

Allergic contact dermatitis caused by phenylethyl resorcinol, a skin-lightening agent contained in a sunscreen

María-Antonia Pastor-Nieto¹, Paloma Sánchez-Pedreño², Teresa Martínez-Menchón², Virginia Melgar-Molero¹, Francisco Alcántara-Nicolás¹ and Pablo de la Cruz-Murie³

¹Dermatology Department, University Hospital of Guadalajara, 19002 Guadalajara, Spain, ²Dermatology Department, University Clinical Hospital Virgen de la Arrixaca, 30120 Murcia, Spain, and ³Pharmacy Department, University Clinical Hospital Virgen de la Arrixaca, 30120 Murcia, Spain

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Phenylethyl resorcinol (CAS no. 85-27-8), a dihydroxylated diphenylmethane derivative with potent tyrosinase inhibitory activity, has been reported to be one of the strongest skin-lightening agents (1). Two new cases of allergic contact dermatitis caused by phenylethyl resorcinol contained in a sunscreen are reported.

Case Reports

Case 1

A 30-year-old woman, working as a hairdresser, presented with erythematous lichenified plaques initially involving her upper lip and progressively spreading to her face (Fig. 1). She was very self-conscious about melasma on her upper lip, which is why she had been applying a sunscreen intended to be used in patients with melasma or hyperpigmentation (Foto Ultra 100 Active Unify Fusion

Fluid®; Isdin, Barcelona, Spain) several times a day on that location for 2 months. Patch tests with the baseline standard Spanish Contact Dermatitis Research Group (GEIDAC), cosmetic, hairdresser and fragrance series (AllergeAZE, Calgary, Canada) and the patient's own products were performed. Positive results were obtained only with the sunscreen 'as is' (3+) on day (D) 2 and D4.

Patch tests were performed with dilutions of the individual ingredients provided by the manufacturer and the sunscreen series, and positive results were obtained with phenylethyl resorcinol in pet. (Fig. 2). The manufacturer confirmed that the concentrations of the provided ingredients were equivalent to the concentrations used in the original product, and stated that the phenylethyl resorcinol concentration was <0.5%. Patch testing in 10 controls gave negative results.

Case 2

A 50-year-old woman with allergic rhinitis came to the emergency room with a facial reaction that the patient attributed to the application of a sunscreen.

Patch tests with the baseline standard GEIDAC and sunscreen Series (Chemotechnique, Vellinge, Sweden) and the patient's sunscreen (Foto Ultra 100 Active Unify

Correspondence: Maria Antonia Pastor-Nieto, Dermatology Department, University Hospital of Guadalajara, C/ Donantes de Sangre s/n, 19002 Guadalajara, Spain. Tel. +0034 949209200 ext. 69435. E-mail: mapastornieto@gmail.com

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Fig. 1. Erythematous lichenified scaly plaques involving the upper lip, eyelids, forehead, nasal bridge, and cheeks. The lesions developed 2 months after the patient had started to apply a sunscreen on her face on a daily basis. Other observations were: (i) very symmetrical eyelid involvement; (ii) recurrence of the rash every time that the patient was patch tested with either the product or the culprit ingredient; and (iii) persistence of the positive reactions for > 3 weeks, which is why we diagnosed a potential component of systemic dermatitis resulting from percutaneous absorption.

Fusion Fluid®; Isdin) 'as is' were performed. Positive results were obtained with the sunscreen (3+ on D4).

The manufacturer provided the raw ingredients, which were appropriately diluted for patch testing. Two percent phenylethyl resorcinol in pet. gave a positive result (3+) on D4. Patch testing in 5 controls gave negative results.

Discussion

Sensitization from phenylethyl resorcinol contained in a skin-lightening essence involving a Japanese woman was first reported in 2013 (2). To the best of our knowledge, no other cases have been published thus far.

Nineteen cases of contact dermatitis caused by depigmenting agents in cosmetics have been published in 14 reports, all involving middle-aged women (2–14). The incriminated bleaching molecules were quite diverse. All cases were caused by lightening creams, except for the 2 cases reported herein, which were caused by a sunscreen (Table 1).

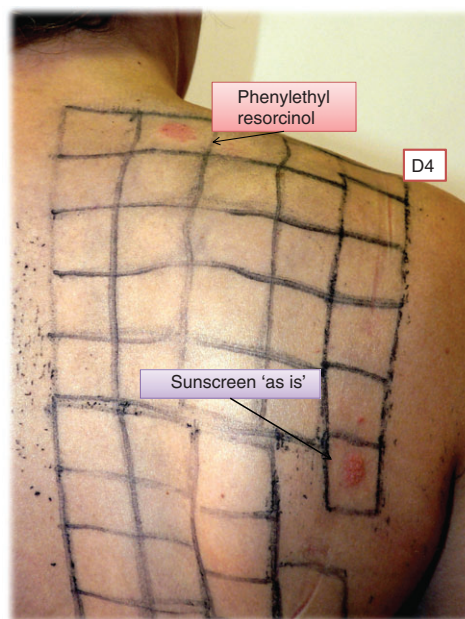


Fig. 2. Patch tests gave positive results with the patient's sunscreen 'as is' and with phenylethyl resorcinol in pet. (at a concentration below 0.5%).

Almost all cases have been reported by either Japanese or Spanish authors. Whether this might reflect regional exposure differences is uncertain, although it is likely that the use of bleaching agents is more widespread in populations with a darker complexion, who are more prone to developing melasma or hyperpigmentation. Ingredients of 338 products in terms of sunscreen, 'anti-ageing' and skin-lightening of 15 dermocosmetic brands available in Spain were assessed in order to determine the presence of resorcinol derivatives with skin-lightening properties (phenylethyl resorcinol, hexyl resorcinol, and butyl resorcinol) (Table 2).

Half of the brands and 36% of the skin-lightening products contained some of the three derivatives. Butyl resorcinol was the most frequently found in skin-lightening creams (almost 20%). Phenylethyl resorcinol was found in only six (1.7%) products from three different brands (four skin-lightening products and two sunscreens, including the culprit product in both presented cases). No other sunscreens were found to contain any of the three substances. Very few products other than skin-lightening products contained resorcinol derivatives. It is important to note, however, that neither hexyl resorcinol nor butyl resorcinol have been incriminated in any cases of contact dermatitis thus far.

Table 1. Literature review on contact dermatitis caused by depigmenting agents in cosmetics. All patients were female.

Skin-lightening agent	Author	Year	Country	Age (years)	Clinical context	Culprit product/ peculiarity
Hydroquinone	Barrientos et al. (3)	2001	Spain	47	Post-peeling	Skin-lightening
	Tatebayashi et al. (4)	2014	Japan	50	–	Skin-lightening/ pigmentation
Kojic acid	Nakagawa et al. (5)	1994	Japan	37, 37, 42, 58, 34	Cloasma (4) Pigmentation (1)	Skin-lightening
	Mata (7)	2005	Spain	40	Post-sclerotherapy postinflammatory hyperpigmentation	Skin-lightening
	Serra-Baldrich et al. (6)	1998	Spain	30	Post-sclerotherapy postinflammatory hyperpigmentation	Skin-lightening
	García-Gavín et al. (8)	2010	Spain	54	Lentigines	Skin-lightening/ pigmentation
Arbutin	Matsuo et al. (9)	2015	Japan	61	–	Skin-lightening
Vitamin C (3-o-ethyl-L-ascorbic acid)	Yagami et al. (10)	2014	Japan	49	–	Skin-lightening
Methyl gentisate	Gallo and Baldari (11)	2006	Italy	38	–	Skin-lightening
	Serra-Baldrich et al. (12)	2009	Spain	44	Melasma	Skin-lightening
5,5'-Dipropylbiphenyl-2, 2'-diol	Suzuki et al. (13)	2011	Japan	45	–	Skin-lightening
	Yagami et al. (14)	2015	Japan	64	–	Skin-lightening
Phenylethyl resorcinol [4-(1-phenylethyl)-1, 3-benzenediol]	Gohara et al. (2)	2013	Japan	52	–	Skin-lightening
	Sánchez-Pedreño	2015	Spain	50	–	Sunscreen
	Pastor-Nieto	2015	Spain	30	Melasma	Sunscreen

Table 2. Assessment of the presence of resorcinol derivatives with skin lightening properties in dermocosmetics available in Spain

Dermocosmetic products in Spain	Sunscreens, n (%)	Anti-ageing, n (%)	Skin-lightening, n (%)	Products, n (%)	Brands, n (%)
With PER	2 (1.2)	0	4 (11)	6 (1.8)	3 (18.7)
With HR	0	2 (1.4)	2 (5.6)	4 (1.2)	2 (12.5)
With BR	0	0	7 (19.4)	7 (2.1)	3 (18.7)
With some resorcinol derivative	2 (1.2)	2 (1.4)	13 (36)	17 (5)	8 (50)
Total	160	142	36	338	16

BR, butyl resorcinol; HR, hexyl resorcinol; PER, phenylethyl resorcinol.

To conclude, we would like to address the following aspects:

1. The newly developed depigmenting molecule phenylethyl resorcinol has been found not only in skin-lightening products but also in sunscreens, and is able to induce allergic contact dermatitis.
2. With the use of sunscreens aimed at a hugely varied profile of users with specific individual needs and the consequent diversification of ingredients, it is likely that we will eventually see cases caused by new components used for purposes other than photoprotection itself. Thus, the currently available

sunscreen series might be insufficient to diagnose these cases.

3. Patch testing the patient with both the suspected products and the individual ingredients provided by the manufacturers is often indispensable for diagnosing new allergens.

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