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REVIEW

Review on photoprotection: a clinician's guide to the ingredients, characteristics, adverse effects, and disease-specific benefits of chemical and physical sunscreen compounds

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Abstract

Photoprotection is a critical health prevention strategy to reduce the deleterious effects of ultraviolet radiation (UVR) and visible light (VL). Methods of photoprotection are reviewed in this paper, with an emphasis on sunscreen. The most appropriate sunscreen formulation for personal use depends on several factors. Active sunscreen ingredients vary in their protective effect over the UVR and VL spectrum. There are dermatologic diseases that cause photosensitivity or that are aggravated by a particular action spectrum. In these situations, sunscreen suggestions can address the specific concern. Sunscreen does not represent a single entity. Appropriate personalized sunscreen selection is critical to improve compliance and clinical outcomes. Health care providers can facilitate informed product selection with awareness of evolving sunscreen formulations and counseling patients on appropriate use. This review aims to summarize different forms of photoprotection, discuss absorption of sunscreen ingredients, possible adverse effects, and disease-specific preferences for chemical, physical or oral agents that may decrease UVR and VL harmful effects.

Keywords Sunscreen · Sunscreen safety · Contact dermatitis · Photodermatoses · Photosensitivity disorders · Melasma · Post-inflammatory hyperpigmentation · Maturational dyschromia · PMLE · Solar urticaria · Photoaggravated dermatoses · Keratinocyte carcinomas · Actinic keratoses · BCC · SCC · Melanoma

Introduction

Photoprotection is a critical health prevention strategy to reduce the deleterious effects of ultraviolet radiation (UVR) and visible light (VL). Photoprotection may prevent and mitigate sunburns, tanning, photoaging, hyperpigmentation, skin cancers, as well as flares of photodermatoses and photoaggravated skin diseases [1, 2]. Photoprotection includes sun avoidance, use of clothing, hats and sunglasses, seeking shade and sunscreen use. The aims of this review are to summarize these different forms of photoprotection with a focus on sunscreens, as the growing arsenal of sunscreen compounds necessitates an update. Sunscreen ingredients, their absorption, possible dermatologic adverse effects, and disease-specific preferences for sunscreens will be reviewed (Table 1). Physicians can facilitate informed product selection by discussing the benefits and possible adverse effects of various sunscreen formulations.

Ultraviolet radiation

Clinically relevant ultraviolet (UV) wavelengths are UVB (290–320 nm) and UVA (320–400 nm) [3]. At temperate latitudes UVB exposure is greatest in the summer, causing acute changes (i.e., tanning, sunburn) as well as DNA damage and photocarcinogenesis [4, 5]. UVA exposure is more constant throughout the year, causing DNA damage

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Table 1 Filtered wavelengths, advantages and disadvantages of active ingredients in chemical and physical sunscreens

Medical ingredient	UVA (UVA 2/short wave 320–340 nm; UVA 1/long wave 340–400 nm)	UVB (290–320)	Visible (400–800)	Advantages	Disadvantages
Chemical sunscreen					
PABA derivatives					
Aminobenzoate		+		Most potent absorber of UVB	None reported
Para-aminobenzoic acid (PABA) - No longer used		+		Most potent absorber of UVB Able to penetrate the stratum corneum layer and bind proteins in the epidermis. Provides a long-lasting sun protection effect [162]	Photooxidation of PABA causes it to turn yellow and stain clothing [32] Most common photoallergen and contact allergen. Thus, it is no longer used
Padimate O		+		None reported	None reported
Cinnamates					
Octinoxate: octyl methoxycinnamate		+		Potent UVB absorber, Not water soluble, useful for water resistant sunscreens [104]	Lacks photostability and degrades in the presence of sunlight [38]
Cinoxate: 2-ethoxyethyl *p*-methoxycinnamate		+		Potent UVB absorber Not water soluble, useful for water resistant sunscreens. [104] Often used in combination with other UVB absorbers to increase the SPF and duration	None reported
Amiloxate: 1-isoamyl *p*-methoxycinnamate		+		Potent UVB absorber	None reported
Salicylates					
Homosalate (homomethyl salicylate)		+		Weak UVB absorber Can reduce degradation of other UV filters, such as oxybenzone and avobenzone. Often added in combination with other active ingredients. [38]	None reported
Octisalate (octyl salicylate)		+		Can reduce degradation of other UV filters, such as oxybenzone and avobenzone. Often added in combination with other active ingredients [38]	None reported
Trolamine salicylate		+		None reported	None reported
Benzyl salicylate		+		None reported	None reported
Benzophenones					
Oxybenzone (benzophenone-3)	+ (Short wave)	+		UVA absorber	May cause photoallergic contact dermatitis, cheilitis [92–99]
Sulisobenzone (benzophenone-4)	+ (Short wave)	+		UVA absorber	None reported
Dioxybenzone (benzophenone-8)	+ (Short wave)	+		UVA absorber	None reported

Table 1 (continued)

Medical ingredient	UVA (UVA 2/short wave 320–340 nm; UVA 1/long wave 340–400 nm)	UVB (290–320)	Visible (400–800)	Advantages	Disadvantages
Dibenzoylmethanes					
Avobenzone (butyl methoxydibenzoylmethane)	+			UVA absorber	Photolabile [38]. Requires additives to help stabilize [163, 164]
Benzotriazole-based					
Methylene bis-benzotriazolyl tetramethylbutylphenol (MBBT), bisoctrizole, or Tinosorb M Bis-ethylhexyloxyphenol methoxyphenyl triazine (BEMT), emotrizinol, or Tinosorb S Butyl methoxydibenzoyl methane (BMDBM) Drometrizole trisiloxane or Mexoryl XL	+	+		The high fat solubility of these agents allows them to be easily added to cosmetic oils The photostability of these agents allow them to be used in combination with other sunscreen components, such as avobenzone, to prevent photodegradation [165]	None reported
Other active ingredients					
Octocrylene		+		Decreased risk of irritation [166]. Often employed in combination to increase SPF potential [167]	Now recognized as a possible photoallergen (included in the European photocontact testing tray)
Ensulizole (phenylbenzimidizole sulfonic acid)		+		Lighter, less oily texture. A common ingredient in cosmetics [167]	None reported
Camphor derivatives (i.e. Ecamsule or Mexoryl SX, terephthydene dicamphor sulfonic acid)	+	(+)		Very photostable and water-resistant with low systemic absorption [163]	None reported
Methyl anthranilate	+			None reported	Rarely used due to a weak filter of UVB and UVA [38]
Physical sunscreen					
Zinc oxide (ZnO)	+	+	+(weak)	Weak filter of visible light	Less efficient at UVB protection than titanium dioxide [38, 59]
Titanium dioxide (TiO_2)	+(Short wave)	+	+(weak)	Smaller in size and has a greater refractive index, which makes it more effective at scattering UVR. Weak filter of visible light	Not effective against long-wave UVA radiation [166] May cause a more notable white cast, making it less cosmetically appealing compared to zinc oxide

Table 1 (continued)

Medical ingredient	UVA (UVA 2/short wave 320–340 nm; UVA 1/long wave 340–400 nm)	UVB (290–320)	Visible (400–800)	Advantages	Disadvantages
Filters not listed as active					
Iron oxide (Fe_2O_3)	+	+	+	Weakly filters a broad spectrum. The unique ability to filter visible spectrum wavelengths is especially useful in skin conditions that involve hyperpigmentation, such as melasma or post-inflammatory hyperpigmentation	None reported

and degradation of elastin and collagen [4, 6–8] leading to photoaging, hyperpigmentation, and photocarcinogenesis. Broad-spectrum protection is required to prevent the adverse effects of UV radiation (UVR) [9, 10].

Visible light (VL)

While UVR accounts for 5% of terrestrial sunlight, 50% is visible light (VL; 400–700 nm) [2]. Exposure is insignificantly increased by electronic devices. Recent literature highlights the importance of protection from VL [2]. VL is part of the action spectrum for chronic actinic dermatitis [11], solar urticaria [12, 13], and the primary action spectrum for porphyrias [14], meaning these wavelengths typically trigger flares of the conditions. VL also worsens melasma, post-inflammatory hyperpigmentation, and maturational dyschromia [15–18].

Types of photoprotection

People should be encouraged to avoid outdoor activities during peak sun hours, seek shade, apply sunscreen, wear sun protective clothing, and sunglasses [19].

Sunscreen

Sunscreen ingredients decrease UVR and VL from reaching the skin. UVR is absorbed or scattered and VL is reflected. Many sunscreens combine chemical (organic) and physical (inorganic) ingredients to maximize UV protection [20]. The American Academy of Dermatology (AAD) and the Canadian Dermatology Association (CDA) recommend a minimum Sun Protection Factor (SPF) of 30 [21]. SPF is a measure of UV-induced erythema, thus primarily denotes UVB protection, as UVB is 1000 times more erythemogenic than UVA [22]. According to Health Canada and the FDA, the term "broad spectrum" means UVA protection with a critical wavelength of at least 370 nm. UVA protection is primarily measured by Critical Wavelength [22]. The European Commission addressed the need to quantify UVA protection with the symbol (UVA), indicating that the UVA protection is at least one third of the stated SPF [23]. VL is not necessarily covered by sunscreen. Filters that cover VL are outlined in the "Physical/Inorganic Sunscreens," "Filters not listed as Active," and "Tinted Sunscreen" sections.

The quantity and frequency of sunscreen application are common concerns. SPF is determined with a standard amount of sunscreen (2 mg/cm^2) under laboratory conditions, but people typically apply much less (0.8 mg/cm^2 in one study) [24]. Early reapplication is also helpful, as two applications of 1 mg/cm^2 produced the same SPF as a single larger application of 2 mg/cm^2 [25].

Use of a sunscreen with a higher SPF partially compensates for the insufficient amount applied [24, 26]. A consumer in-use double-blind randomized split-face study compared the efficacy of sunscreen with SPF 50 versus SPF 85 to assess if there is additional benefit to extra-high SPF. They found that SPF 85 provided significantly more protection against sunburns [27]. Ou-Yang et al. performed a single center, evaluator blinded, randomized trial of 237 participants with Fitzpatrick skin types I–III comparing SPFs 30, 50, 70, and 100 at four different sunscreen densities (0.5, 1.0, 1.5, and 2.0 mg/cm^2) in a controlled laboratory setting [28]. Results demonstrated that mean SPF value was progressively lower with decreasing application densities. However, reduced application densities resulted in proportionately higher mean SPF values for products with higher labeled SPFs. The follow-up study of $n = 65$ compared the same sunscreens at only 0.5 and 1 mg/cm^2 to reflect consumer usage [28]. The mean actual SPF of the 0.5 mg/cm^2 dose was approximately 25% of the labeled SPF for all products. Ou-Yang et al., therefore, suggested using an SPF of 70 and above, which yields at least an actual SPF of 19 when used in concentrations as low as 0.5 mg/cm^2 [28].

The Food and Drug Administration (FDA) and Health Canada suggest sunscreen reapplication every 2 h based on a small observational study [29]. A larger study suggests that a single application remains beneficial for 6 h if there is no water exposure [30]. When active outdoors, sweating, or in contact with water, reapplication is required [26].

Chemical/organic sunscreens Chemical (organic) sunscreens represent 75% of current products [31]. Multiple ingredients are often combined for broad-spectrum coverage [32]. Many are aromatic compounds conjugated with a carbonyl group, which absorb high-energy UVR. The different active ingredients are reviewed in Table 1. There are several chemical filters approved outside of the USA including Mexoryl XL, Tinosorb M and Tinosorb S [33, 34]. Mexoyrl SX has limited use in the USA [35].

Physical/inorganic sunscreens The FDA and Health Canada have approved zinc oxide (ZnO) and titanium dioxide (TiO_2) as physical (inorganic) compounds protecting against a broad range of UVR (Table 1) [36]. The creation of nanoparticles improved the esthetics of these formulations while maintaining UV protection [37]. The photostability of TiO_2 and ZnO is increased by coating them with silica and dimethicone [38].

Filters not listed as Active Iron oxide can be used to reduce VL exposure [2]. However, iron oxide is not listed as an active compound in the FDA and Health Canada monographs. Thus it is listed as an inactive ingredient in the sunscreens that contain it.

Tinted sunscreens Tinted sunscreens contain iron oxides and less commonly pigmentary TiO_2 [39]. Synthetic mica is often used to enhance radiance and create an optical blurring effect to reduce color mismatch [39].

Systemic photoprotection and oral agents Evidence for the use of systemic agents is limited. A comprehensive 2020 review of systemic photoprotection discusses the evidence for vitamins C, E, and D, carotenoids (beta-carotene, lycopene, xanthopylls), nicotinomide, retinoids, and dietary botanicals including polyphenols, polypodium leucotomos extract (PLE), non-steroidal anti-inflammatory drugs (NSAIDs), and afamelanotide [19].

In animal models, PLE upregulates p53 gene expression for enhanced DNA repair, modulates inflammatory cytokines, and inhibits UVR-induced cyclooxygenase-2 expression [40–43]. PLE is reported to be well-tolerated, reduce UVR-induced erythema in human trials, and reduce UV damage at the cellular level [19, 44–49]. However, the protective effect was of short duration and studies to-date are limited [19]. There is no conclusive long-term data from large studies to suggest that oral agents provide sufficient photoprotection when used alone.

Sun protective clothing

The ultraviolet protection factor (UPF) indicates the amount of UVR penetration through different fabrics. UPF does not account for body surface area (BSA) covered [50]. UPF clothing is particularly important for those who are exposed to UVR through their occupation due to increased risk of keratinocyte carcinoma [50]. In 2018 BSA and UPF were both considered when Downs et al. created the garment protective factor (GPF). This has yet to be widely adopted [51].

Less than 30% of cotton fabrics have UPF values of 30 + [51, 52]. The denser the weave of the material and smaller the pore size, the better protection the fabric offers. Natural fabrics (cotton, silk, linen) and lighter colors offer less photoprotection than synthetic fabrics or wool. Darker colors absorb more UVR and looser clothing offers more photoprotection [53–55]. Optical whitening agents and UV-absorbing laundry additives can be used, if available [34]. Clothing specifically made for sun protection will have a labeled UPF.

The Skin Cancer Foundation defined adequate UPF as 30, very good protection as UPF 30–49, and excellent UPF as 50 + [56]. Only European testing standard requires UVA protection thresholds, which is important to inform patients with UVA action spectrum photodermatoses [50].

Wearing appropriate UPF clothing is an effective method of sun protection, although protection can be provided by clothing without a UPF label, determined by color and the factors listed above.

Sunglasses and hats

Sunglasses reduce ocular UVR and VL exposure, thus decreasing the risk of damage to periocular skin (malignancies, photoaging), the lens (cataracts), and cornea (keratitis) [57]. Hats provide important protection for the scalp. An older study using polymer film polysulfone to measure UVR exposure demonstrated wide-brimmed (> 7.5 cm brim) options provide optimal head and neck coverage [58]. Diffey and Cheesman determined that most hat styles provide sufficient forehead coverage, but a brim of at least 7.5 cm is necessary to provide reasonable protection of the nose and cheeks [58].

Adverse effects

Absorption of sunscreens

Superficial cutaneous absorption

The potential for adverse reactions to sunscreen is largely dependent on whether the ingredients penetrate the stratum corneum. In vitro models suggest chemical UV filters (octocrylene, benzophenone, avobenzone, octinoxate, and padimate O) may penetrate the stratum corneum [59–63]. It remains unclear if this exposure causes keratinocyte injury. Anaphylactic reactions to oxybenzone have rarely been reported [64, 65]. UV-induced dehydration of the stratum corneum may increase percutaneous absorption [66]. Certain formulations, such as concentrated sprays or chemical sunscreen compounds encapsulated into mesoporous silica or bio-adhesive nanoparticles optimize delivery and decrease penetration [67–70]. Alcohol-based formulations may penetrate the stratum corneum more easily than lipophilic formulations [71].

The use of nanoparticles in sunscreens with ZnO and TiO_2 initially raised concern about skin penetration, but they do not penetrate the stratum corneum after application in vivo [20, 36, 60, 72–82]. Nanoparticles are undetectable past the stratum corneum on biopsy at 24 and 48 h post-application [83].

Systemic absorption

Studies using benzophenone-3, octylmethoxycinnamate, and 4-methylbenzylidene camphor applied 1–2 times a day showed accumulation in plasma and urinary excretion at 1–2 h after first application continuing until 4–5 days after the last application [84, 85].

After maximal use (4 times a day to 75% body surface area), increasing plasma concentrations above the FDA's safe threshold of 0.5 ng/mL were found between days 1–4 after application [86]. While concentrations for avobenzone, octocrylene, homosalate, octisalate, and octinoxate ranged from 7–50 times the FDA threshold, benzophenone-3 was detected at levels 500 times the FDA approval level [87]. Chemical sunscreen ingredients have also been identified in semen and breast milk [88, 89]. Importantly, there is no evidence to suggest this confers any health risk. Sunscreens have been used for many years without a signal that they are causing harm [90, 91].

Concerns have been raised about sunscreen effects on the endocrine, reproductive, and developmental systems. Most studies use animal models, and the disturbances appear more likely related to biological variation than the application of sunscreen [92–99]. Furthermore, the use of sunscreen in these studies does not always reflect human practice. The report of abnormal uterine growth comes from a 2001 study where rats were fed high doses of chemical sunscreen [100]. Janjua et al. investigated the impact of benzophenone-3, octyl-methoxycinnamate, and 3-(4-methylbenzylidene) camphor on reproductive hormones in humans with whole-body topical application of 2 mg/cm^2 [99]. The study demonstrated that follicle stimulating hormone, luteinizing hormone, and sex hormone binding globulin were unchanged, but a minor statistically significant decrease in testosterone was noted in males [99]. A detailed evaluation of humans' long term use of sunscreen at 2 mg/cm^2 volume is warranted to delineate health risks after decades of use.

For infants, the American Academy of Pediatrics suggests physical sunscreens with a minimum SPF of 30 until more safety data are available on chemical filters [101]. However, the data on absorption of sunscreen ingredients in the pediatric population are scarce. Future investigations are needed to evaluate the safety of chemical UV filters in this population.

Contact dermatitis

Allergic and irritant contact dermatitis (ACD and ICD) are the most common side effects associated with sunscreen use [102–105]. Inactive sunscreen ingredients may also be implicated (e.g., preservatives, fragrances, vehicles).

Photoallergic reactions are rare and have only been reported to a few chemical sunscreen ingredients (Fig. 1). When combined, the strong UV protective effects of physical sunscreens and chemical UVA absorbers may prevent photoallergic reactions to other chemical sunscreen ingredients [106, 107]. Patch and photopatch testing can help determine the culpable allergens [108]. If a contact or photocontact allergy to a particular compound is found on testing, a sunscreen without that compound can be used.

Allergic Contact Dermatitis	Irritant Contact Dermatitis	Photoallergic Contact Dermatitis
Para-aminobenzoic acid (PABA)	Para-aminobenzoic acid (PABA)	Para-aminobenzoic acid (PABA)
Padimate O	Padimate O	Padimate O
Octinoxate	Ethyl-hexyl	Octinoxate
Ethyl-hexyl	methoxycinnamate/Octyl	Cinoxate
methoxycinnamate/Octyl	methoxycinnamate)	Ethyl-hexyl
methoxycinnamate	Octisalate/Octyl salicylate	methoxycinnamate/Octyl
Ethyl cinnamate	Oxybenzone/Benzophenone-3	methoxycinnamate
Amiloxate	Bisoctrizol - MBBT)	Ethyl cinnamate
Homosalate	Methyl anthranilate	Amiloxate
Octisalate/Octyl salicylate	Enzacamene	Homosalate
Trolamine salicylate		Octisalate/Octyl salicylate
Oxybenzone/Benzophenone-3		Oxybenzone/Benzophenone-3
Methanone/Benzophenone-2		Methanone/Benzophenone-2
Dioxybenzone/Benzophenone-8		Dioxybenzone/Benzophenone-8
Mexenone/Benzophenone-10		Mexenone/Benzophenone-10
Sulisobenzone		Sulisobenzone
Avobenzone		Avobenzone
Benzotriazole-based (bisoctrizol - MBBT)		Bisoctrizol - MBBT
Methyl anthranilate		Methyl anthranilate
Octocrylene		Octocrylene
Ensulizole		Ensulizole
Ecamsule		Ecamsule
Enzacamene		Enzacamene

Fig. 1 Active components of chemical sunscreen ingredients reported to trigger allergic, irritant, and photoallergic contact dermatitis. No documented cases of contact dermatitis to physical sunscreens [32].

Vitamin D deficiency

It does not appear that regular use of sunscreen prevents vitamin D synthesis. This may be due to inadequate use of sunscreen [109, 110]. Nevertheless, the AAD recommends a daily oral intake of 1000 International Units of vitamin D for individuals who practice rigorous photoprotection [111].

Disease-specific sunscreen use (Table 2)

Hyperpigmentation: melasma, post-inflammatory hyperpigmentation and maturational dyschromia

Patients with hyperpigmentation require diligent daily application of broad-spectrum UVR and VL protection (i.e., Fe_2O_3) [18, 112, 113]. Tinted broad spectrum sunscreens with iron oxide may reduce the appearance of hyperpigmentation after only 2 months of daily application [18, 114–116]. Broad-spectrum UVA and UVB protection was shown to be more effective in preventing post-inflammatory hyperpigmentation (PIH) with the combination of terephthalylidene dicamphor sulfonic acid (TDSA, MexorylSX) and drometrizole trisiloxane (DT, MexorylXL) compared to TDSA alone [113, 117, 118]. Maturational dyschromia or hyperpigmentation is one reason for recommending broad-spectrum UVR and VL photoprotection for all skin types [119].

The data on possible benefit of PLE for patients with melasma are conflicting, and sample sizes are small [120]. A double-blind, placebo-controlled, randomized trial ($n=40$) evaluated twice daily PLE 240 mg for 12 weeks in patients concomitantly treated with broad-spectrum sunscreen and hydroquinone 4% cream. The group with adjunct PLE treatment had a greater reduction in disease severity [120, 121]. However, another randomized, double-blind study ($n=33$) showed no benefit of PLE [122].

Frontal fibrosing alopecia/lichen planopilaris

There is a controversial, poorly substantiated association between the facial use of sunscreen and frontal fibrosing alopecia (FFA) [123–127]. Only two case reports link long-term use of chemical sunscreen with the onset of LPP [128, 129]. Recent studies demonstrated an association between FFA and many other cosmetics (e.g., moisturizers) [125, 130]. With limited and conflicting data, sunscreen avoidance to prevent FFA is not recommended.

Photosensitivity disorders

Photosensitivity disorders can be divided into those caused by sun exposure (photodermatoses) and those that are

Table 2 Disease-specific topical sunscreen recommendations and action spectrum

	Condition	Action spectrum	Sunscreen recommendation
Diseases requiring visible light coverage	Melasma, post inflammatory hyperpigmentation and maturational dyschromia	Shorter wavelengths of visible light, UVA, UVB	Broad-spectrum sunscreen (SPF50+, UVA, UVB) with visible light blockers (i.e. iron oxide)
	Porphyria	Visible light	
	Chronic actinic dermatitis	Visible light, UVA (very low threshold), UVB	
	Solar urticaria	Predominantly short visible light and UVA, UVB	
Diseases requiring broad spectrum (SPF 50+, UVA, UVB)	Polymorphous light eruption	UVA, UVB	Broad-spectrum sunscreen (SPF50+, UVA, UVB). Finding sunscreens with adequate UVA coverage (circled UVA symbol) is critical
	Actinic prurigo		
	Drug-induced photosensitivity		
	Lupus erythematosus		
	Photoaggravated skin diseases (e.g., atopic dermatitis, acne vulgaris)		
	Hereditary defects causing photosensitivity (xeroderma pigmentosum, Cockayne syndrome)		
	Non-melanoma keratinocyte skin cancer prevention		
	Melanoma prevention		

aggravated by it (photoaggravated diseases). The UV wavelengths that typically trigger flares are the action spectrum for that condition.

Photodermatoses

Photodermatoses can be idiopathic or secondary. Idiopathic photodermatoses include polymorphous light eruption (PMLE), solar urticaria, actinic prurigo, hydroa vacciniforme, and chronic actinic dermatitis [11]. Secondary photodermatoses are triggered by sun exposure, as part of an underlying disease, such as lupus erythematosus and dermatomyositis [131]. Most photodermatoses include UVA in their action spectrum. Therefore, broad spectrum sunscreens are necessary. Solar urticaria and chronic actinic dermatitis include VL in the action spectrum and therefore may benefit from the addition of iron oxide. Depending on severity, protective car window filters and home window coverings can be considered [132].

In addition to broad spectrum sunscreen (± iron oxide), there are photodermatosis-specific therapies beyond the scope of this paper [14].

Drug-induced photosensitivity Drug-induced photosensitive reactions may be phototoxic or photoallergic and are primarily related to UVA exposure with the culprit medication. Common photosensitizing medications include thiazide diuretics, sulfonamide antibiotics, sulfonylureas, phenothiazines, tetracyclines, NSAIDs, amiodarone [11]. The clinical presentation appears as an acute sunburn (phototoxicity) or as a dermatitis (photoallergy). In some cases the reactions persist long after the UV exposure [11]. Continued drug exposure may lead to extreme photosensitivity persisting for months or years after the drug is withdrawn [11]. Management includes drug identification and discontinuation, topical corticosteroids, and sun avoidance [11]. The latter involves using physical barriers and broad-spectrum high SPF sunscreens [11].

Systemic, subacute, and chronic cutaneous lupus erythematosus Consistent photoprotection is critical for patients with systemic (SLE), subacute (SCLE), and chronic cutaneous (CCLE) lupus erythematosus (particularly discoid and tumid lupus) to minimize UV-induced flares [133].

Both UVA and UVB may induce flares [134–139]. UVA penetrates window glass so indoor exposure is often sufficient to trigger skin eruptions [140, 141]. Lesions may appear as late as 3 weeks after UV exposure [133].

In addition to broad spectrum high SPF sunscreens for adequate UVA coverage, there are case reports suggesting

that adjuvant PLE may help reduce flares in patients with SCLE [142–145]. Systemic medication is often required to treat the photosensitive reactions in patients with lupus.

Photoaggravated skin diseases

Photoaggravated skin diseases are worsened by UV exposure. The list of skin conditions is broad including common diseases such as atopic dermatitis (10% photoaggravated), rosacea, and acne vulgaris (can have improvement or photoaggravation) [146]. Given the wide action spectrum, broad-spectrum high SPF sunscreens are recommended. The same suggestion can be made for DNA repair syndromes [14].

In cutaneous porphyrias the action spectrum is primarily VL (400–410 nm), therefore tinted sunscreens containing iron oxide offer the greatest benefit [14].

Keratinocyte carcinomas (non-melanoma skin cancers) and melanoma

The American Cancer Society and the CDA recommend regular use of broad-spectrum sunscreen with SPF30 + to prevent keratinocyte carcinomas [147, 148]. Increased cumulative lifetime sun exposure increases the risk for squamous cell carcinoma (SCC) and actinic keratoses (AKs) [149]. Repeated intermittent high dose UVR exposure is associated with basal cell carcinoma (BCC) and melanoma [19, 150, 151].

Solid organ transplant recipients are 65–250 times more likely to develop SCC [152] and 10 times more likely to develop BCC compared to the general population due to immune suppression [153].

Barriers to sunscreen use: cosmesis, cost, and environmental impact

Esthetic considerations are important. Patients with sensitive skin typically describe stinging, burning and itching sensations, but the pathophysiology remains unclear [154]. Physical sunscreens are recommended for sensitive skin and pigmentary dyschromia (VL coverage), but some have cosmetic disadvantages. Reduced absorption and the scattering of incident light can create a white cast over the skin [104]. Micronization and nanoparticles have greatly improved the cosmesis, but it may remain a concern for patients with darker skin types [155]. Dermatologists should familiarize themselves with acceptable sunscreen options for all skin types [156]. Tints cosmetically enhance physical sunscreen options. Aerosol sprays have some cosmetic advantages because they are light and nongreasy, but they can leave a film and the application process is less controlled [157].

The cost of sunscreen and accessibility should be considered. Knowing more affordable options can be helpful. People can blend the appropriate foundation with sunscreen to provide a tinted option so long as the recommended quantity of sunscreen is still used.

There is concern that UV filters may cause coral bleaching [158, 159]. However, the studies done to date examine coral samples in a laboratory setting with high concentrations of chemical sunscreen ingredients [158]. Ocean warming due to climate change is a major factor in the release of zooxanthelae from coral that leads to bleaching [160]. The possible environmental impact of chemical sunscreen on coral reefs has led to local bans of benzophenone-3 and octinoxate in Hawaii [161].

Conclusion

A personalized approach to sunscreen selection may help in improving patient adherence, short-term and long-term clinical outcomes. Physicians should be aware of sunscreen labeling claims, potential side effects, and sunscreen preferences based on the action spectrum of specific diseases.

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References

1. Green A, Williams G, Neale R, Hart V, Leslie D, Parsons P et al (1999) Daily sunscreen application and betacarotene supplementation in prevention of basal-cell and squamous-cell carcinomas of the skin: a randomised controlled trial. Lancet 354(9180):723–729. https://doi.org/10.1016/s0140-6736(98)12168-2
2. Geisler AN, Austin E, Nguyen J, Hamzavi I, Jagdeo J, Lim HW (2021) Visible light. Part II: photoprotection against visible and ultraviolet light. J Am Acad Dermatol 84(5):1233–1244. https://doi.org/10.1016/j.jaad.2020.11.074
3. Suozzi K, Turban J, Girardi M (2020) Cutaneous photoprotection: a review of the current status and evolving strategies. Yale J Biol Med 93(1):55–67
4. DeBuys HV, Levy SB, Murray JC, Madey DL, Pinnell SR (2000) Modern approaches to photoprotection. Dermatol Clin 18(4):577–590. https://doi.org/10.1016/s0733-8635(05)70208-4
5. Rhodes LE (1998) Topical and systemic approaches for protection against solar radiation-induced skin damage. Clin Dermatol 16(1):75–82. https://doi.org/10.1016/s0738-081x(97)00171-5
6. Marionnet C, Pierrard C, Golebiewski C, Bernerd F (2014) Diversity of biological effects induced by longwave UVA rays (UVA1) in reconstructed skin. PLoS ONE 9(8):e105263. https://doi.org/10.1371/journal.pone.0105263

7. Edstrom DW, Porwit A, Ros AM (2001) Effects on human skin of repetitive ultraviolet-A1 (UVA1) irradiation and visible light. Photodermatol Photoimmunol Photomed 17(2):66–70. https://doi.org/10.1034/j.1600-0781.2001.017002066.x
8. Ikehata H, Kumagai J, Ono T, Morita A (2013) Solar-UV-signature mutation prefers TCG to CCG: extrapolative consideration from UVA1-induced mutation spectra in mouse skin. Photochem Photobiol Sci 12(8):1319–1327. https://doi.org/10.1039/c3pp25444e
9. Hughes MC, Williams GM, Baker P, Green AC (2013) Sunscreen and prevention of skin aging: a randomized trial. Ann Intern Med 158(11):781–790. https://doi.org/10.7326/0003-4819-158-11-201306040-00002
10. Clark A, Hessler JL (2015) Skin care. Facial Plast Surg Clin North Am 23(3):285–295. https://doi.org/10.1016/j.fsc.2015.04.002
11. Lehmann P, Schwarz T (2011) Photodermatoses: diagnosis and treatment. Dtsch Arztebl Int 108(9):135–141. https://doi.org/10.3238/arztebl.2011.0135
12. Beattie PE, Dawe RS, Ibbotson SH, Ferguson J (2003) Characteristics and prognosis of idiopathic solar urticaria: a cohort of 87 cases. Arch Dermatol 139(9):1149–1154. https://doi.org/10.1001/archderm.139.9.1149
13. Botto NC, Warshaw EM (2008) Solar urticaria. J Am Acad Dermatol 59(6):909–920. https://doi.org/10.1016/j.jaad.2008.08.020 (**quiz 21-22**)
14. Lim HW, Hawk JLM, Rosen CF (2018) Chapter 87: photodermatologic disorders. In: Bolognia JL, Schaffer JV, Cerroni L (eds) Dermatology, 4th edn. Elsevier; Amsterdam
15. Grimes PE, Ijaz S, Nashawati R, Kwak D (2019) New oral and topical approaches for the treatment of melasma. Int J Womens Dermatol 5(1):30–36. https://doi.org/10.1016/j.ijwd.2018.09.004
16. Castanedo-Cazares JP, Hernandez-Blanco D, Carlos-Ortega B, Fuentes-Ahumada C, Torres-Alvarez B (2014) Near-visible light and UV photoprotection in the treatment of melasma: a double-blind randomized trial. Photodermatol Photoimmunol Photomed 30(1):35–42. https://doi.org/10.1111/phpp.12086
17. Callender VD, St Surin-Lord S, Davis EC, Maclin M (2011) Postinflammatory hyperpigmentation: etiologic and therapeutic considerations. Am J Clin Dermatol 12(2):87–99. https://doi.org/10.2165/11536930-000000000-00000
18. Dumbuya H, Grimes PE, Lynch S, Ji K, Brahmachary M, Zheng Q et al (2020) Impact of iron-oxide containing formulations against visible light-induced skin pigmentation in skin of color individuals. J Drugs Dermatol 19(7):712–717. https://doi.org/10.36849/jdd.2020.5032
19. Taylor JH, Rosen CF (2020) Systemic photoprotection. Curr Dermatol Rep 9(3):181–188. https://doi.org/10.1007/s13671-020-00306-1
20. Yamada M, Mohammed Y, Prow TW (2020) Advances and controversies in studying sunscreen delivery and toxicity. Adv Drug Deliv Rev 153:72–86. https://doi.org/10.1016/j.addr.2020.02.001
21. What to wear to protect your skin from the sun. American Academy of Dermatology, Rosemont, IL. 2020. https://aad.newmedia-release.com/2020/what_to_wear/. Accessed 3 May 2021
22. Young AR, Boles J, Herzog B, Osterwalder U, Baschong W (2010) A sunscreen's labeled sun protection factor may overestimate protection at temperate latitudes: a human In vivo study. J Investig Dermatol 130(10):2457–2462. https://doi.org/10.1038/jid.2010.144
23. Obelis Group (2006) Stricter labelling principles for sunscreens in Europe. https://www.obelis.net/news/stricter-labelling-principles-for-sunscreens-in-europe/. Accessed 3 May 2021
24. Narbutt J, Philipsen P, Harrison G, Morgan K, Lawrence K, Baczynska K et al (2018) Sunscreen applied at ≥ 2mg/cm^2 during a sunny holiday prevents erythema; a biomarker of UVR-induced DNA damage and suppression of acquired immunity. Br J Dermatol 180:604–614. https://doi.org/10.1111/bjd.17277
25. Teramura T, Mizuno M, Asano H, Naito N, Arakane K, Miyachi Y (2012) Relationship between sun-protection factor and application thickness in high-performance sunscreen: double application of sunscreen is recommended. Clin Exp Dermatol 37(8):904–908. https://doi.org/10.1111/j.1365-2230.2012.04388.x
26. Petersen B, Wulf HC (2014) Application of sunscreen–theory and reality. Photodermatol Photoimmunol Photomed 30(2–3):96–101. https://doi.org/10.1111/phpp.12099
27. Russak JE, Chen T, Appa Y, Rigel DS (2010) A comparison of sunburn protection of high-sun protection factor (SPF) sunscreens: SPF 85 sunscreen is significantly more protective than SPF 50. J Am Acad Dermatol 62(2):348–349. https://doi.org/10.1016/j.jaad.2009.05.025
28. Ou-Yang H, Stanfield J, Cole C, Appa Y, Rigel D (2012) High-SPF sunscreens (SPF ≥ 70) may provide ultraviolet protection above minimal recommended levels by adequately compensating for lower sunscreen user application amounts. J Am Acad Dermatol 67(6):1220–1227. https://doi.org/10.1016/j.jaad.2012.02.029
29. Wright MW, Wright ST, Wagner RF (2001) Mechanisms of sunscreen failure. J Am Acad Dermatol 44(5):781–784. https://doi.org/10.1067/mjd.2001.113685
30. Odio MR, Veres DA, Goodman JJ, Irwin C, Robinson LR, Martínez J et al (1994) Comparative efficacy of sunscreen reapplication regimens in children exposed to ambient sunlight. Photodermatol Photoimmunol Photomed 10(3):118–125
31. Jallad KN (2017) Chemical characterization of sunscreens composition and its related potential adverse health effects. J Cosmet Dermatol 16(3):353–357. https://doi.org/10.1111/jocd.12282
32. Heurung AR, Raju SI, Warshaw EM (2014) Adverse reactions to sunscreen agents: epidemiology, responsible irritants and allergens, clinical characteristics, and management. Dermatitis 25(6):289–326. https://doi.org/10.1097/DER.0000000000000079
33. Fourtanier A, Moyal D, Seité S (2008) Sunscreens containing the broad-spectrum UVA absorber, Mexoryl SX, prevent the cutaneous detrimental effects of UV exposure: a review of clinical study results. Photodermatol Photoimmunol Photomed 24(4):164–174. https://doi.org/10.1111/j.1600-0781.2008.00365.x
34. Wang SQ, Balagula Y, Osterwalder U (2010) Photoprotection: a review of the current and future technologies. Dermatol Ther 23(1):31–47. https://doi.org/10.1111/j.1529-8019.2009.01289.x
35. Sabzevari N, Qiblawi S, Norton SA, Fivenson D (2021) Sunscreens: UV filters to protect us: part 1: changing regulations and choices for optimal sun protection. Int J Womens Dermatol 7(1):28–44. https://doi.org/10.1016/j.ijwd.2020.05.017
36. Nohynek GJ, Lademann J, Ribaud C, Roberts MS (2007) Grey goo on the skin? Nanotechnology, cosmetic and sunscreen safety. Crit Rev Toxicol 37(3):251–277. https://doi.org/10.1080/10408440601177780
37. Schilling K, Bradford B, Castelli D, Dufour E, Nash JF, Pape W et al (2010) Human safety review of "nano" titanium dioxide and zinc oxide. Photochem Photobiol Sci 9(4):495–509. https://doi.org/10.1039/b9pp00180h
38. Kullavanijaya P, Lim HW (2005) Photoprotection. J Am Acad Dermatol 52(6):937–958. https://doi.org/10.1016/j.jaad.2004.07.063 (**quiz 59–62**)
39. Torres AE, Awosika O, Maghfour J, Taylor S, Lim HW (2021) Practical guide to tinted sunscreens. J Am Acad Dermatol. https://doi.org/10.1016/j.jaad.2021.12.040
40. Nestor M, Bucay V, Callender V, Cohen JL, Sadick N, Waldorf H (2014) Polypodium leucotomos as an adjunct treatment of pigmentary disorders. J Clin Aesthet Dermatol 7(3):13–17

41. Siscovick JR, Zapolanski T, Magro C, Carrington K, Prograis S, Nussbaum M et al (2008) Polypodium leucotomos inhibits ultraviolet B radiation-induced immunosuppression. Photodermatol Photoimmunol Photomed 24(3):134–141. https://doi.org/10.1111/j.1600-0781.2008.00352.x
42. Parrado C, Mascaraque M, Gilaberte Y, Juarranz A, Gonzalez S (2016) Fernblock (polypodium leucotomos extract): molecular mechanisms and pleiotropic effects in light-related skin conditions, photoaging and skin cancers, a review. Int J Mol Sci 17(7):1026. https://doi.org/10.3390/ijms17071026
43. Choudhry SZ, Bhatia N, Ceilley R, Hougeir F, Lieberman R, Hamzavi I et al (2014) Role of oral polypodium leucotomos extract in dermatologic diseases: a review of the literature. J Drugs Dermatol 13(2):148–153
44. Nestor MS, Berman B, Swenson N (2015) Safety and efficacy of oral Polypodium leucotomos extract in healthy adult subjects. J Clin Aesthet Dermatol 8(2):19–23
45. Gonzalez S, Pathak MA (1996) Inhibition of ultraviolet-induced formation of reactive oxygen species, lipid peroxidation, erythema and skin photosensitization by Polypodium leucotomos. Photodermatol Photoimmunol Photomed 12(2):45–56. https://doi.org/10.1111/j.1600-0781.1996.tb00175.x
46. González S, Pathak MA, Cuevas J, Villarrubia VG, Fitzpatrick TB (1997) Topical or oral administration with an extract of Polypodium leucotomos prevents acute sunburn and psoralen-induced phototoxic reactions as well as depletion of Langerhans cells in human skin. Photodermatol Photoimmunol Photomed 13(1–2):50–60. https://doi.org/10.1111/j.1600-0781.1997.tb00108.x
47. Prado G, Teplitz R, Winkelmann R, Rosso J, Rigel D (2018) Clinical efficacy and safety of oral polypodium leucotomos extract for photoprotection: a systematic review. Skin J Cutaneous Med. https://doi.org/10.25251/skin.2.6.2.
48. Middelkamp-Hup MA, Pathak MA, Parrado C, Garcia-Caballero T, Rius-Díaz F, Fitzpatrick TB et al (2004) Orally administered Polypodium leucotomos extract decreases psoralen-UVA-induced phototoxicity, pigmentation, and damage of human skin. J Am Acad Dermatol 50(1):41–49. https://doi.org/10.1016/s0190-9622(03)02732-4
49. Winkelmann RR, Del Rosso J, Rigel DS (2015) Polypodium leucotomos extract: a status report on clinical efficacy and safety. J Drugs Dermatol 14(3):254–261
50. Boothby-Shoemaker WT, Mohammad TF, Ozog DM, Lim HW (2022) Photoprotection by clothing: a review. Photodermatol Photoimmunol Photomed. https://doi.org/10.1111/phpp.12776
51. Downs NJ, Harrison SL (2018) A comprehensive approach to evaluating and classifying sun-protective clothing. Br J Dermatol 178(4):958–964. https://doi.org/10.1111/bjd.15938
52. Gambichler T, Rotterdam S, Altmeyer P, Hoffmann K (2001) Protection against ultraviolet radiation by commercial summer clothing: need for standardised testing and labelling. BMC Dermatol. https://doi.org/10.1186/1471-5945-1-6
53. Wilson CA, Bevin NK, Laing RM, Niven BE (2008) Solar protection—effect of selected fabric and use characteristics on ultraviolet transmission. Text Res J 78(2):95–104. https://doi.org/10.1177/0040517508089660
54. Akgun M, Becerir B (2010) Ultraviolet (UV) protection of textiles: a review
55. Saravanan D (2007) UV protection textile materials. Autex Res J 7(1):53–62
56. Skin Cancer Foundation (2019) Sun-protective clothing. https://www.skincancer.org/skin-cancer-prevention/sun-protection/sun-protective-clothing/. Accessed 3 May 2021
57. Behar-Cohen F, Baillet G, de Ayguavives T, Garcia PO, Krutmann J, Peña-García P et al (2014) Ultraviolet damage to the eye revisited: eye-sun protection factor (E-SPF®), a new ultraviolet protection label for eyewear. Clin Ophthalmol 8:87–104. https://doi.org/10.2147/OPTH.S46189
58. Diffey BL, Cheeseman J (1992) Sun protection with hats. Br J Dermatol 127(1):10–12. https://doi.org/10.1111/j.1365-2133.1992.tb14816.x
59. Gabros S, Nessel TA, Zito PM (2020) Sunscreens and photoprotection. StatPearls. StatPearls Publishing, Treasure Island, FL
60. Crosera M, Prodi A, Mauro M, Pelin M, Florio C, Bellomo F et al (2015) Titanium dioxide nanoparticle penetration into the skin and effects on HaCaT cells. Int J Environ Res Public Health 12(8):9282–9297. https://doi.org/10.3390/ijerph120809282
61. Hayden CG, Cross SE, Anderson C, Saunders NA, Roberts MS (2005) Sunscreen penetration of human skin and related keratinocyte toxicity after topical application. Skin Pharmacol Physiol 18(4):170–174. https://doi.org/10.1159/000085861
62. Leite-Silva VR, Le Lamer M, Sanchez WY, Liu DC, Sanchez WH, Morrow I et al (2013) The effect of formulation on the penetration of coated and uncoated zinc oxide nanoparticles into the viable epidermis of human skin in vivo. Eur J Pharm Biopharm 84(2):297–308. https://doi.org/10.1016/j.ejpb.2013.01.020
63. Duracher L, Blasco L, Abdel Jaoued A, Vian L, Marti-Mestres G (2009) Irradiation of skin and contrasting effects on absorption of hydrophilic and lipophilic compounds. Photochem Photobiol 85(6):1459–1467. https://doi.org/10.1111/j.1751-1097.2009.00599.x
64. Spijker GT, Schuttelaar ML, Barkema L, Velders A, Coenraads PJ (2008) Anaphylaxis caused by topical application of a sunscreen containing benzophenone-3. Contact Dermatitis 59(4):248–249. https://doi.org/10.1111/j.1600-0536.2008.01337.x
65. Emonet S, Pasche-Koo F, Perin-Minisini MJ, Hauser C (2001) Anaphylaxis to oxybenzone, a frequent constituent of sunscreens. J Allergy Clin Immunol 107(3):556–557. https://doi.org/10.1067/mai.2001.112430
66. Hikima T, Maibach H (2006) Skin penetration flux and lag-time of steroids across hydrated and dehydrated human skin in vitro. Biol Pharm Bull 29(11):2270–2273. https://doi.org/10.1248/bpb.29.2270
67. Durand L, Habran N, Henschel V, Amighi K (2009) In vitro evaluation of the cutaneous penetration of sprayable sunscreen emulsions with high concentrations of UV filters. Int J Cosmet Sci 31(4):279–292. https://doi.org/10.1111/j.1468-2494.2009.00498.x
68. Warthan MM, Uchida T, Wagner RF Jr (2005) UV light tanning as a type of substance-related disorder. Arch Dermatol 141(8):963–966. https://doi.org/10.1001/archderm.141.8.963
69. Deng Y, Ediriwickrema A, Yang F, Lewis J, Girardi M, Saltzman WM (2015) A sunblock based on bioadhesive nanoparticles. Nat Mater 14(12):1278–1285. https://doi.org/10.1038/nmat4422
70. Li CC, Lin YT, Chen YT, Sie SF, Chen-Yang YW (2015) Improvement in UV protection retention capability and reduction in skin penetration of benzophenone-3 with mesoporous silica as drug carrier by encapsulation. J Photochem Photobiol B 148:277–283. https://doi.org/10.1016/j.jphotobiol.2015.04.027
71. Mancuso JB, Maruthi R, Wang SQ, Lim HW (2017) Sunscreens: an update. Am J Clin Dermatol 18(5):643–650. https://doi.org/10.1007/s40257-017-0290-0
72. Kimura E, Kawano Y, Todo H, Ikarashi Y, Sugibayashi K (2012) Measurement of skin permeation/penetration of nanoparticles for their safety evaluation. Biol Pharm Bull 35(9):1476–1486. https://doi.org/10.1248/bpb.b12-00103
73. Newman MD, Stotland M, Ellis JI (2009) The safety of nanosized particles in titanium dioxide- and zinc oxide-based sunscreens. J Am Acad Dermatol 61(4):685–692. https://doi.org/10.1016/j.jaad.2009.02.051
74. Scalia S, Mezzena M, Iannuccelli V (2007) Influence of solid lipid microparticle carriers on skin penetration of the sunscreen

agent, 4-methylbenzylidene camphor. J Pharm Pharmacol 59(12):1621–1627. https://doi.org/10.1211/jpp.59.12.0003
75. Joshi H, Hegde AR, Shetty PK, Gollavilli H, Managuli RS, Kalthur G et al (2018) Sunscreen creams containing naringenin nanoparticles: formulation development and in vitro and in vivo evaluations. Photodermatol Photoimmunol Photomed 34(1):69–81. https://doi.org/10.1111/phpp.12335
76. Mohammed YH, Holmes A, Haridass IN, Sanchez WY, Studier H, Grice JE et al (2019) Support for the safe use of zinc oxide nanoparticle sunscreens: lack of skin penetration or cellular toxicity after repeated application in volunteers. J Invest Dermatol 139(2):308–315. https://doi.org/10.1016/j.jid.2018.08.024
77. Cross SE, Innes B, Roberts MS, Tsuzuki T, Robertson TA, McCormick P (2007) Human skin penetration of sunscreen nanoparticles: in-vitro assessment of a novel micronized zinc oxide formulation. Skin Pharmacol Physiol 20(3):148–154. https://doi.org/10.1159/000098701
78. Sharma V, Shukla RK, Saxena N, Parmar D, Das M, Dhawan A (2009) DNA damaging potential of zinc oxide nanoparticles in human epidermal cells. Toxicol Lett 185(3):211–218. https://doi.org/10.1016/j.toxlet.2009.01.008
79. Sharma V, Singh SK, Anderson D, Tobin DJ, Dhawan A (2011) Zinc oxide nanoparticle induced genotoxicity in primary human epidermal keratinocytes. J Nanosci Nanotechnol 11(5):3782–3788. https://doi.org/10.1166/jnn.2011.4250
80. Iavicoli I, Leso V, Fontana L, Bergamaschi A (2011) Toxicological effects of titanium dioxide nanoparticles: a review of in vitro mammalian studies. Eur Rev Med Pharmacol Sci 15(5):481–508
81. Tran DT, Salmon R (2011) Potential photocarcinogenic effects of nanoparticle sunscreens. Australas J Dermatol 52(1):1–6. https://doi.org/10.1111/j.1440-0960.2010.00677.x
82. Heng BC, Zhao X, Tan EC, Khamis N, Assodani A, Xiong S et al (2011) Evaluation of the cytotoxic and inflammatory potential of differentially shaped zinc oxide nanoparticles. Arch Toxicol 85(12):1517–1528. https://doi.org/10.1007/s00204-011-0722-1
83. Filipe P, Silva JN, Silva R, Cirne de Castro JL, Marques Gomes M, Alves LC et al (2009) Stratum corneum is an effective barrier to TiO_2 and ZnO nanoparticle percutaneous absorption. Skin Pharmacol Physiol 22(5):266–275. https://doi.org/10.1159/000235554
84. Gonzalez H, Farbrot A, Larkö O, Wennberg AM (2006) Percutaneous absorption of the sunscreen benzophenone-3 after repeated whole-body applications, with and without ultraviolet irradiation. Br J Dermatol 154(2):337–340. https://doi.org/10.1111/j.1365-2133.2005.07007.x
85. Janjua NR, Kongshoj B, Andersson AM, Wulf HC (2008) Sunscreens in human plasma and urine after repeated whole-body topical application. J Eur Acad Dermatol Venereol 22(4):456–461. https://doi.org/10.1111/j.1468-3083.2007.02492.x
86. Matta MK, Zusterzeel R, Pilli NR, Patel V, Volpe DA, Florian J et al (2019) Effect of sunscreen application under maximal use conditions on plasma concentration of sunscreen active ingredients: a randomized clinical trial. JAMA 321(21):2082–2091. https://doi.org/10.1001/jama.2019.5586
87. Matta MK, Florian J, Zusterzeel R, Pilli NR, Patel V, Volpe DA et al (2020) Effect of sunscreen application on plasma concentration of sunscreen active ingredients: a randomized clinical trial. JAMA 323(3):256–267. https://doi.org/10.1001/jama.2019.20747
88. León Z, Chisvert A, Tarazona I, Salvador A (2010) Solid-phase extraction liquid chromatography-tandem mass spectrometry analytical method for the determination of 2-hydroxy-4-methoxybenzophenone and its metabolites in both human urine and semen. Anal Bioanal Chem 398(2):831–843. https://doi.org/10.1007/s00216-010-3947-6
89. Schlumpf M, Kypke K, Wittassek M, Angerer J, Mascher H, Mascher D et al (2010) Exposure patterns of UV filters, fragrances, parabens, phthalates, organochlor pesticides, PBDEs, and PCBs in human milk: correlation of UV filters with use of cosmetics. Chemosphere 81(10):1171–1183. https://doi.org/10.1016/j.chemosphere.2010.09.079
90. Wang SQ, Lim HW (2019) Highlights and implications of the 2019 proposed rule on sunscreens by the US Food and Drug Administration. J Am Acad Dermatol 81(2):650–651. https://doi.org/10.1016/j.jaad.2019.04.007
91. Gilchrest BA (2004) In this issue—if it's not the hamburgers, it's the sunscreens…. J Investig Dermatol 123(1):xi–xii. https://doi.org/10.1111/j.0022-202X.2004.22740.x
92. Suzuki T, Kitamura S, Khota R, Sugihara K, Fujimoto N, Ohta S (2005) Estrogenic and antiandrogenic activities of 17 benzophenone derivatives used as UV stabilizers and sunscreens. Toxicol Appl Pharmacol 203(1):9–17. https://doi.org/10.1016/j.taap.2004.07.005
93. Nashev LG, Schuster D, Laggner C, Sodha S, Langer T, Wolber G et al (2010) The UV-filter benzophenone-1 inhibits 17beta-hydroxysteroid dehydrogenase type 3: virtual screening as a strategy to identify potential endocrine disrupting chemicals. Biochem Pharmacol 79(8):1189–1199. https://doi.org/10.1016/j.bcp.2009.12.005
94. Taurog A, Dorris ML, Doerge DR (1996) Mechanism of simultaneous iodination and coupling catalyzed by thyroid peroxidase. Arch Biochem Biophys 330(1):24–32. https://doi.org/10.1006/abbi.1996.0222
95. Buck Louis GM, Chen Z, Kim S, Sapra KJ, Bae J, Kannan K (2015) Urinary concentrations of benzophenone-type ultraviolet light filters and semen quality. Fertil Steril 104(4):989–996. https://doi.org/10.1016/j.fertnstert.2015.07.1129
96. Ozáez I, Aquilino M, Morcillo G, Martínez-Guitarte JL (2016) UV filters induce transcriptional changes of different hormonal receptors in Chironomus riparius embryos and larvae. Environ Pollut 214:239–247. https://doi.org/10.1016/j.envpol.2016.04.023
97. Ozaez I, Morcillo G, Martinez-Guitarte JL (2016) Ultraviolet filters differentially impact the expression of key endocrine and stress genes in embryos and larvae of Chironomus riparius. Sci Total Environ 557–558:240–247. https://doi.org/10.1016/j.scitotenv.2016.03.078
98. Watanabe Y, Kojima H, Takeuchi S, Uramaru N, Sanoh S, Sugihara K et al (2015) Metabolism of UV-filter benzophenone-3 by rat and human liver microsomes and its effect on endocrine-disrupting activity. Toxicol Appl Pharmacol 282(2):119–128. https://doi.org/10.1016/j.taap.2014.12.002
99. Janjua NR, Mogensen B, Andersson AM, Petersen JH, Henriksen M, Skakkebaek NE et al (2004) Systemic absorption of the sunscreens benzophenone-3, octyl-methoxycinnamate, and 3-(4-methyl-benzylidene) camphor after whole-body topical application and reproductive hormone levels in humans. J Invest Dermatol 123(1):57–61. https://doi.org/10.1111/j.0022-202X.2004.22725.x
100. Schlumpf M, Cotton B, Conscience M, Haller V, Steinmann B, Lichtensteiger W (2001) In vitro and in vivo estrogenicity of UV screens. Environ Health Perspect 109(3):239–244. https://doi.org/10.1289/ehp.01109239
101. Perman MJ (2020) PIC. Groups continue to recommend sunscreen while studies are ongoing. American Academy of Pediatrics. https://www.aappublications.org/news/2020/06/01/focussunprotection060120#:~:text=Sunscreen%20with%20a%20sun%20protection,them%20from%20harmful%20UV%20rays.&text=Wear%20protective%20clothing%20such%20as,swimwear%20with%20UV%2Dprotective%20fabric. Accessed 20 May 2021

102. Gonzalez E, Gonzalez S (1996) Drug photosensitivity, idiopathic photodermatoses, and sunscreens. J Am Acad Dermatol 35(6):871–885. https://doi.org/10.1016/s0190-9622(96)90108-5 (**quiz 86-87**)
103. Gould JW, Mercurio MG, Elmets CA (1995) Cutaneous photosensitivity diseases induced by exogenous agents. J Am Acad Dermatol 33(4):551–573. https://doi.org/10.1016/0190-9622(95)91271-1 (**quiz 74–76**)
104. Scheuer E, Warshaw E (2006) Sunscreen allergy: a review of epidemiology, clinical characteristics, and responsible allergens. Dermatitis 17(1):3–11. https://doi.org/10.2310/6620.2006.05017
105. Deleo VA (2004) Photocontact dermatitis. Dermatol Ther 17(4):279–288. https://doi.org/10.1111/j.1396-0296.2004.04026.x
106. Bilsland D, Ferguson J (1993) Contact allergy to sunscreen chemicals in photosensitivity dermatitis/actinic reticuloid syndrome (PD/AR) and polymorphic light eruption (PLE). Contact Dermatitis 29(2):70–73. https://doi.org/10.1111/j.1600-0536.1993.tb03485.x
107. Macleod TM, Frain-Bell W (1975) A study of physical light screening agents. Br J Dermatol 92(2):149–156. https://doi.org/10.1111/j.1365-2133.1975.tb03051.x
108. Kerr A, Ferguson J (2010) Photoallergic contact dermatitis. Photodermatol Photoimmunol Photomed 26(2):56–65. https://doi.org/10.1111/j.1600-0781.2010.00494.x
109. Rosen CF (2003) Topical and systemic photoprotection. Dermatol Ther 16(1):8–15. https://doi.org/10.1046/j.1529-8019.2003.01602.x
110. Passeron T, Bouillon R, Callender V, Cestari T, Diepgen TL, Green AC et al (2019) Sunscreen photoprotection and vitamin D status. Br J Dermatol 181(5):916–931. https://doi.org/10.1111/bjd.17992
111. Glaser KS, Tomecki KJ (2020) Sunscreens in the United States: current status and future outlook. Adv Exp Med Biol 1268:355–379. https://doi.org/10.1007/978-3-030-46227-7_18
112. Lakhdar H, Zouhair K, Khadir K, Essari A, Richard A, Seité S et al (2007) Evaluation of the effectiveness of a broad-spectrum sunscreen in the prevention of chloasma in pregnant women. J Eur Acad Dermatol Venereol 21(6):738–742. https://doi.org/10.1111/j.1468-3083.2007.02185.x
113. Halder R, Rodney I, Munhutu M, Foltis P, Battie C, Verschoore M et al (2015) Evaluation and effectiveness of a photoprotection composition (sunscreen) on subjects of skin of color. J Am Acad Dermatol 72(5 Suppl 1):AB215
114. Lyons AB, Trullas C, Kohli I, Hamzavi IH, Lim HW (2021) Photoprotection beyond ultraviolet radiation: a review of tinted sunscreens. J Am Acad Dermatol 84(5):1393–1397. https://doi.org/10.1016/j.jaad.2020.04.079
115. Austin E, Geisler AN, Nguyen J, Kohli I, Hamzavi I, Lim HW et al (2021) Visible light. Part I: properties and cutaneous effects of visible light. J Am Acad Dermatol 84(5):1219–1231. https://doi.org/10.1016/j.jaad.2021.02.048
116. Duteil L, Esdaile J, Maubert Y, Cathelineau AC, Bouloc A, Queille-Roussel C et al (2017) A method to assess the protective efficacy of sunscreens against visible light-induced pigmentation. Photodermatol Photoimmunol Photomed 33(5):260–266. https://doi.org/10.1111/phpp.12325
117. Moyal D (2004) Prevention of ultraviolet-induced skin pigmentation. Photodermatol Photoimmunol Photomed 20(5):243–247. https://doi.org/10.1111/j.1600-0781.2004.00111.x
118. Wanitphakdeedecha R, Phuardchantuk R, Manuskiatti W (2014) The use of sunscreen starting on the first day after ablative fractional skin resurfacing. J Eur Acad Dermatol Venereol 28(11):1522–1528. https://doi.org/10.1111/jdv.12332
119. Vashi NA, Kundu RV (2013) Facial hyperpigmentation: causes and treatment. Br J Dermatol 169(s3):41–56. https://doi.org/10.1111/bjd.12536
120. Goh CL, Chuah SY, Tien S, Thng G, Vitale MA, Delgado-Rubin A (2018) Double-blind, placebo-controlled trial to evaluate the effectiveness of polypodium leucotomos extract in the treatment of melasma in Asian skin: a pilot study. J Clin Aesthet Dermatol 11(3):14–19
121. Martin LKMD, Caperton C, Woolery-Lloyd H, Avashia N (2012) A randomized double-blind placebo controlled study evaluating the effectiveness and tolerability of oral polypodium leucotomos in patients with melasma. J Am Acad Dermatol 66(4 Supplement 1):AB21. https://doi.org/10.1016/j.jaad.2011.11.096
122. Ahmed AM, Lopez I, Perese F, Vasquez R, Hynan LS, Chong B et al (2013) A randomized, double-blinded, placebo-controlled trial of oral Polypodium leucotomos extract as an adjunct to sunscreen in the treatment of melasma. JAMA Dermatol 149(8):981–983. https://doi.org/10.1001/jamadermatol.2013.4294
123. Robinson G, McMichael A, Wang SQ, Lim HW (2020) Sunscreen and frontal fibrosing alopecia: a review. J Am Acad Dermatol 82(3):723–728. https://doi.org/10.1016/j.jaad.2019.09.085
124. Aldoori N, Dobson K, Holden CR, McDonagh AJ, Harries M, Messenger AG (2016) Frontal fibrosing alopecia: possible association with leave-on facial skin care products and sunscreens; a questionnaire study. Br J Dermatol 175(4):762–767. https://doi.org/10.1111/bjd.14535
125. Debroy Kidambi A, Dobson K, Holmes S, Carauna D, Del Marmol V, Vujovic A et al (2017) Frontal fibrosing alopecia in men: an association with facial moisturizers and sunscreens. Br J Dermatol 177(1):260–261. https://doi.org/10.1111/bjd.15311
126. Moreno-Arrones OM, Saceda-Corralo D, Rodrigues-Barata AR, Castellanos-Gonzalez M, Fernandez-Pugnaire MA, Grimalt R et al (2019) Risk factors associated with frontal fibrosing alopecia: a multicentre case–control study. Clin Exp Dermatol 44(4):404–410. https://doi.org/10.1111/ced.13785
127. Cranwell WC, Sinclair R (2019) Sunscreen and facial skincare products in frontal fibrosing alopecia: a case–control study. Br J Dermatol 180(4):943–944. https://doi.org/10.1111/bjd.17354
128. Canavan TN, McClees SF, Duncan JR, Elewski BE (2019) Lichen planopilaris in the setting of hair sunscreen spray. Skin Appendage Disord 5(2):108–110. https://doi.org/10.1159/000490362
129. Orlowski T, Reynolds H, Elewski B (2020) Lichen planopilaris associated with spray-on sunscreen. Skin J Cutaneous Med 4:62. https://doi.org/10.25251/skin.4.1.8
130. Ramos PM, Anzai A, Duque-Estrada B, Farias DC, Melo DF, Mulinari-Brenner F et al (2021) Risk factors for frontal fibrosing alopecia: a case–control study in a multiracial population. J Am Acad Dermatol 84(3):712–718. https://doi.org/10.1016/j.jaad.2020.08.076
131. Lehmann P (2006) Diagnostic approach to photodermatoses. J Dtsch Dermatol Ges 4(11):965–975. https://doi.org/10.1111/j.1610-0387.2006.06010.x
132. Samorano LP, Reis VMS (2017) Photoprotection: concept, classification, and mechanism of action. In: Issa M, Tamura B (eds) Daily routine in cosmetic dermatology. Clinical approaches and procedures in cosmetic dermatology. Springer, Cham
133. Kuhn A, Sonntag M, Richter-Hintz D, Oslislo C, Megahed M, Ruzicka T et al (2001) Phototesting in lupus erythematosus: a 15-year experience. J Am Acad Dermatol 45(1):86–95. https://doi.org/10.1067/mjd.2001.114589
134. Kind P, Lehmann P, Plewig G (1993) Phototesting in lupus erythematosus. J Invest Dermatol 100(1):53S-S57. https://doi.org/10.1111/1523-1747.ep12355594

135. Lehmann P, Holzle E, Kind P, Goerz G, Plewig G (1990) Experimental reproduction of skin lesions in lupus erythematosus by UVA and UVB radiation. J Am Acad Dermatol 22(2 Pt 1):181–187. https://doi.org/10.1016/0190-9622(90)70020-i
136. Hasan T, Nyberg F, Stephansson E, Puska P, Häkkinen M, Sarna S et al (1997) Photosensitivity in lupus erythematosus, UV photoprovocation results compared with history of photosensitivity and clinical findings. Br J Dermatol 136(5):699–705
137. Leenutaphong V, Boonchai W (1999) Phototesting in oriental patients with lupus erythematosus. Photodermatol Photoimmunol Photomed 15(1):7–12. https://doi.org/10.1111/j.1600-0781.1999.tb00045.x
138. Nived O, Johansen PB, Sturfelt G (1993) Standardized ultraviolet-A exposure provokes skin reaction in systemic lupus erythematosus. Lupus 2(4):247–250. https://doi.org/10.1177/096120339300200407
139. Wolska H, Błaszczyk M, Jabłońska S (1989) Phototests in patients with various forms of lupus erythematosus. Int J Dermatol 28(2):98–103. https://doi.org/10.1111/j.1365-4362.1989.tb01327.x
140. Klein LR, Elmets CA, Callen JP (1995) Photoexacerbation of cutaneous lupus erythematosus due to ultraviolet A emissions from a photocopier. Arthritis Rheum 38(8):1152–1156. https://doi.org/10.1002/art.1780380819
141. Stern RS, Docken W (1986) An exacerbation of SLE after visiting a tanning salon. JAMA 255(22):3120
142. Breithaupt AD, Jacob SE (2012) Subacute cutaneous lupus erythematosus: a case report of Polypodium leucotomos as an adjuvant therapy. Cutis 89(4):183–184
143. Kuhn A, Gensch K, Haust M, Meuth AM, Boyer F, Dupuy P et al (2011) Photoprotective effects of a broad-spectrum sunscreen in ultraviolet-induced cutaneous lupus erythematosus: a randomized, vehicle-controlled, double-blind study. J Am Acad Dermatol 64(1):37–48. https://doi.org/10.1016/j.jaad.2009.12.053
144. Stege H, Budde MA, Grether-Beck S, Krutmann J (2000) Evaluation of the capacity of sunscreens to photoprotect lupus erythematosus patients by employing the photoprovocation test. Photodermatol Photoimmunol Photomed 16(6):256–259. https://doi.org/10.1034/j.1600-0781.2000.160604.x
145. Herzinger T, Plewig G, Röcken M (2004) Use of sunscreens to protect against ultraviolet-induced lupus erythematosus. Arthritis Rheum 50(9):3045–3046. https://doi.org/10.1002/art.20426
146. Passeron T, Lim HW, Goh C-L, Kang HY, Ly F, Morita A et al (2021) Photoprotection according to skin phototype and dermatoses: practical recommendations from an expert panel. J Eur Acad Dermatol Venereol 35(7):1460–1469. https://doi.org/10.1111/jdv.17242
147. Simon S (2018) Choose the right sunscreen. American Cancer Society. https://www.cancer.org/latest-news/choose-the-right-sunscreen.html. Accessed 15 May 2021
148. Green AC, Williams GM, Logan V, Strutton GM (2011) Reduced melanoma after regular sunscreen use: randomized trial follow-up. J Clin Oncol 29(3):257–263. https://doi.org/10.1200/jco.2010.28.7078
149. Ackerman AB, Mones JM (2006) Solar (actinic) keratosis is squamous cell carcinoma. Br J Dermatol 155(1):9–22. https://doi.org/10.1111/j.1365-2133.2005.07121.x
150. Xiang F, Lucas R, Hales S, Neale R (2014) Incidence of nonmelanoma skin cancer in relation to ambient UV radiation in white populations, 1978–2012: empirical relationships. JAMA Dermatol 150(10):1063–1071. https://doi.org/10.1001/jamadermatol.2014.762
151. Osterlind A, Tucker MA, Hou-Jensen K, Stone BJ, Engholm G, Jensen OM (1988) The Danish case-control study of cutaneous malignant melanoma. I. Importance of host factors. Int J Cancer 42(2):200–206. https://doi.org/10.1002/ijc.2910420210
152. Mittal A, Colegio OR (2017) Skin cancers in organ transplant recipients. Am J Transplant 17(10):2509–2530. https://doi.org/10.1111/ajt.14382
153. Kricker A, Armstrong BK, English DR, Heenan PJ (1995) Does intermittent sun exposure cause basal cell carcinoma? a case–control study in Western Australia. Int J Cancer 60(4):489–494. https://doi.org/10.1002/ijc.2910600411
154. Duarte I, Silveira JEPS, Hafner MFS, Toyota R, Pedroso DMM (2017) Sensitive skin: review of an ascending concept. An Bras il Dermatol 92(4):521–525. https://doi.org/10.1590/abd1806-4841.201756111
155. Maier T, Korting HC (2005) Sunscreens—which and what for? Skin Pharmacol Physiol 18(6):253–262. https://doi.org/10.1159/000087606
156. Song H, Beckles A, Salian P, Porter ML (2021) Sunscreen recommendations for patients with skin of color in the popular press and in the dermatology clinic. Int J Women's Dermatol 7(2):165–170. https://doi.org/10.1016/j.ijwd.2020.10.008
157. Dale Wilson B, Moon S, Armstrong F (2012) Comprehensive review of ultraviolet radiation and the current status on sunscreens. J Clin Aesthetic Dermatol 5(9):18–23
158. Danovaro R, Bongiorni L, Corinaldesi C, Giovannelli D, Damiani E, Astolfi P et al (2008) Sunscreens cause coral bleaching by promoting viral infections. Environ Health Perspect 116(4):441–447. https://doi.org/10.1289/ehp.10966
159. Downs CA, Kramarsky-Winter E, Segal R, Fauth J, Knutson S, Bronstein O et al (2016) Toxicopathological effects of the sunscreen UV Filter, oxybenzone (benzophenone-3), on coral planulae and cultured primary cells and its environmental contamination in Hawaii and the U.S. Virgin Islands. Archiv Environ Contam Toxicol. 70(2):265–288. https://doi.org/10.1007/s00244-015-0227-7
160. Mitchelmore CL, Burns EE, Conway A, Heyes A, Davies IA (2021) A critical review of organic ultraviolet filter exposure, hazard, and risk to corals. Environ Toxicol Chem 40(4):967–988.https://doi.org/10.1002/etc.4948
161. Ouchene L, Litvinov IV, Netchiporouk E (2019) Hawaii and other jurisdictions ban oxybenzone or octinoxate sunscreens based on the confirmed adverse environmental effects of sunscreen ingredients on aquatic environments. J Cutan Med Surg 23(6):648–649. https://doi.org/10.1177/1203475419871592
162. Fisher AA (1992) Sunscreen dermatitis: para-aminobenzoic acid and its derivatives. Cutis 50(3):190–192
163. Latha MS, Martis J, Shobha V, Sham Shinde R, Bangera S, Krishnankutty B et al (2013) Sunscreening agents: a review. J Clin Aesthet Dermatol 6(1):16–26
164. Lacatusu I, Badea N, Murariu A, Meghea A (2011) The encapsulation effect of UV molecular absorbers into biocompatible lipid nanoparticles. Nanoscale Res Lett 6(1):73. https://doi.org/10.1186/1556-276x-6-73
165. Chatelain E, Gabard B (2001) Photostabilization of butyl methoxydibenzoylmethane (Avobenzone) and ethylhexyl methoxycinnamate by bis-ethylhexyloxyphenol methoxyphenyl triazine (Tinosorb S), a new UV broadband filter. Photochem Photobiol 74(3):401–406. https://doi.org/10.1562/0031-8655(2001)074%3c0401:pobmaa%3e2.0.co;2
166. Nash JF (2006) Human safety and efficacy of ultraviolet filters and sunscreen products. Dermatol Clin 24(1):35–51. https://doi.org/10.1016/j.det.2005.09.006

167. Rai R, Shanmuga SC, Srinivas C (2012) Update on photoprotection. Indian J Dermatol 57(5):335–342. https://doi.org/10.4103/0019-5154.100472