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NAVIGATING THE CHALLENGES AND CONTROVERSIES IN SUNSCREEN: A REVIEW

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Abstract
This article explores the controversies and challenges associated with sunscreen use, focusing on the toxicity of UV filters. Sunscreens are critical in protecting against skin cancer and UV-related skin damage, yet certain chemical UV filters, such as oxybenzone and octinoxate, have raised significant health and environmental concerns. These concerns include potential endocrine disruption, allergic reactions, and the harmful impact on marine ecosystems, leading to regulatory bans in some regions. While physical UV filters like zinc oxide and titanium dioxide are generally considered safer, their nanoparticle forms warrant further investigation. The article also examines the role of regulatory bodies in reassessing the safety of these compounds and highlights consumer-driven demand for safer, more sustainable sunscreen options. By reviewing recent research and industry innovations, this article provides a comprehensive overview of the ongoing efforts to balance effective sun protection with the need to minimize risks to human health. The findings underscore the importance of continued research, regulatory oversight, and industry innovation in advancing safer sunscreen formulations that protect both our skin and the planet.

Keywords: Sunscreen, UV filters, toxicity, oxybenzone, octinoxate, safety

Introduction

Sunscreen has become an essential part of daily skincare routines for millions worldwide, recognized for its critical role in protecting against ultraviolet (UV) radiation, which can cause sunburn, premature aging, and skin cancer [1]. The widespread promotion of sunscreen by health organizations underscores its importance in public health strategies aimed at reducing the incidence of skin cancer, the most common form of cancer globally. However, despite its undeniable benefits, the use of sunscreen has not been without controversy. Over the past decade, a series of debates have emerged, focusing on the safety of its ingredients, potential health risks. These controversies have raised significant concerns among consumers, regulators, and researchers, leading to a re-evaluation of sunscreen's role in public health and environmental sustainability.

One of the most prominent controversies revolves around the safety of chemical filters used in sunscreens, such as oxybenzone, avobenzone, and octinoxate. These ingredients have been scrutinized for their potential endocrine-disrupting effects and their ability to penetrate the skin, entering the bloodstream at levels higher than previously anticipated [2].

A study published in Journal of the American Medical Association *(JAMA)* in 2019 revealed that these chemicals can be absorbed into the body at concentrations that exceed the thresholds established by the U.S. Food and Drug Administration (FDA) for requiring further toxicological studies [3, 4]. This has led to growing concerns about the long-term effects of daily sunscreen use, especially as these ingredients are applied over large areas of the skin and often multiple times a day.
Apart from their potential health risks, certain chemicals such as octinoxate and oxybenzone have also been connected to coral reef bleaching, an extremely dangerous phenomenon that affects marine ecosystems. Research has indicated that these substances may result in the demise of coral larvae or hinder their proper development, thereby exacerbating the decline of coral reefs in well-known tourist locations like Hawaii and the Virgin Islands [5]. Because of this, some states have taken action to outlaw the sale of sunscreens that contain these ingredients, which has sparked a larger conversation about the need for more eco-friendly substitutes [6].
The controversy surrounding the efficacy of sunscreen in preventing skin cancer exacerbates the problem even more. Although using sunscreen alone is generally advised as a preventive measure, there is continuous discussion regarding whether it offers enough protection. According to some research, wearing sunscreen alone may give people a false sense of security, causing them to overlook other crucial sun protection strategies like looking for shade, donning protective gear, and avoiding times of peak sun exposure [3, 6].
Consumers are increasingly demanding transparency about the ingredients in their personal care products. This has led to a growing preference for mineral-based sunscreens that use physical blockers like zinc oxide and titanium dioxide, which are perceived as safer alternatives to chemical filters. However, even these ingredients are not without controversy. Questions have been raised about concerns about their ability to penetrate the skin and cause cellular damage [7].
Ten thousand deaths from melanoma are expected in the United States in 2019 out of 74,000 new cases. In a randomized trial conducted in 2011, Green et al. discovered that sunscreen could lower the incidence of melanoma [8]. However, the USA FDA has restricted several UV filters that are currently sold in the European Union. A 2018 national survey in Australia found that 55% of adults thought sunscreen could be used safely on a daily basis. Conversely, 17% of adults felt that frequent use of sunscreen ingredients was harmful to one's health. Removing sunscreen effectively could reduce toxicity and aid in controlling the perceived health risk [9].
Three primary ingredients are found in sun creams. The ingredients that go into making the cream or vehicle, the sun cream filters, preservatives, and other active ingredients. Research has indicated that these filters may pose a risk to skin health due to their degradation and production of reactive oxygen substances when exposed to sunlight. These substances can cause oxidative stress in skin cells, damage to genetic material, premature ageing, and an increased risk of skin cancer [10]. Numerous studies demonstrate that human biological tissues contain UV filters [11,12].
Sunscreens have some requirements to be safe for use in vivo: they must not be absorbed through the skin or if they do so, only in the stratum corneum, must not act as an (Endocrine Disrupting Chemical) EDC, must not have other effects different from the above, must be photostable, must not cause allergies or photosensitivity, must not be bio accumulative, and must be easily degradable [13].
This article review aims to navigate the complex landscape of sunscreen controversies and challenges by critically examining the research, regulatory developments, and public debates. By exploring these issues in depth, this review seeks to provide a comprehensive understanding of the current state of sunscreen use, protecting human health.

1.1 Use of sunscreens for protection against ultraviolet-induced skin damage

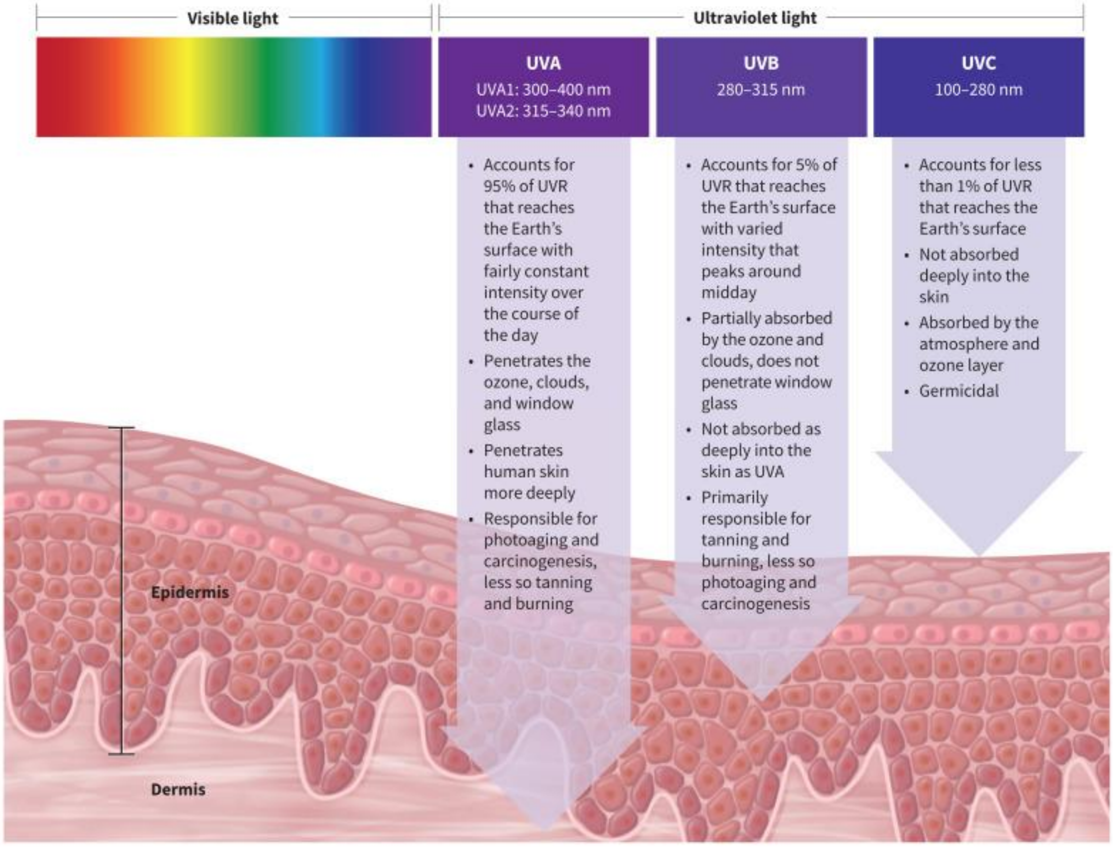

Figure 1UVA UVB UVC effects on skin [108]

With improvements in the medical field and science in general over the twentieth century, it was discovered that the UV portion of light contributes significantly to skin damage. Studies on laboratory rodents provided a better knowledge of UV-induced immunological suppression, carcinogenesis, photodamage, and photoaging [14]. Animals irradiated with UV demonstrated lesser hypersensitivity, and they failed to reject organ implants, unlike the controls which were not irradiated indicating Reduction in the immunological capacities of the irradiated animals [14]. Scientists also discovered that the prevalence of melanoma was higher in communities where sunbathing was widespread. Other extensive investigations revealed that those who used sunscreen on a regular basis saw significantly less skin damage [14].

Numerous cancer agencies have listed UV radiation as one of the major human carcinogens, and widespread research has further characterized the causes of skin cancers [14]. Since then, attempts to raise public awareness have increased sunscreen acceptability and usage. Originally, anti-UVA products were the focus of development; however, most sunscreen formulas now include anti-UVA and anti UVB agents [14].

1.2 Classification of UV filters for Sunscreen:

UV radiation has been linked to the pathophysiology of melanoma and is a major risk factor for the development of nonmelanoma skin cancer [16, 17, 18, 19, 20, 21]. The primary preventive method for lowering the chance of getting skin cancer and attaining a healthy ageing process is photoprotection. Sunscreen use has increased significantly in recent years as a crucial part of photoprotection [22].
Commercially available topical preparations for sun protection involve active ingredients categorized into two main classes:

1.2.1 organic molecules: That principally absorb Ultraviolet Radiation (UVR) energy, and inorganic (or mineral-based physical) molecules that additionally reflect UVR.

1.2.2 Inorganic sunblock: (ZnO and TiO_2) also absorb UVR, though this effect is superimposed with a second mechanism of scattering incident UVR [23, 24].

The components in sunscreens are topical preparations that work to filter, block, reflect, scatter, or absorb ultraviolet (UV) light. Sunscreens can be divided into three categories based on how they work: organic, inorganic, and biological [25]. Emollients, perfumes, emulsifiers, coloring compounds, and a host of additional ingredients, preservatives, or stabilizers are included in these UVFs. Broad spectrum sunscreens are defined by the FDA as those that offer UVA protection proportionate to UVB protection [26, 27]. The sunscreen solutions on the market often contain a blend of organic and inorganic filters with 20 or more components to achieve adequate broad-spectrum coverage [28, 29].

Several investigations have been carried out to evaluate the interference with typical endocrine pathways about the consequences of various synthetic substances in the surroundings [30, 31, 32]. The Organization for Economic Co-operation and Development (OECD) released a document [33] that included standardized testing for assessing possible endocrine disruption chemicals.

1.2.3 Organic Filters

Many organic sunscreen ingredients have one or more aromatic rings that can absorb and distribute UVR energy, such as PABA and its derivatives, cinnamates, avobenzone, octocrylene, salicylates like homosalate, benzophenones like oxybenzone, and octisalate [34].

The most widely utilized filters are organic ones, which offer protection from UVA and UVB rays [35]. The way they work is that they scatter and absorb radiation through chemical processes that result in breakdown products and/or heat. This means that they need to be applied more regularly. Skin absorption accounts for a large number. Inducing irritating or allergic contact dermatitis is more likely when using organic sunscreen [36].

There have been numerous organic UVFs linked to endocrine disruption [37, 39, 40, 41, 42]. In some animal models, benzophenone-3 (BP-3) can be absorbed at a rate of 1% to 9% when applied topically [45]. In other species, BP-3 appears to have systemic effects on the pathways leading to sex and thyroid hormones [40, 41, 43, 44]. It may absorb UVFs more quickly when the skin's barrier function is hindered [45].

The discovery of UVFs in urine [49, 50] placental tissues [48], and breast milk [38, 47] is astounding. Pregnancy-related exposure to BP-3 has been linked to an increased risk of newborn impairment (Hirschprung's illness) [51, 52]. Possible associations between enhanced lung and breast cancer cell motility and uterine leiomyoma formation have been discovered in a number of investigations [53, 54, 55, 56].

In addition to causing allergic contact and/or photo-allergens, UVFs (particularly BP-3, avobenzone, OC, amiloxate, and PABA) also appear to be the cause of several types of irritating dermatitis [52, 57, 58, 59]. Table 1.1 lists the most widely used organic filters [60, 61] and the Environmental Working Group's (EWG) assessment of them [62].

UVB Filters/Risks	UVA Filters/Risks	Broad Spectrum Filters (UVA and UVB)/Risks
PABA and derivates PABA or Endocrine Disrupting Chemical (estrogenic), allergic reactions.	**Benzophenones (BP-3 or Oxybenzone):** EDC effects, bio accumulative, photoallergic reactions, absorbed through the skin, Neurotoxicity. [15, 68]	**Tinosorb M**: Possible environmental contaminant. Acceptable/caution.

Cinnamates - Octinoxate, EHMC): persistent and bio accumulative, absorbed through the skin, appears in breast milk.	**Anthranilates**: less effective than benzophenones.	**Tinosorb**: non-estrogenic. Acceptable/caution. [7, 60]
Homosalate: Highly Polluting, weak EDC, decomposes with light into oxidizing substances harmful skin.	**4-Methylbenzylidene Camphor** EDC, persistent and bio accumulative. Possible thyroid toxicity. Always avoid.	**Iscotrizinol** HEB, diethylhexyl butamido triazone): No data, Acceptable/caution.
Octocrylene: EDC activity, allergies and/or (photo)allergies. [64, 65, 66]	**Mexoryl is** considered safe.	
Ensulizole: produces free radicals (DNA damage and potentially skin cancer. .		
4-Methylbenzylidene Camphor: EDC, persistent and bio accumulative. Possible thyroid toxicity.		

Table 1.1 EWG evaluation of most commonly used Organic filters [62].

1.2.2 Inorganic Filters:

Since these filters do not absorb through the skin, they are the safest and most highly recommended. It has been discovered that these filters have less penetration into living epidermis' Langerhans cells, keratinocytes, and melanocytes.

consequently, have a decreased potential to trigger allergic contact reactions [69]. Two inorganic (mineral) filters, zinc oxide (ZnO) and titanium dioxide (TiO2), have received FDA approval [41, 60, 70].

According to reference [71], ZnO and TiO2 particles have sizes between 200 and 400 nm and 150 and 300 nm, respectively. Larger particle sizes cause the skin's surface to have a white and chalky texture (Environmental Working Group's Sunscreen Guide) [62]. Reduced particle size nanoparticles in new formulations have been spurred by patient dissatisfaction and cosmesis. These ZnO and TiO2 nanoparticles have contributed to the development of a non-greasy, transparent, less expensive formulation that is resistant to UV deterioration [71]. According to the EWG's Sunscreen Guide, approximately 41% of sunscreens in the US are classified as mineral-only in 2018. This indicates a significant rise in inorganic filters [62].

ZnO and TiO2 pose a risk for oxidative stress and cellular toxicity because of their ability to pass through the stratum corneum, the dermis, and eventually the systemic circulation. Nevertheless, research conducted both in vitro and in vivo has revealed that these minerals do not penetrate the skin in any way [70, 72, 74, 75, 76]. The EWG has advised against using powdered products or spray sunscreens containing ZnO and TiO2 due to the possibility of inhalation of these substances [62, 77].

Cerium oxide (CeO2) has been proposed as a potential UV filter. Its high photocatalytic activity, which causes the oxidation and degradation of other formulations' components, leads to the commercialization of this substance with silica coating in some photoprotective formulations [78]. Similar to CeO2, Seixas and Serra have studied cerium phosphate (CePO4) [79]. As a possible future novel, stable, and effective inorganic UV filter, $CePO_4$ has high photocatalytic activity, leaves little white residue on skin, and has increased stability [79].

1.2.3 Biological Sunscreens

Plants and animals have evolved robust defenses against the harmful effects of oxidative stress and ultraviolet radiation (UV) thanks to natural selection and evolution [80]. Sun blockers are examples of natural antioxidants that have garnered a lot of attention. Their exact mode of action as sunscreen molecules hasn't been determined, though. Antioxidant activity is weaker in natural compounds. Their photochemical characteristics are linked to their activity [81]. Safer creams may contain natural compounds that have been shown to absorb UV light, have anti-inflammatory, antioxidant, and immunomodulatory properties. To show their actual efficacy in preventing skin cancer, as well as the recommended dosage and application method, more research in this area is necessary [3, 82]. The most advanced studies and for which there is more data on effectiveness are Lignin: this compound acts as UV blocking agent, with antioxidant properties due to its ability to capture free radicals [83].

- Silymarin: native to the *Silybum marianum*, itis known for its antioxidant properties. Silymarin and its flavonolignans are useful agents that may protect the skin against the adverse impacts of solar radiation [84].
- Marine antioxidants: the potential use of antioxidants derived from marine organisms as radiation-protective agents for skin have been evaluated in several studies [85, 86].
- Plants: recently, many other plant-derived extracts have been used as UV blocking agents:

Sphaeranthus indicus (SI) Linn (Asteraceae): rich in phenols, flavonoids, and mushroom tyrosinase [87].

Elaeagnus angustifolia (*E. angustifolia*): leaf extracts from this plant have been used to develop a topical sunscreen formulation [88].

Moringa oleifera: their extracts are rich in polyphenols such as quercetin, rutin, chlorogenic acid, ellagic acid, and ferulic acid that can be used in sunscreens [89].

Helianthus annuus: its seed oil belongs to the linoleic acid and oleic acid category of oils [90]. The alkyl polyglucoside (APG) emulsifier exhibits good emulsifying properties with a good SPF.

Cistus incanus L. and *Cistus ladanifer* L.: its components in their extracts have abundant polyphenolic that are beneficial sources of sunscreen and preserve the skin from UVR-mediated oxidative damage [91].

Conclusion: Due to UV filters' capacity to permeate skin and enter the bloodstream, some studies have raised concerns about the potential harm they could do to the human body. Urine and blood samples have been found to contain organic UV filters, specifically benzophenone and cinnamate derivatives. It has been reported that nanoparticles related to inorganic filters stay in the stratum corneum without entering the skin. Numerous studies have reported on the possible endocrine disruption caused by UV filters in biological samples. Studies on the potential endocrine disruption effects of UV filter exposure in human embryos have revealed that the frequency of UV filter detection (benzophenone derivatives) varied from 17% to 100%. Of these compounds, benzophenone-4 (BP-4) was the UV filter that tended to accumulate in the placenta the most (concentrations ranging from 0.25 ng/g to 5.41 ng/g).

Using in vivo models, researchers have examined additional detrimental effects of UV filters on neurotoxicity, behavioral abnormalities, and cytotoxicity. Benzophenone and dibenzoylmethane derivatives have been found to contain aromatic ketones, which may be the most toxic filters (causing allergic reactions and other harmful effects). Additionally, the photoisomerization process produces reactive and toxic photodegradation products.

Some UV filters, like cinnamates, octocrylene, and derivatives of camphor, have toxic effects and react with skin proteins to cause skin sensitization reactions and allergic contact dermatitis. These reactions appear to be related to the chemical structure of these UV filters. Oxybenzone and octinoxate are two examples of organic sunscreen filters that have generated controversy because of possible health and environmental hazards. When it comes to inorganic sunscreen filters, ZnO and TiO_2 pose very little health risks to people. This is mostly because they don't absorb through both intact and damaged skin. It is crucial to thoroughly research any compounds that might be utilized in cosmetics and to keep in mind that after years of use, chemicals that we once thought to be safe may need to be changed or forbidden. The final consumer lacks the knowledge and resources necessary to make an informed decision because manufacturers are not required by law to indicate the concentration of each substance on the packaging, even though laws are updated based on scientific evidence regarding safety. The compounds are only ordered depending on the amount present in the final product, which provides qualitative but not quantitative information.

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