tea tree oil allergy need not necessarily be surprising (1).

One final remark on contact allergy as shown by positive patch test reactions to essential oils is that it should be realized that such a positive patch test reaction does not necessarily mean that the patient has become sensitized from the use of this oil. It may be a (pseudo)cross-reaction to other essential oils, but can also result from previous sensitization to an ingredient of the oil (or the commercial test material) from any source, especially when this is present in high concentrations. Thus, patients who are pre-sensitized to eugenol may react to clove oil or bay oil when tested (without ever having had contact with either of them), and patients allergic to geraniol may react to geranium oil and rose oil. Other combinations include cinnamal (cinnamaldehyde) and cinnamon and cassia oil, menthol and peppermint oil, and carvone and spearmint oil. Even some patients sensitized to limonene may sometimes react to tea tree oil (30), even though it will rarely contain > 3% of this chemical.

Indeed, in the absence of clear contact with the oil, many positive patch test reactions to essential oils may be considered to be indicators of fragrance allergy analogous to *M. pereirae* and the fragrance mixes, for which co-reactivity is very frequent (2).

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