Photoprotection for all: Current gaps and opportunities

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The effects of solar radiation on human skin differ based on the skin phototype, presence or absence of photodermatoses, biologic capacity to repair DNA damage, wavelength, intensity of sun exposure, geographic latitude, and other factors, underscoring the need for a more tailored approach to photoprotection. To date, the focus of photoprotection guidelines has been to prevent sunburn and DNA damage induced by UV radiation, both UVB and UVA; however, several recent studies have shown that visible light also generates reactive oxygen and nitrogen species that can contribute to skin damage and pigmentation on the skin, particularly in people with skin of color. Therefore, individuals with dark skin, while naturally better protected against UVB radiation by virtue of the high eumelanin content in melanocytes, may need additional protection from visible light-induced skin damage. The current options for photoprotection products need to expand, and potential strategies against visible light include the addition of iron oxide, titanium dioxide, and biologically relevant antioxidants to sunscreen formulations as well as supplementation with orally active antioxidants. (J Am Acad Dermatol 2022;86:S18-26.)

Key words: photoprotection; skin of color; sunscreen; ultraviolet radiation; visible light.

INTRODUCTION

Sunlight provides heat and energy essential for sustaining human life, but components of solar radiation can have both acute and chronic adverse effects on human skin. The adverse effects of solar radiation on human skin have been attributed primarily to UV radiation (100-400 nm), specifically UVB (290-320 nm), UVA2 (320-340 nm), and UVA1 (340-400 nm) radiation.[1-3] UVB radiation is absorbed primarily in the epidermis, where it induces the inflammatory response of sunburn and directly damages DNA.[4,5] UVA, which makes up the majority of UV radiation that reaches the earth's surface, penetrates into the dermis and can cause oxidative damage and photoaging.[6] UVA may also indirectly cause DNA damage through the generation of reactive oxygen species (ROS) that oxidize guanine bases in DNA, leading to mutagenesis.[4] Compared with UV radiation, the impact of visible light (VL) on human skin has received relatively little attention. Recent studies have focused on the potential adverse effects of VL (400-700 nm) and its role in pigmentary disorders, especially in dark-skinned individuals (ie, Fitzpatrick skin types [FSTs] IV-VI) (Fig 1).[7,8]

The effect of solar radiation on human skin is clearly dependent on skin pigmentation (Fig 2). In dark skin, the damage is limited to the upper layers of the epidermis, whereas in individuals with light skin, the damage occurs in the basal layers of the epidermis as well. The upper epidermal layers in dark skin have a higher melanin content and a higher eumelanin/pheomelanin ratio than light skin.[9] Because melanin, particularly eumelanin, acts as a natural UVB filter, dark skin is better protected from the damaging effects of UVB radiation. In addition, DNA repair is more efficient in dark skin.[10]

UVA radiation and VL also appear to have different effects based on skin tone, causing hyperpigmentation in individuals with skin of color (SOC) skin (FST III-VI).[7] Pigmentation induced by VL was

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shown to be darker and more sustained than UVA1–induced pigmentation in individuals with FST III-VI.[7] Moreover, the pigmentation effect is potentiated when VL is combined with a small percentage of UVA1.[11,12]

Thus, FSTs are affected by solar radiation in different ways, underscoring the need for a comprehensive and targeted approach to photoprotection. The "photoprotection for all" paradigm encompasses the American Academy of Dermatology guidance (see below) but acknowledges that sunscreen protection requirements may vary among individuals of different skin types. In individuals with fair skin, the regular use of a high-sun protection factor (SPF), broad-spectrum sunscreen can help prevent UV-induced erythema and DNA damage, reducing the risk of skin cancer and photoaging. Individuals with dark skin types may not need high UVB protection but may require more protection from the pigment-inducing effects of VL. Individuals of all skin phototypes require protection from the damaging effects of UVA/UVA1. The current armamentarium of sunscreens needs to expand to include products that protect against the effects of UVA1 and VL for individuals with dark skin as well as products for individuals with photodermatoses, acne-prone skin, and other dermatologic needs.

CAPSULE SUMMARY

- Effects of ultraviolet radiation and visible light on human skin depend on pigmentation, with light skin more susceptible to ultraviolet-induced skin damage and dark skin to visible-light–induced damage.
- A personalized approach for photoprotection requires a wider range of sunscreens, including formulations for dark skin that protect against high-energy visible light.

CURRENT GAPS IN PHOTOPROTECTION UNDERSTANDING

Current guidelines from the American Academy of Dermatology focus on protection from UVB and UVA radiation to prevent sunburn and reduce the risk of skin cancer.[13] They recommend (1) seeking shade when outdoors; (2) wearing sun-protective clothing; and (3) using a broad-spectrum, water-resistant sunscreen (SPF ≥30), reapplied every 2 hours or after swimming or sweating.[13]

A recent survey of 540 US dermatologists confirmed that physicians base their recommendations for sunscreen use primarily on the ability to protect against UVB and UVA radiation (ie, SPF level and broad-spectrum protection).[14]

US consumer attitudes toward sunscreen use are also focused primarily on protection from UV-related effects. In a survey of 93 consumers, the main factor influencing the purchase of sunscreen was the SPF level, followed by sensitive skin formulation and water/sweat resistance.[15] Only 34% of consumers considered broad-spectrum protection to be important in their purchasing decision.[15] In a larger survey assessing sunscreen knowledge, only 8.7% of the 334 consumers surveyed correctly understood the concepts of SPF, broad-spectrum, and water resistance.[16]

The American Academy of Dermatology guidelines do not provide guidance on VL protection. Because 50% of sunlight reaching the surface of the earth is VL, it has been estimated that VL is responsible for 50% of free radicals induced by sunlight.[17] With a greater understanding of the effects of VL, future guidelines on photoprotection will need to provide recommendations for protecting skin from the damaging effects of VL.

Current limitations in federal guidance on over-the-counter sunscreens

In February 2019, the US Food and Drug Administration (FDA) issued a proposed rule to provide updated guidance on establishing the safety and efficacy of over-the-counter sunscreen products (Table I).[18] In May 2021, a proposed administrative order was issued.[19] The FDA proposed several changes to the UVA protection and SPF labeling requirements. Many of the currently marketed sunscreen products in the United States do not provide balanced protection against UVB and UVA radiation (ie, UVA protection factor of at least one third of the SPF, as recommended by the European guidelines). A growing body of evidence demonstrates that exposure to UVA, particularly UVA1, is linked to skin cancer and photoaging. To indicate adequate UVA protection, the FDA currently allows sunscreens with SPF values of 15 or higher to be labeled as "broad spectrum" if a critical wavelength of 370 nm or higher has been demonstrated.[18] However, in an evaluation of 20 US sunscreen products by the critical wavelength method and the European Union UVA standard (requiring a UVA protection factor:SPF ratio of higher than 1:3), 19 of 20 tested products met the critical wavelength standard, but only 11 met the European Union standard, suggesting inferior UVA protection compared with sunscreen products in the European Union.[20] In the new proposed guidelines, the FDA has suggested that broad-spectrum products need to have a UVA1/

Abbreviations used:

CPD:	cyclobutane pyrimidine dimer
FDA:	US Food and Drug Administration
FST:	Fitzpatrick skin type
GA:	glycyrrhetinic acid
GRASE:	generally regarded as safe and effective
IL:	interleukin
MMP:	matrix metalloproteinase
ROS:	reactive oxygen species
SPF:	sun protection factor
TiO_2:	titanium dioxide
VL:	visible light
ZnO:	zinc oxide

UV ratio of 0.7 or higher, which would ensure more uniform and balanced protection across the UVA1, UVA2, and UVB ranges.

SOLAR RADIATION EFFECTS ON SKIN: UV AND VL

UV-induced effects

UV radiation has been well established to have acute and chronic effects on human skin. UVB radiation penetrates into the epidermis and induces a cascade of cytokines and vasoactive mediators that results in the inflammatory response known as sunburn.[4] Both UVB and UVA cause DNA damage in human keratinocytes that can lead to skin cancer.

UVA radiation also damages DNA indirectly by generating ROS, such as superoxide anion, hydrogen peroxide, and hydroxyl radical. The nucleotides in DNA are highly susceptible to injury by these ROS. The oxidation of nucleotide bases leads to the mispairing of bases, resulting in mutagenesis. For example, the oxidation of guanine results in a modified nucleotide that tends to pair with adenine rather than cytosine, mutating a guanine/cytosine pair into an adenine/thymine.[4]

Natural DNA repair mechanisms exist to reverse these mutagenic pathways, but if the UV exposure is very high and the DNA damage is too great, the repair mechanisms may fail; in this case, the defective cells may be eliminated via apoptosis or they may acquire mutations that can then lead to skin cancer.[4] The ability to repair UV-induced DNA damage is more efficient in those with FST V-VI due, in part, to the higher melanin content in the epidermis. Individuals with FST I-II may be at higher risk for "dark" cyclobutane pyrimidine dimers (CPDs), DNA lesions that are generated several hours after UVA exposure, due to the higher pheomelanin content in their skin.[21] Antioxidants may help protect the skin from DNA damage induced by UVB and UVA. For example, vitamin E has been shown to inhibit light and dark CPDs as well as oxidative DNA damage in keratinocytes.[22]

Glycyrrhetinic acid (GA) is a compound derived from licorice root, with potent antioxidant and anti-inflammatory properties.[23] In cellular studies, GA has been shown to prevent DNA fragmentation induced by UVB radiation and significantly reduce the generation of intracellular ROS in human keratinocytes irradiated with UVB. The antioxidant activity of GA increased as UVB intensity increased in a dose-dependent manner.[24] GA is also a potent inhibitor of specific mammalian DNA polymerases involved in DNA repair/recombination.[25]

Effects of VL

The effects of VL, particularly high-energy VL, on human skin are not well understood. At high doses, VL can cause erythema, with the intensity and duration dependent on the skin type. Mahmoud et al[7] studied the effects of VL and UVA1 on immediate pigmentation and delayed tanning in volunteers with FST IV-VI and FST II. In the FST IV-VI group, UVA1 induced pigmentation that was gray at first, changed to brown with time, and faded rapidly over 2 weeks, with no erythema observed at any time. The lack of erythema was confirmed by the spectroscopic assessment of oxyhemoglobin levels, which found no dose-response or time-course relationship between UVA1 radiation and oxyhemoglobin level. Irradiation with VL induced immediate pigmentation that was dark brown from the start and surrounded by an ill-defined erythema that disappeared in less than 2 hours. The pigmentation was sustained over the 2 weeks of the study and did not fade.[7] The intensity of the erythema increased with higher doses of VL. In contrast, no pigmentation was observed in individuals with FST II skin, even at higher doses of visible light and UVA1 radiation. In a subsequent study by Randhawa et al,[26] multiple exposures of VLinduced persistent pigmentation, even in Caucasian skin explants.

VL-induced pigmentation also depends on the wavelength, with blue-violet light (415 nm—popularized in the lay press as "high-energy visible light") associated with more hyperpigmentation than red light (630 nm) and pigmentation lasting up to 3 months.[27] Campiche et al[28] found that blue light (450 nm) induced erythema and hyperpigmentation in FST III and IV skin. Unlike UV-induced hyperpigmentation, VL-induced pigmentation is mediated by opsin-3.[28] Blue light activates the opsin-3 receptor in melanocytes, leading to increased calcium flux and, eventually, an upregulation in melanogenesis. The process involves the formation of tyrosinase/tyrosinase-related protein complexes, leading to

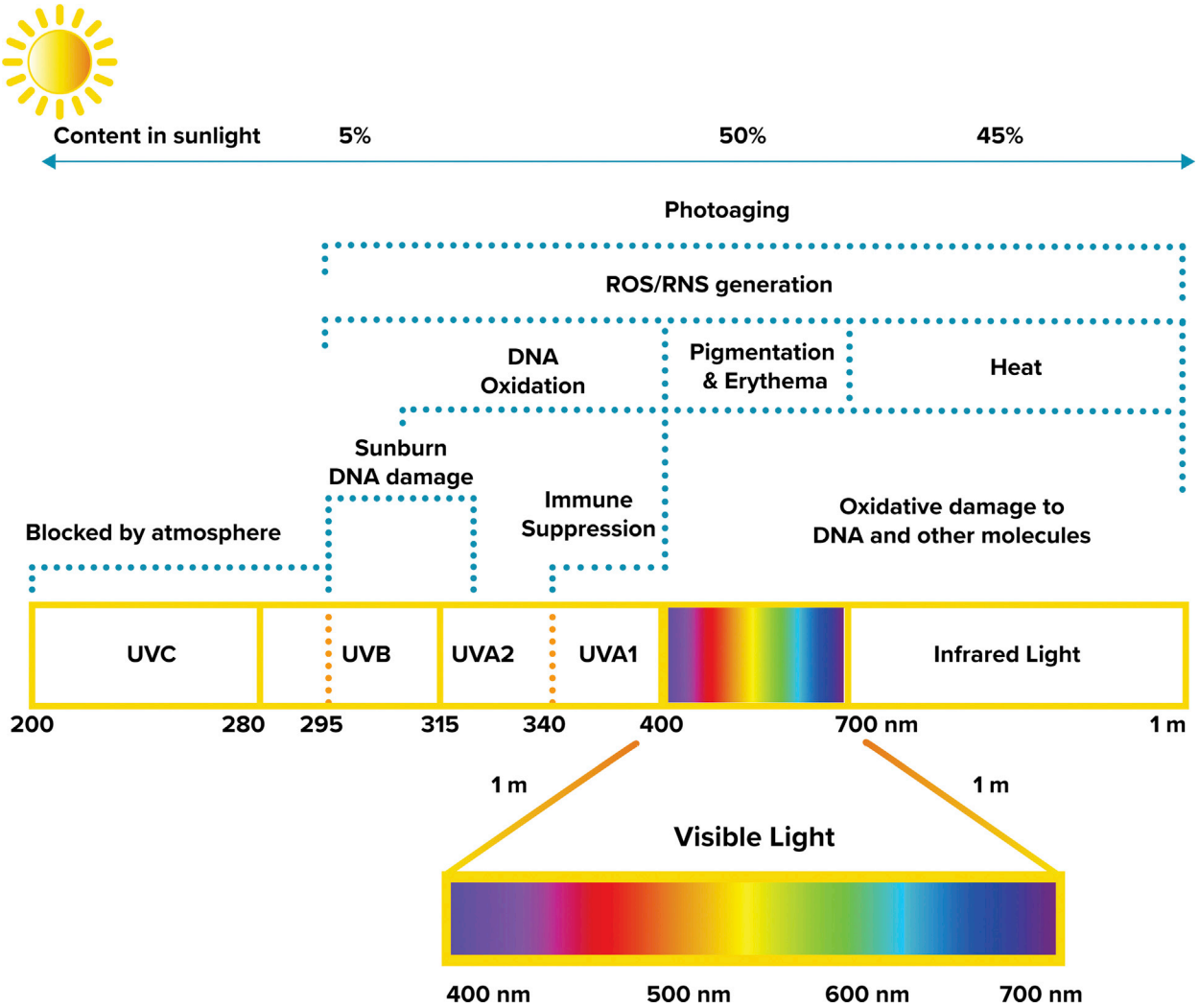

Fig 1. Electromagnetic radiation spectrum. *RNS*, Reactive nitrogen species; *ROS*, reactive oxygen species. (adapted from Dupont et al[5])

sustained tyrosinase activity in melanocytes of FST III and higher. Tyrosinase activity did not change after blue light irradiation in human melanocytes from lightly pigmented (FST I-II) individuals but increased in melanocytes from FST V and VI subjects. These differences may explain why blue light induces hyperpigmentation only in FST III and higher.[29]

VL has been shown to generate ROS in a dose-dependent fashion following the photon-induced activation of endogenous photosensitizers, with the highest ROS levels observed after blue light irradiation.[8,30] VL also induced the release of proinflammatory cytokines, including interleukin 1α (IL-1α), IL-1 receptor antagonist, IL-6, granulocyte colony-stimulating factor (GC-CSF), and IL-8, as well as increased the expression of matrix metalloproteinase 1 (MMP-1) and MMP-9.[8] VL was found to activate the epidermal growth factor receptor pathway in human keratinocytes in a manner similar to UV radiation. The epidermal growth factor receptor pathway has been implicated in the activation of MMPs that can accelerate skin aging.[8]

GAPS IN CURRENT PHOTOPROTECTION PRODUCTS

Organic and inorganic UV filters

Currently available sunscreens in the United States contain one or more FDA-approved UV filters that protect against UVA, UVB, or both (Table II). The 2019 FDA-proposed rule categorizes the active photoprotective agents in current sunscreen products into 3 groups: those generally regarded as safe and effective (GRASE) (Category I), those not GRASE (Category II), and those with insufficient safety data to be classified as GRASE (Category III) (Table I). In this proposed classification, titanium

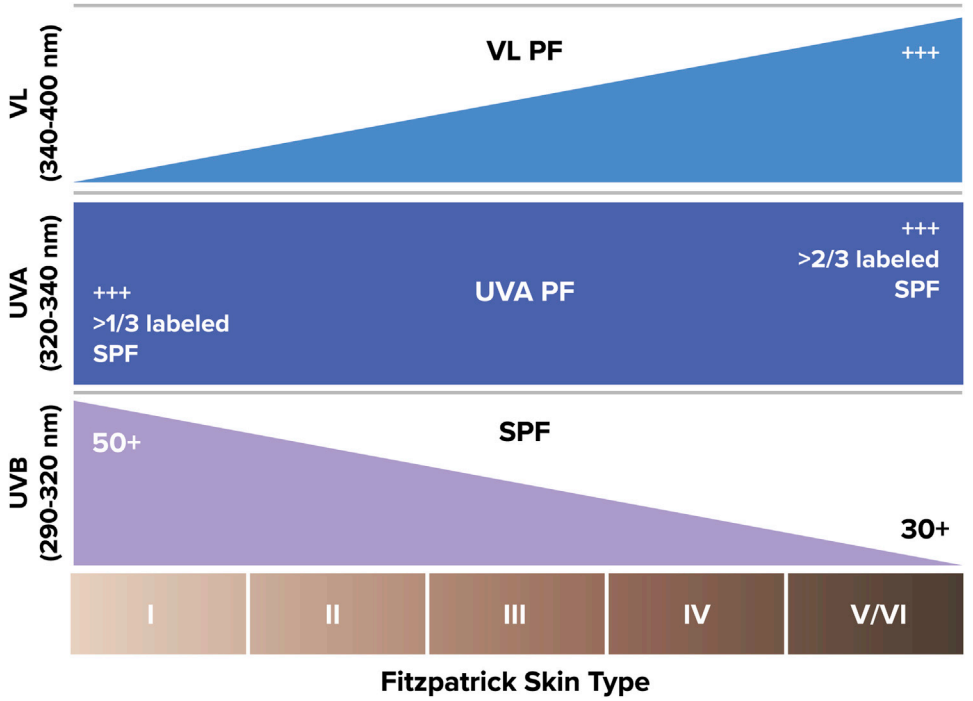

Fig 2. UV and VL protection factors according to skin phototype. *SPF*, Sun protection factor; *PF*, protection factor; *VL*, visible light. (adapted from Passeron et al[9])

Table I. Key components of the 2021 FDA-proposed administrative order on sunscreen

Topic	FDA-proposed rule
Balanced UVB/UVA protection	All sunscreens with SPF 15 or higher must satisfy broad-spectrum test requirements, with a UVA1/UV ratio of 0.7 or higher
SPF limit	Maximum labeled SPF: 60+ Maximum marketed SPF: 80
Sunscreen categorization	I (GRASE): TiO_2, ZnO II (non-GRASE): PABA, trolamine salicylate III (insufficient evidence for GRASE categorization): cinoxate, dioxybenzone, ensulizole, homosalate, meradimate, octinoxate, octisalate, octocrylene, padimate O, sulisobenzone, oxybenzone, avobenzone

FDA, Food and Drug Administration; *GRASE*, generally regarded as safe and effective; *PABA*, para-aminobenzoic acid; *SPF*, sun protection factor; *TiO_2*, titanium dioxide; *UV*, ultraviolet; *ZnO*, zinc oxide.

dioxide (TiO_2) and zinc oxide (ZnO) are classified as Category I (GRASE), while para-aminobenzoic acid and trolamine salicylate are considered Category II, with the risks outweighing the benefits. It should be noted that even before this proposed rule, the latter 2 were no longer being used in sunscreen products in the United States. The remaining 12 active ingredients used in current over-the-counter sunscreens have been classified as Category III.[18]

Sunscreen filters are classified as inorganic (also known as physical or mineral) and organic (also known as chemical).[3] An inorganic filter act as a semiconductive barrier against UV rays by absorbing the radiation and, to a lesser extent, reflecting and scattering the UV radiation.[31,32] They are highly effective immediately on application in preventing UV-induced damage. Larger particles of inorganic filters also scatter and absorb VL. The 2 available inorganic filters, TiO_2 and ZnO, provide protection against both UVB and UVA2. Additionally, ZnO provides protection against UVA1.[33] TiO_2 and ZnO are essentially insoluble in water, preventing their transdermal absorption and minimizing cutaneous irritation.[34] However, they leave a whitish, chalky coat on the skin, which may be aesthetically unacceptable, particularly in individuals with dark skin.[34] Formulation with TiO_2 and ZnO nanoparticles can help reduce the scattering and reflection in the visible region of the spectrum, resulting in a transparent, more cosmetically acceptable form. But the

Table II. FDA-approved sunscreen filters

Filter	Absorption range		
	UVB (290-320 nm)	UVA2 (320-340 nm)	UVA1 (340-400 nm)
Inorganic (mineral, physical)			
Titanium dioxide	x	x	
Zinc oxide	x	x	x
Organic (chemical)			
p-Aminobenzoic acid	x		
Avobenzone		x	x
Cinoxate	x		
Dioxybenzone	x	x	
Ecamsule*		x	x
Ensulizole	x		
Homosalate	x		
Meradimate		x	
Octinoxate	x		
Octisalate	x		
Octocrylene	x		
Oxybenzone	x	x	
Padimate O	x		
Sulisobenzone	x	x	
Trolamine salicylate	x		

FDA, Food and Drug Administration.
X indicates absorption range coverage.
*Ecamsule is approved only at specific concentrations in one commercial line of products.

absorbance range decreases with particle size, and nanoparticles of TiO_2 and ZnO may provide less protection in the UVA range and no protection in the VL range.[34]

Organic filters act by absorbing UV radiation, which is then emitted at higher wavelengths or released as thermal energy.[3] The majority of US-approved organic UV filters provide protection only against UVB, and 3 provide broad-spectrum protection against both UVB and UVA2.[33,35] Only avobenzone has been shown to protect against UVA1.[35] Recent studies have shown that many organic UV filters are readily absorbed through the skin, with detectable plasma levels even days after use.[36,37] Oxybenzone (benzophenone-3), which is present in two thirds of sunscreens in the United States, is a broad-spectrum UV filter that has significant transdermal absorption after topical use. This is of concern because oxybenzone has been reported to disrupt the endocrine system in humans and has been linked to female infertility and low birth weight; further study is needed to evaluate the causality of this association.[38-40] Significant transdermal penetration and detectable plasma levels after maximal usage sunscreen application (ie, to 75% of body surface area, at 2 mg/cm^2) have also been demonstrated for avobenzone, octocrylene, ecamsule, homosalate, octisalate, and octinoxate, even after a single application.[36,37] All 6 active ingredients were detectable in plasma for up to 21 days.[36] Again, additional study is necessary to determine the clinical significance of these results.

Organic UV filters have also been reported to have adverse impacts on marine life and water systems. In laboratory settings, several organic UV filters, including oxybenzone and octinoxate, have been found to be toxic to coral reefs.[41] However, it should be noted that the concentrations to induce these effects in the laboratory setting were 10^3- to 10^6-fold higher than those observed in sea water in a real-life setting.[42]

Ingredients for UV and VL protection

Tinted sunscreens, which contain, in addition to UV filters, a blend of iron oxides and pigmentary TiO_2, protect against VL and UV while avoiding the chalky white appearance of inorganic filters.[43] These tinted sunscreens reduce VL transmission by >90%.[43] In a study comparing a nontinted mineral sunscreen versus tinted products containing iron oxides, the iron-oxide–containing formulations provided better protection against VL-induced pigmentation in patients with FST IV.[44] Iron oxides may be black, red, or yellow; therefore, these pigments, together with pigmentary TiO_2, can be mixed in different amounts to create tinted sunscreens to match a range of skin tones. Tinted sunscreens containing iron oxides have been shown to improve melasma lesions and melasma relapses compared to a UV-only sunscreen.[45] There remains a need for nonpigmented ingredients that can protect from VL to avoid the challenges of matching skin tones and as an alternative for those who do not wish to use pigmented products. The implementation of validated standardized direct immunofluorescence tests for measurements of the impact of VL on skin would be beneficial in improving overall sunscreen development.[46]

Antioxidants can scavenge ROS and may be good candidates to incorporate into sunscreens.[47] Polyphenols are naturally occurring antioxidants that can be found in various plants. They have shown photoprotective properties: inhibiting ROS and ROS-mediated damage to DNA, upregulating DNA repair enzymes, and inhibiting stress-response cell signaling pathways.[33,48] A combination of antioxidants, applied topically, can mitigate the effects of VL, and the addition of a combination of natural antioxidants (feverfew extract, soy extract, and gamma-tocopherol) to a UVA/UVB sunscreen reduced the effects of VL, decreasing ROS by 78%,

IL-1α by 82%, and MMP-1 release by 87%.[8] The antioxidant combination alone also mitigated the release of these mediators.[8] Campiche et al[28] reported that a topical formulation of niacinamide (vitamin B3) plus a polyphenol-rich extract of the green freshwater microalga *Scenedesmus rubescens* reduced pigmentation after blue-light irradiation. A sunscreen formulation containing a UVB/UVA filter with licochalcone A, a potent antioxidant component of licorice extract, was found to protect against VL-induced oxidative stress and prevent the blue-light–induced degradation of carotenoids in the stratum corneum.[30]

Other studies have examined the efficacy of oral/systemic photoprotective agents. *Polypodium leucotomos* is a tropical fern native to South America whose extracts have antioxidant, anti-inflammatory, and photoprotective properties. *P. leucotomos* extracts are available as dietary supplements and have been shown to protect against UVB–induced changes, such as erythema, in subjects with FST I-III as well as against VL-induced pigmentation in subjects with FST IV-VI.[49] Mohammad et al[50] reported a significant decrease in persistent pigmentation after *P. leucotomos* extract administration in 22 subjects with FST IV-VI. Carotenoids, such as β-carotene, can quench UV-induced ROS (eg, singlet molecular oxygen) and may be used in conjunction with sunscreen as photoprotection.[51] In a meta-analysis of 7 studies, dietary supplementation with β-carotene was found to protect against sunburn, with the protective effect increasing with the duration of supplementation.[52]

Currently available sunscreens focus on *protecting* the skin from UV-induced damage. Another approach is to reverse or repair the UV-induced damage after it has occurred, through the use of absorbable DNA repair enzymes (eg, photolyase) in topical sunscreens.[53] Stege et al[54] found that the topical application of photolyase-containing liposomes reduced UVB radiation–induced CPDs, immunosuppressive effects, erythema, and sunburn cell formation. Further, as previously discussed, GA has been shown to have antioxidative properties that prevent DNA fragmentation in human keratinocytes *in vitro*.[24] *In vivo*, GA treatment resulted in 50% fewer CPDs 24 hours after UV irradiation compared to the vehicle-treated control.[55]

Other photoprotective agents that have been studied in populations susceptible to photodamage include nicotinamide, which enhances DNA repair, and afamelanotide, a melanocortin-1 receptor agonist that promotes the synthesis of melanin.[56]

SUMMARY AND CONCLUSION

The impact of VL on human skin is only beginning to be understood. VL, at high doses, induces erythema and hyperpigmentation in subjects with dark FSTs but not in those with light FSTs. VL has also been found to generate reactive oxygen and nitrogen species that may contribute to skin damage and pigmentary disorders. Most of the currently available sunscreen products are designed to protect against UVB and UVA. Tinted sunscreens, which contain iron oxide pigments, are currently the only photoprotection products available in the United States that filter out VL. Other strategies being explored to protect against VL-induced skin damage include the addition of biologically relevant topical antioxidants (eg, GA, polyphenols, licochalcone A) to sunscreen formulations, supplementation with orally active antioxidants (eg, *P. leucotomos* extract, β-carotene), and the development of novel filters that absorb UV radiation and reflect VL. With a greater understanding of the effects of solar radiation on different skin types and the development of sunscreen products that provide protection across the spectrum, from VL to UV, "photoprotection for all" can become an achievable reality in the near future.

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Conflicts of interest

Dr Rigel has served as an advisor/consultant for Almirall, Beiersdorf Inc, Castle Biosciences Inc, DermTech, Ferndale, Johnson & Johnson, Myriad Genetics, Ortho Dermatologics, Pfizer, and Scibase. Dr Lim has served as investigator (grant to institution) for: Incyte, L'Oréal, Pfizer, and Patient-Centered Outcomes Research Institute; consultant for Pierre Fabre, ISDIN, Ferndale, La Roche-Posay, and Beiersdorf Inc; and as a speaker in a general education session for La Roche-Posay and Cantabria Labs. Dr Draelos has served as a consultant for Beiersdorf Inc. Dr Weber is an employee of Beiersdorf Inc. Dr Taylor has served as an investigator for Concert Pharmaceuticals, Croma-Pharma GmbH, Eli Lilly and Company, Immune Tolerance Network, and Pfizer; as a consultant/speaker/advisory board member for AbbVie, Arcutis Biotherapeutics, Beiersdorf Inc, Biorez Inc, CannTec, Evolus, Galderma Laboratories, GloGetter Inc, L'Oréal USA Inc, LuminDX, Medscape/WebMD, Johnson & Johnson Consumer Products, Scientis, and Vichy

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REFERENCES

1. Austin E, Geisler AN, Nguyen J, et al. Visible light. Part I: properties and cutaneous effects of visible light. *J Am Acad Dermatol*. 2021;84(5):1219-1231.
2. Geisler AN, Austin E, Nguyen J, Hamzavi I, Jagdeo J, Lim HW. Visible light. Part II: photoprotection against visible and ultraviolet light. *J Am Acad Dermatol*. 2021;84(5):1233-1244.
3. Singer S, Karrer S, Berneburg M. Modern sun protection. *Curr Opin Pharmacol*. 2019;46:24-28.
4. D'Orazio J, Jarrett S, Amaro-Ortiz A, Scott T. UV radiation and the skin. *Int J Mol Sci*. 2013;14:12222-12248.
5. Dupont E, Gomez J, Bilodeau D. Beyond UV radiation: a skin under challenge. *Int J Cosmet Sci*. 2013;35:224-232.
6. Nichols JA, Katiyar SK. Skin photoprotection by natural polyphenols: anti-inflammatory, antioxidant and DNA repair mechanisms. *Arch Dermatol Res*. 2010;302:71-83.
7. Mahmoud BH, Ruvolo E, Hexsel CL, et al. Impact of long-wavelength UVA and visible light on melanocompetent skin. *J Invest Dermatol*. 2010;130:2092-2097.
8. Liebel F, Kaur S, Ruvolo E, Kollias N, Southall MD. Irradiation of skin with visible light induces reactive oxygen species and matrix-degrading enzymes. *J Invest Dermatol*. 2012;132:1901-1907.
9. Passeron T, Lim HW, Goh CL, et al. Photoprotection according to skin phototype and dermatoses: practical recommendations from an expert panel. *J Eur Acad Dermatol Venereol*. 2021;35(7):1460-1469.
10. Miyamura Y, Coelho SG, Wolber R, et al. Regulation of human skin pigmentation and responses to ultraviolet radiation. *Pigment Cell Res*. 2007;20:2-13.
11. Kohli I, Chaowattanapanit S, Mohammad TF, et al. Synergistic effects of long-wavelength ultraviolet A1 and visible light on pigmentation and erythema. *Br J Dermatol*. 2018;178:1173-1180.
12. Kohli I, Zubair R, Lyons AB, et al. Impact of long-wavelength ultraviolet A1 and visible light on light-skinned individuals. *Photochem Photobiol*. 2019;95:1285-1287.
13. American Academy of Dermatology Association. Sunscreen FAQS. 2021.
14. Farberg AS, Rigel AC, Rigel DS. Online survey of US dermatologists' sunscreen opinions: perceptions, recommendation factors, and self-usage. *J Drugs Dermatol*. 2016;15:1121-1123.
15. Kong BY, Sheu SL, Kundu RV. Assessment of consumer knowledge of new sunscreen labels. *JAMA Dermatol*. 2015;151:1028-1030.
16. Prado G, Svoboda RM, Teplitz RW, Farberg AS, Rigel DS. Patient knowledge of FDA-mandated sunscreen labeling terminology: a cross-sectional survey. *Photodermatol Photoimmunol Photomed*. 2019;35:141-147.
17. Zastrow L, Groth N, Klein F, et al. The missing link—light-induced (280-1,600 nm) free radical formation in human skin. *Skin Pharmacol Physiol*. 2009;22:31-44.
18. US Food and Drug Administration. Rulemaking history for OTC sunscreen drug products. 2019.
19. Lim HW, Mohammad TF, Wang SQ. FDA proposed sunscreen final administrative order: how does it affect sunscreens in the United States? *J Am Acad Dermatol*. 2021. https://doi.org/10.1016/j.jaad.2021.09.052
20. Wang SQ, Xu H, Stanfield JW, Osterwalder U, Herzog B. Comparison of ultraviolet A light protection standards in the United States and European Union through in vitro measurements of commercially available sunscreens. *J Am Acad Dermatol*. 2017;77:42-47.
21. Premi S, Wallisch S, Mano CM, et al. Photochemistry. Chemiexcitation of melanin derivatives induces DNA photoproducts long after UV exposure. *Science*. 2015;347:842-847.
22. Delinasios GJ, Karbaschi M, Cooke MS, Young AR. Vitamin E inhibits the UVAI induction of "light" and "dark" cyclobutane pyrimidine dimers, and oxidatively generated DNA damage, in keratinocytes. *Sci Rep*. 2018;8:423.
23. Kowalska A, Kalinowska-Lis U. 18ß-glycyrrhetinic acid: its core biological properties and dermatological applications. *Int J Cosmet Sci*. 2019;41:325-331.
24. Veratti E, Rossi T, Giudice S, et al. 18beta-glycyrrhetinic acid and glabridin prevent oxidative DNA fragmentation in UVB-irradiated human keratinocyte cultures. *Anticancer Res*. 2011;31:2209-2215.
25. Ishida T, Mizushina Y, Yagi S, et al. Inhibitory effects of glycyrrhetinic acid on DNA polymerase and inflammatory activities. *Evid Based Complement Alternat Med*. 2012;2012:650514.
26. Randhawa M, Seo I, Liebel F, Southall MD, Kollias N, Ruvolo E. Visible light induces melanogenesis in human skin through a photoadaptive response. *PLoS One*. 2015;10:e0130949.
27. Duteil L, Cardot-Leccia N, Queille-Roussel C, et al. Differences in visible light-induced pigmentation according to wavelengths: a clinical and histological study in comparison with UVB exposure. *Pigment Cell Melanoma Res*. 2014;27:822-826.
28. Campiche R, Curpen SJ, Lutchmanen-Kolanthan V, et al. Pigmentation effects of blue light irradiation on skin and how to protect against them. *Int J Cosmet Sci*. 2020;42:399-406.
29. Regazzetti C, Sormani L, Debayle D, et al. Melanocytes sense blue light and regulate pigmentation through opsin-3. *J Invest Dermatol*. 2018;138(1):171-178.
30. Mann T, Eggers K, Rippke F, et al. High-energy visible light at ambient doses and intensities induces oxidative stress of skin-protective effects of the antioxidant and Nrf2 inducer Licochalcone A in vitro and in vivo. *Photodermatol Photoimmunol Photomed*. 2020;36:135-144.
31. Solish N, Humphrey S, Waller B, Vanderveen S. Photoprotection with mineral-based sunscreens. *Dermatol Surg*. 2020;46:1508-1513.
32. Cole C, Shyr T, Ou-Yang H. Metal oxide sunscreens protect skin by absorption, not by reflection or scattering. *Photodermatol Photoimmunol Photomed*. 2016;32:5-10.
33. Glaser KS, Tomecki KJ. Sunscreens in the United States: current status and future outlook. *Adv Exp Med Biol*. 2020;1268:355-379.
34. Schneider SL, Lim HW. A review of inorganic UV filters zinc oxide and titanium dioxide. *Photodermatol Photoimmunol Photomed*. 2019;35:442-446.
35. Yeager DG, Lim HW. What's new in photoprotection: a review of new concepts and controversies. *Dermatol Clin*. 2019;37:149-157.
36. Matta MK, Florian J, Zusterzeel R, et al. Effect of sunscreen application on plasma concentration of sunscreen active ingredients: a randomized clinical trial. *JAMA*. 2020;323:256-267.
37. Matta MK, Zusterzeel R, Pilli NR, et al. Effect of sunscreen application under maximal use conditions on plasma concentration of sunscreen active ingredients: a randomized clinical trial. *JAMA*. 2019;321:2082-2091.

38. Suh S, Pham C, Smith J, Mesinkovska NA. The banned sunscreen ingredients and their impact on human health: a systematic review. *Int J Dermatol*. 2020;59:1033-1042.
39. Arya S, Dwivedi AK, Alvarado L, Kupesic-Plavsic S. Exposure of U.S. population to endocrine disruptive chemicals (parabens, benzophenone-3, bisphenol-A and triclosan) and their associations with female infertility. *Environ Pollut*. 2020;265:114763.
40. Ghazipura M, McGowan R, Arslan A, Hossain T. Exposure to benzophenone-3 and reproductive toxicity: a systematic review of human and animal studies. *Reprod Toxicol*. 2017;73:175-183.
41. Sabzevari N, Qiblawi S, Norton SA, Fivenson D. Sunscreens: UV filters to protect us: part 1: changing regulations and choices for optimal sun protection. *Int J Womens Dermatol*. 2021;7:28-44.
42. Mitchelmore CL, Burns EE, Conway A, Heyes A, Davies IA. A critical review of organic ultraviolet filter exposure, hazard, and risk to corals. *Environ Toxicol Chem*. 2021;40:967-988.
43. Lyons AB, Trullas C, Kohli I, Hamzavi IH, Lim HW. Photoprotection beyond ultraviolet radiation: a review of tinted sunscreens. *J Am Acad Dermatol*. 2021;84:1393-1397.
44. Dumbuya H, Grimes PE, Lynch S, et al. Impact of iron-oxide containing formulations against visible light-induced skin pigmentation in skin of color individuals. *J Drugs Dermatol*. 2020;19:712-717.
45. Boukari F, Jourdan E, Fontas E, et al. Prevention of melasma relapses with sunscreen combining protection against UV and short wavelengths of visible light: a prospective randomized comparative trial. *J Am Acad Dermatol*. 2015;72:189-190.e1.
46. Schalka S, de Paula Correa M, Sawada LY, Canale CC, de Andrade TN. A novel method for evaluating sun visible light protection factor and pigmentation protection factor of sunscreens. *Clin Cosmet Investig Dermatol*. 2019;12:605-616.
47. Solano F. Photoprotection and skin pigmentation: melanin-related molecules and some other new agents obtained from natural sources. *Molecules*. 2020;25:1537.
48. Bosch R, Philips N, Suarez-Perez JA, et al. Mechanisms of photoaging and cutaneous photocarcinogenesis, and photoprotective strategies with phytochemicals. *Antioxidants (Basel)*. 2015;4:248-268.
49. Kohli I, Shafi R, Isedeh P, et al. The impact of oral Polypodium leucotomos extract on ultraviolet B response: a human clinical study. *J Am Acad Dermatol*. 2017;77:33-41.e1.
50. Mohammad TF, Kohli I, Nicholson CL, et al. Oral Polypodium leucotomos extract and its impact on visible light-induced pigmentation in human subjects. *J Drugs Dermatol*. 2019;18:1198-1203.
51. Zerres S, Stahl W. Carotenoids in human skin. *Biochim Biophys Acta Mol Cell Biol Lipids*. 2020;1865:158588.
52. Kopcke W, Krutmann J. Protection from sunburn with beta-carotene—a meta-analysis. *Photochem Photobiol*. 2008;84:284-288.
53. Sondenheimer K, Krutmann J. Novel means for photoprotection. *Front Med (Lausanne)*. 2018;5:162.
54. Stege H, Roza L, Vink AA, et al. Enzyme plus light therapy to repair DNA damage in ultraviolet-B-irradiated human skin. *Proc Natl Acad Sci U S A*. 2000;97:1790-1795.
55. Hong M, Mahns A, Batzer J, et al. Glycyrrhetinic acid: a novel modular of human skin pigmentation and DNA repair. Paper presented at: 39th Annual European Society for Dermatological Research Budapest, Hungary: (ESDR) Meeting; September 9-12, 2009.
56. Lim HW, Arellano-Mendoza MI, Stengel F. Current challenges in photoprotection. *J Am Acad Dermatol*. 2017;76:S91-S99.