The development of efficient sunscreens

Dominique Moyal

L'Oréal Research and Innovation, France

Address for correspondence:
Dominique Moyal, 25-29 Quai Aulagnier - 92665 Asnieres Sur Seine, France.
E-mail: dmoyal@rd.loreal.com

ABSTRACT

Skin exposure to acute or repetitive ultraviolet light induces risks which are now well identified. An efficient photoprotection is thus required for both UVB and UVA radiation. In particular, increasing evidence of the detrimental effects of UVA on skin has led to the development of a new generation of sunscreens that provide effective protection throughout the whole UV radiation spectrum. Many new UV filters have been introduced in the last decade, particularly UVA filters, with improved efficacy and safety. Sunscreen filters must be carefully combined to achieve esthetically pleasing products offering photostable and well-balanced photoprotection.

Key words: Photostability, sunscreens, ultraviolet filters, ultraviolet filters sunscreens, VB/UVA protection

INTRODUCTION

Human exposure to ultraviolet (UV) radiation from sunlight can cause many adverse effects. UVB radiation (290-320 nm) is mainly responsible for the most severe damage: acute damage, such as sunburn, and long-term damage, including cancer. It has a direct impact on cell DNA and proteins.[1] Unlike UVB, UVA radiation (320-400 nm) is not directly absorbed by biological targets,[2] but yet can dramatically impair cell and tissue functions:

- UVA penetrates deeper into the skin than UVB. It particularly affects connective tissue where it produces detrimental reactive oxygen species (ROS). ROS cause damage to DNA, cells, vessels, and tissues.[3-8]
- UVA is a potent inducer of immune suppression[9,10] and there is serious concern about its contribution in the development of malignant melanoma and squamous cell carcinoma.[11,12]
- Photosensitivity reactions and photodermatoses are primarily mediated by UVA.[13]

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As a result, the evidence that most sunscreen products are unable to prevent the harmful effects of UVA has become a major concern. It is important to note that under any meteorological conditions, UVA irradiance is at least 17 times higher than UVB irradiance. For all these reasons, it is evident that sunscreens must contain both UVA and UVB filters to cover the entire range of harmful radiation. In 2006, the European Commission recommended that the minimum level of UVA protection (UVAPF) should be at least one-third of the sun protection factor (SPF), i.e. the SPF/UVAPF ratio should be lower or at the most equal to 3.[14]

REGULATORY STATUS OF ULTRAVIOLET FILTERS

Many new UV filters have been introduced in the last decade, particularly UVA filters, with improved efficacy and safety. They are not available, however, in some countries, such as the USA, for regulatory reasons. For example, 26 UV filters are accepted by Therapeutic Goods Administration in Australia and 31 UV filters are allowed in Japan. In Europe, Annex VII of the Cosmetics Directive lists 26 UV filters, whereas the sunscreen monograph in the USA mentions only 16, including only 10 in common with EU. Thus, most new UVA filters or broad UVB/UVA filters approved for use in Europe, Australia, and Japan [Table 1] are

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Table 1: Regulatory approval status for the main UVB/UVA and UVA filters

Names	Maximum wavelength absorbed (nm)	Major countries where UV filters are approved
Benzophenone-3 (oxybenzone)	288, 329	EU, Japan, Australia, Canada, USA
Butyl methoxy dibenzoyl methane (avobenzone) (BMDM)	355	EU, Japan, Australia, Canada, USA
Terephthalylidene dicamphor sulfonic acid (TDSA)	345	EU, Japan, Australia, Canada, USA (NDA)
Drometrizole trisiloxane (DTS)	303, 344	EU, Japan, Australia, Canada
Disodium phenyl dibenzimidazole tetrasulfonate (DPDT)	335	EU, Australia
Diethylamino hydroxybenzoyl hexyl benzoate (DHHB)	354	EU, Japan
Methylene bis-benzotriazolyl tetramethylbutylphenol (MBBT)	305, 360	EU, Japan, Australia
Bis-ethylhexyloxyphenol methoxyphenyl triazine (BEMT)	310, 343	EU, Japan, Australia
Titanium dioxide	295	EU, Japan, Australia, Canada, USA
Zinc oxide	390	Japan, Australia, Canada, USA

not available in the USA. In addition, there are some limitations on the use of avobenzone in the USA. Combinations with some other UV filters such as titanium dioxide and ensulizole are not permitted, and the maximum level of avobenzone is limited to 3%, instead of 5% in other countries.

DEVELOPMENT OF MORE EFFICIENT SUNSCREENS

An appropriate sunscreen product should provide effective protection against both UVB and UVA radiation, must be stable to heat and to UV-radiation (photostable), and should be cost-effective and user-friendly to encourage frequent application and provide reliable protection. To protect against both UVB and UVA, it must contain a combination of active ingredients (either organic or inorganic) within a complex vehicle matrix. Active ingredients can act either by absorption, or reflection or diffusion of UV radiation (UVR).

Organic ultraviolet filters

Organic filters are active ingredients that absorb UVR energy to a variable extent within a specific range of wavelengths depending on their chemical structure.[15] The molecular structure responsible for absorbing UV energy is called a chromophore. A chromophore consists of electrons engaged into multiple bond sequences between atoms, generally conjugated double bonds. An absorbed UV photon contains enough energy to transfer an electron to a higher energy orbit in the molecule.[15] The filter that was in a low-energy state (ground state) transforms to a higher energy state (excited). From the excited state, the filter molecule can simply deactivate and resume its ground state while releasing the absorbed energy as unnoticeable heat. Alternatively, it may undergo structural transformation or degradation and lose its absorption capacity, in which case it is said to be photounstable.

The control of filter behavior under UV exposure is a critical issue that needs to be thoroughly investigated when new sunscreen products are developed.

Photostability

A number of filters are available for UVB protection. They are photostable except for the most common one, ethylhexyl methoxy cinnamate (EHMC).

Regarding UVA filters, avobenzone (butyl methoxy dibenzoyl methane or BMMD) has a high potency in the UVA1 range (340-400 nm), peaking at 358 nm. However, on UV exposure, it undergoes significant degradation, leading to a decrease in its protective UVA efficacy. Some potent photostabilizers of avobenzone have been identified, such as octocrylene, a UVB filter. To illustrate this point, avobenzone was tested[16] at concentrations of 1%, 3%, and 5% alone and combined with 10% octocrylene. The UVAPF (determined using the persistent pigment darkening (PPD) method[17]) ranged from 2.2 with 1% avobenzone to 4.6 with 5% avobenzone. However, in combination with 10% octocrylene, the UVAPF ranged from 4.6 with 1% avobenzone to 10.6 with 5% avobenzone. This demonstrates that the UVA protective efficacy of avobenzone significantly increases when it is combined with octocrylene. The reason is that the PPD UVA doses affect the photostability of BMDM. It has been checked under real sun exposure conditions[18] that when a photounstable product applied at 1 mg/cm² is exposed to UVA dose ofabout 30 J/cm² (about 2.5 h), there is a dramatic decrease in the UVA absorption properties leading to a substantial decrease in UVA protection efficacy, as reflected by avobenzone.

UVA AND BROAD UVB-UVA FILTERS

In 2005, diethylamino hydroxybenzoyl hexyl benzoate (DHBB) was approved in Europe and Japan. This UVA1 filter has UV-spectral properties similar to avobenzone, but is photostable.

In order to provide full protection over the entire UVA range, it is necessary to have efficient absorption not only in the long UVA but also in the short UVA range. Terephthalylidene dicamphor sulfonic acid (TDSA or Mexoryl SX), with a peak at 345 nm at the boundary between short and long UVA wavelengths, was first approved in Europe in 1993. This was followed in 1998 by the approval of the broad UVB/UVA filter drometrizole trisiloxane (DTS or Mexoryl XL), with two absorption peaks (303 and 344 nm). Since 2000, other photostable short UVA filters, such as disodium phenyl dibenzimidazole tetrasulfonate (DPDT or Neo-Heliopan AP), with an absorption peak at 334 nm, and broadband UVB/UVA filters [methylene bis-benzotriazolyl tetramethylbutylphenol (MBBT) or Tinosorb M, and bis-ethylhexyloxyphenol methoxyphenyl triazine (BEMT) or Tinosorb S] have been approved in Europe.

Synergy of Protection Between Organic Ultraviolet Filters

A synergetic effect can be revealed when organic UV filters are combined. One example is the synergy between TDSA and DTS; the UVAPF of 4% TDSA is 4.3 and that of 4% DTS is 3.5, but the UVAPF of a combination of 2% of both is 6.1. Another example is the synergy between TDSA and BEMT. The SPF of 8% TDSA and 8% BEMT is 5.1 and 10.5, respectively, while the UVAPF is 4.9 and 5.3, respectively. However, the SPF of a combination of 5.5% TDSA and 2.5% BEMT is 22.2 and the UVAPF is 13.4.

Inorganic Ultraviolet Filters

Pigment grade powders of metal oxides such as titanium dioxide or zinc oxide have been used in combination with organic filters to enhance protection in the longer UVA range. Unlike organic filters, they work by reflecting and diffusing UVR. However, these powders also diffuse visible light because of their large particle size and give the skin a white appearance. To overcome this drawback, nanosized powders (<100 nm) of titanium dioxide and zinc oxide have been used. However, minimizing the particle size changes the protective properties of titanium dioxide: the smaller particles shift the protection range from the longer UVA toward the UVB. The absorption properties of these nanoparticle grades increase compared with the hardly absorbing large particles. Zinc oxide has better absorption potency in the long UVA range than titanium dioxide, but is not as effective as organic UVA filters.

Synergy of Protection Between Organic and Inorganic Ultraviolet Filters

When nanosized titanium dioxide is combined with organic UV filters, it allows high sun protection (SPF) products to be formulated with a lower dependence on organic UV filter concentration. In combination with organic UV filters, nanosized titanium dioxide has more a synergistic than an additive effect. For example, the SPF of a combination of three organic UV filters in a total concentration of 12.4% was 23 and that of 3% nanosized titanium dioxide was 4. In contrast, the SPF of a combination of the 12.4% organic UV filters and 3% nanosized titanium dioxide was 39. This synergistic effect between organic UV filters and nanosized titanium dioxide is very useful to reach very high SPF levels.

Well-balanced UVB/UVA Protection

Combinations of highly effective and photostable filters provide optimally balanced protection against both UVA and UVB.[19] The protection against UV-induced skin damage provided by sunscreen products with the same SPF but with different UVA protection factors markedly differs, emphasizing the importance of high UVA protection in preventing cell damage.[20-22] A suitable ratio between UVA and UVB protection levels should be ensured to avoid high UVB protection with low UVA protection. An SPF/UVAPF ratio not higher than 3:1, as defined by the European Commission,[14] should be universally adopted for harmonization of consumer protection.

In order to reach balanced protection, a combination of UV filters is necessary. The criteria for selection of this combination are the following: UV filters should have different maximum absorbance peaks (UVB, short UVA, and long UVA) to cover the entire UV spectrum, filters should be chosen appropriately depending on the different phases of sunscreen emulsion (lipophilic and hydrophilic), and the whole combination has to be photostable.

CONCLUSION

Formulators face many challenges in developing new sunscreen products. The products should afford the best balanced UVB/UVA protection with the minimum amount of UV filters to keep within optimized cost. Sunscreens should also be cosmetically pleasant to allow a sufficient amount to be applied and re-applied by the consumers, ensuring continuous and even coverage of exposed skin. Synergy between UV filters and photostability are the key factors to fulfill these requirements.

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