

Multiple contact allergies to benzophenones

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Sunscreen ingredients are known to induce adverse effects (1). Benzophenones have been used for more than 50 years, and are well-known allergens (2). Several case reports have described contact or photocontact allergy to a single benzophenone. We describe a case of contact sensitization to three different benzophenones in a patient with atopic and chronic actinic dermatitis.

Case Report

A 51-year-old man with a life-long history of atopic dermatitis developed increasing photosensitivity over a period of 10 years. His dermatitis, localized to his face, neck, and arms, was almost constantly active and evolved into chronic actinic dermatitis. Moreover, he also presented with several distinct episodes of acute oozing dermatitis starting 12–24 hr after sun exposure with sunscreen use, requiring courses of oral prednisone. Patch testing and photopatch testing were performed in February 2011. The patient was tested with the North American Contact Dermatitis Group

baseline series and photoallergens series (AllergEAZETTM; SmartPractice[®], Calgary, Canada) applied on Finn Chambers[®] (SmartPractice[®], Phoenix, AZ, USA). He was also tested with his own sunscreens (Neutrogena UltraSheer[®] SPF 85 and Aveeno[®] SPF 60) applied on IQ Ultra[®] chambers (Chemotechnique Diagnostics AB, Vellinge, Sweden) (Table 1). At D1, one set of photopatch allergens was irradiated with 5 J/cm² of ultraviolet A light (UVA). The patches were removed at D2, and the reactions were recorded according to the criteria of the International Contact Dermatitis Research Group at D2 and D4.

The patient had definite positive reactions to benzophenone-3, benzophenone-4, benzophenone-8, triethanolamine salicylate, and his own sunscreens, both of which contain benzophenone-3. Reactivity to methylisothiazolinone was attributed to its presence in Neutrogena UltraSheer[®] sunscreen. Reactivity to colophonium was attributed to past allergic reactions to adhesive dressings. Also, the positive test reaction to triethanolamine salicylate was probably related to past exposure to various other sunscreens. Reactions to thiuram mix and epoxy resin were of undetermined relevance. No photoallergy was shown; all positive reactions were of equal intensity on the irradiated and on the non-irradiated sides. Photosensitivity was obvious, as the patient developed a widespread macular erythema over the entire area that was irradiated with 5 J/cm²

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Table 1. Patch test and photopatch test results

Allergen	Concentration	D2	D4
Baseline series			
Colophonium	20%	2+	2+
Thiuram mix	1%	1+	1+
Bisphenol A epoxy resin	1%	2+	2+
Benzophenone-3	10%	1+	2+
Methylisothiazolinone	200 ppm	—	1+
Photoallergens			
Benzophenone-4	10%	—	1+
Benzophenone-3	10%	—	1+
Benzophenone-8	2%	?	1+
TEA salicylate	5%	—	1+
Own products			
Neutrogena UltraSheer® SPF 85	100%	1+	1+
Aveeno® SPF 60	100%	1+	1+

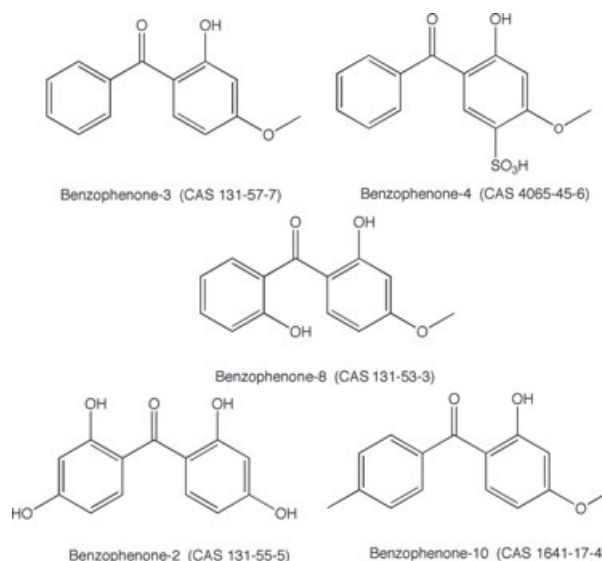
Photopatch testing was performed with ultraviolet A light (5 J/cm²) at D1. All allergens in pet. apart from methylisothiazolinone (aq.)

of UVA. Diagnoses of atopic dermatitis, chronic actinic dermatitis and superimposed allergic contact dermatitis were established on the basis of the clinical presentation, photosensitivity, and multiple contact sensitizations (3). A more comprehensive investigation of the patient's photosensitivity will be carried out at a later date.

Discussion

Benzophenones are chemical ultraviolet filters that are widely incorporated in sunscreens, facial make-up, shampoos, hair sprays and conditioners, lipsticks, and moisturizers. They are also used as preservatives to reduce photodegradation and extend the shelf-life of personal hygiene products, textile, paints, plastics, and rubber products (4, 5).

Benzophenone-3 (oxybenzone), benzophenone-4 (sulizobenzene), benzophenone-8 (dioxybenzone) and benzophenone-10 (mexenone) may be present in sunscreens and cosmetics, with benzophenone-3 being the most frequently used. Recent studies have identified benzophenones as the main sunscreen ingredients giving positive photopatch test results (6). Benzophenone-3 has been responsible for the greatest number of adverse cutaneous reactions, including contact and photocontact dermatitis, contact and photocontact urticaria, and even anaphylaxis (5). Benzophenone-4, which is commonly used in sunscreens, and other cosmetics including hair care products, has been shown in the past few years to be an emergent allergen (4). Cross-reactions between benzophenones are said to occur, but have not been well documented in the current literature (7).

**Fig. 1.** Chemical structures of tested benzophenones.

Our patient had positive patch test reactions to three different benzophenones. Reactivity to benzophenone-3 was of definite relevance, because of its presence in his own sunscreens. A concomitant reaction resulting from previous exposure to benzophenone-4 is possible, because of its ubiquitous presence in cosmetics and hair care products. However, the patient could not recall previous exposure to benzophenone-8.

Interestingly, these three benzophenones share a rather similar molecular structure (Fig. 1). Thus, it is also possible that our patient, having been sensitized to benzophenone-3, exhibited cross-reactions to benzophenone-4 and benzophenone-8. He did not react to benzophenone-2 and benzophenone-10, presumably because of structural differences from the other compounds. We could thus hypothesize that the hydroxyl substitutions at positions 2' and 4' of benzophenone-2 may have prevented its recognition by antigen-presenting cells. Such an assumption is more difficult to put forward with respect to potential cross-reactions with benzophenone-10, which does not differ much from benzophenone-3, benzophenone-4, and benzophenone-8. The retesting technique described by Rustemeyer et al. could prove to be a valuable tool with which to clarify the existence of cross-reactions between benzophenones (8). In order to establish the actual prevalence of such cross-reactions, we suggest that patch and photopatch test series of sunscreen ingredients should include all of the commonly used benzophenones.

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