

Contact allergy to essential oils: current patch test results (2000–2008) from the Information Network of Departments of Dermatology (IVDK)*

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Background: Essential oils are used in perfumery and in products for aromatherapy or balneotherapy. Previous studies have shown some to be important contact sensitizers. A practical diagnostic approach, based on the results of a large, central European network and other evidence, is needed.

Methods: Data of the Information Network of Departments of Dermatology (IVDK; www.ivdk.org) on all patients patch tested between January 2000 and December 2008 with essential oils were retrospectively analysed.

Results: 15 682 patients of 84 716 consulting in the period had been tested with at least one essential oil, and 637 reacted positively to at least one of the essential oils, most commonly to ylang-ylang oil (I and II) (3.1% as weighted mean of positive tests in special series and consecutive testing), lemongrass oil (1.8%), jasmine absolute (1.6%), sandalwood oil and clove oil (1.5% each). Cross-reactivity between distillate and main allergen, if available, was marked.

Conclusions: Patch testing the important essential oils should be considered in patients with a suggestive history. Additionally, culprit products brought in by the patient should be tested, closing a diagnostic gap by (i) including those other essential oils not included in the commercial test series and (ii) providing a means of testing with the oxidized substances to which the patient had actually been exposed.

Key words: contact allergy; essential oils; fragrances. © John Wiley & Sons A/S, 2010.

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In addition to synthetic fragrances and aromas, natural mixtures such as *Myroxylon pereirae* resin or, nowadays, extracts and distillates thereof (1), oak moss (*Evernia prunastri*) or tree moss (*Evernia furfuracea*) absolute are used to compose perfumes. However, a considerable number of other natural distillates in terms of essential oils also play important roles as perfume ingredients or ‘masking’ agents (2). The International Organization for Standardization (ISO) defines essential oils as ‘product obtained from vegetable raw material ... either by distillation with water or steam or ... from the pericarp of *Citrus* fruits by a mechanical process, or ... by dry distillation’ in ISO 9235.2. Beyond perfumery, essential oils are often applied directly to the skin for the treatment of headache or other pains (2), or used in finished products for balneology, phytotherapy and aromatherapy. A number of essential oils are known to be allergenic (2). Their sensitizing potential can sometimes be attributed to constituents having been identified as allergens, such as eugenol in clove oil. Typically, for a natural product, the composition of essential oils varies from harvest to harvest and with the country of origin (3). Table 1 lists the set of potential allergens compiled for this study. Most have been described in detail in a previous publication (2). Table 2 shows additional data for the essential oils tested. For information on International Nomenclature of Cosmetic Ingredients (INCI) nomenclature, the ‘CosIng’ database (<http://ec.europa.eu/enterprise/cosmetics/cosing/>, last accessed April 2010) and EU document 2006/257/EC were used.

The present analysis of patch test data from the Information Network of Departments of Dermatology (IVDK) (www.ivdk.org) describes the results obtained with series of essential oils compiled by the German Contact Dermatitis Research Group (DKG; www.ivdk.org/dkg), commercially available as patch test preparations, in a 9-year period.

Methods

The IVDK, a contact allergy surveillance network in Germany, Switzerland and Austria, has been described elsewhere (6). Briefly, results for all patients patch tested in the participating departments are electronically recorded, along with important demographic and clinical data. The diagnostic procedure follows international guidelines (7) further refined by the DKG (8), of which all IVDK participants are members. All data are transmitted in an anonymous format twice yearly to the data centre in Göttingen, where they are checked and, if satisfying internal quality control criteria (9), analysed according to international guidelines (10),

using SAS software (version 9.2, SAS Institute, Cary, NC, USA).

For the present analysis, data for all patients patch tested between January 2000 and December 2008 ($n = 84\,716$ in the course of 87 103 consultations) with series containing essential oils were included. Some essential oils had been temporarily patch tested in the ‘monitor series’ (11), a temporary supplement to the baseline series, i.e. in consecutive patients, whereas before or after they were tested in the context of special series, as were the remaining essential oils. As the prevalence of positive reactions in consecutive patients is not comparable to the prevalence when only selected patients are tested, being expected to be higher in the latter case, the results are presented separately. Allergens were provided by Almirall-Hermal/Trolab, Reinbek, Germany.

As the composition of these series changed, and for other reasons, such as temporary unavailability of allergens, the number of patients actually tested with the essential oils varied. Weak (+) to strong (+++) positive patch test reactions on the third day after application of the test or, if this was not read, after the fourth day were aggregated as positive outcome and contrasted to non-positive, i.e. non-allergic, reactions, comprising negative, doubtful and irritant reactions.

Results

Of the 84 716 patients consulting in the study period, 15 682 had been tested with at least one essential oil in different versions of special test series or the ‘monitor series’, and 637 reacted positively to at least one of the essential oils. The distribution of important demographic and clinical variables in these three subgroups is given in Table 3. As can be seen, patients with occupational/hand dermatitis, patients with atopic dermatitis and older patients were slightly over-represented among those with at least one positive reaction, and males were less often found to be sensitized to one or more of the essential oils. To identify occupations that may be associated with positive reactions to essential oils, the distributions of occupations were compared between those tested and those with occupational dermatitis who reacted positively. However, a substantial difference was only noted in case of masseurs and physiotherapists (1.1 versus 3.6%, $P < 0.0001$).

Patch test results with the 14 essential oils are given in Table 4. Usually, but not always, sensitization prevalences are higher in the context of patch testing in a special series; however, these differences were significant only for the two most frequent allergens. Whereas about half of the oils elicited positive reactions in a notable proportion

Table 1. Typical composition of essential oils; data taken from the EFFA labelling manual (European Flavour and Fragrance Association, Brussels, www.effa.be/cop_2008.htm) and (4), corrected by analytical purchase data collected for 20 years (E.S.)

Essential oil: official trade name ^a (INCI nomenclature, possibly extended for perfumery use)	Constituents (maximum observed value in %) Allergens listed in the European Cosmetic regulation 76/768/EEC (Annex III) in <i>italics</i>
Ylang-ylang oil (I + II) ^b (<i>Cananga odorata</i> oil) ^c	Germacrene-D (28); (<i>E,E</i>)- α -farnesene (21); caryophyllene (17); <i>linalool</i> (I, 19.0; II, 9.5); <i>benzyl benzoate</i> (8.0); <i>farnesol</i> (4.0); <i>benzyl salicylate</i> (4.0); (<i>E,E</i>)-farnesyl acetate (3.5); <i>geraniol</i> (2.5); <i>isoeugenol</i> (0.8); <i>benzyl alcohol</i> (0.5); <i>eugenol</i> (0.5); <i>p</i> -cresyl methyl ether (I, 5.0; II, 3.5); methyl benzoate (I, 5.5; II, 3.5); <i>benzyl acetate</i> (I, 10.0; II, 5.0); <i>geranyl acetate</i> (I, 15.0; II, 12.0)
Lemongrass oil (<i>Cymbopogon</i> spp. oil)	<i>Citral</i> (85.0); <i>geraniol</i> (7.0); <i>limonene</i> (4.0); <i>geranyl acetate</i> (2.2); caryophyllene (1.6); <i>trans</i> -isocitral (1.4); 6-methyl 5-hepten-2-one (1.3); caryophyllene oxide (1.2); 4-nonanone (1); <i>citronellol</i> (0.8); <i>eugenol</i> (0.3); <i>linalool</i> (0.2) (also according to (5))
Sandalwood oil (<i>Santalum album</i> wood oil)	α -Santalol (55); β -santalol (24)
Clove oils (<i>Eugenia caryophyllus</i> oil)	<i>Eugenol</i> (92.0); caryophyllene (17); <i>eugenyl acetate</i> (15); <i>isoeugenol</i> (0.5)
Jasmine absolute (<i>Jasminum officinale</i> oil)	<i>Benzyl acetate</i> (28); <i>benzyl benzoate</i> (24.0); <i>phytyl acetate</i> (9); <i>isophytol</i> (8.5); <i>phytol</i> (7.4); <i>linalool</i> (7.0); <i>eugenol</i> (4.0); <i>squalene</i> (4); <i>indole</i> (3.5); <i>benzyl alcohol</i> (2.5); <i>cis</i> -3-jasmone (2.5); <i>methyl linolenate</i> (2.0); <i>methyl palmitate</i> (1.4); <i>p</i> -cresol (1.0); <i>cis</i> -3-hexenyl benzoate (1.0); <i>benzyl salicylate</i> (0.4); <i>jasmin lactone</i> (0.9); <i>methyl jasmonate</i> (0.7); <i>isoeugenol</i> (0.4) (also according to (2))
Sweet bay (Laurel) oil (<i>Laurus nobilis</i> oil)	1,8-Cineole (70); β -caryophyllene (11); <i>linalool</i> (11); <i>limonene</i> (5.0); <i>eugenol</i> (2.0); <i>geraniol</i> (0.3)
Cedarwood oil (<i>Juniperus virginiana</i> wood oil)	α -Cedrene (32); <i>thujopsene</i> (25); <i>cedrol</i> (25); β -cedrene (6); <i>widdrol</i> (5); <i>cuparene</i> (traces)
Patchouli oil (<i>Pogostemon cablin</i> oil)	(–)-Patchoulol (35); (+)- α -lulnesene (21); (–)- α -guajene (16); β -pinene (6); (–)- β -patchoulene (3.5); (–)-seychellene (3); <i>pogostol</i> (2.5); α -pinene (2.5); <i>norpatchoulene</i> (1)
Neroli oil (<i>Citrus aurantium</i> flower oil)	<i>Linalool</i> (44); <i>limonene</i> (18); β -pinene (17); <i>linalyl acetate</i> (15); <i>trans</i> - β -ocimene (8); <i>geranyl acetate</i> (5); <i>trans</i> -nerolidol (5); (<i>E,E</i>)-farnesol (4); <i>myrcene</i> (4); <i>farnesol</i> (4.0); <i>geraniol</i> (3.5); <i>citral</i> (0.3)
Peppermint oil (<i>Mentha piperita</i> oil)	(–)-Menthol (49); (–)-menthone (28); (–)-menthyl acetate (8); <i>mentofuran</i> (8); <i>isomenthone</i> (8); <i>neomenthol</i> (6); <i>pulegone</i> (3.5); <i>limonene</i> (3.0); <i>linalool</i> (0.4)
Narcissus absolute (<i>Narcissus poeticus</i> Flower Extract)	α -Terpineol (23.7); <i>trans</i> -isoeugenol methyl ether (20); <i>benzyl benzoate</i> (20); <i>coumarin</i> (5.7); <i>benzyl alcohol</i> (4.0); Δ^3 -carene (3.4); <i>cinnamyl alcohol</i> (2.5); <i>phenylethyl alcohol</i> (2.2); <i>ethyl palmitate</i> (2.2); <i>phenylpropyl acetate</i> (1.7); 1,8-cineole (1.5); caryophyllene (1.0); <i>benzyl acetate</i> (0.7); <i>isoeugenol</i> (0.5); <i>farnesol</i> (0.3) (also according to (2))
Lemon oil (<i>Citrus medica limonum</i> oil)	<i>Limonene</i> (80); β -pinene (16.5); γ -terpinene (12); <i>citral</i> (3.0); <i>geraniol</i> (2.0); <i>neral</i> (1.2); β -bisabolene (0.9); <i>geranyl acetate</i> (0.7); <i>neryl acetate</i> (0.6); <i>linalool</i> (0.3); <i>geraniol</i> (0.2)
Eucalyptus oil (<i>Eucalyptus globulus</i> oil)	1,8-Cineole (58; 70–80 after rectification); α -pinene (22); <i>limonene</i> (8); <i>p</i> -cymene (5); <i>trans</i> -pinocarveol (5); <i>aromadendrene</i> (10); <i>globulol</i> (2.5) (the last two components only traces after rectification)
Orange oil (<i>Citrus aurantium dulcis</i> oil)	<i>Limonene</i> (95.0); <i>linalool</i> (0.7); <i>n-decanal</i> (0.7); <i>citral</i> (0.3); α -sinensal (0.05); β -sinensal (0.06)

^aTaken from ISO/DIS 4720:2009 Essential oils – Nomenclature; International Standardization Organization, Geneva, Switzerland.

^bFour fractions are collected at progressively longer distillation times and are known as 'Extra', 'I', 'II' (the latter two are included in the allergen preparation), and 'III'. The fractions have more or less distinct chemical compositions (4).

^cImprecise representation; *Cananga* oil, extracted from *Cananga odorata* (Lam.) Hook. f. et Thomson, forma *macrophylla*, can be labelled separately only if an unofficial extension of the INCI is used: *Cananga Odorata Macrophylla Flower Oil*.

of patients, doubtful or irritant reactions were more frequent than positive reactions in five test preparations, yielding an overall negative 'reaction index'. The added value of testing essential oils is illustrated in Fig. 1: 1.57% of the 4977 patients tested with fragrance mix I (FM I) and fragrance mix II (FM II) and with essential oils (or 10% of the 779 patients reacting to at least one of the allergens) reacted positively only to the latter.

The concomitant reactivity between ylang-ylang oil and isoeugenol, one of its constituents, is shown in Table 5. There was significant asymmetry of the dichotomized outcomes (positive versus

non-positive), namely $P = 0.002$ (McNemar test), in terms of more patients reacting positively to ylang-ylang oil alone than to isoeugenol alone. Concordance of the dichotomized outcomes was fair [Cohen's $\kappa = 0.32$, and 95% confidence interval (CI) 0.22–0.42]. Regarding ylang-ylang oil and farnesol, a further constituent (Table 1), concomitant reactivity was limited, with a mere 3 patients of 926 tested with both allergens reacting to both, 13 reacting to farnesol only and 50 reacting to ylang-ylang only ($P < 0.0001$, Cohen's $\kappa = 0.085$, 95% CI 0.016–0.15). Of 762 patients tested with all three allergens, 27 reacted positively only to

Table 2. Official botanical terms and reference numbers [CAS (information regarding test allergens supplied by M. Kaebel, Hermal/Allmirel, Reinbek, Germany), EINECS-CAS, EINECS] and ISO Standards for the specification of certain characteristics to facilitate the assessment of quality

Essential oil (official trade name) ^a	Botanical term ^a	CAS	EINECS ^b	EINECS-CAS ^c	Standard(s):year (of current version)
Ylang-ylang oil (I + II)	<i>Cananga odorata</i> (Lam.) Hook. f. et Thomson forma <i>genuina</i>	8006-81-3	281-092-1	83863-30-3	ISO 3063:2004
Lemongrass oil	<i>Cymbopogon flexuosus</i> (Nees ex Steudel) J. F. Watson	8007-02-1	295-161-9	91844-92-7	ISO 4718:2004
	<i>Cymbopogon citratus</i> (DC, ex Nees) Stapf		289-752-0	89998-14-1	ISO 3217:1974
Sandalwood oil	<i>Santalum album</i> L.	8006-87-9	284-111-1	84787-70-2	ISO 3518:2002
Clove oils:					
(a) Bud ^d	<i>Syzygium aromaticum</i> (L.) Merr. & L. M. Perry syn.	(a) 8000-34-8			(a) ISO 3142:1997
(b) Leaf	<i>Eugenia caryophyllus</i> (Spreng.) Bullock & S. G. Harrison	(b) 8015-97-2	284-638-7	84961-50-2	(b) ISO 3141:1997
(c) Stem		(c) 8015-98-3			(c) ISO 3143:1997
Jasmine absolute	<i>Jasminum grandiflorum</i> L.	8022-96-6	283-993-5	84776-64-7	'Standard market quality'
Sweet bay (Laurel) oil	<i>Laurus nobilis</i> L.	8002-41-3	283-272-5	84603-73-6	'Standard market quality'
Cedarwood oil	<i>Juniperus virginiana</i> L.	8000-27-9	285-370-3	85085-41-2	ISO 4724:2004
Patchouli oil	<i>Pogostemon cablin</i> (Blanco) Benth., syn. <i>Mentha cablin</i> Blanco	8014-09-3	282-493-4	84238-39-1	ISO 3757:2002
Neroli oil	<i>Citrus aurantium</i> L. syn. <i>Citrus amara</i> Link syn. <i>Citrus bigaradia</i> Loisel syn. <i>Citrus vulgaris</i> Risso	8016-38-4	277-143-2	72968-50-4	ISO 3517:2002
Peppermint oil	<i>Mentha x piperita</i> L.	8006-90-4	282-015-4	84082-70-2	ISO 856:2006
Narcissus absolute	<i>Narcissus poeticus</i> L.	8023-75-4	290-087-3	90064-26-9	'Standard market quality'
Lemon oil	<i>Citrus limon</i> (L.) Burm. f.	8008-56-8	284-515-8	84929-31-7	ISO 855:2003
Eucalyptus oil	<i>Eucalyptus globulus</i> Labill	8000-48-4	283-406-2	84625-32-1	ISO 770:2002
Orange oil	<i>Citrus sinensis</i> (L.) Osbeck	8008-57-9	232-433-8	8028-48-6	ISO 3140:2005

^aTaken from ISO/DIS 4720:2009 Essential oils – Nomenclature; International Standardization Organization, Geneva, Switzerland.

^bEINECS, European Inventory of Existing Commercial Chemical Substances (<http://ecb.jrc.ec.europa.eu/esis>, last accessed 3 May 2010).

^cThe CAS numbers in EINECS have been generated in the process of compiling the EINECS database. The EINECS-CAS number is a valid CAS number, adding duplicates to the CAS systematic. For ylang-ylang oil, for instance, two different numbers are registered: 'Oils, ylang-ylang' (8006-81-3) and 'Ylang-ylang, ext.' (83863-30-3), respectively. Both numbers are used, for instance, in REACH (Registration, Evaluation, Authorization and Restriction of Chemical Substances, EC 1907/2006).

^dUsed for the allergen preparation.

Table 3. Demographic and clinical characteristics of patients tested in 2000–2008 (Percentages of the "MOAHLFA" index)

		All patients, N = 84 716	Patients tested with at least one essential oil, N = 15 682	Patients positive for at least one essential oil, N = 637
Male	M	38.1	32.8	29.2
Occupational dermatitis	O	14.8	18.3	24.2
Atopic dermatitis	A	17.7	20.3	22.3
Hand dermatitis	H	26.7	30.2	32.7
Leg dermatitis	L	10.9	7.7	11.2
Face dermatitis	F	14.1	18.1	18.2
Age ≥40 years	A	68.3	67.0	77.9

ylang-ylang oil, but neither to isoeugenol nor to farnesol. Concomitant reactivity between clove oil and eugenol is described in Table 6. There was no

significant asymmetry of the dichotomized outcome; that is, about as many patients reacted only to clove oil [containing more than 90% eugenol (see Table 1), i.e. ~1.8% eugenol in the patch test preparation] as reacted only to eugenol (1% petrolatum), and concordance was relatively good (Cohen's $\kappa = 0.52$, 95% CI 0.43–0.61). Lemongrass oil contains a number of single, defined fragrance ingredients (see below), mainly citral. Concomitant reactivity is shown in Table 7; concordance of the dichotomized outcome was good (Cohen's $\kappa = 0.55$, 95% CI 0.44–0.66). Limonene is a constituent of several citrus peel oils. Regarding neroli oil, lemon oil and orange oil, 1526, 1585 and 1527 patients, respectively, had been tested with both of these allergens and limonene. Although 9, 8 and 2 positive reactions, respectively, were observed to the citrus

Table 4. Results with essential oils in Information Network of Departments of Dermatology patients, 2000–2008; all allergens in petrolatum (10)

Allergen	%	Test context	N (tested)	% (?/IR)	% (+)	% (++/+++)	% (pos. std.) (95% CI)	RI	PR
Ylang-ylang (I and II) oil	10	B	3175	1.61	1.86	0.79	2.52 (1.94–3.10)	0.24	70.2
		Sp	2155	1.58	2.27	1.90	3.93 (3.08–4.78)	0.45	54.4
Lemongrass oil	2	B	2435	0.53	0.49	0.12	0.55 (0.26–0.85)	0.07	80.0
		Sp	8445	1.17	1.82	0.67	2.25 (1.93–2.56)	0.36	73.0
Sandalwood oil	10	B	3671	1.28	1.06	0.27	1.26 (0.88–1.64)	0.02	79.6
		Sp	1002	0.60	1.10	0.70	1.80 (0.93–2.67)	0.50	61.1
Clove oil	2	Sp	6893	0.95	0.89	0.60	1.53 (1.22–1.84)	0.26	60.2
Jasmine absolute	5	B	3668	1.06	1.39	0.30	1.52 (1.11–1.92)	0.23	82.3
		Sp	982	1.02	0.51	0.71	1.16 (0.47–1.85)	0.09	41.7
Laurus nobilis leaf oil ^a	2	Sp	6297	0.5	0.54	0.44	1.00 (0.73–1.26)	0.36	55.6
Cedar wood oil	10	Sp	6223	0.73	0.6	0.17	0.83 (0.58–1.09)	0.05	79.6
Patchouli oil	10	B	2446	0.57	0.57	0.04	0.56 (0.26–0.85)	0.03	93.3
		Sp	828	0.72	0.72	0.60	1.43 (0.56–2.30)	0.29	54.6
Neroli oil	2	Sp	6220	0.52	0.64	0.15	0.71 (0.50–0.92)	0.20	81.6
Peppermint oil	2	Sp	6546	0.68	0.48	0.16	0.59 (0.39–0.79)	–0.05	75.6
Narcissus absolute	2	B	2445	0.74	0.53	0.08	0.52 (0.25–0.80)	–0.09	86.7
		Sp	809	0.49	0.49	0.12	0.56 (0.05–1.07)	0.11	80.0
Lemon oil	2	Sp	6467	0.35	0.22	0.07	0.27 (0.14–0.40)	–0.10	77.8
Eucalyptus spp. oil	2	Sp	6680	0.41	0.19	0.06	0.24 (0.11–0.37)	–0.30	73.3
Orange oil	2	Sp	6246	0.56	0.2	0	0.16 (0.05–0.27)	–0.54	100

B, along with baseline series in the 'monitor series'; CI, confidence interval; IR, irritant; PR, positivity ratio; Sp, special series; pos. std., proportion of age-standardized and sex-standardized; RI, reaction index.

^aOil from the seeds of *Laurus nobilis* is not permitted for use in cosmetics (No. 359 of Annex II of EU Cosmetics Directive); other extracts are not restricted. The CAS numbers are not consistently used for extracts from defined parts of the plant.

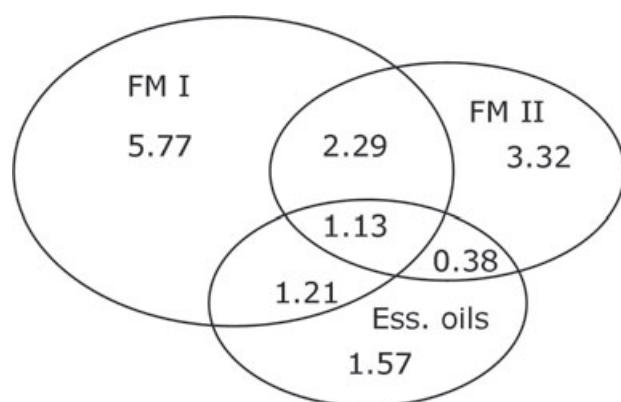


Fig. 1. Pattern of 'detection' of sensitization by fragrance mix I (FM I), fragrance mix II (FM II) and essential oils in the subgroup of 4977 patients tested with the two screening allergens (FM II was introduced only in 2005) and a series of essential oils.

oils in this subgroup, none of these patients was concordantly positive to limonene.

Discussion

A previous European study (2) has already shown that essential oils are important sensitizers, even in consecutively tested patients, the most common allergens being ylang-ylang oil I and II (tested separately, 2.6% and 2.5% positive reactions, respectively), lemongrass oil (1.6% positive), narcissus absolute (1.3% positive), jasmine absolute

Table 5. Cross-reactivity between isoeugenol and ylang-ylang oil in the subgroup of 2276 patients tested with both allergens

Ylang-ylang oil	Isoeugenol				Total ylang-ylang oil
	Negative	?/IR	+	++/+++	
Negative	2090	22	26	7	2145
?/IR	39	2	1	0	42
+	39	0	9	7	55
++/+++	25	0	1	8	34
Total isoeugenol	2193	24	37	22	2276

IR, irritant.

Table 6. Cross-reactivity between eugenol and clove oil in the subgroup of 5634 patients tested with both allergens

Clove oil	Eugenol				Total clove oil
	Negative	?/IR	+	++/+++	
Negative	5135	56	26	4	5221
?/IR	34	13	6	0	53
+	32	4	18	3	57
++/+++	10	1	9	17	37
Total eugenol	5211	74	59	24	5634

IR, irritant.

(1.2% positive) and sandalwood oil (0.9% positive). In contrast, our study is at least partly based on patch test results of patients tested in an aimed fashion, i.e. only in cases of suspected causal exposure to fragrances. Thus, the figures are not directly comparable and would be expected to be higher in the present study, which is mostly the case, but not always – possibly because of marked

Table 7. Cross-reactivity between citral and lemongrass oil in the subgroup of 1777 patients tested with both allergens

Lemongrass oil	Citral				Total lemongrass oil
	Negative	?/IR	+	++/+++	
Negative	1657	13	15	1	1686
?/IR	15	5	4	0	24
+	21	5	15	2	43
++/+++	6	1	7	10	24
Total citral	1699	24	41	13	1777

IR, irritant.

geographical variation, which had been noted in the European study (2). The added value of testing the essential oils has been confirmed; a considerable proportion of patients tested with the series would not have been diagnosed as 'fragrance-allergic' if only the two mixes had been used (Fig. 1) – even though they contain a few of the substances found in essential oils, among an abundance of other compounds (Table 1).

The patch test preparations used here appear to be adequate in terms of a reaction profile, with usually more positive than doubtful or irritant reactions (a positive reaction index) and the occurrence of a 'usual' proportion of ++ or +++ reactions among all positive reactions (a positivity ratio <80%), except for the four most infrequent allergens. However, we were not able to assess the sensitivity or specificity of the preparations, as no validation test, such as repeated open application testing or provocative use testing, was employed. Moreover, relevance had not been documented with sufficient certainty in each single case – probably a common drawback of routine surveillance data used in a retrospective analysis. However, the previous multi-centre study (2) found that 5.2% of patients with a history of adverse reactions to scented products had additionally been detected by using the essential oils series and, conversely, that 10.4% of patients reacting only to one of the essential oils, but not to FM I, had a clear history of fragrance intolerance and another 19% a probable history. These proportions were similar to those found for FM I in the same study, and may be fairly representative for the share of relevant reactions in our study.

Regarding a few of the essential oils, concomitant reactivity to the compounds that are (i) known constituents and (ii) available as standard test preparations has been demonstrated (Table 5–7). For some of these essential oils, a certain correlation can be found between their relative importance and the importance of their single constituents (12); for example, lemongrass oil and citral or clove oil and eugenol are more important than citrus oils and limonene. Nevertheless, a large proportion of reactions occurred only to the essential oil, and

not to the constituent or constituents available for testing.

The three citrus peel oils versus limonene constituted a notable exception regarding concomitant reactivity. The allergenicity of limonene is closely related to oxidation (e.g. (13, 14)), and both limonene and the citrus oils are largely preserved from auto-oxidation when incorporated in pet. Conversely, during shelf storage, and especially during use, after the container is first opened, products containing essential oils are subject to oxidation and auto-oxidation, respectively, to probably varying extents, yielding, for example, oxides, peroxides, hydroperoxides, epoxides and endoperoxides, depending on the substance. Often, this process leads to the formation of a strong or stronger allergens, as shown in case of tea tree oil (15), lavender oil (16) or limonene as a component of citrus peel oils (13), to name but a few examples. As a drawback, irritancy also increases during oxidation, as demonstrated for linalool and *R*-limonene (17), and this has to be considered when patch testing with oxidized compounds. As a consequence, patch testing with unoxidized or weakly oxidized substances may be not entirely suitable for diagnosing the actual clinical problem, which is most likely caused by essential oils that are aged/oxidized to some extent – at least regarding those natural mixtures in which native, unoxidized constituents are merely prehaptenes (18), and the actual allergen or allergens are formed only in the process of ageing. It follows that the prevalences noted in this study may represent a lower limit estimate of the true frequency of problems caused by contact sensitization to those essential oils containing components that are vulnerable to oxidation and relevant for allergen formation. However, regarding the three citrus oils tested in this study, no analytical data on oxidation state are available. An alternative explanation would be sensitization to components of the citrus oils other than limonene, even if these are present only at much lower concentrations (Table 1).

Alas, only a small number of essential oils is available as a patch test preparation, although probably the most relevant ones. Using these available extracts enables specific patch testing and advice to the patient as to future allergen avoidance – even if this has to be based on the INCI nomenclature, which is partly non-specific in this field, as only the botanical names are given. The same botanical name could be used to indicate the use of dried powdered leaves and other material from the plant, which may be quite irrelevant regarding contact sensitization. Nevertheless, the sensitized patient capable of reading and comprehending the INCI listings on products (19) will profit

from this information and be helped to avoid his or her allergen. On the other hand, many essential oils are not available as commercial test preparations. In this situation, a patch test with the incriminated product, such as perfume, cosmetic or aromatherapy oil, ideally followed by breakdown testing of the adequately diluted single ingredients in cases of positive reaction to the product, including essential oils, is a slightly cumbersome, but rewarding, procedure: (i) it may be possible to diagnose the individual allergen – with the prospect of future avoidance as above, without having to resort to a strict ‘fragrance free’ or trial and error strategy; and (ii) this may lead to an accumulating body of evidence regarding the sensitizing properties of this class of natural products. Occasionally, slight irritant reactions in terms of erythema without infiltration might occur when testing alcohol-based perfumes etc.; the frequency of these reactions can be reduced by allowing the patch to dry before it is applied to the skin (20).

Conclusion

Some essential oils are important contact sensitizers; contact sensitization to these can be only partly explained by sensitization to the relatively few single constituents available for patch testing. Patch testing with essential oils – at least with the five most important allergens causing a considerable number of ++ or +++ reactions – should be considered in patients with a history of adverse reactions to perfume and related scented products. Diagnostic sensitivity may be increased if oxidation products of essential oils or of their single main constituents are used for patch testing, for example oxidized limonene (21). Moreover, patch testing with culprit products brought in by the patient, if necessary and feasible, followed by breakdown testing, can help to close the diagnostic gap by: (i) including those other essential oils (or synthetic fragrances, for that matter) not included in the commercial test series; and (ii) providing a means of – unfortunately non-standardized – testing with those oxidation products to which the patient had been exposed.

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