

Fragrance contact dermatitis in Korea: a joint study

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The purpose of this study is to determine the frequency of responses to selected fragrances in patients with suspected fragrance allergy and to evaluate the risk factors. 9 dermatology departments of university hospitals have participated in this study for the past 1 year. To determine allergic response to fragrances, 18 additional fragrances in addition to the Korean standard and a commercial fragrance series were patch-tested in patients with suspecting cosmetic contact dermatitis. Over 80% of the patients were women, and the most common site was the face. Cinnamic alcohol and sandalwood oil (*Santalum album* L.) showed high frequencies of positive responses. Of the specific fragrances, ebanol, α -isomethyl-ionone (methyl ionone- γ) and Lyrall[®] (hydroxyisohexyl 3-cyclohexane carboxaldehyde) showed high positive responses. We compared the results obtained during this study with those of other studies and concluded that including additional fragrance allergens may be useful for the detection of fragrance allergy.

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Fragrance sensitization is a significant clinical problem and contact allergy to fragrances is the most common cause of contact dermatitis due to cosmetics (1).

Positive reactions to fragrance mix (FM) range from 5.5 to 11.4% (2), and FM ranks second or third among the standard series in response frequency in patch tests conducted in various parts of the world for contact allergy (3–7). In a normal non-selected population in Denmark, the prevalence rate of positive reaction to FM was about 1% (8). Despite the usefulness of FM in diagnosis (9), recent work indicates that there may be other allergens that might be useful for the detection of fragrance sensitization (10–14).

Commercially available fragrance allergens are sometimes useful for the detection of fragrance-induced contact dermatitis. As new allergens continuously emerge on the market, fragrance series should be revised periodically. The purpose of this study is to determine the frequency of responses to fragrances in patients with suspected fragrance allergy and to evaluate clinical

characteristics. To investigate this issue, we added fragrance allergens to the commercially available fragrance allergens. Additional fragrance allergens were selected from information as to their usage frequency and potential for allergenicity. This multicentre study was performed by several active members of the Korean Society for Contact Dermatitis and Skin Allergy.

Materials and Methods

Subjects and sources

9 dermatology departments of university hospitals and 1 cosmetic company participated in this study. 422 patients with suspected contact allergy who visited the hospitals over the period April 2002 to June 2003 were patch-tested in 9 university hospitals in Korea.

Test substances

The Korean standard series, which is a variant of the European standard series, and a fragrance series

Table 1. List of fragrance series (Chemotechnique Diagnostics, Malmo, Sweden)

Name (INCI name)	Test concentration (%)
Cinnamic aldehyde (cinnamal)	1
Cinnamic alcohol	2
Amylcinnamaldehyde (amyl cinnamal)	2
Eugenol	2
Isoeugenol	2
Geraniol	2
Oakmoss absolute (Evernia prunastri extract)	2
Hydroxycitronellal	2
Narcissus absolute (Narcissus jonquilla extract)	2
Musk xylene	1
Methyl anthranilate	5
Musk moskene	1
Musk ketone	1
Jasmine synthetic	2
Benzyl salicylate	2
Benzyl alcohol	1
Vanillin	10
Lavender absolute (Lavender augustifolia oil)	2
Cananga oil (Cananga odorata oil)	2
Rose oil Bulgarian	2
Ylang-Ylang oil	2
Geranium oil, Bourbon	2
Jasmine absolute, Egyptian (Jasminum officinale)	2
Sandalwood oil (<i>Santalum album</i> L. oil)	2

INCI = International Nomenclature Cosmetic Ingredient.

(Table 1) were purchased from Chemotechnique Diagnostics, Malmo, Sweden. We selected additional

allergens based on past relevant references and information as to usage frequency. Chemical names, suppliers and test concentrations are summarized in Table 2. The additionally selected 18 fragrances were prepared in batches by the Korean cosmetic company and distributed to researchers at the different hospitals.

Patch test method

Finn Chambers on Scanpor fape (Epitest, Tuusula, Finland) tape was used for patch testing, and the results were evaluated according to the recommendation of the International Contact Dermatitis Research Group (15).

Results

83.4% of the patients were women, and 23.9% had a past history of contact dermatitis, although a small number of cases (6.4%) had a history of atopic dermatitis and photosensitivity (Table 3). The most common site was the face (Table 4). The commonly positive fragrance materials including their frequency are summarized in Table 5. Cinnamic alcohol and sandalwood oil (*Santalum album* L.) produced high frequencies of positive responses (3.1 and 2.4%, respectively), and of the additional fragrances, ebanol, alpha-isomethyl-ionone (methyl ionone gamma) and Lyrall[®] (hydroxyisohexyl 3-cyclohexene carboxaldehyde) showed a high number of positive responses (2.8, 2.1 and 1.7%, respectively).

Table 2. List of additional fragrances

Commercial name (CAS no.)	INCI name (or chemical name)	Supplier	Concentration (%)
Galaxolide 50 (1222-05-5)	Hexamethylindanopyran	IFF	5
Hexadecanolide (109-29-5)	Hexadecanolactone	IFF	5
Ebanol (67801-20-1)	3-methyl-5-(2,2,3-trimethyl-3-cyclopenten-1-yl)-4-penten-2-ol	Givaudan	5
Methyl ionone gamma (127-51-5)	α -isomethyl ionone	Berge	5
Citral (5392-40-5)	Citral	Berge	2
Citronellol (106-22-9)	Citronellol	Kuraray	5
Coumarin (91-64-5)	Coumarin	Berge	5
Cyclacet (54830-99-8)	Tricyclo decenyl acetate or hexahydro-4,7-methanoinden-5 (6)-yl acetate	IFF	5
Dimethyl benzyl carbonyl acetate (DMBCA) (151-05-3)	α,α -dimethyl phenylethyl acetate	Givaudan	5
Triplal (68039-49-6)	2,4-Dimethyl-3-cyclohexene carboxaldehyde	IFF	5
Iso E super (54464-57-2)	7-Acetyl-1,2,3,4,5,6,7,8-octahydro- 1,1,6,7-tetramethyl naphthalene	IFF	5
Lilial (80-54-6)	Butylphenyl methylpropional	Givaudan	5
Linalool (78-70-6)	Linalool	BASF	20
Lyrall (31906-04-4)	Hydroxyisohexyl 3-cyclohexene carboxaldehyde	IFF	5
Methyl salicylate (119-36-8)	Methyl salicylate	Trealt	2
Musk ambrette (83-66-9)	2,6-dinitro-3-methoxy-4-butyltoluene	Penta	1
Ambrettolide (28645-51-4)	Oxacycloheptadec-10-en-2-one or 9-hexadecenolide	Givaudan	5
Spearmint oil (8008-79-5)	Mentha viridis oil	Berge	5

IFF = International Flavours and Fragrances; CAS = Chemical Abstract Service; INCI = International Nomenclature Cosmetic Ingredient.

Table 3. Demographics of subjects

Characteristics	<i>n</i> (cases)	%
Sex (percentage of female)	352	83.4
Past history of contact dermatitis	101	23.9
Past history of atopic dermatitis	27	6.4
Past history of photosensitivity	12	2.8

Discussion

Of the participants, 9.7 and 7.3% reacted to the FM and balsam of Peru (*Myroxylon pereirae* resin), respectively. The response rate to the FM in dermatological patients ranges worldwide from 6 to 11%: Germany 7.5–11.2%, Denmark 6.3%, Belgium 8.3%, Sweden 5.5%, Hungary 10.1%, the USA 11.4%, Australia 6.2%, the UK 7.9% and Greece 8.1%. Positive reactions to FM of 7.8, 8.3 and 7.5% have also been reported in 3 different European joint studies (2). The response rate to FM in Korea is slightly higher than that in other countries reported in those studies.

Fragrances with a positivity rate of $\geq 1.5\%$ included cinnamic alcohol, ebanol, sandalwood oil, methyl ionone gamma, eugenol, cinnamic aldehyde (cinnamal) and Lyrall[®]. Of these, cinnamic alcohol, eugenol and cinnamic aldehyde are constituents of the FM. Several studies have investigated the frequency of allergic reactions to the ingredients of the FM (11, 18–23). Although results vary widely, oakmoss (*Evernia prunastri* extract), isoeugenol and cinnamic aldehyde are major causes of fragrance allergy (2). Moreover, cinnamic alcohol showed the highest positive response rate in the present study, which is

Table 4. Site of skin eruptions in subjects (total 422 cases)

Site	%
Face	63.5
Neck	14.7
Trunk	14.5
Eyelid	10.4
Lips	8.5
Hand	8.3
Arm	7.6
Leg	7.3
Scalp	7.1
Ear	5.0
Foot	2.6
Widespread	1.4

somewhat different from that reported in Japan (24). Cinnamic alcohol, eugenol, cinnamic aldehyde and sandalwood oil are also included in the North American Contact Dermatitis Group perfume screening series (16, 17).

Ebanol (14) and methyl ionone gamma (11) were found to have low positive rates in a previous study, but Lyrall[®] had a high positive rate in several other studies, which recommended its use for testing patients suspected of having contact dermatitis (12, 25–28). In Germany, Lyrall[®] is now included in the national standard series (29).

In our study, 21.8% of patients were positive only to the additional series, while 78.2% of cases were positive to fragrances either in the standard series or in the added fragrance series (Table 6). Some of the patients positive to the additional fragrances were also positive to the FM, which suggests that the FM is still a credible means of detecting fragrance allergy. In conclusion, we believe that a number of

Table 5. Results of patch test with fragrance allergens (total 422 cases)

No.	Fragrance materials	<i>n</i> (positive cases)	% (positive)
19	Fragrance mix	41	9.7
15	<i>Myroxylon pereirae</i> resin	31	7.3
27	Cinnamic alcohol	13	3.1
52	Ebanol	12	2.8
49	<i>Santalum album</i> oil	10	2.4
53	Methyl ionone- γ	9	2.1
29	Eugenol	8	1.9
26	Cinnamal	7	1.7
63	Hydroxyisohexyl-3-cyclohexene-carboxaldehyde	7	1.7
32	<i>Evernia prunastri</i> extract	6	1.4
51	Hexadecanolide	6	1.4
67	<i>Mentha viridis</i> oil	6	1.4
43	<i>Lavendula angustifolia</i> oil	5	1.2
44	<i>Cananga odorata</i> oil	5	1.2
45	Rose oil, Bulgarian	5	1.2
48	Jasmine officinale oil	5	1.2
50	Galaxolide 50	5	1.2
54	Citral	5	1.2
68	Petrolatum (Amojell TM ; Sigma-Aldrich)-vehicle	0	0

1–25 = Korean standard series; 26–49 = Fragrance series; 50–67 = additional fragrances.

Table 6. Pattern of combination of test results obtained with standard series (SS), fragrance series (FS) and additional fragrances (AF)

	AF only	SS or FS (not AF)	FM and AF
Number of positive cases	24	86	12
Percentage	21.8	78.2	10.9

SS = fragrance mix, Myroxylon pereirae resin, colophonium of Korean standard series.

additional fragrance allergens may be necessary for the detection of fragrance allergy, in addition to the commercial fragrance series.

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