

Patch testing with fine fragrances: comparison with fragrance mix, balsam of Peru and a fragrance series

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High frequencies of contact allergy to fragrance ingredients have been reported in recent years. Only approximately 70–80% are detected by fragrance allergens in the standard patch test series. This investigation compares the patch test reactions to fine fragrances with reactions to fragrance mix (FM), balsam of Peru (BP) (*Myroxylon pereirae* resin) and a fragrance series. 641 consecutive patients with eczema were patch tested with the European standard series and with selected fine fragrances. Those who were positive to 1 of the fine fragrances or the FM or BP were also tested with the fragrance series. 95 (14.8%) patients were found to have a positive patch test reaction to FM or BP; 41 (6.4%) had positive results to fragrance no. 1 and 29 (4.5%) to no. 2. 9 (9.5% of the 95 positive patients) had a positive reaction to fine fragrances and a negative reaction to all other fragrance allergens in the standard series. These findings indicate that testing with fine fragrances can add to our evaluation of fragrance-sensitive patients.

Keywords: balsam of Peru; fine fragrances; fragrance mix; fragrance series; *Myroxylon pereirae* resin; patch tests. © Blackwell Munksgaard, 2004.

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According to industry estimates, women's fragrances accounted for 75% of the prestige beauty market in the USA in 1992, and men's fragrances for 15% (1). Contact allergy to fragrance mix (FM) in the standard series is the 2nd most common cause of contact dermatitis after nickel allergy in Denmark (2) and the 3rd most common cause in Israel (3). In the latter study, FM was positive in 8.5% of consecutively patch-tested patients and balsam of Peru (BP) (*Myroxylon pereirae* resin) in 6.6%. In studies conducted in Portugal, Denmark and Germany, patch testing with fine fragrances yielded positive rates of 3.2–11.1% (4–6).

The aims of the present study were to examine patch test reactions to fine fragrances in Israel and to compare the findings to reactions to FM, BP and a fragrance series.

Materials and Methods

The study sample included 641 consecutive patients with eczema, 376 female (59%) and 265 male (41%), attending the Contact Dermatitis Clinic at Rabin Medical Center. Ages ranged from 13 to 95 years (mean 41). All were patch tested with the European standard series and with 2 fine fragrances. Patients who had doubtful or

positive reactions to 1 of the fragrance-related allergens (FM and BP) in the European standard series, or to 1 of the 2 fine fragrances, were tested with a fragrance series.

2 well-known perfumes, Opium® (PO) (Yves Saint Laurent, Paris, France) and Eau de Soir® (PES) (Sisley, Paris, France), were selected for patch testing. Opium was included in 2 previous studies (6, 7) and was shown on chemical analysis to contain 6 of the FM ingredients in concentrations ranging from 0.03 to 1.1% (7). PES has not been tested before. Both were purchased for the study on the Israeli retail market.

All patch tests were applied on the upper back with 2 days of occlusion. The fine fragrances were tested undiluted in Finn Chambers® (Epitest, Tuusula, Finland) with a filter disc, after being allowed to dry for 5 min before application in order to avoid more irritant reactions (6). Readings were taken on D2 and D3. The scale of the International Contact Dermatitis Research Group was used for assessment (8).

Results

A doubtful or positive response to 1 or more of the fragrance allergens in the European standard

Table 1. Positive and doubtful reactions to fragrance allergens

Intensity	Allergen (number of patients)			
	Fragrance mix	Balsam of Peru	Opium®	Eau de Soir®
?+	19	25	18	10
+	33	32	33	22
++	25	7	7	5
+++	2	—	1	2
Total positive	60	39	41	29

series was noted in 127 patients (19.8%), 73 female (57.5%) and 54 male (42.5%). 32 of them (4.9%) had a doubtful reaction and 95 (14.8%) a positive reaction (Table 1). Specifically, 60 patients (9.4%) had a positive reaction to FM, 41 (6.3%) to BP, 41 (6.4%) to PO and 29 (4.5%) to PES.

Positive reactions to at least 1 of the fine fragrances were seen in 31 of the 60 patients (50.8%) with a positive reaction to FM and in 10 of the 41 patients (24.4%) with a positive reaction to BP. In addition, positive reactions to at least 1 of the fine fragrances were seen in 11 of the 65 patients (16.9%) who were negative to FM and in 32 of the 85 patients (37.6%) who were negative to BP (Table 2). 9 patients with positive reactions to the fine fragrances had negative reactions to both FM and BP (9/95, 9.5%). 7 of these were reactive to PO and 5 to PES.

The fragrance series was tested in 91 of the 127 patients with a positive or doubtful reaction to the fragrance allergens (72%). The results are summarized in Table 3. 47 (51.6%) patients had at least 1 positive reaction. The most common allergens with positive results were cinnamic aldehyde (cinnamal) and oak moss absolute (*Evernia prunastri* extract) (also components of the FM). There were 41 positive reactions to FM ingredients and 13 positive reactions to other fragrance allergens.

8 patients who were positive to the fragrance series had negative reactions to both FM and BP.

Table 2. Cross-analysis of fragrance mix (FM) and balsam of Peru (BP) with fine fragrances

	Fine fragrances	
	Positive	Negative
FM		
Positive	31	30
Negative	11	54
BP		
Positive	10	31
Negative	32	53

Table 3. Fragrance patch test series results

Allergen	Intensity				Total positive
	?+	+	++	+++	
Cinnamic aldehyde	5	9	1	—	10
Cinnamic alcohol	6	3	2	—	5
Amylcinnamaldehyde	1	—	—	—	—
Eugenol	2	3	1	—	4
Isoeugenol	3	4	1	—	5
Geraniol	2	3	—	1	4
Oak moss absolute	3	8	2	—	10
Hydroxycitronellal	—	3	—	—	3
Narcissus absolute	1	—	—	—	—
Musk xylene	—	—	—	—	—
Methyl anthranilate	—	—	—	—	—
Musk moskene	1	—	—	—	—
Musk ketone	1	1	—	—	1
Jasmine synthetic	1	—	—	—	—
Benzyl salicylate	—	2	—	—	2
Benzyl alcohol	1	—	—	—	—
Vanillin	—	1	—	—	1
Lavender absolute	1	1	—	—	1
Cananga oil	—	—	1	—	1
Rose oil (Bulgarian)	1	2	—	—	2
Ylang-Ylang oil	2	1	1	—	2
Geranium oil	1	1	—	—	1
Jasmine absolute (Egyptian)	1	—	2	—	2
Sandalwood oil	—	—	—	—	—

7 of them were also negative to fine fragrances (Table 4).

4 of the 9 patients completely negative for FM and BP, but positive to the fine fragrances, were found to have a clinically relevant fragrance allergy. 4 of the 8 patients who were positive to the fragrance series but negative to FM and BP had a clinically relevant allergy. Only 1 of these also had a positive reaction to fine fragrances, but this result was not clinically relevant.

Discussion

Prior to the introduction of FM to the standard series, a few studies reported their results with commercial perfumes as screening agents for fragrance allergy (9,10). Today, however, FM is considered the main indicator and screening test for perfume allergy. Another marker of perfume allergy in the same series is BP. In a study of 176 patients in 7 centres worldwide, Larsen et al. (11) showed a co-reaction to FM and fragrance ingredients in 85.6% of patients.

Johansen et al. (4) investigated the elicitation potential of perfumes in patients with eczema using 17 popular lower-priced cosmetic products. They found that 4.2% of the patients reacted to 1 or more of the wash-off product perfumes and 3.2% reacted to the stay-on product perfumes. Concordant findings between FM and the commercial perfumes were noted for 81.3% of the

Table 4. Cross-analysis of fragrance mix (FM) and balsam of Peru (BP) with fragrance series

	Fragrance series	
	Positive	Negative
FM		
Positive	23	16
Negative	10	42
BP		
Positive	7	22
Negative	26	36

positive reactions to the stay-on products and 52.4% of the reactions to the wash-off products. Bordalo et al. (5) reported that 6.2% of their 1000 patients tested positively to commercial perfumes, and that 8 of 62 patients (13%) were negative to all fragrance allergens. A joint study of Danish and German contact dermatitis clinics showed that patch testing with 2 fine fragrances yielded reactions to at least 1 of them in 11% of patients in Germany and 5.8% in Denmark (6).

Our results are similar to those of Bordalo et al. (5). In our series, 9.5% of the patients with positive results to fragrance markers tested positive to fine fragrances but were negative to all other fragrance allergens. Of the 9 patients who tested positively to fine fragrances but negatively to FM and BP, 4 were found to have a clinically relevant allergy.

The fragrance series does not include fragrance allergens that have recently been identified as important causes of fragrance allergy, such as Lyrall[®] (hydroxyisohexyl 3-cyclohexene carboxaldehyde), citral, coumarin and farnesol (12). Testing with fine fragrances such as those used in our study can detect up to 10% of allergic patients who are not detected with the fragrance allergens (FM and BP) in the European standard series. Until more individual and specific fragrance allergens, e.g. Lyrall[®], are identified as the most appropriate for screening fragrance-allergic patients, the use of fine fragrances can provide a high yield. The ongoing changes in composition of the prestige perfumes also need to be taken into consideration (13).

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