

Positive photocontact responses are not elicited to sunscreen ingredients exposed to UVA prior to application onto the skin

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Photocontact allergic reactions to sunscreen chemicals are investigated by photopatch testing. It has generally been assumed that for photocontact allergy to be shown, the putative pro-allergen must be in the skin at the time of ultraviolet A (UVA) exposure. However, this assumption has not, to our knowledge, been tested. The objective of this study was to determine whether positive photocontact responses can still be elicited when sunscreen chemicals are exposed to UVA prior to application onto the skin. 3 patients known to have positive photocontact reactions to a total of 6 sunscreen chemicals were studied. For conventional photopatch testing, patch test strips were applied onto the back and removed 1 D later, and the area was irradiated with UVA (5 J/cm²). For pre-irradiated testing, patches were exposed to the same dose of UVA immediately before application onto the back and then removed 1 D later. Skin responses were visually assessed by a blinded investigator 1 and 2 D after patch test removal. The same photocontact responses of the same magnitude, as previously documented for each patient, were seen at each of the conventional UVA-exposed patch test sites. However, in no patient was a positive response elicited at any of the sites where pre-irradiated patches had been applied. This study shows that positive photocontact responses to sunscreen chemicals do not occur when the putative pro-allergen is irradiated prior to application onto the skin. This suggests that for a photoallergic reaction to occur, the sunscreen chemical needs to be within the skin when activated by UVA.

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Allergic reactions to sunscreens are rare but clinically important (1–5). They may be because of photocontact allergy, where no problem occurs at the time the sunscreen is applied to the skin; the reaction develops only when sunlight has activated or degraded the chemical in question, rendering it allergenic. Suspected allergy to sunscreen chemicals is investigated by photopatch testing (1).

It has generally been assumed that for photocontact allergy to be shown, the putative pro-allergen must be in the skin at the time of ultraviolet A (UVA) exposure. However, this assumption has not, to our knowledge, been tested.

We performed a study to see if positive photocontact results could still be obtained if the sunscreen ingredients were exposed to UVA prior to application onto the skin. If this were shown to be the case, it would alter our understanding of the

photocontact allergy mechanism and might allow modification of the technique of photopatch testing.

Materials and Methods

This study was approved by the Newcastle and North Tyneside Local Research Ethics Committee. From a database of patients investigated for suspected photosensitivity, we identified individuals in whom we had found a strong (++) (1) positive photocontact reaction to 1 or more sunscreen chemicals and who were also known to have normal minimal erythema responses on irradiation monochromator phototesting and no additional photosensitive disorder such as polymorphic light eruption or chronic actinic dermatitis. We wrote to all 12 of these patients and 3 agreed to participate in the study (Table 1). None of the patients

Table 1. Baseline characteristics of patients

	Patient 1	Patient 2	Patient 3
Age (in years) (sex)	57 (female)	35 (male)	14 (male)
Sunscreen chemical allergies and strength of historical photopatch test result (1)	Benzophenone 3 (++) and benzophenone 4 (++)	Octyl methoxycinnamate (++) and butylmethoxy dibenzoylmethane (++)	Octyl dimethyl PABA (++) and PABA (++)

PABA, para-amino benzoic acid.

was taking immunosuppressive therapy, and none had received significant sun exposure to their back in the 3 months prior to the study.

A photopatch testing schedule (Table 2) was designed to allow conventional photopatch testing (to confirm that the patients were still allergic to the sunscreen chemicals) and also for pre-irradiated patch testing, using 2 radiation sources, with readings at 1 and 2 D after patch test removal.

In each patient, only the previously confirmed photoallergen(s) was tested. A 5 mm length of the commercially available allergen in petrolatum (Trolab, Reinbeck, Germany; info@hermal.de) was dispensed from the supplied 2-ml syringe onto a Finn Chamber (Epitest Ltd, Tuusula, Finland) mounted on Scanpor Tape (Norgesplaster, Vennesla, Norway). The allergen was dispersed on the Finn Chamber to achieve a thin film prior to irradiation or application to the back.

2 radiation sources were used to deliver 5 J/cm² of UVA (Table 2):

- (1) An irradiation monochromator coupled to a xenon arc lamp was set to a central wavelength of 350 nm (bandwidth of ± 15 nm or

30 nm) and the radiation passed through an optical filter (WG335) and then through a 5 mm internal diameter liquid-filled light guide (5). Irradiance was measured using a calibrated thermopile. For conventional photopatch testing, the patch test strip was removed from the patient's back, any excess allergen removed by wiping the skin, and the area was then irradiated using the light guide. For the pre-irradiated testing, the patch test strips were placed immediately below the distal end of the light guide during irradiation.

- (2) A bank of 8 UVA fluorescent lamps (TL-09; Philips, Eindhoven, The Netherlands) were used to pre-irradiate 2 of the patch test strips. Irradiance was measured using a calibrated radiometer, and the patches were placed 10 cm from the lamps during irradiation.

All patch test strips were applied to the patient's back, avoiding the immediate paravertebral area. Each patient had a total of 6 patches applied for each allergen under test (2 for conventional

Table 2. A summary of the conventional and pre-irradiated photopatch test protocols

Site number and description	Day			
	1	2	3	4
Control (unirradiated) patch	Apply patch	Remove patch		Read result
Conventional photopatch testing	Apply patch	Remove patch; skin wiped and exposed to UVA (5 J/cm ²) using an irradiation monochromator		Read result
Pre-irradiated photopatch testing, read 2 D after removal of patches	2 sets of each patch applied: (1) 1 set pre-irradiated with UVA (5 J/cm ²) using an irradiation monochromator and (2) 1 set pre-irradiated with UVA (5 J/cm ²) using a bank of fluorescent lamps		Remove patches	Read result
Pre-irradiated photopatch testing, read 1 D after removal of patches		2 sets of each patch applied: (1) 1 set pre-irradiated with UVA (5 J/cm ²) using an irradiation monochromator and (2) 1 set pre-irradiated with UVA (5 J/cm ²) using a bank of fluorescent lamps	Remove patch	Read result

UVA, ultraviolet A.

photopatch testing and 4 for pre-irradiated testing) (Table 2). Skin responses were assessed by a blinded investigator and graded using conventional methodology (1).

Results

Each patient completed the study. The same photocontact reactions of the same magnitude as previously documented for each patient (++) (Table 1) were shown at each of the conventional UVA-exposed patch test sites. However, in no patient was a positive response elicited at any of the sites where pre-irradiated patches had been applied (Fig. 1).

Discussion

We have shown for 6 sunscreen chemicals that positive photopatch test results are not obtained when the putative allergen is irradiated prior to application onto the skin.

Using 2 different irradiation sources and by paying attention to the irradiation geometry and dosimetry, we aimed to maximize the chance of finding a positive result with pre-irradiation of the test samples. Fluorescence of each sunscreen sample was easily observed during irradiation, indicating that some photochemical process was occurring. Although we only studied 3 patients and 6 allergens, the results clearly indicate that for these allergens at least, the chemical must be within the skin at the time of irradiation for a positive photopatch test result to be obtained. This suggests that the active and potentially allergenic photoproduct is either short-lived and therefore has to be within the skin at the time of its production to achieve a biological effect or is only produced when the sunscreen is dispersed within the stratum corneum.

The stability of a sunscreen product when exposed to ultraviolet (UV) is important both in terms of maintaining efficacy during use and with regards to allergenic potential. The photostability of UV-absorbing chemicals can also be influenced by the vehicle or the solute used in the sunscreen formulation (6). Following UV exposure, sunscreen chemicals may undergo photofragmentation or photoisomerization as well as producing free radicals or other reactive intermediates (6). Which of these potential changes is important for the pathogenesis of photoallergy is currently unknown.

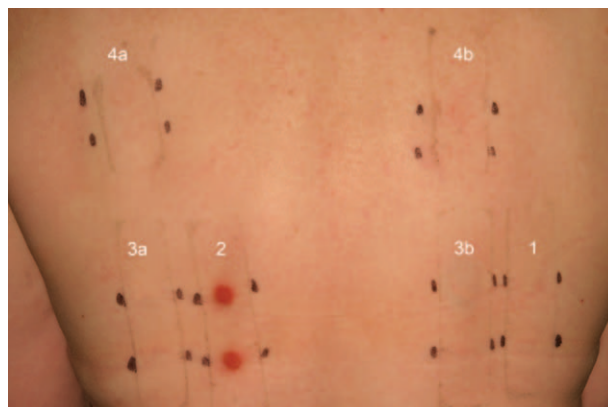


Fig. 1. Results from patient 1 who was tested to benzophenone 3 (upper test site in each pair) and benzophenone 4. Site 1: no reaction at control (unirradiated) patches. Site 2: strong (++) (1) positive reaction at the conventional UVA-exposed patch test site. Sites 3a–4b: no reaction at any site where pre-irradiated patches were applied, using either the irradiation monochromator (3a and 4a) or the bank of fluorescent lamps (3b and 4b), with readings at 2 D (3a and 3b) or at 1 D (4a and 4b) after removal of patches. UVA, ultraviolet A.

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