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Allergic contact dermatitis from the synthetic fragrances Lyral and acetyl cedrene in separate underarm deodorant preparations

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The case is reported of a 28-year-old man who developed allergic contact dermatitis from 2 synthetic fragrance ingredients, Lyral (3- and 4-(4-hydroxy-4-methylpentyl)-3-cyclohexene-1-aldehyde) and acetyl cedrene, in separate underarm deodorant preparations. The implications of the patient's negative patch test reactions to the European standard series (Trolab) and cosmetics and fragrance series (both Chemotechnique Diagnostics) are discussed. The importance is stressed of patch testing with the patient's own preparations when cosmetic dermatitis is suspected, and of identifying and reporting offending fragrance ingredients, with a view possibly to updating the European standard series and commercially available cosmetics and fragrance series.

Key words: allergic contact dermatitis; fragrances; Lyral; acetyl cedrene; underarm deodorants; cosmetics and toiletries; patch testing technique. © Munksgaard, 1994.

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Fragrances are stated to be the most frequent cause of cosmetic allergy (1, 2). They are a blend of natural plant and flower oils, or synthetic compounds such as alcohols, aldehydes or ketones. Patch test screening with the European standard series' fragrance mix (eugenol, isoeugenol, oak moss absolute, geraniol, cinnamic aldehyde, amyl cinnamaldehyde, hydroxycitronellal and cinnamic alcohol, emulsified in sorbitan sesquioleate) (3) is estimated to detect only 70–80% of cases of fragrance allergy (4).

As new fragrances are continuously being developed, it is important constantly to update knowledge of the most common allergens by identifying the fragrance ingredient(s) responsible in any patient who develops perfume dermatitis. This can be a lengthy and unrewarding task, as cosmetic formulations are often a closely guarded secret. In this regard, we report a patient who developed allergic contact dermatitis from 2 synthetic fragrance compounds, Lyral and acetyl cedrene, in separate underarm deodorants. Only 3 previous cases of Lyral sensitivity have been reported (2, 5, 6) and allergy to acetyl cedrene is hitherto unrecognized.

Case Report

A 28-year-old man developed dermatitis of both axillae after 3 months' use of 2 separate deodorant preparations (A and B). Patch testing showed positive reactions at 3 days to both preparations (as is), and negative responses to the European standard series (Trolab), including fragrance mix, balsam of Peru and colophony, and cosmetics and fragrance series (both Chemotechnique Diagnostics). He was advised against further use of these preparations and his rash settled quickly with topical corticosteroids with no subsequent recurrence.

The manufacturer kindly provided the individual constituents of the 2 deodorants, and patch testing showed positive responses to the perfume used in each of them. The suppliers of these perfumes were asked to provide the ingredients of their preparations with a view to identification of the fragrance allergens.

One perfume company initially provided 4 fractions of their perfume compound (I) and patch testing showed a positive response to fraction 2. 5 further ingredients of fraction 2 (fraction 2, fraction 2 ingredients 3, 4, 6 (each separate), fraction 2 ingredients 1/2/5 (one sample)) were supplied and patch testing showed positive responses to fraction 2 and fraction 2 ingredient 6, which the company identified as Lyral and provided us with the product safety data sheet of.

The other perfume company initially provided 4 fractions of their compound (II) (esters, aldehydes

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plus ketones, alcohols, naturals) and patch testing showed a positive response to the aldehyde and ketone fractions. 4 further ingredients of the aldehyde and ketone fraction were provided (ketone A, aldehyde Z, aldehyde Y, ketone B) and positive patch test responses were obtained to aldehyde Z and ketone B, which the company then identified as Lyral (aldehyde Z), and acetyl cedrene (ketone B). Relevant product safety and data sheets were provided.

Thus, the allergen in perfume compound I (deodorant A) was Lyral (3- and 4-(4-hydroxy-4-methylpentyl)-3-cyclohexene-1-aldehyde), and the allergens in perfume compound II (deodorant B) were Lyral and acetyl cedrene. These findings are summarized in Table 1. The patient showed positive 3-day patch test reactions to (1) Lyral (0.075%, 0.125%, 0.25% in petrolatum (pet.) and Lyral 6.5% in diisopropylene glycol (DIPG) (2) acetyl cedrene (10.8% DIPG). Patch tests to acetyl cedrene in dilutions of 0.108%, 0.54%, 1.08% were all negative. Negative results were obtained in all 20 controls (attending the patch test clinic for other unrelated reasons) on patch testing to Lyral (0.25% pet., 6.5% DIPG) and acetyl cedrene (10.8% DIPG).

9 months after initial presentation, the patient was diagnosed as having allergic contact dermatitis from the synthetic fragrance ingredients Lyral and acetyl cedrene.

Discussion

This patient developed allergic contact dermatitis from 2 synthetic fragrance ingredients, Lyral (an aldehyde) and acetyl cedrene (a ketone), in separate underarm deodorant preparations. This case is of interest as it aptly demonstrates the difficulties and time involved in identifying fragrance allergens in patients with cosmetic dermatitis. In addition, only 3 cases of Lyral sensitivity have previously been reported (2, 5, 6) and, to our knowledge, contact allergy to acetyl cedrene has not hitherto been recognized.

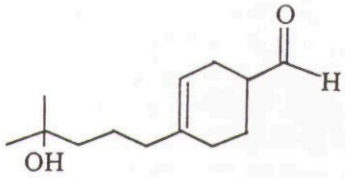
Contact allergy to Lyral was proven by: (a) positive patch testing to concentrations between 0.075–6.5%; Research Institute for Fragrance Materials (RIFM) test data show Lyral to be non-irritating in concentrations of 10% pet. on human patch testing; (b) negative responses to Lyral in control patients. The case for acetyl cedrene allergy in this patient is less certain. Alternative explanations for the positive patch test response to acetyl cedrene (10.8% DIPG) could be: (a) false-positive irritant reaction; (b) cross-reactivity between Lyral and acetyl cedrene. We believe that the positive patch test response to acetyl cedrene (10.8%) is a true allergic rather than false-positive irritant response on the basis that: (a) RIFM test data shows acetyl cedrene 30% pet. to be non-irritating

Table 1. Patch testing identification of allergens in perfume compound I (deodorant A) and perfume compound II (deodorant B)

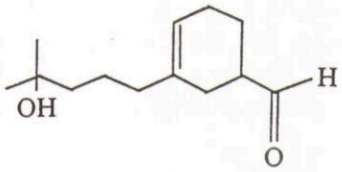
Perfume Compound I	
Patch testing to	Positive response (grade)
(i) fractions 1, 2, 3, 4 (all 5% pet.)	fraction 2 (+) (contains 0.075% Lyral)
(ii) fraction 2	fraction 2 (+)
fraction 2, ingredients 3, 4, 6	fraction 2, ingr. 6 (+)
fraction 2, ingredients 1, 2, 5 (all 1%, 2% pet.)	(contains 0.125%, 0.25% Lyral)
Perfume Compound II	
Patch testing to	Positive response (grade)
(i) (a) esters 29% DIPG (b) alcohols 24% DIPG (c) naturals 15% DIPG (d) alcohols/Ketones 32% DIPG (all 5% pet.)	(d) alcohols/ketones (++)
(ii) Components of alcohols/ketones:	
(a) 5.3% ketone A+94.7% DIPG	
(b) 1.1% aldehyde Y+98.9% DIPG	(c) aldehyde Z (++) (6.5% Lyral)
(c) 6.5% aldehyde Z+93.5% DIPG	
(d) 10.8% ketone B+89.2% DIPG (all as is)	(d) ketone B (++) (10.8% acetyl cedrene)
(iii) Dilutions of 10.8% ketone B+89.2% DIPG:	
(a) 1% pet. (0.108% acetyl cedrene)	none
(b) 5% pet. (0.54% acetyl cedrene)	
(c) 10% pet. (1.08% acetyl cedrene)	

NB. pet.: petrolatum
DIPG: diisopropylene glycol.
+: faint erythema: ++: marked erythema.

(a) Lyral: a mixture of isomers



and



(b) Acetyl cedrene (Vertofix Coeur) – a complex reaction mixture of which a principal constituent is methyl cedryl ketone

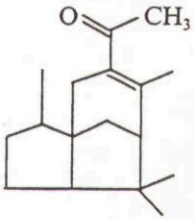


Fig. 1. Chemical structures of (a) Lyral (b) acetyl cedrene.

on human patch testing; (b) patch testing with acetyl cedrene (10.8% DIPG) showed no positive responses in control patients. The negative patch test responses obtained with acetyl cedrene dilutions between 0.108–1.08% were most likely because these allergen concentrations were too low to provoke a cutaneous immune response. In our opinion, cross-reactivity between Lyral and acetyl cedrene is unlikely due to their completely different chemical structures (Fig. 1).

It is noteworthy that patch test screening with the European standard series (specifically fragrance mix, and the indicators of fragrance sensitivity balsam of Peru and colophony) and the Chemotechnique cosmetics and fragrance series (neither of which contain Lyral or acetyl cedrene) was negative in this patient. This stresses the importance of (1) patch testing to the individual preparations concerned in suspected cases of cosmetic dermatitis, and (2) identifying and reporting offending fragrance ingredients in individual cases of perfume dermatitis, with a view to possibly updating the the European standard series and commercially available cosmetics and fragrance series.

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References

1. Adams R M, Maibach H I. A 5-year study of cosmetic reactions. *J Am Acad Dermatol* 1985: *13:* 1062–1069.
2. De Groot A C, Bruynzeel D P, Weyland J W et al. The allergens in cosmetics. *Arch Dermatol* 1988: *124:* 1525–1529.
3. De Groot A C, White I R. Cosmetics and skin care products. In: Rycroft R J G, Menné T, Frosch P J, Benezra C (eds): *Textbook of contact dermatitis.* Berlin, New York: Springer Verlag, 1992: 459–475.
4. Larsen W G, Maibach H I. Fragrance contact allergy. *Semin Dermatol* 1982: *1*: 85–90.
5. De Groot A C. Contact allergy to cosmetics: causative ingredients. *Contact Dermatitis* 1987: *17:* 26–34.
6. Benke G M, Larsen W G. Safety evaluation of perfumed shampoos: Dose/response relationships for product use testing by presensitised subjects. *Journal of Toxicology – Cutaneous and Ocular Toxicology* 1984: *3:* 65–67.

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