Photoprotection

Part II. Sunscreen: Development, efficacy, and controversies

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Dr Lam has served as consultant for Ferndale, La Roche-Posay, Pierre Fabre, Uriage, and Palatin. He has received research grants from Clinswel and Esteé Lauder. Mr Osterwalder is a full-time employee of BASF. Dr Wang has served on the advisory board of L’Oreal. Drs Burnett and Jansen have no conflicts of interest to declare.

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Learning Objectives:
After completing this learning activity, participants should be able to describe the evolution of sunscreen technology; summarize new photoprotective technologies; and discuss and explain current sunscreen controversies.

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867.e1
In addition to the naturally occurring, physical, and systemic photoprotective agents reviewed in part I, topical ultraviolet radiation filters are an important cornerstone of photoprotection. Sunscreen development, efficacy, testing, and controversies are reviewed in part II of this continuing medical education article. (J Am Acad Dermatol 2013;69:867.e1-14.)

**Key words:** oxybenzone; photoprotection; photostability; Sun Protection Factor; sunscreen; sunscreen controversies; ultraviolet filter.

### SUNSCREENS: TOPICAL PHOTOPROTECTIVE AGENTS

#### Key points
- Ideal sunscreens provide uniform protection against ultraviolet A and ultraviolet B light.
- Ideal sunscreens have aesthetically pleasing compositions that enhance compliance.

#### The notion of the “ideal sunscreen”

Since the first commercial sunscreen was introduced in 1928, the use of sunscreens as an integral part of photoprotection strategy has expanded worldwide. Table I highlights the historical development of sunscreens.5,4

Two factors must be addressed to produce an “ideal” sunscreen.5 It should provide uniform protection across the range of ultraviolet B light (UVB) and ultraviolet A light (UVA), a property referred to as “spectral homeostasis,” which assures that the natural spectrum of sunlight is attenuated in a uniform manner (Fig 1).6 This is particularly useful for protection against immunosuppression, which has a broad action spectrum.7 An “ideal” sunscreen should also have pleasing sensory and tactile profiles that enhance the user’s compliance.

<table>
<thead>
<tr>
<th>CAPSULE SUMMARY</th>
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<tbody>
<tr>
<td>• Ideal sunscreens provide uniform protection across the ultraviolet B and ultraviolet A light range while maintaining sensory and tactile features that enhance the user's experience.</td>
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<tr>
<td>• Sunscreen efficacy depends on ultraviolet filter type (organic or inorganic), photostability, and the addition of Sun Protection Factor—boosting agents.</td>
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<td>• New US Food and Drug Administration regulations regarding sunscreen testing and labeling aim to improve the clarity of photoprotection of sunscreens.</td>
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<td>• While there are controversies involving sunscreen ingredients, formulations, and side effects, based on current data, the risk–benefit ratio indicates that it is appropriate to include the use of sunscreen as an important component of photoprotection strategy.</td>
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#### Ultraviolet filters

Principles of ultraviolet radiation absorption by organic ultraviolet filters. In order to absorb ultraviolet radiation (UVR), an organic ultraviolet (UV) light filter must contain a suitable chromophore that has conjugated \( \pi \)-electron systems. Increasing the number of conjugated double bonds in the molecule shifts the absorption maximum to longer wavelengths and also gives rise to a larger absorption cross section and, therefore, stronger absorption. In general, the larger the molecular weight of the chromophore, the more the absorption maximum will be shifted towards longer wavelengths. This is the reason that UVB light filters have smaller molecular weights compared to UVA light or broad-spectrum filters.

Currently, all organic UV absorbers used in sunscreens are aromatic compounds, each containing multiple conjugated \( \pi \)-electron systems (Tables II and III).8 The type of substituents and their position at the aromatic ring are important for the UV spectroscopic properties. Especially advantageous are disubstituted systems with an electron-donor (+M-) and an electron-acceptor (−M-) group in paraposition (so-called push−pull systems). Fig 2 shows a
comparison of the absorption spectra of ethylhexylidimethyl paraaminobenzoate (United States Adopted Name [USAN], padimate O), with substituents in a paraposition, and a UV absorber with similar groups but in orthoposition, menthyl anthranilate (USAN, meradimate). Because of the substituents in paraposition, padimate O is a more efficient UV filter than meradimate.

### Photostability

Absorption of a UV photon transfers the UV absorber molecule into an excited electronic state. If the absorbed energy is not sufficiently and speedily dissipated into heat, chemical bonds of the UV absorber may break, resulting in degradation of the UV filter. A reversible isomerization (tautomerism) in the excited state can stabilize an UV absorber. This principle is realized, for instance, in the menthyl anthranilate molecule because of the orthoamino group (Fig 2), resulting in excellent photostability. In others, this is realized via electronic state. If the absorbed energy is not sufficiently and speedily dissipated into heat, chemical bonds of the UV absorber may break, resulting in degradation of the UV filter. A reversible isomerization (tautomerism) in the excited state can stabilize an UV absorber.9,10 This principle is realized, for instance, in the menthyl anthranilate molecule because of the orthoamino group (Fig 2), resulting in excellent photostability. In others, this is realized via an orthohydroxy group forming hydrogen bonds (eg, bemotrizinol and bisoctrizole).

Most of the UV absorbers used in sunscreens are photostable under the conditions of use. Two exceptions are avobenzone (AVO) and octinoxate.11 AVO undergoes rapid photodegradation, which can be stabilized by UV filters octocrylene and bemotrizinol. The latter is not yet available in the United States (Fig 3). In addition, AVO and octinoxate enhance the photodegradation of each other. For this reason, these 2 filters should not be used in combination.12-14

### Principles of ultraviolet protection with inorganic ultraviolet filters

Micronized inorganic oxides used in sunscreens (TiO₂ and ZnO) attenuate UV mainly by absorption and some scattering.15 Depending on particle size, these materials are semiconductors that absorb photons at different wavelengths. The smaller the primary particles, the shorter its peak absorption spectrum.16 The primary particle sizes of TiO₂ used in sunscreens are between 10 and 30 nm. However, in dispersion, the particles form aggregates with sizes usually around 100 nm. With ZnO, primary particle sizes from 10 to 200 nm are available, but mainly the grades with larger particles are used. Because of the photocatalytic effect, TiO₂ for sunscreen applications is coated with aluminum oxide or silica in order to prevent oxygen radical formation. In addition, the rutile crystal form is used in most cases. Rutile is the most common form of TiO₂, has a high refractive index, and can absorb UVR. Although the anatase form of TiO₂ has many of the same properties as the rutile form, it has lower UVR absorption and higher tendency for photocatalysis.

### Particulate organic ultraviolet filters

Sunscreens, especially those with a high Sun Protection Factor (SPF), contain a considerable amount of UV filters. Therefore, solubility of the active substance can be a significant problem.17 For this reason, particulate organic UV filters were developed that allow high SPF products to be developed with relatively lower concentrations of UV filters. Examples of these UV filters include methylene bis-benzotriazolyl tetramethylbutylphenol (biscotrizole) and tris-biphenyl triazine. These filters have extremely low solubility in oil and in water, but can be micronized in an aqueous phase.17,18 Particulate biscotrizole shows a broad absorption up to 380 nm.

### Regulations of ultraviolet filters

The safety of UV filters has to be shown in an extensive program of toxicologic studies. In Europe and Japan, UV absorbers are regulated as cosmetics, in the United States as over the counter drugs and in Australia as therapeutic drugs.19 An overview of common UV filters in sunscreen is shown in Table II. Australia and Europe have the most UV filters for sunscreen formulation. By contrast, the United States has the least number of UV filters available.

### Limitations of available ultraviolet filters in United States

While sufficient filters are available in the UVB and UVA2 range, only 4 UVA1 (340-400 nm) filters, all with limitations, are approved in the United States (Figs 4 and 5). AVO is the most efficient UVA1 filter, but it is not photostable. In the United States, the maximal concentration is 3%, and it is not approved for combination with TiO₂ because enhanced photodegradation of AVO is observed in the presence of TiO₂. AVO is also not approved in combination with ZnO for lack of data to show the

### Abbreviations used:

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
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<tr>
<td>AAP</td>
<td>American Academy of Pediatrics</td>
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<td>AO</td>
<td>antioxidant</td>
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<td>AVO</td>
<td>avobenzone</td>
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<td>BEMT</td>
<td>bemotrizinol</td>
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<td>CW</td>
<td>critical wavelength</td>
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<td>EU</td>
<td>European Union</td>
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<td>FDA</td>
<td>Food and Drug Administration</td>
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<td>ISO</td>
<td>International Organization for Standardization</td>
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<td>MED</td>
<td>minimal erythema dose</td>
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<td>PPD</td>
<td>persistent pigment darkening</td>
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<td>ROS</td>
<td>reactive oxygen species</td>
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<td>SPF</td>
<td>Sun Protection Factor</td>
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<tr>
<td>TiO₂</td>
<td>titanium dioxide</td>
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<tr>
<td>UK</td>
<td>United Kingdom</td>
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<tr>
<td>USAN</td>
<td>United States Adopted Name</td>
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<td>UV</td>
<td>ultraviolet</td>
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<td>ultraviolet A</td>
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<td>ultraviolet B</td>
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<td>UVR</td>
<td>ultraviolet radiation</td>
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<tr>
<td>ZnO</td>
<td>zinc oxide</td>
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</table>

$\text{Abbreviations used:}$
enhancement of UVA protection potential of ZnO in the presence of AVO. Ecamsule, the most recent UV filter approved in the United States (2006), is available only for the sponsor of the new drug application (ie, it can only be used in certain products). The third organic UVA1 filter, meradimate (Fig 2), is rather weak and limited to use at concentrations ≤ 5%. The fourth UVA1 filter is ZnO, which has low E1,1 value. While it can be used in concentrations of ≥ 25%, in practice, cosmetic limitations exist at such high concentrations.

Sun Protection Factor—boosting agents. Better film forming of sunscreen on the skin leads to a more uniform distribution and therefore to a higher SPF. The use of organic UV filters to stabilize inherently unstable UV filters, such as AVO, leads to a higher SPF and/or better UVA protection. It should be noted that some of the emollients, photostabilizers, and other ingredients in sunscreen products are also UV absorbers, although they do not appear on the actives list on the drug fact sheet (Table III).

Ultraviolet filters not yet available in the United States. In the UVB/UVA2 range, 2 UV filters are frequently used outside of the United States: octyl triazone and diethylhexyl butamido triazone. As seen in Figs 6 and 7, they are the most efficient UVB filters, with a maximal E1,1 value >1400. Less frequently used is amiloxate, a homologue of octinoxate with isopentyl instead of the ethyl-hexyl group. A unique UV filter is polysilicon-15. It has a low E1,1 value of just ≤ 150. However, because it has a polymeric structure, it spreads extremely well on the surface of the skin, contributing significantly to the SPF.

All new UV filters that reach into the UVA1 range are photostable and shown in Table II. The most efficient broad-spectrum UV filter is bemotrizinol. Bisoctrizole is a particulate organic UV filter with especially broad UVB and UVA absorbance. The inclusion of only a few percent of bisoctrizole boosts the critical wavelength (CW) to >370 nm.

**SUNSCREEN USE**

**Key points**
- The SPF value primarily measures the level of protection against UVB and UVA2, and is based on the ratio of MED on sunscreen-
protected skin compared to unprotected skin.

- Methods for assessment of UVA protection. vary by country; in the US critical wavelength method is used.

Evaluation of efficacy

The SPF and the UVA protection profile are the 2 common indices used to quantify the efficacy of sunscreens. The measurement of SPF depends on minimal erythema dose (MED), which is defined as "the smallest UV dose that produces perceptible redness of the skin (erythema) with clearly defined borders at 16 to 24 hours after UV exposure." Improved understanding of the deleterious effects of UVA radiation has underpinned the development of better UVA filters and testing standards for determining UVA protection in a reproducible manner.

Methods for testing UVA protection have been adopted by regulatory bodies in Japan, the European Union (EU), United Kingdom (UK), Australia, and the United States. However, the methodologies vary by country. Japan uses persistent pigment darkening (PPD) as a clinical endpoint. PPD measures the minimal UVA radiation dose required to induce the first perceptible pigmentation changes (ie, minimal pigmenting dose) in sunscreen-protected skin compared to unprotected skin. Sunscreen products are then rated as PA+, PA++, PA++++, or PA++++ (where PA indicates the protection grade from UVA). The EU requires UVA protection factor to be at least one-third of the labeled SPF, with PPD method as the assessment of the UVA protection. For example, a sunscreen with a SPF of 30 must have a UVA protection factor of at least 10. In the UK, the ratio of UVA absorbance to mean UVB absorbance is measured in vitro; a star rating system is used. Australia adopted the in vitro test procedure ISO 24443:2012 for determining broad-spectrum performance, which is similar to the European assessment. The adoption of this UVA testing method, which determines the spectral absorbance characteristics of UVA protection, has led to the development of sunscreens with 10 to 20 times the protection against UVA radiation when compared to sunscreens complying with the old standard.

In 2011, the US Food and Drug Administration (FDA) mandated the use of in vitro CW for testing of UVA protection. Briefly, the CW test is conducted by applying the test product to 3 different polymethyleneacrylate plates at a density of 0.75 mg/cm². Transmittances are then measured from 290 to 400 nm. CW is defined as the wavelength at which 90% of the total area under the absorbance curve occurs (Fig 8). Sunscreens that have a CW of ≥ 370 nm are then allowed to claim broad-spectrum status.

Immune protection factor. Photoimmunosuppression by UVR is an in vivo parameter forming the basis for the index of protection known as immune protection factor. Immune protection factor can be assessed by measuring the UVR-induced suppression of either the induction or elicitation arms of the delayed-type or contact hypersensitivity responses. However, standardization of both the definition and the method for determination of immune protection factor has yet to be established.

Factors affecting sunscreen efficacy

Knowledge and behavioral barriers. Sunscreen should always be used in conjunction with other photoprotective measures (Table IV). Many consumers lack a fundamental understanding of the relationship between UVA/UVB and sunscreen protection ratios. In practice, most people often apply only 25% to 50% of the amount used for SPF testing. This results in an effective SPF that is ≤ 33% of the labeled SPF. Recently, a modification of the "teaspoon rule" for sunscreen application has been proposed. Namely, to achieve 2 mg/cm² of density, the following should be done: 1 teaspoon of sunscreen to the face/head/neck, 1 teaspoon to each upper extremity, a total of 2 teaspoons to the front
<table>
<thead>
<tr>
<th>INCI abbreviation</th>
<th>INCI CE no.</th>
<th>INCI abbreviation</th>
<th>Trade name</th>
<th>USAN</th>
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<td>Bis-ethylhexyloxyphenol</td>
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<td>Uvinul A Plus</td>
<td><strong>DHHB</strong></td>
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<td>Bisdisulizole disodium</td>
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<td>Methylene bis-benzotriazolyl tetramethylbutylphenol</td>
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<td>Mexoryl SX</td>
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<tr>
<td>Ethylhexyl methoxycinnamate</td>
<td>S 28</td>
<td>Octinoxate</td>
<td>Uvinol MC 80</td>
<td>EHMCS</td>
<td>10</td>
<td>10</td>
<td>20</td>
<td>7.5</td>
<td>10</td>
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</tr>
<tr>
<td>Ethylhexyl salicylate</td>
<td>S 13</td>
<td>Octisalate</td>
<td>Neo Heliopan EHS</td>
<td>OS</td>
<td>5</td>
<td>5</td>
<td>10</td>
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<td>10</td>
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<td>Ethylhexyl triazine</td>
<td>S 69</td>
<td>Octyltriadione</td>
<td>Uvinol T 150</td>
<td><strong>EHT</strong></td>
<td>5</td>
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<td>Homomenthyl salicylate</td>
<td>S 12</td>
<td>Homosalate</td>
<td>Eusolex HMS</td>
<td><strong>HMS</strong></td>
<td>15</td>
<td>10</td>
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<tr>
<td>Isoamyl p-methoxyxycinnamate</td>
<td>S 27</td>
<td>Miloxate</td>
<td>Neo Heliopan IMC</td>
<td>—</td>
<td>—</td>
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<tr>
<td>Octocrylene</td>
<td>S 32</td>
<td>Octocrylene</td>
<td>Uvinol N 539 T</td>
<td>OCR</td>
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</tr>
</tbody>
</table>
and back torso, and 2 teaspoons to each lower extremity.

Studies have shown the incorrect application and reapplication of sunscreen by the lay public and the need for avoidance of unnecessary sun exposure after its application.32,34 It is clear that a sustained effort in public education is still needed.

Initiatives to enhance clarity and consistency of sunscreen use

**Updating the 2011 US Food and Drug Administration regulations.** Effective December 2012, sunscreens that have an SPF $\geq 15$ and CW $\geq 370$ nm can display the claim that “if used as directed with other sun protection measures, decrease the risk of skin cancer and early skin aging caused by the sun.”30,31 For sunscreens that are not broad-spectrum (ie, CW $<370$ nm) or are broad-spectrum but with an SPF $<15$, these above claims will not be allowed on the label.

In addition, the terms “sunblock,” “water proof,” “sweat proof,” or “all day protection” are not allowed. Going forward, labels may only contain the statement “water resistant (40 minutes)” or “water resistant (80 minutes),” reflecting the actual water resistant testing wherein test subjects are immersed in a whirlpool twice for 20 minutes or 4 times for 20 minutes, followed by measurement of the SPF. Lastly, as of this writing, the US FDA has yet to make the final determination on the following proposed items: SPF capped at 50, sunscreens in the form of oils, lotions, creams, gels, butter, pastes, and ointment as eligible dosage forms, sunscreens in the form of wipes, towelettes, powders, body wash, and shampoo are not eligible, and safety of sprays.

**SUNSCREEN CONTROVERSIES**

**Oxybenzone**

**Key points**

* Oxybenzone has been shown to have estrogenic effect, both in vitro and in an in vivo animal model.
* It has been used in the United States since the 1970s, and no untoward cause and effect relationship in humans has been reported.

The potential hormonal disruption effect of oxybenzone, an organic UV filter with an absorption profile ranging from 270 to 350 nm, has been discussed in the past few years. It has been used in the US since the 1970s, and prevalence of exposure to the compound among the US population is estimated to be 96%.35

In vitro experiments using human breast cancer cells suggest that oxybenzone can exert both
estrogenic\textsuperscript{36-39} and antiandrogenic\textsuperscript{39,40} effects. In an in vivo study, Schlumpf et al\textsuperscript{38} found that the weight of the uteri in 21-day-old rats fed with oxybenzone ([1500 mg/kg/day]) was 23\% greater than uteri of the control group. However, the dosage of oxybenzone used in this study was exceedingly high, and Wang et al\textsuperscript{41} estimated that it would take 277 years of daily application of sunscreens with 6\% oxybenzone to attain the same level of exposure in humans.

In humans, in a single-blinded, short-term clinical study, exposure to oxybenzone did not produce clinically relevant effects on hormonal homeostasis.\textsuperscript{42} Oxybenzone was detected in urine of studied subjects in the United States and Denmark; however, it was not correlated with the use of sunscreens.\textsuperscript{35,43} One or more UV filters were detected in 85\% of human milk samples in a study conducted in

### Table III. Emollients and photostabilizers ("boosters") with ultraviolet light—absorbing properties

<table>
<thead>
<tr>
<th>Name</th>
<th>Trade name*</th>
<th>UV light absorption</th>
</tr>
</thead>
<tbody>
<tr>
<td>Butyloctyl salicylate</td>
<td>Hallbrite BHB</td>
<td>Max (E1,1) 140 306</td>
</tr>
<tr>
<td>Benzotriazolyl dodecyl p-cresol</td>
<td>TinoGard TL</td>
<td>Max (nm) 350/380 304/337</td>
</tr>
<tr>
<td>Ethylhexyl methoxycrylene</td>
<td>Solastay S1</td>
<td>320 340</td>
</tr>
<tr>
<td>Polyester-8</td>
<td>Polycrylene</td>
<td>160 306</td>
</tr>
<tr>
<td>Diethylhexyl syringyldienemalonate</td>
<td>Oxynex ST</td>
<td>370 338</td>
</tr>
<tr>
<td>Diethylhexyl 2,6-naphthalate</td>
<td>Corapan TQ</td>
<td>310/60 295/350</td>
</tr>
</tbody>
</table>

\textsuperscript{E1,1}, Extinction at 1-cm pathlength and 1\% concentration; UV, ultraviolet.

\*Trade names are the property of their respective manufacturers.

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**Fig 2.** Ultraviolet light absorption spectra of ethylhexyl-dimethyl p-amino benzoate (padimate O) and menthyl anthranilate (meradimate). \textit{E1,1}, Specific extinction.

**Fig 3.** Photostability of avobenzone, alone and in presence of octocrylene and bemotrizinol.

**Fig 4.** UVB and UVA2 light filters commonly used in the United States. \textit{UVA}, Ultraviolet A; \textit{UVB}, ultraviolet B.

**Fig 5.** UVA1 and broad-spectrum UV light filters commonly used in the United States. \textit{UV}, Ultraviolet; \textit{UVA}, ultraviolet A.
Switzerland, and high oxybenzone levels in mother’s urine were associated with decreased birth weight in girls and increased birth weight and head circumference in boys.44 While no cause and effect relationship was established in the above studies, continued careful observation is warranted.

Retinyl palmitate

Key points
- Concerns have been raised regarding the photocarcinogenic potential of retinyl palmitate.
- Analysis of results of animal studies, and experience on its use in humans, failed to indicate any compelling evidence of photocarcinogenesis of retinyl palmitate.

Vitamin A is an essential nutrient that plays a major role in a number of important physiologic functions.45 As the storage form of vitamin A, retinyl palmitate (RP) has been approved for use by the FDA in foods as a fortifier, over the counter and prescription drugs, cosmetic products, and sunscreens as an antioxidant (AO). However, the use of RP in sunscreens has raised concerns regarding the potential photocarcinogenic effect of the compound.

An in-depth review of this topic has been conducted by Wang et al.46 Briefly, 8 in vitro studies were conducted to evaluate the photocarcinogenicity of RP between 2002 and 2009. Of these, 4 showed the formation of free radicals by RP after exposure to UVA radiation.47-49 The FDA National Toxicology Program subsequently conducted a large scale in vivo study using SKH-1 hairless mice, which have a thin epidermis and a predisposition to developing skin cancer. RP cream (0.1% and 0.5%) was applied, and mice were then exposed to UVR (6.75 mJ/cm² or 13.7 mJ/cm²).50 Only mice that received 0.5% RP and that were exposed to low-dose UVR revealed a statistically significant increase in the rate of cancerous lesion formation. Therefore, no clear evidence on photocarcinogenesis could be established based on this study.

In addition, the medical community has a long-standing history of safely using a number of oral and topical forms of vitamin A derivatives. Therefore, conclusive evidence is lacking that RP increases the risk of cutaneous carcinogenesis in humans.

Ultraviolet filters and inflammation

Key point
- Ultraviolet filters may have antiinflammatory properties.
A study on the antiinflammatory properties of UV filters was performed in a mouse model, using ear inflammation induced by topical phorbol-myristate-acetate application. The authors concluded that many of the common UV filters have significant antiinflammatory properties. If confirmed in UV-induced inflammation in humans, this finding could contribute to the understanding on the assessment of the SPF values and biologic effects of sunscreens. It should be emphasized that the protective property of sunscreens against acute and chronic effects of UV has now been well established.

Nanoparticles

Key points

• Concerns have been raised on the ability of metal oxide nanoparticles to generate cytotoxic reactive oxygen species and the penetration of these particles through the epidermis.
• Published evidence indicates that as used in cosmetic products, including sunscreens, micro- and nanosized ZnO and TiO$_2$ do not pose a risk to humans.

Micro- and nanosized ZnO and TiO$_2$ (diameter <100 nm) can generate reactive oxygen species (ROS) upon UV exposure. Studies on the toxicity to animal and human cells have yielded conflicting results. In view of the potential toxicity, manufacturers have coated the nanosized ZnO and TiO$_2$ with compounds such as aluminum oxide and SiO$_2$, both to minimize the formation of ROS and to reduce cytotoxicity by preventing adherence of nanoparticles to cells. It is also important to remember that the endogenous AO systems in the skin can neutralize ROS generated by these metal oxides.

Concern also exists regarding the percutaneous penetration of nanoparticles. To date, numerous in vitro and in vivo studies, conducted in both animal and human skin, have shown that nanoparticles are confined to the level of the stratum corneum after topical application, even in skin where the barrier function has been altered. The shedding and turnover of stratum corneum further prevents accumulation of nanoparticles. Along the same mechanism, the outward direction of hair shaft growth and flow of sebum push nanoparticles out of the hair follicle.

Based on current evidence, the EU’s Scientific Committee on Emerging and Newly Identified Health Risks concluded that the topical use of TiO$_2$ and ZnO in cosmetic products does not pose a risk to humans. However, until more data are available, their use at sites with severely impaired barrier function should be minimized.

Antioxidants

Key points

• Antioxidants incorporated into sunscreens have the potential of added protection against the effects of ultraviolet radiation.
• A 2011 study concluded that all tested sunscreens had no or minimal antioxidant properties.

AOs have been incorporated into many sunscreen products to neutralize the cytotoxic effects of ROS generated by UV exposure. In human studies, after UVR exposure, it has been shown that subjects who applied sunscreen that contained meticulously stabilized AOs had greater reduction in matrix metalloproteinase-1 levels and less pigment induction and epidermal proliferation when compared to controls. However, Wang et al found that many sunscreen products in the United States that claimed to contain AO ingredients actually had no or negligible AO capability, most likely because of the lack of stability of AOs.

Vitamin D synthesis

Key points

• Rigorous photoprotection, including the use of sunscreens, is associated with vitamin D insufficiency.
• However, because of inadequate application, serum 25-hydroxyvitamin D levels are not affected with normal usage of sunscreens.

A growing body of evidence has shown an important role for vitamin D in human health. In 2011, the Institute of Medicine concluded that the available data supported only the benefits of vitamin D in skeletal health, while no conclusive evidence was available to support the extraskeletal health benefits. The Institute of Medicine report issued guidelines defining vitamin D deficiency at a serum 25-hydroxyvitamin D (25(OH)D) level of 12 ng/mL. The guidelines also stated that most normal individuals are considered to have sufficient vitamin D at a serum 25(OH)D level of 20 ng/mL. The committee recommended daily requirements of 400 IU for infants <1 year of age, 600 IU vitamin D for adults <70 years if age, and 800 IU/d for those >70 years of age. Three sources of vitamin D exist: vitamin D–rich food, dietary supplements, and cutaneous synthesis after exposure to UVB. Currently available data indicate that dietary or supplemental vitamin D should be the preferred modern-day method of maintaining normal serum levels.
erythropoietic protoporphyria, sunscreens and photoprotection have been shown to be associated with low 25(OH)D levels. However, Norval et al concluded through a review of the literature that normal usage of sunscreen does not generally result in vitamin D insufficiency. Similarly, Linos et al found that in whites, seeking shade and wearing long sleeves were associated with low 25(OH)D levels, while frequent sunscreen use had no effect on 25(OH)D levels. The most likely explanation for these findings is that most individuals do not adequately apply sunscreens (ie, <2 mg/cm²).

Photoallergic dermatitis and allergic contact dermatitis. While UV filters can cause both allergic and photoallergic contact dermatitis, the latter condition occurs more frequently. It should be emphasized that considering the widespread use of sunscreens, contact and photoccontact dermatitis is uncommon. Photoallergic dermatitis from sunscreens is from organic UV filters, with benzophenone-3 (also known as oxybenzone) being the most common cause.

Use in pediatric populations

Key points
- In children, as in adults, broad-spectrum sunscreens should be used only as adjunct to other photoprotective measures.
- For those <2 years of age, if needed, sunscreens containing inorganic UV filters could be used on exposed areas.

Epidemiologic data have shown that childhood sun exposure increases the risk of cutaneous carcinogenesis in adulthood. The latest FDA sunscreen final monograph, published in 1999, indicated that physicians should be consulted for the use of sunscreens in infants <6 months of age. More recent guidelines issued by the American Academy of Pediatrics (AAP; 2011) and Centers for Disease Control and Prevention (CDC; 2003) both recommend that UVR exposure in children be reduced or prevented as a first-line strategy against solar UVR damage, with sunscreen used as a complementary measure. Specifically, the AAP does permit the use of sunscreen on small areas of skin when other photoprotective measures are not possible. Contrary to these recommendations, in practice, sunscreens remain the primary method of photoprotection used in children. Given the long-term risks of UVR exposure, proper photoprotective practice in the pediatric population, similar to adults, should include providing shade, wearing protective clothing, wide brim hat, sunglasses and, only on the uncovered areas, the use of broad-spectrum sunscreen.

The increasingly widespread use of sunscreens among the pediatric population has generated concern regarding their safety. Compared to adults, the higher body surface area—volume ratio of children and unique microstructure of immature skin suggest that children, especially infants, may absorb a greater fraction of topically applied substances. In addition, the capacity to metabolize and excrete absorbed substances may not yet be fully mature in young children and infants, putting them at risk for side effects and toxicities not seen in adults. Although firm data are lacking, because of the controversy on the systemic absorption of UV filters, especially benzophenones, and the evidence from numerous studies showing the lack of percutaneous penetration of inorganic UV filters, it is a prudent clinical practice to recommend the use of sunscreens with only inorganic UV filters in children <2 years old.

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