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(54) **Title**: COMPOSITION AND COMBINATION OF BMDBM PHOTOSTABILIZERS AND SUNSCREENS

(57) **Abstract**: The present invention concerns a composition containing a photostabilized combination of Butyl Methoxydibenzoylmethane (BMDBM), Bis-Ethylhexyloxyphenol Methoxyphenyl Triazine (BEMT), and Methylene Bis- Benzotriazolyl Tetramethylbutylphenol (MBBT) wherein: (i) - the BEMT/BMDBM mass ratio is greater than or equal to 1 and preferably greater than or equal to 1.5; (ii) - the content of BMDBM is comprised between 1% and 5% by weight with regard to the total weight of the composition; (iii) - the quantity of MBBT is comprised between 3% and 7% by weight with regard to the total weight of the composition, said combination containing no octocrylene, PABA or ethylhexyl methoxycinnamate, and a pharmaceutically or cosmetically acceptable excipient.

COMPOSITION AND COMBINATION OF BMDBM PHOTOSTABILIZERS AND SUNSCREENS

The present invention concerns a combination of sunscreens for photostabilization of Butyl Methoxydibenzoylmethane (BMDBM).

Protection against UVA (320-400 nm) must be substantial to limit damage related to prolonged exposure that could lead to changes in the skin, acceleration of photoaging, loss of skin elasticity, etc.

First of all, we will review the nomenclature and abbreviations of the main filters involved in the scope of the present invention:

- Butyl Methoxydibenzoylmethane (BMDBM) = avobenzone = CAS Registry Number: 70356-09-1, which filter is sold under the DSM trademark Parsol1789®,
- 2,4-Bis[4-(2-ethylhexyloxy)-2-hydroxyphenyl]-6-(4-methoxyphenyl)-1,3,5-triazine = Bis-Ethylhexyloxyphenol Methoxyphenyl Triazine (BEMT) = Bemotrizinol = CAS Registry Number: 187393-00-6,

which filter is sold under the BASF trademark Tinosorb S®,

- 2,2'-Methylene-bis-(6-(2H-benzotriazole-2-yl)-4-(1,1,3,3-tetramethylbutyl)-phenol = Methylene Bis-Benzotriazolyl Tetramethylbutylphenol (MBBT) = Bisoctrizole = CAS Registry Number: 103597-45-1, which filter is sold under the BASF trademark Tinosorb M®.

Butyl Methoxydibenzoylmethane (BMDBM) is not a UV radiation stable filter. A cleavage of the molecule takes place, which breaks down into various chemical elements with no absorbent activity.

In combination with other filters (for example ethylhexyl methoxycinnamate), BMDBM can still break down and lose its photoprotective properties.

BMDBM is often combined with octocrylene, which photostabilizes it, or even PABA® (para-aminobenzoic acid). However, octocrylene has the drawback of being a powerful allergen which causes contact eczema in children and cross allergies with ketoprofen.

More recently, the prior art includes document US20110212040 which teaches the stabilization of BMDBM by addition of synthetic or natural phytoene or phytofluene.

The goal of the present invention is to offer a new alternative for photostabilizing BMDBM while developing a photoprotective system according to current regulations.

The present invention concerns a combination containing Butyl Methoxydibenzoylmethane (BMDBM), Bis-Ethylhexyloxyphenol Methoxyphenyl Triazine (BEMT), and

Methylene Bis-Benzotriazolyl Tetramethylbutylphenol (MBBT) characterized in that:

- the BEMT/BMDBM mass ratio is greater than or equal to 1 and preferably greater than or equal to 1.5 and
- said combination does not contain octocrylene.

The present invention concerns a photostabilized combination containing Butyl Methoxydibenzoylmethane (BMDBM), Bis-Ethylhexyloxyphenol Methoxyphenyl Triazine (BEMT), and Methylene Bis-Benzotriazolyl Tetramethylbutylphenol (MBBT):

i. - the BEMT/BMDBM mass ratio is greater than or equal to 1 and preferably greater than or equal to 1.5 and
ii. the content of BMDBM is comprised between 1% and 5% by weight with regard to the total weight of the composition,
iii. the quantity of MBBT is comprised between 3% and 7% by weight with regard to the total weight of the composition,

said combination containing no octocrylene, PABA or ethylhexyl methoxycinnamate.

In one particular embodiment of the invention, the BEMT/ BMDBM mass ratio is less than or equal to 5, preferably less than or equal to 4 and even more preferentially less than or equal to 3.

Preferentially, the BEMT/BMDBM mass ratio will be chosen in the range from 1 to 5, preferentially 1.5 to 5 and even more preferentially 1.5 to 3.

According to another characteristic of the invention, the BEMT content is comprised between 2% and

6% by weight with regard to the total weight of the composition.

In the framework of the present invention, the BEMT/BMDBM mass ratio has to be considered as a predominantly characteristic feature. That means that the concentration of the different solar filters BEMT, BMDBM and MBBT will have to be adjusted within each concentration rate in order for said mass ratio to be first and foremost respected.

Another subject of the present invention concerns a composition containing a combination of BMDBM, BEMT and MBBT characterized in that:

- the BEMT/BMDBM mass ratio is greater than or equal to 1 and preferably greater than or equal to 1.5 and
- said combination does not contain octocrylene,
- the quantity of MBBT is comprised between 3 % and 7% by weight with regard to the total weight of the composition,
- and with a pharmaceutically or cosmetically acceptable excipient.

Another subject of the present invention concerns a composition containing a combination of BMDBM, BEMT and MBBT characterized in that:

- the BEMT/BMDBM mass ratio is greater than or equal to 1 and preferably greater than or equal to 1.5,
- said combination contains no octocrylene, PABA or ethylhexyl methoxycinnamate.
- the quantity of MBBT is comprised between 3 % and 7% by weight with regard to the total weight of the composition,

- and with a pharmaceutically or cosmetically acceptable excipient.

According to another characteristic of the present invention, the composition above also has a content of Bis-Ethylhexyloxyphenol Methoxyphenyl Triazine (BEMT) comprised between 2 and 6% by weight with regard to the total weight of the composition.

According to another characteristic of the present invention, the composition above also has a content of Butyl Methoxydibenzoylmethane (BMDBM) comprised between 1 and 5 % by weight with regard to the total weight of the composition.

Finally, according to another characteristic of the present invention, the composition above also has another filter, preferably between 1 and 10 % by weight with regard to the total weight of the composition.

According to another aspect, the invention also concerns the use of a combination of Butyl Methoxydibenzoylmethane (BMDBM) Bis-Ethylhexyloxyphenol Methoxyphenyl Triazine (BEMT), and Methylene Bis-Benzotriazolyl Tetramethylbutylphenol (MBBT), in which the BEMT/BMDBM mass ratio is greater than or equal to 1 and preferably greater than or equal to 1.5, and in the absence of octocrylene, PABA and ethylhexyl methoxycinnamate to photostabilize BMDBM in a photoprotective composition.

"Photostabilization, photostable or photostability" mean, in the sense of the present invention, that after irradiation of 5 MED and preferably 10 MED, the following is retained:

- at least 80% and preferably at least 85% and even more preferentially at least 90% of the total SPF (290 to 400 nm); and
- at least 80% and preferably at least 85% and even more preferentially at least 90% for the UVA part (320 to 400 nm) of the total SPF.

Preferably, the combination or composition according to the present invention also contains no PABA®.

Combinations according to the present invention represent photostable photoprotective systems combining organic fat-soluble filters (such as BMDBM and BEMT) which are perfectly and evenly distributed on the skin and organic screens (like MBBT) dispersed in the aqueous phase for a better absorption response and therefore better efficacy.

Preferably, the compositions according to the present invention are adjusted so as to obtain a photoprotective system:

- having the broadest possible UV absorption spectrum (maximum spectral coverage of 290 to 400 nm)
- according to current regulations, that is having a critical wavelength λc greater than or equal to 370 nm and an SPF/UVA ratio less than or equal to 3.

More preferentially, the composition according to the present invention may correspond to the maximum category in terms of sun protection, that is, having SPF 50+.

One or more of the following UVB filters can be added to the composition according to the invention:

- Salicylates: Homosalate, ethylhexyl salicylate
- Phenylbenzimidazole Sulfonic Acid
- Ethylhexyl Triazone, Diethylhexyl Butamido Triazone
- TiO2
- Tris-biphenyl triazine.

The UVB filters indicated above are UVB filters considered satisfactory from the point of view of tolerance, toxicity, photostabilization and UV absorption. Thus, as a precaution regarding homosalate, preferably the following UVB filter or filters are preferred:

- Ethylhexyl salicylate
- Phenylbenzimidazole Sulfonic Acid
- Ethylhexyl Triazone, Diethylhexyl Butamido Triazone
- TiO2
- Tris-biphenyl triazine.

Furthermore, the composition will preferentially be stable to light, air, humidity and temperature.

Another subject of the present invention concerns a composition containing a photostabilized combination comprising

- Butyl Methoxydibenzoylmethane (BMDBM), Bis-Ethylhexyloxyphenol Methoxyphenyl Triazine (BEMT), and Methylene Bis-Benzotriazolyl Tetramethylbutylphenol (MBBT) wherein:

i. the BEMT/BMDBM mass ratio is greater than or equal to 1 and preferably greater than or equal to 1.5 and
ii. the content of BMDBM is comprised between 1% and 5% by weight with regard to the total weight of the composition,

iii. the quantity of MBBT is comprised between 3% and 7% by weight with regard to the total weight of the composition,

- in addition, one or more UVB filters chosen from among the following filters:
  - Ethylhexyl salicylate
  - Phenylbenzimidazole Sulfonic Acid
  - Ethylhexyl Triazone, Diethylhexyl Butamido Triazone
  - TiO2
  - Tris-biphenyl triazine

and a pharmaceutically or cosmetically acceptable excipient.

In one particular embodiment of the invention, the quantity of the UVB filter or filters is comprised in total between 1 and 10% by weight with regard to the weight of the composition.

In another embodiment of the invention, the composition contains a single additional UVB filter in an amount of 1% to 10% by weight with regard to the weight of the composition and preferably in an amount of 1% to 5% by weight with regard to the weight of the composition.

In one particular embodiment of the invention, the composition will contain a single UVB filter chosen from among the following filters:

- Ethylhexyl salicylate
- Phenylbenzimidazole Sulfonic Acid
- Ethylhexyl Triazone, Diethylhexyl Butamido Triazone
- TiO2
- Tris-biphenyl triazine

The present invention finally concerns the use of a combination containing:

- Butyl Methoxydibenzoylmethane (BMDBM), Bis-Ethylhexyloxyphenol Methoxyphenyl Triazine (BEMT), and Methylene Bis-Benzotriazolyl Tetramethylbutylphenol (MBBT), in which the BEMT/BMDBM mass ratio is greater than or equal to 1 and preferably greater than or equal to 1.5,
- one or more UVB filters chosen from among the following filters and preferably only 1 UVB filter chosen from among the following filters:
    - Ethylhexyl salicylate
    - Phenylbenzimidazole Sulfonic Acid
    - Ethylhexyl Triazone, Diethylhexyl Butamido Triazone
    - TiO2
    - Tris-biphenyl triazine

to photostabilize BMDBM in a photoprotective composition.

"Pharmaceutically or cosmetically acceptable excipient" means any adjuvant or excipient for manufacturing, preserving or administering the composition.

Compositions according to the invention may more particularly be sunscreen compositions. They are particularly intended for protecting skin (face and/or body) and/or hair from ultraviolet radiation.

The present invention also concerns a method for protecting skin (face and/or body) and/or hair from ultraviolet radiation comprising applying a composition

described previously onto the skin (face and/or body) and/or hair.

Compositions according to the invention may also comprise conventional cosmetic or pharmaceutical adjuvants, in particular chosen from among fats, organic solvents, thickeners, softeners, opacifiers, stabilizers, emollients, anti-foaming agents moisturizers, fragrances, preservatives, polymers, fillers, sequestering agents, bactericides, odor absorbers, basifying or acidifying agents, surfactants, free-radical scavengers, antioxidants, vitamins E and C, alpha-hydroxy acids or any other ingredient usually used in cosmetics or pharmaceuticals, particularly for the manufacture of sunscreen compositions.

The fats may consist of an oil or wax or mixtures thereof, and they also include fatty acids, fatty alcohols and fatty acid esters. The oils may be chosen from among animal, vegetable, mineral or synthetic oils and notably Vaseline oil, paraffin oil, volatile or nonvolatile silicone oil, isoparaffins, polyolefins and fluorinated and perfluorinated oils. Likewise, the waxes may be chosen from among animal, fossil, vegetable or synthetic waxes such as beeswax, candelilla wax, carnauba wax, petroleum wax (or microcrystalline wax), paraffin, and mixtures thereof.

The composition may further comprise a water-miscible polyol at room temperature (around 25°C), in particular chosen from among polyols having from 2 to 20 carbon atoms, preferably having 2 to 10 carbon atoms, and preferentially having 2 to 6 carbon atoms, such as glycerin; glycol derivatives such as propylene

glycol, butylene glycol, pentylene glycol, hexylene glycol, dipropylene glycol and diethylene glycol; glycol ethers such as C1-C4 alkyl ethers of mono-, di- or tri-propylene glycol, C1-C4 alkyl ethers of mono-, di-or triethylene glycol and mixtures thereof.

The composition may also comprise thickeners or rheology modifying agents, such as, for example, non-ionic ethoxylated hydrophobically modified urethanes, polycarboxylic acid thickeners such as acrylates/steareth 20 methacrylate copolymers, carbomers, crosslinked acrylate copolymers and mixtures thereof.

The composition may also comprise acids and bases to adjust the pH zone of said composition. The bases may be mineral (sodium hydroxide, potassium hydroxide, ammonia, etc.) or organic such as mono-, di- or triethanolamine, aminomethylpropanediol, N-methylglucamine, basic amino acids such as arginine and lysine, and mixtures thereof.

The composition may also comprise skin conditioners. Examples of skin conditioners include, but are not limited to, anionic, cationic and nonionic surfactants such as sodium lauryl sulfate, sodium dioctyl sulfosuccinate, sodium stearate, ester sorbitan, ethoxylated fatty acids, ethoxylated fatty alcohols such as trideceth-9 and PEG-5 ethylhexanoate; any other emulsifier and conditioning agent known to the skilled person, and mixtures thereof.

Compositions according to the invention may further comprise additional active agents chosen in particular from among from moisturizers, desquamating

agents, agents for improving barrier function, depigmenting agents, antioxidants, skin tighteners, anti-glycation agents, agents stimulating the synthesis of dermal and/or epidermal macromolecules and/or preventing their degradation, agents stimulating fibroblast or keratinocyte proliferation and/or keratinocyte differentiation, NO synthase inhibitors, agents increasing the activity of the sebaceous gland, tensioning agents, lipo-restructuring agents, slimming agents, agents promoting skin microcirculation, soothing and/or irritant agents, sebo-regulating or anti-seborrheic agents, astringents, wound healing agents, anti-inflammatory agents, anti-acne agents, and mixtures thereof.

Compositions according to the invention may be presented in any appropriate form for topical application, especially on the skin and/or hair. In particular, they may be in the form of emulsions obtained by dispersing a fatty phase in an aqueous phase, for example one or multiple oil-in-water or water-in-oil emulsions, or in the form of a gel or an anhydrous liquid, pasty or solid product, or in the form of a dispersion in the presence of spherules. Compositions according to the invention may also be less fluid and may be in the form of a white or colored cream, ointment, milk, lotion, serum, paste, mask, powder, solid stick or optionally, an aerosol, foam or spray. These compositions may also be water resistant.

In vitro method of evaluating total UV and UVA photostability

A) Material

- *UV spectrophotometer:*

The spectrophotometer measures the spectral transmittance through a plate with and without a layer of a sunscreen composition on its surface.

The spectrophotometer should allow measurements comprised between 290 nm and 400 nm. To reduce variability between measurement readings and to compensate for the lack of uniformity of the product layer, it is recommended that the reading zone of the sites be at least 0.5 cm^2.

The spectrophotometer used for these measurements is the Labsphere® UV-1000S or 2000S.

- *Plate:*

The plate is the material onto which the sunscreen composition is applied. This material must be transparent to UV, non-fluorescent, photostable and inert with regard to the compounds of the compositions tested. For this protocol, polymethyl methacrylate (PMMA) plates proved ideal.

- *UV Source:*

The UV source is a solar simulator with a xenon arc lamp diffusing a visible + UVA + UVB spectrum. The UV source used for this study is Suntest CPS+ (Atlas).

B) Method:

- *Measuring transmission through an untreated plate:*

Firstly, it is necessary to determine UV transmission through a control plate. This is prepared by spreading a few microliters of glycerin so that the surface of the plate is completely covered.

- *Sample application:*

The sample to be tested is applied onto the PMMA plate in an amount of 1.3 mg/cm^2 (actual quantity remaining on the plate). To guarantee the accuracy of the amount and the reproducibility of the results, the application zone is larger than 10 cm^2.

The sample to be tested is applied in the form of a large number of small drops of the same volume, distributed over the entire surface of the plate.

In order to ensure that the quantity of the product is correct, a method of validating the quantity of product applied must be adopted (for example: weigh the plate before and after application of the product).

After application of the defined quantity of sample, the sample should be spread over the entire plate as quickly as possible (less than 30 seconds).

The sample is then placed for 15 minutes in the dark at room temperature in order to promote the formation of a homogenous film.

- *Measuring transmission through a plate treated with a sample:*

The plate treated with the sample is analyzed with the spectrophotometer and the mean value of UV radiation transmission through the sample is determined for each wavelength from 290 nm to 400 nm (using the

monochromatic absorbance data measured on the different areas of the plate).

- *Number of measurements:*

At least three PMMA plates should be prepared for each sample. Each plate should be measured in at least nine different regions unless almost the entire surface is measured by spectrophotometry.

C) Calculation of photostability:

Calculation of SPF and UVA (PPD) in vitro from absorbance data A(λ) before and after irradiation with doses of 5 and 10 MED.

$$\text{SPF in vitro} = \frac{\int_{\lambda=290\,nm}^{\lambda=400\,nm} E(\lambda) * S(\lambda) * d\lambda}{\int_{\lambda=290\,nm}^{\lambda=400\,nm} E(\lambda) * S(\lambda) * 10^{-A(\lambda)} * d\lambda}$$

Wherein:

- E(λ) = Erythemal effectiveness spectrum
- S(λ) = Solar spectral irradiance
- A(λ) = Sample absorbance
- dλ = Wavelength variation (1 nm)

$$\text{PPD in vitro} = \frac{\int_{\lambda=320\,nm}^{\lambda=400\,nm} P(\lambda) * I(\lambda) * d\lambda}{\int_{\lambda=320\,nm}^{\lambda=400\,nm} P(\lambda) * I(\lambda) * 10^{-A(\lambda)} * d\lambda}$$

Wherein:

$P(\lambda)$ = PPD action spectrum (Persistent Pigment Darkening)

$I(\lambda)$ = Solar spectral irradiance

$A(\lambda)$ = Sample absorbance

$d\lambda$ = Wavelength variation (1 nm)

Calculation of photostability from the following formulas:

$$\text{Total UV photostability} = \frac{\text{SPF before irradiation}}{\text{SPF after irradiation}}$$

$$\text{UVA photostability} = \frac{\text{PPD before irradiation}}{\text{PPD after irradiation}}$$

Composition examples

COMPOSITION 1

Ingredients	%
Butyl Methoxydibenzoylmethane	1-5
Bis-Ethylhexyloxyphenol Methoxyphenyl Triazine	2-6
Methylene Bis-Benzotriazolyl Tetramethylbutylphenol	3-7
Glycerin	10.0
Demineralized water	QSP 100
Na2EDTA	0.1
Xanthan gum	0.3
C12-C15 alkyl benzoate	25.0
Preservatives	qs
Stearyl alcohol	2.5
Glycerol monostearate	2.5
Potassium cetyl phosphate	1.8

COMPOSITION 2

Ingredients	%
Butyl Methoxydibenzoylmethane	1-5
Bis-Ethylhexyloxyphenol Methoxyphenyl Triazine	2-6
Methylene Bis-Benzotriazolyl Tetramethylbutylphenol	3-7
UVB filter	1-10
Glycerin	10.0
Demineralized water	QSP 100
Na2EDTA	0.1
Xanthan gum	0.3
C12-C15 alkyl benzoate	25.0
Preservatives	qs
Stearyl alcohol	2.5
Glycerol monostearate	2.5
Potassium cetyl phosphate	1.8

Photostability results

Photostability:	Composition 1	Composition 2
Total UV - 5 MED	96%	93%
UVA - 5 MED	95%	92%
Total UV - 10 MED	92%	90%
UVA - 10 MED	91%	89%

CLAIMS

1. Composition containing a photostabilized combination of Butyl Methoxydibenzoylmethane (BMDBM), Bis-Ethylhexyloxyphenol Methoxyphenyl Triazine (BEMT), and Methylene Bis-Benzotriazolyl Tetramethylbutylphenol (MBBT) wherein:
   i. the BEMT/BMDBM mass ratio is greater than or equal to 1 and preferably greater than or equal to 1.5,
   ii. the content of BMDBM is comprised between 1% and 5% by weight with regard to the total weight of the composition,
   iii. the quantity of MBBT is comprised between 3% and 7% by weight with regard to the total weight of the composition,

   said combination containing no octocrylene, PABA or ethylhexyl methoxycinnamate,

   and a pharmaceutically or cosmetically acceptable excipient.

2. Composition according to claim 1, characterized in that the BEMT content is comprised between 2% and 6% by weight with regard to the total weight of the composition.

3. Composition according to claim 2, characterized in that it contains one or more additional filters present in an amount of 1% to 10% by weight in all with regard to the weight of the composition.

4. Composition according to claim 3, characterized in that the additional filter is a UVB filter chosen from among the following filters:

- Ethylhexyl salicylate
- Phenylbenzimidazole Sulfonic Acid
- Ethylhexyl Triazone, Diethylhexyl Butamido Triazone
- TiO2
- Tris-biphenyl triazine

as well as mixtures thereof.

5. Composition according to claim 4, characterized in that it contains a single additional UVB filter present in an amount of 1% to 10% by weight with regard to the weight of the composition and preferably present in an amount of 1% to 5% by weight with regard to the weight of the composition.

6. Composition according to any one of claims 1 to 5, for its use as a photoprotective system.

7. Use of a combination of Butyl Methoxydibenzoylmethane (BMDBM) Bis-Ethylhexyloxyphenol Methoxyphenyl Triazine (BEMT), and Methylene Bis-Benzotriazolyl Tetramethylbutylphenol (MBBT), in which the BEMT/BMDBM mass ratio is greater than or equal to 1 and preferably greater than or equal to 1.5, and in the absence of octocrylene, PABA and ethylhexyl methoxycinnamate to photostabilize BMDBM in a photoprotective composition.

8. Use according to claim 7, characterized in that the BMDBM content is comprised between 1% and 5% by weight with regard to the total weight of the composition.

9. Use according to one of claims 7 or 8, characterized in that the BEMT content is comprised between 2% and 6% by weight with regard to the total weight of the composition.

10. Use according to one of claims 7 to 9, characterized in that the MBBT content is comprised between 3 % and 7% by weight with regard to the total weight of the composition.

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(54) Title: COMPOSITION AND ASSOCIATION OF SUNSCREENS FOR PHOTOSTABILIZING BUTYL METHOXYDIBENZOYLMETHANE (BMDBM)

(57) Abstract: The present invention concerns a composition containing a photostabilized combination of Butyl Methoxydibenzoylmethane (BMDBM), Bis-Ethylhexyloxyphenol Methoxyphenyl Triazine (BEMT), and Methylene Bis- Benzotriazolyl Tetramethylbutylphenol (MBBT) wherein: (i) - the BEMT/BMDBM mass ratio is greater than or equal to 1 and preferably greater than or equal to 1.5; (ii) - the content of BMDBM is comprised between 1% and 5% by weight with regard to the total weight of the composition; (iii) - the quantity of MBBT is comprised between 3% and 7% by weight with regard to the total weight of the composition, said combination containing no octocrylene, PABA or ethylhexyl methoxycinnamate, and a pharmaceutically or cosmetically acceptable excipient.

INTERNATIONAL SEARCH REPORT

International application No
PCT/EP2013/051777

A. CLASSIFICATION OF SUBJECT MATTER
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B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
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Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
EPO-Internal, CHEM ABS Data, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	EP 1 308 153 A2 (BEIERSDORF AG [DE]) 7 May 2003 (2003-05-07) pages 16-19; examples 2.5,4.3,6.3 claims 1,3,7	1-10
A	WO 02/43656 A2 (AVON PROD INC [US]; KALAFSKY ROBERT E [US]; PECHKO ANDREW H [US]) 6 June 2002 (2002-06-06) page 10; example 2	1-10
A	EP 1 764 081 A1 (JOHNSON & JOHNSON CONSUMER FR [FR]) 21 March 2007 (2007-03-21) page 13; example 1	1-10
A	DE 101 35 258 A1 (BEIERSDORF AG [DE]) 6 February 2003 (2003-02-06) pages 17-18; examples 1.5,4.4,5.3	1-10

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[X] Further documents are listed in the continuation of Box C.

[X] See patent family annex.

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"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
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Name and mailing address of the ISA/	Authorized officer
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INTERNATIONAL SEARCH REPORT

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C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
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X	EP 1 093 797 A1 (OREAL [FR]) 25 April 2001 (2001-04-25) pages 12-13, paragraphs 0001,0022,0030-0031,0040; claims 14,21	1-10
A	GB 2 439 618 A (RECKITT & COLMANN PROD LTD [GB]) 2 January 2008 (2008-01-02) claims 1-3	1-6

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International application No
PCT/EP2013/051777

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权利要求书1页 说明书9页

(54)发明名称

用于光稳定丁基甲氧基二苯甲酰基甲烷(BMDBM)的防晒剂的组合物和组合

(57)摘要

本发明涉及一种含有丁基甲氧基二苯甲酰基甲烷(BMDBM)、双-乙基己氧基苯酚甲氧基苯基三嗪(BEMT)和亚甲基双-苯并三唑基四甲基丁基苯酚(MBBT)的经光稳定化的组合和药物可接受或化妆品可接受的赋形剂的组合物,其中:(i)-BEMT/BMDBM质量比大于或等于1,且优选大于或等于1.5;(ii)-所含BMDBM的含量以组合物的总重量计在1重量%和5重量%之间;(iii)-所含MBBT的量以组合物的总重量计在3重量%和7重量%之间,所述组合不含氰双苯丙烯酸辛酯、PABA或乙基己基甲氧基肉桂酸酯。

CN 104080437 A

1. 含有丁基甲氧基二苯甲酰基甲烷 (BMDBM)、双 - 乙基己氧基苯酚甲氧基苯基三嗪 (BEMT) 和亚甲基双 - 苯并三唑基四甲基丁基苯酚 (MBBT) 的经光稳定化的组合和药物可接受或化妆品可接受的赋形剂的组合物，其中 ：

i. BEMT/BMDBM 质量比大于或等于 1，且优选大于或等于 1.5，

ii. 所含 BMDBM 的含量以组合物的总重量计在 1 重量％和 5 重量％之间，

iii. 所含 MBBT 的量以组合物的总重量计在 3 重量％和 7 重量％之间，

所述组合不含氰双苯丙烯酸辛酯、PABA 或乙基己基甲氧基肉桂酸酯。

2. 根据权利要求 1 所述的组合物，其特征在于，所含 BEMT 含量以组合物的总重量计在 2 重量％和 6 重量％之间。

3. 根据权利要求 2 所述的组合物，其特征在于，其含有以组合物的重量计以总共 1 重量％至 10 重量％的量存在的一种或多种另外的滤光剂。

4. 根据权利要求 3 所述的组合物，其特征在于，所述另外的滤光剂为选自如下滤光剂的 UVB 滤光剂 ：

- 乙基己基水杨酸酯
- 苯基苯并咪唑磺酸
- 乙基己基三嗪酮、二乙基己基丁酰胺基三嗪酮
- TiO_2
- 三 - 联苯三嗪

以及它们的混合物。

5. 根据权利要求 4 所述的组合物，其特征在于，其含有以组合物的重量计以 1 重量％至 10 重量％的量，优选以组合物的重量计以 1 重量％至 5 重量％的量存在的单个另外的 UVB 滤光剂。

6. 用作光防护体系的根据权利要求 1 至 5 中任一项所述的组合物。

7. 丁基甲氧基二苯甲酰基甲烷 (BMDBM)、双 - 乙基己氧基苯酚甲氧基苯基三嗪 (BEMT) 和亚甲基双 - 苯并三唑基四甲基丁基苯酚 (MBBT) 的组合在不存在氰双苯丙烯酸辛酯、PABA 和乙基己基甲氧基肉桂酸酯的情况下用以光稳定光防护组合物中的 BMDBM 的用途，其中 BEMT/BMDBM 质量比大于或等于 1，且优选大于或等于 1.5。

8. 根据权利要求 7 所述的用途，其特征在于，所含 BMDBM 含量以组合物的总重量计在 1 重量％和 5 重量％之间。

9. 根据权利要求 7 或 8 中任一项所述的用途，其特征在于，所含 BEMT 含量以组合物的总重量计在 2 重量％和 6 重量％之间。

10. 根据权利要求 7 至 9 中任一项一项所述的用途，其特征在于，所含 MBBT 含量以组合物的总重量计在 3 重量％和 7 重量％之间。

用于光稳定丁基甲氧基二苯甲酰基甲烷(BMDBM)的防晒剂的组合物和组合

技术领域

[0001] 本发明涉及一种用于丁基甲氧基二苯甲酰基甲烷(BMDBM)的光稳定的防晒剂的组合。

背景技术

[0002] 对抗UVA(320-400nm)的保护必须实质上限制与可导致皮肤的变化、光老化的加速、皮肤弹性的损失等的长时暴露相关的损害。

[0003] 首先,回顾本发明的范围中涉及的主要滤光剂的命名和缩写:

[0004] -丁基甲氧基二苯甲酰基甲烷(BMDBM)=阿伏苯宗=CAS注册号:70356-09-1,所述滤光剂以DSM商标Parsol1789®销售,

[0005] -2,4-双[4-(2-乙基己氧基)-2-羟基苯基]-6-(4-甲氧基苯基)-1,3,5-三嗪=双-乙基己氧基苯酚甲氧基苯基三嗪(BEMT)=Bemotrizinol=CAS注册号:187393-00-6,所述滤光剂以BASF商标Tinosorb S®销售,

[0006] -2,2'-亚甲基-双-(6-(2H-苯并三唑-2-基)-4-(1,1,3,3-四甲基丁基)-苯酚=亚甲基双-苯并三唑基四甲基丁基苯酚(MBBT)=Bisoctrizole=CAS注册号:103597-45-1,所述滤光剂以BASF商标Tinosorb M®销售。

[0007] 丁基甲氧基二苯甲酰基甲烷(BMDBM)不是UV辐射稳定滤光剂。分子发生分裂,其分解成不具有吸收剂活性的各种化学元素。

[0008] 当与其他滤光剂(例如乙基己基甲氧基肉桂酸酯)组合时,BMDBM仍然可分解并损失其光防护性质。

[0009] BMDBM通常与使其光稳定的氰双苯丙烯酸辛酯,或甚至PABA(对氨基苯甲酸)组合。然而,氰双苯丙烯酸辛酯具有这样的缺陷:其作为强大的变应原,在儿童中导致接触性湿疹,并与酮洛芬交叉过敏。

[0010] 最近,现有技术包括文献US20110212040,所述文献教导了通过添加合成或天然八氢番茄红素或六氢番茄红素而稳定BMDBM。

[0011] 本发明的目的在于提供用于光稳定BMDBM,并同时根据目前的规定而开发光防护体系的新的替代方案。

发明内容

[0012] 本发明涉及一种含有丁基甲氧基二苯甲酰基甲烷(BMDBM)、双-乙基己氧基苯酚甲氧基苯基三嗪(BEMT)和亚甲基双-苯并三唑基四甲基丁基苯酚(MBBT)的组合,其特征在于:

[0013] -BEMT/BMDBM质量比大于或等于1,且优选大于或等于1.5,且

[0014] -所述组合不含有氰双苯丙烯酸辛酯。

[0015] 本发明涉及一种含有丁基甲氧基二苯甲酰基甲烷 (BMDBM)、双 - 乙基己氧基苯酚甲氧基苯基三嗪 (BEMT) 和亚甲基双 - 苯并三唑基四甲基丁基苯酚 (MBBT) 的经光稳定化的组合 :

[0016] i.-BEMT/BMDBM 质量比大于或等于 1,且优选大于或等于 1.5,且

[0017] ii. 所含 BMDBM 的含量以组合物的总重量计在 1 重量%和 5 重量%之间,

[0018] iii. 所含 MBBT 的量以组合物的总重量计在 3 重量%和 7 重量%之间,

[0019] 所述组合不含氰双苯丙烯酸辛酯、PABA 或乙基己基甲氧基肉桂酸酯。

[0020] 在本发明的一个特定实施方案中,BEMT/BMDBM 质量比小于或等于 5,优选小于或等于 4,甚至更优先小于或等于 3。

[0021] 优先地,BEMT/BMDBM 质量比选择为在 1 至 5,优先 1.5 至 5,甚至更优先 1.5 至 3 的范围内。

[0022] 根据本发明的另一特性,所含 BEMT 含量以组合物的总重量计在 2 重量%和 6 重量%之间。

[0023] 在本发明的框架中,必须将 BEMT/BMDBM 质量比考虑为主要特性特征。这意味着必须在每个浓度比率内调节不同的太阳滤光剂 BEMT、BMDBM 和 MBBT 的浓度,以首先且最重要地遵守所述质量比例。

[0024] 本发明的另一主题涉及一种含有 BMDBM、BEMT 和 MBBT 的组合的组合物,其特征在于 :

[0025] -BEMT/BMDBM 质量比大于或等于 1,且优选大于或等于 1.5,且

[0026] - 所述组合不含有氰双苯丙烯酸辛酯,

[0027] - 所含 MBBT 的量以组合物的总重量计在 3 重量%和 7 重量%之间,

[0028] - 具有药物可接受或化妆品可接受的赋形剂。

[0029] 本发明的另一主题涉及一种含有 BMDBM、BEMT 和 MBBT 的组合的组合物,其特征在于 :

[0030] -BEMT/BMDBM 质量比大于或等于 1,且优选大于或等于 1.5,

[0031] - 所述组合不含氰双苯丙烯酸辛酯、PABA 或乙基己基甲氧基肉桂酸酯。

[0032] - 所含 MBBT 的量以组合物的总重量计在 3 重量%和 7 重量%之间,

[0033] - 并具有药物可接受或化妆品可接受的赋形剂。

[0034] 根据本发明的另一特性,如上组合物也具有含量以组合物的总重量计在 2 和 6 重量%之间的双 - 乙基己氧基苯酚甲氧基苯基三嗪 (BEMT)。

[0035] 根据本发明的另一特性,如上组合物也具有含量以组合物的总重量计在 1 和 5 重量%之间的丁基甲氧基二苯甲酰基甲烷 (BMDBM)。

[0036] 最后,根据本发明的另一特性,如上组合物也具有优选以组合物的总重量计在 1 和 10 重量%之间的另一滤光剂。

[0037] 根据另一方面,本发明也涉及丁基甲氧基二苯甲酰基甲烷 (BMDBM)、双 - 乙基己氧基苯酚甲氧基苯基三嗪 (BEMT) 和亚甲基双 - 苯并三唑基四甲基丁基苯酚 (MBBT) 的组合在不存在氰双苯丙烯酸辛酯、PABA 和乙基己基甲氧基肉桂酸酯的情况下用以光稳定光防护组合物中的 BMDBM 的用途,其中 BEMT/BMDBM 质量比大于或等于 1,且优选大于或等于 1.5。

[0038] “光稳定化、光稳定或光稳定性”就本发明的意义上说意指在照射 5MED,优选 10MED

之后，保持如下：

[0039] - 总 SPF(290 至 400nm) 的至少 80％，优选至少 85％，甚至更优先至少 90％；和

[0040] - 总 SPF 的 UVA 部分 (320 至 400nm) 的至少 80％，优选至少 85％，甚至更优先至少 90％。

[0041] 优选地，根据本发明的组合或组合物也不含PABA®。

[0042] 根据本发明的组合代表光稳定光防护体系，所述光稳定光防护体系组合完全且均匀分布于皮肤上的有机脂溶性滤光剂（如 BMDBM 和 BEMT）以及分散于水相中以获得更好的吸收响应并因此获得更好的功效的有机防晒剂（如 MBBT)。

[0043] 优选地，调节根据本发明的组合物，以获得如下光防护体系：

[0044] - 具有最广可能 UV 吸收光谱 (290 至 400nm 的最大光谱覆盖）

[0045] - 遵守目前的规定，即具有大于或等于 370nm 的临界波长 λ_c 和小于或等于 3 的 SPF/UVA 比。

[0046] 更优先地，根据本发明的组合物可对应于就防晒而言最大的类别，即具有 SPF 50+。

[0047] 可将如下 UVB 滤光剂中的一种或多种添加至根据本发明的组合物中：

[0048] ➢ 水杨酸酯：胡莫柳酯、乙基己基水杨酸酯

[0049] ➢ 苯基苯并咪唑磺酸

[0050] ➢ 乙基己基三嗪酮、二乙基己基丁酰胺基三嗪酮

[0051] ➢ TiO_2

[0052] ➢ 三 - 联苯三嗪。

[0053] 如上所述的 UVB 滤光剂就耐受性、毒性、光稳定和 UV 吸收方面而言被认为是令人满意的 UVB 滤光剂。因此，作为有关胡莫柳酯的预防措施，优选地，优选如下一种或多种 UVB 滤光剂：

[0054] ➢ 乙基己基水杨酸酯

[0055] ➢ 苯基苯并咪唑磺酸

[0056] ➢ 乙基己基三嗪酮、二乙基己基丁酰胺基三嗪酮

[0057] ➢ TiO_2

[0058] ➢ 三 - 联苯三嗪。

[0059] 此外，所述组合物优先对光、空气、湿气和温度稳定。

[0060] 本发明的另一主题涉及一种含有经光稳定化的组合和药物可接受或化妆品可接受的赋形剂的组合物，所述经光稳定化的组合包含

[0061] - 丁基甲氧基二苯甲酰基甲烷 (BMDBM)、双 - 乙基己氧基苯酚甲氧基苯基三嗪 (BEMT) 和亚甲基双 - 苯并三唑基四甲基丁基苯酚 (MBBT)，其中：

[0062] i. BEMT/BMDBM 质量比大于或等于 1，且优选大于或等于 1.5，且

[0063] ii. 所含的 BMDBM 的含量以组合物的总重量计在 1 重量％和 5 重量％之间，

[0064] iii. 所含的 MBBT 的量以组合物的总重量计在 3 重量％和 7 重量％之间，

[0065] - 另外，一种或多种 UVB 滤光剂选自如下滤光剂：

[0066] ➢ 乙基己基水杨酸酯

[0067] ➢ 苯基苯并咪唑磺酸

[0068] ➢ 乙基己基三嗪酮、二乙基己基丁酰胺基三嗪酮

[0069] ➢ TiO_2

[0070] ➢ 三 - 联苯三嗪。

[0071] 在本发明的一个特定实施方案中，所含的一种或多种 UVB 滤光剂的量以组合物的重量计总共在 1 和 10 重量％之间。

[0072] 在本发明的另一实施方案中，所述组合物含有以组合物的重量计 1 重量％至 10 重量％的量，优选以组合物的重量计 1 重量％至 5 重量％的量的单个另外的 UVB 滤光剂。

[0073] 在本发明的一个特定实施方案中，所述组合物含有选自如下滤光剂的单个 UVB 滤光剂：

[0074] ➢ 乙基己基水杨酸酯

[0075] ➢ 苯基苯并咪唑磺酸

[0076] ➢ 乙基己基三嗪酮、二乙基己基丁酰胺基三嗪酮

[0077] ➢ TiO_2

[0078] ➢ 三 - 联苯三嗪

[0079] 本发明最后涉及含有如下的组合用以光稳定光防护组合物中的 BMDBM 的用途：

[0080] - 丁基甲氧基二苯甲酰基甲烷 (BMDBM)、双 - 乙基己氧基苯酚甲氧基苯基三嗪 (BEMT) 和亚甲基双 - 苯并三唑基四甲基丁基苯酚 (MBBT)，其中 BEMT/BMDBM 质量比大于或等于 1，且优选大于或等于 1.5，

[0081] - 选自如下滤光剂的一种或多种 UVB 滤光剂，优选选自如下滤光剂的仅 1 种 UVB 滤光剂：

[0082] ➢ 乙基己基水杨酸酯

[0083] ➢ 苯基苯并咪唑磺酸

[0084] ➢ 乙基己基三嗪酮、二乙基己基丁酰胺基三嗪酮

[0085] ➢ TiO_2

[0086] ➢ 三 - 联苯三嗪。

[0087] “药物可接受的或化妆品可接受的赋形剂”意指用于制造、保存或施用所述组合物的任何佐剂或赋形剂。

[0088] 根据本发明的组合物可更特别地为防晒组合物。它们特别地旨在保护皮肤（面部和 / 或身体）和 / 或毛发免于紫外辐射。

[0089] 本发明也涉及一种用于保护皮肤（面部和 / 或身体）和 / 或毛发免于紫外辐射的方法，所述方法包括将之前描述的组合物施用至皮肤（面部和 / 或身体）和 / 或毛发上。

[0090] 根据本发明的组合物也可包含特别地选自如下的常规化妆品或药物佐剂：脂肪、有机溶剂、增稠剂、软化剂、不透明剂、稳定剂、润肤剂、消泡剂、保湿剂、芳香剂、防腐剂、聚

合物、填料、螯合剂、杀菌剂、气味吸收剂、碱化或酸化剂、表面活性剂、自由基清除剂、抗氧化剂、维生素 E 和 C、α－羟基酸，或通常用于化妆品或药物中，特别是用于制造防晒组合物的任何其他成分。

[0091] 脂肪可由油、蜡或它们的混合物组成，它们也可包括脂肪酸、脂肪醇和脂肪酸酯。油可选自动物油、植物油、矿物油或合成油，特别是凡士林油、石蜡油、挥发性或非挥发性硅油、异链烷烃、聚烯烃，和氟化及全氟化的油。同样地，蜡可选自动物蜡、地蜡、植物蜡或合成蜡，如蜂蜡、小烛树蜡、巴西棕榈蜡、石油蜡（或微晶蜡）、石蜡，和它们的混合物。

[0092] 所述组合物还可包含在室温下（大约 25℃）水可溶混的多元醇，所述多元醇特别地选自具有 2 至 20 个碳原子，优选具有 2 至 10 个碳原子，优选具有 2 至 6 个碳原子的多元醇，如甘油；二醇衍生物，如丙二醇、丁二醇、戊二醇、己二醇、二丙二醇和二乙二醇；二醇醚，如一丙二醇、二丙二醇或三丙二醇的 C1-C4 烷基醚、一乙二醇、二乙二醇或三乙二醇的 C1-C4 烷基醚，和它们的混合物。

[0093] 所述组合物也可包含增稠剂或流变改性剂，例如非离子乙氧基化的疏水改性的氨基甲酸酯、聚羧酸增稠剂，如丙烯酸酯 / 硬脂醇聚醚 20 甲基丙烯酸酯共聚物、卡波姆 (carbomer)、交联丙烯酸酯共聚物，和它们的混合物。

[0094] 所述组合物也可包含酸和碱以调节所述组合物的 pH 区。碱可为无机的（氢氧化钠、氢氧化钾、氨等）或有机的，如单乙醇胺、二乙醇胺或三乙醇胺、氨基甲基丙二醇、N- 甲基葡糖胺、碱性氨基酸（如精氨酸和赖氨酸），以及它们的混合物。

[0095] 组合物也可包含皮肤调节剂。皮肤调节剂的例子包括但不限于阴离子、阳离子和非离子表面活性剂，如月桂基硫酸钠、二辛基磺基琥珀酸钠、硬脂酸钠、酯脱水山梨糖醇、乙氧基化的脂肪酸、乙氧基化的脂肪醇（如十三烷醇聚醚 -9 和 PEG-5 乙基己酸酯）；本领域技术人员已知的任何其他乳化剂和调节剂，以及它们的混合物。

[0096] 根据本发明的组合物还可包含特别地选自如下的另外的活性剂：保湿剂、剥离溶解剂 (desquamating agent)、用于改进阻挡功能的试剂、脱色剂、抗氧化剂、皮肤紧致剂、抗糖化剂、刺激真皮和 / 或表皮大分子的合成和 / 或防止它们的降解的试剂、刺激成纤维细胞或角化细胞增殖和 / 或角化细胞分化的试剂、NO 合成酶抑制剂、增加皮脂腺的活性的试剂、张力调节剂、脂肪重构剂 (lipo-restructuring agents)、减肥剂 (slimming agent)、促进皮肤微循环的试剂、安抚剂和 / 或刺激剂、皮脂调节或抗皮脂溢剂、收敛剂、伤口愈合剂、抗炎剂、抗痤疮剂，和它们的混合物。

[0097] 根据本发明的组合物可以以用于局部施用（尤其是在皮肤和 / 或毛发上）的任何适当的形式呈现。特别地，它们可为通过将脂肪相分散于水相中而获得的乳状液 (emulsion) 的形式（例如一种或多种水包油或油包水乳状液），或为凝胶或无水液体、糊状或固体产品的形式，或为在小球的存在下的分散体的形式。根据本发明的组合物也可为更少的流体，并可为白色或有色霜剂、软膏、乳状物 (milk)、乳液、浆液、糊剂、面膜、粉剂、固体棒或任选的气溶胶、泡沫或喷剂的形式。这些组合物也可为耐水的。

具体实施方式

[0098] 评价总体 UV 和 UVA 光稳定性的体外方法

[0099] A) 材料

[0100] -UV 分光光度计：

[0101] 分光光度计测量在表面上具有和不具有防晒组合物的层的情况下通过板的光谱透射率。

[0102] 分光光度计应该允许在 290nm 和 400nm 之间的测量。为了降低测量读数之间的变化性，并弥补产品层的均匀性的缺乏，推荐的是位点的读数区域为至少 0.5cm^2。

[0103] 用于这些测量的分光光度计为 Labsphere® UV-1000S 或 2000S。

[0104] - 板：

[0105] 板为其上施用防晒组合物的材料。该材料必须对 UV 透明、非荧光的、光稳定的且相对于所测试的组合物的配混物为惰性的。对于此方案，聚甲基丙烯酸甲酯 (PMMA) 板经证实为理想的。

[0106] -UV 源：

[0107] UV 源为具有传播可见光 +UVA+UVB 光谱的氙弧灯的太阳模拟器。用于所述研究的 UV 源为 Suntest CPS+(Atlas)

[0108] B) 方法：

[0109] - 测量通过未经处理的板的透射率：

[0110] 首先，必须确定通过对照板的 UV 透射率。这通过铺展数微升甘油，从而完全覆盖板的表面而制得。

[0111] - 样品施用：

[0112] 将待测试的样品以 1.3mg/cm^2 的量（保持在板上的实际量）施用至 PMMA 板上。为了确保量的准确性和结果的再现性，施用区域大于 10cm^2。

[0113] 待测试的样品以分布于板的整个表面上的相同体积的大量小滴的形式施用。

[0114] 为了确保产品的量正确，必须采用验证施用的产品的量的方法（例如：对在施用产品之前和之后板称量）。

[0115] 在使用限定量的样品之后，应该尽可能快地（小于 30 秒）在整个板上铺展样品。

[0116] 然后将样品置于室温下黑暗中 15 分钟，以促进形成均匀的膜。

[0117] - 测量通过用样品处理的板的透射率：

[0118] 使用分光光度计分析用样品处理的板，对于从 290nm 至 400nm 的每个波长，确定通过样品的 UV 辐射透射率的平均值（使用在板的不同区域上测得的单色吸光度数据）。

[0119] - 测量次数：

[0120] 对于每个样品，应该制备至少三个 PMMA 板。每个板应该在至少九个不同的区域中进行测量，除非几乎整个表面通过分光光度法测量。

[0121] C) 光稳定性的计算：

[0122] 来自用 5 和 10 MED 的剂量照射之前和之后吸光度数据 A（λ）的体外 SPF 和 UVA(PPD) 的计算。

[0123]

$$\text{体外 SPF} = \frac{\int_{\lambda=290\,nm}^{\lambda=400\,nm} E(\lambda)*S(\lambda)*d\lambda}{\int_{\lambda=290\,nm}^{\lambda=400\,nm} E(\lambda)*S(\lambda)*10^{-A(\lambda)}*d\lambda}$$

[0124] 其中：

[0125] -E(λ)＝红斑效力光谱

[0126] -S(λ)＝太阳光谱辐照度

[0127] -A(λ)＝样品吸光度

[0128] -dλ ＝波长变化(1nm)

[0129]

$$\text{体外 PPD} = \frac{\int_{\lambda=320\,nm}^{\lambda=400\,nm} P(\lambda)*I(\lambda)*d\lambda}{\int_{\lambda=320\,nm}^{\lambda=400\,nm} P(\lambda)*I(\lambda)*10^{-A(\lambda)}*d\lambda}$$

[0130] 其中：

[0131] P(λ)＝PPD 作用光谱(持续性色素变黑)

[0132] I(λ)＝太阳光谱辐照度

[0133] A(λ)＝样品吸光度

[0134] dλ ＝波长变化(1nm)

[0135] 由下式计算光稳定性：

[0136]

$$\text{总 UV 光稳定性} = \frac{\text{照射之前的SPF}}{\text{照射之后的SPF}}$$

[0137]

$$\text{UVA 光稳定性} = \frac{\text{照射之前的PPD}}{\text{照射之后的PPD}}$$

[0138] 组合物实施例

[0139] 组合物 1

[0140]

成分	%
丁基甲氧基二苯甲酰基甲烷	1-5
双-乙基己基氧基苯酚甲氧基苯基三嗪	2-6
亚甲基双-苯并三唑基四甲基丁基苯酚	3-7

甘油	10.0
脱矿质水	QSP 100
Na2EDTA	0.1
黄原胶	0.3
苯甲酸 C12-C15 烷基酯	25.0
防腐剂	qs
硬脂醇	2.5
单硬脂酸甘油酯	2.5
十六烷基磷酸钾	1.8

[0141] 组合物 2

[0142]

成分	%
丁基甲氧基二苯甲酰基甲烷	1-5
双 - 乙基己基氧基苯酚甲氧基苯基三嗪	2-6
亚甲基双 - 苯并三唑基四甲基丁基苯酚	3-7
UVB 滤光剂	1-10
甘油	10.0
脱矿质水	QSP 100
Na2EDTA	0.1
黄原胶	0.3
苯甲酸 C12-C15 烷基酯	25.0
防腐剂	qs
硬脂醇	2.5
单硬脂酸甘油酯	2.5

十六烷基磷酸钾	1.8

[0143]

[0144] 光稳定性结果

[0145]

光稳定性：	组合物 1	组合物 2
总 UV-5MED	96％	93％
UVA-5MED	95％	92％
总 UV-10MED	92％	90％
UVA-10MED	91％	89％