New Combination of Ultraviolet Absorbers in an Oily Emollient Increases Sunscreen Efficacy and Photostability

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ABSTRACT

Introduction: It is now recognized that to adequately protect skin from sun damage, sunscreens require a photostable combination of ultraviolet (UV) filters with a suitable level of UVA protection. The total amount of UV filters should be as low as possible to avoid adverse skin reactions, potential environmental impact, and to ensure acceptable texture for better application and usage.

Methods: A synergistic combination of UV filters was selected to obtain a high sun protection factor (SPF) and UVA protection factor (UVA-PF). An oily vehicle was then added to the formula to improve the solubility and the photostability of the lipophilic UV filters.

Results: The combination of filters, i.e., terephthalylidene dicamphor sulfonic acid (TDSA), bis-ethylhexyloxyphenol methoxyphenyl triazin (BEMT), and butyl methoxy dibenzoyl methane (BMDM), obtained an elevated SPF as well as a high UVA-PF. Isopropyl lauroyl sarcosinate (ILS), a derivative of a natural amino acid (sarcosine, also known as N-methylglycine) was introduced in this formulation in order to dissolve the oil-soluble UV absorbers and to photostabilize BMDM. The new sunscreen formulation obtained with this combination is photostable and contains a reduced amount of UV filters compared to other sunscreens with the same level of efficacy.

Conclusion: This report described the steps resulting in the formulation of a new combination of UV filters in an oily emollient, which presents a high UVA-PF (UVA-PF = 38) and a SPF 50+, is photostable, and offers good protection against UV-induced biological damage.
Keywords: Isopropyl lauroyl sarcosinate; Photoprotection factors; Photostability; Sunscreen; Sun protection factor; UV absorbers; UV filters; UV protection

INTRODUCTION

Most people use sunscreens to avoid sunburn, whilst the more educated of those also know that sunscreen can protect their skin from premature aging and cancer [1]. However, the use of sunscreens is far from what could be expected [2]. The reason frequently conveyed by consumers for avoiding sunscreen use is that they are too greasy and leave an unpleasant feeling on the skin. If they are used, they are not applied in sufficient quantity, perhaps due to their unpleasant texture, but also a lack of information regarding their correct usage [3]. Furthermore, skin reactions to sunscreen agents may be an issue. Contact dermatitis and photocontact sensitization can be a concern for some people [4, 5], although it is mostly subjective irritation or discomfort that is the actual problem [6]. Finally, a rising objection to sunscreen use is the potential risk to the environment, particularly for aquatic organisms. However, these concerns may be addressed by lowering the concentration of ultraviolet (UV) filters in the formulations. This has to be achieved without compromising efficacy, which is a difficult challenge.

Increasing evidence of the damaging effects of UVA impel sunscreen formulators to use new UVA filters [7]. Consumers, as well as the European Commission (EC), have also requested greater and wider protection against solar UVA radiation [8]. To meet these demands, researchers developed UVA filters [9]. One of the first filters available was butyl methoxy dibenzoyl methane (BMDM). Unfortunately, it has been shown that this molecule loses part of its absorbance under UV-exposure; it is photo-labile or photo-unstable [10].

For many years, BMDM was the only long-wave UVA filter (maximum wavelength = 357 nm) allowed in Europe and the US. However, photostability has been, and remains, a primary focus for formulators. Photostability is obtained by removing certain UV filters and excipients known to be deleterious to BMDM, and by including ingredients known to improve its photostability [11].

A further challenge for the sunscreen formulator is to reduce the total amount of chemical filters without compromising the efficacy. Therefore, the authors set out to find a synergetic combination of UV filters in terms of sun protection factor (SPF) and UVA protection factor (UVA-PF). In addition, an oily vehicle, which could improve the solubilization of the lipophilic UV filters, as well as ensuring BMDM photostability, was added to this combination.

The photostability, SPF, UVA-PF, and the in vivo efficacy in the prevention of photoreactions observed after yearly sun exposure [e.g., polymorphous light eruption (PLE)] were evaluated for this new complete sunscreen formulation.

MATERIALS AND METHODS

Sunscreen Products

The list of active materials [trade names, International Nomenclature of Cosmetic Ingredients (INCI) names, and maximum absorption for the UV filters] is given in Table 1. The first part of the work was performed with simplex formulas, detailed in
Table 2, and the second part with complete SPF 50+ formulations, listed in Table 3.

**Photostability**

To evaluate the photostability of the BMDM, the residual concentration of 2% of BMDM was introduced in the simplex oil in water emulsion with and without bis-ethylhexyloxyphenol methoxyphenyl triazin (BEMT) and isopropyl lauroyl sarcosinate (ILS), a derivative of a natural amino acid (sarcosine, also known as N-methylglycine) (Sunscreens F, G, and H). This was measured by high-performance liquid chromatography (HPLC) after exposure to UV solar simulated radiation (SSR) with an Atlas Suntest® CPS (Atlas, Chicago, IL, USA), as previously described [12, 13]. The duration of

Table 1 Characteristics of ultraviolet filters

| Trade name  | Manufacturer                                      | Abbreviation | Wavelength at which maximum absorption occurs (nm) |
|-------------|---------------------------------------------------|--------------|---------------------------------------------------|
| Uvinul® 539 | BASF Aktiengesellschaft, Ludwigshafen, Germany    | OC           | 303                                               |
| Mexoryl® SX | L’Oréal, Paris, France                            | TDSA         | 340                                               |
| Tinosorb® S | BASF Aktiengesellschaft, Ludwigshafen, Germany    | BEMT         | 310–345                                           |
| Mexoryl® XL | L’Oréal, Paris, France                            | DTS          | 304–340                                           |
| Parsol® 1789| Givaudan Roue, New Jersey, USA                    | BMDM         | 355                                               |
| Uvinul® T 150| BASF Aktiengesellschaft, Ludwigshafen, Germany  | ET           | 314                                               |
| Eldew® SL-205| Ajinomoto Co., Inc., Tokyo, Japan                 | ILS          | –                                                 |

BEMT bis-ethylhexyloxyphenol methoxyphenyl triazin, BMDM butyl methoxydibenzoylmethane, DTS drometrizole trisiloxane, ET ethylhexyl triazon, ILS isopropyl N-lauroyl sarcosinate, OC octocrylene, TDSA terephthalylidene dicamphor sulfonic acid

Table 2 Composition of ultraviolet filters in Sunscreens A–H

| Chemical          | Sunscreen | A   | B   | C   | D   | E   | F   | G   | H   |
|-------------------|-----------|-----|-----|-----|-----|-----|-----|-----|-----|
| TDSA (%)          |           | –   | 8.11| 2.46| –   | –   | –   | –   | –   |
| BEMT (%)          |           | 8.11| –   | 5.65| –   | 5.65| –   | 2.00| –   |
| BMDM (%)          |           | –   | –   | 1.96| 0.76| 2.00| 2.00| 2.00| –   |
| OC (%)            |           | –   | –   | –   | 6.15| 1.70| –   | –   | –   |
| Total amount of UV absorbers (%) | | 8.11| 8.11| 8.11| 8.11| 8.11| 2.00| 4.00| 2.00|
| Other components (ILS) (%) | | –   | –   | –   | –   | –   | –   | –   | 10.00|

BEMT bis-ethylhexyloxyphenol methoxyphenyl triazin, BMDM butyl methoxydibenzoylmethane, ILS isopropyl N-lauroyl sarcosinate, OC octocrylene, TDSA terephthalylidene dicamphor sulfonic acid, UV ultraviolet
exposure was calculated in order to deliver 18 J/cm² of UVA (320–400 nm), which corresponds to the dose received during a 1 h exposure to the zenithal sun.

Furthermore, the absorption spectra of Sunscreens H and I were measured by UV spectrophotometry after exposure to SSR. Two different doses were given for each sunscreen: one dose was 45 J/cm² of UVA, the other was 75 J/cm² of UVA.

**Table 3** Composition and characteristics of ultraviolet absorbers of SPF 50+ Sunscreens I and J

| Chemical                      | Sunscreen | I    | J    |
|-------------------------------|-----------|------|------|
| TDSA (%)                      | 0.50      | 0.75 |
| BEMT (%)                      | 0.50      | 2.00 |
| BMDM (%)                      | 3.00      | 3.00 |
| Other UV filters (DTS, OC, ET) (%) | 10.00    | 6.00 |
| Total amount of UV absorbers (%) | 14.00   | 11.75 |
| ILS                           | No        | Yes  |
| SPF                           | 62.30 ± 5.70 | 69.60 ± 4.50 |
| UVA-PF                        | 28.40 ± 6.30 | 38.40 ± 9.50 |

*BEMT* bis-ethylhexoxyphenol methoxyphenyl triazin, *BMDM* butyl methoxy dibenzoyl methane, *DTS* drometrizole trisiloxane, *ET* ethylhexyl triazon, *ILS* isopropyl N-lauroyl sarcosinate, *OC* octocrylene, *SPF* sun protection factor, *TDSA* terephthalylidene dicamphor sulfonic acid, *UVA-PF* ultraviolet A protection factor

**SPF and UVA-PF**

The SPF was measured in vivo using the international SPF test method [14]. The UVA-PF, based on the persistent pigment darkening method, was measured using the method used in Japan [15]. The measurements were performed on the simplex emulsions A, B, and C, as well as on the complete Sunscreens I and J (Tables 2, 3). Ten subjects were used for each measurement.

**Protective Effect of Sunscreens Against Reactive Oxygen Species**

RealSkin™ (SkinEthnic laboratories, Lyon, France; 4 cm² full-thickness skin equivalents) is a reconstructed skin (RS) model made of an epidermis and a living dermis. The generation of reactive oxygen species (ROS) was measured using the oxidant sensing probe, 2′,7′-dichlorodihydrofluorescein diacetate (DCFH-DA), as previously described [16]. The RS was loaded by systemic application with freshly prepared DCFH-DA solution for 30 min before the application of sunscreen (A, B, C, D, and E), vehicle treatment, or nothing (the UVA control), which was applied 20 min prior to UVA exposure (10 J/cm², 320–400 nm). The UVA source was the 1.000 W Oriel® (Newport Corporation, CA, USA) solar simulator fitted with Schott AG optical filters UG11 and WG335. Immediately after UVA exposure, ROS generation was measured by spectrofluorimetry (excitation 485 nm; emission 535 nm; Tecan Spectrafluor Plus, Tecan Group Ltd, Switzerland). Each essay was performed on three different RS batches.

In addition, two-photon excited fluorescence (2PEF) was used to detect UV-induced ROS within RealSkin reconstructed epidermis (RE) with three-dimensional (3D) subcellular resolution. Multiphoton imaging was performed using a Zeiss LSM510 Meta microscope. 2PEF was excited by a femtosecond titanium–sapphire laser adjusted to 760 nm, with typically 3 mW power at the sample. Samples were maintained between two cover slides and imaged by use of a 40×, 1.1 numerical aperture, water-immersed, objective lens. The acquisition time per pixel was 2.05 µs. The authors recorded three $210 \times 210 \times 100 \, \mu m^3$
z-stacks in every sample, with 1 μm z-step and 0.6 μm pixel size. Two-dimensional images were combined using Image software (W. Rasband, National Institutes of Health), and quantified (average intensity of fluorescence in each stack).

**In-Vivo Efficacy**

The efficacy of Sunscreen J in preventing cutaneous skin reactions associated with PLE, such as itching, burning, and urticarial papules, was evaluated during an “in use” test conducted under dermatological control during early summer in Cape Town, South Africa. No ethic committee approval was required for this test. Forty-one volunteers of Caucasian origin prone to PLE (at least three episodes, with one during the last summer), were recruited. After receiving instructions for use, the volunteers were asked to apply the product instead of their usual sunscreen at least once a day on their face, neck, and arms for 2 weeks. After swimming, volunteers had to re-apply the product. Volunteers were asked to report any cutaneous reactions during the test, which were confirmed by dermatologist examination, and to complete a questionnaire about the cosmetic qualities of the product.

**RESULTS**

The Association of Terephthalylidene Dicamphor Sulfonic Acid and BEMT Has a Synergistic Effect in Terms of Protection Factors

With a total concentration of 8.11% of UV filters [Sunscreen C: 2.46% terephthalylidene dicamphor sulfonic acid (TDSA), 5.65% BEMT] in a simplex emulsion, the authors obtained a

![Fig. 1 SPF and UVA-PF comparison of sunscreens A, B, and C showing the synergistic effect of the association TDSA and BEMT. BEMT bis-ethylhexyloxyphenol methoxyphenyl triazin, SPF sun protection factor, TDSA terephthalylidene dicamphor sulfonic acid, UVA-PF ultraviolet A protection factor](image)
SPF value of 22.2 ± 3.5 and a UVA-PF of 13.4 ± 1.5 (Fig. 1). With 8.11% TDSA alone in the same emulsion (Sunscreen B), the SPF was 4.6 ± 1.1 and the UVA-PF 4.9 ± 0.1. With 8.11% BEMT alone in the same emulsion (Sunscreen A), the SPF was 9.2 ± 2 and the UVA-PF 5.3 ± 0.9 (Fig. 1).

**Association of TDSA and BEMT Offers Optimal Protection Against UVA-Induced Oxidative Stress**

Reactive oxygen species detection induced by UVA can be used to rate different sunscreen products from the most to the least effective in reducing oxidative stress. Figure 2 shows ROS detection induced by UVA, and suggests that Sunscreen A ≈ B ≈ C > E > D > vehicle > UVA control. These sunscreen products all have the same total UV filter content (8.11%, Table 2).

Sunscreens C, D, and E have a similar UV absorption spectrum. To validate this result in the different epidermis layers, the authors performed a multiphoton acquisition test, as shown in Fig. 3.

**BMDM is Photostabilized by Association with BEMT or ILS**

After 1 h of exposure to SSR, which includes 18 J/cm² of total UVA, only 30% of the initial 2% of BMDM introduced in a simplex emulsion (Sunscreen F) was detected by HPLC. When 2% BEMT was added to this simplex emulsion (sunscreen G), a higher percentage of BMDM remained (approximately 78%). Similarly, the addition of 10% ILS (which is not a filtering molecule) to this simplex emulsion (Sunscreen H) allowed up to 75% photostabilization of BMDM, as shown on Fig. 4.

**Fig. 2** Photoprotective efficacy of Sunscreens A, B, C, D, and E (same total UV filter content of 8.11%) against UVA-induced ROS measured by spectrofluorimetry after DCFH-DA incubation on reconstructed human skin. Sunscreen C containing TDSA and BEMT offers good protection against UVA-induced oxidative stress. **BEMT** bis-ethylhexyloxyphenol methoxyphenyl triazin, **DCFH-DA** 2',7'-dichlorodihydrofluorescein diacetate, **ROS** reactive oxygen species, **TDSA** terephthalylidene dicamphor sulfonic acid
The association of UV filters, including TDSA, BEMT, BMDM, and ILS, increased both the SPF and the UVA-PF even if the total amount of UV absorbers decreased from 14% in Sunscreen I (without ILS) to 11.75% in Sunscreen J (with ILS). The SPF and UVA-PF (±SD) values are given at the bottom of Table 3.

**SPF and UPA-PF of Sunscreens I and J**

The association of UV filters, including TDSA, BEMT, BMDM, and ILS, increased both the SPF and the UVA-PF even if the total amount of UV absorbers decreased from 14% in Sunscreen I (without ILS) to 11.75% in Sunscreen J (with ILS). The SPF and UVA-PF (±SD) values are given at the bottom of Table 3.

**Sunscreen J is Photostable**

Figure 5 shows the UV absorption spectra of Sunscreen J before and after SSR exposure, which included 45 or 75 J/cm² of UVA. These spectra are the mean of 15 scans and are given in adjusted normalized mean monochromatic absorption factor (mAF; lambda).

**Sunscreen J Prevents PLE**

Under “in-use” test conditions, under the South African sun, only one subject of the 41 participants had a notable reaction, which was diagnosed by a dermatologist as sunburn due to overexposure and/or poor application of the tested product. Sunscreen J was judged to be efficient in preventing skin reactions...
Fig. 4 Comparison of the remaining percentage of BMDM in Sunscreen F, G, and H evaluated by HPLC after 1 h SSR-exposure. BMDM is photostabilized by association with BEMT or ILS. BEMT bis-ethylhexyloxyphenol methoxyphenyl triazin, BMDM butyl methoxy dibenzoyl methane, HPLC high-performance liquid chromatography, ILS isopropyl lauroyl sarcosinate, SSR solar simulated radiation.

Fig. 5 UV absorption spectra of Sunscreen J before and after exposure to SSR doses, including either 45 or 75 J/cm² UVA, and demonstrating the photostability of this formula. SSR solar simulated radiation.
(declarative judgment) associated with PLE by 85% of the volunteers. Sunscreen J was also highly appreciated for its cosmetic qualities (83% of the volunteers) and its efficacy against sunburn (95% of the volunteers).

**DISCUSSION**

Over the past 20 years, an increasing number of publications have reported the damaging effects of UVA radiation. It has been proven that UVA radiation induces molecular, cellular, and clinical damage, which may lead to photo-induced aging, immune system depression, altered gene expression, oncogenes, and tumor suppressor gene modulation partly responsible for skin cancer development [17].

In parallel to this increased knowledge, progress has been achieved in sunscreen technology. A variety of UVA filters are now available and the present authors have combined them with UVB filters to produce a high protection and photostability with a minimum concentration of active ingredients. However, further UVA filters could be investigated for their synergistic qualities. There remains a need to improve sun-care formulations, particularly to provide broad UVA protection without losing cosmetic properties. Additionally, further development of new filter combinations with a low environmental impact should be continued.

As knowledge increases in photochemistry and photobiology, formulators face many challenges when developing new sunscreens. Simply including UV filters in a formulation base does not ensure efficacy, photostability, or an aesthetically pleasing texture that is easy to apply, i.e., a product that the consumer will apply and continue to re-apply.

The fact that there is an increasing concern about the possible impact of chemical filters on the environment pushes formulators to try to reduce the amount of filters without decreasing the efficacy. This is an additional challenge.

To address these demands, a combination of UV filters was selected and was shown to be synergistic in terms of SPF and UVA-PF. In addition, the spectrofluorimetry measurements validated the performance of the TDSA and BEMT combination in reducing oxidative stress in both the stratum corneum and the living epidermis layers.

The ILS, an oily vehicle, was expected to improve the solubility of the lipophilic UV filters, as well as BMDM photostability. The authors successfully developed a new sunscreen formulation that included the filters TDSA, BEMT, and BMDM within the ILS vehicle. The present results clearly showed that this new association of filters with ILS oil technology obtained both high sunscreen photoprotective efficacy and photostability over the entire UV range.

In conclusion, the UVA filters, TDSA, BEMT, and BMDM, solubilized in the oily derivative of the ILS, and combined with an UVB filter (octocrylene) and titanium dioxide, produce a sunscreen with a high UVA-PF (UVA-PF 38) and a SPF 50+. This product is photostable even after >4 h exposure under zenithal sun. It prevents UV-induced biological damage as well as skin reactions of PLE.

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**Conflict of interest.** All authors are employees of L’Oréal, France.

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