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Abstract: This review provides an overview of important concepts and trends in photoprotection. From the use of protective clothing to latest-generation oral photoprotectives, this article covers these topics from two points of view: 1) the physical blockade (absorption and/or reflection) of UV photons by topical sunscreens; 2) topical compounds with antioxidant properties that thereby protect from the consequences of UV-mediated photooxidation. The last section is devoted to the development of strong antioxidant oral compounds and discusses their possibilities as adjuvants in skin protection and repair and regeneration.

Keywords: Photoprotection, sunscreens, oral antioxidants, dietary photoprotectants.

INTRODUCTION

UV filters ("sunscreens") are designed to protect the skin from the harmful effects of solar radiation, particularly the UV band. UV radiation can be roughly divided into two segments according to wavelength: UVB (~290-320 nm) and UVA (~320-400 nm). UVB is erythematogenic, carcinogenic, induces photoaging and mutagenic damage to nucleic acids, e.g. RNA and DNA. UVA, on the other hand, is also mildly erythematogenic, but promotes ROS (Reactive Oxygen Species) accumulation. ROS also induce direct cell damage, carcinogenesis and contribute to photoaging.

The basic idea underlying photoprotection is to establish a physical barrier between the sun and the skin; hence most of these compounds exert their protective effect when used topically. However, a new trend is emerging, consisting of increasing the basal antioxidant threshold of the body to improve the response to oxidative damage, including that due to exposure to the sun. Thus, new substances that include potent antioxidant capability are starting to be used systemically, for example orally.

UV-based skin damage can be divided into two major categories: 1) acute, including necrosis, erythema and inflammation, and 2) chronic, termed photoaging, and characterized by the appearance of wrinkles, changes in skin color and skin cancer. The acute effects of UV exposure are mainly caused by high energy-containing photons, which are relatively easy to stop using molecules or molecular complexes that absorb, reflect, or scatter high-energy UV photons. Consequently, the major components of most topical sunscreens include barrier components as described above. However, most sunscreens cannot stop the lower-energy UV photons that cause photoaging. These photons do not cause erythema, but they can induce immunosupression as well as mutations in the DNA of the most exposed cells of the epidermis and superficial dermis. These effects are amplified by the increased oxidative damage that results from the energy transfer of these photons to destroy naturally-occurring photoprotective molecules in the skin as well as to produce reactive oxygen species (ROS). The consequences of increased oxidation include extracellular matrix (e.g. collagen) deterioration, cellular apoptosis, plasma membrane destruction, direct DNA damage and increased mutagenesis [1-5].

Visible light can also harm the skin if there is a previous skin condition, e.g. chronic actinic dermatosis, or erythropoietic porphiria. Current UV filters do not protect against visible light; opaque filters are required, including clothing or “old school” preparations of physical filters, such as ZnO or TiO2 ([6] and see below).

From these facts, it can be inferred that proactive strategies to combat oxidative damage are highly desirable. This concept underlies the possibility of using oral antioxidants to combat the effects of photoaging. Some of the new substances used as oral photoprotectives contain one, or many, antioxidant active principles that can stop UV-induced skin damage, or even collaborate to repair previously induced damage. Future scenarios in the treatment and prevention of sun-induced skin pathologies contemplate synergic protection conferred by complementation of topical and oral sunscreens.
THOU SHALL NOT PASS! PREVENTING UV PHOTONS FROM REACHING THE SKIN

1. Clothing and Glasses

Appropriate clothing and sunglasses are basic tools to fight sun-induced damage from both the UV and visible parts of the spectrum. The American Society of Photobiology and the American Academy of Dermatology have highlighted the importance of the use of adequate cloths, hats and eyewear to protect from UV radiation. Clothing photoprotection directly depends on thickness (thicker is usually better), color (reflective colors, such as white), moisture and tightness. Highly efficient photoprotective textiles are available, e.g. nylon made from BASF fibers, which has TiO2 particles embedded in the fabric. Also, some laundry products can endow or enhance photocatalytic properties, which protect from UV radiation.

Solar erythema in the eyes often appears as “pink eye” (inflammation of the conjunctiva). In more severe cases, it can cause solar keratitis and irreversible damage to the vision [8, 9]. Chronic damage includes cataracts and macular degeneration [3, 4]. Interestingly, use of appropriate goggles significantly decreases the risk of these events. There are well-defined, FDA-approved parameters for sunglasses: less than 0.001% of photons between 200-320 nm are accepted through the protective material, whereas the percentage is <0.01 % for less damaging wavelengths (320-400 nm) [10].

2. Topical Sunscreens

Topical sunscreens include substances: 1) that reflect or scatter UV photons, 2) that absorb them, preventing their incidence on the cells of the skin acceptors; 3) substances with antioxidant properties. The main goals are to protect against UVB radiation [11] and long-wavelength UVA radiation [12]; scavenge ROS; activate cellular repair systems, including DNA repair (Table 1).

Their activity is established according to their SPF (Sun Protection Factor), which is a measurement of their capability to stop UV photons: higher SPF means higher efficiency. A sunscreen SPF is usually measured using solar-simulated radiation (SSR) and a defined sunscreen application density (2 mg·cm⁻²), and calculated according to the following formula:

\[
\text{Minimal Erythema Dose (MED) with sunscreen} = \frac{\text{MED without sunscreen}}{\text{SPF}}
\]

Other parameters utilized are: 1) Ery-PF (Erythema protection factor), which only takes into account the erythematos response after 24 hours; 2) PFA (Protection Against UVA), which is mainly used in the European Union; 3) Immune protection factor, for which there is no standardized protocol. One of the most utilized is the suppression of contact hypersensitivity by UV [13]. Additionally, sunscreens should (and some are) be tested for their antimutagenic and antioxidant properties.

Table 1. Main Photoprotector Groups

<table>
<thead>
<tr>
<th>1. Topical Photoprotective Agents</th>
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<tr>
<td>a) Physical blockers</td>
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<tr>
<td>i) Zinc oxide (ZnO)</td>
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<td>ii) Titanium dioxide (TiO₂)</td>
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<td>b) Chemical and biological filters</td>
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<td>i) Cinnamates</td>
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<td>ii) Benzophenones</td>
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<td>• Oxybenzone</td>
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<td>• Avobenzone</td>
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<td>iii) Mexoryl SX</td>
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<td>v) Tinosorb M</td>
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<td>vi) Tinosorb S</td>
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<td>c) Antioxidants</td>
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<td>i) Hydrocinnamic acids</td>
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<td>ii) Polyphenolics</td>
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<td>• Flavonoids</td>
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<td>• Green tea Extract</td>
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<td>• Astaxanthin</td>
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<td>iii) Anthocyanins and tannins</td>
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<td>iv) Pycnogenol® (French Maritime pinus extract)</td>
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<td>v) Fernblock® (Polypodium leucotomos extract)</td>
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<td>vi) Others</td>
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<td>• Diydroxyacetone</td>
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<td>• Caffeine and caffeine sodium benzoate</td>
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<td>• Polyuron multiflorum thumb</td>
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<td>• N-(4-pyridoxylmethylene)-l-serine</td>
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<td>• Creatine</td>
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<td>• Idebenone</td>
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<td>• COX-2 inhibitors</td>
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<td>• DNA repair systems</td>
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<td>- Photolyase</td>
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<td>- T4 endonuclease</td>
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<td>• DNA oligonucleotides</td>
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<td>• AC-11</td>
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<th>2) Oral Photoprotective Agents</th>
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<td>a) Vitamin derivatives</td>
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<td>b) Dietary animal and botanic extracts</td>
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<td>i) Genistein</td>
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<td>ii) α³ polysaturated fatty acids</td>
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<td>iii) Fernblock® (Polypodium leucotomos extract)</td>
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<td>iv) Green tea polyphenols</td>
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High SPF sunscreens always contain a physical filter and at least two organic filters; one with optimal screening for UVB wavelengths and the other for UVA photons.

Topical sunscreens are presented as ointments, lotions, creams or sprays. Due to their ease of use, they are the most common photoprotective measure in environments of high exposure, e.g. seaside, mountain and countries with with low incidence of rain, e.g. countries in Oceania. Population studies have been conducted in some of these countries. For example, a study in Australia showed that consistent use of sunscreens (SPF ≥15) significantly reduced the occurrence of some types of skin cancers [14]. A major caveat of most of these studies is that they fail to address the long-term effect of sunscreens in preventing photoaging. A few studies are emerging on the use of sunscreens to prevent photoaging. An early clinical trial in humans showed that use of a sunscreen (SPF=29) for two years reduced photoaging [15]; recently, sunscreens containing Mexoryl SX were found to reduce wrinkle depth in long-term studies [16]. However, these
studies need to be standardized for future use as a general screening for topical sunscreens and to avoid false claims on efficacy.

**Components of Topical Sunscreens**

- **Physical blockers**: Blocking agents are made of big particles (diameter is ~0.1-1 μm) that scatter, reflect or absorb solar radiation in the UV, visible and even infrared wavelengths. By far, the two most common physical blockers are zinc oxide (ZnO) and titanium dioxide (TiO₂). Microfine zinc oxide is a better blocker than titanium dioxide [17]. However, both components are somewhat photosensitive and can react with light, inhibiting their efficiency or even causing tissue damage [18]. In addition, microfine ZnO or TiO2 do not protect against visible light. To prevent this, both compounds are usually caged. The most common caging substances are dimethicone or silica [19]. Additional stabilizers include carnauba wax, which contains cinnamates that synergize with TiO₂ resulting in stable solutions that can hold SPF up to 50 [20-22].

- **Filters (chemical or biological)**: These include:
  a) **UVB filters**: They are efficient (90%) UVB blockers [23]. Cinnamates are frequently used in combination with other substances, e.g. salicylates, which are very stable and insoluble in water, which allows them to retain their properties once applied on the skin [24, 25]. Salicylates can also be used to dissolve other sunscreen ingredients, such as benzophenones [26].
  b) **UVA Filters**: Most sunscreens protect well from UVB; however, these do not necessarily protect from UVA as well. Specific filters exist to absorb UVA photons, including oxybenzone (Bp-3; Eusolex 4360) and avobenzone (Parsol 1789) [23]. A major caveat is that these are easily oxidized and degraded.
  c) **Dual UVB/ UVA filters**: Newer filters have been developed that can absorb both UVA and UVB. Some examples include the Mexoryl series. Mexoryl SX is the commercial name of terephthalalidene dicamphor sulfonic acid. This compound is quite stable, and frequently used together with avobenzone in broad-spectrum sunscreens [1]. Several studies suggest a significant effect for Mexoryl SX-based formulations in preventing several aspects of photoaging [16, 27, 28]. Mexoryl XL is drometrizol trisiloxane and it absorbs UVB and UVA2 radiation. Mexoryl XL synergizes with Mexoryl SX for enhanced photoprotection [28]. Other dual filters include Tinosorb M (methylene-bis-benzotriazoyl tetramethylbutylphenol), which is made of microfine, water-soluble organic particles [25]; Tinosorb S (bis-ethyhexyloxyphenol methoxyphenyl triazine), which is another high-molecular mass broadband sunscreen filter (280-380 nm) that can absorb and also reflect UV photons. It also synergizes with other blocking substances, such as OMC (2-ethylhexyl-4-methoxycinnamate) and avobenzone [29]. Different biophysical techniques have been used to improve the efficacy and applicability of these filters, e.g. their encapsulation in sol-gel glass silica microcapsules of ~1 μm diameter [30]. These approaches decrease penetration beyond the epidermis and immunogenicity and improve photostability.

- **Antioxidants**: Antioxidants are commonly included in commercial sunscreens to reduce the photo-oxidative damage that results from UV-induced ROS production. These include several well-characterized vitamins including vitamins C, E and β-carotene [31]. Other common substances are:
  a) **Hydroxycinnamic acids**, e.g. caffeic or ferulic acids. They prevent UVB-induced erythema in vivo and in vitro [24], and decrease UV-induced oxidative damage in skin cells and lymphocytes [32-34].
  b) **Polyphenolics**, e.g. flavonoids and phenolic acids. Several of them have antioxidant, anti-inflammatory and antitumoral activities [35]. Several of these are used in sunscreens, including:
    - **Flavonoids**: they are vegetal isoflavones endowed with antioxidant and antitumoral properties [36, 37]. Genistein is a specific inhibitor of protein tyrosine kinases and a phytoestrogen that effectively blocks UVB and also from PUVA-induced photodamage and molecular alterations in hairless mouse skin [40, 41]. It also bears antiphotocarcinogenic and antiphotoaging properties [39]. Silymarin is a plant flavonoid isolated from the seeds of milk thistle (Silybum marianum). It is a combination of silybin, silydianin and silychristin that prevents ultraviolet light-induced immune suppression and oxidative stress in a mouse model [42]. Equol can be purified from red clover (Trifolium pretense) in its precursor form, daidzein [43], and also from Punica granatum [44]. Equol protects from UV erythema and may prevent photocarcinogenesis [45, 46] and photoaging [47]. **Quercetin** is a very potent antioxidant used to successfully inhibit UVB-induced skin damage in rodent models [48, 49]. Apigenin decreases UV-induced skin tumorigenesis and inhibits tumor cell growth in vitro [50, 51]. Its mechanism includes inhibition of UV-induced upregulation of COX-2 [52].
Green tea polyphenols (GTPP) is used to refer to several potent antioxidants that appear in green tea leaves. The most abundant is epigallocatechin-3-gallate (EGCG). EGCG reduces lipid peroxidation induced by UVB, and also decreases UVA-induced skin damage and immunosuppression [53]. EGCG inhibits activation of pro-inflammatory transcription factors such as AP-1 and NF-κB, collagenase expression and collagen cross-linking [54, 55]. Due to its intrinsic instability on skin, it needs to be mixed with butylated hydroxytoluene [56].

Resveratrol is a polyphenolic phytoalexin present in several fruits, particularly grapes. Its topical use on hairless mice before UVB irradiation decreased erythema, ROS production and inflammation [57, 58]. Its effect on delaying UV-induced tumorigenesis has also been reported [59].

Astaxanthin is a natural xantophilic pigment that sequesters ROS and thus inhibits accumulation of free polyamines induced by UVA [60]. It also attenuates the UVA-induced up-regulation of matrix metalloproteinases and elastase in human dermal fibroblasts [61].

- **Anthocyanins and tannins** are present in several fruits, e.g. grapes or pears, and are endowed with antioxidant and anti-inflammatory properties. Used topically, they protect against the adverse effects of UV radiation, inhibiting UVB-dependent activation of NF-κB, MAP kinase and COX-2 pathways downstream of the signaling kinases MKK4, MEK1, and Raf-1 [62, 63].

- **Pycnogenol** is an extract of French maritime pine (*Pinus pinaster Ait*). It bears antioxidant, anti-inflammatory and anticarcinogenic properties. Pycnogenol prevents UV-induced erythema as well as longer-term effects, such as immunosuppression and tumor formation [64, 65]. It also possesses regenerative skin properties [66], and prevents UVB-induced photoaging [67].

- **Fernblock** is an extract obtained from the fern *Polypodium leucotomos*. Topical application of *Polypodium leucotomos* extract (PL) inhibited UVB- and PUVA therapy-induced erythema in vivo [68]. PL is a potent antioxidant and has shown immunomodulating capability and inhibition of pro-inflammatory cytokines, such as TNF-α or IL-6 [69]. PL also inhibits the depletion of Langerhans cells induced by irradiation with UV light and PUVA therapy [68, 70, 71] and reduces chronic elastosis and matrix metalloprotease expression [72, 73].

- **Other photoprotective agents**: We include miscellanea of compounds that have been used in different skin formulations. Some are:

  - Dihydroxyacetone is a photoprotective agent that provides SPF 3-4 and protects against UVA photons [74]. Its main drawback is that it tints the skin and rare cases of contact dermatitis have been reported [75].

  - **Caffeine and caffeine sodium benzoate (SB)** inhibit UVB-induced apoptosis. Additional studies have shown that caffeine-SB strongly inhibited UVB-induced carcinogenesis [76].

  - **Polygonum multiflorum thumb (PM)** is an extract that possesses antibacterial properties. PM decreases oxidative stress induced by UVB irradiation [77].

  - N-(4-pyridoxylmethylene)-L-serine (PYSer) is an antioxidant that suppresses iron-catalyzed ROS generation, and has shown promise in the treatment of UVB-induced photoaging [78].

  - **Creatine** is a metabolic reservoir of energy in the muscle. It has been suggested that boosting the energy metabolism in the skin may improve skin aging and photoaging [79]. Consistently, topical use of creatine has been shown to decrease UV-induced damage *in vivo* and *in vitro* [80], and postulates it use to fight photoaging [81].

  - **Idebenone** is a synthetic analog of coenzyme Q10 [82, 83]. A clinical study using a compound based on idebenone has suggested its efficacy in preventing photoaging [84], but other studies have suggested otherwise [85, 86]. In addition, cases of contact dermatitis have been documented [87].

  - **COX-2 inhibitors**: COX-2 is a metabolic enzyme linked to tumorigenesis and cancer progression. Consequently, COX-2 makes an excellent target for the development of antitumor drugs, which has turned out a bumpy road due to unforeseen side effects [88]. Regarding their topical use, celecoxib, a COX-2 inhibitor, has been shown to decrease UVB-mediated erythema, inflammation and prostaglandin E2 (PGE2) production [89, 90]. It also inhibited UVB-induced papilloma formation [91] as well as the appearance of skin tumors after adoptive transfer of tumor cells [92].

  - **DNA repair enzymes** constitute an emerging approach to enhance DNA repair after UV exposure. Some examples are:

    - **Photolyase** is isolated from the cyanobacteria *Anacystis nidulans*. It promotes DNA repair and also decreases the number of UV-induced thymidine dimers [93, 94].

    - **T4 endonuclease** has been assayed in patients with xeroderma pigmentosum [95, 96]. Treatment with a liposomal preparation of T4 endonuclease, T4N5, prevents sunburn and local
suppression of contact- and delayed-type hypersensitivity [95, 97].

- DNA oligonucleotides can enhance the cellular response to subsequent UV irradiation, regardless the existence of previous DNA damage [98]. The most commonly assayed are thymidine dinucleotides as well as homologues of the telomere 3-prime overhang sequence (T-oligos). The latter exhibited enhanced melanogenesis and increased DNA repair in response to UV irradiation [99].

- AC-11 (C-Med-100) is obtained from cat’s claw (Uncaria tomentosa). It promotes DNA repair (8-hydroxyguanine and strand breaks) after UVB exposure. Possible mechanisms include enhanced base excision repair or an inherent antioxidant effect. A single-blind, right side-left side beach sun exposure pilot study described a significant decrease in erythema and blistering by application of 0.5% topical AC-11 with an SPF-15 sunscreen compared to application of SPF-15 sunscreen alone [100].

THE ROAD LESS TAKEN: ORAL PHOTOPROTECTIVE AGENTS

Oral photoprotection is a novel approach to skin care. Evidently, they cannot be used in lieu of topical sunscreens, as they do not prevent erythema but they complement their use by preventing photaging and photocarcinogenesis. The amount of mechanistic information on their effects is still limited, but they are believed to increase the basal threshold amount of mechanistic information on their effects is still limited, but they are believed to increase the basal threshold amount of mechanistic information on their effects is still limited, but they are believed to increase the basal threshold amount of mechanistic information on their effects is still limited, but they are believed to increase the basal threshold amount of mechanistic information on their effects is still limited, but they are believed to increase the basal threshold amount of mechanistic information on their effects is still limited, but they are believed to increase the basal threshold amount of mechanistic information on their effects is still limited, but they are believed to increase the basal threshold amount of mechanistic information on their effects is still limited, but they are believed to increase the basal threshold amount of mechanistic information on their effects is still limited, but they are believed to increase the basal threshold amount of mechanistic information on their effects is still limited, but they are believed to increase the basal threshold amount of mechanistic information on their effects is still limited, but they are believed to increase the basal threshold amount of mechanistic information on their effects is still limited, but they are believed to increase the basal threshold amount of mechanistic information on their effects is still limited, but they are believed to increase the basal threshold amount of mechanistic information on their effects is still limited, but they are believed to increase the basal threshold amount of mechanistic information on their effects is still limited, but they are believed to increase the basal threshold amount of mechanistic information on their effects is still limited, but they are believed to increase the basal threshold amount of mechanistic information on their effects is still limited, but they are believed to increase the basal threshold amount of mechanistic information on their effects is still limited, but they are believed to increase the basal threshold amount of mechanistic information on their effects is still limited, but they are believed to increase the basal threshold amount of mechanistic information on their effects is still limited, but they are believed to increase the basal threshold amount of mechanistic information on their effects is still limited, but they are believed to increase the basal threshold amount of mechanistic information on their effects is still limited, but they are believed to increase the basal threshold amount of mechanistic information on their effects is still limited, but they are believed to increase the basal threshold amount of mechanistic information on their effects is still limited, but they are believed to increase the basal threshold amount of mechanistic information on their effects is still limited, but they are believed to increase the basal threshold amount of mechanistic information on their effects is still limited, but they are believed to increase the basal threshold amount of mechanistic information on their effects is still limited, but they are believed to increase the basal threshold amount of mechanistic information on their effects is still limited, but they are believed to increase the basal threshold amount of mechanistic information on their effects is still limited, but they are believed to increase the basal threshold amount of mechanistic information on their effects is still limited, but they are believed to increase the basal threshold amount of mechanistic information on their effects is still limited, but they are believed to increase the basal threshold amount of mechanistic information on their effects is still limited, but they are believed to increase the basal threshold amount of mechanistic information on their effects is still limited, but they are believed to increase the basal threshold amount of mechanistic information on their effects is still limited, but they are believed to increase the basal threshold amount of mechanistic information on their effects is still limited, but they are believed to increase the basal threshold amount of mechanistic information on their effects is still

• Vitamin derivatives: They include:

- Carotenoids. Lycopene is the major carotenoid present in tomatoes and a very efficient singlet oxygen quencher. Recent studies have suggested beneficial photoprotective effects [103]. Lutein and zeaxanthin are xanthophyll carotenoids that exhibit a moderate photoprotective effect in combination with topical application [104].

- Tocopherol and ascorbate exhibit moderate oral photoprotective effect when used in combination [105]; interestingly, a combination of lycopene, beta-carotene, alpha-tocopherol and selenium yeast reduced UV-induced damage [106]. Other combinations include Seresis®, which contains carotenoids (β-carotene and lycopene), ascorbate, tocopherol, selenium yeast and proanthocyanidins. Oral use of Seresis® delays the onset of UVB-induced erythema and inhibits the expression of matrix metalloproteinases, postulating an effect on photoaging [107].

- Dietary animal and botanical extracts: Their composition is rather heterogenous, but most contain dietary flavonoids and phenolics. Some examples include:

  - Genistein, which can be used as a dietary complement as well as in topical formulations (see above). Oral genistein decreases UVB-induced skin photaging and tumorigenesis in a rodent model [39], postulating its use as a natural cancer preventive [108].

  - ω-3 polyunsaturated fatty acids are a popular dietary supplement obtained from fish oil. Regarding their use as oral skin photoprotectors, high doses have been shown to decrease UVB-induced erythema and inflammation [109].

  - Polypodium leucotomos extract (PL) can also be administered orally with very low toxicity. In addition to its antioxidant properties, PL can exert immunomodulatory effects. Oral PL scavenges free radicals and reactive oxygen species such superoxide anion, singlet oxygen, hydroxyl radical and hydrogen peroxide, and prevents lipid peroxidation [110, 111]. Oral administration also induced photoprotection against UVB radiation and during PUVA therapy without significantly affecting the efficacy of the treatment [70, 71]. Supplementation with PL significantly decreased erythema and depletion of Langerhans cells [70, 71]. PL also prevents oxidative DNA damage (8-hydroxyguanine) and accelerates repair of thymine dimers [71, 112]. In addition, it also inhibited trans-urocanic acid photo-induced isomerization and inactivation [113]. Analysis of its in vivo and in vitro protective effects have revealed several molecular mechanisms of action [68, 114, 115], including abrogation of UV-induced TNF-α and nitric oxide (NO) production [116]; potentiation of the endogenous antioxidant response [117]; inhibition of photoimmunosuppression [118]; and modulation of the inflammatory response [112]. A recent study notes that oral administration reduces UVA-induced cyclobutane pyrimidine dimer deletions and mitochondrial DNA damage [119].

  - Green tea polyphenols (GTPPs), e.g. epigallocatechin-3-gallate (EGCG). Oral use of EGCG prevents UV-induced skin tumorigenesis in mice. Several mechanisms underlie this effect, e.g. induction of interleukin 12, which prevents immunosuppression and boosts DNA repair through excision repair mechanisms dependent; inhibition of angiogenic factors and stimulation of T cell-dependent cytotoxicity and tumor cell clearance [120]. Oral GTPPs can also decrease UV-induced expression of skin matrix metalloproteinases, postulating an effect on photaging [121].

CONCLUDING REMARKS AND FUTURE PERSPECTIVES

This review offers a non-comprehensive account of several compounds with proven effect in photoprotection. Most of the topical compounds used topically are well
proven tools to prevent erythema and the acute deleterious effects of UV exposure; However, the jury is still out regarding their efficacy in preventing chronic damage and photoaging. On the other hand, oral photoprotectives exert often modest effects. It is necessary to mention that they are not meant to be silver bullets in photoprotection, i.e. they cannot and are not intended to substitute sunscreens or to increase the threshold of what is considered healthy exposure to the sun. It is the general consensus that they are intended to fight the long term effects of UV exposure, particularly photoaging and skin tumorigenesis. Future studies will undoubtedly reveal the complementary effect of topical and oral photoprotection.

The mechanisms of photoprotection of most of these compounds are not fully defined yet; most of them are based on powerful antioxidant activities; others promote regeneration through yet-unknown mechanisms, making this an active and attractive field for basic and clinical research. Therefore, further clinical trials will be required to validate the preventive and therapeutic value of these products. In summary, oral sunscreens have a demonstrated therapeutic value in the prevention and treatment of sun damage, and are likely in their way to become a mainstream method of protection that complements traditional screening methods.

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