ATTACHMENT 3
UV-A PROTECTION WITH NEW CLASS OF UV ABSORBER
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Abstract
The Sun Protection Factor (SPF) measurement is based on erythema; mainly caused by Ultraviolet B radiation (UV-B). Therefore, SPF more appropriately describes a Sunburn Protection Factor. On the other hand, the awareness for the need of protection against UV-A radiation is rising and the claim for UV-A or broadband protection can already be seen on sunscreen bottles around the world. Several in vivo and in vitro methods to assess the UV-A protection are available. However, the availability of efficient and photostable UV-A absorbers is far from ideal.

With the new UV-A-absorber Ciba® TINOSORB™ M, the formulator is offered a UV-filter that fulfills the need for better UVA protection. TINOSORB M defines a new class of UV absorber, consisting of microfine, organic particles, combining the best of the two conventional categories; chemical/soluble and physical/insoluble. TINOSORB M does indeed combine the best of both worlds. As a particle, it provides UV protection by reflection and scattering. Furthermore, classical absorption plays an important role due the organic nature of the substance. In this paper the high efficacy and exceptional photostability of this new UVA filter is shown and the incorporation into sunscreen formulations is discussed.

Background of photo protection
Solar radiation in the range of infrared is perceived as heat, in the visible as color, and in the ultraviolet as the result of photochemical reactions. Such photochemical reactions may ultimately stimulate melanin production and tanning, or lead to genetic mutatins and to aberrant cell behavior.

The fact that the radiation energy increases with the decrease of the wavelength, and that longer waves are less reflected by an object holds also true for UV-radiation. Short wave UV-radiation is more likely to induce photochemical reactions. Long wave UV will penetrate deeper into the skin. Hence, the biological effects induced by UV-radiation changes with the wavelength.

UV-B (wavelengths between 290 nm - 320 nm)
UV-B radiation stimulates the production of Vitamin D. It affects especially the epidermal layer of the skin, where it causes Erythema (sun burn). Frequent and intense exposure to UV-B induces lesions on the DNA and suppresses the immune response of the skin. In turn, UV-B enhances the risk of fatal mutations eventually leading to skin cancer and reduces the chance that a malignantly transformed cell is recognized and destroyed (1).
**UV-A (wavelengths between 320 nm - 400 nm).**

UV-A radiation penetrates down to the dermal layers of the skin. It stimulates tanning and pigmentation and relates to skin aging. UV-A may act in an indirect way by creating free radicals and reactive oxygen species (2).

The chance of developing permanent damage increases with the dose of sun light accumulated over a lifetime. The risk of detrimental UV-induced effects eventually depends on the accumulated dose and not only on the UV-wavelength. This holds especially true in the context of exposure to natural sun light where UV-A contributes to about 95% and UV-B only to 5% of the radiation.

UV-related health hazards can be minimized by proper protection and shielding. Sun protective agents have been on the market for more than 60 years. They were first developed to protect the skin against sunburn, i.e. to shield the skin preferentially from UV-B and to permit tanning by UV-A. The conventional sun protection factors (SPF) still relate to the protection from UV-induced Erythema.

With the growing awareness of UV-A, it became obvious that for reducing the risk of sun exposure-related cancers the skin has to be protected not only from UV-B but from the whole UV-A/UV-B range (3, 4). In consequence, a new concept has evolved: An efficient sunscreen should not only prevent sunburn, but also minimize the accumulation of all radiation induced damages in the skin which eventually enhance the risk of fatal alterations (5-7).

**Requirements for cosmetic UV absorbers**

UV protection means conversion of the radiation energy of sun light into an harmless form. UV-absorbers for cosmetics must therefore be chemically and photochemically inert. If they are not, chemical bonds may be rearranged leading to new molecules the UV-absorbance of which might be diminished or even lost, and the toxicological properties may be altered. Radicals may react to form reactive oxygen species leading to biological damage. Moreover, fluorescence and phosphorescence, though not dangerous, are not desirable. Therefore, the light energy absorbed by UV-filters (if not scattered or reflected) should only be transformed into harmless thermal energy.

**Discussion of available UV-A absorbers**

Several UV absorbers have been developed to satisfy the growing need for better UV-A protection (8, 9). Table 1 lists these filters in the order of the absorption maximum in the UV-A range. Butyl Methoxydibenzoyl Methane is the most efficient UV-A filter, covering almost the entire UV-A range. One drawback of this filter is its lack of inherent photostability (10). Formulators can overcome this problem to a certain extent by adding Octocrylene or 4-Methybenzylidene Camphor to their formulations (11). However, these routes of stabilization are unfortunately blocked for many companies by
patent restrictions (12). Another filter with reasonable UV-A coverage is Terephthalidene dicamphor sulfonic acid, but this is available only for captive use by one company. With the physical UV filter Zinc Oxide UV-A protection can also be achieved. Rather high concentrations of ZnO are required however and there will be a trade off with the cosmetic elegance of the formulation.

With the year 2000 a new era in UV-A protection is emerging. For the first time a truly photostable, full spectrum UV-A filter is freely available on the market.

**TABLE 1 List of UV-A Filters before 1999**

<table>
<thead>
<tr>
<th>INCI name</th>
<th>Absorption Max.</th>
<th>Remark</th>
</tr>
</thead>
<tbody>
<tr>
<td>Butyl Methoxydibenzoyl Methane</td>
<td>357 1)</td>
<td>not photostable, stabilization possible under patent restrictions</td>
</tr>
<tr>
<td>Terephthalidene dicamphor sulfonic acid</td>
<td>345 2)</td>
<td>not freely available</td>
</tr>
<tr>
<td>Menthyl Anthranilate</td>
<td>336 1)</td>
<td>not permitted in Europe and Japan</td>
</tr>
<tr>
<td>Benzophenone-3</td>
<td>325 1)</td>
<td>covers only part of UVA</td>
</tr>
<tr>
<td>Benzophenone-4</td>
<td>324 1)</td>
<td>covers only part of UVA</td>
</tr>
<tr>
<td>Zinc Oxide</td>
<td>none</td>
<td>physical sunscreen</td>
</tr>
</tbody>
</table>

1) measured in Ethanol, 2) in water

**New class of UV absorber**

Ciba Specialty Chemicals has developed a new class of UV absorber. For the first time microfine particle technology is applied to organic UV absorbers combining the typical properties of organic (strong absorbance) with those of particulate UV filters (scattering and reflection). The organic molecules used have an inherent extraordinary photostability. The result is a highly efficient sunscreen due to its triple action: UV absorption, light scattering and light reflection. The new class is combining the best features of both conventional classes of UV filters.
Ciba® TINOSORB™ M, the first representative

TINOSORB M is the first representative of this new class of UV absorber. It is a 50% aqueous dispersion of colorless organic microfine particles with a size below 200 nm ($d_{0.5}$). The small particles are stabilized in their size by a surfactant.

Composition of TINOSORB M:

<table>
<thead>
<tr>
<th>Ingredient</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Organic micropigment</td>
<td>50.0 %</td>
</tr>
<tr>
<td>Surfactant (Decyl glucoside)</td>
<td>7.5 %</td>
</tr>
<tr>
<td>Thickener (Xanthan gum)</td>
<td>0.2 %</td>
</tr>
<tr>
<td>Propylene glycol</td>
<td>0.4 %</td>
</tr>
<tr>
<td>Water</td>
<td>ad 100 %</td>
</tr>
</tbody>
</table>
TABLE 2 Data of active ingredient

<table>
<thead>
<tr>
<th>Particle size</th>
<th>Chemical Structure</th>
</tr>
</thead>
<tbody>
<tr>
<td>![Image of particle size]</td>
<td>![Chemical structure image]</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Chemical name</th>
<th>2,2'-Methylene-bis-(6-(2H-benzotriazole-2-yl)-4-(1,1,3,3-tetramethylbutyl)-phenol)</th>
</tr>
</thead>
<tbody>
<tr>
<td>INCI name</td>
<td>Methylene Bis Benzotriazoyl Tetramethylbutylphenol</td>
</tr>
<tr>
<td>Absorption Maximum</td>
<td>350 nm</td>
</tr>
<tr>
<td>Molecular Formula</td>
<td>C_{46}H_{50}N_{6}O_{2}</td>
</tr>
<tr>
<td>Molecular Mass</td>
<td>658.86 g/mol</td>
</tr>
<tr>
<td>Tm</td>
<td>195°C</td>
</tr>
<tr>
<td>Solubility in H_{2}O:</td>
<td>&lt; 10^{-6} g/l</td>
</tr>
</tbody>
</table>

**Dispersion Stability of TINOSORB M**

The stability of particles against aggregation depends on their zeta-potential. At the isoelectric point particles may aggregate. The zeta-potential of TINOSORB M was determined as a function of the pH.

In the neutral range, the potential amounts to about -26 mV. With decreasing pH the value of the potential slowly increases eventually reaching the isoelectric point at a pH of about 2 (see FIGURE 1). Within the pH-range commonly used for cosmetic formulations the particles are stable.

![Graph showing zeta potential as a function of pH]  
**FIGURE 1** Zeta potential of Tinosorb M as a function of pH
Absorption spectrum of TINOSORB M

The spectra of TINOSORB M have been measured in dispersion. Sandwich-like cuvettes of 8 μm optical path length have been employed for the quantitative analysis of the extinction, that means the molar extinction or the E(1,1), using different concentrations between 0 and 3% active. With these range one is close to or even within the range of the concentrations employed in sunscreen formulations.

Each spectrum at an individual concentration was measured 10 times and then the average was taken. Because of the scattering an integration sphere attachment has been used (Perkin Elmer Lambda 20 Spectrophotometer).

FIGURE 2 Absorption Spectrum of TINOSORB M

Performance of TINOSORB M

UV-A assessment

The efficacy of a modern sunscreen is characterized not only by its UV-B shielding capacity but also by its UV-A attenuation. Three methods are widely used to document the UV-A performance of a sunscreen. The method required by the Australian authorities, the “Australian Standard”, relates directly to the absolute reduction of UV-A radiation reaching the skin. In contrast, the λc concept and the UV-A/UV-B ratio are measures for the amount of UV-A protection by a specific sunscreen in relation to its overall protection or to its protection in the UV-B, respectively.

In Australia, UV-A protection is recognized when a sunscreen preparation transmits between 320 nm and 360 nm (at a pathlength of 8 μm) less than 10% of the incoming light (13).

3.3% active ingredient (6.6% of TINOSORB M) are necessary to fulfill the requirement of the Australian Standard if no other filters are present.

FIGUR 3 Australian UV-A Standard
The critical wavelength \( \lambda_c \) is a measure of a sunscreen’s extinction capacity in the UV-A range in relation to its overall extinction between 290 nm and 400 nm. The extinction capacity is given by the area under the extinction curve. \( \lambda_c \) is defined as the wavelength at which the area corresponds to 90% of the total area \( A_{290-400} \). The higher the critical wavelength of a sunscreen, the better its UV-A performance (14).

\[
\int_{290}^{\lambda_c} E(\lambda) d\lambda = 0.9 \int_{290}^{400} E(\lambda) d\lambda
\]

Critical wavelength for TINOSORB M comes to 388 nm

**FIGURE 4 Critical Wavelength**

The UV-A/UV-B ratio defines the performance of a sunscreen in the UV-A range (200-400 nm) in relation to its performance in the UV-B range (290-320 nm). It is calculated as the ratio between the areas defined by the UV A and UV B extinction capacity. Both areas are normalized to the range of wavelength involved.

\[
\frac{\int_{320}^{400} A(\lambda) d\lambda}{\int_{290}^{400} A(\lambda) d\lambda} \div \frac{\int_{290}^{400} d\lambda}{\int_{290}^{400} d\lambda}
\]

UV-A/UV-B ratio of TINOSORB M alone amounts to 1.0

**FIGURE 5 UV-A/UV-B ratio**

The ratio 1, indicating a UV filter to absorb comparably in UV-A and UV-B, does not refer to the absolute filtering capacity of a product. If a sunscreen absorbs poorly in the UV-B, the UV-A/UV-B ratio may be higher than 1. If UV-B protection is high, even high absorption in UV-A leads to a ratio <1.
Synergistic effect of TINOSORB M and Octyl Methoxy Cinnamate (OMC)

In combination with UV-B absorbers such as OMC, TINOSORB M can boost the SPF. Two reasons may explain this phenomenon:

- TINOSORB M is also absorbing in the UV-B and short UV-A range
- TINOSORB M is dispersed in the water phase, thus acting complementary to oil-soluble filters.

FIGURE 6 SPF boosting effect with OMC

Photostability of TINOSORB M

TINOSORB M proved extremely photostable. The photostability was measured according to Berset et al. (15) in a solar simulator.

The recovery of TINOSORB M (7% active ingredient in aqueous suspension, 2μl/cm² on a rough quartz plate) after irradiation by 10 MED amounted to > 99 % and by 50 MED to > 98 %. Efficient energy dissipation of the active ingredient, intramolecular hydrogen transfer in the excited state, followed by internal conversion and thermal deactivation (16), may have accounted for the high photostability.

Recovery of TINOSORB M after irradiation according to Berset et al (15)

MED

Minimal Erythema Dose defines the unity of UVR exposure for sun-sensitive individuals (skin phototype II). Its value is 200 J/m².

FIGURE 7 Photostability of TINOSORB M
Compatibility with OMC and its stabilization

TINOSORB M is compatible with other UV filters and may have a stabilizing effect on them. The experiment with OMC shows the positive effect of TINOSORB M.

![Recovery of Octyl Methoxycinnamate (OMC) O/W](image)

After irradiation with 10 MED, 27% of the OMC, when used alone is lost. In the presence of TINOSORB M this loss is only 8%.

**FIGURE 8 Stabilizing effect on OMC**

Incorporation of TINOSORB M

TINOSORB M can readily be incorporated into O/W emulsions, since it comes as an aqueous dispersion. On the other hand incorporation into W/O emulsions is difficult. We therefore only recommend incorporation into O/W emulsions.

Recommendation for use:

- Tinosorb M is best diluted by deionised water. Electrolytes may influence the distribution of the particles.
- Tinosorb M can be added prior to emulsification to the water phase or after preparation of the emulsion, always under slight stirring.
- Tinosorb M may be adjusted to the desired pH (e.g. 5.5) by cosmetically acceptable acids (e.g. 25% citric acid) or by acidic components of the formulation.

Concentrations:

In sunscreen formulations 8-20% (= 4-10% active substance) are recommended. If TINOSORB M is used as the only UV absorbing agent in a sunscreen, a minimum of 6.6 % (= 3.3% active ingredient) is necessary to fulfill the Australian UV-A standard (see above). In combination with oil soluble UV-B absorbers such as OMC or with polymers such as PVP, TINOSORB M can boost the SPF values by synergy.

Safety/Registration Status of TINOSORB M (Active Ingredient)

<table>
<thead>
<tr>
<th>Country</th>
<th>max. Concentration (A.I.)</th>
<th>year of approval</th>
</tr>
</thead>
<tbody>
<tr>
<td>European Union</td>
<td>10%</td>
<td>2000</td>
</tr>
<tr>
<td>Brazil</td>
<td>10%</td>
<td>2000</td>
</tr>
<tr>
<td>Switzerland</td>
<td>10%</td>
<td>1999</td>
</tr>
</tbody>
</table>
Summary
TINOSORB M fulfills all basic requirements for UV filters as defined by De Polo (8) in TABLE 3.

Furthermore TINOSORB M:

- offers the broadest coverage of UV-A
- is inherently photostable
- does contribute considerably to the SPF (boosting effect)
- is compatible with UV-B absorbers
- stabilizes other UV absorbers

**TABLE 3 Requirements for UV Filters and fulfillment by TINOSORB M**

<table>
<thead>
<tr>
<th>Sunscreen agents should possess the following properties (8):</th>
<th>Fulfillment of criteria</th>
<th>TINOSORB M</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 possess absorption maxima in the UV-B and/or UV-A</td>
<td>✓</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2 show high effectiveness at low dosage</td>
<td>✓</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3 be chemically and physically stable</td>
<td>✓</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4 be non-volatile</td>
<td>✓</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5 be compatible with other ingredients of the formulation</td>
<td>✓</td>
<td></td>
<td></td>
</tr>
<tr>
<td>6 be sufficiently soluble in either cosmetic oils/emollients or in water</td>
<td>✓</td>
<td>disperisible in water phase</td>
<td></td>
</tr>
<tr>
<td>7 absence of dermato-toxicological reactions (in darkness and under irradiation)</td>
<td>✓</td>
<td></td>
<td></td>
</tr>
<tr>
<td>8 show minimum skin penetration</td>
<td>✓</td>
<td></td>
<td></td>
</tr>
<tr>
<td>9 be resistant to removal by perspiration</td>
<td>✓</td>
<td></td>
<td>under investigation</td>
</tr>
<tr>
<td>10 be non-staining to the skin and tissues</td>
<td>✓</td>
<td></td>
<td></td>
</tr>
<tr>
<td>11 be practically odorless, tasteless and colorless</td>
<td>✓</td>
<td></td>
<td></td>
</tr>
<tr>
<td>12 be compatible with the ecosystem</td>
<td>✓</td>
<td></td>
<td>EC environmental risk assessment: no concern</td>
</tr>
</tbody>
</table>
References


