Fragrance contact allergy: a 4-year retrospective study

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Background: Fragrance chemicals are the second most frequent cause of contact allergy. The mandatory labelling of 26 fragrance chemicals when present in cosmetics has facilitated management of patients allergic to fragrances.

Objectives: The study was aimed to define the characteristics of the population allergic to perfumes detected in our hospital district, to determine the usefulness of markers of fragrance allergy in the baseline GEIDAC series, and to describe the contribution made by the fragrance series to the data obtained with the baseline series.

Material and methods: We performed a 4-year retrospective study of patients tested with the Spanish baseline series and/or fragrance series. There are four fragrance markers in the baseline series: fragrance mix I (FM I), Myroxylon pereirae, fragrance mix II (FM II), and hydroxyisohexyl 3-cyclohexene carboxaldehyde.

Results: A total of 1253 patients were patch tested, 117 (9.3%) of whom were positive to a fragrance marker. FM I and M. pereirae detected 92.5% of the cases of fragrance contact allergy. FM II and hydroxyisohexyl 3-cyclohexene carboxaldehyde detected 6 additional cases and provided further information in 8, enabling improved management. A fragrance series was tested in a selected group of 86 patients and positive results were obtained in 45.3%. Geraniol was the allergen most frequently found in the group of patients tested with the fragrance series.

Conclusions: Classic markers detect the majority of cases of fragrance contact allergy. We recommend incorporating FM II in the Spanish baseline series, as in the European baseline series, and using a specific fragrance series to study patients allergic to a fragrance marker.

Key words: allergic contact dermatitis; epidemiology; fragrances; patch test. © John Wiley & Sons A/S, 2010.

Conflict of interests: The authors have declared no conflicts.

Accepted for publication 7 March 2010

There are about 3000 fragrance chemicals available and a single perfume may contain 10–300 different fragrance chemicals (1, 2). They are also present in cosmetics, cleaning products, industrial products, and topical medicaments. Fragrances may be responsible for clinical conditions, including irritant contact dermatitis, allergic contact dermatitis, photosensitivity, immediate contact reactions (contact urticaria), and pigmented contact dermatitis (1).

Fragrances are considered to be the second most frequent cause of contact allergy after metals (3). Furthermore, together with preservatives, they are the most important sensitizers in cosmetics. Fragrance contact allergy affects approximately 1% of the general population, and 6–14% of patients with contact dermatitis (1–9).

In recent years, there has been a greater awareness of the importance of fragrance contact allergy, as shown by the change made in the labelling of cosmetics in accordance with the seventh Amendment of the European Cosmetic Directive (10), which requires the labelling of 26 specific fragrance
We have marked the constituents analysed in our study.

- Constituent of FM I.
- Constituent of FM II.
- Present in fragrance series.

Table 1. List of ingredients that must be declared on the labelling of cosmetics, according to the seventh Amendment of the Cosmetics Directive

<table>
<thead>
<tr>
<th>Constituent</th>
<th>Concentration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cinnamal</td>
<td>Farnesol</td>
</tr>
<tr>
<td>Geraniol</td>
<td>Benzyl alcohol</td>
</tr>
<tr>
<td><em>Eversnia prunastri</em></td>
<td>Benzyl salicylate</td>
</tr>
<tr>
<td>Cinnamyl alcohol</td>
<td>Linalool</td>
</tr>
<tr>
<td>Eugenol</td>
<td>Limonene</td>
</tr>
<tr>
<td>Hydroxycitronellal</td>
<td>Butylphenyl methylpropional</td>
</tr>
<tr>
<td>Isoeugenol</td>
<td>Anisyl alcohol</td>
</tr>
<tr>
<td>α-Amyl cinnamal</td>
<td>Benzyl cinnamate</td>
</tr>
<tr>
<td>Citral</td>
<td>Benzyl benzoate</td>
</tr>
<tr>
<td>Coumarin</td>
<td>Methyl-2-octynoate</td>
</tr>
<tr>
<td>hydroxyisohexyl 3-cyclohexene carboxaldehyde</td>
<td>α-isomethyl ionone</td>
</tr>
<tr>
<td>Citronellol</td>
<td><em>Eversnia fufuracea</em></td>
</tr>
<tr>
<td>α-Hexyl cinnamal</td>
<td>Amyl cinnamal alcohol</td>
</tr>
</tbody>
</table>

The baseline series of the Spanish Group for Research into Contact Dermatitis and Skin Allergy (GEIDAC) contains various allergens that may be considered markers of fragrance allergy. Traditionally, these markers have been fragrance mix I (FM I), *Myroxylon pereirae* and colophonium. Fragrance mix II (FM II) and hydroxyisohexyl 3-cyclohexene carboxaldehyde have recently been included (11–13). It is also possible to perform patch tests with a specific series of fragrance allergens (Chemotechnique Diagnostics®, Vellinge, Sweden).

Before the change in labelling of cosmetics and household cleaning products came into effect, there was limited use in knowing which specific fragrance chemical an individual was allergic to. Now, we believe that using a fragrance series to test patients who are positive for a fragrance marker in the baseline series may be of importance in the subsequent management of these patients.

We performed a retrospective and descriptive study of all the patients seen by us in the last 4 years who were patch tested with the baseline and/or fragrance series (Chemotechnique®). The objectives of this study were as follows:

1. To define the characteristics of the population allergic to perfumes detected in our hospital district;
2. To determine the usefulness of markers of fragrance allergy in the baseline GEIDAC series;
3. To describe the contribution made by the fragrance series to the data obtained with the baseline series.

Material and Methods

This is a retrospective and descriptive study carried out at the Cutaneous Allergy Unit of a tertiary referral hospital, between October 2004 and June 2008. All patients tested with the baseline Spanish Group series were reviewed, as well as patients tested with the fragrance series either because they were positive to the baseline series or because there was clinical suspicion.

The clinical data recorded on each patient were age, sex, profession, site of lesions, series tested, positive allergens and number of positive reactions, their relevance, origin of the sensitization, and patient’s diagnosis.

The MOALFHA index was used to study the characteristics of the patients seen. This index records the percentage of the following characteristics: male, occupational dermatitis, atopic dermatitis, leg dermatitis, face dermatitis, hand dermatitis, and age >40 years. A history of atopy was not adequately recorded and so it is not included in our study.

The allergens used both in the standard series and in the fragrance series were supplied by Chemotechnique Diagnostics®. The markers of the baseline Spanish Group series used in our study to detect fragrance allergic contact dermatitis were: the ‘traditional’ markers (*M. pereirae* and FM I), hydroxyisohexyl 3-cyclohexene carboxaldehyde (included as of October 2005), and FM II (included as of January 2007). FM I consists of eight components: *Eversnia prunastri* (1%), isoeugenol (1%), eugenol (1%), cinnamal (1%), hydroxycitronellal (1%), geraniol (1%), cinnamyl alcohol (1%), and α-amylcinnamal (1%). Both *M. pereirae* and FM I contain sorbitan sesquioleate as an emulsifying agent. FM II is made up of six substances: hydroxyisohexyl 3-cyclohexene carboxaldehyde (2.5%), citral (1%), farnesol (2.5%), citronellol (0.5%), α-hexyl cinnamal (5%), and coumarin (2.5%) (12).

The fragrance series (Chemotechnique®) contains 30 substances (Table 2). We added sorbitan sesquioleate to this series to detect false positives to fragrance chemical allergens prepared using this substance. The individual components of FM II were included in this series in January 2007.

The patches were prepared using Finn Chambers® fixed with Scanpor® adhesive and removed after 2D in contact with the skin. Readings
Table 2. Constituents of the specific fragrance series (Chemotechnique®), concentration used in the patch test, and frequency of reactions found in the population in whom this series was tested (86 patients tested)

<table>
<thead>
<tr>
<th>Components of the fragrance series</th>
<th>Concentrationa (%)</th>
<th>Frequency n (％)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Geraniol</td>
<td>2.0</td>
<td>17 (19.7)</td>
</tr>
<tr>
<td>Eugenol</td>
<td>2.0</td>
<td>12 (13.9)</td>
</tr>
<tr>
<td>Ylang-ylang oilb</td>
<td>2.0</td>
<td>12 (13.9)</td>
</tr>
<tr>
<td>Cinnamyl alcohol</td>
<td>2.0</td>
<td>12 (13.9)</td>
</tr>
<tr>
<td>Isoeugenol</td>
<td>2.0</td>
<td>11 (12.8)</td>
</tr>
<tr>
<td>Geranium oil bourbonb</td>
<td>2.0</td>
<td>8 (9.3)</td>
</tr>
<tr>
<td>Hydroxycitronellalb</td>
<td>5.0</td>
<td>7 (8.1)</td>
</tr>
<tr>
<td>3-cyclohexene carboxaldehyde</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cinnamal</td>
<td>2.0</td>
<td>7 (8.1)</td>
</tr>
<tr>
<td>Rose oil absoluteb</td>
<td>2.0</td>
<td>6 (7.0)</td>
</tr>
<tr>
<td>Hydroxycitronellalb</td>
<td>5.0</td>
<td>6 (7.0)</td>
</tr>
<tr>
<td>Jasmine absolute, Egyptian</td>
<td>2.0</td>
<td>3 (3.5)</td>
</tr>
<tr>
<td>Cananga oil</td>
<td>2.0</td>
<td>3 (3.5)</td>
</tr>
<tr>
<td>Jasmine synthetic</td>
<td>2.0</td>
<td>3 (3.5)</td>
</tr>
<tr>
<td>Evernia prunastri</td>
<td>2.0</td>
<td>2 (2.3)</td>
</tr>
<tr>
<td>Benzyl alcohol</td>
<td>1.0</td>
<td>2 (2.3)</td>
</tr>
<tr>
<td>Benzyl salicylate</td>
<td>2.0</td>
<td>2 (2.3)</td>
</tr>
<tr>
<td>Lavender absoluteb</td>
<td>2.0</td>
<td>2 (2.3)</td>
</tr>
<tr>
<td>Sandalwood oil</td>
<td>2.0</td>
<td>2 (2.3)</td>
</tr>
<tr>
<td>Citral</td>
<td>2.0</td>
<td>2 (2.3)</td>
</tr>
<tr>
<td>Farnesol</td>
<td>5.0</td>
<td>1 (1.2)</td>
</tr>
<tr>
<td>Coumarin</td>
<td>5.0</td>
<td>1 (1.2)</td>
</tr>
<tr>
<td>α-Amyl cinnamal</td>
<td>2.0</td>
<td>0</td>
</tr>
<tr>
<td>Narcissus absolute</td>
<td>2.0</td>
<td>0</td>
</tr>
<tr>
<td>Musk xylene</td>
<td>1.0</td>
<td>0</td>
</tr>
<tr>
<td>Musk moskene</td>
<td>1.0</td>
<td>0</td>
</tr>
<tr>
<td>Musk ketone</td>
<td>1.0</td>
<td>0</td>
</tr>
<tr>
<td>Vanillin</td>
<td>10</td>
<td>0</td>
</tr>
<tr>
<td>Methyl anthranilate</td>
<td>5</td>
<td>0</td>
</tr>
<tr>
<td>Citronellalb</td>
<td>1.0</td>
<td>0</td>
</tr>
<tr>
<td>α-Hexyl cinnamal</td>
<td>10</td>
<td>0</td>
</tr>
</tbody>
</table>

aPetrolatum was used as the vehicle for all the constituents of the fragrance series.
bFragrances that contain geraniol or that have cross reactions with geraniol.

were taken at D2 and D4, with the evaluation criteria (+, ++, and ++++) recommended by the ICDRG. If the result was doubtful, a late reading was taken at D7. The relevance was considered current if the clinical picture could be attributed totally or partially to the fragrance obtained, past if this positivity explained only previous dermatitis, and unknown if the clinical picture could not be attributed to the use of these fragrances.

Patients who were positive to any fragrance marker in the GEIDAC baseline series (M. perirela, FM I, hydroxyisohexyl 3-cyclohexene carboxaldehyde, or FM II) were identified, and the percentage of patients positive to each of the markers was determined.

The characteristics of the population seen were compared with those of the population with a positive fragrance marker, according to the MOALFHA index (11).

We studied the relevance of the positivity to classical markers of the baseline series.

In patients patch tested with a specific fragrance series, the frequency of positive reactions to each of the fragrances present in the series was determined. We also studied the percentage of positivity in the subgroup of patients negative to a classical marker of the standard series and in the subgroup of patients positive to a classical marker. Furthermore, in the latter subgroup we distinguished between whether the marker was M. perirela, FM I, or both, and studied which individual fragrances were most frequently positive in each subgroup.

Results

Between October 2004 and June 2008, patch tests were performed in a total of 1253 patients, all of whom were tested with the baseline Spanish Group series. Of these patients, 852 were tested with hydroxyisohexyl 3-cyclohexene carboxaldehyde and 450 with FM II. A total of 86 patients were tested with the Chemotechnique® fragrance series.

Standard series markers

Frequencies. Of the 1253 patients, 117 (9.3%) had at least one positive fragrance marker in the baseline Spanish Group series. In our population, the sum of these four markers represents the second most frequent cause of allergic contact eczema (9.3%) after metals.

M. perirela was positive in 80 of 1253 patients (6.4%) and FM I was positive in 56 of 1253 patients (4.5%), whereas FM II was positive in 7 of 1253 patients (1.5%) and hydroxyisohexyl 3-cyclohexene carboxaldehyde in 9 of 1253 patients (1.1%). We found patients who were positive to various markers – 29 patients (2.31%) were positive to M. perirela and FM I. Only one patient (0.08%) was positive to M. perirela and FM II. Two patients (0.16%) were positive to M. perirela and hydroxyisohexyl 3-cyclohexene carboxaldehyde, and three patients (0.24%) were positive to hydroxyisohexyl 3-cyclohexene carboxaldehyde and FM I. Three patients (0.24%) were positive to FM I and FM II, and two of these were also positive to hydroxyisohexyl 3-cyclohexene carboxaldehyde (Fig. 1). It is remarkable that of the patients allergic to FM II, only three were positive to this marker alone. Similarly, of the patients allergic to hydroxyisohexyl 3-cyclohexene carboxaldehyde, only three were positive to this marker alone. Therefore, these two markers together detected six additional cases of fragrance allergy.

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Epidemiological data. The characteristics of the total patch test population studied using the MOALFHA index are shown in Table 3, together with those of the population with a positive marker; the differences were statistically significant ($P < 0.05$) for each index, except for occupational dermatitis and hand dermatitis when we analysed with Fisher’s exact test. The finding of higher percentage of men (51.3 versus 38% in the general population) and of patients over 40 years old (74.4 versus 56.4% in the general population) in patients with a positive fragrance marker in the baseline series is notable. The most frequent site was the hands, both in the population with a positive marker and in the general population studied (32.5 versus 29.7%), but there was greater involvement of the legs (12 versus 6.8%) and less involvement of the face (8.5 versus 16.4%) in the population with a positive marker.

Relevance. The relevance of positivity to *M. pereirae* was considered current in 53 (66.2%) cases, past in 6 (7.5%) cases, and unknown in 21 (26.25%) cases. The relevance of FM I was considered current in 52 (92.8%) cases and unknown in 4 (7.2%) cases.

Fragrance series

Of the 117 patients with a positive marker in the baseline series, 54 were subsequently tested with the fragrance series. In addition, this series was used to test 32 patients with clinical symptoms compatible with fragrance contact dermatitis, despite not having any positive fragrance marker in the baseline series. In total, 86 patients were tested with the fragrance series.

Fragrance chemical frequencies. Of the 86 patients tested with the Chemotechnique® fragrance series, 39 (45.3%) were positive to an allergen. The most frequent allergens found in our population in the fragrance series were geraniol, eugenol, ylang-ylang oil, cinnamyl alcohol, isoeugenol, geranium oil bourbon, and hydroxyisohexyl 3-cyclohexene carboxaldehyde. It should be mentioned that the frequency of hydroxyisohexyl 3-cyclohexene carboxaldehyde is probably underestimated, as it was included in the baseline series 12 months after the

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Table 3. Demographic description of the populations studied using the MOALFHA index (except for atopic dermatitis, which was not recorded in our database)

<table>
<thead>
<tr>
<th></th>
<th>Population treated in our unit</th>
<th>Population with a positive fragrance marker</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Total</td>
<td>Percentage</td>
</tr>
<tr>
<td>Patients studied</td>
<td>1253</td>
<td>100</td>
</tr>
<tr>
<td>M Men</td>
<td>476</td>
<td>38</td>
</tr>
<tr>
<td>O Occupational dermatitis</td>
<td>175</td>
<td>14</td>
</tr>
<tr>
<td>A Atopic dermatitis</td>
<td>Not recorded in our database</td>
<td></td>
</tr>
<tr>
<td>L Leg dermatitis</td>
<td>85</td>
<td>6.78</td>
</tr>
<tr>
<td>F Face dermatitis</td>
<td>205</td>
<td>16.4</td>
</tr>
<tr>
<td>H Hand dermatitis</td>
<td>372</td>
<td>29.7</td>
</tr>
<tr>
<td>A &gt;40 years</td>
<td>706</td>
<td>56.4</td>
</tr>
</tbody>
</table>

*a* Results statistically significant ($P < 0.05$).

*b* Results not statistically significant ($P > 0.05$).
study was started. It is notable that we found only two cases positive to *Evernia prunastri* (Table 2).

**Patients with a positive fragrance marker in the standard series.** We used the specific fragrance series to test 54 patients with a positive fragrance marker (Fig. 2). In total, 17 patients were positive to *M. pereirae* and FM I, 12 to *M. pereirae* only, 19 to FM I only, and 6 to hydroxyisohexyl 3-cyclohexene carboxaldehyde or FM II. Of the 54 patients, 39 (72%) were positive to fragrances in the specific fragrance series.

Of the 17 patients positive to FM I and *M. pereirae* tested with the fragrance series, 11 (64.7%) exhibited some positivity (Fig. 3). The most frequent positive allergens in this group were eugenol, isoeugenol (always in combination with eugenol), and ylang-ylang. Three patients (17.7%) were allergic to sorbitan sesquioleate and, therefore, were false negatives.

Of the 12 patients positive to *M. pereirae* alone, 3 (25%) exhibited some positivity in the fragrance series (Fig. 3). It is notable that in this group, there was only one patient allergic to cinnamyl alcohol and none allergic to cinnamal.

Of the 19 patients who were positive to only FM I, 16 (84.2%) exhibited some positivity to the fragrance series (Fig. 3). The main allergens detected in these cases were geraniol, hydroxycitronellal, rose oil absolute, and geranium oil bourbon (the latter two were almost always associated with geraniol).

In total, 36 patients were positive to FM I and 27 of these (75%) were positive to some markers in the fragrance series.

**Patients with negative fragrance markers in the standard series.** Of the 32 patients studied with negative fragrance markers in the baseline series, 3 (9.3%) exhibited some positivity (Fig. 2). Two of the patients were allergic to constituents of FM I (false negatives).

If we compare the demographic characteristics of our population allergic to fragrances with those of the general population, the high percentage of men (51.3 versus 38%) and an age of over 40 years (74.4% in those allergic to fragrances versus 56.4% in the general population) were found to be significant. This contrasts with the results obtained in studies of most published series in which women were found to be the most affected (18–20). The explanation for our findings remains unclear, although there are other studies which reported no differences in terms of gender (1, 21).

With regard to the distribution of eczema, the hands were most frequently affected in our study, which correlates with most of the data in the literature (10, 20, 22–25). In our study, we found greater involvement of the legs and less of the face, compared with that in the general population (these results were statistically significant). However, in other studies, the face was found to be most frequently involved (1, 20, 21, 25). The greater involvement of the legs may be attributed to the fact that among the population allergic to fragrances, many patients had vascular ulcers on the legs as a result of repeated exposure to topical drugs that

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**Discussion**

The most frequent adverse reaction to fragrances is allergic contact dermatitis, although it is believed to be an underestimated problem as many individuals may be aware of the perfumed products they tolerate and those they do not, and rarely consult a dermatologist about this problem.

In our study, fragrance contact allergy was second only to allergy caused by metals (9.3%), and this is in agreement with the data in the literature reviewed (6, 14, 15). In our population, *M. pereirae* occupied the sixth position of the allergens tested, with a frequency of 6.22%, and FM I occupied the seventh place, with a frequency of 4.46%.

Our data are similar to those obtained by other groups, such as the Portuguese group in which FM I and *M. pereirae* occupy the fifth and sixth place, respectively, with a frequency of 7.6 and 6% (16). In the epidemiological study carried out by the Spanish Group in 2001, similar results were found: FM I occupied the fifth place (5.03%) and *M. pereirae* the seventh (3.20%) (17).
frequently contained fragrance (18, 26–28). One of the most frequently used topical drugs for treating leg ulcers in Spain is Blastoestimulina® (Almirall), which contains geraniol.

In our study, the markers FM I and *M. pereirae* identified more than 90% of our cases. In other studies, FM I and *M. pereirae* have been shown to detect 70–80% of the cases of allergic contact dermatitis to fragrances (4–6, 8). Some of these studies have used Trolab® (Hermal Almirall, Reinbeck, Germany) allergens, where the concentration of some allergens varies from that used by Chemotechnique®, which could explain this variation. Some authors even detected 85% of the cases just with FM I (12, 21).

FM II and hydroxyisohexyl 3-cyclohexene carboxaldehyde have been used since 2005 as markers of fragrance allergy, although they are less powerful markers than FM I. Nevertheless, in our study, hydroxyisohexyl 3-cyclohexene carboxaldehyde and FM II included in the baseline series identified six new patients allergic to fragrances. In addition, they were concomitantly positive in nine patients who were also allergic to *M. pereirae* and FM I, thereby allowing more comprehensive fragrance avoidance information to be provided to these patients (29). We therefore consider that it would be advisable to include them in the baseline Spanish Group series, as has occurred in other European countries such as Germany and UK (4, 12, 13, 30–33).

The current relevance found in our study was very high, 92.8% for FM I and 66.2% for *M. pereirae*. Although this may seem excessive, according to De Groot and Frosch (5, 33, 34), at least 55–65% of the cases with positive results have clinical relevance and in the latest epidemiological study of the Spanish Group, current relevance for *M. pereirae* was found in 85.71% of the cases and for FM I in 79.79% (19). We are convinced that very often fragrance allergic contact dermatitis acts as an aggravating factor for atopic dermatitis, irritant dermatitis, and other previous cases of dermatosis, especially on the hands, and unless personal hygiene and cleaning products containing fragrances are avoided, previous dermatosis will not improve despite appropriate treatment and protective measures. De Groot and Frosch consider that a strong positive reaction is more likely to have clinical relevance than a weak positive reaction (5, 6). If there is high clinical suspicion and the results are not conclusive, many authors recommend using the standard series again (35, 36).

The fragrance series has proved to be very useful as we found positivity in 45.3% of the cases. We did not find any earlier studies that reviewed the usefulness of applying a specific commercial fragrance series.
The fragrance found most frequently was geraniol, whereas *Evernia prunastri* absolute was rarely detected. Other fragrances that contain geraniol, such as ylang-ylang oil, geranium oil bourbon, and rose oil absolute, have also been frequently found. This differs from the European studies in which the most frequently detected individual fragrances were *Evernia prunastri*, isoeugenol, and cinnamal, whereas geraniol was one of the less frequent (1, 5, 11, 37). Some authors have suggested removing geraniol and α-amyl-cinnamal from FM I, because of the small percentage of positivity (5, 21, 36, 38). We have not found any previous reports that support our results and there seems to be no clear explanation. However, we believe that removing geraniol would not be convenient in our region and probably also in most other areas of Spain (38, 39).

When we tested patients allergic to FM I with the fragrance series, we found positivity for some of the individual components in 75% of the cases. Kiec et al. obtained similar results (72%) (40), although they are high when compared with those found in most studies, which vary from 40 to 60% (5, 8, 41). There may be three possible reasons for this discrepancy: (i) positivity to FM I may be false because of the irritative capacity of the mix. In our study, there is high concordance and this could be used as a marker of the quality of our readings. (ii) It could be a false negative to the constituents of the fragrance series because of the fact that the concentrations of the individual components are too low, or that absorption of FM I is increased by the emulsifier sorbitan sesquioleate. In this case, it would be necessary to adjust the concentrations of the individual fragrances used for patch testing. (iii) The other possibility is the existence of an allergy to a combination of two or more ingredients of FM I (42).

Patch testing a fragrance series in patients who are allergic to only *M. pereirae* is not as worthwhile as testing in patients allergic to FM I, as positive results were obtained in only 25% of the cases. Therefore, from the practical point of view, we were obliged to recommend that patients use entirely unperfumed products in 75% of the cases, whereas in 25% we could be more specific. It is also notable that of all the patients allergic to cinnamyl alcohol and/or cinnamal, only one was allergic to *M. pereirae* despite the fact that the former two were components of the latter (43); however, eugenol and isoeugenol, which were also components of *M. pereirae*, have been found quite frequently in patients who exhibited positivity to both FMI and *M. pereirae*. There are probably multiple allergens present in *M. pereirae* and what appears to be clear is that the constituents of the fragrance series account for only a small percentage of them (41, 43).

Including sorbitan sesquioleate in the fragrance series enabled us to find that 17.7% of patients with positive patch test to both *M. pereirae* and FM I had a false positive, as they were in fact allergic to sorbitan sesquioleate. We, therefore, recommend including sorbitan sesquioleate in the fragrance series.

Using a fragrance series in patients with no fragrance marker but with a high clinical suspicion detected positivity in only 9.3% of the cases. This indicates that there are good markers in our baseline series with few false negatives.

**Conclusions**

The usual markers of the standard series, FM I and *M. pereirae*, detected 90% of the cases, and so we believe them to be of great use. Adding hydroxyisohexyl 3-cyclohexene carboxaldehyde and FM II to the baseline series made it possible to diagnose new cases and study patients with known fragrance allergy in more detail. We think that it is necessary to include theses allergens in the Spanish baseline series as in other national series and the European baseline series.

Testing with a fragrance series proved to be of great use as it was possible to identify more clearly which allergens were involved, mainly when the positive marker in the baseline series was FM I.

The fragrance we found most frequently involved was geraniol, in contrast to the situation in most European countries.

We consider that identifying the fragrances involved in a patient’s clinical condition enables better treatment to be given, especially because of the change in legislation that makes it compulsory to include a list of 26 fragrances in the labelling of cosmetics and because they became commercially available for patch testing (Trolab® and Chemotechnique®).

**References**


30. Geier J, Brasch J, Schnuch A et al. For the Information Network of Departments of Dermatology (IVDK) and the German Contact Dermatitis Research Group (DKG). Lyral has been included in the patch test standard series in Germany. *Contact Dermatitis* 2002: 46: 295–297.


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