

Recent information on photoaging mechanisms and the preventive role of topical sunscreen products

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Abstract

The main environmental element causing photoaging is ultraviolet (UV) light, and this involves an extrinsic mechanism of skin aging superimposed on an intrinsic process. Clinical (evident) characteristics of photoaging include the presence of deep wrinkles, deterioration of skin laxity, and hyperpigmentation. In the UV light spectrum, UVA and UVB radiation cause the most damage in photoaging. UVB light has shorter wavelengths and is mostly absorbed by the *stratum corneum*, causing erythema and changes in the epidermis, whereas UV rays with longer wavelengths (i.e., UVA) penetrate to the deepest layer of the skin (i.e., the dermis) and interact with DNA. As a result of UV radiation, chemical reactions in the skin produce reactive oxygen species (ROS), which cause protein denaturation, impairment of RNA and DNA synthesis, and damage to the skin structure. Using local sunscreen agents can not only prevent sunburn, but also help prevent photocarcinogenesis and photoaging. Therefore, many epidemiological studies have been conducted with results showing credible and positive evidence for the safety and efficacy of sunscreen to prevent photoaging and photocarcinogenesis.

Keywords: photoaging mechanisms, UV radiation, actinic elastosis, reactive oxygen species, sunscreens

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Introduction

The pathophysiology and etiology of the aging process of human skin is complex. Degeneration of the skin is evident in all of its layers (the epidermis, dermis, and subcutaneous tissue), but dermal changes are the most obvious. Skin aging may be classified as intrinsic or extrinsic (1). Unavoidable elements, such as race, hormonal changes, and anatomical diversity of the skin, contribute to intrinsic aging, and this progresses with age (2). Environmental temperature, medications, and exposure to natural light are responsible for extrinsic aging. Ultraviolet (UV) light is the main environmental element that causes photoaging, a process typically superimposed on intrinsic skin aging (3). Extrinsic aging is clinically characterized by marked cutaneous alterations including deep wrinkles, skin laxity, hyperpigmentation, roughness, freckled pigmentation, telangiectasia, and progressive atrophy of the dermis (4, 5). Skin is the primary shield against UV light, but it does not provide complete protection, which causes a significant portion of UV light to penetrate the outer layer of the skin, causing 80% of obvious aging marks (6). Compared to intrinsic aging (marks are evident after age 50), photoaging begins at an early age (in the late teens) and has a strong association with the pigmentation level of the skin (7).

UV light in daylight, especially UVA and UVB, is the main source of photoaging. This light causes reactive oxygen species (ROS), which cause protein denaturation, reduce RNA and DNA synthesis, and affect skin structure. Although both UVA and UVB are included in the extrinsic skin aging process, UVA light causes deterioration and sagging of skin by penetrating into its deeper layers, whereas wrinkles are most commonly produced by UVB exposure (8, 9). Skin exposure to UV light results in multiple acute and chronic forms of damage, including erythema and hyperpigmentation as acute effects, whereas photocarcinogenesis

and aging are the most important chronic effects. The effects are prominent at the molecular and cellular levels (e.g., DNA damage, ROS production, inflammatory mediator production, and apoptosis) (10).

Damage from sun exposure can be prevented by spending time around midday indoors, when there is the highest UV light intensity, and by wearing protective clothing when spending time outdoors. Sunscreen products prevent acute sunburn and can also be effective as a supplementary photoaging preventive measure. The results of numerous studies that examined the relationship between sunscreen use and preventing photoaging show credible and positive evidence of the safety and efficacy of sunscreen.

Photoaging mechanisms as an extrinsic skin-aging process

Following UV exposure, it is believed that activation of inflammatory pathways plays an important role in the intrinsic aging process and carcinogenesis (11, 12). The UV light spectrum is divided into UVA (320–400 nm), UVB (290–320 nm), and UVC (200–290 nm) (13). Complete absorption of UVC occurs in the ozone layer, whereas UVA and UVB completely penetrate the atmosphere (14). UVA typically accounts for most of the UV light arriving at the Earth's surface, whereas only 4 to 5% of the UV light reaching the surface is UVB (15). In contrast to UVA intensity, which remains relatively constant throughout the day, the highest intensity of UVB is around midday (10). In contrast to UVB light, an interesting feature of UVA light is its ability to penetrate glass. This is why intense UVA light exposure may be experienced even indoors. Regarding skin damage, UVB mostly induces erythema and changes in the epidermis because almost 70% of it is absorbed by the *stratum corneum*, and 20% reaches the lower layers of the epidermis, with only 10% reaching the dermis (and only its upper layer) (16).

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UVA reaches the deepest dermis and causes DNA interactions because the longer wavelengths penetrate deeper, which is why it is considered the main culprit in skin photoaging, marked by wrinkle formation, loss of skin tone, and reduction of skin elasticity (17–21). The acute effects of UV exposure consist of erythema, hyperpigmentation, acquired immunosuppression of the skin's innate immunity responses, and a decrease in blood pressure (mostly an effect of UVA exposure) (22, 23). Chronic damage includes carcinogenesis and photoaging.

In terms of the effect of UV exposure on the skin, it is important to understand its mechanisms. For a photochemical reaction to take place, light must be absorbed by a chromophore (24). Skin chromophores are well defined, and they include DNA, nucleic acids, urocanic acid, tryptophan and tyrosine, NADH, quinones, porphyrins, and flavins. UV light absorption induces chemical excitation of the chromophore with the capacity to transfer energy received to other substances, which can result in photodamage (24).

Oxidative processes due to ultraviolet light exposure and their involvement in photoaging

About 0.5% of UV exposure damage is the result of free radical production, and direct cellular injury accounts for the remainder (25). Cellular responses caused by UV light arise because of oxidative processes triggered by photosensitization. After absorption of UV light by chromophores in the skin cells, they transfer the energy received to another element (i.e., oxygen), and radicals are generated (e.g., singlet oxygen, hydrogen peroxide, or hydroxyl elements) (24, 26). The majority of endogenous cellular chromophores absorb photons in the UVB spectrum. Cutaneous chromophores that absorb UVA photons are still mostly undiscovered, with the exception of trans-urocanic acid, although, interestingly, more oxidation incidents can be caused by UVA than by UVB (26). The ROS produced by UV exposure can damage multiple skin elements, including cellular proteins, nucleic acids, lipids, cell membranes, and organelles (27). ROS entities activate nuclear factor kappa B (NF- κ B), which then promotes cytokine secretion from keratinocytes and dermal cells, including interleukin type 1 (IL-1), epidermal growth factor (EGF), and tumor necrosis factor alpha (TNF- α) (28). UV and infrared (IR-A) light can also negatively affect functioning of the mitochondria in skin fibroblasts by disturbing the electron transport chain (29). Although the skin has a complex antioxidant mechanism to manage UV-induced oxidative stress, chronic UV light can lead to further damage by overwhelming this mechanism and the skin's capacity (30). *In vivo* investigations have shown so far that high levels of free radical production in the skin can also be caused by visible light, which can also lead to premature cutaneous photoaging (31, 32). Addressing these aspects may be imperative for broad-spectrum sunscreens covering the UV and visible light spectrum with the possible addition of antioxidants because results show that visible light mostly leads to ROS-mediated damage (31).

There are multiple substances that, as part of antioxidant group (e.g., apigenin, chrysin, and beta-carotene), have the ability to neutralize oxidative reactions and damage, although there is not yet strong evidence of their ability to suppress or prevent ROS production (33–35). Nuclear factor erythroid-derived 2-like 2 (Nrf2) activation upregulates antioxidant chemicals and molecules, and detoxifies enzymes important in clearance of cellular damage caused by ROS products, which is why Nrf2 may play a central role in oxidative stress manipulation (36). Nevertheless, their antioxi-

dativ effects may be helpful in preventing photoaging because the same study showed that it is still questionable whether they protect against photocarcinogenesis; in fact, some hypothesize they may actually promote it (37). Another antioxidant mechanism is called autophagy and is an intracellular process of oxidized lipid and metabolic waste degradation in order to minimize the photoaging progress (38). Therefore ROS-modified proteins are cleared by proteasomal and lysosomal cellular mechanisms (39). However, clearance mediated by autophagy decreases with time, leading to higher concentrations of damaged proteins and lipids (i.e., waste), causing dermal accumulation of waste products and consequently photoaging (40).

Other mechanisms involved in photoaging

Epidermal cells' DNA absorbs UVB light, which leads to the production of DNA alterations; for example, pyrimidine dimers (41). Products of DNA damage thereby act as melanogenesis initiators, protecting the skin from further UV damage (41). On the other hand, impaired DNA leads to inhibition of RNA synthesis and activation of p53 proteins, leading to keratinocyte apoptosis and production of "sunburn" epidermal cells. Extended irradiation has the ability to suppress apoptosis mediated by the p53 mechanism, which can result in impaired cell accumulation and initiation of skin carcinogenesis (42). As shown in some studies, UVA also contributes to impairment of DNA through guanine oxidation, forming 8-hydroxyguanine and 8-oxoguanine (8oG). The mechanisms of DNA photodamage are mostly part of the photocarcinogenesis process but can also be an important aspect of the photoaging process (24).

Exposure to sunlight also results in the activation of inflammation processes in skin due to NF- κ B signaling enhancement while activating endothelial cells in skin vasculature, lymphocytes, macrophages, and other immune cells (43). This signaling pathway forces keratinocytes to secrete cytokines that enhance inflammation (IL-1, IL-3, IL-6, IL-8, IL-7, IL-10, and TNF- α) (43). Exposure to UV light also activates lipoxygenase and cyclooxygenase pathways (LOX and COX-2 X), resulting in production of leukotrienes and prostaglandins (43, 44). This complex cascade of inflammatory reactions may eventually "hyperactivate" immune cells and cause further possible skin damage (24).

UVA exposure also has an effect on the dermal matrix. ROS upregulates activator protein 1 (AP1; i.e., transcription factor) and increases matrix metalloproteinase (MMP) production (43). MMPs are endopeptidases with the ability to disintegrate extracellular matrix (ECM) proteins. ECM protein damage leads to wrinkling and solar elastosis (i.e., aged clinical presentation of the skin). AP-1 also inhibits synthesis of dermal collagen by inhibiting transforming growth factor beta (TGF- β) and by reducing type I and III procollagen gene expression (43, 45, 46). Therefore photoaged skin shows reduction of type I and III collagen precursors and an increased type III/I collagen ratio (24, 43, 45). Thus, chronic exposure to UV light results in a loss of dermal collagen net formation due to its degradation and impairment of synthesis, consecutively leading to dermal atrophy (24, 43, 45). The important histopathological hallmark of photoaging is mid-dermal accumulation of elastotic material (yellowish thickening of the skin as a clinical observation and histopathological accumulation of basophilic material) (5). Although acute exposure to UV light induces upregulation of elastin synthesis, it also leads to reflux of neutrophils that eventually degrade elastic fibers by activation of

the aforementioned MMPs and elastase enzyme (24). Degraded elastin fibers are then phagocytosed by fibroblasts and destroyed in their lysosomes (24). Exposure to UVA upregulates the activity of lysosomes in fibroblasts on the one hand, but on the other hand aged fibroblasts lose their ability to phagocytose fragments of elastin, which may be why elastin fragments accumulate in the dermis. This mechanism is similar to the one previously explained by the clearance of ROS-mediated intracellular waste products, and it is thought to be one of the most important mechanisms for how cells age in general (24). All the mechanisms of photodamage in photoaging are described in Figure 1.

Photoprotection as the main preventive measure against photoaging

The primary preventative strategy for photoaging should include sun avoidance during high UV indices (around midday in summer and in higher-elevation areas where shorter wavelengths are detected), wearing sun-protective clothing, and applying appropriate sunscreen agents (47). Photoprotective clothing includes clothing with impenetrable, tightly woven, synthetic, and thick (e.g., denim) material and material prewashed with broad-spectrum ultraviolet absorbers (48). Clothes made of fabrics with darker colors are also considered photoprotective (48). In fact, photoprotective clothes have a UV protection factor (UPF) greater than 40 (the UPF is a measure for rating the amount of UV light that penetrates through fabric), and they are considered adequate for resisting possible factors that may decrease UPF value (49).

Another important part of preventing photoaging is sunscreen agents. UV filters are sunscreen ingredients that provide skin protection against UV light damage. Currently, there are seventeen Food and Drug Administration (FDA)-approved active sunscreen ingredients or filters, divided into inorganic/physical filters (mechanism of action: reflection and dispersal of UV light, the two main ones being zinc oxide and titanium dioxide) and organic/chemi-

cal filters (mechanism of action: absorption of specific UV light photons, most commonly avobenzone, oxybenzone, or octinoxate) (50). Although chemical UV filters have cosmetic precedence in comparison to physical UV filters, their poor photostability and their safety are problematic (51–53). Consequently, Cozzi et al. recently investigated and compared the skin penetration, skin surface retention, and photostability of organic sunscreen formulations with the same filter composition (avobenzone and octocrylene, Eusolex® OCR), but in different forms: encapsulated and free (54). The importance of that study is its results, which show that encapsulation technology for developing organic sunscreens can reduce skin penetration while improving overall safety and significantly extending the photostability of organic agents (54).

Sunscreen can be protective against UVB and UVA, and formulations that protect against both are called broad-spectrum sunscreens (47). The sun protection factor (SPF) is a measure that shows the efficacy of protection against UVB light and does not take UVA light into account, which is why the 2011 guidelines on assessing UV protection were published by the FDA, which included both UVB and UVA (i.e., broad-spectrum sun protection) (55). Assessing broad-spectrum UV protection is done by using the critical wavelength (CW) method (the wavelength where 90% of the total area under the absorbance curve resides across the UV spectrum of 290 nm and 400 nm) (50, 55). Today, according to this assessment, a sunscreen's CW must be ≥ 370 nm for it to be called broad-spectrum (50, 55). Along with assessment of the type of UV protection, other important factors for greater sunscreen agent efficacy are the total amount (the recommended amount is 2 mg/cm²) and the uniformity of the agent's skin application, the specific absorption/reflection spectrum of the agent used, and providing stable photoprotection during the UV exposure period (48, 56). In addition, current specialists' recommendations are to apply the sunscreen agent 15 to 30 minutes before sun exposure and to reapply it every 2 to 3 hours (or more frequently if sweating and after swimming) (57).

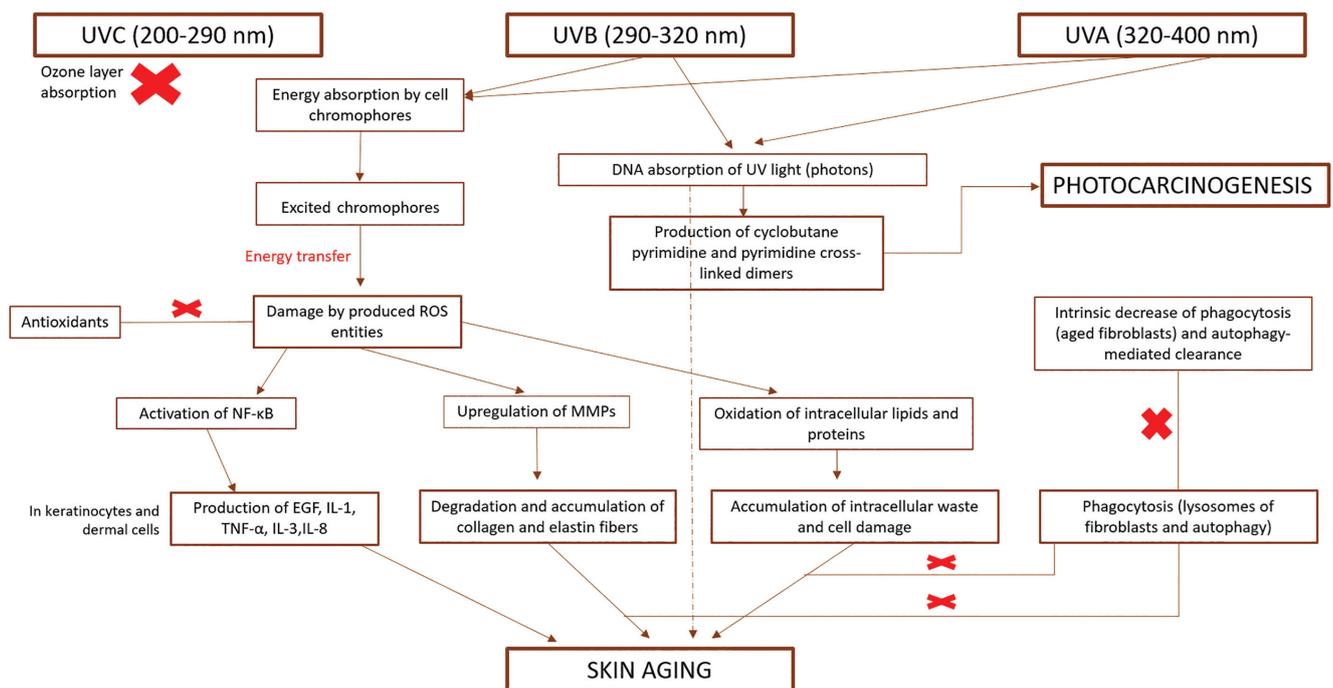


Figure 1 | Mechanisms of photoaging: processes through which UVA and UVB radiation cause photoaging. This includes the main path of ROS production and its multiple ways of causing photoaging, and the path of DNA damage that mainly causes photocarcinogenesis but also photoaging through negative influence on cell functions and cell death. UV = ultraviolet, ROS = reactive oxygen species, NF-κB = nuclear factor kappa B, EGF = epidermal growth factor, TNF = tumor necrosis factor, MMP = matrix metalloproteinase.

Overall efficacy of sunscreen agents against photoaging

The main use of sunscreen agents is for photoprotection against malignant damage to skin by UV light, but there are some sunscreens properties that can be effective in protection against photoaging, which is why many studies have been conducted on this topic. One such study was published by Seité et al., in which the authors exposed young volunteers to repeated low doses of solar-simulated radiation (SSR) for 6 weeks on nonprotected and UV-protected skin (daily photostable broad-spectrum sunscreen) (58). After 6 weeks of exposure, the authors showed that low doses of SSR reduced type I procollagen production in the dermis along with a slight increase of lysozyme and alpha-1 antitrypsin deposits in elastin fibers. Interestingly, the results observed were present even where strong pigmentation was induced (supposedly acting as skin self-protection) (58). As another part of their study, the authors showed that application of sunscreen with photoprotection properties significantly prevented all the photodamage examined in the research (58). It is important to emphasize that the area below the dermoepidermal junction, where the authors found the aforementioned reduced expression of procollagen type I, has been reported in previous studies to be a collagen neosynthesis location, which increases the importance of understanding the use of photoprotection (24). Similarly, Seité et al. showed in a later study that daily application of moisturizers with broad-spectrum sunscreen prevented transcriptional expression of genes associated with skin aging (mainly MMP-1) and acted as an antioxidative response to UV exposure (59). The authors also showed that protection from photodamage is similar when comparing products that have different SPF values but the same UVA-PF (59).

Another two studies, which were similar in design, evaluated the efficacy of daily sunscreen use against photoaging in female volunteers. A study performed by Nawaz et al. was conducted for 6 months on 11 female volunteers using sunscreen products containing ecamsule, with application on only one cheek of each volunteer (60). In another study, performed by Randhawa et al., volunteers applied broad-spectrum photostable SPF 30 sunscreen (composition: avobenzone 3%, homosalate 12%, octyl salicylate 5%, octocrylene 1.7%, and oxybenzone 3%) over a 52-week period to the entire face in the morning and a simple moisturizer without any active antiaging components in the evening (also to the entire face) (61). In the first study, the authors evaluated skin changes using Cutometer®, Mexameter®, and Corneometer® devices, and in the second study data analysis was performed by the dermatologist using professional clinical evaluation. Results from a study by Nawaza et al. showed more negative changes in gross elasticity (0.72%), net elasticity (0.66%), viscoelasticity (0.77%), and biological elasticity (1.39%), higher melanin production (1.99%), erythema (2.01%), and worse hydration (3.15%) in unprotected skin than in photoprotected skin (60). Dermatologists' evaluation of photodamage parameters (crow's feet, skin tone evenness, overall skin tone, texture, and skin clarity) in a study by Randhawa et al. showed significant improvement of the parameters evaluated after 1 year of daily sunscreen application ($p \leq 0.05$) (61). The authors concluded that broad-spectrum sunscreen may even improve photodamage that had previously accumulated, and not only prevent possible future damage (61). In addition, a pivotal randomized controlled trial by Hughes et al. showed that a group of participants that used broad-spectrum SPF 15+ sunscreen daily for 4.5 years experienced significantly slower progression of skin

aging; during the trial period, such aging was 24% less evident in the test group than in a control group that used sunscreen on a discretionary basis (photoaging changes were measured using microtopography of surface of the skin on the back of the left hand at the beginning and end of the study) (62). The authors also examined the effect of antioxidant oral beta-carotene supplement use on photoaging but did not find a significant positive effect on preventing skin aging (62).

In the last 10 years, many studies have questioned the effect of sunscreens containing topical antioxidants in reducing photoaging damage. Two published studies showed that daily application of broad-spectrum sunscreen combined with antioxidants may reduce the production of ROS, cytokines, and MMP-1, may suppress UV-induced pigmentation, and may be superior to sunscreen alone (31, 63). However, there are limitations to topical antioxidant use in terms of its stability and diffusion into the epidermis, and whether it may promote photocarcinogenesis (37, 64).

It is also important to emphasize that cumulative UV exposure may be an important factor that contributes to skin aging in comparison to intermittent exposure, and that photoprotection should be applied daily (65).

The importance of SPF values in preventing photoaging

SPF is a relative measure that indicates the percentage of UVB light that is blocked by the photoprotection used. In this way, SPF 15, 30, 50, and 100 block 93%, 97%, 98%, and 99% of UVB radiation, respectively. Abundant evidence has recently emerged suggesting that the higher the SPF, the better the sun protection efficacy (although SPF value is not multiplicative; e.g., an SPF 20 agent is not twice as effective as SPF 10). In a randomized double-blind clinical trial, Williams et al. demonstrated that 55.3% of their participants experienced sunburn on the side protected with SPF 50+ in comparison to 5% of participants that experienced sunburn on the side with SPF 100+ protection (66). The design of the trial included split-face use of sunscreens, simultaneously during activities (on one side SPF 50+ and the other SPF 100+) with natural sunlight exposure (66). The authors also showed that 40.7% of participants had higher and more frequent erythema on the side protected with SPF 50+ in comparison to 13.6% of participants that experienced erythema on the side protected with SPF 100+ (66).

The objective of another study by Cole et al. was to determine whether high-SPF sunscreen has the ability to protect against cellular photodamage if doses of UV exposure are similar to the sunscreen's SPF value (67). In that study, each of nine subjects underwent four different treatments performed on four different skin sites: the first was an untreated and unprotected site (as a negative control), the second was an unprotected skin site treated with 1 minimal erythema dose (MED; MED value was determined for every individual), the third was an unprotected skin site treated with 3 MEDs, and the last site was protected with SPF 55+ and UVA-PF 22 broad-spectrum sunscreen and was exposed to 55 MEDs of UV radiation (67). Researchers took skin biopsies from all four skin sites and evaluated the presence of sunburn cells, Langerhans cells, thymine dimers, p53, and MMP-1 and MMP-9 activity evidence (67). The 1 MED untreated site showed significantly prominent signs of damage when compared with the negative control, and, in addition, all the signs showed significantly more photodamage in comparison to 3 MED unprotected sites and the negative control (67). In the comparison of sunscreen-protected skin sites with unprotected and MED-exposed sites, all

of the markers of photodamage evaluated showed no statistical difference in comparison to the 1 MED exposed area, but for MMP-9 and p53 sunscreen-protected skin areas were statistically less damaged than the 1 MED exposed sites (67). These results showed that broad-spectrum high-SPF protection is similarly effective as an effect of “minimal erythema” protection, and it may provide even better protection against underlying cellular photodamage than its SPF value (67).

Recently, industry and research have been working to create and test novel solar-specific skincare with a protection range from UV to IR (68). Results from a recent study conducted by Tanaka et al. showed improvement in skin texture and luminosity, and significant improvement in skin redness and hyperpigmentation after 1 year of daily application of such novel solar-specific skincare formulations (also protecting against near-IR radiation), which pushes the benchmark for sunscreen development (68).

Table 1 lists and summarizes the result of all the studies cited in this section concerning the efficacy of photoprotection for preventing photoaging.

Possible negative impacts of sunscreens on health and the environment

Recently, the question arose whether large-scale use of sunscreen products may have negative impacts on overall health and natu-

ral homeostasis. Many studies have investigated this. Physical filters have been shown to be most effective and safest, but they have inferior cosmetic characteristics (69). On the other hand, chemical filters have limited absorption ranges. They provide a better and more pleasing cosmetic appearance, but they need to be combined for adequate photoprotection. Studies have shown that oxybenzone and octinoxate are largely responsible for contact allergic reactions and are considered to disrupt the endocrine system in humans because they can penetrate intact skin (their concentration can be measured in urine and serum) (70). These filters have been shown to have an anti-androgenic and estrogenic effect, they may affect pregnancy duration, and they have been linked to coral reef bleaching (70–72). Although there are conflicting data about the safety of chemical filters (some studies dismiss the theory of endocrine disruption) (73, 74), safe and appropriate use of sunscreen products should be encouraged.

Conclusions

Photoaging is an important and possibly preventable extrinsic skin aging process. The mechanism of photoaging is multi-variable and there are some etiological principles that overlap and cause photodamage to the skin (e.g., rhytides, pigmentary changes, and telangiectasias). Many recent studies present hard evidence that regular sunscreen use provides quality photoaging

Table 1 | Summary of studies cited on protective effects of sunscreen against photodamage.

| Study | UV protection | Results |
|-------------------------------|--|--|
| Seité & Fourtanier, 2008 (58) | Broad-spectrum | Application of UV protection prevents enhanced expression of tenascin, reduces expression of type I procollagen, and increases lysozyme and alpha-1 antitrypsin deposits in elastin fibers. |
| Seité et al., 2012 (59) | Broad-spectrum | Daily use of UV-protection prevents expression of skin aging genes (i.e., MMP-1) and reflects the skin's antioxidative stress defense response. |
| Nawaz et al., 2019 (60) | Broad-spectrum (SPF 60+) | Application of sunscreen showed no significant difference in gross, net, and biological elasticity and viscoelasticity, but there was a significant difference in hydration, melanin, and erythema. |
| Randhawa et al., 2016 (61) | Broad-spectrum (SPF 30+) | All photodamage parameters (crow's feet, skin tone evenness, overall skin tone, texture, and skin clarity) significantly improved after 1 year of daily sunscreen application, $p \leq .05$. |
| Hughes et al., 2013 (62) | Broad-spectrum | Skin aging (measured by change in microtopography) was 24% less in participants that used sunscreen daily than in a discretionary sunscreen group (relative odds 0.76 [95% CI, 0.59–0.98]). |
| Liebel et al., 2012 (31) | Broad-spectrum with antioxidant | Application of UV protection plus antioxidants significantly reduced antioxidant stress <i>in vivo</i> in humans and reduced production of ROS, cytokines, and MMP expression <i>in vitro</i> . The results also showed that visible light irradiation produces high free radical activity. |
| Grether-Beck, 2015 (63) | Broad-spectrum (with and without antioxidants) | Exposure to IR-A radiation significantly upregulated MMP-1 expression. This effect was also significantly reduced with the application of SPF30 sunscreen with an antioxidant, in contrast to UV protection without antioxidants. |
| Phillips et al., 2000 (65) | Broad-spectrum (SPF 15+ and 29+) | At sites lacking photoprotection there was a statistically significant increase in the number of sunburn cells, degree of inflammation, and intensity of lysozyme staining, and a decrease in the number of Langerhans cells in comparison to non-irradiated control and participant groups that used photoprotection daily. |
| Williams et al., 2018 (66) | Broad-spectrum (SPF 100+ and SPF 50+) | SPF 100+ sunscreen is significantly more effective in photoprotection than SPF 50+ sunscreen (5% of participants in comparison to 55.3% in terms of sunburn, and 13.6% of participants versus 40.7% in terms of increased erythema scores). |
| Cole et al., 2014 (67) | Broad-spectrum (SPF 55+) | Exposure to 55 MEDs at sunscreen-protected sites showed significantly less p53 and MMP-9 expression in keratinocytes than unprotected sites exposed to 1 MED. |
| Tanaka, 2019 (68) | Broad spectrum + topical solar repair at night | Improvements were seen in skin texture and luminosity via digital photography after 1 year of daily application of photoprotection and topical solar repair. |

UV = ultraviolet, MMP = matrix metalloproteinase, ROS = reactive oxygen species, IR-A = infrared, SPF = sun protection factor, MED = minimal erythema dose, CI = confidence interval.

prevention. Daily use of broad-spectrum sunscreen with an SPF of 30 or higher is the latest recommendation by expert groups for effective overall photoprotection. The main reason for the lower efficacy of sunscreens is customers' misuse. An important fact is that there are no photoprotective products that can completely protect against photodamage, and avoiding sun is the most important for preventing photoaging, photocarcinogenesis, and melanogenesis. To respond to these possible effects of appropri-

ate photoprotection, industry is constantly developing new and improved UV filters, broad-spectrum sunscreens, and innovative technologies to provide safe and pleasant application with the best cosmetic prospects to improve the frequency of sunscreen use. It is therefore dermatologists' duty to inform and educate patients with the latest information about appropriate and effective photoprotection.

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