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Daily photoprotection to prevent photoaging

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Abstract

Background

Extrinsic skin aging or photoaging was previously thought to be almost exclusively due to solar ultraviolet (UV) radiation. However, recent literature has described other contributing factors and clarification is thus required as to what extent and what type of daily photoprotection is needed to mitigate extrinsic skin aging.

Methods

We reviewed the existing scientific evidence on daily photoprotection, and specific requirements at the product level, to prevent extrinsic skin aging. We critically reviewed the existing evidence on potential ecological and toxicological risks which might be associated with daily photoprotection.

Results

Evidence shows that broad protection against the entire solar range of UVB, UVA, UVA1, visible light and short infrared (IRA) is required to prevent extrinsic aging. Other exposomal factors, such as air pollution and smoking, also contribute to skin aging. Daily broad-spectrum sunscreen photoprotection should thus contain antioxidant ingredients for additional benefits against UV, IRA and pollution-induced oxidative stress as well as anti-aging active ingredients to provide clinical benefits against skin aging signs, such as wrinkles and dark spots. Broad-spectrum sunscreen containing pigments, such as iron oxide, may be required for melasma prevention. There is no conclusive clinical evidence that daily sunscreen use is unsafe or that it compromises vitamin D synthesis.

Conclusion

Daily use of broad-spectrum sunscreen containing antioxidant and anti-aging active ingredients can effectively reduce extrinsic aging.

Keywords: photoaging, photoprotection, sunscreens, wrinkles, pigmentary disorders

Introduction

Chronic exposure to sunlight is known to have detrimental effects on human skin by causing skin cancer. In this regard the use of sunscreens has received considerable attention and corresponding public campaigns have been conducted to educate consumers that regular sunscreen use can effectively reduce skin cancer risk.[1-3]

In addition to causing skin cancer, exposure to sunlight also contributes to extrinsic skin aging. Until recently, exposure to solar ultraviolet (UV) radiation was regarded as the major, if not the only, cause of extrinsic skin aging. As one consequence, cosmetic products for daily photoprotection are being advocated as a potentially effective preventive measure to slow down skin aging. More recently, however, it has become increasingly clear that the situation is much more complex. The solar spectrum is composed of various wavelengths and there are wavelengths in other spectral regions beyond UV which contribute to extrinsic skin aging. Furthermore, it is now generally accepted that the skin aging exposome includes several other factors, such as air pollution and tobacco smoke.[4] This leaves consumers unsure as to what extent and what type of daily photoprotection is needed to prevent external skin aging. Furthermore, ecological and toxicological concerns have been raised about the daily use of sunscreen products. We therefore felt it was appropriate and timely to review the existing scientific evidence that daily photoprotection is efficient in preventing extrinsic skin aging. Finally, we discuss specific requirements at the product level and critically review the existing evidence as it concerns ecological and toxicological risks which might be associated with daily photoprotection.

Clinical signs of extrinsic skin aging

Wrinkles, laxity, roughness and telangiectasia are clinical hallmarks of both intrinsic and extrinsic skin aging processes, while pigmentary conditions (including lentigines, postinflammatory hyperpigmentation [PIHP], melasma), yellowing and uneven skin tone are strongly linked to extrinsic skin aging and usually observed on the face, neck, chest, and dorsal hands.[5-7] Clinical signs of photoaging differ depending on age, gender, and especially skin phototype and ethnicity.[8-12] In general, wrinkles appear 10 to 20 years earlier in fair skin than in Asian skin, while dark skinned individuals from Asian and African ethnic groups are more prone to actinic lentigines and hyperpigmentation.[8, 9]

The role of ultraviolet B and ultraviolet A in photoaging

Acute UVB irradiation results in decreased dermal and epidermal hyaluronic acid (HA) content and photoexposed skin is characterized by distinct homeostasis of HA.[13, 14] Skin aging is associated with loss of skin moisture and one dramatic histochemical change observed in aged skin is the marked disappearance of epidermal HA that has unique capacity in retaining water.[15]

Both UVB (290 – 320 nm) and UVA (320 – 400 nm), particularly long wave UVA1 (340 – 400 nm), cause photoaging. Because of its physical properties, UVB radiation mainly affects the epidermis, whereas UVA rays can penetrate more deeply into the dermal compartment and directly affect dermal fibroblasts. The dermis is the skin compartment which is primarily affected by photoaging. UVB effects on the dermis are thus thought to be mediated by keratinocyte-derived, UVB-inducible soluble mediators such as selected cytokines, but also matrix metalloproteinases (MMPs), which diffuse down into the dermis where they affect the extracellular matrix (ECM).[16] In contrast, long-wave UVA (UVA1) radiation can directly cause macromolecular damage in dermal fibroblasts and generate mitochondrial DNA deletions for example. Recent evidence suggests that there is interplay between these mechanisms, resulting in controlled dermal ECM turnover.[17] Over time, these result in fibroblast senescence and the production of a fibroblast secretome, which is thought to be a major driver of skin aging.[18]

In vitro, ex vivo and in vivo studies in human skin cells, 3-D skin models and human skin are consistent with the assumption that both UVB and UVA rays contribute to the formation of skin wrinkles and the development of uneven skin pigmentation including the generation of age spots (solar lentigines).[19, 20]

It has been demonstrated that UVA1 exposure induces skin darkening to a similar extent in skin phototypes III to VI with similar cellular changes in all skin phototypes, which highlights the importance of broad-spectrum sunscreen even in dark skinned individuals.[21]

The role of visible light and infrared A radiation in skin photoaging

Although chronic UV exposure is widely considered as the major cause of photoaging, all spectral regions (UV, visible light [VL] and near infrared [IR]) cause free radical formation and hence can promote premature skin aging by modulating the expression of ECM molecules, MMPs, and inflammatory cell infiltration in human skin.[22-26] Visible light and short infrared (IRA) penetrate into the hypodermis and thus could potentially impact all the compartments of the skin. Furthermore, VL and IRA may play a role in photoaging in both light and darker skin types so even people with darker skin need solar protection.[27, 28]

IRC (3000 nm - 1 mm) and IRB (1400 - 3000 nm) are absorbed at the skin surface or the upper layers of the epidermis and do not contribute to skin aging. In contrast, IRA (700 – 1400 nm) can penetrate deeper to directly affect cells in the epidermis, dermis, and subcutis to contribute to photoaging.[29] Both murine and human studies showed that IRA causes wrinkles.[25] Furthermore, IRA radiation has been shown to induce MMP-1 upregulation, which was reduced by applying a sunscreen supplemented with an antioxidant cocktail, whereas sunscreen alone did not protect against IRA.[30]

The relevance of VL for skin aging remains unclear and there has been no demonstration of skin wrinkling induced by VL.[31, 32] VL, as well as synergistic effects of long-wavelength UVA1 and VL, have been shown to induce long-lasting skin pigmentation in dark skin but not in fair-skinned individuals,[33, 34] and it likely interacts with the same melanin precursor as UV.[35] The shorter wavelengths of VL (blue-violet light), via the opsin 3 receptor in melanocytes, cause melanin synthesis.[36, 37] There is also circumstantial evidence that VL might also contribute to the pathogenesis of melasma,[38] which might be viewed as a form of skin aging.[39] Adding VL protection (iron oxide) in a well-balanced UVB/UVA containing sunscreen significantly decreased hyperpigmentation.[40]

Exposome factors beyond solar radiation contribute to photoaging

In addition to solar radiation (UV, VL, IR), other exposome factors may contribute to skin aging, including air pollution, smoking, and lifestyle factors (nutrition and sleeping patterns).[4, 41] Both epidemiological and mechanistic studies have demonstrated a role of traffic-related air pollution exposure (particulate matter [PM], soot and nitrogen dioxide) and tropospheric ozone skin damage causing premature skin aging with lentigenes and/or wrinkle formation in Caucasians and East Asians.[4, 41-45] Epidemiological findings suggest that associations of UV radiation with facial skin aging can be negatively affected by PM exposure, which might be explained by the fact that increased PM concentrations in the troposphere reflect and absorb UV rays and thereby reduce the UVB dose reaching the skin. Under certain circumstances, however, UV and PM might be additive for skin aging, as was suggested by in vitro experiments assessing a combined effect of pollution and long ultraviolet A (UVA1) on the skin.[46, 47] Additionally, tobacco smoke is an important environmental factor that has been associated with skin aging, causing increased wrinkles and tissue laxity, driven by loss of dermal elastic fibres;[48] smoking also results in pigmentary changes, including hyperpigmentation.[49-51] To protect against high exposure to air pollution, broad-spectrum sunscreens should be combined with additional skin care benefits, e.g. antioxidants, to prevent skin pigmentation and extracellular matrix degradation.[52, 53] Ideally daily photoprotection strategies should include complete protection against all factors of photoaging.

Does daily photoprotection with broad-spectrum suncreen prevent photoaging?

Initial studies in Caucasians showed that daily use of topical, broad-spectrum sunscreen prevents photoaging. In the first study, the effects of chronic sunscreen use on the histologic changes of photoaging were evaluated in a study including 46 patients of mean age 63 years and with a history of skin cancer who were randomized to apply either sun protection factor (SPF) 29 UVB/ UVA (short wavelength UVA2) sunscreen or vehicle daily for 24 months. At 24 months, a decrease in solar elastosis was observed between the treatment versus placebo of punch biopsy specimens of preauricular skin analyzed by computer enhancement.[54]

In a larger, randomized, controlled study in younger subjects aged <55 years old (mean age 39 years), which was conducted in Australia in 903 subjects, the effects of regular sunscreen use were assessed at the level of clinical symptoms. Subjects were randomly assigned to apply SPF 15+ broad-spectrum sunscreen daily for 4.5 years (with instructions on how to apply it properly) or to the control group who could apply sunscreen on a discretionary basis (which was usually recreational use). The daily sunscreen group showed no detectable increase in skin aging and 24% less skin aging, as measured by microtopography of dermal elastosis on the back of the hands, than in the discretionary sunscreen group (relative odds, 0.76 [95% CI, 0.59 -0.98]).[55] As that study was performed between 1992 and 1996 with a broad-spectrum SPF 16 sunscreen with low UVA protection, more recent sunscreens with better UVA protection may be expected to be even more effective at preventing photoaging.[56]

Daily use of a facial UVA/UVB broad-spectrum, photostable sunscreen with SPF 30 (UVA-PF not specified) in 32 subjects for 52 weeks significantly improved clinical evaluation of photoaging (overall photodamage, overall skin tone, crow's feet, fine lines, mottled pigmentation, discrete pigmentation, evenness of skin tone, clarity, and texture). Assessments included dermatologist evaluations and subjects' self-assessment. At week 52, all subjects showed improvements in skin texture and clarity, and the greatest improvements were observed in mottled and discrete pigmentation (52% and 42% mean improvements from baseline, respectively).[57] This study demonstrated that daily use of a facial broad-spectrum photostable sunscreen can prevent uneven pigmentation and may visibly reverse the signs of existing photodamage, in addition to preventing wrinkles and additional sun damage. The authors speculated that daily use of a product with a higher SPF (and a higher UVA-PF) would provide even greater protection and greater improvements in photoaging.[57]

Several studies have been performed in East Asian and South Asian subjects with darker skin types. A single arm interventional study in 14 elderly Japanese people of mean age 79.6 years old (range: 62–91 years) with photoaged skin, investigated the effects of sunscreen application for 18 months. At the beginning of the study, subjects received instructions from the dermatologist on the proper method of application and were given a leaflet illustrating how much to apply (~2 mg/cm2) with a sample photograph. Despite this, there were large differences in total amount of sunscreen used. After 18 months of sunscreen application, the only significant difference was observed for skin surface hydration. However, the changes in the number of spots and skin tone uniformity during the study period showed good correlation with the amount of sunscreen used.[58]

A randomized, uncontrolled and investigator-blinded study was conducted in India in 216 subjects, aged 18–45 years old, with skin phototype IV and V with pigmentation irregularities (actinic lentigines and post-inflammatory hyperpigmentation), who did not previously use sunscreens. Participants were randomized to apply twice daily either sunscreen product A (sun protection factor 50 with high UVA protection factor PA+++) or sunscreen product B (sun protection factor 19 with high UVA protection factor PA+++) before sun exposure for ≥2 h for 12 weeks. The clinical assessment of the density of pigmented spots and skin radiance showed significant ($P<0.001$) improvement in both groups compared to baseline.[59] There were no significant differences detected when the two treatment groups were compared with each other.

In the aggregate, these studies provide compelling evidence that regular use of sunscreens is effective in preventing the development of wrinkles and uneven pigmentation in different ethnic groups.

It has also been speculated that the efficacy of daily photoprotection might be increased by supplementing UV filters with actives that have anti-skin-aging properties and/or that extend the protection beyond the UV spectrum. There is indeed evidence that such combination products are capable of partially preventing and even reverting clinical signs of skin aging.[19, 60, 61] As an example, a 6-month, randomized, double-blind, vehicle-controlled study of 346 subjects with photoaged skin, as defined by the presence of wrinkles in the periorbital region, evaluated the efficacy of SPF 15 sunscreen and a cream formulation of 0.05% isotretinoin. After once-daily application for 6 months, subjects using sunscreen with 0.05% isotretinoin had statistically significant improvement in the appearance of wrinkles associated with photoaged skin compared with the vehicle group.[62]

The additional benefit of protecting against visible light was shown in a randomized controlled trial in 40 melasma patients comparing two UVA/UVB sunscreens, one of which was supplemented with VL protection (tinted and contained iron oxides). The use of the sunscreen with VL protection prevented melasma relapses compared to the UV only sunscreen, as measured by the evolution of Melasma Area and Severity Index score.[63] Similarly, in a double-blind, randomized trial in 68 melasma patients, UV-VL sunscreen enhanced the depigmenting efficacy of hydroquinone compared with UV-only sunscreen in the treatment of melasma.[64] Similarly, addition of antioxidants to UV filter-containing sunscreens was found to be effective in protecting against IRA-induced molecular events indicative of skin aging. A vehicle controlled, double-blind, randomized study in 30 healthy volunteers evaluated the effectiveness of an SPF 30 sunscreen versus the same sunscreen supplemented with an antioxidant cocktail containing grape seed extract, vitamin E, ubiquinone and vitamin C to protect human skin against IRA radiation-induced MMP-1 upregulation. The sunscreen supplemented with antioxidants protected human skin against IRA radiation, which contributes to photoaging, whereas the regular sunscreen did not.[30] Of note, this study used IRA-induced MMP-1 mRNA expression as a surrogate marker for wrinkle formation. A human study comparing regular use of sunscreens with and without IRA protection, however, has not yet been conducted.

At present, there is no clear evidence that topical application of DNA repair enzymes or nicotinamide, which is highly effective in preventing actinic keratosis, have benefits in reducing the incidence of chronic sun exposure-related photoaging.[65-67]

Current concerns and controversies in the use of topical photoprotection

The studies described above support the beneficial effects of sunscreen to prevent photoaging. However, certain challenges remain, as discussed in a recently published review by Krutmann et al.[68]

Should photoprotection include UVA protection? Sunscreens were originally developed to minimize erythema (sunburn) and were thus primarily UVB absorbers. Sun protection factor (SPF) is mainly an index of UVB protection, measuring eythema. However, it is now widely accepted that other acute and chronic pathogenic effects may occur after cumulative exposure to sub-erythemal doses of solar UVR, including UVA and an ideal sunscreen should protect against the entire solar UVB/UVA range.[20, 69]

Does photoprotection impair vitamin D synthesis? There are concerns that sunscreen may block the beneficial effects of UVR, e.g., vitamin D synthesis, antimicrobial effects, tanning and photoadaptation. Several recently published reviews have concluded that broad-spectrum sunscreens for daily use in real-life settings are unlikely to compromise vitamin D synthesis, even after application of proper amounts.[70, 71] Vitamin D screening for vitamin D supplementation should be restricted to those at risk of hypovitaminosis, such as patients with photosensitivity disorders requiring strict sun avoidance and photoprotection.[71]

Is sunscreen photoprotection safe for daily use? As photoaging prevention requires daily use of sunscreen, the safety of these products is critical. UV absorbers are regulated as cosmetics in most countries in Europe and Latin America, as well as Japan, as over-the-counter drugs in the United States and Canada, and as therapeutic drugs in Australia. Similarly, various different UV filters are available in the different regions. The United States Food and Drug Administration (FDA) published a prior pilot study on 4 commercially available organic sunscreen products (lotion, aerosol spray, non-aerosol spray and pump spray)[72] and a randomized clinical trial on the effect of sunscreen application on plasma concentration of 6 sunscreen organic filters under single dose and maximal use conditions.[73] All 6 tested active ingredients and all of the formulations, resulted in measurable blood levels of the active ingredient. However, this study was conducted in situations that do not accurately reflect the reality of sunscreen applications (dose per cm^2, surface, and frequency of application). The authors suggest performing larger-scale studies to assess the clinical implications of these findings, as the fact that an ingredient is absorbed through the skin and into the blood does not necessarily mean that the ingredient is unsafe. Furthermore, daily photoprotection concerns limited surface areas which are exposed to the sun all year long, such as the face and hands. The FDA calls for further industry testing to determine the safety and effect of systemic exposure of sunscreen ingredients, especially with chronic use and these results do not indicate that individuals should refrain from the use of sunscreen. Inorganic sunscreens have been linked to frontal fibrosing alopecia but at present there remains insufficient evidence to establish a direct causal relationship.[74]

Is sunscreen photoprotection deleterious for the environment? Another controversial topic is the environmental impact of sunscreen, especially organic UVR filters and their toxic effects on marine ecosystems and aquatic organisms.[75-78] The chronic effects of common sunscreen UV filters and preservatives were tested on the photosynthetic efficiency of scleractinian coral and several organic UV filters were shown not to cause a significant decrease in coral photosynthetic efficiency or coral bleaching, but zinc oxide was more toxic.[79] To put these concerns into perspective we would like to emphasize that the major cause for coral bleaching is global warming and the concomitant increase in water temperature, although oxybenzone may further weaken coral experiencing global warming.[80] Further studies are warranted on the in-situ concentrations of UV filters and preservatives as well as their individual and combined effects on corals.[79]

Requirements for daily photoprotection for skin aging prevention

Dermatologists advocate a multi-pronged approach to minimizing UVR exposure including lifestyle modifications, UVR protective clothing and sunglasses, and topically applied sunscreen products.[74] The main criteria for topical sunscreens for daily photoprotection to prevent photoaging are summarized in Table 1. A high UVA-PF should take priority over high SPF values, which may have insufficient long UVA1 protection. In general, an SPF of at least 30 should ensure UV protection over the whole day even if small amounts are applied. However, the skin type, latitude and altitude should be taken into consideration and a higher SPF for example may be required at lower latitudes. Furthermore, while high-SPF products require higher concentrations of actives and thus have potentially higher health risks if they penetrate the skin and higher environmental risks, sunscreen is generally under-applied at only 25% of the recommended dose, which may compromise photoprotection. Analysis by UV imaging in 57 participants revealed that eyelid and periorbital regions were disproportionately missed during routine sunscreen application (median 14% missed in the eyelid region vs 7% of rest of face missed, $P<0.01$).[81] This highlights the importance of sunscreens with good cosmeticity and tolerability, as well as wearing sunglasses. Sunscreens should contain antioxidant ingredients to provide additional benefits against UV, IRA and pollution-induced oxidative stress and contain anti-aging active ingredients to optimise clinical benefits against skin aging signs such as wrinkles and dark spots. Formulations that leave white residues are not desirable, especially for dark-skinned individuals, whereas formulations that are easy and pleasant to apply are likely to result in better adherence to daily photoprotection. Tinted broad-spectrum sunscreens containing pigments such as iron oxide to protect against VL may be required for melasma prevention and for the prevention of cutaneous hyperchromias (actinic lentigo).[40]

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TABLE 1 Summary of the main criteria for topical sunscreens for daily photoprotection to prevent photoaging

	Topical sunscreen criteria
Sunscreen application	Apply daily Apply proper amount Apply on whole face including eyelid and periorbital regions
Protection against UVB, UVA, UVA1, and VL	SPF of at least 30 with high UVA-PF (the PF should be adapted to the latitude and skin type)
Additional protection against IRA and pollution	Antioxidant ingredients
Prevention of skin aging signs	Anti-aging active ingredients
Prevention of melasma and actinic lentigo	Tinted sunscreen with UVB, UVA1 and HEV protection
Obtain optimal compliance	Good cosmeticity, sensoriality and tolerability Avoid white residues

IRA infrared, SPF sun protection factor, UV ultraviolet, VL visible light, HEV, high energy visible blue-violet light