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Photoallergic Contact Dermatitis due to Combined UVB (4-Methylbenzylidene Camphor/Octyl Methoxycinnamate) and UVA (Benzophenone-3/Butyl Methoxydibenzoylmethane) Absorber Sensitization

Key Words

Photoallergic contact dermatitis
4-Methylbenzylidene camphor
Octyl methoxycinnamate
Benzophenone-3
Butyl methoxydibenzoylmethane
Mexoryl® SX

Abstract

In a 71-year-old male Caucasian patient with persistent eczema on light-exposed skin, photocontact allergy was demonstrated to the UV filter substances 4-methylbenzylidene camphor (UVB), octyl methoxycinnamate (UVB), benzophenone-3 (UVA) and butyl methoxydibenzoylmethane (UVA) present in sunscreen products used by the patient over several years. A significantly reduced UVB sensitivity of 25 mJ/cm² in this patient (normal minimal erythema dose in our laboratory = 70–130 mJ/cm²) was considered an early indication of a persistent light reaction. Topical anti-inflammatory treatment over 2 weeks together with consequent application of a sunscreen containing Mexoryl® SX/titanium dioxide led to complete remission. Taking into account the widespread use of the above UV filter substances not only in sun protection products, but also in cosmetics such as antiaging lotions and day care products, the possible risk of allergy to these chemicals has to be taken seriously. The substitution of known photocontact sensitizers in UV filters by photostable compounds and detailed product information are the basis of preventive strategies.

Introduction

The rising awareness of the western population regarding the UV-radiation-related risks of skin cancer and aging resulted in a tremendous increase in the application of sunscreen products [1]. These UV filter substances are furthermore common ingredients of textiles and other colored products for protection against light-dependent degradation [2, 3]. At the same time, numerous publications reported photoallergic skin reactions, identifying UV filter chemicals as the relevant photoallergens in the majority of the cases and not so much other ingredients as perfumes or preservatives [4–8]. Studies of the Department of Dermatology of the University Hospital of Göttingen and the German Working Group on Photopatch Testing revealed a high rate of positive patch test reactions to the UV filter compounds 4-iso-

propyldibenzoylmethane, 3-(4'-methylbenzylidene) camphor and benzophenone-3 with cross-reactions to structurally similar substances [8–10].

Case Report

History

We present the case of a 71-year-old Caucasian man (skin type III) with a 5-month history of persisting eczema on light-exposed skin, which had appeared for the first time during a skiing vacation. There was neither any evidence of atopy in the patient's history nor of any other UV-related dermatosis or systemic medication. To protect himself from sunburn, the patient had, as on several occasions in previous years, applied Piz Buin sunscreen products (Piz Buin Sonnenmilch SF 10, Piz Buin Sun Stick SF 10, Piz Buin Clas-

sic Brown Bräunungsmilch SF 2; Piz Buin-Greiter AG, Altstätten, Switzerland/Johnson & Johnson GmbH, Bad Honef, Germany).

The application of the above products, however, did not prevent the occurrence of eczematous lesions on the face, the neck and the back of both hands.

Dermatological Examination

Clinical examination revealed pruritic eczematous lesions with hazy delimitation restricted to the light-exposed skin areas. These showed numerous papules and papulovesicles, mild exudation as well as lichenification and lamellar white scaling. Areas that were protected by the patient's sun glasses, the submental triangle and the retroauricular region showed no alterations (fig. 1, 2).

Complete and persistent healing was achieved after an anti-inflammatory treatment lasting 2 weeks supported by conse-

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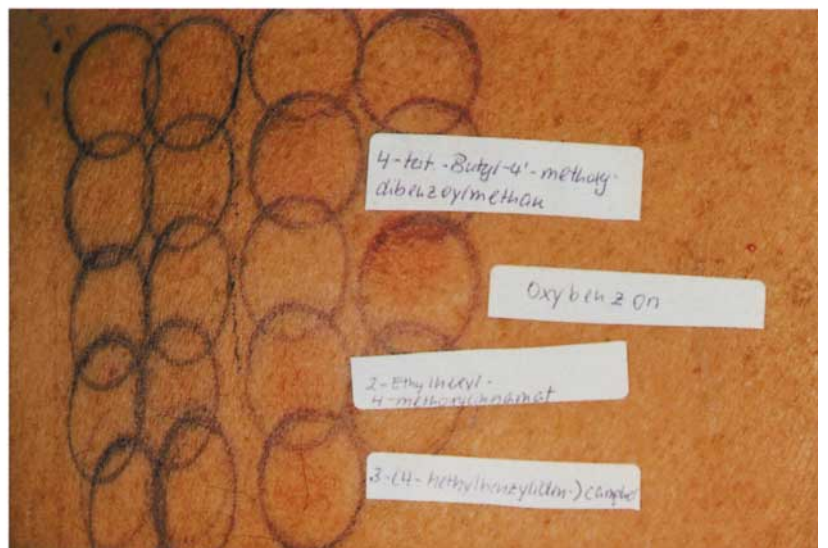
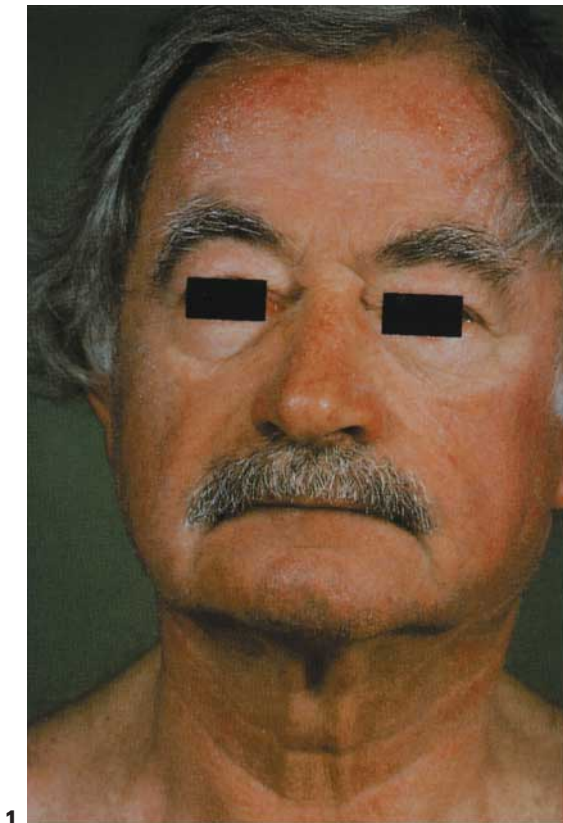


Fig. 1. Eczematous lesions exclusively restricted to light-exposed skin sites with sun-protected regions being spared.

Fig. 2. Eczematous lesions show marked lichenification and scaling. There is no sharp but hazy delimitation characteristic of a photoallergic contact reaction.

Fig. 3. Positive photopatch test reaction to benzophenone-3, butyl methoxydibenzoylmethane, octyl methoxycinnamate and 4-methylbenzylidene camphor.

quent application of Mexoryl® SX, a new photostable UVA filter, combined with titanium dioxide, a physical UVB/UVA filter (Anthelios® T) onto the eczematous skin lesions.

Laboratory Analysis

Laboratory tests including autoantibody screening did not reveal any significant abnormalities.

Determination of Minimal Erythema Dose for UVA and UVB

The patient's individual UV sensitivity was determined by phototesting of non-light-exposed gluteal skin with radiation doses ranging from 25 to 200 mJ/cm² and 5–40 mJ/cm² for UVB and 30–48 J/cm² for UVA, respectively. The tests were carried out with the UV 800 K detector (Waldmann, Villingen-Schwenningen, Germany) equipped

with UVA fluorescent illuminators TL-K 40W/09 emitting a radiation spectrum of 320–365 nm with a corresponding maximum at 355–365 nm and UVB illuminators TL 20W/12 emitting a spectrum ranging from 285 to 350 nm with a maximum at 310–315 nm. Based on the detected average UVA/UVB minimal erythema dose (MED) the doses for further phototesting were determined.

Table 1. Equipment and modalities for experimental reproduction of lesions in persistent light reaction

Location	nonaffected non-light-exposed skin
Size of test area	5×8 cm
UV emitters	UVA fluorescent illuminator TL-K 40W/09 (Phillips) UVB fluorescent illuminator TL 20W/12 (Phillips) visible light diaprojector (Leitz) with filter GG 420
UV doses	UVA: 1, 10, 30 J/cm ² UVB: 0.5, 1, 1.5×UVB MED visible light: 30 J/cm ²
Readings	24, 48, 72 h following irradiation performed on 3 consecutive days

Table 2. Results of photopatch and patch testing

No.	Substances	Concentration %	Patch test 24–96 h	Photopatch test		
				24 h	48 h	72 h
1	tetrachlorosalicylanilide	0.1	–	–		
2	bromosalicylanilide	1.0	–	–		
3	hexachlorophene	1.0	–	–		
4	bithionol	1.0	–	–		
5	sulfanilamide	5.0	–	–		
6	promethazine	0.1	–	–		
7	quinidine sulfate	1.0	–	–		
8	musk ambrette	5.0	–	–		
9	perfume mix	8.0	–	–		
10	<i>p</i> -aminobenzoic acid	10.0	–	–		
11	2-ethylhexyl- <i>p</i> -dimethylaminobenzoate	10.0	–	–		
12	1-(4-isopropylphenyl)-3-phenyl-1,3-propanedione	10.0	–	–		
13	4- <i>tert</i> -butyl-4'-methoxydibenzoylmethane	10.0	–	+	++	++
14	<i>p</i> -methoxycinnamonic acid isoamylate	10.0	–	–		
15	2-ethylhexyl- <i>p</i> -methoxycinnamate ¹	10.0	–	++	+++	+++
16	3-(4-methylbenzylidene) camphor ¹	10.0	–	+	++	++
17	phenylbenzimidazolesulfone acid	10.0	–	–		
18	2-hydroxy-4-methoxybenzophenone ¹	10.0	–	+	++	+++
19	sulisobenzone	10.0	–	–		

–=No reaction; +=erythema; ++=erythema, infiltration; +++=erythema, infiltration, papular vesicles.

¹ Ingredients of the sun protection products used by our patient.

Photoprovocative Testing

Phototesting was performed on 5×8 cm test fields of nonaffected and non-light-exposed skin of the gluteal region. Test fields were exposed to increasing doses of UVA (1, 10, 30 J/cm²) and UVB irradiation (0.5, 1, 1.5×UVB MED) on 3 successive days. To test the response of the patient to visible radiation we used a Leitz slide projector combined with an absorption filter (Schott GG 420) and a dose of 30 J/cm² was given. Results were read immediately after each irradiation and 24, 48, 72 h and 7 days after provocation (table 1).

Contact and Photoallergy Patch Tests

Apart from the standard patch test series of the German Contact Allergy Group, the substances listed in table 2 were used for photopatch tests, which were carried out in accordance with the standards of the German Working Group on Photopatch Testing [11, 12] featuring a test block (Hermal), which was attached to the left and right sides of the patient's back using the Finn chamber technique. The first reading was done after 24 h with subsequent UVA irradiation of *one* test block with the UV Test (Waldmann), equipped with fluorescent illuminators TL-K 40/12

and a dose of 10 J/cm², i.e. a dose well below the patient's UVA MED. A first reading of the irradiated test block was done after 20 min followed by further readings of *both* test blocks after 24, 48 and 72 h.

Results

Phototesting

The UVB MED was significantly reduced to 25 mJ/cm² (normal values in our laboratory: 70–130 mJ/cm²). The UVA MED was within normal limits.

Moreover test fields of photoprovocation revealed dermatitis with eruption of pruritic papulovesicles in two of the three UVB test sites (1, 1.5×UVB MED) 2 days after cessation of irradiation. No evidence of porphyria or other photoaggravated skin diseases including photoinduced dermatitis to UVA irradiation or visible light was observed in later readings at the other photoprovocation test sites.

Patch and Photopatch Testing

Positive skin reactions (from ++ to +++) were provoked by the UVA filter substances benzophenone-3 and butyl methoxydibenzoylmethane as well as by the UVB filter substances 4-methylbenzylidene camphor and octyl methoxycinnamate on the irradiated test sites only, whereas no skin reactions were observed on the nonirradiated test sites (table 2). The same positive skin reactions were demonstrated in parallel test series carried out with the sun care products used by our patient.

As the products used by our patient contain combinations of the above UV filter substances [9], the findings were regarded to be clinically relevant.

Therapy and Clinical Outcome

Complete and persistent healing of photoallergic contact dermatitis was achieved by short-term treatment with topical corticosteroids supported by consequent application of Mexoryl® SX, a new photostable UVA filter, combined with titanium dioxide, a physical UVB/UVA filter (Anthelios® T) onto the eczematous skin lesions.

Discussion

Coupled photocontact allergies with positive skin reactions to 4-isopropylidibenzoylmethane and 4-methylbenzylidene camphor also known as a combination named Eusolex 8021® has first been described by Schauder in 1996 [9]. Here we add a new case of combined photocontact allergy to four commonly used UV filter substances. The patient presented suffered from a severe eczematous skin disease which had developed after application of sunscreen products and sun exposure during his skiing vacation.

Photopatch tests evoked a characteristic crescendo reaction to butyl methoxydibenzoylmethane (Parsol 1789), benzophenone-3 (oxybenzone/Eusolex 4360), 4-methylbenzylidene camphor (Eusolex 6300) and octyl methoxycinnamate (Parsol MCX). The significantly reduced UVB sensitivity of 25 mJ/cm² was diagnosed as an early form of persistent light reaction. To our knowledge, no such case has been reported before.

In comparison to phototoxic reactions, photoallergies show a markedly lower incidence [10]. Besides the established photosensitizers such as nonsteroidal antiinflammatories, phenothiazines, perfumes or preservatives, UV filter substances gain more and more importance as photoallergic substances [10].

Whereas the photoallergic potential of dibenzoylmethanes and benzophenones is well known, isolated photocontact sensitization to cinnamates and camphor derivatives is a rare event. The increased use of combinations

of UV filters with higher and lower photoallergenic potential as contained in the majority of the currently available sunscreen products may provoke marked photoallergic skin reactions even to the compounds regarded as low potential sensitizers [9].

In our patient concomitant photoallergic reactions to certain structurally not related UV filter substances were demonstrable. Due to the suspected diagnosis of persistent light reaction, there was a need for sunscreen products. Therefore the daily application of a combination of a chemical and physical (titanium dioxide) UV filter system [13] was used and very well accepted by the patient.

Although still a matter of current debate, this case report provides clear evidence that photocontact dermatitis evoked by chemical UV absorbers may result in persistent light reaction, a form of chronic actinic dermatitis developing from prior localized photocontact dermatitis. Therefore more and more attention has to be drawn to the problem of light-induced eczema caused by UV filter substance sensitization.

The widespread use of the above UV filter chemicals not only in sun protection products but also in various cosmetics such as antiaging lotions, day care products, lipsticks and shampoos without attachment of a detailed product information denies the patient the possibility to effectively avoid the substances in question. Therefore preventive approaches should aim at eliminating the relevant photocontact allergens in the patient's everyday life.

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