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Visible Light Part II. Photoprotection against visible and ultraviolet light

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Abstract

Cutaneous photobiology studies have focused primarily on the UV portion of the solar spectrum. However, VL comprises 50% of EMR that reaches the earth's surface, and, as discussed in Part I of this CME, VL has cutaneous biologic effects such as pigment darkening and erythema. Photoprotection against VL includes sun avoidance, seeking shade, and the use of photoprotective clothing. Organic and inorganic UV filters used in sunscreens do not protect against VL; only tinted sunscreens do. In the US, these filters are regulated by the FDA as an over-the-counter drug and are subjected to more stringent regulations than in Europe, Asia, and Australia. There are no established guidelines regarding VL photoprotection. Alternative measures to confer VL photoprotection are being explored. These novel methods include topical, oral, and subcutaneous agents. Further development should focus on better protection in the range of UVA1 (340–400nm) and VL while enhancing the cosmesis of the final products.

Keywords

visible light; ultraviolet light; visible light photoprotection; photoprotection; organic filter; inorganic filter; photolyase; light filter; sunscreen; sunblock

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I. TYPES OF PHOTOPROTECTION

Key points

- VL (400–700 nm) accounts for 50% of electromagnetic radiation that reaches the earth's surface.
- Photoprotective measures against VL include avoiding the sun, seeking shade, and using photoprotective clothing.
- Tinted sunscreens are the only currently available topical photoprotection products for VL.

Electromagnetic radiation.

The adverse effects of sun exposure on the skin are well-established.[1] The sun emits broad-spectrum electromagnetic radiation (EMR) with a peak in the visible light (VL) (400–700 nm) range.[2–7] The majority of EMR that reaches the earth's surface is composed of UVB (290–320 nm), UVA2 (320–340 nm), UVA1 (340–400 nm), VL (400–700 nm), and infrared (IR) (700 nm-1 mm) radiation.[2–8] Cutaneous photobiology studies have focused primarily on the ultraviolet (UV) portion of the solar spectrum, as the erythema peak is around 295nm.[3,9–11] However, VL compromises 50% of EMR that reaches the earth's surface (versus UV, which is responsible for only 5%) and has been shown to induce pigment darkening and erythema as discussed in Part I.[3,11–19,17,20–24] Environmental exposure to VL is primarily from the sun, but also from electronic devices such as smartphones, tablets, and computer screens.[25–28] However, the cumulative dose of blue light emitted by these low-intensity sources is not relevant for VL biologic effects as it does not reach the dose demonstrated to induce hyperpigmentation.[28]

Photoprotection modalities.

Photoprotection is critical to maintain skin health, minimize post-inflammatory hyperpigmentation, and prevent photoaging and photocarcinogenesis. Photoprotective measures include avoiding the sun, seeking shade, using photoprotective clothing, wearing wide-brimmed hats and sunglasses, and applying broad-spectrum sunscreens.[26,29] UV filters used in sunscreens may be either organic (i.e., chemical) or inorganic (i.e., mineral) (Table 1).[2,17,22,23,30] While these terms are used interchangeably, organic and inorganic filters are the terms recommended by the US Food and Drug Administration (FDA).[2,17,22,23,30] All UV filters, including mineral filters [zinc oxide (ZnO) and titanium dioxide (TiO_2)] are "chemicals".[2,17,22,23,30] It is a misconception that mineral filters are "physical blockers" as they absorb UV photons, especially in nanosized form.[2,17,22,23,30] Nanosized inorganic filters (i.e., ZnO, TiO_2) do not have VL photoprotective properties, but non-nanosized inorganic filters do.[15,17,24,31–33] For proper photoprotection, sunscreens should be combined with measures outlined above.[33–38]

Organic filters.

Organic filters are composed of an aromatic ring and functional groups of electron donors and acceptors that delocalize electrons upon UV irradiation and absorption.[6,16,22,39–41] There are five main types of organic filters: para-aminobenzoic acid (PABA) derivatives, benzophenones, salicylates, cinnamates, and other.[6] Oxybenzone is the most commonly used benzophenone and absorbs UVB and short UVA.[6] UV filters are often combined to increase photostability and spectral performance.[2,4,42] The structure of organic filters allow for UVR, but not VL, to be absorbed, resulting in molecular conformational changes.[43–45] As the molecule returns from the excited to the ground state, energy is released as heat (Figure 1).[22,43–45]

Inorganic filters.

The two FDA-approved inorganic filters, ZnO and TiO_2, are metal oxides that effectively absorb, reflect, or scatter EMR.[2,3,7,22,25,32,39,40,46,47] Inorganic filters are nontoxic, nonallergenic, and largely unaffected by light-induced reactions, unlike organic filters.[2,3,47] Products with inorganic filters might give skin a chalky white appearance that limits usage due to cosmesis, especially in skin of color (SOC).[12,15–17,24,26,32,37,51–53] Micronized formulations make inorganic filters more cosmetically appealing, but less protective for UVA and VL.[2,3,7,12,20,29,30,32,35,39,46,47,54–57] Larger opaque pigments confer superior protection against photodermatoses induced by VL, such as erythropoietic protoporphyria (EPP).[2,3,7,12,20,21,29,30,32,35,38,39,46,47,54–57]

Tinted (colored) sunscreens:

Since neither organic nor inorganic UV filters used in sunscreens protect against VL, tinted (colored) sunscreens are available to protect against VL.[48,58] Tinted sunscreens consist of a blend of iron oxides (Fe_2O_3) and TiO_2 pigments that function as VL and UV blockers.[24,58] Depending on the oxidation state, Fe_2O_3 may appear yellow, red, or black.[24] Yellow Fe_2O_3 protects melanocompetent subjects from VL-induced pigmentation.[59] Tinted sunscreens reduce VL transmission by 93–98%.[2,3,7,22,24,25,32,39,40,46,47]

Daily application of tinted sunscreens reduced the appearance of cutaneous hyperchromias after 60 days.[58,60] One study compared a combination of Fe_2O_3 and TiO_2 to a non-tinted mineral SPF 50+ sunscreen with ZnO and TiO_2 for protection against VL-induced pigmentation.[60,61] Expert grading and colorimetry demonstrated that the Fe_2O_3-containing formulations better protected against VL-induced pigmentation than non-tinted mineral sunscreen in Fitzpatrick IV individuals.[60,61]

Fe_2O_3-containing formulations in women's facial products, including foundations, have a dual function in covering pigmentary blemishes and reducing the development of further pigmentation induced by sunlight.[60] The availability of foundations in multiple shades and tones can offer daily, customized protection beyond the UV spectrum for individuals of all skin phototypes.[60] Foundations that contain Fe_2O_3 to even skin tone and cover blemishes have been demonstrated to protect against blue light.[59]

Photoprotection against VL is relevant for SOC, as VL may contribute to melasma and post-inflammatory hyperpigmentation.[9,12,13,20,24,26,27,32,33,36,47–49] Tinted sunscreens which include mineral pigments improve the Melasma Area and Severity Index (MASI) score.[50] A study compared the use of broad-spectrum UV protection that contained Fe_2O_3 as a VL-absorbing pigment (UV-VL) and a regular UV-only broad-spectrum sunscreen in 61 patients with melasma, receiving 4% hydroquinone as a depigmenting treatment.[62] At 8 weeks, UV-VL protection showed a 15%, 28%, and 4% greater improvement in MASI, colorimetric values, and melanin assessments, respectively.[62] In addition to improving melasma lesions after 8 weeks, broad-spectrum sunscreens containing Fe_2O_3 alone or in combination with ZnO and TiO_2 prevented relapses after 6 months.[60]

Application of sunscreens.

Sunscreen efficacy is measured by the sun protection factor (SPF), an assessment of the ratio of the minimal erythemal dose (MED) of UVR on filter protected skin compared to unprotected skin (MED protected/MED unprotected).[25,63] For SPF testing, sunscreen is applied at 2 mg/cm^2, which corresponds to 30 mL (1 oz) for the entire body surface.[44] SPF is a measure of the erythemogenic effect of UVB, and to a lesser extent, UVA2.[33] In the US, sunscreens labeled as “broad-spectrum” must have a critical wavelength (CW) of ≥370 nm.[1,3,9,29,46,64] To meet this criterion, at least 90% of the product’s total absorbance must be at or above this CW value when measured using UV wavelengths ranging from 290 to 400 nm.[29,57] Broad-spectrum sunscreens with an SPF >15 may claim protection from skin cancer and early skin aging.[3,35,46] Theoretically, for someone who burns typically after 10 minutes, wearing SPF 15 would allow them to stay outside 15 times longer (2.5 hours) without burning if sun exposure is constant.[65,66] However, most individuals tend to underapply sunscreens.[2,3,44,46,64,67,68] Therefore, the in-use SPF is significantly lower than the labeled SPF. Furthermore, SPF alone does not indicate protection against UVA nor VL.[65,66,69,70]

The FDA and US Preventive Services Task Force recommend the use of a broad-spectrum filter with SPF>15, while the American Academy of Dermatology (AAD) recommends SPF>30.[46,71] Products with SPF 15, 30, and 60 allow 6.7%, 3.3%, and 1.7% UVR to be transmitted to the skin surface, respectively, based on topical application at 2 mg/cm^2; however, consumers usually apply 0.5–1.0 mg/cm.[2,3,44,46,64,67,68] While the difference between SPF 30 and 60 (3.3% vs. 1.7% transmission) is relatively minimal for a single acute exposure, with daily application over time, the more than 2-fold difference might significantly affect chronic UV effects on the skin.[72] The “Teaspoon Rule of Applying Sunscreen,” which advises 1 teaspoon of sunscreen to the face/head/neck, 1 teaspoon to each upper extremity, 2 teaspoons to the torso, and 2 teaspoons to each lower extremity, was proposed to help achieve 2 mg/cm^2 of density.[23,35,67]

Other photoprotective strategies.

Pollutants, clouds, and fog may reduce the intensity of UVR, VL, and IR; ozone absorbs UVC (99%), some UVB (90%), but little to no UVA or VL (50%).[5,73] The US National Weather Service calculation of the UV index assumes that clear skies allow 100% of UV transmission, scattered clouds 89%, broken clouds 73%, and overcast skies 31%.[5,73] Clear

glass allows up to 90% of VL (assessed from 400–780 nm), 72% of UV (from 300–400 nm), and 83% of solar heat to penetrate.[74,75] Tinted or reflective glass transmits less VL, UV, and IR radiation; however, US federal standards mandate at least 70% VL transmission through the windshield.[5,47,74] All types of glass block transmission of UVB (280–315 nm).[5,47,74] Darkly tinted sunglasses may block UVA and VL but can obscure vision.[47] UVB may damage the cornea and lens, whereas VL can affect the retina.[11,47,74] Glasses with blue lenses absorb VL between 400–500nm.[74,76–80] Orange and yellow lenses provide the best protection against both UV and VL.[81] Wide-brimmed hats may offer an SPF of up to 7.[5,64] The UV protection factor (UPF) is a measure of protection against UV through clothing.[5,23,73,82] A UPF of 15–24 indicates good protection, 25–39 very good protection, and 40–50 excellent protection, with tightly woven and dark fabrics being superior.[5,46] The pigments in makeup and tanning preparations (e.g., dihydroxyacetone) protect against UVA and VL by their oxidation effects that change skin color to orange-brown.[32,47] The color remains adherent to the stratum corneum and confers an SPF of 2.[5,47] Systemic agents may also protect against VL as discussed later.

II. GLOBAL DIFFERENCES IN REGULATIONS OF UV FILTERS

Key points

- In the US, the FDA regulates UV filters as an over-the-counter drug.
- The FDA categorize inorganic filters as generally recognized as safe and effective.
- VL photoprotection regulations and guidelines are lacking in the US and globally.

United States FDA regulations.

In the US, the FDA regulates UV filters as an over-the-counter drug.[3,6,16,29,30,42,83,84] The FDA proposed its first set of rules regarding UV filters in 1978, and the original FDA monograph listed 16 approved UV filters (Table 1).[1,30,46,47] Another UV filter available in the US, ecamsule, was approved as part of New Drug Application in 2006.[30,47] From 1997 to 2009, the percentage of low SPF products (SPF 4–14) decreased from 27% to 6%, the number of products that filter against UVA increased from 5% to 70%, and 68% of the products tested in 2009 attained CW >370 nm.[85] There is a trend toward more broad-spectrum coverage in the UVA and VL range. The FDA proposed rule, released on February 2019, classified the 16 approved UV filters in the monograph into 3 categories: Category 1 (zinc oxide and titanium dioxide): generally recognized as safe and effective (GRASE), Category 2 (PABA, trolamine salicylate): not GRASE, and Category 3 (remaining 12 UV filters): insufficient data to determine GRASE.[25,31,86] However, guidelines addressing VL are insufficient.[7,20]

Other countries.

Compared to Europe, Asia, Central, and South America, Canada, and Australia, the US has fewer available UV filters, which offer less superior UVA protection due to stringent requirements.[3,6,29,31,35,87,88] UV filters are regulated as cosmetics in Europe, quasi-drugs in Japan, and therapeutic drugs in Australia.[3,6,16,30,35,42,47,89,90] Currently, there are 29 UV filters approved in Europe.[3,47] Several UV filters with broadband UV protection have been approved in Europe and other parts of the world since the 1990s; however, they are not yet approved by the US FDA.[1,3,6,34,88,89]

III. SAFETY OF UV FILTERS

Key points

- Safety concerns regarding UV filters include photoallergic reactions and potential systemic absorption.
- The use of sunscreens has been associated with frontal fibrosing alopecia, b no causal relationship has been established.
- The AAD and the National Council on Skin Cancer Prevention recommend receiving vitamin D through the diet and oral supplementation and avoiding intentional UV radiation exposure to induce production.
- Data currently support the regular use of UV filters as the benefits greatly outweigh the limited data regarding its risks.

Photoallergic reactions.

UV filters may induce irritant and allergic contact reactions, photoallergy, and phototoxic effects.[3,16,35,46,47,73] In a 10-year retrospective analysis of almost 24,000 patients patch-tested, 0.9% had a sunscreen allergy, and 70% of those were due to oxybenzone.[15,34,35,47,91] The American Contact Dermatitis Society named oxybenzone contact allergen of the year, and the European Scientific Committee on Consumer Safety has recommended its replacement with other broad-spectrum filters.[14,15,34,73,92] However, its use continues in the US because the FDA has not yet approved alternative filters.[6,15] The Centers for Disease Control and Prevention estimate that 96.8% of the US population has been exposed to oxybenzone since its first use in 1978.[15,52,92–94]ut Thus, in regards to its widespread use, the development of photoallergic reactions are uncommon.[47,73]

Systemic absorption of UV filters.

In vitro and animal studies report endocrinologic effects of UV filters, but the results are equivocal in human studies.[6,15,30,34,47,73,93,95–97] Metal oxide nanoparticles do not penetrate the stratum corneum but are deposited in the openings of pilosebaceous follicles, sweat glands, and skin folds.[30,34,35,39,40,51,54,55,98,99] In vitro, nanoparticles generate reactive oxygen species (ROS) when exposed to UVA and UVB light.[39,40,73,98] However, their safety in sunscreen products is well established.[39,40,73,98] In sunscreens, nanoparticles are coated with silica or aluminum hydroxide that minimize ROS formation

and cytotoxicity.[25,31,34,35,57,100] Additionally, endogenous antioxidants in the skin can neutralize ROS.[35]

Possible link to frontal fibrosing alopecia.

Survey data demonstrates an association between sunscreen use and frontal fibrosing alopecia (FFA) in men and women.[33,101–106] TiO_2 has been found in the hair shafts of FFA patients, and the dominant putative mechanism for the association is that UV filters penetrate the follicular infundibulum and elicit a lichenoid reaction.[104,106] Overall incidence of FFA remains low compared to the prevalence of sunscreen use, and not all patients with FFA endorse exposure to UV filters.[106] Thus, there is insufficient evidence to establish a direct causal relationship.[106]

Vitamin D.

While questions exist about UV filters reducing the production of UVB-induced vitamin D synthesis, this is not a concern due to the underapplication of sunscreen by the public.[3,33,35,73,89,107–111] The AAD and the National Council on Skin Cancer Prevention recommend receiving vitamin D through the diet and oral supplementation and avoiding intentional UV radiation exposure to induce production.[33,36,107,109–113] The benefits of regular sunscreen use outweigh the risks.[6,16,83]

IV. ENVIRONMENTAL IMPACT OF UV FILTERS

Key points

- UV filters may enter the aquatic environment and cause coral reef bleaching and death.
- Hawaii became the first state to ban the use of two light filters, oxybenzone and octinoxate.
- Except for the US, oxybenzone is no longer commonly used in sunscreens in many parts of the world.

Damage to coral reefs.

It is estimated that as much as 14,000 tons of UV filters are released into the coral reefs annually.[92,94,114–115] Oxybenzone was added to the Environmental Protection Agency High Production Volume Challenge Program, which identifies ingredients manufactured or imported into the US in amounts equal to or greater than one million pounds per year.[92] Organic filters cause coral bleaching and death.[31,52,92,94,115,117–121] However, a study done in Oahu, Hawaii, showed that the concentrations detected in seawater were 1000^{th}-fold lower than those reported to be cytotoxic to coral reefs in vitro.[115] Multiple studies have concluded that ocean water warming is a major contributing factor in coral bleaching.[6,31,52,94,122–128] In many parts of the world, because of the availability of other filters, oxybenzone is no longer commonly used in sunscreens; this is not the case in the US due to the limited availability of filters to replace oxybenzone.[14,25,33,46,68,92,94,129]

Environmental regulations.

Hawaii became the first state to ban the sale of two UV filters, oxybenzone, and octinoxate, by January 1, 2021.[14,25,33,46,68,92,94,129] The US Virgin Islands, Palau, Bonaire, the nature reserves of Mexico, and Key West enacted similar bans, while active discussions are occurring in Brazil and Europe.[31,52,94,117]

V. ROLE OF ANTIOXIDANTS AND OTHER AGENTS IN PHOTOPROTECTION AND PHOTOREPAIR

Key points

- Emerging evidence exists for the beneficial effects of sunscreen containing photolyases, enzymes that repair DNA damage.
- Early studies show that oral and topical antioxidants might confer VL photoprotection.

Photorepair with photolyase.

There is emerging evidence for the beneficial effects of sunscreen containing photolyases.[21,130–132] Photolyases are enzymes that repair cyclobutane pyrimidine dimers (CPDs) upon exposure to blue light.[15,131,133–139] After photodynamic therapy (PDT), daily application of a sunscreen with photolyases was associated with a reduction in the number of new AK lesions compared to conventional sunscreen.[15,21,130,140] The combination of topical antioxidants and photolyases may have a synergistic effect.[15,132] However, photolyases are not effective when used with VL blockers as they are activated by blue light.[15,133–135]

Antioxidant mechanism of photoprotection.

UVB-induced erythema results from direct DNA damage (i.e., CPDs), while UVA effects are largely mediated by ROS.[33] VL exposure may contribute up to one-half of ROS generated in the skin.[7,11,25,133,136] The addition of antioxidants to sunscreens reduces ROS formation by an additional 1.7-fold for SPF 4 and 2.4-fold for SPF 15 products.[130] Antioxidants modulate the effects of VL on a molecular level by reducing interleukin-1a and matrix metalloproteinase expression.[5,6,11,15,17,18,25,32,34,35,141,142] In one study, topical application of a sunscreen containing an antioxidant complex reduced immediate erythema and pigmentation in subjects with skin phototypes I-III and IV-VI, respectively, after irradiation with VL and UVA1.[60] However, this protective effect was not observed at day 7, indicating that antioxidants may be more effective at reducing pigmentation mediated by photo-oxidation than pigmentation caused by de novo melanin synthesis.[60]

Topical, oral, and systemic agents for VL photoprotection.

In addition to offering superior VL protection, topical antioxidants are non-toxic.[5,22,81,143–149] However, in an analysis of sunscreens with antioxidant ingredients, 10 of 12 sunscreens had no antioxidant activity, and the other 2 had only low activity.[34,35]

More research is needed to determine how to stabilize antioxidants into a biologically active product.[34,35]

Oral photoprotective agents (Table 2)[11,15,21,22,25,33,53,142,147–155] offer the advantage of protecting the skin surface without being affected by external factors such as washing, perspiration, or rubbing.[12,21,73,81] Oral *Polypodium leucotomos* extract has photoprotective, chemoprotective, anti-inflammatory, and immunomodulatory properties that mitigate VL-induced effects, including persistent pigment darkening and delayed tanning.[154] Subcutaneous afamelanotide, an analog of α-melanocyte stimulating hormone, stimulates melanin production and has antioxidative properties, and is approved for the management of EPP, a VL-induced photodermatosis.[32,150,156,157]

VI. RECOMMENDATIONS, FUTURE DIRECTIONS, AND CONCLUSION

Key points

- Sunscreens have undergone fundamental improvements, but there is still a need for additional research on VL photoprotection.
- Further development should focus on better protection in the range of UVA1 and VL, enhancing cosmesis, and incorporating antioxidants to enhance photoprotection.

Photoprotection against VL includes seeking shade during peak hours, wearing photoprotective clothing and accessories, and applying tinted broad-spectrum sunscreens.[1,52,67,85,94] While sunscreens have undergone significant improvements, there is still a need for additional VL photoprotection research. Further development should focus on better protection in the range of UVA1 and VL, enhancing cosmesis of these filters (especially for susceptible SOC individuals), and the use of effective antioxidants and other agents to enhance photoprotection.[29,48,85,87,94,158]

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Conflict of Interest Disclosure(s):

Henry W. Lim is an investigator for Incyte, L'Oreal, Pfizer, and PCORI, has served as a consultant for Pierre Fabre, ISDIN, Ferndale, Galderma, and La Roche-Posay, and has participated as a speaker in general educational session for Johnson and Johnson, Ra Medical System, La Roche-Posay, and Cantabria labs. Indermeet Kohli is an investigator (grant funding received by the institution) for Ferndale, Estee Lauder, L'Oreal, Unigen, Johnson and Johnson, Allergan, and Bayer and is a consultant (fee and equipment received by the institution) for Pfizer, Johnson and Johnson, and Bayer. Jared Jagdeo is a member of the GlobalMed Scientific advisory board and a consultant for UV Biotek. Iltefat Hamzavi is an investigator for Estee Lauder, Ferndale Laboratories, Galderma, Bayer, Loreal, Lenicura, and Unigen.

ABBREVIATIONS

AK	actinic keratoses
AAD	American Academy of Dermatology
CW	critical wavelength
CPD	cyclobutene pyrimidine dimer
EMR	electromagnetic radiation
EPP	erythropoietic protoporphyria
FAD	flavin adenine dinucleotide
FDA	Food and Drug Administration
FFA	frontal fibrosing alopecia
GRASE	generally recognized as safe and effective
IR	infrared
MASI	Melasma Area and Severity Index
MED	minimal erythemal dose
PABA	para-aminobenzoic acid
PDT	photodynamic therapy
ROS	reactive oxygen species
SOC	skin of color
SPF	sun protection factor
TiO_2	titanium dioxide
UV	ultraviolet
UPF	UV protection factor
UVR	UV radiation
WWTP	wastewater treatment plant
VL	visible light
ZnO	zinc oxide

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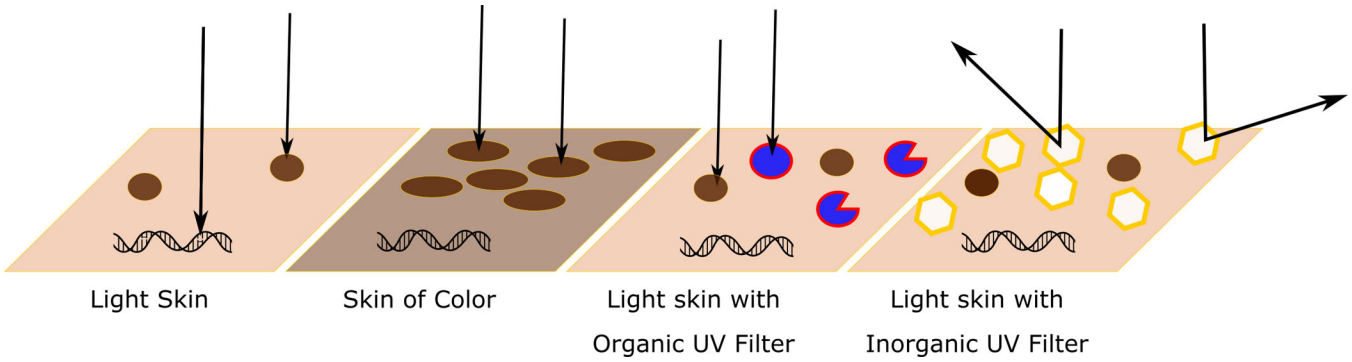

Figure 1. Mechanism of action of organic and inorganic UV filters.
Note that as the diameter of the inorganic filters decreases, they do absorb UVB.

Table 1.

Approved UV filters listed in the 1999 United States Food and Drug Administration sunscreen monograph.[30,46,73]

Light filter	Maximum Approved Concentration (%)	Peak Absorption (nm)	Action spectrum
Organic Filters			
PABA derivatives			
PABA	15%	283	UVB
Padimate O	8%	311	UVB
Benzophenones			
Dioxybenzone	3%	352	UVB, UVA2
Oxybenzone	6%	288, 325	UVB, UVA2
Sulisobenzone	10%	366	UVB, UVA2
Salicylates			
Homosalate	15%	306	UVB
Octisalate	5%	307	UVB
Trolamine salicylate	12%	260–355	UVB
Cinnamates			
Cinoxate	3%	289	UVB
Octinoxate	7.5%	311	UVB
Other			
Avobenzone	3%	360	UVA2, UVA1
Ensulizole	4%	310	UVB
Meradimate	5%	340	UVA2
Octocrylene	10%	303	UVB, UVA2
Inorganic			
Titanium dioxide	25%		UVB, UVA2, UVA1
Zinc oxide	25%		UVB, UVA2, UVA1

*PABA (para-aminobenzoic acid), Padimate O (octyl dimethyl PABA), Dioxybenzone (benzophenone-8), Oxybenzone (benzophenone-3), sulisobenzone (benzophenone-4), Homosalate (homomethyl salicylate), Octisalate (octyl salicylate), Trolamine salicylate (triethanolamine salicylate), Cinoxate (2-ethyoxyethyl p-methoxycinnamate), Octinoxate (octyl methoxycinnamate), Avobenzone (butyl methoxydibenzoyl methane), Ensulizole (phenylbenzimidazole sulfonic acid), Meradimate (menthyl anthranilate)

Table 2.

Non-topical forms of photoprotection[15]

Photoprotective agent	Source	Mechanism	Clinical Use
Polypodium leucotomos extract	Tropical fern of the *Polypodiaceae* family	• Neutralization of superoxide anions, lipid peroxides, and hydroxyl radicals • Reduced COX-2 expression (induced by light exposure and involved in mutagenesis) • p53 suppressor gene activation • Decreased formation of CPDs, sunburn cells, and inflammatory infiltrate	• Reduces persistent pigment darkening and delayed tanning (VL) • Increases minimal erythemal dose to UVB • Down-regulates development of polymorphic light eruptions • Protect against light-induced retinal damage and age-related macular degeneration
Nicotinamide	Active form of vitamin B3 (niacin)	• Prevent light-induced intracellular depletion of ATP • Enhanced DNA repair • Protection against photooxidative stress and light-induced immunosuppression	• Chemoprevention of actinic keratosis and nonmelanoma skin cancers
Afamelanotide	Analogue of alpha-melanocyte-stimulating hormone	• Stimulates eumelanin production in the epidermis without light-induced cellular damage • Eumelanin absorbs light, reduces free radicals and ROS	• Photoprotective in patients with EPP and XLPP • Possible role in polymorphous light eruption, solar urticaria, and actinic keratosis in patients with organ transplants. Accelerates repigmentation in vitiligo in conjunction with narrowband UVB

*COX-2 (cyclooxygenase-2), CPDs (cyclobutene pyrimidine dimers), UV (ultraviolet), UVR (UV radiation), ATP (adenosine triphosphate), ROS (reactive oxygen species), EPP (erythropoietic protoporphyria), XLPP (X-linked protoporphyria)