

CONTACT ALLERGY TO PRESERVATIVES AND PERFUMED COMPOUNDS USED IN SKIN CARE PRODUCTS

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Synopsis

Contact allergy and irritation to cosmetic constituents, in particular perfumed compounds and preservatives, are a major problem, which is exacerbated because such substances are also greatly spread in the environment.

This report records data on contact dermatitis from cosmetic products among 19,546 unselected patients affected by eczematous dermatitis. The most common forms of this affection are caused by perfumed compounds (4%), eye cosmetics (2.1%), lip products (1.6%), and hair preparations (0.5%). Data on allergy to fragrances refers to the same individuals who have been tested with fragrance mix and its single components; 78.4% of the cases concern women; the main constituents are oak moss and cinnamaldehyde.

The highest rate of positive reactions was observed with parabens (1.9%) and Kathon CG (1.6%), some of the most common preservatives. Other preservatives are formaldehyde-releasers, butylhydroxyanisole and sodium metabisulfite.

Riassunto

Le allergie da contatto e le irritazioni verso gli ingredienti dei cosmetici, in particolare verso i profumi ed i conservanti, sono un grosso problema, che è ulteriormente esacerbato dalla diffusa presenza di queste sostanze nell'ambiente.

Questo lavoro registra i dati sulle dermatiti da contatto causate da prodotti cosmetici in 19.546 pazienti consecutivamente osservati ed affetti da eczema. Le forme più comuni di questa affezione sono causate dai profumi (4%), dai cosmetici per gli occhi (2,1%), dai prodotti per labbra (1,6%) e dai prodotti per capelli (0,5%). I dati sulle allergie ai profumi fanno riferimento agli stessi soggetti che sono stati testati con una miscela di fragranze e con i suoi singoli componenti. Il 78,4% dei casi riguarda donne; gli ingredienti principali sono il muschio di quercia e la cinnamaldeide.

Il più alto tasso di reazioni positive è stato registrato con i parabeni (1,9%) ed il Kathon CG (1,6%), che sono fra i conservanti più comuni. Altri conservanti sono quelli che liberano la formaldeide, il butilidrossianisolo ed il metabisolfito di sodio.

INTRODUCTION

Cosmetic products do not induce large-scale undesired effects, though they are used daily by a great number of people. Intolerance to cosmetic products ranges from 2 to 8% (1-4), allergic reactions accounting for 80% and irritation for 16% (5-11). Irritation is thus much less frequent than contact allergy. This is true, however, only in respect of a studied and tested population. If we consider the general population, irritation is actually much more frequent, since contact dermatitis disappears fairly rapidly when the contact ceases, and it is often unreported. The greatest part of patients suffering from both allergy or contact irritation are women. The major allergens are perfumed compounds and preservatives.

This work presents some of our data on contact allergy to cosmetic products and their constituents. It concerns 19,546 patients with various kinds of dermatitis, who have been consecutively observed and tested.

FRAGRANCES

Table 1 shows the major groups of contact dermatitis due to cosmetic products. Most commonly, this affection is caused by perfumed compounds (4%), eyelid cosmetic products (2.1%) (5,12), and cheilitis due to lipsticks and toothpastes (1.6%) (5,13). Contact dermatitis due to hair preparations is not very frequent (0.5%). This may be accounted for by the fact that the cosmetic product is in contact with the cutis only for a short time, and that, when used, it is diluted with water (10).

Natural and synthetic fragrances are the most frequent allergens causing contact dermatitis due to cosmetic products (10,14,18). They can also occasionally cause irritant contact dermatitis, photodermatitis (berloque dermatitis), contact urticaria and depigmentation. The high rate of allergy to fragrances is due to their large presence in cosmetics as well as in a greater variety of other products, such as detergents, toiletries, toothpastes, local treatments, food and beverages (16). Women comprise 78.4% of the patients affected by

this kind of allergy. Eczematous dermatitis affects various areas.

Table 2 shows cases of allergy following ulcerative vascular dermatitis of the legs due to the use of local remedies containing perfumed compounds.

Table 3 shows contact allergy to the various compounds (single mix constituents) as observed in our 19,546 eczematous patients, where oak moss and cinnamaldehyde prevail.

In addition to traditional direct cutaneous contact, contact with perfumed compounds may also occur through the air (airborne contact dermatitis) (19). We have observed two young women with armpit contact dermatitis and high sensitivity to fragrances (cinnamic aldehyde). After visiting some perfumery where samples of perfume had been sprayed, the two women suffered from facial and, mainly eyelid erythematous edematous rashes. In one of the two cases, in a test carried out in our Allergology Department, spraying resulted in eyelid erythema and edema after some hours (19).

Finally, we have observed that fragrances can often induce two different clinical pictures in the same person at the same time: contact allergy (cell-mediated pathogenesis) and contact urticaria (immediate mechanism).

Table I

INCIDENCE OF SOME GROUPS OF CONTACT DERMATITIS (CD) DUE TO COSMETICS IN 19,546 ECZEMATOUS PATIENTS.

CD to fragrances	4.0%
CD of the eyelids	2.1%
Contact cheilitis	1.6%
CD to hair cosmetics	0.5%

Table II

SITES OF ALLERGIC CONTACT DERMATITIS TO FRAGRANCES IN 19,546 SUBJECTS WITH DERMATITIS.

Face and/or axillae and/or neck	57.0%
Hands	16.7%
Legs (ulcerative dermatitis)	15.5%
Other sites	10.8%

Table III
PERFUME MIXTURE RESULTS.

Substance	Patients tested	Positive reactions (%)
Perfume mixture	19,546	4.0
Oak moss		1.2
Cinnamaldehyde		1.0
Eugenol		0.6
Cinnamic alcohol		0.4
Hydroxycitronellal		0.3
Geraniol		0.3
Isoeugenol		0.2
Alfa-amyl cinnamaldehyde		0.1

Table IV
POSITIVE REACTIONS TO SOME PRESERVATIVES IN PATIENTS WITH DERMATITIS.

Substance (conc.)	Patients tested	Positive reactions (%)
Parabens (15% pet.)	19,546	1.9
Kathon CG (100 ppm, aq.)	10,795	1.6
Sodium metabisulfite (1% pet.)	980	1.4
Chloracetamide (0.2% pet.)	1250	0.6
Formaldehyde (1% aq.)	19,546	0.3
Triclosan (2% pet.)	1250	0.3
Butylhydroxyanisole (2% pet.)	980	0.3
Imidazolidinyl urea (2% pet.)	13,647	0.2
Bronopol (0.5 pet.)	2852	0.2
Quaternium 15 (1% pet.)	14,897	0.1
Butylhydroxytoluene (2% pet.)	980	0

PRESERVATIVES

Preservatives are the second class of cosmetic compounds, after fragrances, which are the most frequent causes of contact allergy.

Table 4 shows the results of tests in eczematous patients. The highest numbers of positive reactions were obtained with parabens (1.9%) and Kathon CG (1.6%). Almost all the other preservatives induced a low rate of responses (below 1%), consistent with the relevant literature (11, 20, 22). Preservatives such as parabens and formaldehyde are known to cause contact allergy. However, it is necessary also to monitor sensitization to other less known preservatives, such as some formaldehyde-releasers (Quaternium 15, Bronopol, Germall 115 or imidazolidinyl urea), butylhydroxyanisole and sodium metabisulfite. The latter is present in cosmetic products and local remedies, and may cross-react with other sulfites.

Parabens

Para-hydroxybenzoic acid esters (parabens) are the most widely used preservatives throughout the world. They are included in cosmetic products and

local remedies in a concentration of 0.1-0.3%. The sensitization power of parabens is low, according to maximization and Draize tests in man (23, 24). In literature, contact allergy to parabens, ranges from 0.3 to 6%. Our results from a series of 19,546 patients show an incidence of 1.9% which is comparable with the incidence reported by most authors (25-27).

Figure 1 shows the incidence of contact allergy to parabens observed between January 1968 and May 1991. In 1983 it decreased and has remained around 1% ever since. It is important to note that reduction in 1983 seems to have coincided with replacement of parabens by other preservatives in most of local remedies.

Table 5 gives important data on the incidence of contact allergy to parabens in various groups of patients tested for different forms of eczematous dermatitis. The highest incidence of allergy is found with leg ulcers (11%), and traumas (8.5%), followed by perianal contact dermatitis (3%) and hand contact dermatitis (2.2%). Incidence is lower for face contact dermatitis (1%) or atopic dermatitis (0.2%). This data leads to the following analysis. First of all, contact allergy to parabens was induced by local remedies applied directly over the dermis

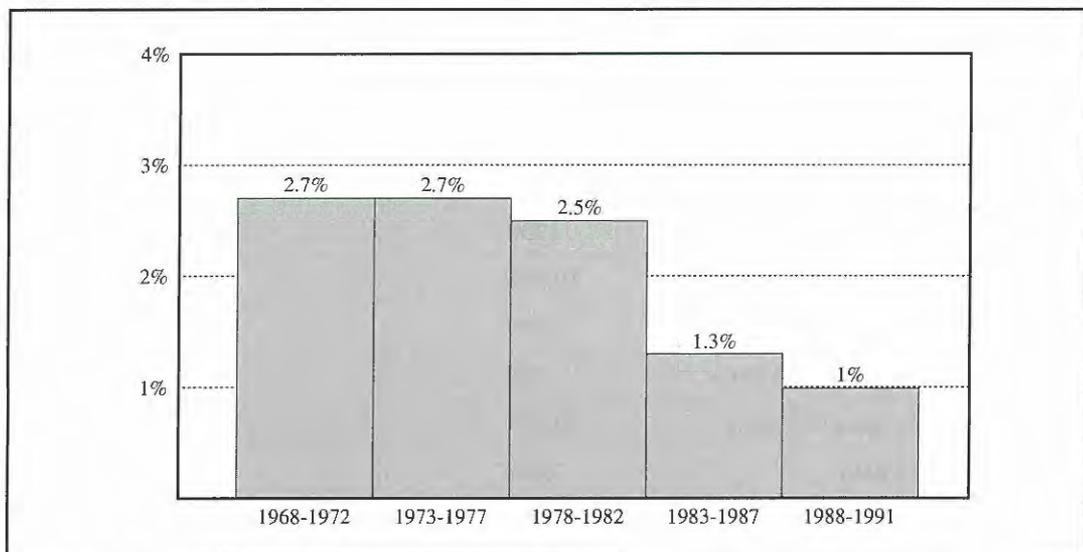


Fig. 1 - Incidence of contact allergy to parabens from 1968 to May 1991 in 19,546 patients with dermatitis.

Table V

INCIDENCE OF POSITIVE REACTIONS TO PARABENS IN 19,546 PATIENTS WITH DIFFERENT DERMATITIS (1968-1991).

Dermatitis	%
Leg ulcers	11.0
Traumatic injury	8.5
Perianal dermatitis	3.0
Occupational contact dermatitis	2.2
Jewellery and apparel dermatitis	2.2
Pompholyx	1.9
Contact dermatitis of face	1.0
Atopic dermatitis	0.2
Others	0.1

Table VI

CUTANEOUS SITES AND RISK OF SENSITIZATION TO PARABENS.

Group	Notes
Leg ulcers/traumatic lesions	very high risk area
Anoperianal eczema	high risk area
Hands	moderate risk area
Face	low risk area
Atopic dermatitis	low risk area

wounded skin (dermatitis due to other causes), as Table 5 shows (28). This means that parabens are easily absorbed when the skin filter is lacking (ulcers and traumas) or in case of dermatitis.

Our data reveal that allergy to parabens is due to the use of local remedies. On the other hand the literature indicates that the allergy to parabens can exceptionally be caused by the use of the cosmetic products which contain them (29). Parabens can thus be safely used on sound skin. This is the so-called "paradox effect" which is typical of these substances. Individuals with allergy to parabens contained in topical medicaments may tolerate the same substance when contained in cosmetic products on sound skin (30).

On the basis of this analysis, we may state that the risk of allergy to parabens varies according to the

region of the body, in reference with particular cutaneous lesions and, obviously, with different degrees of absorption (Table 6).

Leg ulcers, traumas and the ano-perianal region present a high sensitization risk, as stated by other authors (31-35). Our data also show that allergy to parabens more often affects people around 50 and 60, in relation with the greater incidence of leg ulcers due to vascular diseases at this age (32).

The absence of systemic contact dermatitis has been observed in patients affected by contact allergy to parabens, after introducing parabens through oral or injected remedies. This is most likely to be another "paradox effect" linked to these substances. Only one case exists in literature (36). We have carried out the oral challenge on 35 and 20 cases of contact allergy to methyl and propylparabens respectively. We have not observed any secondary reaction, at least in the concentrations used (37) (Table 7).

We have tested the single constituents of the mix on 45 patients with positive reactions to parabens, and we have obtained a greater incidence of positive responses to methylparaben (Table 8).

Simultaneous responses to two or more constituents have been often observed. This may be linked to cross or concomitant sensitization, since these constituents are found together in the various remedies (27).

Benzylparaben induced a low incidence of positive reactions, probably because of its molecular weight which is more or less twice that of methylparaben. The different reactivity, however, may be also due to a different bioavailability of vaseline esters. In this regard, the single esters should be tested using the same molar concentrations in order to make a real comparison (27).

Kathon CG

Kathon CG, a widely used preservative in cosmetic products, was introduced into our standard series in 1983. Since then, it has been tested (100 ppm in water: 0.01%) in 10,795 eczematous patients consecutively observed. Some data on this substance has formed the object of our previous studies (38-40).

Table VII

PERORAL TESTS IN SUBJECTS WITH CONTACT ALLERGY DUE TO PARABENS.

Substance	Peroral test	Cases No	Positive test
Methylparaben	20 mg	35	0
Propylparaben	5 mg	20	0

Table VIII

PATCH RETESTING WITH INDIVIDUAL ESTERS (ALL IN PET.) IN 45 SUBJECTS WITH A POSITIVE REACTION TO PARABEN MIXTURE.

Substance	Positive reactions (%)
Methylparaben	93.3
Ethylparaben	46.6
Propylparaben	45.0
Butylparaben	45.0
Benzylparaben	20.0

Table IX

SITES AND INCIDENCE OF CONTACT ALLERGY TO KATHON CG IN 10,795 SUBJECTS WITH DERMATITIS.

Site	Positive reactions (%)
Hands	52.4
Face	38.5
Forearms	9.7
Neck	8.9
Trunk	4.8
Legs	2.4

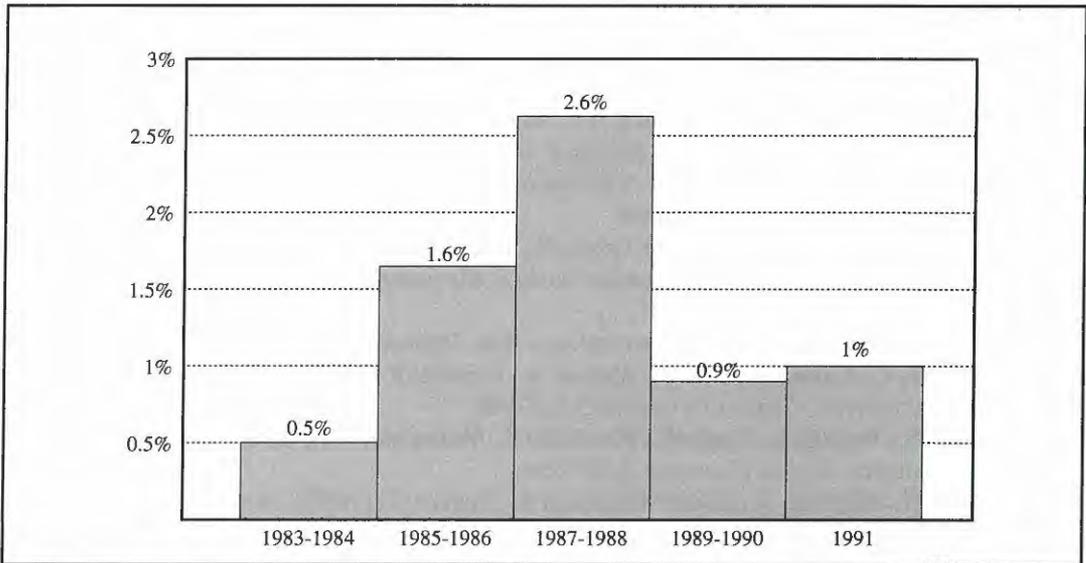


Fig. 2 - Incidence of contact allergy to Kathon CG from 1983 to May 1991 in 10,795 patients with dermatitis.

The overall incidence of contact allergy in our patients is 1.6%. This rose progressively from 1983 (0.5%) to 1988 (2.6%). The elimination of this substance from many cosmetic products, also for preventive purposes, resulted in a decreased incidence of 1% (Figure 2).

Contact allergy to Kathon CG is more frequently found in women (82%) than in men (18%). Most of the positive reactions were relevant, since the anamnesis revealed the use of cosmetic products containing isothiazolinones. In our opinion, it is important to highlight the morphologic features of the positive patch test. This test is regularly erythematous-edematous-vesicular, but has always given well defined roundish limits, without erythema propagation.

Table 9 shows that, unlike parabens, allergy to Kathon CG affects mainly the face and the hands. Another important finding which is also confirmed in literature (40) was that retesting of the substance after 10-15 days following the first positive patch test, gave positive results in 88% of the cases. This good reproducibility suggests that the reactions observed in the first test are to be considered as true allergic reactions.

A multi-centre work on Kathon CG in which we par-

ticipated (40), revealed the highest incidence of contact allergy (11%) to be recorded in Italy. This was probably due to the use of Kathon CG in concentrations highly exceeding the recommended values.

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