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Review Article

Sunscreens: What Might the Future Hold?

Lily Guo[1], Cynhia Hsu[1], Peter Lio, MD[2]

[1] Rosalind Franklin University of Medicine and Science, [2] Dermatology, Northwestern University

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Skin cancer trends continue to rise with the majority of cases attributable to ultraviolet radiation exposure. Studies show that regular sunscreen use reduces the risk of both melanoma and non-melanoma skin cancers. However, limitations and flaws exist with the current generation of sunscreens– both chemical filters and physical blockers. Innovative sun protection solutions are needed on the market to assuage patient concerns regarding the safety of sunscreens, broad spectrum and visible light coverage, and their potential impact on the environment. This narrative review aims to highlight promising new filter technologies that may have better safety profiles and provide comparable or superior sun protection to current available sunscreens.

I. INTRODUCTION

The incidence of skin cancer worldwide is steadily increasing, and it has become the most common cancer diagnosed in the United States. From 1990 to 2019, the incidence of melanoma increased from 12.6 to 17.0 per 100,000 persons, and the incidence of non-melanoma skin cancer (NMSC), both basal cell carcinoma (BCC) and squamous cell carcinoma (SCC), increased from 402 to 787 per 100,000 persons.[1] While mortality rates have declined—presumably as a result of earlier detection and treatment—morbidity remains significant. Exposure to ultraviolet (UV) light is largely responsible for both melanoma and non-melanoma skin cancer, in addition to sunburn and photoaging. It is thought that the increased incidence of NMSCs can be attributed to an increase in exposure to UV radiation secondary to ozone depletion, increase in human longevity resulting in higher cumulative UV dose, and societal sun-seeking behaviors,[2] among other factors. The use of tanning beds reached their peak between 1990-2000. However, it was not until 2015 that the U.S. Food and Drug Administration (FDA) proposed age restrictions limiting their use in minors. While there have been increased efforts to prioritize sun protection and implement skin cancer prevention programs, current sunscreens on the market have their limitations and barriers to consistent sunscreen use remain.

II. PROBLEMS WITH CURRENT SUNSCREENS

In 1928, the first commercially available sunscreen was released, consisting of benzyl salicylate and benzyl cinnamate. Regulatory body involvement for sunscreen was introduced in the 1970s and have since played an important role in reviewing the safety and efficacy of ingredients of commercial sunscreens. Current broad-spectrum sunscreens protect against sunlight on the UVA (320-400 nm) and UVB (290-320 nm) spectrum. UVA constitutes more than 90% of the ultraviolet radiation in sunlight, and can penetrate deep into both the epidermis and dermis of the skin causing premature photoaging. UVB is a minor component of sunlight; however, it is capable of causing sunburn, inducing DNA damage, and ultimately leading to skin cancer. Randomized control trials have shown that sunscreen use reduces the risk of melanoma and NMSCs, and the American Academy of Dermatology recommends regular sunscreen use with a sun protective factor (SPF) of 30 or higher for people of all skin types.[3] Current sunscreens on the market can be divided into two groups, organic (or chemical) filters and inorganic (or physical, mineral-based) blockers. Chemical sunscreens (eg benzophenones (BPs), avobenzone, octocrylene) absorb UV rays (UVR) and are less visible when applied to the skin, compared to physical sunscreens. Physical sunscreens are composed of mineral particles (eg titanium dioxide [TiO2] and/or zinc oxide [ZnO]), which absorb and reflect UVR as well as some visible light, and can leave behind a white residue or 'cast' which is especially problematic for those with more richly-pigmented skin.

Chemical filters have recently gained traction in the media as a threat to public health due to possible mutagenic, carcinogenic, and endocrine disruptive properties and their potential impact on marine life. Benzophenone-3 (BP-3), also known as oxybenzone, is one of the most widely used BP type UV filters and is found in sunscreens and various other consumer products including cosmetics. While approved by the FDA and in widespread use for decades, BP-3 has the potential to trigger contact dermatitis, erythema, urticaria, and photoinduced dermatitis when applied to the skin.[4] In humans, BP-3 is systemically absorbed, and has been detected in urine, serum, and breast milk samples worldwide. Its major metabolite, benzophenone-1 (BP-1), which has been detected in placental tissues of delivering women, possesses even stronger estrogenicity than its parent compound.[5] Furthermore, these ingredients have long half-lives, suggesting that regular sunscreen use may lead to accumulation within the body.[6]

The widespread use of BP-3 has resulted in the release of this compound and its derivatives into aquatic environ-

ments around the world. The compound can be directly released into the environment from the skin during recreational activities such as swimming in oceans and lakes, or indirectly released via waste products from cosmetics or sunscreen manufactures and industries.[5] Acute and chronic adverse effects of BP-3 on aquatic organisms including invertebrates, algae, and fish have been documented.[5] Marine copepods exposed to benzophenone exhibit decreased egg viability and hatching success.[7] Exposure to BP-3 has resulted in adverse effects on reproduction,[8] brain and liver development,[9] and steroidogenesis[10] in various species of fish. BP-3 further poses a threat for aquatic ecological integrity by reducing the ability of corals to adapt to climate variation and impair additional coral recruitment.[11,12]

UV chemical filters such as oxybenzone, octocrylene, and octinoxate have been banned in various jurisdictions worldwide including Hawaii, Key West, U.S. Virgin Islands, Palau, parts of Mexico, and the Caribbean islands.[13] Octocrylene has a similar structure to oxybenzone, and is one of the 17 US FDA active ingredients approved for use in SPF over-the-counter drugs. Octocrylene-containing commercial products may not only be contaminated by benzophenone, but levels of benzophenone accumulate from the degradation of octocrylene as the product ages.[4] Furthermore, octocrylene in itself has been established as an endocrine disruptor and a metabolic stressor to mammal, fish, and coral models.[4]

In contrast to chemical sunscreens, physical sunscreens are not systemically absorbed, offer broad-spectrum coverage (protection from both UVA and UVB rays), and are photostable resulting in fewer adverse skin reactions.[14] The most common physical sunscreens are TiO2 and ZnO. TiO2 is primarily a UVB absorbing compound, whereas ZnO is more effective in the UVA range. Combinations of both filters are frequently used to offer broad-spectrum coverage.

While considered a safer alternative to chemical sunscreens, physical sunscreens possess their own limitations. The large particle size of TiO2 and ZnO often results in an opaque formulation, which leaves white residue on the skin, potentially resulting in decreased adherence and sunscreen underapplication. Nanoscale preparations have been developed for aesthetic enhancement; however, there is a question of potential penetration and absorption into systemic circulation. Some studies show negligible amounts of zinc nanoparticles are able to penetrate the uppermost layer of the stratum corneum, with none being able to pass through the lower stratum corneum to reach viable cells.[15,16]

Physical sunscreens have generally been deemed better for the environment compared to chemical sunscreens, however both zinc oxide and titanium dioxide may cause damage to the marine environment.[13] Generation of reactive oxygen species by uncoated TiO2 specifically, has a toxic effect on marine phytoplankton and toward the crustacean, *Cladocera*.[17] Some TiO2 is coated, and the coating may dissolve in an aquatic environment. Similarly, uncoated ZnO nanoparticles may permanently bleach coral.[18]

III. PATIENT ADHERENCE

While sunscreen is well-established to prevent skin cancer, public use and adherence remains low. Studies show 14.3% of men and 29.9% of women regularly use sunscreen on both their face and exposed areas.[19] Barriers to use may include lack of motivation and interest, forgetting, inconvenience of application, and a desire to tan.[20] Additionally, dislike of the feeling or appearance of sunscreen, time constraints, and cost may play a role.[21] Observational studies have shown that when patients do apply sunscreen, they typically underapply, with use ranging between 20% and 50% of the recommended amount.[22,23] Choosing a sunscreen to use has become increasingly difficult for patients as companies launch a wide range of sunscreens with only subtle differences and often minor improvements in formulation. Furthermore, concerns of systemic absorption and potential toxicities may deter sunscreen use. However, the degree to which this contributes to underutilization is unknown. New and innovative sun protection solutions are needed in the market to assuage public concerns regarding the safety of current sunscreen formulations.

IV. FUTURE DIRECTIONS FOR SUNSCREEN

The sunscreen market is constantly evolving to meet the demand for better sun protection options and is projected to reach $24.4 billion worldwide by 2029.[24] Public interest in sunscreens and sunscreen ingredients has grown significantly over the last 10 years, with search trends expanding from general categories of sunscreens (“chemical sunscreen,” “mineral sunscreen,” “tinted sunscreen”) to specific UV filters such as “avobenzone,” “homosalate,” and “meradimate.”[25] Beyond new filters, a variety of novel technologies and approaches are currently being explored, holding promise for solutions to many of the problems of existing sunscreens.

4.1. NEW FILTER TECHNOLOGY

Currently, there are 17 UV filters approved for use in the US, compared to 29 available in the European Union (EU). Of the 17 approved filters, only 10 are considered suitable for adequate and effective UV protection when incorporated into sunscreen products.[26] No new UV filters have been approved by the FDA since 1999 due to strict regulations regarding dosage and labeling restrictions. UV filters are treated as over-the-counter drugs in the US (instead of cosmetic products as seen in the EU) and are thus subject to FDA safety standards requiring data gathered from non-clinical animal studies (to determine carcinogenicity and toxicities) as well as human clinical studies (eg irritation, sensitization, absorption, and pediatric safety).[27] Filters must meet Generally Recognized as Safe and Effective (GRASE) determination before it can be added to the FDA sunscreen monograph, which identifies the permitted ingredients, concentrations, directions, and conditions of use for OTC products.[26,28]

Bis-Ethylhexyloxyphenol Methoxyphenyl Triazine (BEMT), also known as bemotrizinol (Tinosorb®), is a newer sunscreen ingredient that is being considered for inclusion on the FDA monograph. Bemotrizinol is a photostable, oil-soluble, organic compound that is added to sunscreens and offers protection against both UVA and UVB rays. 10% BEMT has been in global use outside of the US since 2000. However, in order for the new ingredient to be included in the OTC sunscreen monograph, it must complete a Maximal Usage Trial (MUsT) to assess the extent of dermal penetration and systemic exposure as well as possible differences in populations or conditions. An open-label trial revealed 6% BEMT concentrations rarely exceeded FDA's defined threshold (0.5 ng/mL) in plasma and there was no evidence for BEMT accumulation or steady-state concentrations above threshold.[26] Furthermore, no estrogenic effects have been shown in vitro.[29]

Bis (diethylamino hydroxybenzoyl benzoyl) piperazine (BDBP) is another UV filter of interest that was approved by the Scientific Committee on Consumer Safety (SCCS) of the European Commission in 2021.[27] The organic filter demonstrated superior protection against pigmentation caused by wavelengths from the ultraviolet radiation (UVR)- visible light (VL) boundary region (385-405 nm) when studied against an identical formula without BDBP.[30]

4.2. NATURAL COMPOUNDS/ "GREEN PRODUCTS"

Natural compounds, defined as substances produced by a living organism found in nature, are gaining popularity. They present multiple advantages including their safety profile, cost effectiveness, and obtainment from renewable sources. Examples of common natural ingredients used in sunscreens include propolis, plants, herbs, cyanobacteria, and lichen species.

ALGAE DERIVATIVES

Cyanobacterium, also known as blue-green algae, are not truly algae but are a phylum of photosynthetic bacteria. The terrestrial cyanobacterium *Nostoc commune* tolerates high levels of UV radiation and possesses UV-protecting capabilities. Cyanobacteria produce two types of sunscreen pigments, scytonemin and mycosporine-like amino acids (MAAs). These secondary metabolites are thought to play multiple roles against several environmental stressors. MAAs are secreted in response to UV light and have light absorptive properties.[31] Scytonemin is a unique sunscreen pigment produced only in cyanobacteria. Similar to MMAs, biosynthesis of scytonemin is activated during UV (preferentially UVA) light exposure. It can prevent 90% of UVA light from penetrating into cells and has strong radical scavenging activity, similar to that of MAA.[32]

Lichen are complex life forms that are a symbiotic partnership of two separate organisms, fungus and algae. Usnic acid is a dibenzofuran derivative synthesized exclusively by lichen species (eg Usnea, Cladonia, Ramalina spp.). Usnic acid has been tested on human volunteers and found to have UV protection factors comparable to a commercial sunscreen spray with an SPF of 5, octyl methoxycinnamate (OMC), and butyl meth-oxydibenzoylmethane (BM-DBM). Among the three, usnic acid was found to be the best UVB filter.[33] The compound absorbs UV radiation similarly to octocrylene and when used concurrently with formulations containing octocrylene, it was found to enhance photoprotective potential. Usnic acid has good bioavailability and can easily be derived from a large population of lichen species, however some studies point to potential hepatotoxicity and there are reports of contact allergy.[34]

PLANT AND HERB DERIVATIVES

Plant derived products, including green coffee oil (GCO), have arisen as potential candidates to replace the chemical filters in "green" sunscreen formulations. GCO is a rich source of antioxidants and polyphenols, and when compared to other natural oils such as raspberry, avocado, Brazil nut, carrot, and spent coffee oil, GCO showed the highest SPF of 5. GCO has potential to improve SPF in sunscreens and allow for a decrease in the concentration of chemical filters in formulations. GCO further shows a high synergistic effect when associated with ethylhexyl methoxycinnamate in synthetic sunscreens, leading to an increase of 20% in SPF.[35] Other plant oils such as sesame oil resists 30% of UV rays, whereas coconut, peanut, olive, and cottonseed oils block approximately 20%.[36] The main active ingredient in green tea, epigallocatechin-3-gallate (EGCG), works as an anti-inflammatory agent, antioxidant, and sunscreen. Topical green tea applied to human skin yields a photoprotective effect, reducing the number of sunburns cells, protecting epidermal Langerhans cells from UV damage, and reducing the DNA damage that forms after UV radiation. Green tea further decreases melanoma cell formation after topical and oral administration in mice. However, most cosmeceutical products containing tea extracts have not been tested in controlled clinical trials.[36]

The root extract of the Krameria triandra plant, also known as the Peruvian Rhatany, has antioxidant and photoprotective potential. In cultured human keratinocytes exposed to UVB radiation, Krameria triandra root extract significantly and dose-dependently decreased the loss of cell viability and intracellular oxidative damage.[37] It was also found to absorb 25% to 30% of the amount of UV radiation typically absorbed by octyl methoxycinnamate.[36]

Propolis, also known as bee glue, is a natural product derived from plant resins and collected by honeybees. Its polyphenolic components have UV-absorbing, photoprotective, and photodamage preventive properties. In vitro measurements of the sun protection factor show formulations containing 40% of the hydroalcoholic propolis extract possess an SPF value of 10. When compared to common commercial UV filters (bemotrizinol, oxybenzone, octinoxate, and padimate O), Italian propolis extract has shown superior photoprotection.[38] When propolis is added to titanium dioxide, the SPF value increases from 20 to 50–60 showing a synergistic effect. Furthermore, green propolis extract has antioxidant activity, with topical application on mice resulting in reduced cutaneous inflammation, immunosuppression, and lipid peroxidation induced by UV exposure.[39]

4.3. BROAD-SPECTRUM COVERAGE INCLUDING VISIBLE LIGHT

In order for a sunscreen to be labeled "broad-spectrum," the FDA requires the UV filter to have a critical wavelength greater than 370 nm. A higher critical wavelength provides more UV protection, especially from UVA rays which have longer wavelengths.[27] The European Union standards for UVA blocking capability are more stringent than that of the US, requiring UVA protection to be at least one-third the sun protection factor (SPF) of the sunscreen.[40] As a result, US sunscreens block UVB rays but generally do not block UVA rays as effectively as EU sunscreens. Furthermore, compared to the wide variety of UVB filters available, there are only two FDA-approved filters for UVA, zinc oxide and avobenzone. In addition to UVA and UVB-light, visible light (400–760 nm) similarly penetrates the skin and plays a role in inducing erythema and hyperpigmentation depending on skin tone.[41,42] Currently, the most widely studied visible light filter is iron oxide. Adding iron oxide to zinc oxide formulations has been found to significantly reduce the transmission of visible light, while improving cosmetic appearance.[43,44] Visible light has shown to increase reactive oxygen species. Therefore, potential benefits from antioxidants have been raised. Antioxidants are frequently included in sunscreens. However, their protective properties are mainly based on laboratory tests and their role in skin protection in vivo is poorly understood.[24]

4.4. ANTIOXIDANTS

Topical and systemic antioxidants are emerging as potential agents of photoprotection. Ascorbate, tocopherols, carotenoids, polyphenols, and flavonoids may be added to sunscreens to counter reactive oxygen species (ROS) radicals generated by UV radiation. Carotenoid action is based on absorption of UV light and quenching of singlet oxygen, polyphenols join light absorption with quenching ROS, and tocopherols are a family of antioxidant molecules especially effective in preventing cell membrane oxidation. Two flavonoids, quercetin and rutin, were tested as potential topical sunscreen factors in human beings and found to provide protection in the UVA and UVB range. When used in association with titanium dioxide, the SPF obtained was around 30.[45] Silymarin is a flavonoid compound found in the seeds of milk thistle (*Silybum marianum*) that prevents UVB-induced immune suppression, decreases oxidative stress leading to apoptotic cell death, and has antitumor effects in vivo.[36,46,47]

Polypodium leucotomos extract, derived from the leaves of a tropical fern found in Central and South America, demonstrate photoprotective properties by enhancing endogenous antioxidant systems, inhibiting the generation of free radicals, and thus decreasing UV-mediated oxidative DNA damage. The extract, taken as an oral supplement, has demonstrated a favorable safety profile while protecting against UVR-induced sunburn reaction and UVA-induced phototoxicity.[48-50]

Despite these findings, studies have established that sunscreens that claim antioxidant activity have little to no actual antioxidant activity; they cannot yet be stabilized within sunscreen formulations to remain biologically active.[3] Further research is needed to improve the thermal and photo stability of natural, antioxidant-containing extracts. A combination of several different natural derivatives and antioxidants may be the key to creating sunscreens that offer safe, effective, broad-spectrum UV protection.

V. CONCLUSION

Skin cancer is the most common cancer in the United States and also largely preventable. In addition to sun avoidance and sun protective clothing, the use of sunscreen is an effective and important strategy in preventing skin cancer as well as sunburns and photoaging. While there are multiple FDA approved UV filters currently available for commercial use in the United States, there are many unmet needs and areas for improvement.

The future of sunscreens is promising. New ingredients, some of which are already approved in the EU, are being studied for commercial use in the US. Natural products such as algae and herb derivatives have also gained popularity and have been shown to provide photoprotection potential. Cyanobacterium can tolerate high levels of UV radiation lending to its UV-protecting capabilities. Formulations with propolis, derived from plant resins and collected by honeybees, enhance SPF by providing synergistic effects. Beyond new ingredients, the rise of sunscreens with broad-spectrum coverage and the incorporation of antioxidants encourages improved protection by shielding against both UVA and UVB rays as well as free radicals and oxidative stress.

As consumer needs and preferences continue to evolve, a variety of safe, effective, and sustainable sunscreen options will be necessary to keep up with the demand. Future sunscreens should include UVB protection but also significant protection from UVA and high-energy visible light. Consideration of environmental impact will also be important for manufacturers to problem solve to avoid injury to the aquatic ecosystem. Lastly, continued studies of new sunscreen technologies will encourage the use of sunscreen for both UV protection as well as optimal skin health.

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Table 1. Select new filter technologies

	Experimental Design	Route Administered	Mechanism of Action	Findings
Synthesized compounds				
Bis-Ethylhexyloxyphenol Methoxyphenyl Triazine (BEMT)	In vitro skin permeation test	Topical	Absorbs UVA and UVB rays ranging from 280-400 nm	Maximal topical applications of 6% BEMT in sunscreen formulation did not contribute to systemic exposure or estrogenic effects[26,29]
Bis (diethylamino hydroxybenzoyl benzoyl) piperazine (BDBP)	In vivo	Topical	Absorbs wavelengths in the UV/visible border region (385-405 nm)	The addition of BDBP affords more protection against pigmentation than a conventional formulation with the 385 nm source[30]
Natural compounds				
Cyanobacterium, syctonemin	In vivo (mice model) and in vitro	Topical	Secrete mycosporine-like amino acids in response to UV-AB light, which have UV absorption properties	Inhibits skin inflammation by down-regulating NF-kB activity and decreasing expression of TNF-a. Performs as a multi-function ingredient for skin care[31,51]
Usnic acid	In vivo and in vitro	Topical	Contains UV absorbing properties	Demonstrated UV protection factors superior to a commercial sunscreen spray with an SPF of 5, octyl methoxycinnamate (OMC), and butyl meth-oxydibenzoylmethane (BM-DBM)[33,34,52]
Green coffee oil	In vivo and in vitro	Topical	Rich source of antioxidants and polyphenols. High chlorogenic acid activity to facilitate wound healing	GCO showed a synergistic effect in SPF value when it was associated with the synthetic sunscreen ethylhexyl methoxycinnamate, leading to an increase of 20% in SPF[35,53–55]
Sesame oil	In vitro	Topical	Contains vitamin E and phenolic compounds to absorb UV rays and act as antioxidant and anti-inflammatory agents	Sesame oil resists 30% of UV rays, whereas coconut, peanut, olive, and cottonseed oils block out about 20%[36,53,54]
Green tea	In vivo (mice model) and in vitro	Topical or oral	The main active ingredient, epigallocatechin-3-gallate (EGCG), works as an anti-inflammatory agent, antioxidant, and sunscreen	Topical green tea applied to human skin yields a photoprotective effect, reducing the number of sunburns cells, protecting epidermal Langerhans cells from UV damage, and reducing the DNA damage that forms after UV radiation. Green tea further decreases melanoma cell formation after topical and oral administration in mice[36,55]
Krameria triandra root extract	In vitro	Topical	Rich in tannins to provide UV protection and reduce inflammation	Significantly and dose-dependently decreased the loss of cell viability and intracellular oxidative damage, absorbed 25% to 30% of the amount of UV radiation typically absorbed by octyl methoxycinnamate[36, 37]
Propolis	In vivo (mice model) and in vitro	Topical	Antioxidant, contains broad spectrum UVB and UVA photoprotection	Formulations containing 40% of the hydroalcoholic propolis extract possess an SPF value of 10.[38] When propolis is added to

				titanium dioxide, the SPF value increased from 20 to 50–60 showing a high synergic effect[39]
Silymarin	In vivo (mouse model)	Topical	Antioxidant, activates p53, prevents UVB-induced immune suppression	Mice treated with silymarin either before or after UV exposure illustrated diminished infiltration of leukocytes especially, CD11b+ and also decreased number of cells producing H2O2 and nitric oxide suggesting silymarin to be an anticarcinogenic and anti-inflammatory agent[36,46,47,56]
Polypodium leucotomos extract	In vivo (mouse and human models)	Oral	Antioxidant, inhibits release of cytokines	Demonstrated a favorable safety profile while protecting UVR-induced sunburn reaction and UVA-induced phototoxicity[47–50]

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