

Positive Patch-Test Reactions to Essential Oils in Consecutive Patients From North America and Central Europe

Erin M. Warshaw, MD, MS,*†‡ Kathryn A. Zug, MD,§ Donald V. Belsito, MD,|| Joseph F. Fowler, Jr, MD,¶|| Joel G. DeKoven, MD,# Denis Sasseville, MD,** Howard I. Maibach, MD,†† C.G. Toby Mathias, MD,‡‡ Vincent A. DeLeo, MD,§§ James S. Taylor, MD,|||| Anthony F. Fransway, MD,¶¶ James G. Marks, Jr, MD,## Melanie D. Pratt, MD,*** Matthew J. Zirwas, MD,††† Johannes Geier, MD,‡‡‡ and Wolfgang Uter, MD§§§

Background: Synthetic fragrances and natural essential oils (EOs) are used in perfumery and found in various cosmetics. Essential oils are also increasingly used to promote wellness. In previous studies, the sensitization potential of some EOs has been identified; however, the current prevalence of sensitivity is largely unknown.

Objectives: The aim of this study was to determine frequency of positive patch-test reactions to EOs tested in the baseline series, along with 3 fragrance markers (FMs) (fragrance mix I, fragrance mix II, and *Myroxylon pereirae*), in consecutive patients in the US/Canadian North American Contact Dermatitis Group (NACDG) (2009–2014) and the central European, trinational Information Network of Departments of Dermatology (IVDK) (2010–2014).

Methods: This study used a retrospective analysis of patch-test results and relevant demographic/clinical data collected electronically by the networks, obtained with *Santalum album* 10% petrolatum (pet) (IVDK only); *Cananga odorata* 2% (NACDG) and 10% (IVDK) pet; *Jasminum* species 2% (NACDG) and 5% (IVDK) pet; *Mentha piperita* 2% pet; *Melaleuca alternifolia*, oxidized (tea tree oil), 5% pet; and *Lavandula angustifolia* 2% pet (latter 3 NACDG only).

Results: Overall, 62,354 patients were tested to 3 FMs and EOs (NACDG, 13,398; IVDK, 48,956); 11,568 (18.6%) reacted to at least 1 FM or EO, whereas 857 (1.4%) reacted to 1 or more EOs but none of the 3 FMs. For both the NACDG and IVDK populations, individuals who were positive to 1 or more of the 9 study allergens were significantly less likely to be male, have occupational skin disease, or have hand involvement and significantly more likely to have leg dermatitis and be 40 years and older (P 's ≤ 0.005). Prevalence rates for EOs were as follows: *S. album*, 1.4% IVDK; *C. odorata*, 1.1% NACDG and 2.4% IVDK; *Jasminum* species, 0.7% NACDG and 1.4% IVDK; *M. piperita*, 0.9% NACDG; *L. angustifolia*, 0.3% NACDG; and *M. alternifolia*, 0.3% NACDG. Of the 140 NACDG patients who reacted to 1 or more of the 5 NACDG EOs but none of the FMs, *M. alternifolia* yielded most positive reactions (45%); half of these reactions were strong (++ or +++, 50.8%) and of definite/probable clinical relevance (52.4%). Of the 717 IVDK patients who reacted to 1 or more of the 3 IVDK EOs but none of the 3 FMs, 38% were positive to *C. odorata*, 38% to *S. album* and 36% to *Jasminum* species."

Conclusions: Testing to EOs may be important for detecting sensitivity not detected by FMs alone. In North America, *M. alternifolia* is an important and clinically relevant sensitizer often not detected by FM. In Europe, as well as in North America, clinical relevance is often difficult to evaluate because (1) labeling of EOs when used as fragrance is not mandatory, and (2) these mixtures may indicate sensitization to 1 or more of their individual constituents from other sources, including synthetic fragrances.

From the *Department of Dermatology, Minneapolis Veterans Affairs Medical Center; †HMC Parkside Occupational and Contact Dermatitis Clinic; and ‡Department of Dermatology, University of Minnesota Medical School, Minneapolis; §Dartmouth-Hitchcock Medical Center, Lebanon, NH; ||Department of Dermatology, Columbia University Medical Center, New York, NY; ¶University of Louisville, KY; #Division of Dermatology, Sunnybrook Health Sciences Centre, University of Toronto, Ontario; and **Division of Dermatology, Montreal General Hospital, McGill University, Quebec, Canada; ††Department of Dermatology, University of California, San Francisco; ‡‡Department of Dermatology, University of Cincinnati, OH; §§Department of Dermatology, Keck School of Medicine, Los Angeles, CA; ||||Department of Dermatology, Cleveland Clinic, OH; ¶¶Associates in Dermatology, Fort Myers, FL; ##Department of Dermatology, Pennsylvania State University, State College; ***Division of Dermatology, University of Ottawa, Ontario, Canada; †††Ohio State

University, Columbus; and ‡‡‡Information Network of Departments of Dermatology at the University of Gottingen; and §§§Department of Medical Informatics, Biometry and Epidemiology, University of Erlangen-Nuremberg, Germany.

No reprints available.

This material is the result of work supported with resources and the use of facilities at the Minneapolis Veterans Affairs Medical Center. There are no other sources of funding for this work.

The contents do not represent the views of the US Department of Veterans Affairs or the US Government.

DOI: 10.1097/DER.0000000000000293

© 2017 American Contact Dermatitis Society. All Rights Reserved.

Synthetic fragrances and natural essential oils (EOs) are used in perfumery, foods, beverages, medicinal products, and personal care products. Many are sensitizers.^{1–3} Essential oils, complex substances obtained by distillation of plants, are also increasingly used to promote wellness.^{4–6} A 2002 survey of 31,044 US adults found that up to 70% of 31- to 40-year-old patients reported using herbal products.⁷ In a 2009 study of 400 Italian dermatology outpatients, the top reason cited for using topical herbal remedies was perceived safety of botanical products as compared with traditional medicaments.⁸ De Groot and Schmidt⁹ documented 79 EOs reported to cause contact allergy.

In previous studies, the sensitization potential of some EOs has been identified^{10–14}; however, the current prevalence of sensitivity is largely unknown. This study reviews data collected by 2 large patch-test groups, one in North America and the other in Central Europe. We provide prevalence rates of positive patch-test reactions and patterns of coreaction and compare results between the 2 regions.

METHODS

North American Contact Dermatitis Group Database

Methods for patch testing and data recording by the North American Contact Dermatitis Group (NACDG) have been previously reported.¹⁵ Briefly, patients were tested to a screening series of 70 allergens. Information recorded included patient age, sex, and race; atopic history (hay fever, eczema, and asthma); site(s) of dermatitis (up to 3 sites); strength of reactions; final interpretation (allergic vs not allergic); and clinical relevance of allergy. This analysis focused on patients tested from January 1, 2009, to December 31, 2014, to the 8 fragrance markers (FMs)/EO allergens on the NACDG screening series (Table 1). Although jasmine absolute is not technically an EO, for simplicity and ease of discussion we have included it in the EO category. Allergens were supplied by Chemotechnique Diagnostics AB (Malmö, Sweden) and Allergeaze (SmartPractice, Calgary, Alberta, Canada). A positive reaction was defined as a final interpretation code of “allergic.”

Information Network of Departments of Dermatology

The Information Network of Departments of Dermatology (IVDK) is a network of presently 56 departments of dermatology in Central Europe; 50 are located in Germany, 5 are located in Switzerland, and 1 is located in Austria. Patch-test material has been uniformly obtained by Hermal/Almirall, Reinbek, Germany, whereas use of different chambers and tapes is accepted. Exposure time was 2 days in most departments (n = 45) and patients (n = 43,851), and 1 day in the remainder. The methods have been described previously.¹⁶ Briefly, patch-test results are collected along with demographic and clinical information and transmitted twice yearly to the data center in Göttingen in an anonymous format. After quality verification, data are pooled for scientific analyses. The present analysis is composed of patients tested between January 1, 2010, and December 31, 2014, with 3 baseline screening allergens for fragrance allergy and

3 EOs (Table 1). Reactions morphologically + to +++ on day (D) 3, except on D4 when no D3 reading was available, were regarded as allergic, whereas all other reactions were regarded as nonallergic.

Statistical Analysis

Descriptive (stratified) statistical analysis focused on prevalence estimates accompanied by 95% confidence intervals. Differences in proportions across groups were statistically tested with the χ^2 test. For statistical analysis, the R software package¹⁷ (version 3.3.2, <http://www.r-project.org>) was used. In this exploratory analysis, no adjustment techniques were used for multiple comparisons; $P < 0.05$ was considered significant.

RESULTS

Study Population

Overall, there were 62,354 patients tested to 3 FMs (*Myroxylon pereirae* is regarded here as a “natural fragrance mix”) and EOs; 11,568 (18.6%) reacted to at least 1 FM or EO, whereas 857 (1.4%) reacted to 1 or more EOs but none of the 3 FMs (Table 2). Of the 13,398 NACDG patients patch tested to all 8 allergens, 18.6% (n = 2494) reacted to 1 or more of these allergens; there were 140 patients who reacted to 1 or more EOs but none of the 3 FMs. Of the 48,956 IVDK patients tested to all 6 study allergens, 18.5% (n = 9074) reacted to 1 or more of these allergens; there were 717 patients who had 1 or more positive reactions to EOs but did not react to any of the 3 FMs. There were no significant differences concerning the proportions of positive reactions to each of the 6 target allergens between IVDK departments using 1- versus 2-day patch-test exposure

TABLE 1. Fragrance Markers and EOs Tested by the NACDG and IVDK

Allergen	Concentration*	
	NACDG	IVDK
FMs		
Fragrance mix I	8%	8%
Fragrance mix II	14%	14%
<i>M. pereirae</i>	25%	25%
EOs		
<i>C. odorata</i> †	2%	10%
<i>Jasminum</i> species‡	2%	5%
<i>S. album</i>	NT	10%
<i>M. piperita</i>	2%	NT
<i>M. alternifolia</i> , oxidized	5%	NT
<i>L. angustifolia</i>	2%	NT

*All in petrolatum.

†Ylang-ylang oil as a volatile product is not generally collected as a whole oil but in 5 successive fractions during the course of distillation. These 5 fractions, known respectively as “extra super,” “extra,” “first” (I), “second” (II), and “third,” are the oils usually found in the trade (ISO 3063:2004). The patch-test preparation includes I and II.

‡Absolute is technically not an EO; for simplicity, we have grouped jasmine absolute with EOs.

NT indicates not tested.

TABLE 2. Patient Characteristics

Characteristic	NACDG			IVDK			Total (NACDG + IVDK)		
	Tested to All FMs and EOs (n = 13,398)	≥1 FM or EO (n = 2494)	FM ⁺ , EO ⁺ (n = 140)	Tested (n = 48,956)	≥1 FM or EO (n = 9074)	FM ⁺ , EO ⁺ (n = 717)	Tested to All FMs and EOs (n = 62,354)	≥1 FM or EO (n = 11,568)	FM ⁺ , EO ⁺ (n = 857)
Male	4167 (31%)	700 (28%)	34 (24%)	17,882 (37%)	2964 (33%)	234 (33%)	22,049 (35%)	3664 (32%)	268 (31%)
Occupational dermatitis	1270 (9%)	189 (8%)	16 (11%)	8337 (17%)	1309 (14%)	101 (14%)	9607 (15%)	1498 (13%)	117 (14%)
Atopic dermatitis	3576 (27%)	611 (24%)	33 (24%)	11,264 (23%)	1949 (22%)	169 (24%)	14,840 (24%)	2560 (22%)	202 (24%)
Hand*	2665 (20%)	435 (17%)	29 (21%)	14,557 (30%)	2347 (26%)	175 (24%)	17,222 (28%)	2782 (24%)	204 (24%)
Leg*	589 (4%)	136 (5%)	14 (10%)	5285 (11%)	1301 (14%)	108 (15%)	5874 (9%)	1437 (12%)	122 (14%)
Face*	2101 (16%)	412 (17%)	20 (14%)	8169 (17%)	1638 (18%)	135 (19%)	10,270 (16%)	2050 (18%)	155 (18%)
Age ≥40 y	9032 (67%)	1888 (76%)	95 (68%)	35,584 (73%)	7515 (83%)	535 (75%)	44,616 (72%)	9403 (81%)	630 (74%)

*As the primary location for NACDG and main presenting anatomical site for IVDK.

($P > 0.47$; for jasmine absolute, $P = 0.059$). The proportions of positive reactions to FMs and/or EOs for the 2 groups are shown in Figure 1.

MOAHLFA characteristics¹⁸ (male, occupational dermatitis, atopic dermatitis, hand dermatitis, leg dermatitis, face dermatitis, and age >40 years) are listed in Table 2. For both the NACDG and IVDK populations, each was considered separately, but the more so if combined, individuals who were positive to 1 or more of the 9 study allergens were more likely to be female and older than 40 years and have leg or face dermatitis. They were also less likely to have occupationally related skin disease, atopic dermatitis, and hand dermatitis as compared with the remainder of the patch-tested population. All differences were significant ($P \leq 0.002$) for the IVDK subgroup; for the smaller NACDG sample, differences were significant for sex, hand and occupational dermatitis, and age 40 years or older ($P \leq 0.005$), as well as atopic and leg dermatitis ($P \leq 0.024$), but not face dermatitis ($P = 0.31$).

Reaction Prevalence Rates

Positive reaction prevalence rates to the 9 study allergens are listed in Table 3. Of the FMs, for both the NACDG and IVDK, fragrance mix I had the highest number of positive reactions (10.8% and 9.5%, respectively). Reaction prevalence rates to FMs were similar for the NACDG and IVDK. For EOs, prevalence rates were higher for the IVDK (all 3 >1.4%) than the NACDG (all 5 <1.1%). Of the EOs, for both the NACDG and IVDK, *Cananga odorata* had the highest number of positive reactions (1.1% and 2.4%, respectively). *Lavandula angustifolia* had the lowest number of positive reactions (0.3%).

Relevance of Reactions to EOs Without FM Positivity

Of the NACDG patients, 140 (1.04%) reacted to 1 or more of the 5 NACDG EOs but none of the FMs. In this group, *Melaleuca alternifolia* yielded the highest proportion of positive reactions (45%, $n = 63$); half of these reactions were strong (++ or +++, 50.8%) and were of definite or probable clinical relevance (52.4%; Table 4).

Of the IVDK patients, 1.46% reacted to 1 or more of the 3 IVDK EOs but none of the FMs. In this group, 272 patients (38%) were positive to *C. odorata* (I/II) 10%, 270 (38%) were positive to *Santalum album* 10%, and 255 (36%) were positive to jasmine absolute 5%. In this subgroup, coupled reactions to *C. odorata* and *S. album* were much more common than any other combination (Fig. 2).

DISCUSSION

This study explored the positive patch-test reaction prevalence rates to 3 FMs and 6 EOs. There are several key findings. As expected, sensitivity to FMs was higher (5.2%–10.8%) than that to EOs (0.3%–2.4%). Despite the high reaction prevalence to FMs, there were 857 (1.4% overall, 140 NACDG and 717 IVDK) individuals who reacted to 1 or more EOs but none of the FMs. Finally, positivity to EOs was generally higher in Central Europe as compared with North America.

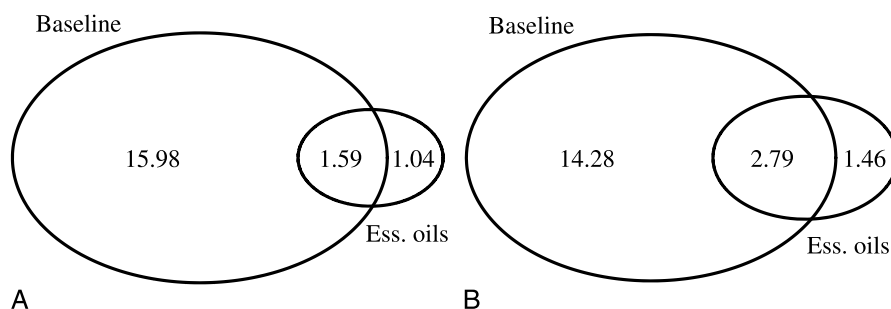


Figure 1. Proportionate Venn (Euler) diagrams of percent positive reactions to baseline fragrance screening markers and/or EOs for NACDG (A) and IVDK (B).

Demographics

In both North American and Central European populations, individuals who were positive to 1 or more of the 9 study allergens were more likely to be female and older than 40 years and have leg or face dermatitis as compared with the remainder of the patch-test population. They were also less likely to have occupationally related skin problem, atopic dermatitis, and hand dermatitis. In an Italian study on botanical product use, the highest rate of use was in 31- to 40-year-olds (72%), who used botanical agents in creams/ointment/lotions (36%) on the face (31%).⁹ In 127 patients in Belgium with allergic contact dermatitis (ACD) to FMs and EOs in topical pharmaceutical products, women were more frequently affected than men, and the legs/hands/face were the most commonly affected body sites.¹⁹

Although prevalence rates to FMs were similar in the 2 study groups, reactions to EOs were higher in the IVDK group (>1.4%) as compared with the NACDG group (<1.1%). Reasons for this could include a higher use of products containing these EOs in Europe or differences in methodology between the 2 groups, predominantly the differing patch-test concentrations (Table 1), which are higher by a factor of 5 (*C. odorata*) and 2.5 (jasmine absolute), respectively, in the IVDK. In addition, allergen occlusion is 24 to 48 hours for the IVDK and 48 hours for the NACDG; the IVDK delayed reading is

generally performed at 72 hours, whereas the NACDG varies from 96 to 168 hours.

Coreactivity of FM and EO

In this study, of the 353 NACDG patients positive to at least 1 EO, 60% also reacted to at least 1 FM. Of the 2081 IVDK patients positive to at least 1 EO, 66% also reacted to at least 1 FM (Fig. 1). This is similar to a previous study of 637 IVDK patients reacting to at least 1 EO, which found that more than half (55%) also reacted to fragrance mix I, 35% reacted to fragrance mix II, and 63% reacted to one of these mixes.¹³ Of 193 patients reacting to fragrance mix I in the Netherlands, 15 (7.7%) also reacted to ylang-ylang oil, and 13 (6.7%) reacted to jasmine.²⁰ Coreactivity to fragrance mix for individual EOs in a European multicenter study was as follows: ylang-ylang oil, 36 (86%) of 42, and jasmine absolute, 11 (55%) of 20.²¹ Of 283 Portuguese patients with a positive reaction to fragrance mix I, 190 reacted to *M. pereirae* (42.4%).²² In a subgroup of these patients tested to EOs (n = 67), 9 (13.4%) reacted to ylang-ylang oil, 4 (6.6%) reacted to sandalwood oil, and 4 (6.6%) reacted to lavender.²¹

Coreactivity between and within FMs and EOs is not unexpected. The chemical composition of FMs and EOs is complex. Composition

TABLE 3. Positive Reaction Prevalence

Allergen	NACDG		IVDK	
	n	% (95% CI) (n = 13,398)	n	% (95% CI) (n = 48,956)
FMs				
Fragrance mix I	1453	10.8 (10.3–11.4)	4652	9.5 (9.2–9.8)
Fragrance mix II	695	5.2 (4.8–5.6)	2535	5.2 (5.0–5.4)
<i>M. pereirae</i> (balsam of Peru)	991	7.4 (7.0–7.9)	3944	8.1 (7.8–8.3)
EOs				
<i>C. odorata</i> (ylang-ylang)	146	1.09 (0.92–1.28)	1175	2.40 (2.27–2.54)
<i>Jasminum</i> species (jasmine absolute)*	89	0.66 (0.53–0.82)	703	1.44 (1.33–1.55)
<i>S. album</i> (sandalwood)	NT	NT	676	1.38 (1.28–1.49)
<i>M. piperita</i> (peppermint)	71	0.53 (0.41–0.67)	NT	NT
<i>M. alternifolia</i> , oxidized (tea tree)	123	0.92 (0.76–1.09)	NT	NT
<i>L. angustifolia</i> (lavender)	43	0.32 (0.23–0.43)	NT	NT

*Absolute is technically not an EO; for simplicity, we have grouped jasmine absolute with EOs.

CI indicates confidence interval; NT, not tested.

TABLE 4. Clinical Relevance* of Reactions to EOs in Patients Negative to FMs

Substance	Positive, n (%) (n = 13,398)	Second Read				Clinical Relevance			
		+++	++	+	+/-†	Definite	Probable	Possible	Past/Unknown
<i>C. odorata</i>	35 (0.3)	5 (14.3)	12 (34.3)	12 (34.3)	6 (17.1)	0 (0.0)	5 (14.3)	21 (60.0)	9 (25.7)
<i>Jasminum</i> species	23 (0.2)	2 (8.7)	8 (34.8)	7 (30.4)	64 (26.1)	0 (0.0)	7 (30.4)	16 (69.6)	0 (0.0)
<i>M. piperita</i>	26 (0.2)	1 (3.8)	3 (11.5)	17 (65.4)	5 (19.2)	2 (7.7)	4 (15.4)	12 (46.2)	8 (30.8)
<i>M. alternifolia</i>	63 (0.5)	19 (30.2)	13 (20.6)	27 (42.9)	4 (6.3)	8 (12.7)	25 (39.7)	10 (15.9)	20 (31.7)
<i>L. angustifolia</i>	11 (0.1)	0 (0.0)	0 (0.0)	7 (63.6)	4 (36.4)	0 (0.0)	4 (36.4)	3 (27.3)	4 (36.4)

Definite indicates use test or patch test with a product containing the EO was positive; possible, the EO was likely present in products that the patient was exposed to; probable, the EO could be verified as present in the patient's product(s).

*NACDG data only.

†Doubtful reaction (macular erythema).

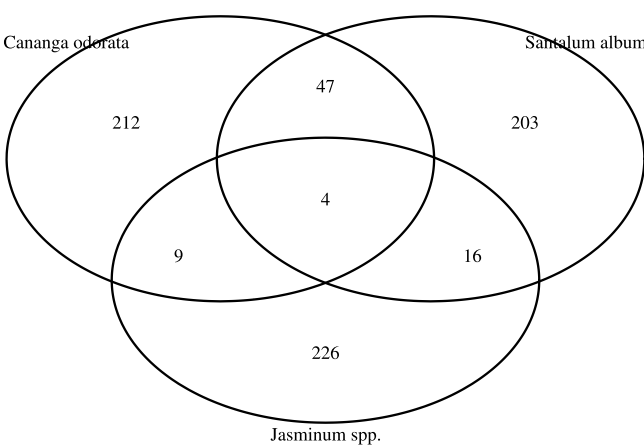


Figure 2. Coreactivity of EOs (IVDK).

of these botanicals varies by factors including species, harvest location, and extraction method.²³ Most EOs contain 100 to 250 individual components.²⁴ As described hereinafter, many allergenic compounds are shared among EOs.

Ylang-ylang

Ylang-ylang oil is the EO obtained from the flowers of the ylang-ylang tree, *C. odorata forma genuina*, which is primarily found in Southeast Asia. It is different from *Cananga* oil, which is derived from the macrophylla form. Ylang-ylang oil is used as a floral fragrance in perfumery and personal care products. It is also used in drinks, chewing gum, ice cream, candy, and bakery items. Medicinal uses range from treating depression, hypertension, and anxiety to skin diseases.²⁵

Ylang-ylang oil as a volatile product is not generally collected as a whole oil but in 5 successive fractions during the course of distillation. These 5 fractions, known respectively as “extra super,” “extra,” “first” (I), “second” (II), and “third,” are the oils usually found in the trade (ISO 3063:2004). The patch-test preparation includes I and II. There are at least 52 compounds in ylang-ylang oil, including linalool, germacrene D, methyl benzoate, and β -caryophyllene.²⁶ The composition of the 5 different EOs varies considerably; hence, the subtype of ylang-ylang oil used in a study should ideally be defined.

There are many reports of ACD to ylang-ylang oil. The major sensitizer, dihydro-isoeugenol, was eliminated in the 1990s in Japan with a subsequent reduction in ACD cases there, including “pigmented cosmetic dermatitis.”²⁷ Other major allergens include caryophyllene and linalool.¹³ The role of oxidation products of linalool has been well established for purified linalool from natural sources or synthetic linalool²⁸; however, the question to which extent oxidation products of linalool (or of other autooxidation-prone constituents) are relevant in ylang-ylang oil (or other EOs) is hitherto unclear. The range of positivity to ylang-ylang oil in 14 studies involving 37,356 patients (including, but not limited to, NACDG and

IVDK studies) from 1976 to 2012 was 0.7% to 2.6%.²⁴ Our study prevalence rates were 1.1% (NACDG) and 2.4% (IVDK).

Jasmine

The jasmine absolute tested by the IVDK and NACDG is the EO from *Jasminum grandiflorum* L. flowers (Spanish jasmine), a flowering shrub native to Africa and Asia. An absolute differs from an EO in that absolutes are products obtained by extraction with ethanol. There are more than 40 reports of ACD to jasmine absolute.²⁴ The major allergens include eugenol and linalool.¹³ The range of positivity to jasmine in 12 studies involving 32,708 patients from 1983 to 2012 was 0.3% to 1.5%.²⁴ Our study prevalence rates were 0.7% (NACDG) and 1.4% (IVDK).

Sandalwood

There are 3 main varieties of sandalwood: East India (*S. album* L.), Australia (*Santalum spicatum* R. Br.), and New Caledonia (*Santalum austrocaledonicum*). Sandalwood is an evergreen tree used in furniture. The EO is used as a fragrance agent in many personal care products and extensively in aromatherapy.²⁹ De Groot and Schmidt³⁰ analyzed the constituents and identified more than 90 compounds; these included bergamotol, bisabolol, farnesol, lanceol, nuciferol, and santalols. The major allergen is presumably santalol, although this has not been investigated adequately.¹³

Allergic contact dermatitis to sandalwood oil has been documented in 30 publications including pigmented cosmetic dermatitis and photoallergic contact dermatitis.³¹ The range of positivity to sandalwood oil in 8 studies involving 10,921 patients from 1983 to 2008 was 0.1% to 2.4%.²⁴ The prevalence in our study was 1.4% (IVDK).

Peppermint

Peppermint, the EO derived from the leaves of *Mentha piperita* L., is cultivated in many parts of the world and prized for its stomach-soothing digestive properties. This oil contains more than 30 known compounds including menthyl acetate, menthofuran, eucalyptol, limonene, and menthol.²³ The major allergens are caryophyllene, limonene, menthol, α -pinene, piperitone, and pulegone.¹³ Because of its high menthol content, it is used as a flavoring agent in beverages, sweets, chewing gum, and oral hygiene products. Peppermint oil was the fifth highest traded EO (3300 tons) in 2007, after sweet orange oil (51,000 tons), cornmint oil (32,000 tons), lemon oil (9200 tons), and eucalyptus oil (4000 tons).³¹

De Groot and Schmidt²⁴ found more than 45 publications documenting sensitivity to peppermint oil, especially in oral hygiene materials.^{22,32,33} The range of positivity to peppermint oil in 10 studies involving 14,326 patients from 1970 to 2012 was 0.3% to 1.8%.²⁴ The prevalence in our study was 0.5% (NACDG).

Tea Tree

Commercial tea tree oil is from the native Australian *M. alternifolia* tree. Tea tree oil is highly prized as a "natural" remedy for dermatologic

conditions, especially bacterial, fungal, and viral infections. Exposure to air and light (autooxidation) increases allergenicity 3-fold.³⁴ There are almost 100 compounds in the oil; major allergens include aromadendrene, ascaridole, D-carvone, L-carvone, 1,8-cineole, p-cymene, D-limonene, myrcene, α -phellandrene, α -terpinene, terpinen-4-ol, terpinolene, 1,2,4-trihydroxymenthane, sabinene, and viridiflorene.¹³

Many cases of ACD to tea tree oil have been reported. Application of undiluted tea tree oil directly on damaged skin is a major culprit.²⁴ The range of positivity to tea tree oil in 19 studies involving 44,964 patients from 1997 to 2013 was 0.1% to 2.7%.²⁴ The prevalence in our study was 0.9% (NACDG). Importantly, most (68.3%) of the reactions not associated with FM positivity had current clinical relevance, and more than half (50.8%) were strong (++) or very strong (+++).

Lavender

Lavender oil is obtained from the flowers of the Mediterranean evergreen shrub, *L. angustifolia*. Dried lavender boughs are used indoors to deter moths and flies. The oil is used for flavoring drinks, sweets, and chewing gum. It is widely used in herbal medicine and in traditional medical settings as aromatherapy for its calming properties.^{24,35}

De Groot and Schmidt²⁴ documented more than 450 chemicals in lavender and more than 40 publications involving lavender sensitivity. The main allergens likely are caryophyllene, linalyl acetate, and linalool.¹⁵ The range of positivity to lavender in 3 studies involving 8953 patients from 2002 to 2012 was 0.1% to 1.2%.²⁴ Our prevalence of 0.32% is consistent with these reports. Wu and James,³⁵ as well as de Groot and Schmidt,¹⁴ describe many case reports of occupational and nonoccupational ACD to lavender, especially from massage oils and aromatherapy oils.

Limitations

There are several limitations associated with this study. First, there are differences in methodology between the NACDG and IVDK such as patch-test reading schedules and collected variables (eg, relevance). Therefore, direct comparisons are difficult. Second, concentrations and suppliers of EOs tested by the NACDG and IVDK differed. Third, these data were retrospective and have, in part, been previously published. Finally, the study populations represent tertiary referral populations that are representative neither of the general population nor of the average population of dermatology patients with or without suspected contact dermatitis.

CONCLUSIONS

This study found that 1.04% of NACDG patients and 1.46% of IVDK patients reacted to 1 or more EOs but none of the FMs. Testing to EOs can be important for detecting sensitivity not detected by FMs alone. Whereas the fragrance sensitivity markers (fragrance mix I, fragrance mix II, and *M. pereirae*) are top prevalence allergens, to

date, sensitivity to EO is not as common. Expanded use and exposure may increase this level of sensitivity. Limited screening trays will miss EO allergy. Improved labeling is desirable and could, in the future, aid patch testing and subsequent allergen avoidance.

REFERENCES

- Ernst E. Adverse effects of herbal drugs in dermatology. *Br J Dermatol* 2000;143:923–929.
- Schaller M, Kortling HC. Allergic airborne contact dermatitis from essential oils used in aromatherapy. *Clin Exp Dermatol* 1995;20:143–145.
- Kiken DA, Cohen DE. Contact dermatitis to botanical extracts. *Am J Contact Dermat* 2002;13:148–152.
- Sienkiewicz M, Kowalczyk E, Wasiele M. Recent patents regarding essential oils and the significance of their constituents in human health and treatment. *Recent Pat Antiinfect Drug Discov* 2012;7(2):133–140.
- Bedi MK, Shenefelt PD. Herbal therapy in dermatology. *Arch Dermatol* 2002;138:232–242.
- Eisenberg DM, Kessler RC, Foster C, et al. Unconventional medicine in the United States. Prevalence, costs, and patterns of use. *N Engl J Med* 1993;328:246–252.
- Barnes PM, Powell-Griner E, McFann K, et al. Complementary and alternative medicine use among adults: United States, 2002. *Adv Data* 2004;343:1–19.
- Corazza M, Borghi A, Lauriola MM, et al. Use of topical herbal remedies and cosmetics: a questionnaire-based investigation in dermatology outpatients. *J Eur Acad Dermatol Venereol* 2009;23(11):1298–1303.
- De Groot AC, Schmidt E. Essential oils, part I: introduction. *Dermatitis* 2016;27(2):39–42.
- Mortimer S, Reeder M. Botanicals in dermatology: essential oils, botanical allergens and current regulatory practices. *Dermatitis* 2016;27(6):317–324.
- Uter W, Johansen JD, Börje A, et al. Categorization of fragrance contact allergens for prioritization of preventative measures: clinical and experimental data and consideration of structure-activity relationships. *Contact Dermatitis* 2013;69:196–230.
- De Groot AC, Schmidt E. Essential oils, part IV: contact allergy. *Dermatitis* 2016;27(4):170–175.
- Uter W, Schmidt E, Geier J, et al. Contact allergy to essential oils: current patch test results (2000–2008) from the Information Network of Departments of Dermatology (IVDK). *Contact Dermatitis* 2010;63(5):277–283.
- De Groot AC, Schmidt E. Essential oils, part V: peppermint oil, lavender oil, and lemongrass oil. *Dermatitis* 2016;27(6):325–332.
- DeKoven JG, Warshaw EM, Belsito DV, et al. North American Contact Dermatitis Group patch test results 2013–2014. *Dermatitis* 2017;28(1):33–46.
- Schnuch A, Geier J, Lessmann H, et al. Surveillance of contact allergies: methods and results of the Information Network of Departments of Dermatology (IVDK). *Allergy* 2012;67(7):847–857.
- R Core Team. *R: A Language and Environment for Statistical Computing*. Vienna, Austria: R Foundation for Statistical Computing; 2016.
- Schnuch A, Geier J, Uter W, et al. National rates and regional differences in sensitization to allergens of the standard series. Population adjusted frequencies of sensitization (PAFS) in 40,000 patients from a multicenter study (IVDK). *Contact Dermatitis* 1997;37:200–209.
- Narelli A, D'Hooge E, Dreighe J, et al. Allergic contact dermatitis from fragrance components in specific topical pharmaceutical products in Belgium. *Contact Dermatitis* 2009;60:303–313.
- De Groot AC, Coenraads PJ, Bruynzeel DP, et al. Routine patch testing with fragrance chemicals in the Netherlands. *Contact Dermatitis* 2000;42:184–185.
- Frosch PJ, Johansen JD, Menné T, et al. Further important sensitizers in patients sensitive to fragrances. *Contact Dermatitis* 2002;47:279–287.
- Brites MM, Gonçalves M, Figueiredo A. Contact allergy to fragrance mix—a 10-year study. *Contact Dermatitis* 2000;43:181–182.
- Herro E, Jacob SE. *Mentha piperita* (peppermint). *Dermatitis* 2010;21:327–329.
- De Groot AC, Schmidt E. Essential oils, part III: chemical composition. *Dermatitis* 2016;27(3):161–169.
- De Groot AC, Schmidt E. *Essential Oils: Contact Allergy and Chemical Composition*. Boca Raton, FL: CRC Press Taylor & Francis Group; 2016.
- Tan LT, Lee LH, Yin WF, et al. Traditional uses, phytochemistry, and bioactivities of *Cananga odorata* (Ylang-ylang). *Evid Based Complement Alternat Med* 2015;2015:896314.
- Sugawara M, Nakayama H, Watanabe S. Contact hypersensitivity to ylang-ylang oil. *Contact Dermatitis* 1990;23:248–249.
- Deza G, García-Bravo B, Silvestre JF, et al. Contact sensitization to limonene and linalool hydroperoxides in Spain: a GEIDAC* prospective study. *Contact Dermatitis* 2017;76(2):74–80.
- Erligmann A. Sandalwood oils. *Int J Aromather* 2001;11(4):186–192.
- De Groot AC, Schmidt E. Essential oils, part VI: sandalwood oil, ylang-ylang oil, and jasmine absolute. *Dermatitis* 2017;28(1):14–21.
- De Groot AC, Schmidt E. Part II: general aspects. *Dermatitis* 2016;27(2):43–49.
- Morton CA, Garioch J, Todd P, et al. Contact sensitivity to menthol and peppermint in patients with intra-oral symptoms. *Contact Dermatitis* 1995;32:281–284.
- Tran A, Pratt M, DeKoven J. Acute allergic contact dermatitis of the lips from peppermint oil in a lip balm. *Dermatitis* 2010;21:111–115.
- Hausen BM, Reichling J, Harkenthal M. Degradation products of monoterpenes are the sensitizing agents in tea tree oil. *Am J Contact Dermat* 1999;10:68–77.
- Wu P, James WD. Lavender. *Dermatitis* 2011;22(6):344–347.