

Review

Toxicity of Different Chemical Components in Sun Cream Filters and Their Impact on Human Health: A Review

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Abstract: Some chemical components in sun cream filters have endocrine-disrupting activity or can be carcinogenic, neurotoxic, bioaccumulative, allergens, or be toxic for human reproduction. It is important that sunscreens have safety requirements. The objective of this work is to compare sun cream filters used in conventional commercial sunscreens and those that are considered natural products, especially focused on endocrine-disrupting effects. In order to achieve the above objective, the compositions of different conventional and natural sun cream filters were evaluated and compared, taking into account the presence of the different sun cream filters whose effects were evaluated on the website specialized in safety and cosmetics, Environmental Working Group (EWG), and in the Register of chemical substances and mixtures in the EU Registration, Evaluation, Authorization and Restriction of Chemicals (REACH) Regulation. The currently available evidence of each sun cream filter and their degree of safety has been summarized. Several organic sun cream filters present a potential risk to health and the environment; however, inorganic sun cream filters such as titanium dioxide and zinc oxide (ZnO and TiO₂) show a very low risk in humans as they are not absorbed through intact or damaged tissues. The legislation does not oblige manufacturers to specify the concentration of each substance, which provides qualitative but not quantitative information for the consumer.

Keywords: sunscreen filters; sun cream filters; solar filters; UV filters; endocrine-disrupting chemical (EDC)



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1. Introduction

At the European level, the REACH (Registration, Evaluation, Authorization, and Restriction of Chemicals), was created to protect human/animal health and the environment from chemicals. REACH is intended not only to mitigate the environmental damage that new compounds can cause, but also to protect human health. European companies and industries have been forced to incorporate this type of regulation into their manufacturing and industrialization processes since its implementation (1 June 2007). Currently, there are more than 80,000 chemical substances registered for use in Europe. REACH applies to all chemical substances: those involved in industrial processes and those that are present in objects in our daily life, such as cosmetics, including sun creams [1,2].

According to Commission Regulation 2018/605 amending the Plant Protection Regulation No. 1107/2009 adopted by the European Commission, a substance shall be considered as having endocrine disrupting activity in humans if: it shows an adverse effect in an intact organism or its progeny leading to functional changes; it has an endocrine mode of action (anti-estrogenic, androgenic or anti-androgenic activity, steroidogenesis alteration and thyroid and anti-thyroid hormone activity); the adverse effect is a consequence of the endocrine mode of action [3]. The Endocrine Society and the World Health Organization

(WHO) define an endocrine-disrupting chemical (EDC) as “an exogenous substance or mixture that alters function (s) of the endocrine system and consequently causes adverse health effects in an intact organism, or its progeny, or (sub)populations” [4,5]. There are many harmful effects that EDC can have on health at any age, such as malformations and/or malfunction of the reproductive system, obesity, and cancer [6–9], in particular hormone-dependent cancers (such as breast, endometrium, prostate, testis, and thyroid) [6].

Endogenous hormones and EDCs share many structural similarities which may lead to hormone-dependent cancers interfering with hormone receptor function [10]. Parabens (methylparaben, butylparaben, ethylparaben, propylparaben, isopropylparaben, isobutylparaben, benzylparaben) are an example of EDCs [11]. There is an important link between alterations of reproductive and metabolic health as a result of EDC exposure, such as from bisphenol A, bisphenol S, bisphenol F, phthalate metabolites, and mercury [6–8,10].

Sun creams are made up of three main ingredients. The excipients that create the cream or vehicle, the additives, preservatives, and other active substances, and finally the sun cream filters. The safety of UV filters for humans and the environment has been questioned recently. It has been studied that these filters can be harmful to the skin because when they come into contact with sunlight, they degrade and produce reactive oxygen substances that generate oxidative stress in skin cells, damage to genetic material, premature aging, and predisposition to skin cancer [12]. Multiple investigations reveal the presence of UV filters in human biological tissues [13,14].

It is important that 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 EDC, must not have other effects different from the above, must not favor the absorption of other chemical substances, must be photostable, must not cause allergies or photosensitivity, must not be bioaccumulative, and must be easily degradable and not affect flora and fauna. Thus, the ideal photoprotector would meet all these requirements, have adequate cosmetic effects, and not have harmful effects on health [15]. Could it be possible?

The objective of this research is to compare sun cream filters used in conventional commercial sunscreens and those that are considered natural products.

2. Materials and Methods

In order to achieve the above objective, the compositions of different conventional and natural sunscreens have been evaluated and compared, taking into account the presence of different sun cream filters whose effects have been consulted on the website specialized in safety and cosmetics, Environmental Working Group (EWG), which summarizes the currently available evidence of each of them and their degree of safety and in the Register of chemical substances and mixtures in the EU (REACH Regulation).

In addition, published safety data on solar filters were updated by searching publications in peer-reviewed journals available on PubMed Database at the end of September 2022. The following search terms were used: ‘solar filters’ OR ‘sun cream filters’ OR ‘sunscreens’. The inclusion criteria were possible side effects of selected UV-filters in cosmetics, especially in sun creams. Putting the focus above all on those sunscreens with endocrine disruptive effects. No limits for publication dates were set. The articles were screened by two reviewers based on titles and abstracts. All articles dealing with environmental effects of sun creams filters were excluded. Those articles not published in English or Spanish were excluded. Finally, a manual search of data available in gray literature was conducted.

3. Results

Ultraviolet radiation (UV) is a fundamental risk factor for the development of non-melanoma skin cancer and it is also implicated in the pathogenesis of melanoma [16–21]. Photoprotection is the main preventive strategy for reducing the risk of developing skin cancer and achieving healthy aging. In recent years, the use of sunscreens has become widespread as an essential component of photoprotection [22].

Commercially available sun-protective topical formulations utilize active agents classified into two major classes: organic molecules that principally absorb UVR energy, and inorganic (or mineral-based physical) molecules that additionally reflect UVR. Inorganic sunblocks (ZnO and TiO₂) also absorb UVR, though this effect is superimposed with a second mechanism of scattering incident UVR [23,24]. Sunscreens are topical preparations whose compounds have the function of filtering, blocking, reflecting, scattering or absorbing ultraviolet (UV) light. According to their mode of action, we can classify sunscreens into organic, inorganic, and biological [25].

Sunscreens contain one or more ultraviolet filters (UVFs) that may be physical, chemical, or both. A UVF is a specific compound that impedes the passage of UV light. UVFs can be divided into chemical agents (absorbing UV rays and converting them to thermal energy) vs. physical agents (reflecting UV rays). They can be categorized in several ways, for example: organic vs. inorganic, lipophilic vs. hydrophilic, which is how environmental chemists do it. The National Library of Medicine databases sometimes refer to these compounds as suncreening agents (confusing terms) and define them as chemical or physical agents that protect the skin from sunburn and erythema by absorbing or blocking ultraviolet radiation. UVFs are also used in consumer cosmetics (makeup, nail polish, shampoo, etc.) and in industry (plastics, paints, sealants, etc.) to protect against photodegradation.

In addition, these UVFs contain many other substances, preservatives, or stabilizers, such as emollients, fragrances, emulsifiers, and coloring compounds. The FDA define broad spectrum sunscreens as products that provide UVA protection that is proportional to its UVB protection [26,27]. In order to ensure sufficiently broad-spectrum coverage, the sunscreen formulas available on the market usually include a mixture of organic and inorganic filters with 20 or more components [28,29].

Multiple studies have been conducted to assess the disruption of normal endocrine pathways in the context of the effects of multiple man-made chemicals in the environment [30–32]. A document was published by The Organization for Economic Co-operation and Development (OECD) with standardized tests to evaluate potential endocrine disruption molecules [33].

3.1. Organic Filters

Several organic sunscreen agents (including PABA and derivatives, cinnamates, avobenzone, octocrylene, salicylates including homosalate, benzophenones including oxybenzone, and octisalate among others) contain one or more aromatic rings, capable of absorbing and distributing energy from incident UVR [34].

Organic filters can protect against both UVA and UVB radiation and are the most commonly used [35]. They act by scattering and absorbing radiation through chemical reactions that produce heat and/or degradation byproducts; however, they must be applied more frequently. Many are absorbed through the skin. Organic sunscreens show a higher risk of inducing irritant or allergic contact dermatitis [36].

Several organic UVFs have been associated with endocrine disruption [37–42]. Benzophenone-3 (BP-3) seems to have systemic effects on sex and thyroid hormone pathways in animal models [40,41,43,44] and can be absorbed at a rate of 1% to 9% with topical application in some models [45].

When the skin barrier function is compromised, it may absorb UVFs more rapidly [46]. It is remarkable that UVFs have been found in breast milk [38,47], placental tissues [48], and urine [49,50]. During pregnancy an increased incidence of neonatal dysfunction (Hirschprung's disease) due to exposure to BP-3 has been observed [51,52]. In several studies, possible correlations with uterine leiomyoma formation and increased mobility of breast and lung cancer cells have been found [53–56].

UVFs (especially BP-3, avobenzone, OC, amiloxate, and PABA) seem to cause various forms of irritant dermatitis as well as allergic contact and/or photo-allergens [52,57–59].

The most commonly used organic filters [60,61] and their evaluation by the EWG [62] are described in Table 1.

Table 1. The most used organic filters and their possible risks (based on EWG classification).

UVB Filters/Risks	UVA Filters/Risks	Broad Spectrum Filters (UVA and UVB)/Risks
<p>PABA and derivatives</p> <ul style="list-style-type: none"> - Octyldimethyl PABA or Padimate O: EDC (estrogenic), liberator of free radicals, allergic reactions. Always avoid. - Ethylhexyl triazone (octyl triazone): Free radical liters with sunlight. Prudence. 	<p>Benzophenones (BP-3 or Oxybenzone): EDC effects, bioaccumulative, photoallergic reactions, absorbed through the skin, passing into breast milk. Neurotoxicity. Always avoid</p>	<p>Tinosorb M (Methylene bis-benzotriazolyl tetramethylbutylphenol): Possible environmental contaminant. Acceptable/caution.</p>
<p>Cinnamates</p> <ul style="list-style-type: none"> - Octinoxate (Octyl Methoxycinnamate, OMC, Ethylhexyl Methoxycinnamate, EHMC): confirmed EDC, persistent and bioaccumulative, absorbed through the skin, appears in breast milk. Always avoid. - Cinoxato (2-Ethoxyethyl-P-Methoxycinnamate): In disuse. Little data on its safety. Avoid as a precaution. 	<p>Anthranilates: less effective than benzophenones.</p>	<p>Tinosorb S (Bis-Ethylhexyloxyphenol methoxyphenyl triazine): non-estrogenic. Acceptable/caution.</p>
<p>Salicylates: Better security profile.</p> <ul style="list-style-type: none"> - Octisalate (ethylhexyl salicylate, 2-Ethylhexyl 2-Hydroxybenzoate): Acceptable chemical filter. - Homosalate (3,3,5-Trimethyl-Salicylate Cyclohexanol; 3,3,5-Trimethylcyclohexyl 2-Hydroxybenzoate): Highly Polluting, weak EDC, decomposes with light into oxidizing substances harmful skin. Increases the absorption of other substances. Avoid. 	<p>Avobenzone (Butyl Methoxydibenzoylmethane): Rare allergies. The most recommended by the EWG.</p>	<p>Iscotrizinol (Uvasorb HEB, diethylhexyl butamido triazone): No data, Acceptable/caution.</p>
<p>Octocrylene: EDC activity, allergies and/or (photo)allergies. Avoid.</p>	<p>Mexoryl SX (Tetraphthalidine sulfonic acid dialcamphor): also considered safe.</p>	
<p>Ensulizole (2-Pheny 1H-benzimidazole 5-Sulfonic acid, PBSA): produces free radicals (DNA damage and potentially skin cancer. Avoid.</p>		
<p>4-Methylbenzylidene Camphor: EDC, persistent and bioaccumulative. Possible thyroid toxicity. Always avoid.</p>		

In Figure 1 each type of filter and how they act is described.

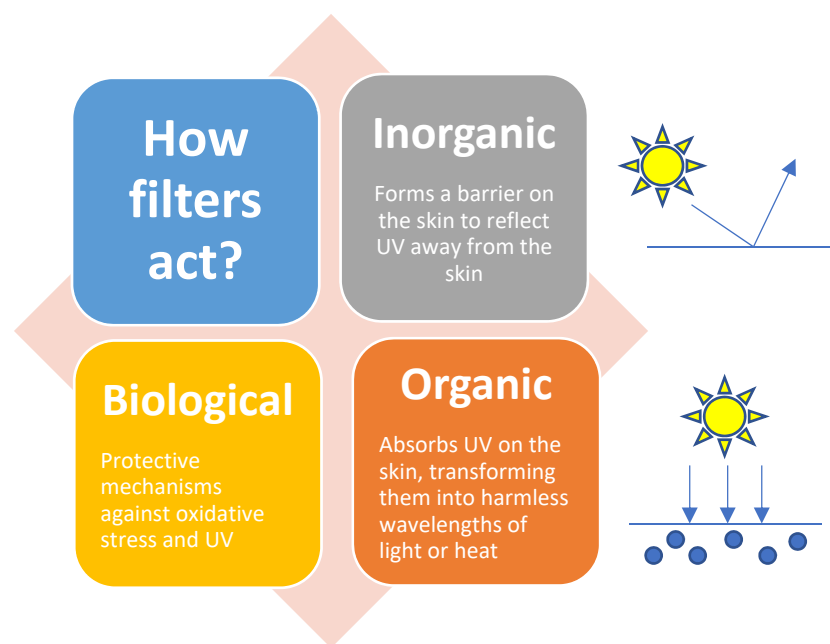


Figure 1. Type of filters and its mechanism of action.

3.1.1. UVB Filters

UV filters allowed in cosmetic products in Europe are regulated in Annex VI of Cosmetics Regulation (EC) No. 1223/2009 [63].

- PABA and derivatives:
 - Octyldimethyl PABA or Padimate O: EDC (estrogenic), liberator of free radicals, allergen reactions, ecotoxin and environmental pollutant. Always avoid (EWG sec 5 fair)
 - Ethylhexyl triazone (octyl triazone): Not authorized in the USA. Increases the effectiveness of other filters. Free radical released in sunlight. Very little data. Prudence (EWG 1 None)
- Cinnamates:
 - Octinoxate (Octyl Methoxycinnamate, OMC, Ethylhexyl Methoxycinnamate, EHMC): confirmed EDC, persistent and bioaccumulative, is absorbed through the skin and can increase the absorption of other substances. It appears in breast milk. Ecotoxic. One of the most problematic filters today. Banned in Denmark in creams for children. It pollutes rivers and affects the populations of fish and other aquatic animals. It appears in tap water and even some bottled water. Always avoid (EWG 6 limited)
 - Cinoxato (2-Ethoxyethyl-P-Methoxycinnamate): In disuse. There is little data on its safety. Avoid as a precaution (EWG 3 limited)
- Salicylates: They are weaker; they increase the power of other UVB radiation absorbers. Better safety profile.
 - Octisalate (ethylhexyl salicylate, 2-Ethylhexyl 2-Hydroxybenzoate): It is quite safe, it is frequently used in association with Avobenzone to extend the duration of protection. Ecotoxin. Today, it is an acceptable chemical filter (EWG sec 3)
 - Homosalate (3,3,5-Trimethyl-Salicylate Cyclohexanol; 3,3,5-Trimethylcyclohexyl 2-Hydroxybenzoate): Highly polluting, weak endocrine disruptor, decomposes with light into oxidizing substances that are harmful to the skin. Increases the absorption of other substances. Avoid (EWG 4 limited)
- Octocrylene or octocrilene (CAS n. 6197-30-4) (2-ethylhexyl 2-cyano-3,3-diphenyl-2-propenoate; 2-ethylhexyl 2-cyano-3,3-diphenylacrylate or the 2-ethylhexyl ester of 2-

cyano-3,3-diphenyl acrylic acid): It is an organic ultraviolet (UV) filter with an aromatic structure, which absorbs mainly UVB radiation and short UVA wavelengths [64]. It is used in sunscreens with other UV filters to provide an adequate sun protection factor (SPF) due to its UV radiation absorption properties [65]. According to regulation, octocrylene is authorized as a UV filter in cosmetic formulations at a maximum concentration of 10.0% in acid form in Europe (Annex VI/10). Octocrylene seems to have endocrine disrupting activity and may cause allergies and/or (photo)allergies. It is included in the list elaborated in 2019 by the European Commission that collected 14 ingredients with potential disrupting properties used in cosmetic products [66].

- Ensulizole: (2-Pheny 1H-benzimidazole 5-Sulfonic acid, PBSA): In contact with the sun, it produces free radicals that can damage DNA and potentially cause skin cancer. Avoid if possible (EWG 3 limited)
- 4-MBC (4-Methylbenzylidene Camphor) (1,7,7-Trimethyl-3- [(4-Methylphenyl) Methylene] Bicyclo [2.2.1] Heptan-2-On)): EDC, persistent and bioaccumulative. Not authorized in the US for sun creams. Possible thyroid toxicity. Important environmental contaminant, affects aquatic populations. Always avoid. (EWG 7 fair)

Some studies have reported that Sulphonated compounds act as DNA alkylating agents, and genotoxic agents in bacterial and mammalian cells [67].

3.1.2. UVA Filters

- Benzophenones: benzophenone-3, (2-hydroxy-4-methoxyphenyl) phenyl- methanone; 2-benzoyl-5-methoxyphenol; 2-hydroxy-4-methoxybenzophenone; (2-hydroxy-4-methoxyphenyl) phenylmethanone; 4-methoxy-2-hydroxybenzophenone; advastab 45; ai3-23644; anuvex; b3; benzophenone. Widely used, although less and less since it is one of the worst chemical filters that exists, especially BP-3 or Oxybenzone, which has multiple endocrine disrupting effects, is bioaccumulative, persistent in the environment, is associated with photoallergic reactions, is absorbed in significant amounts through the skin, passes into breast milk. There is evidence of neurotoxicity and ecotoxicity affecting many aquatic species [15,68]. With the current data, it should be prohibited. The CDC found it in the bodies of 97% of Americans tested in one study. Always avoid. (EGW 8 fair)
- Anthranilates: They are weak UVB absorbers and mainly UVA absorbers, but less effective than benzophenones.
- Avobenzone (Butyl Methoxydibenzoylmethane, Parsol 1798) Today one of the safest chemical filters. Allergies rare. It degrades easily in sunlight, losing its effectiveness, although it can be stabilized with other safe substances such as Octisalate. Ecotoxin. The most recommended by the EWG. (EWG 2 limited)
- Mexoryl SX: Tetraphthalidine sulfonic acid dialcamphor: Broad UVA absorber with efficacy similar to avobenzone. It is also considered safe. (EWG sec 2 limited)

Figure 2 shows how UV filters can affect the human body.

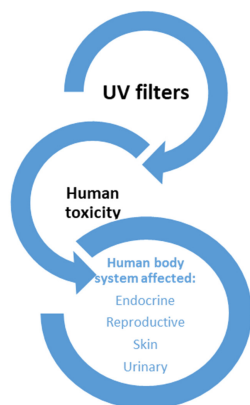


Figure 2. How human body is affected by UV filters.

3.1.3. Broad Spectrum Filters (UVA and UVB)

In recent years, new filters have appeared that absorb, reflect, and scatter light, and are a hybrid between mineral and chemical filters. They have been created to avoid the problems of the old chemical filters. They are larger, are not absorbed, are not very allergenic and for the time being they appear to be safe [7,60].

- Tinosorb M (Methylene bis-benzotriazolyl tetramethylbutylphenol) is not absorbed, is photostable, and there are few studies on it. Possible environmental contaminant. Not allowed in the USA. Acceptable filter but caution due to lack of studies. (EWG 1 limited).
- Tinosorb S (Bis-Ethylhexyloxyphenol methoxyphenyl triazine: Photostable and non-estrogenic. Few studies on toxicity. Acceptable but caution due to lack of studies. (EWG 0 limited). Not allowed in the USA.
- Iscotrizinol (Uvasorb HEB, diethylhexyl butamido triazone) No data, acceptable/caution. (EWG 2 limited).

Table 2 shows a classification of the most used compounds as organic filters.

Table 2. Classification of different compounds used as filters.

Inorganic Filters	Organic Filters	Biological Filters
Titanium dioxide	PABA and derivatives	Lignin
Zinc Oxide	Cinnamates	Silimarine
	Salicylates	Marine antioxidants
	Octocrylene	Plant-derived extracts
	Ensulizole	
	4-Methylbenzylidene Camphor	
	Benzophenones	
	Anthranilates	
	Avobenzone	
	Mexoryl SX	

3.2. Inorganic Filters (Minerals)

These filters are the safest and most recommended, since they are not absorbed through the skin. It has been found that these filters have lower penetration into Langerhans cells, keratinocytes, and melanocytes (living epidermis), and thus present a lower risk of inducing allergic contact reactions [69]. U.S. Food and Drug Administration (FDA) has approved two inorganic (mineral) filters: titanium dioxide (TiO₂) and zinc oxide (ZnO) [41,60,70]. These particles act by absorbing, reflecting, and refracting UV photons but its primary function in photoprotection is absorbing UV radiation [23]. Sunscreens utilize ZnO and TiO₂ since they reflect and absorb UV photons. These particles have the ability to protect against UV exposure, directly related to particle size.

The size of ZnO and TiO₂ particles ranges from 200 to 400 nm and 150 to 300 nm, respectively [71]. White and chalky texture on the skin's surface is due to larger particle size (EWG's Sunscreen Guide) [62]. Patient dissatisfaction and cosmesis have encouraged new formulations with nanoparticles with decreased particle size. These nanoparticles of ZnO and TiO₂ have helped to create of a non-greasy formulation, transparent, cheaper and which is not degraded with UV radiation exposure [71]. In 2018, the EWG reported that a large increase in these inorganic filters with ~41% of sunscreens in the United States designated as mineral only (EWG's Sunscreen Guide) [62].

ZnO and TiO₂ are able to penetrate the stratum corneum, enter the dermis and ultimately the systemic circulation, risking oxidative stress and cellular toxicity. However,

in vivo and in vitro studies have found that these minerals do not permeate the skin to any degree [70,72–76].

The lungs are unable to clear nanoparticles. Inhalation of these substances is considered to be a potential risk, so the EWG has recommended not use powdered products or spray sunscreens containing ZnO and TiO₂ [62,77].

One possible UV filter that has been suggested is cerium oxide (CeO₂). Some photo-protective formulations commercialize this substance with silica coating because of its high photocatalytic activity, responsible for oxidation and degradation of other formulations' components [78]. Seixas and Serra have studied cerium phosphate (CePO₄) similarly to CeO₂ [79]. CePO₄ possesses high photocatalytic activity, low amount of white residue when applied on the skin, and increased stability being a potential future novel, stable, and efficient inorganic UV filter [79].

3.3. Biological Sunscreens

Natural selection and evolution have ensured that plants and animals have developed effective protective mechanisms against the deleterious side effects of oxidative stress and ultraviolet radiation (UV) [80].

Natural antioxidants such as sun blockers have drawn considerable attention. However, their mechanism of action as sunscreen molecules has not been clearly elucidated. Natural compounds show weaker antioxidant activities. Their activity is associated with their photochemical properties [81]. It is known that natural compounds that absorb UV, have antioxidant, anti-inflammatory, and immunomodulatory effects, so they could be part of safer creams. However, more studies in this regard are needed to demonstrate their real effectiveness in preventing skin cancer, recommended dose, and mode of application [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*, it is 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].

4. Discussion

Some studies reported the possible negative impact of UV filters in the human body because UV filters have the ability to penetrate the skin and reach the blood circulation, triggering concerns. Regarding organic UV filters, particularly benzophenone and cinnamate derivatives, their presence in urine and blood samples has been detected [92]. Regarding inorganic filters, it was reported that nanoparticles remain in the stratum corneum without penetrating into the skin [19].

The potential endocrine disruption of UV filters in biological samples have been reported in several studies [14,93,94]. The possible endocrine disrupting effects resulting from UV filters exposure in human embryos has been studied [13] showing that the frequency of detection of UV filters (benzophenone derivatives) varied between 17% and 100%. Benzophenone-4 (BP-4) was the UV filter that tended to accumulate in the placenta the most among these types of compounds (concentrations between 0.25 ng/g and 5.41 ng/g) [13].

Other negative effects of UV filters on cytotoxicity, behavioral changes, and neurotoxicity have been studied using in vivo models [95–102].

Aromatic ketones have appeared in benzophenone and dibenzoylmethane derivatives, possibly being the most toxic filters (toxic and allergic reactions) [103], and also because of the photoisomerization process leading to the formation of toxic and reactive photodegradation products [104].

The chemical structure of other UV filters such as cinnamates, octocrylene [105], and camphor derivatives seems to be implicated in their toxic effects and reactions with skin proteins producing skin sensitization reactions and allergic contact dermatitis [106]. The toxicity range of different compound used in organic/inorganic filters is shown in Table 3.

Table 3. Toxicity range of organic/inorganic filters (based on EWG’s Sunscreen Guide).

Compounds in Organic/Inorganic Filters	Toxicity Range (1–10)
Oxybenzone	High Danger: 7–10
Ethylhexyl methoxycinnamate	High Danger: 7–10
Homosalate	High Danger: 7–9
Octisalate	High Danger: 7–9
Octocrylene	Medium Danger: 3–6
Titanium dioxide	Low Danger: 1–2
Zinc oxide	Low Danger: 1–2

It seems that natural compounds from plants as potential sunscreen ingredients are the safest and the most effective UV filters. When these compounds are compared to synthetic products, they have higher UV assimilation and antioxidant capacities. The long-term effects of new substances are not studied before they are used. From time to time, new evidence appears relating to substances that we considered innocuous and end up being either modified or prohibited after years of use.

One of the objectives of the Regulation (EC) No. 1223/2009 of the European Parliament and of the Council, of 30 November 2009 is to ensure that cosmetic products are safe under normal or reasonably foreseeable conditions of use. In particular, a rationale based on the balance between risks and benefits should not serve as a justification for a risk to human health. Chapter X of the aforementioned regulation on application measures and additional provisions says that when there is a potential risk to human health derived from the use of substances in cosmetic products that must be addressed at Community level, the Commission may make changes to their use in order to adapt them to scientific and technical progress.

Recently, the Commission Regulation (EU) 2022/1176 of 7 July 2022 was published which modifies Regulation (EC) No. 1223/2009 of the European Parliament and of the Council regarding the use of certain ultraviolet filters in cosmetic products, by modifying the safe concentrations of the filters 2-hydroxy-4-methoxybenzophenone/oxybenzone or benzophenone-3 and 2-cyano-3,3-diphenylacrylic acid 2-ethylhexyl ester/octocrylene or octocrylene.

5. Conclusions

Organic sunscreen filters such as oxybenzone and octinoxate have become controversial due to their potential health and environmental risks.

Regarding inorganic sunscreen filters, the health risks of ZnO and TiO₂ to humans is extremely low, primarily due to a lack of absorption across both intact and damaged skin.

It is important to study in detail possible compounds that could be used in cosmetics and note that substances we have considered innocuous could be either modified or prohibited after years of use.

Although the legislation is being updated according to scientific evidence on safety, the final consumer does not have enough tools or information to make their own decision since the legislation does not oblige manufacturers to specify the concentration of each substance on the packaging. 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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References

1. Anastas, P.T.; Warner, J.C. *Green Chemistry: Theory and Practice*; Oxford University Press: Oxford, UK, 1998; p. 148.
2. Bopp, S.K.; Kienzler, A.; Richarz, A.N.; van der Linden, S.C.; Paini, A.; Parissis, N.; Worth, A.P. Regulatory Assessment and Risk Management of Chemical Mixtures: Challenges and Ways Forward. *Crit. Rev. Toxicol.* **2019**, *49*, 174–189. [[CrossRef](#)] [[PubMed](#)]
3. Berardesca, E.; Zuberbier, T.; Sanchez Viera, M.; Marinovich, M. Review of the safety of octocrylene used as an ultraviolet filter in cosmetics. *European Academy of Dermatology and Venereology. J. Eur. Acad. Dermatol. Venereol.* **2019**, *33* (Suppl. S7), 25–33. [[CrossRef](#)] [[PubMed](#)]
4. Vom Saal, F.S.; Woodruff, T.J.; Soto, A.M.; Skakkebaek, N.E.; Gore, A.C.; Doan, L.L.; Brown, T.R.; Zoeller, R.T. Endocrine-Disrupting Chemicals and Public Health Protection: A Statement of Principles from The Endocrine Society. *Endocrinology* **2012**, *153*, 4097–4110. [[CrossRef](#)]
5. WHO. *State of the Science of Endocrine Disrupting Chemicals 2012*; WHO Press: Geneva, Switzerland, 2013.
6. Bokobza, E.; Hinault, C.; Tirolle, V.; Clavel, S.; Bost, F.; Chevalier, N. The Adipose Tissue at the Crosstalk Between EDCs and Cancer Development. *Front. Endocrinol.* **2021**, *12*, 691658. [[CrossRef](#)]
7. Komarowska, M.D.; Grubczak, K.; Czerniecki, J.; Hermanowicz, A.; Hermanowicz, J.M.; Debek, W.; Matuszczak, E. Identification of the Bisphenol A (BPA) and the Two Analogues BPS and BPF in Cryptorchidism. *Front. Endocrinol.* **2021**, *12*, 694669. [[CrossRef](#)]
8. Rodprasert, W.; Toppari, J.; Virtanen, H.E. Endocrine Disrupting Chemicals and Reproductive Health in Boys and Men. *Front. Endocrinol.* **2021**, *12*, 706532. [[CrossRef](#)]
9. Zhang, Y.; Lu, Y.; Ma, H.; Xu, Q.; Wu, X. Combined Exposure to Multiple Endocrine Disruptors and Uterine Leiomyomata and Endometriosis in US Women. *Front. Endocrinol.* **2021**, *12*, 726876. [[CrossRef](#)]
10. Delfosse, V.; Maire Al Balaguer, P.; Bourguet, W. A Structural Perspective on Nuclear Receptors as Targets of Environmental Compounds. *Acta Pharmacol. Sin.* **2014**, *36*, 88–101. [[CrossRef](#)]
11. Fransway, A.F.; Fransway, P.J.; Belsito, D.V.; Yiannias, J.A. Paraben Toxicology. *Dermatitis* **2019**, *30*, 32–45. [[CrossRef](#)]
12. Kockler, J.; Oelgemöller, M.; Robertson, S.; Glass, B.D. Photostability of sunscreens. *J. Photochem. Photobiol. C Photochem. Rev.* **2012**, *13*, 91–110. [[CrossRef](#)]
13. Valle-Sistac, J.; Molins-Delgado, D.; Díaz, M.; Ibáñez, L.; Barceló, D.; Silvia Díaz-Cruz, M. Determination of parabens and benzophenone-type UV filters in human placenta: First description of the existence of benzyl paraben and benzophenone-4. *Environ. Int.* **2016**, *88*, 243–249. [[CrossRef](#)] [[PubMed](#)]
14. Rehfeld, A.; Egeberg, D.L.; Almstrup, K.; Petersen, J.H.; Dissing, S.; Skakkebaek, N.E. EDC IMPACT: Chemical UV filters can affect human sperm function in a progesterone-like manner. *Endocr. Connect.* **2018**, *7*, 16–25. [[CrossRef](#)] [[PubMed](#)]
15. López-Hera, D. Medicina de Familia en la Red. Cremas Para el Sol Seguras: Como Elegir Fotoprotectores Solares No Tóxicos y Respetuosos Con El Medio Ambiente. Available online: <https://www.drlopezheras.com/2014/07/cremas-para-el-sol-seguras-como-elegir.html> (accessed on 1 September 2022).
16. Skotarczak, K.; Osmola-Mańkowska, A.; Lodyga, M.; Polańska, A.; Mazur, M.; Adamski, Z. Photoprotection: Facts and controversies. *Eur. Rev. Med. Pharmacol. Sci.* **2015**, *19*, 98–112. [[PubMed](#)]

17. Narbutt, J. Does the use of protective creams with UV filters inhibit the synthesis of vitamin D?—For and against. *Prz. Pediatric* **2009**, *41*, 75–81.
18. Yeager, D.G.; Lim, H.W. What's new in photoprotection: A review of new concepts and controversies. *Dermatol. Clin.* **2019**, *37*, 149–157. [[CrossRef](#)]
19. Wang, S.Q.; Balagula, Y.; Osterwalder, U. Photoprotection: A review of the current and future technologies. *Dermatol. Ther.* **2010**, *23*, 31–47. [[CrossRef](#)]
20. De Gruijl, F.R.; van Kranen, H.J.; Mullenders, L.H. UV-induced DNA damage, repair, mutations and oncogenic pathways in skin cancer. *J. Photochem. Photobiol. B* **2001**, *63*, 19–27. [[CrossRef](#)]
21. Liu, F.C.; Grimsrud, T.K.; Veierød, M.B.; Robsahm, T.E.; Ghiasvand, R.; Babigumira, R.; Shala, N.K.; Stenehjem, J.S. Ultraviolet radiation and risk of cutaneous melanoma and squamous cell carcinoma in males and females in the Norwegian Offshore Petroleum Workers cohort. *Am. J. Ind. Med.* **2021**, *64*, 496–510. [[CrossRef](#)]
22. Duro Mota, E.; Campillos Páez, M.T.; Causín Serrano, S. El sol y los filtros solares. *Medifam* **2003**, *13*, 39–45. [[CrossRef](#)]
23. 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. [[CrossRef](#)]
24. Kollias, N. The absorption properties of “physical” sunscreens. *Arch. Dermatol.* **1999**, *135*, 209–210. [[CrossRef](#)] [[PubMed](#)]
25. Garrote, A.; Bonet, R. Fotoprotección. Factores de protección y filtros solares. *Offarm* **2008**, *27*, 63–73.
26. Food and Drug Administration (US). CFR—Code of Federal Regulations Title 21; 2017, FDA Approved UV Filters for Sunscreens. Available online: <https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr> (accessed on 15 April 2022).
27. FDA Advances New Proposed Regulation to Make Sure That Sunscreens are Safe and Effective. Federal Register 84FR6204, 2019-03019. 2019. Available online: <https://www.fda.gov/news-events/press-announcements/fda-advances-new-proposed-regulation-make-sure-sunscreens-are-safe-and-effective> (accessed on 18 May 2022).
28. Danovaro, R.; Bongiorni, L.; Corinaldesi, C.; Giovannelli, D.; Damiani, E.; Astolfi, P.; Greci, L.; Pusceddu, A. Sunscreens cause coral bleaching by promoting viral infections. *Environ. Health Perspect.* **2008**, *116*, 441–447. [[CrossRef](#)] [[PubMed](#)]
29. Watkins, Y.S.D.; Sallach, J.B. Investigating the exposure and impact of chemical UV filters on coral reef ecosystems: Review and research gap prioritization. *Integr. Environ. Assess Manag.* **2021**, *17*, 967–981. [[CrossRef](#)] [[PubMed](#)]
30. National Institute of Health 2020. Endocrine Disruptors. Available online: <https://www.niehs.nih.gov/health/topics/agents/endocrine/index.cfm> (accessed on 13 June 2022).
31. Environmental Protection Agency (US). Nanomaterial Case Studies: Nanoscale Titanium Dioxide in Water Treatment and in Topical Sunscreen (Final). EPA/600/R-09/057F. 2010. Available online: <https://cfpub.epa.gov/ncea/risk/recorddisplay.cfm?deid=230972> (accessed on 13 June 2022).
32. Environmental Protection Agency (US). Endocrine Disruptor Screening Program. 2010. Available online: <https://www.epa.gov/endocrine-disruption> (accessed on 14 July 2022).
33. OECD. *Revised Guidance Document 150 on Standardised Test Guidelines for Evaluating Chemicals for Endocrine Disruption*; OECD Publishing: Paris, France, 2018.
34. DeLeo, V. Sunscreen. In *Bologna J. Dermatology*; Elsevier: London, UK, 2012; pp. 2197–2204.
35. Garnacho Saucedo, G.M.; Salido Vallejo, R.; Moreno Giménez, J.C. Effects of solar radiation and an update on photoprotection. *An. Pediatr.* **2020**, *92*, 377. [[CrossRef](#)]
36. Maier, T.; Korting, H.C. Sunscreens—Which and what for? *Skin Pharm. Physiol.* **2005**, *18*, 253–262. [[CrossRef](#)]
37. Heneweer, M.; Muusse, M.; van den Berg, M.; Sanderson, J.T. Additive estrogenic effects of mixtures of frequently used UV filters on p52-gene transcription in MCF-7 cells. *Toxicol. Appl. Pharmacol.* **2005**, *208*, 170–177. [[CrossRef](#)]
38. Schlumpf, M.; Cotton, B.; Conscience, M.; Hailer, V.; Steinmann, B.; Lichtensteiger, W. In vitro and in vivo estrogenicity of UV screens. *Environ. Health Perspect.* **2001**, *109*, 239–244. [[CrossRef](#)]
39. Coronado, M.; De Haro, H.; Deng, X.; Rempel, M.A.; Lavado, R. Estrogenic activity and reproductive effects of the UV-filter oxybenzone (2-hydroxy-4-methoxyphenyl-methanone) in fish. *Aquat. Toxicol.* **2008**, *90*, 182–187. [[CrossRef](#)]
40. Krause, M.; Klit, A.; Blomberg Jensen, M.; Søbørg, T.; Frederiksen, H.; Schlumpf, M.; Lichtensteiger, W.; Skakkebaek, N.E.; Drzewiecki, K.T. Sunscreens: Are they beneficial for health? An overview of endocrine disrupting properties of UV-Filters. *Int. J. Androl.* **2012**, *35*, 424–436. [[CrossRef](#)]
41. Broniowska, Z.; Slusarczyk, J.; Starek-Swiechowicz, B.; Trojan, E.; Pomierny, B.; Krzyzanowska, W.; Basta-Kaim, A.; Budziszewska, B. The effect of dermal benzophenone-2 administration on immune system activity, hypothalamic-pituitary-thyroid axis activity and hematological parameters in male Wistar rats. *Toxicology* **2018**, *1*, 1–8. [[CrossRef](#)]
42. Krzyzanowska, W.; Pomierny, B.; Starek-Swiechowicz, B.; Broniowska, Z.; Strach, B.; Budziszewska, B. The effects of benzophenone-3 on apoptosis and the expression of sex hormone receptors in the frontal cortex and hippocampus of rats. *Toxicol. Lett.* **2018**, *296*, 63–72. [[CrossRef](#)] [[PubMed](#)]
43. Schreurs, R.; Lanser, P.; Seinen, W.; van der Burg, B. Estrogenic activity of UV filters determined by an in vitro reporter gene assay and an in vivo transgenic zebrafish assay. *Arch. Toxicol.* **2002**, *76*, 257–261. [[CrossRef](#)] [[PubMed](#)]
44. Akhiyat, S.; Olasz-Harken, E.B. Update on human safety and the environmental impact of physical and chemical sunscreen filters: What do we know about the effects of these commonly used and important molecules? *Pract. Dermatol.* **2019**, 48–51. Available online: <https://practicaldermatology.com/articles/201> (accessed on 31 October 2022).

45. Klimova, Z.; Hojerova, J.; Beránková, M. Skin absorption and human exposure estimation of three widely discussed UV filters in sunscreens—In vitro study mimicking real-life consumer habits. *Food Chem. Toxicol.* **2015**, *83*, 237–250. [CrossRef]
46. Joensen, U.N.; Jorgensen, N.; Thyssen, J.P.; Petersen, J.H.; Szecsi, P.B.; Stender, S.; Andersson, A.M.; Skakkebaek, N.E.; Frederiksen, H. Exposure to phenols, parabens and UV filters: Associations with loss-of-function mutations in the filaggrin gene in men from the general population. *Environ. Int.* **2017**, *105*, 105–111. [CrossRef]
47. Schlumpf, M.; Durrer, S.; Faass, O.; Ehnes, C.; Fuetsch, M.; Gaille, C.; Henseler, M.; Hofkamp, L.; Maerkel, K.; Reolon, S.; et al. Developmental toxicity of UV filters and environmental exposure: A review. *Int. J. Androl.* **2008**, *31*, 144–151. [CrossRef]
48. Kim, S.; Choi, K. Occurrences, toxicities, and ecological risks of benzophenone-3, a common component of organic sunscreen products: A mini-review. *Environ. Int.* **2014**, *70*, 143–157. [CrossRef]
49. Olson, E. The rub on sunscreen. *New York Times*, 19 June 2006.
50. DiNardo, J.C.; Downs, C.A. Dermatological and environmental toxicological impact of the sunscreen ingredient oxybenzone/benzophenone-3. *J. Cosmet. Dermatol.* **2018**, *17*, 15–19. [CrossRef]
51. Huo, W.; Cai, P.; Chen, M.; Li, H.; Tang, J.; Xu, C.; Zhu, D.; Tang, W.; Xia, Y. The relationship between prenatal exposure to BP-3 and Hirschsprung's disease. *Chemosphere* **2016**, *144*, 1091–1097. [CrossRef]
52. DiNardo, J.C.; Downs, C.A. Can oxybenzone cause Hirschsprung's disease? *Reprod. Toxicol.* **2019**, *86*, 98–100. [CrossRef] [PubMed]
53. Alamer, M.; Darbre, P.D. Effects of exposure to six chemical ultraviolet filters commonly used in personal care products on motility of MCF-7 and MDA-MB-231 human breast cancer cells in vitro. *J. Appl. Toxicol.* **2018**, *38*, 148–159. [CrossRef] [PubMed]
54. Pollack, A.Z.; Buck Louis, G.M.; Chen, Z.; Sun, L.; Trabert, B.; Guo, Y.; Kannan, K. Bisphenol A, benzophenone-type ultraviolet filters, and phthalates in relation to uterine leiomyoma. *Environ. Res.* **2015**, *137*, 101–107. [CrossRef] [PubMed]
55. Phiboonchaiyanan, P.P.; Busaranon, K.; Ninsontia, C.; Chanvorachote, P. Benzophenone-3 increases metastasis potential in lung cancer cells via epithelial to mesenchymal transition. *Cell Biol. Toxicol.* **2017**, *33*, 251–261. [CrossRef]
56. Wang, W.Q.; Duan, H.X.; Pei, Z.T.; Xu, R.R.; Qin, Z.T.; Zhu, G.C.; Sun, L.W. Evaluation by the Ames assay of the mutagenicity of UV filters using benzophenone and benzophenone-1. *Int. J. Environ. Res. Public Health* **2018**, *15*, 1907. [CrossRef]
57. Lim, H.W.; Thomas, L.; Rigel, D.S. Photoprotection. In *Photoaging*; Rigel, D.S., Weiss, R.A., Lim, H.W., Eds.; Marcel Dekker: New York, NY, USA, 2004; pp. 73–88.
58. Schauder, S.; Ippen, H. Contact and photocontact sensitivity to sunscreens. Review of a 15-year experience and of the literature. *Contact Dermat.* **1997**, *37*, 221–232. [CrossRef]
59. Heurung, A.R.; Raju, S.L.; Warshaw, E.M. Adverse reactions to sunscreen agents: Epidemiology, responsible irritants and allergens, clinical characteristics, and management. *Dermatitis* **2014**, *25*, 289–326. [CrossRef]
60. Carrascosa, J.M. El futuro se hace presente en fotoprotección solar. *Rev. Piel* **2011**, *26*, 311–314. [CrossRef]
61. Sánchez Saldaña, L.; Lanchipa Yokota, P.; Pancorbo Mendoza, J.; Regis Roggero, A.; Saenz Anduaga, E.M. Fotoprotectores tópicos. *Rev. Peru. Dermatol.* **2002**, *12*, 156–163.
62. EWG's Low Danger: 1–2. 2018. Available online: <https://www.ewg.org/sunscreen/report/executive-summary/#.WxcjvVMvxmB> (accessed on 26 September 2021).
63. Cosmetics Regulation (EC) No. 1223/2009. Available online: <https://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2009:342:0059:0209:es:PDF> (accessed on 26 September 2021).
64. Manová, E.; von Goetz, N.; Hungerbühler, K. Ultraviolet filter contact and photocontact allergy: Consumer exposure and risk assessment for octocrylene from personal care products and sunscreens. *Br. J. Dermatol.* **2014**, *171*, 1368–1374. [CrossRef]
65. Bury, D.; Belov, V.N.; Qi, Y.; Hayen, H.; Volmer, D.A.; Brüning, T.; Koch, H.M. Determination of urinary metabolites of the emerging UV filter octocrylene by online-SPE-LC-MS/MS. *Anal. Chem.* **2018**, *90*, 944–951. [CrossRef] [PubMed]
66. Available online: https://ec.europa.eu/growth/content/call-data-ingredients-potential-endocrine-disrupting-properties-used-cosmetic-products_en (accessed on 26 January 2021).
67. Elder, D.P.; Snodin, D.J. Drug substances presented as sulfonic acid salts: Overview of utility, safety and regulation. *J. Pharm. Pharmacol.* **2009**, *61*, 269–278. [CrossRef] [PubMed]
68. Fivenson, D.; Sabzevari, N.; Qiblawi, S.; Blitz, J.; Norton, B.B.; Norton, S.A. Sunscreens: UV filters to protect us: Part 2-Increasing awareness of UV filters and their potential toxicities to us and our environment. *Int. J. Womens Dermatol.* **2020**, *7*, 45–69, PMID:PMC7838327. [CrossRef] [PubMed]
69. Scheuer, E.; Warshaw, E. Sunscreen allergy: A review of epidemiology, clinical characteristics, and responsible allergens. *Dermatitis* **2006**, *17*, 3–11. [CrossRef]
70. Osmond, M.J.; McCall, M.J. Zinc oxide nanoparticles in modern sunscreens: An analysis of potential exposure and hazard. *Nanotoxicology* **2010**, *4*, 15–41. [CrossRef]
71. Hanigan, D.; Truong, L.; Schoepf, J.; Nosaka, T.; Mulchandani, A.; Tanguay, R.L.; Westerhoff, P. Trade-offs in ecosystem impacts from nanomaterial versus organic chemical ultraviolet filters in sunscreens. *Water Res.* **2018**, *139*, 281–290. [CrossRef] [PubMed]
72. Smit, T.G.; Pavel, S. Titanium dioxide and zinc oxide nanoparticles in sunscreens: Focus on their safety and effectiveness. *Nanotechnol. Sci. Appl.* **2011**, *4*, 95–112. [CrossRef]
73. Schilling, K.; Bradford, B.; Castelli, D.; Dufour, E.; Nash, J.F.; Pape, W.; Schulte, S.; Tooley, I.; van den Bosch, J.; Schellau, F. Human safety review of “nano” titanium dioxide and zinc oxide. *Photochem. Photobiol. Sci.* **2010**, *9*, 495–509. [CrossRef]

74. Senzui, M.; Tamura, T.; Miura, K.; Ikarashi, Y.; Watanabe, Y.; Fujii, M. Study on penetration of titanium dioxide (TiO₂) nanoparticles into intact and damaged skin in vitro. *J. Toxicol. Sci.* **2010**, *35*, 107–113. [CrossRef]
75. Dussert, A.S.; Gooris, E.; Hemmerle, J. Characterization of the mineral content of a physical sunscreen emulsion and its distribution onto human stratum corneum. *Int. J. Cosmet. Sci.* **1997**, *19*, 119–129. [CrossRef]
76. Zvyagin, A.V.; Zhao, X.; Gierden, A.; Sanchez, W.; Ross, J.A.; Roberts, M.S. Imaging of zinc oxide nanoparticle penetration in human skin in vitro and in vivo. *J. Biomed. Opt.* **2008**, *13*, 064031. [CrossRef] [PubMed]
77. Scientific Committee on Consumer Safety (SCCS). Opinion on Zinc Oxide (Nano Form). 2012. Available online: http://ec.europa.eu/health/scientific_committ (accessed on 24 February 2021).
78. Yabe, S.; Sato, T. Cerium oxide for sunscreen cosmetics. *J. Solid State Chem.* **2003**, *171*, 7–11. [CrossRef]
79. Seixas, V.C.; Serra, O.A. Stability of sunscreens containing CePO₄: Proposal for a new inorganic UV filter. *Molecules* **2014**, *19*, 9907–9925. [CrossRef]
80. He, H.; Li, A.; Li, S.; Tang, J.; Li, L.; Xiong, L. Natural components in sunscreens: Topical formulations with sun protection factor (SPF). *Biomed Pharmacother.* **2021**, *134*, 111161. [CrossRef] [PubMed]
81. Matsui, M.S.; Hsia, A.; Miller, J.D.; Hanneman, K.; Scull, H.; Cooper, K.D.; Baron, E. Non-sunscreen photoprotection: Antioxidants add value to a sunscreen. *J. Investig. Dermatol. Symp. Proc.* **2009**, *14*, 56–59. [CrossRef] [PubMed]
82. Landaeta, K.V.; Piombo, M.E. Estrés oxidativo, carcinogénesis cutánea por radiación solar y quimioprotección con polifenoles. *Piel* **2012**, *27*, 446–452. [CrossRef]
83. Li, S.X.; Li, M.F.; Bian, J.; Wu, X.F.; Peng, F.; Ma, M.G. Preparation of organic acid lignin submicrometer particle as a natural broad-spectrum photo-protection agent. *Int. J. Biol. Macromol.* **2019**, *132*, 836–843. [CrossRef]
84. Netto, M.G.; Jose, J. Development, characterization, and evaluation of sunscreen cream contain-ing solid lipid nanoparticles of silymarin. *J. Cosmet. Dermatol.* **2018**, *17*, 1073–1083. [CrossRef]
85. Álvarez-Gómez, F.; Korbee, N.; Casas-Arrojo, V.; Abdala-Díaz, R.T.; Figueroa, F.L. UV photoprotection, cytotoxicity and immunology capacity of red algae extracts. *Molecules* **2019**, *24*, 341. [CrossRef]
86. Garcia-Pichel, F.; Wingard, C.E.; Castenholz, R.W. Evidence regarding the UV sunscreen role of a mycosporine-like compound in the cyanobacterium *Gloeocapsa* sp. *Appl. Environ. Microbiol.* **1993**, *59*, 170–176. [CrossRef]
87. Ahmad, H.I.; Khan, H.M.S.; Akhtar, N. Development of topical drug delivery system with *Sphaeranthus indicus* flower extract and its investigation on skin as a cosmeceutical product. *J. Cosmet. Dermatol.* **2020**, *19*, 985–994. [CrossRef] [PubMed]
88. Ahmady, A.; Amini, M.H.; Zhakfar, A.M.; Babak, G.; Sediqi, M.N. Sun protective potential and physical stability of herbal sunscreen de-veloped from afghan medicinal plants. *Turk. J. Pharm. Sci.* **2020**, *17*, 285–292. [CrossRef] [PubMed]
89. Baldisserotto, A.; Buso, P.; Radice, M.; Dissette, V.; Lampronti, I.; Gambari, R.; Manfredini, S.; Vertuani, S. Moringa oleifera leaf extracts as multifunctional ingredients for “natural and organic” sunscreens and photoprotective preparations. *Molecules* **2018**, *23*, 664. [CrossRef] [PubMed]
90. Banerjee, K.; Thiagarajan, N.; Thiagarajan, P. Formulation and characterization of a *Heli annuus*-alkyl polyglucoside emulsion cream for topical applications. *J. Cosmet. Dermatol.* **2019**, *18*, 628–637. [CrossRef] [PubMed]
91. Gawel-Beben, K.; Kukula-Koch, W.; Hoian, U.; Czop, M.; Strzepak-Gomółka, M.; Antosiewicz, B. Characterization of *Cistus × incanus* L. and *Cistus ladanifer* L. ex-tracts as potential multifunctional antioxidant ingredients for skin protecting cosmetics. *Antioxidants* **2020**, *9*, 202. [CrossRef]
92. Hiller, J.; Klotz, K.; Meyer, S.; Uter, W.; Hof, K.; Greiner, A.; Göen, T.; Drexler, H. Systemic availability of lipophilic organic UV filters through dermal sunscreen exposure. *Environ. Int.* **2019**, *132*, 105068. [CrossRef]
93. Witorsch, R.J.; Thomas, J.A. Personal care products and endocrine disruption: A critical review of the literature. *Crit. Rev. Toxicol.* **2010**, *40*, 515563. [CrossRef]
94. Rehfeld, A.; Dissing, S.; Skakkebaek, N.E. Chemical UV filters mimic the effect of progesterone on Ca²⁺ signaling in human sperm cells. *Endocrinology* **2016**, *157*, 4297–4308. [CrossRef]
95. Ponzio, O.J.; Silvia, C. Evidence of reproductive disruption associated with neuroendocrine changes induced by UV-B filters, phtalates and nonylphenol during sexual maturation in rats of both gender. *Toxicology* **2013**, *311*, 41–51. [CrossRef]
96. Axelstad, M.; Boberg, J.; Hougaard, K.S.; Christiansen, S.; Jacobsen, P.R.; Mandrup, K.R.; Nellemann, C.; Lund, S.P.; Hass, U. Effects of pre- and postnatal exposure to the UV-filter Octyl Methoxycinnamate (OMC) on the reproductive, auditory and neurological development of rat offspring. *Toxicol. Appl. Pharmacol.* **2011**, *250*, 278–290. [CrossRef]
97. Ozáez, I.; Martínez-Guitarte, J.L.; Morcillo, G. Effects of in vivo exposure to UV filters (4-MBC, OMC, BP-3, 4-HB, OC, OD-PABA) on endocrine signaling genes in the insect *Chironomus riparius*. *Sci. Total Environ.* **2013**, *456*, 120–126. [CrossRef] [PubMed]
98. Li, A.J.; Law, J.C.F.; Chow, C.H.; Huang, Y.; Li, K.; Leung, K.S.Y. Joint Effects of Multiple UV Filters on Zebrafish Embryo Development. *Environ. Sci. Technol.* **2018**, *52*, 9460–9467. [CrossRef] [PubMed]
99. Li, V.W.T.; Tsui, M.P.M.; Chen, X.; Hui, M.N.Y.; Jin, L.; Lam, R.H.W.; Yu, R.M.K.; Murphy, M.B.; Cheng, J.; Lam, P.K.S.; et al. Effects of 4-methylbenzylidene camphor (4-MBC) on neuronal and muscular development in zebrafish (*Danio rerio*) embryos. *Environ. Sci. Pollut. Res.* **2016**, *23*, 8275–8285. [CrossRef]
100. Balázs, A.; Krifaton, C.; Orosz, I.; Szoboszlai, S.; Kovács, R.; Csenki, Z.; Urbányi, B.; Kriszt, B. Hormonal activity, cytotoxicity and developmental toxicity of UV filters. *Ecotoxicol. Environ. Saf.* **2016**, *131*, 45–53. [CrossRef] [PubMed]
101. Chen, T.H.; Hsieh, C.Y.; Ko, F.C.; Cheng, J.O. Effect of the UV-filter benzophenone-3 on intra-colonial social behaviors of the false clown anemonefish (*Amphiprion ocellaris*). *Sci. Total Environ.* **2018**, *644*, 1625–1629. [CrossRef]

102. Carvalhais, A.; Pereira, B.; Sabato, M.; Seixas, R.; Dolbeth, M.; Marques, A.; Guilherme, S.; Pereira, P.; Pacheco, M.; Miei-ro, C. Mild effects of sunscreen agents on a marine flatfish: Oxidative stress, energetic profiles, neurotoxicity and behaviour in response to titanium dioxide nanoparticles and oxybenzone. *Int. J. Mol. Sci.* **2021**, *22*, 1567. [[CrossRef](#)]
103. Bahia, M.F. *Proteção Solar—Atualização*, 1st ed.; Universidade do Porto: Porto, Portugal, 2003.
104. Bonda, C.A.; Lott, D. Sunscreen photostability. In *Principles and Practice of Photoprotection*; Springer: Berlin/Heidelberg, Germany, 2016; pp. 247–273.
105. Tarras-Wahlberg, N.; Stenhagen, G.; Larko, O.; Rosen, A.; Wennberg, A.M.; Wennerstrom, O. Changes in ultraviolet absorption of sunscreens after ultraviolet irradiation. *J. Investig. Dermatol.* **1999**, *113*, 547–553. [[CrossRef](#)]
106. Stiefel, C.; Schwack, W. Reactions of cosmetic UV filters with skin proteins: Model studies of esters with primary amines. *Trends Photochem. Photobiol.* **2013**, *15*, 105–116.

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