

Sunscreen Allergy: A Review of Epidemiology, Clinical Characteristics, and Responsible Allergens

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Although allergy to sunscreen represents a small proportion (< 1%) of allergic contact dermatitis reactions in North America, it is one of the most common causes of photoallergy. The epidemiology and clinical characteristics of sunscreen allergy are summarized in this review. In addition, a detailed discussion of specific chemical sunscreen allergens is provided.

SUNSCREENS have traditionally been divided into chemical absorbers and physical blockers.¹ Chemical sunscreens absorb ultraviolet (UV) radiation and incorporate its energy into the structure of the sunscreen molecule itself, exciting the molecule to a higher energy state. This in turn converts the ultraviolet energy into less dangerous wavelengths. Chemical sunscreens can absorb in the ultraviolet B (UVB) (290–320 nm), ultraviolet A II (UVA II) (321–340 nm), and ultraviolet A I (UVA I) (341–400 nm) ranges.² By contrast, physical blockers reflect and scatter UV radiation and dissipate the energy into the surrounding environment.¹

Although chemical sunscreens were first introduced in the 1930s, widespread use of these products has occurred only in the last 20 years as the photocarcinogenic and photoaging properties of UV radiation have been increasingly recognized by the general population.³ Consequently, in the United States, allergic reactions to sunscreens have also become more common. Allergic and photoallergic reactions have been reported with several chemical sunscreen families.^{4,5}

Photoallergic contact dermatitis is a T-cell-mediated delayed-type hypersensitivity reaction. It occurs in response to a photoallergen or antigen in a person previously sensitized to the same substance or to a cross-reacting substance. It occurs in response to both UV (most commonly UVA) and visible light.^{6,7} The mechanism by which UV light contributes to photoantigen formation is not well un-

derstood. Two mechanisms have been proposed. The skin has several endogenous chromophores (including keratin proteins, porphyrins, lipoproteins, hemoglobin, melanin, and amino acids) that can absorb UV radiation.⁷ These chromophores may be transduced to an excited state after exposure to UV radiation and, upon reversion to the ground state, may conjugate with a carrier. Alternatively, UV radiation may induce a stable photoproduct that serves as a hapten. The hapten would then conjugate with a carrier protein to serve as a complete antigen.⁶ Once complete antigen formation occurs, the pathophysiology of photoallergic contact dermatitis is identical to that of allergic contact dermatitis.^{6–8}

In addition to reacting to active sunscreens, patients may demonstrate allergy or photocontact allergy to inactive ingredients in sunscreen formulations. Most significant among these are fragrances, formaldehyde releasers, preservatives, and lanolin alcohol.^{9,10} A full discussion of inactive sunscreen allergens is beyond the scope of this review; the purpose of this discussion is to present a comprehensive overview of the epidemiology and clinical characteristics of allergic and photoallergic contact dermatitis from active sunscreen agents and to provide a detailed description of each allergen.

Prevalence of Contact Dermatitis from Active Sunscreen Agents

The prevalence of allergy in the general population to sunscreen agents is unknown. Among individuals referred for patch testing, the prevalence of allergy to active sunscreen ingredients is low, probably less than 1%. The North American Contact Dermatitis Group (NACDG), a research organization of American and Canadian dermatologists who specialize in patch testing, periodically reports findings

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from their combined data sets. NACDG screening agents for sunscreen allergy have included benzophenone (added in 1998) and cinnamic aldehyde. From 1998 to 2002, the prevalence of reactions to benzophenone was 0.6%^{11,12}; 59% of these reactions were deemed to be of definite, possible, or probable relevance. From 2003 to 2004, the prevalence of allergy to benzophenone was reported as 0.5% (Erin Warsaw [NACDG member], personal communication, March 2005). From 2003 to 2004, 70.3% of reactions to benzophenone-3 were considered to be of definite, probable, or possible relevance. The prevalence of patch-test reaction to cinnamic aldehyde (which is not specific for chemical sunscreens but which may also indicate a perfume or flavoring allergy) was 3.6% from 1998 to 2002¹² and 2.3% from 2003 to 2004.

Prevalence of Photocontact Allergy to Active Sunscreen Agents

The prevalence of sunscreen sensitization in individuals referred for evaluation of photosensitivity is much higher.^{13–15} Journe and colleagues evaluated 370 patients in France who had photodistributed eczematous eruptions. They observed 107 positive patch-test reactions and 126 positive photopatch-test reactions; 15.4% of these positive reactions were related to sunscreens, and 72% were deemed relevant. Eighteen patients were diagnosed with contact allergy, and 39 patients had photocontact allergy to active sunscreen ingredients.¹⁶ From 1981 to 1996, Schauder and Ippen evaluated 402 patients who had been referred to a photobiology unit in Germany with suspected photosensitivity. The patients were patch-tested and photopatch-tested with common UV absorbers and with commercial sunscreen products as well as with fragrance materials, preservatives, and emollients found in these products. Eighty patients (20%) had relevant allergic or photoallergic contact dermatitis from UV absorbers.¹⁴

Other reports in the literature suggest a lower frequency of sunscreen allergy in patients referred for photodistributed eczematous eruptions. From 1992 to 1996, Ang and colleagues from Singapore reviewed the records of 48 patients who had been referred for suspected light-related dermatoses and who underwent photopatch testing. These patients were patch-tested with a standard sunscreen series that included oxybenzone, mexenone, Parsol, octyl dimethyl para-aminobenzoic acid (PABA), and cinnamate. Three patients (6.3%) had allergic reactions to these active sunscreen ingredients, and two patients (4.2%) had photoallergic reactions to these same ingredients.¹⁵ Darvay and colleagues patch- and photopatch-tested 2,715 patients

referred for presumed photosensitivity disorders from 1983 to 1998. Sixty-two patients (2.3%) exhibited photoallergic reactions, and of these reactions, 65% were due to UV absorbers. Forty-nine patients (1.8%) had non-photoallergic contact reactions, 68% of which were due to UV absorbers.¹⁷

Risk Factors

Sunscreen use by the general public has increased markedly over the last 20 years as the photocarcinogenic and photoaging properties of UV radiation have become recognized. Chemical absorbers are frequently incorporated not only into dedicated sunscreens but also into personal products such as moisturizers, lip care products, and foundations.^{4,5,10}

The risk factors for sunscreen allergy are largely unknown but may include gender, preexisting photodermatoses, outdoor occupation, and atopy. In their retrospective study, Schauder and Ippen found that of individuals with relevant allergic or photoallergic contact dermatitis, 65% (52 of 80) were female.¹⁴ They postulated that this could be due to either a higher use of sunscreen and cosmetic products by women or greater use of dermatologic services among women.

Several studies have demonstrated an increased prevalence of sunscreen allergy in patients with idiopathic photodermatoses.^{13,14,18,19} In Schauder and Ippen's study, 59% (47 of 80) of individuals with allergy had known photodermatoses¹⁴; not surprising, diagnosis varied by gender. Sixty-eight percent of men (19 of 28) with demonstrated allergy had photodermatoses; the most common condition was chronic actinic dermatitis (16 of 19 [84%]). Among women, 53% (28 of 52) had known photodermatoses; polymorphous light eruption (PMLE) was the most common condition (18 of 28 [64%]). Bilsland and Ferguson evaluated 45 patients with chronic actinic dermatitis (CAD) and 54 patients with PMLE and patch-tested them with benzophenones, dibenzoylmethanes, aminobenzoates, cinnamates, and Eusolex 6300 (Merck KGaA, Darmstadt, Germany).¹⁸ One hundred fifteen nonphotosensitive subjects served as controls. Ten (22%) of the 45 patients with CAD and 2 (3.7%) of the 54 patients with PMLE demonstrated sunscreen allergy on patch tests. Only 4 (3.4%) of the 115 controls demonstrated allergy ($p = .0001$). Benzophenones accounted for most of the positive results. Photopatch tests were not performed in this study.

Other potential patient risk factors for sunscreen sensitization include the use of sunscreen products on previously damaged skin, a history of atopic dermatitis, and an outdoor occupation.^{13,20,21}

Clinical Features of Sunscreen Allergy

The clinical features of allergic and photoallergic responses to sunscreens are often indistinguishable because sunscreens are typically applied to body sites that are exposed to light. Both reactions are characterized by an eczematous dermatitis that may be acute, subacute, or chronic. Photoallergic contact dermatitis in any form logically affects sun-exposed areas such as the face, the “V” of the anterior neck, the dorsal hands, and forearms. Typically, the upper eyelids, upper lip, and submental and postauricular areas are spared. Any skin area that receives sufficient light and is exposed to a photosensitizing chemical may be affected, however.⁴ Unilateral involvement may be seen after application of the photosensitizing sunscreen agent to a particular body site or after greater exposure of one body site as compared to another. Transfer from one body site to another may also occur.

Patch Testing and Photopatch Testing

Because sunscreen allergy may be photoinduced, the evaluation of suspected patients usually includes both standard and photopatch testing. A full discussion of photopatch-testing procedures is beyond the scope of this review. Briefly, prior to patch application, minimal erythema dose (MED) testing is often performed to assess the minimal erythemogenic dose for skin that is not exposed to sunlight. For most fair-skinned individuals, the MED in the UVA range is 20 to 30 J/cm². Most photoallergens will be defined by smaller doses, however, and the dose of UVA used to irradiate photopatch tests for sunscreen allergy ranges from 1 to 10 J/cm² in most studies.^{4,20,22} MED testing with UVB is often done at the same time to assess general (nonallergic) sensitivity at this wavelength. Allergen patches are placed on the back, as in standard patch testing, but are done so in duplicate. One set of photoallergens is irradiated with UVA, and the other set serves as a control. If patches on both sides show a positive reaction, contact allergy is confirmed. If only the irradiated side shows a positive reaction, photocontact allergy is present.²⁰

Sunscreen allergen concentrations and vehicles used for patch testing and photopatch testing are not well characterized. Hasan and colleagues suggested that in eliciting a photoresponse, the allergen concentration is much more important than the actual dose of UVA; they suggested 5 J of UVA for standard testing.⁹ Petrolatum is most often used as the diluent for sunscreen antigens; however, the bioavailability of the antigens tested may be limited with the use of this vehicle. For this reason, ethanol has been

suggested for detecting PABA sensitivity.²¹ Other problems inherent in photopatch testing include the “masked patch test” (so called when the patient is so photosensitive that the UVA dose alone will elicit a reaction), irritant reactions, inadvertent sensitization, and false-positive or false-negative reactions owing to the selection of an inappropriate type or amount of light.^{4,22}

Sunscreen Allergens

para-Aminobenzoic Acid

PABA and its esters were among the earliest UV absorbers to be introduced in the United States, and sensitization was documented as early as 1947.²³ PABA is a member of the “para” group of antigens; these antigens are frequent sensitizers and consist of chemicals with a free amino group in the para position of a benzene ring.²⁴ PABA is a potent UVB absorber but does not absorb UVA.²⁵ PABA requires an alcohol vehicle for use in sunscreen commercial products. It may stain clothing, and it has been associated with a number of adverse reactions, including allergic and photoallergic contact dermatitis.¹ Ester derivatives of PABA include octyl dimethyl PABA, amyl dimethyl PABA (padimate A), and glycerol PABA. These derivatives have become more popular for use in sunscreen products because of a higher compatibility with other cosmetic vehicles and a decreased propensity for staining. Reports of photoallergy to PABA and its ester counterparts, however, have led to their near removal from sunscreen manufacturing. Today, PABA products are used only rarely in sunscreen formulations. The promotion of PABA-free sunscreens is now common.^{1,21,26}

In addition to demonstrating allergic reactions, patients may report a transient stinging or burning sensation after application of PABA-containing products. This phenomenon is deemed to be more common than true allergy and may lead patients to falsely believe they are allergic to this chemical. As a result, several sunscreen products have been marketed as “hypoallergenic” because they are PABA free, but they may obviously still contain other chemical UV absorbers to which patients may become allergic.

The mechanism leading to the formation of common allergenic haptens remains unclear. The haptens deemed to be responsible in the case of PABA and its cross-reacting compounds are quinine amines, oxidation products of para-amino chemicals.²⁵ The degree of allergenic cross-reactivity between different para-amino compounds is variable and may be explained by the ability of different patients to transform these products into their quinolamine metabolites.

Patients allergic to PABA may also react to other para-amino allergens such as para-phenylenediamine, para-aminosalicylic acid ester anesthetics, sulfonamides, and azo dyes.⁴ Uter and colleagues conducted a retrospective review of the cross-sensitivity to para-amino compounds in clinical patch testing.²⁴ They examined the results of 638 patients who were patch-tested with a “para-amino series” that included PABA, para-aminophenol, para-toluenediamine, sulfanilamide, Disperse Orange 3, para-aminoazobenzene, 4,4'-diaminodiphenylmethane, and para-phenylenediamine. They found a heterogeneous pattern of reactivity to different para-amino compounds among their patients and suggested that patch-test screening should use several para-amino compounds to ascertain an individual's spectrum of allergic contact sensitization to these products. The most common para-amino sensitizer in their study was para-aminoazobenzene, which induced positive reactions in 16.2% of patients tested.

Recommended patch-test concentrations for PABA have ranged from 1 to 10%. False-negative results may occur if petrolatum is used as a vehicle.²⁷ Table 1 lists the most common para-amino compounds found in sunscreens and indicates their suggested patch-test concentrations.

Benzophenones

Benzophenones were first used in sunscreen products in the 1950s.²⁸ Benzophenone-3 (2-hydroxy-4-methoxybenzophenone) is the most frequently used benzophenone in the United States and is currently one of the most common causes of photocontact allergy.⁴ It is marketed elsewhere under the names oxybenzone, Eusolex 4360 (Merck), methanone, Uvinul M40 (BASF Japan Ltd., Tokyo, Japan),

and diphenylketone.²⁷ Benzophenones are primarily UVB absorbers although benzophenone-3 and sulisobenzene absorb UVB through UVA II (321–340 nm) and are considered broad-spectrum chemical sunscreens.²⁷ In addition to their use as chemical sunscreens, benzophenones may also function as preservatives. They are known to protect against sunlight-induced discoloration of cosmetic products and are often incorporated for similar purposes into textiles, plastics, paints, and rubber products.²⁹

The first description of a contact reaction to benzophenones in sunscreen products was published in 1972 by Ramsay and colleagues, who described a 54-year-old African American man with a papular eruption in photo-distributed areas of the ears, face, neck, and arms.³⁰ The patient exhibited not only an immediate positive wheal and flare response to scratch testing with two benzophenones (1% sulisobenzene and 2-hydroxy-4-methoxybenzophenone) but also a delayed hypersensitivity reaction to 5% sulisobenzene in water.

In addition to causing contact and photocontact delayed-type hypersensitivity reactions, benzophenone-3 has been reported to induce photocontact urticaria, contact urticaria, and anaphylaxis.^{31–34} Bourrain and colleagues reported on a 31-year-old man with recurrent facial dermatitis exacerbated by sunlight.³¹ The patient demonstrated normal results on MED testing. Patch testing and photopatch testing was performed with benzophenone-3 and benzophenone-10 as well as with the patient's own sunscreen, which contained benzophenone-3. Urticarial reactions occurred within minutes of irradiation to the aforementioned test sites and disappeared within 30 minutes. Nonirradiated sites were unaffected. Furthermore, no delayed reactions were found at readings performed at 48 and 96 hours. Yesudian and King reported a similar case of a 40-year-old woman who developed a pruritic eruption on the face, trunk, and limbs after applying sunscreen to her daughter.³⁵ On patch testing, she developed an urticarial wheal and flare reaction to benzophenone-3 (photopatch testing was not performed on this patient). Emonet and colleagues reported on a 22-year-old woman with an atopic diathesis who developed generalized urticaria, dyspnea, and fainting after the application of an oxybenzone-containing sunscreen to normal skin.³² Patch tests with the sunscreen demonstrated a local wheal and flare reaction within 5 minutes of application and a similar reaction to oxybenzone after 15 minutes. Results of skin-prick tests with both the patient's personal sunscreen product and oxybenzone were positive as well.

The severity of a urticarial reaction to benzophenone may depend on the body surface area to which it is applied.

Table 1. para-Amino Compounds Used in Sunscreens

<i>Compound</i>	<i>Patch-Test Concentration*</i>
PABA, 4-amino benzoic acid	2–5% or 10% pet
Amyl dimethyl PABA (padimate A, isoamyl-p-N,N-dimethylaminobenzoate, Escalol 506, pentyl dimethyl PABA)	1% or 5% pet
Octyl dimethyl PABA (padimate O, Escalol 507, Eusolex 6007, octyl dimethylaminobenzoate, 2-ethylhexyl-4-dimethylaminobenzoate)	2% or 5% pet
Glycerol PABA	2%, 5%, or 10% pet

PABA = para-aminobenzoic acid; pet = petrolatum.

*Recommended concentrations (adapted from Chemotechnique Diagnostics³⁶; De Groot AC⁴⁷; Trolab/Hermal⁴⁸).

Table 2. Benzophenones*

<i>Compound</i>	<i>Patch-Test Concentration[†]</i>
Benzophenone-3 (2-hydroxy-4-methoxybenzophenone, Eusolex 4360, Escalol 567, oxybenzone, Uvinul M40)	10% pet
Mexenone (2-hydroxy-methoxymethylbenzophenone, benzophenone-10)	10% pet
Benzophenone-4 (2-hydroxy-4-methoxybenzophenone-5-sulfonic acid, sulisobenzone, Uvinul MS40)	10% pet
Benzophenone-8 (dioxibenzene, dihydroxy-4-methoxybenzophenone)	2% pet

pet = petrolatum.

*Benzophenones-1 to -12 are used in chemical sunscreens; the most common of these to cause allergy are listed.

[†]Recommended concentrations (adapted from Chemotechnique Diagnostics³⁶; De Groot AC⁴⁷; Trolab/Hermal⁴⁸).

A small and localized application may induce only a local contact urticaria whereas the application of larger amounts may lead to an anaphylactic reaction. Benzophenone-3 has been shown to cross the epidermal barrier, and its metabolites are known to be excreted in the urine after widespread topical application.³²

For patch testing, a 10% oxybenzone concentration in petrolatum is recommended and generally serves as a marker for allergy to benzophenones.³⁶ Detection of allergy to this product may be complicated by the combination of this chemical sunscreen with other sunscreen agents. Patients must be alerted to the other names for benzophenone-3 when practicing avoidance. Table 2 lists the most common benzophenones found in sunscreens and indicates their recommended patch-test concentrations.

Cinnamates

The cinnamates are a group of related substances used in flavorings, fragrances, and (less frequently) sunscreens.²⁷ In sunscreen products, they are often used in combination with the benzophenones.³⁷ The cinnamates are primarily UVB absorbers. Given their poor water solubility, they are often used in sunscreens marketed as “water-proof.” The most commonly used cinnamate in sunscreens is ethylhexyl-p-methoxycinnamate, also known as Parsol MCX (Roche Vitamins Inc., Parsippany, NJ). 2-Ethoxyethyl-p-methoxycinnamate, or cinoxate, is less commonly used.

Allergy to cinnamates is deemed to be infrequent.⁴ Journe and colleagues evaluated 370 French patients with

suspected contact or photocontact allergy to sunscreens by patch testing and photopatch testing.¹⁶ Their cinnamate markers included *e*-ethylhexyl-p-methoxycinnamate and isoamyl p-methoxycinnamate. Photoallergy alone to *e*-ethylhexyl-p-methoxycinnamate was demonstrated by two patients. No cases of allergy or photoallergy were detected among those patients tested with isoamyl p-methoxycinnamate. Whereas allergy to these cinnamate sunscreen ingredients is uncommon, more significant is their cross-reactivity with flavorings and fragrances that include balsam of Peru, coca leaves, cinnamic acid, cinnamic aldehyde, and cinnamon oils.³⁷

An extensive literature search revealed no reports of contact urticaria from cinnamates used in sunscreen products. Urticaria from cinnamates used in other cosmetic products has been reported, however, and cross-reaction with cinnamates in sunscreen agents is certainly possible.^{38,39} According to Nater and colleagues, cinnamic aldehyde has a “histamine-liberating” effect resulting in nonimmunologic urticaria.³⁹

For patch testing, cinnamic aldehyde is used as a 1% preparation in petrolatum and serves as a marker for cinnamate allergy on the NACDG standard series.¹² Table 3 lists the most common cinnamates used in sunscreen preparations and indicates their suggested patch-test concentrations.

Salicylates

Benzyl salicylate was the first cosmetic sunscreen used in the United States.⁴⁰ Currently, octyl salicylate is the major salicylate component of sunscreens.⁴¹ The salicylates are weak UVB absorbers; as such, they are used in high concentrations.⁴¹ Salicylates have been used as a standard for determining sun protection factors because of their safety profile. Furthermore, they are able to solubilize insoluble

Table 3. Cinnamates

<i>Compound</i>	<i>Patch-Test Concentration*</i>
Parsol MCX (2-ethylhexyl-4-methoxycinnamate, Escalol 557)	10% pet
Isoamyl p-methoxycinnamate (amylcinnamate)	10% pet
Cinoxate (2-ethoxyethyl-p-methoxycinnamate, octyl methoxycinnamate)	2% pet
Ethyl cinnamate	4% pet

pet = petrolatum.

*Recommended concentrations (adapted from Chemotechnique Diagnostics³⁶; De Groot AC⁴⁷; Trolab/Hermal⁴⁸).

sunscreens like the benzophenones but are themselves insoluble in water. They are easily incorporated into other agents and are thus often used in cosmetic products that are marketed as concomitant sunscreens.

Allergic contact dermatitis from salicylates has been reported only rarely.²¹ The first report dates back to 1968 and cites benzyl salicylate as a potential allergen in soaps and detergents.⁴² In 1978, Rietschel and Lewis reported two cases of contact dermatitis with follicular accentuation from benzyl salicylate found in sunscreen products.⁴⁰ The authors postulated that hapten conjugation was occurring with an unknown substance found only in the infundibular region of the hair follicle. A literature search revealed no reports of contact urticaria from salicylates used in sunscreen products.

For patch testing, octyl salicylate is used at a 5% concentration in petrolatum. Other salicylates commonly used in patch testing are 2-ethylhexyl salicylate, menthyl salicylate, benzyl salicylate, and homosalate. Their patch-test concentrations are listed in Table 4.

Dibenzoylmethanes

The dibenzoylmethanes were introduced as sunscreens in Europe in 1980.⁴³ In 1997, 4-tert-butyl-4'-methoxy-dibenzoylmethane (more commonly known as Parsol 1789 [Roche Vitamins Inc.,] or avobenzone) was approved for use in the United States. The dibenzoylmethanes possess a broad absorption spectrum with maximal absorption in the UVA range,⁴⁴ and their use has increased as a result of reported sensitivities to benzophenones and PABA products.¹⁴

Both contact allergy and photocontact allergy to dibenzoylmethanes have been reported.^{43,45,46} Most of the reports describe photoallergy to isopropyl dibenzoylmethane (Eusolex 8020, Merck & Co., Inc., Whitehouse Station, NJ). In Schauder and Ippen's study, 15.4% (62 of 402) of patients who were evaluated for suspected photosensitive dermatitis had either contact allergy or photocontact al-

lergy to isopropyl dibenzoylmethane.¹⁴ This product was removed from the market in 1993 owing to its photosensitizing effects.⁴ Currently, 4-tert-butyl-4'-methoxy-dibenzoylmethane is the most common dibenzoylmethane found in sunscreen products in the United States. Reports of allergies to 4-tert-butyl-4'-methoxy-dibenzoylmethane exist, but several of these allergies may have resulted from cross-reactivity caused by prior exposure to the isopropyl derivative (Eusolex 8020).^{21,44,46}

Avobenzone is often combined with UVB-blocking agents in commercial sunscreens for broad-spectrum protection, and physicians must be aware of this when patch-testing patients with the patients' personal sunscreen products. The recommended patch-test concentration for 4-tert-butyl-4'-methoxy-dibenzoylmethane is 10% in petrolatum.³⁶

Anthranilates

Anthranilates are derivatives of ortho-aminobenzoic acid. They absorb UVA radiation of wavelengths between 322 and 350 nm. They are often combined with UVB absorbers to give broad-spectrum protection. Unlike their para-amino counterparts, anthranilates are not common sensitizers.⁴¹ A comprehensive literature search found no reports of allergy or photoallergy to these chemicals. Anthranilates are currently part of the sunscreen series recommended for photopatch testing by the NACDG. Methylantranilate is tested at 5% in petrolatum.

Methylbenzylidene Camphor

3-(4-Methylbenzylidene) camphor (Eusolex 6300, Merck) is a sunscreen agent used in Europe.²² It absorbs best in the UVB spectrum.⁴ There have been several case reports of allergy and photoallergy to this chemical.^{16,43,44} Buckley and colleagues reported on a 56-year-old woman with a photoinduced pruritic eruption after application of a personal sunscreen product containing 3-(4-methylbenzylidene) camphor and isopropyl dibenzoylmethane (a combination known as Eusolex 8021).⁴³ On photopatch testing, she demonstrated strong reactions to both chemicals as well as to her own sunscreen. Most of the 37 patients who demonstrated allergy or photoallergy to methylbenzylidene camphor in a study by Schauder and Ippen demonstrated concomitant photosensitization to isopropyl dibenzoylmethane.⁴⁴

De Groot recommended patch-testing with methylbenzylidene camphor in petrolatum at a 2% concentration⁴⁷ although it is commercially available at a 10% concentration.^{36,48}

Table 4. Salicylates

<i>Compound</i>	<i>Patch-Test Concentration*</i>
Octyl salicylate (ethylhexyl salicylate)	5% pet
Menthyl salicylate	2% olive oil
Benzyl salicylate	1% pet
Homosalate (homomenthyl salicylate)	5% pet

pet = petrolatum.

*Recommended concentrations (adapted from Chemotechnique Diagnostics³⁶; De Groot AC⁴⁷; Trolab/Hermal⁴⁸).

Octyl Triazone

Octyl triazone (2,4,6-trianalino-[p-carbo-2'-ethylhexyl-1'oxy] 1,3,5 triazine) is a UVB absorber unrelated to any of the aforementioned chemical sunscreens. It is highly polar and completely insoluble in water. A literature search found one case report of photoallergy to this compound. Sommer and colleagues described a 66-year-old woman with an erythematous bullous eruption on sun-exposed areas after sunscreen use.⁴⁹ She reacted to both octyl triazone and Parsol 1789 at UVA-irradiated patch-test sites only. Both products were found in her personal sunscreen. Patch-test concentrations were not reported.

2-Phenylbenzimidazole-5-Sulfonic Acid

2-Phenylbenzimidazole-5-sulfonic acid (also known as Eusolex 232 and Novantisol, Merck & Co., Inc.) absorbs in the UVA spectrum. Allergy to this chemical agent is rare. On routine photopatch testing of 355 patients with suspected photosensitivity in Sweden, Berne and Ros found two patients with photocontact allergy to this chemical.⁵⁰ Schauder and Ippen reported one allergic reaction and seven photoallergic reactions to this agent over a 15-year period.¹⁴ Two additional cases were described in 1998.⁵¹ Commercial sources provide 2-phenylbenzimidazole-5-sulfonic acid at a 10% concentration^{36,38} although a 2% concentration is also recommended.⁴⁷

Octocrylene

Octocrylene (2-ethylhexyl-2-cyano-3,3-diphenylacrylate) is a UVB chemical photoprotectant that has been used in sunscreens for less than a decade.⁵² It is sometimes grouped with the cinnamates because of structural similarities. Two patients with photoallergy to this unique agent were reported by Carotte-Lefebvre and colleagues in 2003.⁵² These are the only known case reports of allergy to this relatively new agent. Octocrylene is tested in a petrolatum vehicle at a 10% concentration³⁶ although a 1% concentration has also been used.⁴⁷

Other Chemical Sunscreen Agents

Other chemical sunscreen agents incorporated into commercial products include etocrilene (ethyl 2-cyano-3,3-diphenylacrylate), drometrizole trisiloxane, bisethylhexyloxyphenol methoxyphenol triazine, drometrizole (2-(2-hydroxy-5-methylphenyl)benzotriazole), dioctyl butamido triazone, and terephthalylidene dicamphor sulfonic acid (Mexoryl SX, L'Oreal, Aulnay Sous Bois, France). A literature search revealed no cases of allergy or photoallergy

to these products, nor were any patch-test concentrations referenced.⁵³

Physical Ultraviolet Light Blockers

Some of the first physical UV blockers used in the United States were opaque formulations that scattered or reflected UV radiation.¹ Poor cosmetic acceptability initially limited the use of these products. Recently, however, micro-sized forms have become available. Titanium dioxide and zinc oxide are the most common physical UV blockers used today. These agents have not been reported to cause contact dermatitis or photoallergy.^{4,21} Of interest, several sources in the literature do suggest that these agents may block the appearance of photoallergy to sunscreens or other agents because of their strong UV-blocking effects.^{18,54}

Management and Differential Diagnosis of Sunscreen Allergy

As sunscreen allergy has become one of the most important causes of photoallergy over the last several decades, the management of this problem begins with the proper identification of the sunscreen allergen through patch testing and photopatch testing. Education for proper avoidance is critical. Patients must be made aware of the antigen's synonyms. As the physical blockers have been shown to cause neither allergy nor photoallergy, their use should be encouraged although the patient must be aware of commercial products that contain both physical blockers and chemical absorbers. The Contact Allergen Replacement Database⁵³ may be useful in providing a list of allergen-free products for these patients.

Other photosensitivity disorders that should be considered in the differential diagnosis of sunscreen allergy include PMLE, chronic actinic dermatitis, persistent light eruption, lupus, and porphyrias.

Conclusion

Contact allergy and photocontact allergy to sunscreen agents are uncommon but not rare. Their prevalence may increase as sunscreen use continues to become more widespread. We have reviewed the epidemiology and clinical characteristics of sunscreen allergy and have provided an up-to-date discussion of sunscreen allergens and their appropriate patch-test concentrations. More research is needed to further elucidate the mechanisms and responsible moieties involved in both allergy and photoallergy to sunscreens.

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