# **ORIGINAL ARTICLES**

# Allergic Contact Dermatitis to Cosmetics

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Abstract. Introduction. Contact dermatitis to cosmetics is a common problem in the general population, although its prevalence appears to be underestimated. We reviewed cases of allergic contact dermatitis to cosmetics diagnosed in our dermatology department over a 7-year period with a view to identifying the allergens responsible, the frequency of occurrence of these allergens, and the cosmetic products implicated.

Methods. Using the database of the skin allergy department, we undertook a search of all cases of allergic contact dermatitis to cosmetics diagnosed in our department from January 2000 through October 2007.

Results. In this period, patch tests were carried out on 2485 patients, of whom 740 were diagnosed with allergic contact dermatitis and the cause was cosmetics in 202 of these patients (170 women and 32 men), who accounted for 27.3 % of all cases. A total of 315 positive results were found for 46 different allergens. Allergens most often responsible for contact dermatitis in a cosmetics user were methylisothiazolinone (19%), paraphenylenediamine (15.2 %), and fragrance mixtures (7.8 %). Acrylates were the most common allergens in cases of occupational disease. Half of the positive results were obtained with the standard battery of the Spanish Group for Research Into Dermatitis and Skin Allergies (GEIDAC). The cosmetic products most often implicated among cosmetics users were hair dyes (18.5 %), gels/soaps (15.7 %), and moisturizing creams (12.7 %).

Conclusion. Most patients affected were women. Preservatives, paraphenylenediamine, and fragrances were the most frequently detected cosmetic allergens, in line with previous reports in the literature. Finally, in order to detect new cosmetic allergens, cooperation between physicians and cosmetics producers is needed.

Key words: ontact dermatitis, cosmetics, methylisothiazolinone, paraphenylenediamine, fragrances, acrylates.

#### DERMATITIS ALÉRGICA DE CONTACTO POR COSMÉTICOS

Resumen. Introducción. La dermatitis de contacto por cosméticos es un problema frecuente entre la población general, sin embargo, parece ser que su prevalencia está infraestimada.

Revisamos en este trabajo los casos de dermatitis de contacto alérgica por cosméticos diagnosticados en el Departamento de Dermatología en un periodo de 7 años con el objetivo de detectar los alergenos responsables, la frecuencia de los mismos, así como los productos cosméticos implicados.

Métodos. Utilizando la base de datos de la sección de Alergia Cutánea se realiza una búsqueda de todos los casos de dermatitis de contacto alérgica por cosméticos diagnosticados en nuestro departamento entre enero de 2000 y octubre de 2007.

Resultados. Durante este periodo se realizaron pruebas epicutáneas a 2.485 pacientes. De todos ellos, 740 fueron diagnosticados de una dermatitis de contacto alérgica, 202 pacientes (170 mujeres/32 varones), es decir, el 27,3 % lo fueron por cosméticos. Se detectaron un total de 315 parches positivos y 46 alergenos diferentes. Los alergenos que con más frecuencia produjeron una dermatitis de contacto en el usuario fueron las metilisotiazolinonas (19 %), la parafenilendiamina (15,2%) y la mezcla de perfumes (7,8%). Los acrilatos fueron los alergenos más frecuentes en aquellos casos que tenían un origen laboral. Con la batería estándar del Grupo Español en Investigación en Dermatitis y Alergia Cutánea (GEIDAC) se detectaron la mitad de las pruebas positivas. Los productos cosméticos implicados con mayor frecuencia en el usuario fueron los tintes capilares (18,5 %), los geles/jabones (15,7 %) y las cremas hidratantes (12,7%).

Conclusión. La mayoría de los pacientes afectados fueron mujeres. Los conservantes, la parafenilendiamina y los perfumes fueron los alergenos cosméticos más frecuentes, tal y como había sido publicado previamente en la lite-

tivos y las casas comerciales.

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Palabras clave: dermatitis de contacto, cosméticos, metili-

ratura. Finalmente, con el objetivo de detectar nuevos aler-

genos cosméticos debe existir colaboración entre los faculta-

sotiazolinonas, parafenilendiamina, perfumes, acrilatos.

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## Introduction

Contact dermatitis due to cosmetics has traditionally been estimated to account for between 2% and 4% of all dermatology consultations, 1 but its true prevalence is probably much higher.<sup>2</sup> Indeed a large portion of the population is susceptible to this allergic condition due to the widespread use of cosmetic products such as soap, shampoo, deodorant, toothpaste, face cream, sunscreens, and perfume. Furthermore, not all patients with mild forms of contact dermatitis seek medical consultation, preferring instead to simply stop using the suspect product. Irritant reactions to cosmetics generally occur in patients with sensitive skin such as those with atopy or rosacea, 3 but they can also occur as a result of incorrect use such as leaving on rinse-off products for hours, as if they were leave-on cosmetics, instead of washing them off after a few minutes as is indicated.

Cosmetics generally remain in close contact with the skin for long periods of time, thus favoring allergic sensitization to the numerous chemical substances they contain. Identifying the allergens responsible for allergic contact dermatitis (ACD) due to cosmetics was greatly facilitated in 1997, when it became mandatory in Europe to include the ingredients on the labeling of cosmetic products. From that moment on, the clinical relevance of patch test positivity could be determined by checking whether the sensitizing allergen was present in any of the cosmetic products used by the patient and by determining whether those products were responsible for the allergic reaction.

We reviewed all the cases of ACD due to cosmetics diagnosed at the Consorcio Hospital General Universitario de Valencia (CHGUV), Spain, between 2000 and 2007 in order to identify the offending allergens and determine their prevalence. We also wished to determine in which type of cosmetic products these allergens were generally used.

#### **Materials and Methods**

We searched the database maintained by the skin allergy unit at the dermatology department of the CHGUV for cases of ACD due to cosmetics diagnosed between January 2000 and October 2007. Of the 2485 patients patch tested during this period (using allergen series supplied by Martí Tor laboratories in Barcelona, Spain), 740 had been diagnosed with contact dermatitis and 202 of these with ACD due to cosmetics. For these 202 patients we recorded the sex of the patient, the source of sensitization (workplace/cosmetics use), the offending allergens, the cosmetic products containing these allergens, and the relevance of patch test positivity.

#### Results

We reviewed the cases of 202 patients (170 women and 32 men) diagnosed with ACD due to cosmetics. In these 202 patients, contact with cosmetic products such as hair dyes, creams, and soap was for personal use in 185 whereas it was occupational in 17 (6 hairdressers and 11 beauticians). There were 315 positive patch test results to 46 different allergens. Half (50.8%) of the positive results were detected using a standard allergen series and the rest were detected using the following series: preservatives and cosmetics (13%), perfumes (10.5%), hairdressing products (8.8%), acrylates (7%), plastics and glues (5.4%), and sunscreens (3.5%). The most common allergens detected were methylisothiazolinones (Kathon CG) (responsible for 19% of all positive results), paraphenylenediamine (PPD) (15.2%), fragrance mix (7.8%), Euxyl K-400 (5.6%), propyl gallate (5.6%), and toluenesulfonamide formaldehyde resin (5.6%) (Table 1).

The above allergens were found in hair dyes (18.5%), gels and creams (15.7%), moisturizing creams (12.7%), perfumes and colognes (9.2%), shampoos (8.9%), lipstick (8.6%), nail polish (6.8%), sunscreens (5.1%), black henna tattoos (5.1%), cleansing wipes (3.8%), deodorants (2.4%), after shave (0.7%), hair gels (0.7%), hair removal wax products (0.7%), and toothpaste (0.3%).

The 17 patients diagnosed with occupational ACD all had hand eczema. Of the 6 hairdressers in this group, 3 were found to be sensitized to PPD, 1 to PPD and 4-aminophenol, 1 to PPD and toluene-2,5-diamine sulfate, and 1 to methylisothiazolinones present in a shampoo. Of the 11 beauticians, 10 were sensitized to multiple acrylates and 1 to both colophony (hair removal wax) and toluenesulfonamide formaldehyde resin (nail polish) (Table 2).

The relevance of the patches was classified as present in all patients except 7, who had sensitization to PPD of past relevance.

### **Discussion**

In our review of ACD cases diagnosed at the CHGUV between January 2000 and October 2007, we found 2485 patients who had been patch tested; 740 were diagnosed with ACD and the cause was cosmetics in 202 (27.3%). The vast majority of patients were women (n=170).

Preservatives, PPD, and perfumes were the most common cosmetic sensitizers identified, a finding that is consistent with previously published data.<sup>5-7</sup> Half of the positive patch test results were detected using a standard allergen series. Of the 29 allergens contained in this series, the following can cause ACD due to cosmetics: PPD, fragrance mix, Kathon CG, Euxyl K-400, colophony, Peruvian balsam, formaldehyde, quaternium 15, lanolin alcohols, and paraben mix.

Table 1. Allergens Detected in Cosmetics Users in Order of Frequency and Cosmetic Products Containing These Allergens

Allergens (in Order of Frequency)	No. of Cases	Cosmetic Product No. of Case	
Kathon CG (methylchloroisothiazolinone and methylisothiazolinone)	54	Gel/soap Moisturizing cream Shampoo Cleansing wipes After shave Hair gel	24 14 13 6 2 1
Paraphenylenediamine (PPD)	43	Hair dye 28 Black henna tattoo 15	
Fragrance mix	22	Perfume 9 Gel/soap 5 Moisturizing cream 5 Shampoo 2 Deodorant 1 Hair gel 1	
Euxyl K-400 (phenoxyethanol and methyldibromo glutaronitrile or 1,2-dibromo-2,4-dicyanobutane)	16	Moisturizing cream7Cleansing wipes4Gel/soap2Make-up2Sunscreen1	
Propyl gallate	16	Lipstick	16
Toluenesulfonamide formaldehyde resin	16	Nail polish	16
Octyl gallate	9	Lipstick	9
3-Aminophenol	8	Hair dye	8
Toluene-2,5-diamine sulfate	7	Hair dye	7
Cocamidopropyl betaine	7	Shampoo Gel/soap	4 3
o-nitro-PPD	7	Hair dye	7
Geraniol	7	Cologne Gel/soap Shampoo Moisturizing cream	
Formaldehyde	6	Nair hardener Gel/soap Toothpaste Shampoo	
Quaternium 15	5	Shampoo 2 Moisturizing cream 1 Gel/soap 1 Deodorant 1	
Methyldibromo glutaronitrile	5	Moisturizing cream Cleansing wipes	4 1
4-Aminophenol	4	Hair dye	4
Hydroxycitronellal	4	Cologne Shampoo Moisturizing cream	
soeugenol	4	Gel/soap 2 Cologne 1 Deodorant 1	
Peruvian balsam	4	Moisturizing cream Deodorant Perfume	2 1 1

Table 1. Allergens Detected in Cosmetics Users in Order of Frequency and Cosmetic Products Containing These Allergens (Continuation)

Allergens (in Order of Frequency)	No. of Cases	Cosmetic Product	No. of Cases
Nitrocellulose	3	Nail polish	3
Geranium oil	3	Cologne	3
Lyral (hydroxyisohexyl 3-cyclohexene carboxaldehyde)	3	Deodorant Gel/soap	2 1
2-Ethylhexyl-4-methoxycinnamate	3	Sunscreen	3
Isopropyl myristate	3	Sunscreen	3
3-(4'-Methylbenzylidene) camphor	3	Sunscreen	3
4-Tert-butyl-4'-methoxy dibenzoylmethane	2	Sunscreen	2
2-Hydroxy-4-methoxybenzophenone	2	Sunscreen	2
Colophony	2	Hair removal wax	2
Eugenol	2	Cologne Deodorant	1 1
Oak moss absolute	2	Gel/soap Cologne	1 1
Bulgarian rose oil	2	Cologne Gel/soap	1 1
Cinnamic alcohol	1	Cologne	1
Synthetic jasmine	1	Gel/soap	1
Ylang-Ylang oil	1	Gel/soap	1
Musk ambrette	1	Cologne	1
Xylene musk	1	Cologne	1
Sandalwood oil	1	Cologne	1
Isoamyl p-methoxycinnamate	1	Sunscreen	1
2-Bromo-2-nitropropane-1,3-diol (bronopol)	1	Moisturizing cream	1
Paraben mix	1	Moisturizing cream	1

Preservatives are one of the most common types of allergen found in cosmetics. While newer molecules such as Kathon CG and Euxyl K-400 are less toxic than preservatives that have been used for years such as formaldehyde and paraben mix, they have been found to exhibit greater allergenic potential. Because cosmetic ingredients are listed by their INCI (International Nomenclature of Cosmetic Ingredients) name, we believe that it is important for health professionals to avoid using commercial names to prevent confusion among patients. Kathon CG, which contains 2 active ingredients, methylchloroisothiazolinone and methylisothiazolinone, is a very effective preservative found in numerous products such as moisturizing creams, gels, shampoos, and cleansing wipes. 9,10 In our series, it was the most common allergen in

patients with non-occupational ACD, occurring in 54 cases (Figure 1). Euxyl K-400, for its part, contains a mixture of phenoxyethanol and methyldibromo glutaronitrile (MDBGN), also known as 1,2-dibromo-2,4-dicyanobutane. Although the preservative contains 2 active ingredients, MDBGN tends to be responsible for the majority of sensitizations. In the preservative and cosmetic allergen series used in our group, the 2 ingredients are tested separately. We found 16 positive test results to Euxyl; 5 patients were tested with phenoxyethanol and MDBGN separately and in all 5 cases the offending allergen was MDBGN, with no positive results for phenoxyethanol. These findings are consistent with reports that almost all cases of sensitization to Euxyl are caused by MDBGN. We found 6 cases of sensitization to

formaldehyde. This substance used to be a common ingredient in cosmetic products but has now been largely replaced by preservatives that release formaldehyde in the presence of water. Examples are quaternium 15 (Figure 2), 2-bromo-2-nitropropane-1,3-diol (bronopol) diazolidinyl urea, imidazolidinyl urea, and diaminodiphenylmethane (DMDM) hydantoin. Quaternium 15 and bronopol were responsible for sensitization in 5 and 1 of our patients, respectively. Of the 315 positive patch test results detected in our review, just 1 was caused by a paraben, yet another indication that that these preservatives have been unfairly labeled as sensitizers. Parabens received such bad press that some cosmetics manufactures even claimed that their products were *paraben free*.

Together with preservatives, fragrances and perfumes rank among the most common allergens responsible for ACD due to cosmetics. In our series, we found 55 positive patch test results to perfumes (22 using the fragrance mix from the standard allergen series and 33 using the specific fragrance series). The 33 fragrances that caused sensitization from the specific series were geraniol (7 cases), hydroxycitronellal (4 cases), isoeugenol (4 cases), geranium oil (3 cases), Lyral or hydroxyisohexyl 3-cyclohexene carboxaldehyde (3 cases), oak moss absolute (2 cases), eugenol (2 cases), Bulgarian rose oil (2 cases), cinnamic alcohol (1 case), jasmine synthetic (1 case), ylang-ylang oil (1 case), musk ambrette (1 case), musk xylene (1 case), and sandalwood oil (1 case). It has been easier to evaluate the relevance of patch test positivity to a particular fragrance ever since European labeling regulations made it mandatory for manufacturers to indicate the presence of 26 potentially allergenic fragrances if the product contains more than 10 parts per million (ppm) in the case of leave-on cosmetics or more than 100 ppm in the case of rinse-off cosmetics.<sup>2,13</sup> Prior to this, the only indication on the product label was that it contained perfume. Several fragrances found to be responsible for photoallergic reactions in the 1970s were banned years ago. Nonetheless, we found 1 case of sensitization to such a fragrance (musk ambrette) with present relevance in a patient who had bought a cologne on the street.

PPD remains an important cause of ACD due to cosmetics, both at the workplace (hairdressers with hand eczema) and in the home (notably women with hair dye allergy) (Figure 3). In recent years, however, a new source of primary sensitization to PPD has emerged with the growing popularity of temporary black henna tattoos. In many cases, this allergy has affected children. <sup>14</sup> We are particularly concerned about this new source of sensitization and have notified the Spanish Pharmacovigilance System of this concern. <sup>15</sup> We found 43 cases of positive patch results to PPD, the second most common allergen among cosmetics users in our series; 28 of these results were detected in hair dye users and 15 in children who had had a

Table 2. Allergens in Occupational Contact Allergic Dermatitis Due to Cosmetics

Allergens -	Positive Patch Tests, No.	Cosmetic Product
Ethyleneglycol dimethacrylate	7	Artificial nails
Hydroxyethyl methacrylate	7	Artificial nails
Triethyleneglycol dimethacrylate	4	Artificial nails
n-Butyl acrylate	2	Artificial nails
1,4-Butanediol-dimethacrylate	1	Artificial nails
Tetraethyleneglycol dimethacryla	ate 1	Artificial nails
Paraphenylenediamine	5	Hair dye
Kathon CG	1	Shampoo
Colophony	1	Hair removal wax
Toluenesulfonamide formaldehyde resin	1	Nail polish
Toluene-2,5-diamine sulfate	1	Hair dye
4-Aminophenol	1	Hair dye





Figure 1. Allergic contact dermatitis due to a shower gel containing methylisothiazolinones, the most common allergens found in our review.





Figure 2. Allergic contact dermatitis due to quaternium 15 in a shampoo used by the patient.



Figure 3. Acute eczema caused by a hair dye containing parapheny-lenediamine.

black henna tattoo applied. Of the 17 patients with occupational ACD in our group, 5 were sensitized to PPD. Other hair dye allergens detected using the hairdressing allergen series were 3-aminophenol (8 cases), toluene-2,5-diamine sulfate, o-nitro-PPD (7 cases), and 4-aminophenol (5 cases).

Cocamidopropyl betaine (CAPD) is a surfactant that has been widely used as an ingredient in cosmetics. <sup>16</sup> In our review, we found 7 cases of ACD to CAPD, present in shampoo in 4 cases and in soap in 3. While CAPD seems to be less common than it used to be due to the growing use of other surfactants, there are still cases of patients who, though allergic to commercial CAPB, test negative to CAPB in patch testing but positive to 3-dimethylaminopropylamine (DMAPA), an intermediate molecule in CAPB synthesis. Many cases are unfortunately not diagnosed because DMAPA is not included in all cosmetic allergen series, even though it seems to be the main allergenic fraction in CAPB. <sup>17</sup>

While sunscreens rarely cause ACD, they are the most common cause of photoallergic contact dermatitis to cosmetics. <sup>18</sup> We found 11 positive tests to sunscreens in 6 patients, 4 of whom were diagnosed with photoallergic contact dermatitis. The allergens were 2-ethylhexyl-4-methoxycinnamate (3 cases), 3-(4'-methylbenzylidene) camphor (3 cases), 2-hydroxy-4-methoxybenzophenone (2 cases), 4-tert-butyl-4'-methoxydibenzoylmethane (2 cases), and isoamyl p-methoxycinnamate.

Acrylic resins, together with hair dyes, are the most common cause of occupational ACD, and the number of cases has increased in the last 6 years with the growing popularity of sculptured (artificial) nails. While beauticians are affected most often, people who wear these nails may also develop an allergic reaction. <sup>19</sup> Contact dermatitis due to acrylates tends to manifest as chronic eczema affecting the fingers and hands. It is a common cause of occupational

disability as these resins are capable of penetrating both rubber (vinyl) and plastic (nitryl) gloves. In our review, we found 10 beauticians with ACD due to acrylic resins (22 positive tests to 6 different allergens).

Of all the oxidants used in cosmetics, those that most frequently cause ACD are gallic acid esters (gallates), used above all in lipsticks. Although octyl gallate (E-311) has much greater sensitization potential than other gallates, in the current review, we detected almost twice as many positive results for propyl gallate (n=16) as for octyl gallate (n=9), supporting a recent finding by our group that positivity to propyl gallate was more common than that to either octyl or dodecyl gallate.<sup>20</sup>

Toluenesulfonamide formaldehyde resin, also known as tosylamide or arylsulfonamide, is the main allergen responsible for contact dermatitis due to nail polish<sup>21</sup> (Figure 4). In our review, we found 16 positive patch test results, making this resin the fourth most common allergen outside the workplace, together with Euxyl K-400 and propyl gallate. Other allergens present in nail polish in our series were formaldehyde (as a component of nail hardener) and nitrocellulose (3 cases).

Peruvian balsam may occasionally serve as a marker of allergy to perfumes. <sup>22,23</sup> In our review of patients with ACD due to cosmetics, it yielded 4 positive patch test results. In 2 patients, it was present in a moisturizing cream; one of these patients also tested positive for a fragrance mix and the other for fragrance mix and isoeugenol. In the other 2 patients, balsam had been found in a perfume and a deodorant and the patients in those cases also tested positive for isoeugenol and for eugenol and isoeugenol, respectively. Colophony (a hair wax removal product ingredient) yielded positive patch test results in 3 patients: 1 beautician and 2 normal users. <sup>24</sup>

Emerging cosmetic allergens are not found in standard allergen series and can only be identified with the help of the firm that manufactures and distributes the suspect product. An example of such an allergen is dicaprylyl maleate, also known as dioctyl maleate. Although initial tests on this ingredient showed low irritant potential and inability to cause ACD, several authors have since reported that dicaprylyl maleate in moisturizing and sunscreen products has allergenic potential.<sup>25</sup> The most recent report was from a multicenter study involving 22 patients, most of whom had used products from the same manufacturer.<sup>26</sup> The manufacturer collaborated with the authors of the study by supplying them with the ingredient. Based on the results of the study, the company began to withdraw all its products containing dicaprylyl maleate from the market in 2003. We identified 3 cases of ACD (2 due to eye liner and 1 to mascara) in which we were unable to determine the offending allergens, either because they did not appear on the product label or because not all of the ingredients were available for analysis.





Figure 4. Contact eczema caused by nail polish containing toluenesulfonamide formaldehyde resin. This was an airborne form of contact dermatitis and therefore affected the eyelids, cheeks, and perioral area, but not the fingers.

Finally, we would like to highlight the fact that the mandatory labeling of cosmetic ingredients introduced in Europe in 1997 (and in force in the United States since the 1970s) has improved the prognosis of patients with ACD. We would also like to emphasize the important role that manufacturers can play by aiding researchers in their identification of emerging allergens responsible for ACD.

#### **Conflicts of Interest**

The authors declare no conflicts of interest.

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