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Photoprotection: new concepts, controversies and trends in 2022

Photoprotection appeared, on technical if not scientific bases, in the 1930's.

It was created for permitting tanning without burn. This concept lasted until the 1980's and then evolved, due to both scientific advances permitting to reach higher SPF's, but also more and more concern of the population about the noxious effects of sun exposure on the occurrence of skin cancers. At that time, it was demonstrated that sun radiation was not only able to favour the development of carcinomas and melanomas, but also to speed up the visible signs of skin aging. This made that nowadays, photoprotection turns to be a responsible act and a daily routine.

This paper intends to update the current knowledge about photoprotection. We lastly discovered that not only UVA/UVB but also visible light and infrared radiation, i.e. the complete sun spectrum, is negatively impacting the skin, hence the necessity of creating a full spectrum photoprotection. Dark cyclobutane pyrimidine dimers formation following sun exposure is becoming an urgent concern, and photolyases are probably a solution to reduce the formation of these compounds and repair the damages they are susceptible to cause in the skin. Other concerns are also the levels of vitamin D in the organism, which could be impacted by the regular use of high SPF photoprotection, the frequent use of mineral nanoparticles as sunscreens, the possible impact of certain sunscreens on the human health and also the potential environmental damage they may cause. Finally, an evolution of sunscreens toward more elegant, pleasant and easy to use formulations is certainly the guarantee of a better compliance of the patients with photoprotection.

Keywords

Photoprotection, UVA, UVB, SPF-factor, vitamin D.

1. Introduction

Along years, it was discovered that the solar radiation was playing a critical role in various phenomena. In 1798, Robert Willan was the first to describe a photodermatosis: solar eczema [1]. In 1896, Unna reports for the first time an association between sun exposure and occurrence of skin cancers [2]. Finally, Albert Kligman first suggested in 1969 that apart from intrinsic aging factors, sun exposure causes skin damage and aging [3].

During the second half of 20th century and beginning of 21st, lots of investigations showed that UV-A (320–400 nm) penetrate into the dermis and damages DNA by producing reactive oxygen species. UV-A favour the production of cyclobutane pyrimidine and pyrimidine dimers, responsible for skin-aging and carcinogenesis [4]. They are considered as being the major contributor to photoaging [5]. UV-B (290–320 nm), in contrast, is responsible for sunburns and directly damages DNA by the formation of 6-4 cyclobutane pyrimidine dimers (CPDs) and pyrimidine (6-4) pyrimidone photo-products [6]. Both UV-A and UV-B exposure

increase the risk of basal cell carcinoma, squamous cell carcinoma, and melanoma. According to the Skin Cancer Foundation, 90 % of nonmelanoma skin cancers and 86 % of melanomas are related to sun exposure and UVR [6]. Obviously, photoprotection is one of the most important preventative health strategies, ranging from behavioural modifications, such as seeking shade when outdoors and wearing protective clothing, wide-brimmed hats, and sunglasses to the use of topical sunscreens to prevent or counteract the damaging effects of UVR.

2. History of sun protection

Since around 3100 BC the ancient Egyptians used methods of sun protection for cosmetic reasons, considering that lighter skin was more desirable than darker one. Among the ingredients used: rice bran, jasmine and lupine. Amazingly, it was recently discovered that rice bran absorbs ultraviolet [UV] light, jasmine helps repair DNA, and lupine lightens skin [7]. Later, the ancient Greeks and Romans used olive oil to protect their skin from the sun and for care after sun exposure, a custom still

alive among the populations neighbouring the Mediterranean Sea. Recently, Kaur et al. were demonstrating that olive oil had a SPF rating close to 8 [8]. During the early 20th century there were attempts to develop topical sunscreens: we can mention Unna in 1910 (*Zeozon* and *Ultrazeozon*), and later E. Schüller, the founder of l'Oréal («Ambre Solaire» — 1935) and Greiter («Piz Buin» — 1938) [9].

In the 70's the US Food and Drug Administration (FDA) begins to regulate the booming sunscreen market, helped by its homologs in Australia and Europe which introduced the notion of SPF.

In parallel, the population's behaviour was also changing. Whilst in previous centuries there was a search for lighter skin, in order to assess social superiority, Coco Chanel popularizes from 1920 onward the idea of tanning. This trend was amplified by the occurrence of paid vacations in Western European countries by 1930's, leading the workers to go to the seaside and tanning there. The use of sunscreens was already popular, with the unique concern of avoiding sunburns. The cult of tanning had its peak in the 1970's, especially with the French actress Brigitte Bardot as its muse. Later, from 1980's onward the SPF values of sunscreens were steadily growing to 15, 30, 50 and even 100 before SPFs higher than 50+ were banned by Health Authorities. Today, in 2022, the use of sunscreens turned from occasional (summer holidays, outdoor activities) to a daily routine.

3. The growing importance of visible light

Until recently, the focus of photoprotection were UV-A and UV-B. The visible light (VL) spectrum, which includes the wavelengths between 400 and 700 nm was traditionally left aside. However, VL was found to induce skin pigmentation in subjects with skin types IV to VI [10]. In addition, visible light-induced pigmentation was observed up to 2 weeks after the irradiation. Contrarily, these pigmentation effects were not observed in lighter skin patients of skin type II. Visible light-induced migration of melanin from the basal layer to the upper layers in the epidermis was observed by histology. Furthermore, exposure to a light source emitting visible light and a small amount of UV-A1 (0.5%) resulted in more intense pigmentation compared with exposure to pure visible light [11]. Obviously, these findings demonstrate that visible light irradiation could have a negative outcome in conditions aggravated by sun exposure such as melasma, lentigo or post-inflammatory hyperpigmentation. Hence the need of an effective protection against visible light. The fact is that the current topical photoprotectors usually do not offer VL-protection, as the chemical filters and mineral

sunscreens commonly used in their formulation are not effective in the VL-spectrum. A good alternative are photoprotectors containing melanin, especially synthetic, fragmented melanin in their formula. Melanin was shown to be able to absorb VL-wavelengths and the products are cosmetically acceptable by the patients.

4. Infrared radiation must be taken into account

In the same manner as visible light, during a long time infrared (IR) wavelengths were not submitted to any investigation regarding their eventual noxious effects on the skin.

Obviously, IR irradiation has as a consequence skin heating, leading to the degradation of lycopene and carotenoids which have antioxidant functions in the skin [12]. It was also shown that IRs cause the formation of ROS in the skin [13]. IRs are associated with accelerated growth of more aggressive tumours and a higher number of malignant tumours in the skin [14]. Further it was reported that IRs increase the expression of MMP-1, whose increase is the base of the formation of wrinkles [15] and repeated exposure to IRs was shown to be the cause of the occurrence of deep wrinkles in mice [16]. Heat produced by IRs was also associated with inflammation, elastosis and rupture of collagen fibres [17]. As a conclusion, IRs appear to have a major role in the premature skin-aging [18]. Although non-micronized form of zinc oxide or titanium dioxide would physically block IR transmission, this would only be with high concentrations, and the chalky white appearance of these agents would make them aesthetically not acceptable to users. Similar to exposure to UVR or visible light, IR-exposure generates reactive oxygen species; therefore, it is possible that antioxidants could play a role in decreasing the skin alterations caused by IR-irradiation.

5. Dark cyclobutane pyrimidine dimers formation

Melanin has traditionally been thought to be protective against UVR-induced DNA damage and skin cancer development [5]. However, Premi et al. have recently reported that melanin may also be carcinogenic by contributing to the formation of cyclobutane pyrimidine dimers (CPDs), even after the completion of UV-A radiation [19]. It was further shown that pheomelanin was a more potent generator of dark CPD formation than eumelanin. One of the benefits of the delayed formation of CPDs for up to 3 hours after UV exposure, should this occur in humans as it does in rodents, is the opportunity for intervention during this time [5].

Topical application or intake of antioxidants would probably be helpful at this stage.

6. Photolyases in sunscreens

Photolyases are enzymes that have the property of repairing CPDs. Naturally occurring in bacteria, plants, and animals that experience high UV exposure, they are absent in humans.

Both *in vitro* and *in vivo* studies have supported the beneficial properties of photolyases in preventing photodamage [20]. In a study, it was found that the combined presence of topical antioxidants and photolyases resulted in the greatest reduction in CPDs and free radical-induced protein damage compared with the sunscreen that contained either ingredient alone, suggesting that antioxidants and photolyases might have a synergistic effects [21]. The use of this kind of combination would certainly open new ways in photoprotection.

7. The concern about vitamin D

UV-B is responsible for the conversion of epidermal 7-dehydrocholesterol into active vitamin D₃ (cholecalciferol). *In vitro* and animal studies have proven that vitamin D enhances antimicrobial responses, suppresses proinflammatory mediators, and diminishes inflammation after skin injury [22]. Due to the importance of adequate levels of vitamin D in the human organism, global concern about vitamin D deficiency has fuelled debates on photoprotection and the importance of solar exposure to meet vitamin D requirements [23].

The results of a meeting gathering an international panel of 13 experts in endocrinology, dermatology, photobiology, epidemiology and biological anthropology were that a serum level of ≥ 50 nmol/L 25(OH)D was a target for all individuals [23]. Further, it was agreed on that broad-spectrum sunscreens that prevent erythema are unlikely to compromise vitamin D status in healthy populations. Screening and supplementation in vitamin D are only advised for the group of patients at risk of hypovitaminosis, such as patients with photosensitivity disorders. The conclusion of this panel was that sunscreen use for daily and recreational photoprotection does not compromise vitamin D synthesis, even when applied under optimal conditions [23].

8. Oral photoprotection

Oral forms of photoprotection are gaining interest recently.

They could be an alternative to current topical photoprotection, which is not protecting against the negative effects of visible light and infrared radiation.

Polypodiumleucotomos is a plant native in Latin America with antioxidant and anti-inflammatory

properties. Human studies have shown that P leucotomos extract increases the UV dose required for immediate pigment darkening, minimal erythema dose, and minimal phototoxic dose [24]. It was also reported that it could be beneficial in preventing photodermatoses such as solar urticaria or polymorphous light eruption [25].

Nicotinamide (vitamin D₃) is also of interest as it is essential in DNA repair in the skin [26].

In human keratinocytes, nicotinamide was shown to block the inhibitory effect of UV on adenosine triphosphate production, enhance DNA repair and decrease the formation of CPDs [27]. In two clinical trials, subjects with sun-damaged skin taking 500 mg once or twice daily had 29 % and 35 %, respectively, fewer actinic keratoses at 4 months [28], 23 % lower rates of new non-melanoma skin cancers and 11 % fewer actinic keratosis compared with placebo at 12 months [29].

Other vitamin derivatives with antioxidant properties may also be valuable candidates for oral photoprotection, for instance carotenoids, which are pigments existing in a wide variety of vegetables and fruits. Lycopene is the predominant carotenoid present in tomatoes and other vegetables and red fruits. Other carotenoids, e.g., lutein, astaxanthin, and zeaxanthin, have all been shown to prevent photodamage induced by sunlight [30].

Vitamin E and vitamin C also feature good candidates.

Omega-3 polyunsaturated fatty acids have also been considered to treat skin conditions related to UVR exposure.

The role of probiotics in photoprotection is promising, but it is necessary to carry out more extensive clinical trials before making a definitive recommendation on the use of probiotics as oral photoprotective agents [31].

Various botanicals have also been mentioned, such as Green Tea polyphenols, Cocoa extract, also rich in polyphenols, isoflavones including genistein, silymarin, quercetin [32].

9. The concern of nanoparticles in sunscreens

As mineral sunscreens, TiO₂ (titanium dioxide) and ZnO (zinc oxide) are commonly used. When formulated in non-micronized form, they are leaving a chalky appearance on the skin which is cosmetically unpleasant and not accepted by the consumers. For this reason, formulators of sunscreens are using more likely micronized forms of both TiO₂ and ZnO.

Both were under scrutiny. First, a wave of *in vitro* investigations with nanoparticles of TiO₂ (TiO₂-NPs) was published, rising concern. It was demonstrated in human keratinocytes that TiO₂-NPs accumulate at the cell surface and are taken up by

endocytosis. Following, the level of ROS is increased and mitochondrial damage occurs [33]. Still in human keratinocytes, under UV-A irradiation, the stress induced by TiO₂-NPs triggers the apoptosis and induces cell-death [34]. In human endothelial cells in vitro, it was also assessed that aggregates of TiO₂-NPs of 300 nm or smaller strongly inhibited cell proliferation and induced apoptosis and cell necrotic death [35]. Further, the genotoxicity of TiO₂-NPs from a sunscreen composition was demonstrated on strains of *Salmonella typhimurium* [36]. The question which was rapidly raised was whether or not nanoparticles were able to penetrate human skin. In previous animal studies in intact skin of hairless rats, TiO₂-NPs of 50 nm did not penetrate intact skin [37] whilst TiO₂-NPs of 20 nm penetrated the intact skin after 60 days dermal exposure, reaching different tissues and inducing pathological lesions in various organs (skin, liver) [38]. In intact pig skin ZnO-NPs and TiO₂-NPs of 50 nm and 35 nm do not penetrate porcine stratum corneum [39]. After 30-days application on porcine skin, TiO₂-NPs (4 and 60 nm) can penetrate through horny layer and be located in deeper layers of epidermis [40].

In both rats and pigs, NPs are widely distributed into the groove and hair follicles after topical application of commercial sunscreens but do not permeate into intact skin [41].

In rats, barrier perturbation by tape stripping does not cause penetration, but abrasion allowed NPs to penetrate deeper into the dermal layers [42]. Now what's about human skin?

It was shown by tomography that ZnO-NPs after one application penetrate only in the outermost layers of stratum corneum, furrows and hair follicles, but do not reach viable dermis [43]. In voluntaries applying sunscreen with ZnO-NPs (two groups, 20 nm and 100 nm) during 5 days, followed by sun exposure on the beach, penetration of ZnO-NPs beyond the dermis was demonstrated in both groups [44]. In 2012, COLIPA has concluded that «the use of ZnO and TiO₂ nanoparticles, at a concentration up to 25 % as a UV-filter in sunscreens, can be considered not to pose a risk of adverse effects in humans after dermal application» [45, 46].

10. UV blocked vs. Transmitted

A well-known concept, SPF, means the effectiveness of a sunscreen in protecting against erythema-induced radiation (EIR). SPF is representing a percent of EIR absorbed and not percent of EIR transmitted, which can be misleading. Many people believe for instance that SPFs beyond 30 provide only minimal additional protection [47]. It should

be more appropriate considering photons that are transmitted and absorbed by the skin, with biologic effects, than photons absorbed by the sunscreen. For example, when comparing percent absorbed of SPF-30 with SPF-60, it is 96.7 % EIR absorbed compared with 98.3 % EIR absorbed. However, if comparing the number of photons transmitted when exposed to 60 photons, SPF-30 allows 2 photons to be transmitted, and SPF-60 only 1 photon [5]. This means that, as sunscreen SPF is presented as percent of EIR absorbed compared with percent transmitted, dermatologists may underestimate the increased protection provided by the higher SPF sunscreen [48].

11. Safety of sunscreens

Recently, there is growing concern about the effects of photoprotection on human health.

A study [49] published in September 2020 investigated the effects of UV filters on human health. Results found that current evidence was not sufficient to support the causal relationship between the elevated systemic level of oxybenzone or octinoxate and adverse health outcomes. The major concern is about the suspicion that various sunscreens commonly used in photoprotectors could possess endocrine-disrupting properties. Endocrine disruptors are chemicals that disrupt the normal functioning of the endocrine system, leading to a variety of health problems, including reproductive problems, deficiencies, and female and male cancers [50]. Exposure to endocrine disruptors begins in the womb and never stops throughout life, as these chemicals are present in a variety of everyday products, including food, bottled water, and cosmetics [50]. Some of the ingredients in sun cosmetics show potential endocrine disrupting properties [51]. Oxybenzone (benzophenone-3 BP) exhibits anti-estrogenic and antiandrogenic activity in vivo in fish [52]. In humans, a reduction in birth weight in girls and an increase in boys may also be associated with maternal exposure to oxybenzone [53] which has also been detected in breast milk. Benzophenone-1 also has estrogenic and antiandrogenic properties demonstrated in fish and rats [54]. Endometriosis in women, an estrogen-dependent disease, is associated with exposure to benzophenone compounds and especially with exposure to BP1 [55]. Octylmethoxycinnamate has known endocrine disrupting properties [51], exhibiting anti-estrogenic and androgenic/antiandrogenic activity but no estrogenic activity. It would also have a possible impact on the function of the hypothalamus-pituitary-thyroid axis [56]. Its presence in human milk leads to exposure of neonates, a particular concern. 4-Methyl benzylidene camphor and 3-benzylidene camphor dis-

rupt normal endocrine function in rats, fish, aquatic molluscs, and insects [57]. All the currently allowed sunscreens should be revisited according to these toxicological aspects and based on the results, the current listing should be updated.

12. Environmental impact of sunscreens

There are consistent environmental and health impacts associated with photoprotection.

In a critical review [58] investigators reviewed all of the published photoprotection studies up to June 2020, 32 in total. They identified 14 various organic UV filters found in seawater near coral reefs in the nanograms per liter range. Also, the review found 9 papers that reported toxicological findings in the micrograms per liter to milligrams per liter range.

When compared with concentrations in seawater, toxic effects of UV filters were found at 1000 to 1 million-fold higher concentrations. The review concluded that there is currently limited evidence suggesting coral reefs are adversely affected by exposure to UV filters, however, the authors noted major data gaps that should be immediately addressed with high-quality monitoring, fate, and toxicity studies [58]. However, BP-3, octinoxate, OCTO and sulisobenzone have been considered threats to coral reefs around the world and an estimated 14,000 tons of sunscreen, some containing up to 10 % BP-3, are washed into areas of coral reefs annually [59]. Apart from corals, the mentioned sunscreens have a detrimental effect on planktonic crustaceans, amphipod crustaceans, molluscs, algae, bacteria, sea urchins, zebrafish, fathead minnows and rainbow trout [60]. Many organic filters are also lipophilic and have been found to accumulate in the fat of many freshwater and marine species, making them theoretically capable of bioaccumulating up the food chain [60].

13. Increased importance of skin aging in patients' behaviour

Since Kligman's publication in 1969 [2] it is unanimously accepted that sun exposure causes photoaging. This is obviously known by all dermatologists, but also by a large part of the public. Skin aging consists in epidermal thickness, increases in pigment heterogeneity and dermal elastosis, degradation of collagen in the dermis, development of ectatic vessels, and increases in mutagenesis of keratinocytes and melanocytes in the skin [61]. Visible symptoms include an increase in rhytides, telangiectasias, dyspigmentation including lentiginos and ephelides, volume loss, and cutaneous malignancies [61]. In today's society, the value placed on a youthful appearance is reflected in the multibillion-dollar industry centered around anti-

aging products [62]. Therefore, despite the emphasis of the market on the reversal of skin aging, the best defence against cutaneous age-related changes is through prevention with rigorous photoprotection. Thanks to this growing awareness of the population associating sun exposure with photoaging and, hence, more and more extended use of photoprotectors, the second benefit is also in a better protection against the occurrence of carcinomas and melanomas, with decreasing numbers as regards their incidence. Step by step, our patients are considering photoprotection as a daily routine, especially among the young and middle-aged age ranges.

14. A need for cosmetically elegant sunscreens

Given the necessity of this daily routine, a key challenge for sunscreens of the future is to ensure compliance and a general good adherence to photoprotection. Factors like easy-to-use formats including ultra-light textures, convenient sprays and non-greasy formulations are key to encourage the regular use of sunscreens [63]. Good ocular safety for a facial sunscreen is also important as stinging eyes is one of the main cited reasons for not using sunscreens while engaging in outdoor activities [64]. Sunscreens must also be compatible with the use of coloured cosmetics and makeup. Compact cream sunscreens can be a good option for persons wearing makeup to reapply sunscreen over the make-up throughout the day if needed [65]. Light and evanescent textures should be preferred to heavier ones. The case of patients with acne is also important to consider, guaranteeing that the sunscreen would not be comedogenic. Skin of colour patients must also find photoprotectors adapted to their needs. Some companies have created sunscreen products with marked cosmetic acceptability, even on darker skin tones. While micronized inorganic ingredients may be more cosmetically appealing, it still may not be sufficiently cosmetically appealing for individuals with very dark skin tones [66].

15. Photoprotection in special populations

In addition to the general recommendations, it is important to tailor these to the individual, in terms of both behavioural modifications and appropriate sunscreen products. Depending on their specific situation and health status, certain factors should be taken into consideration because health beliefs and behaviours are complex and may relate to perceived risks and benefits [67]. Special population groups can broadly be categorised into five groups:

1. *Those undertaking recreational, acute, and intermittent high-to-extreme UV exposure* (e.g., at the beach or skiing) where the user principally wants to be protected from sunburn.

Let's remember that UVB is the main causative agent for solar erythema and SPF is the most relevant indicator because it is directly indicative of sunburn protection. High protection must be provided in these extreme conditions.

2. *Photoprotection in patients with photodermatoses.* Polymorphic light eruption and lupus erythematosus are triggered by UVA and UVB; thus, in addition to protection with clothing, exposed areas require a broad-spectrum sunscreen with high SPF and high UVA protection [68]. In subjects with pigmentary disorders such as melasma and post-inflammatory hyperpigmentation we must keep in mind the important role of visible light and prefer sunscreens protecting not only from UVA/UVB but also from visible light.

3. *Immunocompromised patients.* Organ transplant recipients represent a high-risk group for skin cancers as a result of their posttransplant immunosuppressive therapy. This is also the case of patients receiving immunosuppressive therapies for other diseases. Strict sun avoidance and use of very high SPF products are essential; consequently, vitamin D supplementation may be required.

4. *Children* because of a physiologically immature immune system, and also because they generally spend a greater amount of time outdoors, are therefore requiring a careful approach to photoprotection and reliance on adults to enforce it.

5. *Outdoor workers* are exposed to UVR for the majority of their working life and need permanent and high photoprotection, at least SPF 50+.

16. Regulatory advances

In September 2021, USFDA recently updated its sunscreen regulations, in response to new scientific information or safety issues. USFDA proposed changes to sunscreen regulations that «would have severely restricted the options for sunscreen actives», by removing all of the organic filters, making zinc oxide and titanium dioxide the only options left. It also proposes to raise the maximum proposed SPF value on sunscreen labels from SPF 50+ to

SPF 60+. It is also expected that European Union regulations follow a similar way.

17. How to advise our patients?

With more areas of the world considering the ban of some UV filters for health and environmental reasons, and the rapid diffusion of this information, patients may be reluctant or confused when choosing a sunscreen or other form of photoprotection.

Physicians must advise their patients to seek shade, wear protective clothing – such as sunglasses and wide-brimmed hats – and apply broad spectrum, tinted sunscreen of SPF-30 or more to exposed areas. For patients concerned about the safety for health of organic sunscreens or by their environmental effect, they can shift to mineral sunscreens.

On the other hand, it is recommendable to insist on that photoprotectors are strictly regulated, which should help to give confidence to the patients. But the practice of photoprotection is essential!

Conclusions

Since the first sunscreens were formulated, almost 80 years have passed. From their first function of permitting tanning without burn under special circumstances, step by step they turned to be more and more protective, and used on daily bases not only in the prevention of skin cancer but also of skin aging. To the eldest of us (the author of this paper is part of them) photoprotection was not even taught during our medical cursus. Along the years, photoprotection took more and more importance as it is now a daily concern for most of our patients. Our duty is advising them in the adequate way, and for this reason we must constantly update our knowledge, especially in this period marked by so important changes.

In the coming years, the concept of photoprotection that most of us have learnt will be totally subverted, not only in terms of habits and concerns of our patients, but also of a complete renewal of the formulations.

References

1. Urbach F. The historical aspects of sunscreens // *J. Photochem. Photobiol. B.*— 2001.— Vol. 64 (2–3).— P. 99–104.
2. de Grujil F.R. Skin cancer and solar UV radiation // *Eur. J. Cancer.*— 1999.— Vol. 35 (14).— P. 2003–2009.
3. Kligman A.M. Early destructive effect of sunlight on human skin // *JAMA.*— 1969.— Vol. 210 (13).— P. 2377–2380.
4. Cadet J., Douk T. Oxidatively generated damage to DNA by UVA radiation in cells and human skin // *J. Invest. Dermatol.*— 2011.— Vol. 131.— P. 1005–1007.
5. Yeager D.G., Lim H.W. What's New in Photoprotection. A Review of New Concepts and Controversies // *Dermatol. Clin.*— 2019.— Vol. 37 (2).— P. 149–157.
6. Cohen L.E., Grant R.T. Sun protection: current management strategies addressing UV exposure // *Clin. Plast. Surg.*— 2016.— Vol. 43.— P. 605–610.
7. Aldahan A.S., Shah V.V., Mlacker S. et al. The history of sunscreen // *JAMA Dermatol.*— 2015.— Vol. 151 (12).— P. 1316.
8. Kaur C.D., Saraf S. In vitro sun protection factor determination of herbal oils used in cosmetics // *Pharmacognosy Res.*— 2010.— Vol. 2 (1).— P. 22–25.
9. Drissi M., Carr E., Housewright C. Sunscreen: a brief walk through history // *Proc. (Bayl. Univ. Med. Cent.)*— 2021.— Vol. 35 (1).— P. 121–123.
10. Mahmoud B.H., Ruvolo E., Hessel C.L. et al. Impact of long-wavelength UVA and visible light on melano-competent skin // *J. Invest. Dermatol.*— 2010.— Vol. 130.— P. 2092–2097.

11. Kohli I., Chaowattanapanit S., Mohammad T.F. et al. Synergistic effects of long-wavelength ultraviolet A1 and visible light on pigmentation and erythema // *Br. J. Dermatol.*— 2018.— Vol. 178.— P. 1173–1180.
12. Darvin M.E., Fluhr J.W., Caspers P. et al. In vivo distribution of carotenoids in different anatomical locations of human skin: comparative assessment with two different Raman spectroscopy methods // *Exp. Dermatol.*— 2009.— Vol. 18.— P. 1060–1063.
13. Darvin M.E., Gersonde I., Albrecht H. et al. In vivo Raman spectroscopic analysis of the influence of IR radiation on the carotenoid antioxidant substances beta-carotene and lycopene in the human skin. Formation of free radicals // *Laser Phys. Lett.*— 2007.— Vol. 4.— P. 318–321.
14. Jantschitsch C., Weichenthal M., Maeda A. et al. Infrared radiation does not enhance the frequency of ultraviolet radiation-induced skin tumors, but their growth behavior in mice // *Exp. Dermatol.*— 2011.— Vol. 20.— P. 346–350.
15. Schieke S., Stege H., Kurten V. et al. Infrared-A radiation-induced matrix metalloproteinase 1 expression is mediated through extracellular signal regulated kinase – activation in human dermal fibroblasts // *J. Invest. Dermatol.*— 2002.— Vol. 119.— P. 1323–1329.
16. Schroeder P., Lademann J., Darvin M.E. et al. Infrared radiation-induced matrix metalloproteinase in human skin: implications for protection // *J. Invest. Dermatol.*— 2008.— Vol. 128.— P. 2491–2497.
17. Kim H.H., Lee M.J., Lee S.R. et al. Augmentation of UV-induced skin wrinkling by infrared irradiation in hairless mice // *Mech. Ageing. Dev.*— 2005.— Vol. 126.— P. 1170–1177.
18. Robert I., Bonnet M., Marques S. et al. Low to moderate doses of infrared a irradiation impair extracellular matrix homeostasis of the skin and contribute to skin photodamage // *Skin Pharmacol. Physiol.*— 2015.— Vol. 28 (4).— P. 196–204.
19. Premi S., Wallisch S., Mano C.M. et al. Photochemistry. Chemiexcitation of melanin derivatives induces DNA photo-products long after UV exposure // *Science.*— 2015.— Vol. 347.— P. 842–847.
20. Kabir Y., Seidel R., McKnight B. et al. DNA repair enzymes: an important role in skin cancer prevention and reversal of photodamage – a review of the literature // *J. Drugs Dermatol.*— 2015.— Vol. 14.— P. 297–303.
21. Emanuele E., Spencer J.M., Braun M. An experimental double-blind irradiation study of a novel topical product (TPF 50) compared to other topical products with DNA repair enzymes, antioxidants, and growth factors with sunscreens: implications for preventing skin aging and cancer // *J. Drugs Dermatol.*— 2014.— Vol. 13.— P. 309–314.
22. Scott J.F., Das L.M., Ahsanuddin S. et al. Oral vitamin D rapidly attenuates inflammation from sunburn: an interventional study // *J. Invest. Dermatol.*— 2017.— Vol. 137.— P. 2078–2086.
23. Passeron T., Bouillon R., Callender V. et al. Sunscreen photoprotection and vitamin D status // *Br. J. Dermatol.*— 2019.— Vol. 181 (5).— P. 916–931.
24. Choudhry S.Z., Bhatia N., Ceilley R. et al. Role of oral Polypodiumleucotomos extract in dermatologic diseases: a review of the literature // *J. Drugs Dermatol.*— 2014.— Vol. 13.— P. 148–153.
25. Caccialanza M., Recalcati S., Piccinno R. Oral polypodiumleucotomos extract photoprotective activity in 57 patients with idiopathic photodermatoses // *G. Ital. Dermatol. Venereol.*— 2011.— Vol. 146.— P. 85–87.
26. Chen A.C., Martin A.J., Choy B. et al. A phase 3 randomized trial of nicotinamide for skin-cancer chemoprevention // *N. Engl. J. Med.*— 2015.— Vol. 373.— P. 1618–1626.
27. Lim H.W., Arellano-Mendoza M.I., Stengel F. Current challenges in photoprotection // *J. Am. Acad. Dermatol.*— 2017.— Vol. 76.— P. S91–99.
28. Surjana D., Halliday G.M., Martin A.J. et al. Oral nicotinamide reduces actinic keratoses in phase II double-blinded randomized controlled trials // *J. Invest. Dermatol.*— 2012.— Vol. 132.— P. 1497–1500.
29. Chen A.C., Martin A.J., Choy B. et al. A phase 3 randomized trial of nicotinamide for skin-cancer chemoprevention // *N. Engl. J. Med.*— 2015.— Vol. 373.— P. 1618–1626.
30. Palombo P., Fabrizi G., Ruocco V. et al. Beneficial long-term effects of combined oral/topical antioxidant treatment with the carotenoids lutein and zeaxanthin on human skin: a double blind, placebo-controlled study // *Skin Pharmacol. Physiol.*— 2007.— Vol. 20.— P. 199–210.
31. Baquerizo Nole K.L., Yim E., Keri J.E. Probiotics and prebiotics in dermatology // *J. Am. Acad. Dermatol.*— 2014.— Vol. 71.— P. 814–821.
32. Parrado C., Philips N., Gilaberte Y. et al. Oral Photoprotection: Effective Agents and Potential Candidates // *Front Med.*— 2018.— Vol. 5.— P. 188.
33. Jaeger A., Weiss D.G., Jonas L., Kriehuber R. Oxidative stress-induced cytotoxic and genotoxic effects of nano-sized titanium dioxide particles in human HaCaT keratinocytes // *Toxicology.*— 2012.— Vol. 296.— P. 27–36.
34. Kim I.Y., Lee T.G., Reipa V. et al. Titanium Dioxide Induces Apoptosis under UVA Irradiation via the Generation of Lysosomal Membrane Permeabilization-Dependent Reactive Oxygen Species in HaCat Cells // *Nanomaterials (Basel, Switzerland).*— 2021.— Vol. 11 (8).— P. 1943.
35. Montiel-Dávalos A., Ventura-Gallegos J.L., Alfaro-Moreno E. et al. TiO₂ nanoparticles induce dysfunction and activation of human endothelial cells // *Chem. Res. Toxicol.*— 2012.— Vol. 25 (4).— P. 920–930.
36. Jomini S. Effets des nanoparticules de dioxyde de titane sur les bactéries : de la cellule à la communauté // *Ecotoxicologie. Université de Lorraine.*— 2014. Français.fNNT: 2014LOR R0098ff. ffilet-01750816.
37. Adachi K., Yamada N., Yoshida Y. et al. Subchronic exposure of titanium dioxide nanoparticles to hairless rat skin // *Exp. Dermatol.*— 2013.— Vol. 22 (4).— P. 278–283.
38. Wu J., Liu W., Xue C. et al. Toxicity and penetration of TiO₂ nanoparticles in hairless mice and porcine skin after subchronic dermal exposure // *Toxicol. Lett.*— 2009.— Vol. 191 (1).— P. 1–8.
39. Gamer A.O., Leibold E., van Ravenzwaay B. The in vitro absorption of microfine zinc oxide and titanium dioxide through porcine skin // *Toxicol. in Vitro.*— 2006.— Vol. 20 (3).— P. 301–307.
40. Senzui M., Tamura T., Miura K. et al. Study on penetration of titanium dioxide (TiO₂) nanoparticles into intact and damaged skin in vitro // *J. Toxicol. Sci.*— 2010.— Vol. 35 (1).— P. 107–113.
41. Zhang L.W., Monteiro-Riviere N.A. Assessment of quantum dot penetration into intact, tape-stripped, abraded and flexed rat skin // *Skin Pharmacol. Physiol.*— 2008.— Vol. 21.— P. 166–180.
42. Darvin M.E., König K., Kellner-Hoefer M. et al. Safety assessment by multiphoton fluorescence/second harmonic generation/hyper-Rayleigh scattering tomography of ZnO nanoparticles used in cosmetic products // *Skin Pharmacol. Physiol.*— 2012.— Vol. 25 (4).— P. 219–226.
43. Gulson B., McCall M., Korsch M. et al. Small amounts of zinc from zinc oxide particles in sunscreens applied outdoors are absorbed through human skin // *Toxicol. Sci.*— 2010.— Vol. 118 (1).— P. 140–149.
44. Scientific Committee on Consumer Safety. Opinion on Titanium Dioxide (nano form) COLIPA n° S75.— P. 2012.
45. Scientific Committee on Consumer Safety. Opinion on zinc oxide (nano form) COLIPA n° S76.— 2013.
46. Your burning questions, answered. Our scientific sunscreen testing exposes startling truths about product claims and effectiveness // *Consum. Rep.*— 2016.— Vol. 81.— P. 21–29.
47. Herzog S.M., Lim H.W., Williams M.S. et al. Sun protection factor communication of sunscreen effectiveness: a web-based study of perception of effectiveness by dermatologists // *JAMA Dermatol.*— 2017.— Vol. 153.— P. 348–350.
48. Suh S., Pham C., Smith J., Mesinkovska N.A. The banned sunscreen ingredients and their impact on human health: a systematic review // *Int. J. Dermatol.*— 2020.— Vol. 59 (9).— P. 1033–1042.

49. Colborn T., vom Saal F.S., Soto A.M. Developmental effects of endocrine-disrupting chemicals in wildlife and humans // *Environ. Health Perspect.*— 1993.— Vol. 101 (5).— P. 378–384.
50. Schlumpf M., Cotton B., Conscience M. et al. In vitro and in vivo estrogenicity of UV screens // *Environ. Health Perspect.*— 2001.— Vol. 109 (3).— P. 239–244.
51. Blüthgen N., Zucchi S., Fent K. Effects of the UV filter benzophenone-3 (oxybenzone) at low concentrations in zebrafish (*Danio rerio*) // *Toxicol. Appl. Pharmacol.*— 2012.— Vol. 263 (2).— P. 184–194.
52. Wolff M.S., Engel S.M., Berkowitz G.S. et al. Prenatal phenol and phthalate exposures and birth outcomes // *Environ. Health Perspect.*— 2008.— Vol. 116 (8).— P. 1092–1097.
53. Kunz P.Y., Galicia H.F., Fent K. Comparison of in vitro and in vivo estrogenic activity of UV filters in fish // *Toxicol. Sci.*— 2006.— Vol. 90 (2).— P. 349–361.
54. Kunisue T., Chen Z., Buck Louis G.M. et al. Urinary concentrations of benzophenone-type UV filters in U.S. women and their association with endometriosis // *Environ. Sci. Technol.*— 2012.— Vol. 46 (8).— P. 4624–4632.
55. Klammer H., Schlecht C., Wuttke W. et al. Effects of a 5-day treatment with the UV-filter octyl-methoxycinnamate (OMC) on the function of the hypothalamo-pituitary-thyroid function in rats // *Toxicology.*— 2007.— Vol. 238 (2–3).— P. 192–199.
56. Maipas S., Nicolopoulou-Stamati P. Sun lotion chemicals as endocrine disruptors // *Hormones (Athens).*— 2015.— Vol. 14 (1).— P. 32–46.
57. Mitchelmore C.L., Burns E.E., Conway A. et al. A Critical Review of Organic Ultraviolet Filter Exposure, Hazard, and Risk to Corals // *Environ. Toxicol. Chem.*— 2021.— Vol. 40 (4).— P. 967–988.
58. Schneider S.L., Lim H.W. Review of environmental effects of oxybenzone and other sunscreen active ingredients // *J. Am. Acad. Dermatol.*— 2019.— Vol. 80 (1).— P. 266–271.
59. Fivenson D., Sabzevari N., Qiblawi S. et al. Sunscreens: UV filters to protect us: Part 2-Increasing awareness of UV filters and their potential toxicities to us and our environment // *Int. J. Women's Dermatol.*— 2021.— Vol. 7 (1).— P. 45–69.
60. Yaar M., Gilchrist B.A. Photoageing: mechanism, prevention and therapy // *Br. J. Dermatol.*— 2007.— Vol. 157.— P. 874–887.
61. Anti-Aging Products-Market Study by Global Industry Analysts, Inc. [Internet]. [cited 2021 Mar 10]. Available from: <https://www.strategyr.com/market-report-anti-aging-products-forecasts-global-industry-analysts-inc.asp>.
62. Wang S.Q., Virmani P., Lim H.W. Consumer acceptability and compliance: the next frontier in sunscreen innovation // *Photodermatol. Photoimmunol. Photomed.*— 2016.— Vol. 32.— P. 55–56.
63. Narda M., Ramos-Lopez D., Mun G. et al. Three-tier testing approach for optimal ocular tolerance sunscreen // *Cutan. Ocul. Toxicol.*— 2019.— Vol. 7.— P. 1–9.
64. Krutmann J., Passeron T., Gilaberte Y. et al. Photoprotection of the future: challenges and opportunities // *J. Eur. Acad. Dermatol. Venereol.*— 2020.— Vol. 34 (3).— P. 447–454.
65. Morquette A.J., Waples E.R., Heath C.R. The importance of cosmetically elegant sunscreen in skin of color populations // *J. Cosmet. Dermatol.*— 2022.— Vol. 21 (4).— P. 1337–1338.
66. Cercato M. et al. Sun protection among Spanish beachgoers: knowledge, attitude and behaviour // *J. Cancer Educ.*— 2015.— Vol. 30 (1).— P. 4–11.
67. Granger C., Narda M., Andres P. et al. Photoprotection: Key Concepts, Current Status, and Special Patient Groups // *EMJ Dermatol.*— 2020; doi: 10.33590/emjdermatol/20-00002.

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ФОТОЗАХИСТ — НОВІ КОНЦЕПЦІЇ, СУПЕРЕЧКИ ТА ТЕНДЕНЦІЇ 2022 р.

Питання про необхідність створення фотозахисту виникло на технічних, якщо не наукових засадах, ще у 30-х роках минулого століття.

Фотозахист був призначений для набуття засмаги без опіків. Ця концепція проіснувала до 80-х років, а потім її було доопрацьовано завдяки науковим досягненням, які дали змогу досягти більш високих значень SPF, а також через усе більшу занепокоєність населення щодо шкідливих наслідків впливу сонця на виникнення раку шкіри. Тоді ж було встановлено, що сонячне випромінювання здатне не тільки спричинити розвиток карциноми і меланому, а й прискорювати видимі ознаки старіння шкіри. Це призвело до того, що сьогодні фотозахист перетворюється на відповідальну дію і щоденну рутину.

Цей документ має на меті оновити сучасні знання про фотозахист. Ми дійшли висновку, що не лише UVA/UVB, а й видиме світло та інфрачервоне випромінювання, тобто весь сонячний спектр, негативно впливає на шкіру, отже, необхідно створити повний спектр фотозахисту. Утворення темних димерів циклобутанового піримідину після перебування на сонці стає актуальним питанням, і фотоліази, ймовірно, є рішенням для зменшення утворення цих сполук і усунення пошкоджень, які вони можуть спричинити на шкірі. Іншими важливими питаннями є також рівень вітаміну D в організмі, на який може вплинути регулярне застосування SPF із високим фотозахисним фактором, часте використання мінеральних наночастинок як сонцезахисних засобів, можливий вплив деяких сонцезахисних кремів на здоров'я людини, а також потенційна шкода навколишньому середовищу, яку вони можуть завдати. Нарешті, еволюція сонцезахисних кремів до більш елегантних, приємних і простих у використанні хімічних складів є безумовною гарантією кращого фотозахисту для пацієнтів.

Ключові слова: фотозахист, UVA, UVB, SPF-фактор, вітамін D.

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