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Potential Systemic Toxicity of UV Filters in Sunscreen: A Review

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ABSTRACT

For over 75 years, the use of UV filters in the composition of sunscreen and some products of cosmetics has been continuing for the purpose of the protection of the skin from acquiring damaging frequencies and wavelengths of sunlight. Even before 1500 BC, people were already conscious of the results of UV rays on the application of skin in which they used clothing for their protection against its harmful effects. In today's time, modern sunscreens are commonly used for the same purpose, mainly for protecting the skin from sunburn-inducing UV radiation. Moreover, sunscreens contain UV filters that could help lessen such occurrences. Reports indicated in this review are the common effects of UV filters that are used for the consumers on sunscreen usage, and those reasons of why consumers do not use sunscreens. Also, the paper will be discussing the health concerns and toxicities that UV filters might cause as it will be utilised as skin protectors in sunscreen formulation.

Keywords: Toxicities of UV filters, sunscreens, skin protectors, health concerns, UV filters

Introduction

Various skin maladies are formed when exposed to ultraviolet (UVA/UVB) radiation such as cancer, degenerative aging, and inflammation. Three subdivisions of UV energy consist of shorter and longer wavelengths with distinct and overlapping wavelength-dependent skin effects. Longer-wavelength UVA harms the skin by causing oxidative reactions that alter lipids, proteins, and DNA, as well as being immunosuppressive. Increased effects of ultraviolet B, on the other hand, results in sunburn and mutation of the formation of DNA dimer leading to cancer. The shortest wavelength with the highest energy, UVC, is the most detrimental out of the three forms of ultraviolet which enables it to kill unicellular organisms on exposure. Fortunately, only UVA and UVB predominate in ambient sunlight due to the absorption and protection of the atmospheric ozone from UVC ^[1]. Furthermore, lifestyle and environment, for instance, are one of the external factors owing to sunburn, skin pigmentation, photoaging, and eventually skin cancer from UV exposure.

Individual UV exposure is defined not only by the amount of solar radiation, but also by the overall length of time spent outdoors for work or enjoyment, as well as the utilization of shade, UV-protective clothing, and sunscreen. The progressive intensity of UV radiation differs geographically where sunlight hits the Earth directly in locations closest to the Equator such as in the Philippines, Colombia, Ecuador, Brazil, etc. As a result, those living in equatorial areas face a higher risk of skin diseases owing to higher UV doses than those living in temperate climes.^[2]

UV radiation is considered carcinogenic and thus must be avoided or reduced from its harmful effects. As a consequence, UV filters have been utilized as active components in the manufacture of cosmetic goods since they mainly protect and defend the human skin from getting radiation from the sun. A sun protective cosmetic might be described as *"a certain cosmetic product that has UV filters to shield the skin from the sun's damaging UV-light, so minimizing or limiting the damages that such radiation may bring to people's health."* ^[2]. UV filters were originally used in beach sunscreen, and thereafter in outdoor sports. Currently, it is added to a broad range of skincare and other cosmetics, including in different kinds of creams, serums, moisturizers, make-up, and even in hair care products ^[3].

People have been conscious of the effects of UV radiation as early as 1500 BC. Civilizations in Mesopotamia and in Egypt discovered weaving which enabled them to use clothing for photoprotection ^[4]. Olive oil, lead paints, chalks, inorganic clays and mineral powders were utilized by the Egyptians to

protect their skin from darkening as they thought pale skin was more beautiful than darker complexion. When practicing for the Olympic Games in ancient Greece, participants coated their skin with a protective combination of oil along with the sand. Arsenic and Mercury derivatives were then used by Queen Elizabeth I of England in the 16th century for face whitening and sun protection. Years later, UV rays were discovered, and melanin was revealed to work as a built-in sunscreen in our skin for protection ^[5]. Hammer employed numerous topical therapies to prevent sunburn in 1981 and documented it in his photoprotection monograph as he was the first to advocate the use of certain chemical sunscreens to protect against sunburn ^[4]. Despite the fact that we now have far more options for protecting our skin from both short-term and long-term sun harm than it has been, there is still tremendous potential for improvement ^[4].

UV filters must be constructed in such a manner whereby they are chemically compatible, do not react with other matrix chemicals, and are physically stable. There are two types of chemical compounds used as UV filters: inorganic UV filters (physical UV filters) and organic UV filters (chemical UV filters). To improve product efficiency, UV filters should typically stay on the surface or in the stratum corneum's upper layers. However, there is the possibility of absorption into and through the skin, raising concerns about possible systemic toxicity ^[4].

Materials and Methods

The review of literatures was carried out using Google Scholar (scholar.google.com) and other open-access databases, with the keywords "sunscreen toxicities", "ultraviolet filters", "UV filters", "sunscreen" and "sunscreen UV filters" as keywords. The article selection period for the review was limited to the last ten years (March 2012 to March 2022). More than 300 papers were reviewed, with only those studies focused on ultraviolet attenuation from sunscreen UV filters; benefits and risks of using sunscreens; UV filter toxicities in sunscreens; health concerns of UV filters in skin protectors; *in vitro* and *in vivo* UV filter effects. This article contains a total of 43 papers that were reviewed.

UV attenuation from sunscreen UV filters

For almost 75 years, sunscreen or other cosmetic products have featured UV filtersto shield the human skin from the sun's harmful rays. The awareness UV filters were developed in response to the detrimental effects of UV radiation on the skin. UV filters absorb UV light, reducing the harmful effects of sun exposure. Because of the large variety of combinations sold depending on the features and expected level of protection, people are shielded from the bulk of UV-induced skin damage ^[6]. UV filter compounds have various aromatic structures with double bond carbon-carbon conjugates and/or carbonyl moieties that hamper the transmission of energetic sun photons that reach the Earth's surface. After the photons are absorbed by the UV filters, the energy is thermally released via vibrational transitions or vibrational relaxation. If the UV filters do not deteriorate, they absorb more photons and continue the procedure, resulting in UV-protected skin. Thus far, there are a variety of commercial preparations with varying compositions that are manufactured to provide UV-A (320-400 nm) and UVB (280-320 nm) protection ^[7].

There are around 55 UV filters that are permitted for use in the manufacture of sunscreens globally, with each filter being accepted or refused based on regional standards. There are two sorts of UV filter classifications available: inorganic particulates (e.g. zinc oxide and titanium dioxide) and organic particulates (UVB or UVA filters). The mechanisms of action for ultraviolet attenuation are determined through its absorption, reflection (backward scattering), and scattering ^[4]. Organic UV filters inhibit both UVB and UVA rays by scattering and reflection, whereas inorganic particles protect us from significant UV radiation by absorbing, scattering, and reflecting UVB and UVA rays. The total effect of UV filters for titanium dioxide (inorganic UV filter), for instance, can be represented by the sum of scattering and absorption ^[4]:

Extinction = Scattering + Absorption

UV filters absorb or scatter the energy of electromagnetic rays. Inorganic particles diffuse by scattering and reflecting electromagnetic energy while also having the propensity take in UV radiation. When a UV photon is absorbed by an organic UV filter, the electron's highest occupied molecular orbital (HOMO) is converted to the lowest unoccupied molecular orbital (LUMO) (Figure 1)^[7]



Figure 1. Organic UV filter energy absorption^[7]

UV filters, in general, deactivate electrons collected from electromagnetic energy from an excited state into a ground state by losing energy in a process of simple vibrational relaxation and/or fluorescence (visible radiation). However, in physical sunscreens, compounds such as Avobenzone (organic UV filter) exhibit intersystem bridging or instability and may be regulated by phosphorescence, T-T transfer, and photochemical processes ^[7]. From the standpoint of product design, such photo-stable sunscreen formulation can be accomplished by developing and testing combinations of UV filters, emollients, stabilizers, and preservatives to achieve the desired biological efficacy, physical stability parameters, microbial robustness, cosmetic aesthetic attributes, and photostability properties ^[4].

Benefits and Risks of using Sunscreens

Sunscreens are used as a protection for skin against harmful UV rays. There are other benefits that sunscreens can provide to the skin such as the following: when used regularly it could help to avoid sunburn, skin cancer, and premature ageing of the skin^[8] by lessening the damaging effects of the sun's ultraviolet (UV) light, reduces tanning and blotchiness particularly in the face, and may help to inhibit the loss of elasticity of the skin that leads to wrinkling, additionally, there are sunscreen products declares that there product has a potential to protect skin against those free radicals ^[9]. There is a study found by the FDA about the dangers of sunscreen, although the dangers are uncertain there could still be a possibility of rising risks. According to an article medically reviewed by Fischer ^[10], without further testing, active substances should not be retained in the skin and in the bloodstream at amounts greater than 0.5 nanograms per milliliter (ng/mL). However, researchers discovered that when oxybenzone was administered on the skin every two hours as stated on the bottle, it was absorbed at a level of 258.1 ng/mL in which it exceeded the FDA's limit by 516 times. Research studies about this are inconsistent, there are concerns that oxybenzone may interfere with the body's normal hormone function. Furthermore, according to a dermatologist, it is unclear whether oxybenzone poses a real health danger. Thus, sunscreen disadvantages are yet unclear but ingredients involved in the formulation of each sunscreen must be monitored for safety use.

UV Filter Toxicities in Sunscreens

Two types of UV filters exist that are classified on their properties: (1) Physical UV filters, also known as inorganic UV filters, reflect and dispersed the UV rays; and (2) chemical Ultra violet filters, also recognized as natural or organic UV filters, UV filters, absorb light. ^[111]. Moreso, In the field of ultraviolet light absorption, a type of carbon-based molecule that is made to utilize UV light is also known as an organic UV filter. They should not undergo any chemical changes as a result of frequent UV irradiation in order to preserve their effectiveness over time. Many conventional organic UV filters absorb Infrared radiation and attain energy-dense energy state, however they are frequently unable to rapidly release the excited state energy and return to their ground state, where they are stable and ready to absorb more UV radiation [12]. Inorganic UV filters, on the other hand, include titanium dioxide (TiO2) and zinc oxide (ZnO). They were created from nano particles or nanometric particles that reflect the minimum amount of visible light, resulting in a diminished white pigmentation appearance during the application to the skin. These oxides have unique qualities coming from the standpoint of photoprotective efficacy ^[13]. Further, ZnO and TiO2 are known as the active photocatalysis that are widely employed in heterogeneous photocatalysis to degrade organic environmental contaminants. TiO2 and ZnO have been shown to produce highly

oxidizing radicals including OH as well as other reactive oxygen species (ROS) like H2O2 and singlet oxygen, 1O2, which are both cytotoxic and genotoxic when photoactivated by UV light ^[12].

In line with this, continuous increase in skin cancer incidence rate has been registered. Skin cancer looks to be a public health issue that must be addressed as the number of cases increases. International health analysts have suggested people to protect themselves from the harmful effects of UV radiation. In order to avert exposure to the sun during peak radiation hours and donning protective clothing and using sunscreens ^[14]. According to a study published in 2020, there are controversies surrounding the toxicity of UV sunscreens, including hormonal imbalances, allergic reactions, increased oxidative stress, and phototoxic events.^[15].

There have been several studies that have shown that using sunscreen effectively prevents sunburns. However, there is inconclusive data to support their claim that they protect against melanoma skin cancer. In addition, a recent study mentioned in the article that a massive wave of animal and in vitro experiments demonstrated that certain UV-filters may also have adverse effects on the endocrine system as endocrine disruptors as well ^[16]. Moreso, regardless of these rhetoric, the manner in which sunscreens are tested is critical for ensuring their safety. While mandated phototoxicity testing is included in sunscreen regulation, however, it's not recommended to use photo-genotoxicity testing combined with the normal program of photosafety testing ^[15]. A number of currently available analyses do not usually yield dependable results, primarily as a result of limitations related to the nature of the assessed phototoxic effect, cell UV sensitivity, and the irradiation protocols used. Sunscreens must pass a number of tests before they can be sold because they are an FDA-regulated product ^[7].

Health concerns of UV filters in Skin Protectors

Over the years, there has been a rise in the use of sunscreens due to a shift in public awareness about the potential dangers of excessive sun exposure. Sunscreens contain UV filters that protect against UV radiation. These compounds absorb and filter UV rays in sunscreens. Although these filters protect the skin, significant concern about its safety remains as cellular damages and biologic changes challenge its potential each day ^[18].

Ultraviolet radiation is one of the critical environmental factors that can trigger various skin problems such as burning, erythema, premature skin aging, and skin cancer ^[19]. The first sunscreens and their UV filters (organic or inorganic) were manufactured mainly for the purpose of preventing UV erythema, more commonly known as sunburn ^[20]. Now, modern sunscreens incorporate a number of organic and inorganic UV filters, or even a combination of both, to provide broad UV spectrum protection that reaches the highest level of UV protection ^[21]. However, because of its seemingly demanding role in consumer life, the presence of UV filters in sunscreens has been the focus of numerous research raising concerns about their safety.

In principle, sunscreens are designed to be applied externally to the skin. However, the ability of UV filters, specifically organic filters, to cross the skin barrier puts the safety of UV filters into question mainly on the grounds that they can be toxic. It has been reported that the UV filter and its broken-down products may penetrate the skin and reach the circulatory system due to its stability and lipophilicity ^[22-23]. Many studies have also shown

that some UV filters have been found in urine, confirming the fact that they make their way inside the human body and cause detrimental effects to health ^[24]. For instance, a study conducted by Ao et. al. quantified the levels of four commonly used organic UV filters in Eastern China, and later on found out that benzophenone-3, a UV filter, is present and abundant in the urine samples ^[25]. Possible estrogenic effects are also related to the usage of organic UV filters, which are a result of the organic filters' hormone-disrupting potential. It was not until 2001 that researchers found the detrimental effects of organic UV filters on the endocrine gland, and various studies have been undertaken since then to study the possible impairment of the endocrine system induced by these filters ^[19]. However, further investigation is still needed regarding the endocrine disruptive effects of UV filters as studies today are still conflicting.

Apart from the risk for systemic toxicity, medications used topically may induce unpleasant skin responses. With the ever-increasing usage of sunscreens and exposure to UV filters in daily-used topicals, soluble UV filters have emerged as increasingly common photo allergens and contact allergies ^[25]. Although the incidence is rare, it has been observed to range between 1% and 40% in individuals with a history of photosensitivity. In a recent study that focused on profiling photoallergic manifestations of common UV filters in Canada, a total of 99 out of 160 patients had photoallergic reactions. They tested common UV filters such as benzophenone-3, octyl dimethyl para-aminobenzoic acid, and butylmethoxydibenzoylmethane. Among the 160, 54 individuals had one photoallergic reaction at a minimum, 19 experienced irritation due to light, and 29 suffered from both photoallergy and allergic reactions. While these dermal problems have resulted from exposure to UV filters, it is important to note that these test allergens should be consistently standardized to provide a concrete and reliable explanation for the overall occurrence of allergic reactions ^[26].

In vitro and In vivo penetration

Organic and inorganic ultraviolet filters are being used in sunscreens and other preparations to minimize or reduce Ultraviolet damage. The increased use of these filters has resulted in an increase in the number of studies looking into the potential effects on health and the environment^[19]. Regarding the benefits of using filters, some disadvantages of them are their contents, which cause human toxicity, impact on the environment, and photo instability, even though these are some of the considerations in terms of creating new, safer, and effective photoprotective agents.^[27]. The analyses employed in vitro algae cultures that have been utilized to directly test the UVF exposure toxicity. According to the studies, toxicity is found in the ranges of species (10x to 100x, the revealed concentrations from different locations around the world) and 10 to 300 micrograms per liter depending on UVF^[28]. In-vivo, the use of human skin is essential in monitoring skin penetration in-vitro as long as regulation requires it. A study was conducted using the oestrogenic activity of the following benzophenone organic filter derivatives: benzophenone-1, benzophenone-2, and benzophenone-3. For their estrogenic activity in vitro, these benzophenone derivatives should be present in MCF-7 cells^[29]. Most in vitro studies on the oestrogenic effects of UV filters discovered that benzophenone-3, 4-methylbenzylcathinone, octylmethoxycinnamate, and octyl-dimethyl-PAB all had oestrogenic effects. The suspected oestrogenic actions of 3benzylidene-camphor, octyl-methoxycinnamate, benzophenone-3, and 4-methylbenzylidene camphor, on the other hand, were applied in an increased uterine weight through ophorectomized rats and some immature rats in acute

tests in vivo. However, not all UV-filters that appear oestrogenic in vitro were also oestrogenic in acute in vivo models.^[30].

Those certain negative effects of ultraviolet filters have been reported by several research groups that used in-vivo models of fish, insects, rats, etc. The damaging impact of UV filters on the endocrine system includes effects on the estrogen, androgen, and thyroid, but some other intrinsic effects have been shown, including cell toxicities, behavioral changes, and neurotoxicity ^[31]. Probably, dibenzoylmethane and benzophenone are extremely toxic UV filters since they have aromatic ketones, which are unknown metabolic enzymes produced in humans ^[32].

Results and Discussions

The production of cosmetics and other industrial products that contain ultraviolet filters is in high demand since many people are using these kinds of products. Due to the investigated endocrine damaging effects of UV filters, such a topic has become a subject of concern that as a result, researchers have been finding wars to improve risk assessment of chemicals present as well as their metabolites ^[33]. A significant number of *in vitro* studies as well as in vivo animal studies have reported a variety of negative effects of UV filters present in sunscreens and cosmetics. Several results usually involve developmental and reproductive effects that appear to be caused by these chemicals' endocrine-disrupting actions ^[34].

	Generic name	Product name	Max concentration (%)	Spectrum of action	Approved
Chemical UV- filters	Benzophenone- 3	BP-3	6b–10a,c	UV-A, UV-B	EU, US, AU
	2-Cyano-3,3- diphenyl acrylic acid	OCT	10	UV-B	EU, US, AU
	3-Benzylidene camphor	3-BC	2	UV-B	EU
	3-(4-Methyl- benzylidene) camphor	4-MBC	4	UV-B	EU, AU
	2-Ethylhexyl 4- methoxy cinnamate	OMC	7.5b–10a,c	UV-B	EU, US, AU
	Homosalate	HMS	10a–15b,c	UV-B	EU, US, AU
	2-Ethylhexyl 4- dimethylamino benzoate	OD-PABA	8	UV-B	EU, US, AU
	4- Aminobenzoic acid	РАВА	15b,c	UV-B	US, AU
Physical UV- filter	Titanium dioxide		25	Physical	EU, US, AU
	Zinc oxide		25-no limit	Physical	US, AU

Table 2. CAS numbers, chemical formulas, molecular weights, log P, European Union and US maximum approved concentrations, solubility and absorption spectra of several organic UV filters^[29]

Compoun ds	CAS numbe r	Chemica l Formula	Molecul ar weight (gmol-1)	Log P	Maximum authorized concentrati ons in European Union (%)	Maximum authorized concentratio ns in United- States FDA (%)	Solubility	Absorption spectrum
Para- aminobenz oic acid	150-13- 0	C7-H7- N-O2	137.1	0.830	5	15	Hydrophilic	UVB
Avobenzon e	70356- 09-1	C20- H22-O3	310.4	4.510	5	3	Lipophilic	UVAI
Octocrylen e	6197- 30-4	C24- H27-N- O2	361.5	6.890	10	10	Lipophilic	UVB
Benzophen one 3	131-57- 7	C14- H12-O3	228.2	3.790	10	6	Lipophilic	UVB, UVAII
3-(4'- methylbenz ylidene) camphor	36861- 47-9	C18- H22-O	254.4	3.390	2	4	Lipophilic	UVB
Octyl- methoxycin namate	5466- 77-3	C18- H26-O3	290.4	5.800	10	7.5	Lipophilic	UVB
Octyl- triazone	88122- 99-0	C48- H66-N6- O6	823.1	15.50	5	5	Lipophilic	UVB
Octyl- salicylate	118-60- 5	C15- H22-O3	250.3	5.934	5	5	Lipophilic	UVB
Homosalat e	119-36- 8	C8H8O3	152.2	5.940	10	15	Lipophilic	UVB
2-phenyl- benzimidaz ole-5- sulfonic acid	27503- 81-7	C13- H10-N2- O3-S	274.3	2.100	8	4	Hydrophilic	UVB

Table 3. Shown in this table are the analyses of uni- and multivariate logistic regression regarding the factors associated with sunscreen use. Abbreviations OR, CI, and NA stand for odds ratio, confidence interval, and not applicable, respectively.^[32]

	Factor		Univariate analysis			Multivariate analysis			
			Never used sunscreen <i>n</i> (%)	Use sunscreen n (%)	P value	OR	959	% CI	P value
Participants			496 (49%)	515 (51%)	NA	NA	NA	NA	NA
Gender		Male* Female	380 (74%) 116 (23%)	130 (26%) 385 (77%)	<0.001	1 10.038	7.219	13.957	<0.001
College year		Junior* Senior	260 (49%) 236 (49%)	270 (51%) 245 (51%)	0.998	1 0.932	0.674	1.287	0.668

The factors correlated with the use of sunscreen include the highest income of the family, gender, application of tanning bed, use of other sunscreens and history of sunburn. Results show that there is no difference between using sunscreen among the junior and senior students. Moreover, the majority of females used sunscreen more than males. Regarding the history of sunburn, the students with the greatest sunburn in the past most likely used sunscreen over 5 times. Those people who use tanning beds presumably use sunscreen.



Figure 1. The rationale of using sunscreen ^[33]

Sunburn prevention (62 percent), dark skin spot avoidance (51 percent), and finally skin cancer prevention (46 percent) were the top three reasons why students used sunscreen.



Figure 2. The rationale for not using sunscreen^[33]

Time constraints (36 percent), inconvenience or disruption (31 percent), and inefficiency are the primary reasons why students choose not to apply sunscreen to their bodies (19 percent). Other reasons include expense (11 percent), a lack of understanding of what sunscreen is all about, and a skin allergy (1 percent).

Table 4. Summary of Sunscreen Toxicities

Sunscreen toxicity	Cases in percentage				
A. Allergies ^[15]					
Allergic reactions ^[35]	11.3%				
Photoallergy (PA) ^[35]	4.4%				
Contact allergy (CA) ^[35]	5.5%				
Combination of Photoallergy and Contact allergy ^[35]	1.3%				
B. Neurotoxic ^[31]					
Endocrine Disruptor ^[36]	15%				
Developmental toxicity ^[37-38]	60.89%				
Reproductive Hormonal levels ^[39]	10.3%				
Oxidative stress ^[40]	0.05%				
Melanoma (Skin Cancer) ^[41]	1.0%				

Based on the data collected, Allergies (Part A) indicated that 130 patients experienced allergic reactions (11.3%), 51 had photoallergy (4.4%), contact allergy (5.5%), and 15 both had contact and photoallergy (1.3 percent). In addition, under Neurotoxic (Part B), it is shown that (15%) of 48 healthy participants experienced endocrine disruptors leading to neuronal propagation, synaptic plasticity, and neurodegeneration, that (60.89%) of 473 pairs of participants experienced developmental toxicity, that (10.3%) of 106 participants were associated with Reproductive Hormonal changes, and that (1.0%) of 6 participants had Melanoma (skin cancer).

In support to the Allergies category of sunscreen toxicities, Oxybenzone, DL-alpha-tocopherol, and fragrance mix have been reported to be the top three (3) responsible irritants and allergens which were identified in a standard patch testing conducted in 23 908 patients, wherein there were 219 positive reactions . Similarly, an opinion paper published by the European Scientific Committee on Consumer Safety (SCCP) concluded that oxybenzone is a photoallergen in sunscreen agents photo-patch testing, including oxybenzone, based on their review of 20 articles/studies involving 6378 patients, where 159 positive reactions were discovered. Contact urticaria has also been reported in the use of cosmetics containing substances such as polyaminopropyl, phenoxyethanol, oxybenzone, and others, with oxybenzone being associated with contact-mediated anaphylaxis. Based on the findings of Heurung et al ^[42], the American Contact Dermatitis Society named benzophenones, such as oxybenzone, as the 2014 Allergen of the Year, with both contributing to allergy and photoallergy reactions. The sunscreen ingredient octocrylene, as well as ketoprofen, a topical nonsteroidal antiinflammatory, demonstrated substantial levels of cross-reactivity with oxybenzone^[43]. Ultimately, there appears to be enough evidence that oxybenzone has the potential to cause contact allergy, photocontact allergy, and contact urticaria responses in humans.

Conclusion

While the sun provides incredibly beneficial light, its damaging ability and long-term damage from prolonged exposure are something to be wary of. UV filters must be made in such a way that they are chemically compatible, do not react with the other chemicals in the formulation, and are physically stable; and most, if not all, sunscreens in the market contain combinations of different UV filters. Since most sunscreens only give effective protection in a restricted area of the UV spectrum, combining several UV filters to get the required SPF is all that is required. However, developing a less toxic sunscreen with lesser allergenic potential can be difficult as it requires further technical attention to maintain stability. As a result, researchers are still in the works, looking for ways to improve sunscreen formulations by adding new active compounds and/or possible new combinations and developing novel cosmetic systems that are generally safe and less toxic. Furthermore, although recent experimental reports have sparked concerns about the safety and toxicities of these UV filters in skincare products, the lacking and inconsistent information regarding how these filters produce harmful effects on the body still warrants further investigations.

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