

## Analysis of Hypersensitivity in Fragrance Series by Patch Testing

### Abstract

**Introduction:** Allergic contact dermatitis (ACD) is an inflammatory disorder, which occurs as a result of repeated contact with an allergen. Fragrances are the products obtained naturally or produced synthetically. The purpose of this study is to detect the fragrance allergens producing ACD. **Materials and Methods:** This is an open-label prospective observational study. Patients of age above 18 years with history of using cosmetic products with dermatitis lesions over face, neck, axilla and hands were included. Patch testing was done with fragrance series by using the standard technique. The results were interpreted on day 2 and day 4 as recommended by International Contact Dermatitis Research Group criteria. **Results:** Totally 27 patients were included in this study. Of them, 12 were males and 15 were females; the mean age was 43 years. The mean duration of symptoms was 12.5 months. The most common site of involvement was hands. Housewives and office workers were the most commonly affected occupational groups. The most commonly used category of cosmetic product was talcum powders by 13 (48.1%) patients. In this study, 85.18% patients showed at least one fragrance antigen positivity. Fragrance mix II is the most frequent allergen in this study. **Discussion:** We conclude that the fragrance mix II is an important marker to find out fragrance allergy. Hand dermatitis is the most common presentation in patients with fragrance allergy. Perfumed talcum powders, soaps and perfumes are the leading sources of sensitization to fragrance allergens.

**Keywords:** Allergic contact dermatitis, cosmetics, fragrances, hand dermatitis, patch testing

### Introduction

Allergic contact dermatitis (ACD) is an inflammatory disorder, which occurs as a result of repeated contact with an allergen, leading to the rapid activation of T cells and further release of cytokines.<sup>[1]</sup> In the sixth century, Aetius Amidenus, a physician to the Byzantine court first used the word “eczema”. Eczema may present clinically as scaling, clustered papulovesicles, associated with erythema, pruritus and fissuring. It is caused by a different variety of external and internal factors.<sup>[2]</sup> Patch testing is considered as the gold standard and only reliable method to identify the contact allergens.<sup>[3]</sup>

Cosmetics is defined as the substances which are intended to be poured, rubbed, sprinkled or sprayed on skin, applied to a normal or previously sensitized skin for cleansing, promoting attractiveness, beautifying, or to alter the appearance of the human skin or body.<sup>[4]</sup> Cosmetics and toiletries are being used by most of the people for hygiene and personal care of

the body to enhance the attractiveness of consumers, get pleasant smell, protection and masking the defects present in the skin.<sup>[5]</sup> Cosmetics are complex mixtures made up of preservatives, perfumes, emulsifiers, stabilizing agents, various types of lipids, alcohols and so on.<sup>[6]</sup>

Fragrances are the products obtained naturally or produced synthetically. Natural fragrances, such as balsams, concretes, essential oils and absolutes are available, with a few animal products such as musk, civet and ambergris, which also can be manufactured synthetically.<sup>[7]</sup> Masking fragrances are used mainly in topical medicaments and cosmetic products by labeling them as “fragrance free”. But they contain original fragrances.<sup>[8]</sup> The purpose of this study is to detect all the fragrance allergens which cause ACD.

### Materials and Methods

This is an open-label prospective observational study conducted from March 2017 to July 2018 in a tertiary care hospital. All patients of age above 18 years who

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attended our dermatology outpatient department with the history of using various topical cosmetic products such as perfumes, detergent soap, after shave lotion, moisturizers, facial makeup creams, with dermatitis lesions over face, neck, axilla and hands were included in the study. Age below 18 years, who have not used any cosmetic products, who are on systemic corticosteroids, immunosuppressants, pregnant, lactating females, were excluded from the study.

The study was reviewed and approved by an institutional ethical committee, and all patients gave their voluntary informed consent to participate in this study. Detailed history regarding duration, occupation, systemic illness was obtained and recorded [Table 1]. Patch testing with fragrance series [Figure 1] was done by using the standard technique, that is, 0.1 ml of each antigen was placed in an aluminum Finn chamber, mounted on an adhesive tape [Figure 2], which was applied over the back of all the patients [Figure 3]. A total of 42 patch test antigens [Table 2] are present in the fragrance series obtained from chemotechnique diagnostics, AB Sweden. The results were interpreted on days 2 and 4 as recommended by International Contact Dermatitis Research Group (ICDRG) criteria [Table 3].

## Results

A total of 27 patients were included in this study and patch testing was done with fragrance series. Of them, 12 (44.4%) were males and 15 (55.5%) were females; the mean age was 43 years (range 18-68 years). The mean duration of symptoms was 12.5 months (range 1-24 months). The most common site of involvement was hands [Figure 4], which



Figure 1: Fragrance series antigens (Chemotechnique diagnostics, AB Sweden)

Table 1: Demographic data of all 27 patients

Age/sex	Occupation	Areas involved	Duration of symptoms	Cosmetic products used	Total number of antigens positive
54/F	Housewife	Face, neck	1 month	Giordani gold cream	2
64/M	Navy man	Face, neck,	2 months	Yardley lavender powder	9
36/M	Office worker	Axilla, hands	8 months	Dermicool powder	1
37/M	Painter	Neck	6 months	Power detergent soap	4
34/M	Painter	Hand, face	3 months	Dermicool powder, perfume	0
21/F	Office worker	Face, hand	1 month	Ponds powder, enchanter spray	3
18/M	Textile labour	Face, hands	1 year	Fair & Lovely cream, Savlon soap, aftershave lotion	2
20/F	Office worker	Hands	4 months	Venusia max cream, Rin detergent soap	2
46/F	Housewife	Hands, neck	6 months	Fair & Lovely cream, Gokul sandal powder, Mysore sandal soap	2
55/F	Office worker	Hands	6 months	Anti-hair fall shampoo, Vim bar soap	0
50/M	Business	Neck	3 months	Jasmine perfumes, Fogg body spray	1
18/F	Office worker	Hands, neck	1.5 years	Saffron face wash, Pond's powder, Mysore sandal soap	0
54/F	Agriculture	Face	8 months	Pond's powder, Hamam soap	4
40/F	Housewife	Neck	1 month	Surf Excel detergent, Mysore sandal soap	6
60/M	Agriculture	Face, neck	2 years	Gokul sandal powder, perfumes	1
31/F	Housewife	Face, hands	6 months	Gokul sandal powder, perfumes	3
36/F	Housewife	Face, hands	6 months	Mysore sandal soap, perfumes	4
54/F	Painter	Hands	1 month	Moisturex cream, herbal soap	5
30/F	Office worker	Hands	8 months	Moisturizing cream, perfumes, sunscreen lotion	4
65/M	Agriculture	Axilla, hands	2 months	Gokul sandal powder, Fair & Lovely cream	4
26/M	Business	Face, hands	2 years	Keraglo ad shampoo, Fair And Handsome cream	0
60/F	Cement worker	Hands, neck	3 months	Gokul sandal powder, Lifebouy soap, Arasan soap	3
55/F	Agriculture	Hands, neck	1 month	Hamam soap, Arasan soap	4
59/M	Cement worker	Hands, axilla	1 month	Lifebouy soap, body spray, moisturizers	2
40/M	Agriculture	Hands, neck, axilla	1.5 years	Perfumes, body spray, Pond's powder	3
55/M	Machine operator	Hands, axilla	2 years	Mysore sandal soap, sunscreen lotion	3
68/F	Housewife	Face, neck	6 months	Moisturizers, sunscreen lotion, Mysore sandal soap	3



**Figure 2: Patch testing: Antigens are placed in aluminum Finn chambers mounted over an adhesive tape**



**Figure 4: Hyperpigmented scaly lesions over the hands**

was observed in 19 (70.3%) patients [Table 4], followed by neck [Figure 5] in 12 (44.4%) patients.

The most commonly seen occupational groups with dermatitis features were housewives 6 (22.2%) and office workers 6 (22.2%) patients [Table 5]. The most commonly used category of cosmetic products by these patients were talcum powders by 13 (48.1%) patients [Table 6] followed by scented soaps in 12 (44.4%) patients.

Out of the 27 patients, 8 (29.6%) were atopic individuals and 19 (70.3%) were non-atopic individuals. Of the 27 patients, 23 (85.18%) patients showed at least one antigen positivity, and 4 (14.8%) patients were negative to all antigens. The most frequent allergen to become positive in this study is fragrance mix II [Figure 6] in eight (29.6%) patients [Table 7], followed by cinnamic aldehyde and cinnamic alcohol in seven (25.9%) patients each [Figure 7].

## Discussion

ACD is one of the commonest examples of type IV hypersensitivity reaction which usually affects the



**Figure 3: Patch test antigens applied over the back of patients**



**Figure 5: Erythema and scaling seen over the neck**

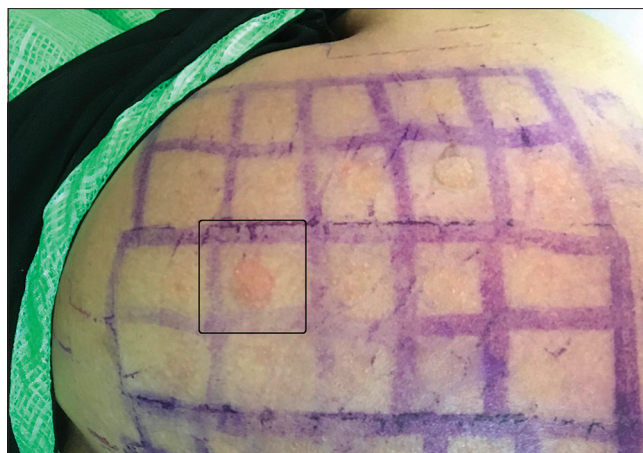
previously sensitized persons. The contact allergens are very small molecules which are able to penetrate deeper layers of the skin and produce sensitization.<sup>[2]</sup> Fragrances are the most common cause of allergic reactions to

**Table 2: Fragrance series antigens (Chemotechnique Diagnostics, AB Sweden)**

Antigen	Concentration (%)
Control	
Cinnamic aldehyde	1
Cinnamic alcohol	2
Amyl cinnamaldehyde	2
Eugenol	2
Isoeugenol	2
Geraniol	2
Oakmoss absolute	2
Hydroxycitronellal	2
Narcissus Absolute	2
Musk xylene	1
Methyl anthranilate	5
Musk moskene	1
Musk ketone	1
Jasmine synthetic	2
Benzyl salicylate	1
Benzyl alcohol	10
Vanillin	10
Lavender absolute	2
Cananga oil	2
Rose oil. Bulgarian	2
Ylang-Ylang oil	2
Geranium oil Bourbon	2
Jasmine absolute, Egyptian	2
Sandalwood oil	2
Lylal	5
Citral	2
Farnesol	5
Citronellol	1
Hexyl Cinnamic aldehyde	10
Coumarin	5
Fragrance mix II	14
Amyl cinnamic alcohol	5
Anise alcohol	10
Benyl benzoate	10
Benzyl cinnamate	10
Butyl phenyl methyl propional	10
Evernia furfuracea	1
Alpha-iso methyl ionone	10
d-Limonene	10
Linalool	10
Methyl-2-octynoate	0.2

cosmetics. Fragrances can enter into the body through nose into lungs, upper airways, ingestion, skin, and it can cause irritation of eyes, throat and nose, headaches, dizziness, forgetfulness and easy fatigability.<sup>[9]</sup>

In our study, females outnumbered males in fragrance hypersensitivity reactions by nearly 10%. The fact that there is a high prevalence of fragrance allergy in women than men could be due to the frequent use of skin care, personal hygiene and face care products by the female population.



**Figure 6: Patch test: Same patient shown in Figure 4, showed positive reaction to fragrance mix II**

In this study, housewives and office workers are the occupational groups who developed fragrance allergy most frequently, which is seen in six (22.2%) patients in each occupational group. DeGroot *et al.*<sup>[7]</sup> found that fragrance allergy from perfumes, deodorants and aftershave lotions is commonly encountered in Swedish college students.

In this study, most commonly 19 (70.3%) patients had lesions over the hands, and next frequent site was over the neck in 12 (44.4%) patients. Our findings correlate well with the studies conducted by Santucci and Malten;<sup>[7]</sup> they found that hand dermatitis was the most common presentation with 41% and 52% positivity, respectively, because of frequent contact of the fragrance products such as soaps, fairness creams, shampoos and topical medications with hands before application at various sites of the body.<sup>[7]</sup>

In this study, the most common category of cosmetic products used were talcum powders by 13 (48.1%) patients and scented soaps by 12 (44.4%) patients. An observational study found that the skin care products such as lotions, creams were the cosmetic categories which were blamed for the positive reactions in patch testing in 37% of patients; 30% of positive cases had used personal care products and 13% used deodorants and antiperspirants.<sup>[5]</sup> According to Cornelis *et al.*, soaps were used by 87% of the people, 82% people used toothpaste, shampoos were used by 80%, deodorants and antiperspirants by 61%, talcum powder and body spray were used by nearly 45% of the study population.<sup>[5]</sup>

In this study, we found that the most frequent allergen to show positivity was fragrance mix II in eight (29.6%) patients. The second most common allergens were cinnamic aldehyde and cinnamic alcohol in seven (25.9%) patients, which is followed by Geranium oil Bourbon and Lavender absolute in five (18.5%) patients. Our observations are similar to a study conducted by Johansen *et al.*: who stated that the most common allergens are fragrance mix II and

**Table 3: Interpretation of Patch Test Results (ICDRG Criteria)**

Notation	Description
Negative	No changes in the tested skin area
?+	Non-palpable faint erythema
1+	Palpable erythema with moderate edema or infiltrate, no papules or vesicles
2+	Strong infiltrate and erythema, numerous papules or vesicles
3+	Many vesicles coalesced to form bulla or ulceration
NT	Not tested
IR	Inflammation is sharply limited to an exposed area, lack of infiltrate, small petechiae, pustules with papules and vesicles

ICDRG=International Contact Dermatitis Research Group

**Table 4: Location of dermatitis lesions**

Location	Number of patients	Percentage
Neck	12	44.4
Face	11	40.7
Hands	19	70.3
Axilla	5	18.5

**Table 5: Various occupational groups presented with dermatitis**

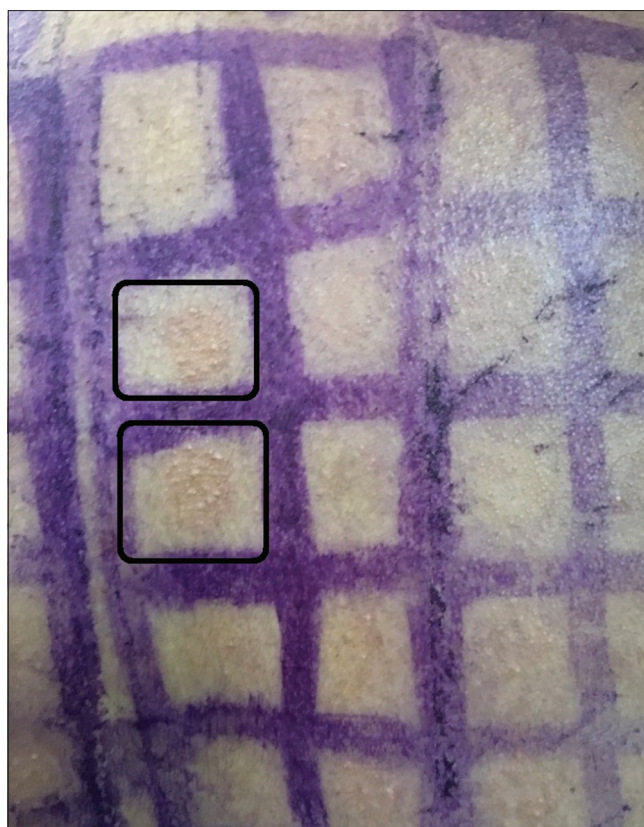
Occupation	Number of patients	Percentage
Housewife	6	22.2
Navy man	1	3.7
Office worker	6	22.2
Painter	3	11.1
Business	2	7.4
Textile laborer	1	3.7
Agriculture	5	18.5
Cement worker	2	7.4
Machine operator	1	3.7

**Table 6: Categories of the cosmetic products used by the patients**

Category	Number of patients	Percentage
Perfumes	9	33.3
Soaps	12	44.4
Detergents	5	18.5
Moisturizers	5	18.5
Talcum powders	13	48.1
Fairness creams	5	18.5
Sunscreens	3	11.1
Shampoo	2	7.4
Aftershave lotion	1	3.7

balsam of peru.<sup>[10]</sup> Santucci *et al.* identified 54 out of 92 patients were sensitive to fragrance mix II.<sup>[7]</sup>

Various studies have been conducted in various countries to know the incidence of fragrance allergy, but only a few studies are available for our Indian skin type. This

**Figure 7: Patch test: Same patient shown in Figure 5, showed positive reaction to cinnamic alcohol and cinnamic aldehyde**

is because the fragrance allergy is usually not reported to the dermatologists by the patients. In USA, the most frequent sensitizer was fragrance mix II. In Netherlands, isoeugenol is followed by oak moss absolute. In a European study, they found that oak moss absolute is the most frequently positive fragrance allergen followed by isoeugenol.<sup>[10]</sup>

In this study, a total of 27 patients were included with dermatitis. Of them, 8 (29.6%) patients were known atopic and 19 (70.3%) patients were non-atopic individuals. But Katsarma *et al.*<sup>[10]</sup> stated that more than 50% of ACD patients were with atopic diathesis in their study. Caress and Maria *et al.*<sup>[11]</sup> also concluded that the fragrance-induced ACD is most commonly seen in atopic eczema cases.

In this study, we did not experience any adverse events or intolerability to patch testing. All the 27 patients came for regular follow-up and also for the readings taken on day 2 and day 4. Once the patient is diagnosed as a case of ACD by patch testing, pamphlets were issued regarding the awareness of how to avoid contact with the particular allergens. Cosmetics are not very safe as claimed by the manufacturing companies, and it may contain many fragrance allergens. ACD induced by cosmetics was more prevalent in urban people than rural because of the health awareness and attitude towards cosmetics in urban people.<sup>[12]</sup>

**Table 7: Frequency of fragrance allergen positivity**

Antigens	Number of patients showed positivity	Percentage
Cinnamic aldehyde	7	25.9
Cinnamic alcohol	7	25.9
Isoeugenol	4	14.8
Oakmoss absolute	4	14.8
Lavender absolute	5	18.5
Geranium oil Bourbon	5	18.5
Fragrance mix II	8	29.6
Benzyl cinnamate	4	14.8

### Conclusion

Patch testing is a simple method to diagnose the causative agent of ACD. It shortens the time lapse from the first visit to final diagnosis and increases the period of remission, which in turn reduces the cost of treatment. We conclude that fragrance mix II is an important marker to find out fragrance allergy. Hand dermatitis is the most common presentation in patients with fragrance allergy. Perfumed talcum powders, soaps and perfumes are the leading source of sensitization to fragrance allergens producing fragrance allergy.

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### Conflicts of interest

There are no conflicts of interest.

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