Abstract

Photostable sunscreen composition for topical application

The sunscreen composition includes dibenzoylmethane derivative in 1 to 5% by weight of the composition, octyl-methoxycinnamate in 1 to 10% by weight of the composition and dermatologically acceptable excipients in 79 to 97% by weight of the composition containing 60 – 75% aqueous phase stabilised with 1-(4-methoxy-5-benzofuranyl)-3-phenyl 1, 3 propanedione (pongamol) in 0.9 to 6% by weight of the composition.

FIELD OF THE INVENTION

This invention relates to a photostable sunscreen composition and a method of preparing the same

BACK GROUND OF THE INVENTION:

Ultraviolet (UV) light or radiation is classified as UVA, UVB and UVC depending upon the wavelength thereof, UVA being the longest of the three at 320-400 nm. UVA is further divided into two wavelength ranges, UVA I measuring 340-400 nm and UVA II measuring 320-340 nm. UVB wavelength ranges from 290 to 320 nm. Both the UVA and UVB radiations penetrate into the atmosphere and play an important role in causing health problems and conditions such as premature skin aging, eye damage (including cataracts) and skin cancers. Shorter rays of UVC in the wavelength range of 100 to 290 nm are mostly absorbed by the ozone layer and do not reach the earth. Harmful effects of UV-B radiation may be aggravated by UV-A radiation. In order to prevent and mitigate the harmful effects of exposure to UVA and UVB radiations, there are several sunscreen, cosmetic or dermatological formulations available, which comprise one or more UV absorbers or UV filters.

UV filters used in the sunscreen preparations are mainly derivatives of 3-benzylidenecamphor, ethylhexyl salicylate, p-methoxy-cinnamic acid esters such as 2-ethylhexyl p-methoxycinnamate or 2-ethylhexyl(2E)-3-(4-methoxyphenyl)pro-2-

enoate(octyl-methoxycinnamate) or dibenzoylmethane derivative such as 4-(tert-butyl)-4′-methoxydibenzoyl methane (also called avobenzone, CAS No 70356-09-1). Some of the UV absorbing organic compounds employed in sunscreen compositions, avobenzone in particular, undergo rapid photo degradation on exposure to UV radiation and do not give effective protection from sun damage over a period. To overcome this problem, sunscreen preparations generally contain photostabilizers to enhance their photostability.

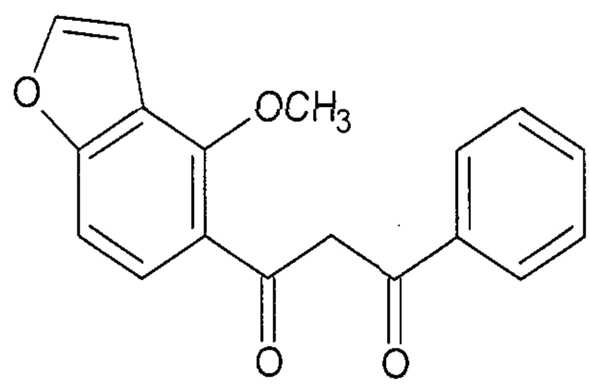
Deflandre et al teach stabilization of dibenzoylmethane derivative in a cosmetic composition comprising a cosmetically acceptable vehicle containing atleast one fatty phase and alkyl β-β-diphenylacrylate or α-cyano-β-β-diphenylacrylate (US 5576354). Raspanti et al teach photostable cosmetic compositions comprising combination of dibenzoylmethane derivative and benzopheride derivative (US 5776439). Bonda et al describe a sunscreen composition comprising dibenzoylmethane derivative such as 4-(1,1-dimethylethyl)-4'-methoxydibenzoylmethane and a benzoate stabilizer for the dibenzoylmethane derivative (US 5788954). Bonda et al also describes a sunscreen composition comprising dibenzoylmethane derivative stabilized with salicylate (US 5849273).

Gonzenbach et al teach cosmetic compositions comprising at least one fatty phase, dibenzoymethane derivative and water soluble p-methoxycinnamate derivative stabilized with 3,3-diphenylacrylate derivative or benzylidene camphor derivative (US 5985251). Gonzenbach also teach photostable, cosmetic sunscreen composition comprising dibenzoylmethane derivative stabilized with α-cyano-β,β diphenylacrylate (US 6033649). Cole et al teach sunscreen compositions comprising a dibenzoylmethane derivative stabilized with a combination of a benzophenone derivative and a diester or polyester of a naphthalene dicarboxylic acid (US 6444195). Meyer et al describe sunscreen compositions containing avobenzone and zinc oxide stabilized with phenylbenzimidazole sulfonic acid (US 7244416). Wagner et al teach a sunscreen composition comprising dibenzoylmethane derivative stabilized with merocyanine derivatives (US8535648).

Stabilising agents used in the above compositions are all synthetic compounds which are generally considered to be unsafe. Preparation of synthetic compounds generally gives rise to byproducts which create environmental hazards and problems. Synthetic stabilisers are also usually required in large amounts. There is thus need for stabilisers for stabilizing UV absorbers in sunscreen compositions, which are safe, environment friendly and cost effective.

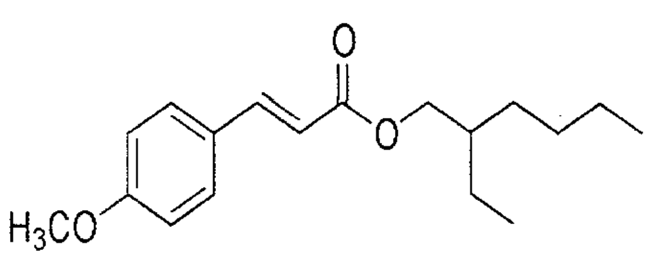
DESCRIPTION OF THE INVENTION

1-(4-Methoxy-5-benzofuranyl)-3-phenyl 1,3 propanedione (pongamol), is a natural compound extracted from Pongamia pinnata (Karanja) seed oil and is a known UV absorber. We have found out by extensive research and experimentation that 1-(4-methoxy-5-benzofuranyl)-3-phenyl 1, 3 propanedione can stabilize UV absorbers comprising dibenzoylmethane derivative and 2-ehtylhexyl (2E)-3-(4-methoxyphenyl) prop-2-enoate (octyl-methoxycinnamate). Pongamol has the following structural formula 1:



Formula 1

Octyl methoxycinnamate (OMC) has the following structural formula 2 :



Formula 2

Dibenzoylmethane derivative is preferably 1-(4-methoxyphenyl)-3-(4-tert-butylphenyl) propane-1,3-dione (avobenzone) having the following structural formula 3:

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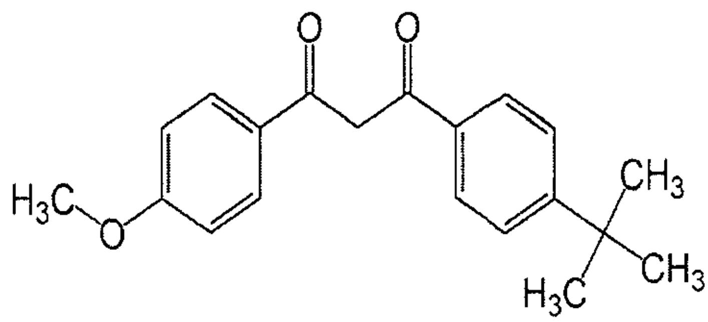

Formula 3

According to the invention there is provided a photostable sunscreen composition comprising UV absorbers in combination with dermatologically acceptable excipients, wherein the UV absorbers comprise diebenzoylmethane derivative in 1 to 5% by weight of the composition and octyl-methoxycinnamate in 1 to 10% by weight of the composition and wherein the composition further comprises 1-(4-methoxy-5-benzofuranyl)-3-phenyl 1, 3 propanedione in at least 0.9 to 6% by weight of the composition to stabilize the UV absorbers in the composition, the balance being the dermatologically acceptable excipients in 65 to 97.1% by weight of the composition.

According to the invention there is also provided a method of preparing a photostable sunscreen composition comprising UV absorbers in combination with dermatologically acceptable excipients, wherein the UV absorbers comprise dibenzoylmethane derivative in 1 to 5% by weight of the composition and octyl-methoxycinnamate in 1 to 10% by weight of the composition and wherein the UV absorbers in the composition are stabilized with 1-(4-methoxy-5-benzofuranyl)-3-

phenyl 1, 3 propanedione in at least 0.9 to 6% by weight of the composition, the balance being the dermatologically acceptable excipients in 65 to 97.1% by weight of the composition.

According to the invention there is also provided use of 1-(4-methoxy-5-benzofuranyl)-3-phenyl 1,3 propane dione in stabilizing UV absorbers in a photostable sunscreen composition comprising dibenzoylmethane derivative in 1 to 5% by weight and octyl-methoxycinnamate in 1 to 10% by weight in combination with dermatologically acceptable excipients, wherein the 1-(4-methoxy-5-benzofuranyl)-3-phenyl 1, 3 propanedione is used in at least 0.9 to 6% by weight of the composition, the balance being the dermatologically acceptable excipients in 65 to 97.1% by weight of the composition.

Preferably, the 1-(4-methoxy-5-benzofuranyl)-3-phenyl 1, 3 propanedione is used in 1 to 6% by weight of the composition. Preferably, the dibenzoylmethane derivative is in 1.5% to 5% by weight of the composition. Preferably, the dibenzoylmethane derivative is 4-(tert-butyl)-4'-methoxy dibenzoyl methane. Preferably, the octyl-methoxycinnamate is in 8 to 10% by weight of the composition. The UV absorbers may comprise additional UV absorbers selected from the group consisting of Tinosorb M (methylene bis-benzotriazolyl tetramethylbutylphenol), ethyl hexyl triazone, octyl dimethyl PABA (para-aminobenzoic acid), TiO2 and ZnO upto 14%

by weight of the composition. Preferably, the 1-(4-methoxy-5- benzofuranyl)-3-phenyl 3 propanedione is of 98% purity. The sunscreen composition may be in any applicable form such as cream, lotion, gel, oil or spray.

Dermatologically acceptable excipients used in the sunscreen composition are those commonly used in sunscreen preparations and include vitamins such as A, C, E, K or PP and derivatives or precursors thereof, alone or as mixtures thereof; antioxidants such as tocopheryl acetate or BHT (butylated hydroxytoluene); free-radical scavengers such as tocopheryl acetate or BHT (butylated hydroxytoluene); anti glycation agents such as carnosine green tea extract; calmatives such as C-β-D-xylopyranoside-2-bydroxypropane; NO-synthase inhibitors such as NG-monomethyl-L-arginine or methyl ester of NG-nitro-L-arginine; agents for stimulating the synthesis of dermal or epidermal macromolecules and/or for preventing their degradation such as globularia cordifolia extract; agents for stimulating fibroblast proliferation such as sophorolipid; agents for stimulating keratinocyte proliferation such as globularia cordifolia extract; muscle relaxants such as acetyl hexapeptide-3 or spilanthol; dermo-relaxing agents such as adenosine or manganese gluconate, keratolytic agents such as salicyclic acid; desquamating agents such as capryolyl salicyclic acid; moisturizers such as polyols such as glycerol, butylene glycol or propylene glycol; anti-inflammatory agents such as alpha bisabolol, Portulaca oleraceae extract; agents that act on the energy metabolism of cells such as euglena extract; insect repellents such as octyldodecyl neopentanoate; substance P or CGRP antagonists such as sendide or spantide II; anti-wrinkle agents such as argireline or knotgrass flavonoids; anti-ageing agents such as hyaluronic acid; astringent agents such as extract of gallnut or extract of centella; sebum-regulating agents and anti-seborrhoeic agents such as benzoyl peroxide or selenium disulphide and agents that protect formulation from microbials such as iodopropyl butylcarbamate.

According to the invention the stabilizing agent consisting of pongamol is a natural extract and is safe. Raw Material for the extract namely karanja seed oil is easily available. Extraction of pongamol is easy and convenient and cost effective and does not give rise to byproducts which are harmful to environment. Effective amount of pongamol required for stabilization of the UV absorbers is low. The invention is thus efficient and cost effective.

The following experimental examples are illustrative of the invention but not limitative of the scope thereof :

Example 1

Comparative spectrophotometric studies of two sunscreen compositions comp[rising avobenzone (1.5% by wt, 100% purity) and octyl-methoxycinnamate (8% by wt, 100% purity) with and without pongamol (1% by wt, 98% purity) were carried out to determine their physical and chemical stability to UV light according to the test procedure described in "A statistical application allowing comparison between the spectrums of two or several products to evaluate if they are statistically equivalent", D. Lutz and S. Miksa. *In vitro comparison - A new accessible and reliable statistical* method to compare the global UV protection properties of cosmetics. H&PCToday and Monographic supplement SUN CARE - Vol 8(4) July/August 2013, P23-27 by Helio Screen.

Both the compositions were exposed to UV, 4.8 (Minimal Erythemal Dose) which is equivalent to 72 min exposure to the zenith sun with erythemal power of 4 MED/h.After normalization of the evolution of the level of sun protection of the two compositions while being UV exposed, a root mean square error (RMSE) test was conducted to determine whether there was a significant association between the two spectrums. Graphic representations of the test results were as shown in Figs 1 and 2 below. In a RMSE test, if the RMSE (Root Mean Square Error) has a value lower than 5%, both curves can be considered as statistically equivalent and can be compared. If the RMSE has a value greater than 5% both curves are statistically different and not comparable.

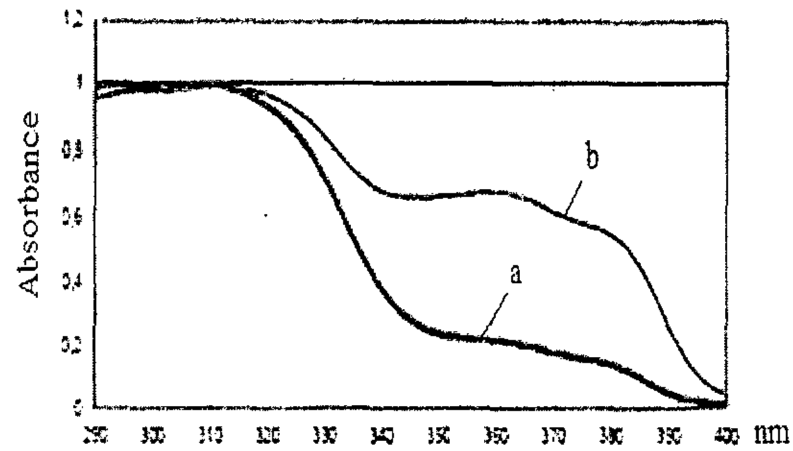

Fig 1

Curves a and b in Fig 1 represent product mixture of avobenzone and octyl-methoxycinnamate before and after UV radiation respectively. Fig 1 clearly depicts that the product before and after UV irradiation is not the same, as the composition has undergone degradation after the 72 min exposure to the zenith sun. Deviation from the original product measured as RMSE is 28.7% .This shows that both spectrums are not statistically equivalent, so the product mixture was not photostable.

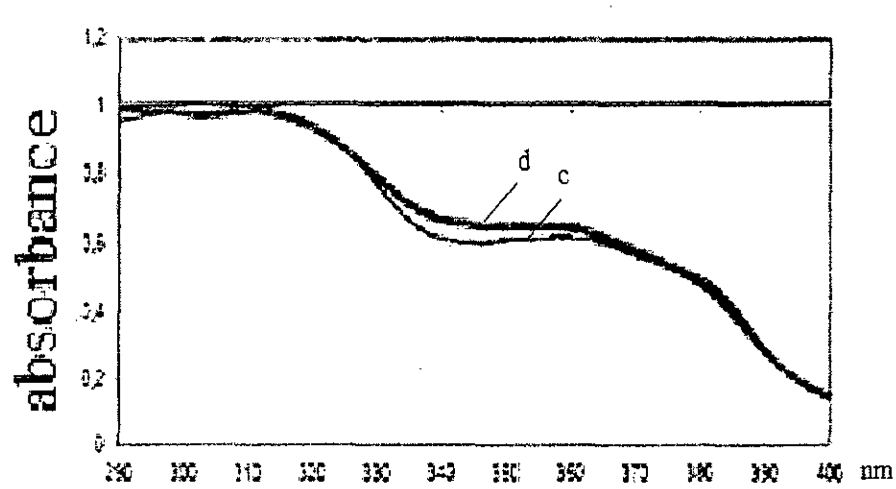

Fig 2

Curves c and d represent product mixture of avobenzone, octyl-methoxycinnamate and pongamol before and after UV radiation respectively. Fig 2 clearly shows that the product before and after UV irradiation is the same. Only a negligible degradation of the composition has occurred after the exposure to 72 min the zenith sun. Deviation from the original product measured as RMSE is 3%. This shows that both peaks are statistically equivalent and the product mixture is photostable.

Example 2

Spectrophotometric studies were conducted according to the test procedure described in Example 1 on product mixtures without pongamol and with different concentrations of pongamol and the results were as given in the Table 1 below:

Table 1

Product Mixture	without pongamol	with pongamol at 0.2%	with pongamol at 0.5%	with pongamol at 1.0%	with pongamol at 3.0%	with pongamol at 6.0%
Comparison of spectrum curve						
Tolerance threshold of RMSE	5%	5%	5%	5%	5%	5%
RMSE percent calculated	28.7%	26%	13%	3%	3%	3%

RMSE values of the products with different pongamol concentrations were plotted as shown in the graph in Fig 3 below:

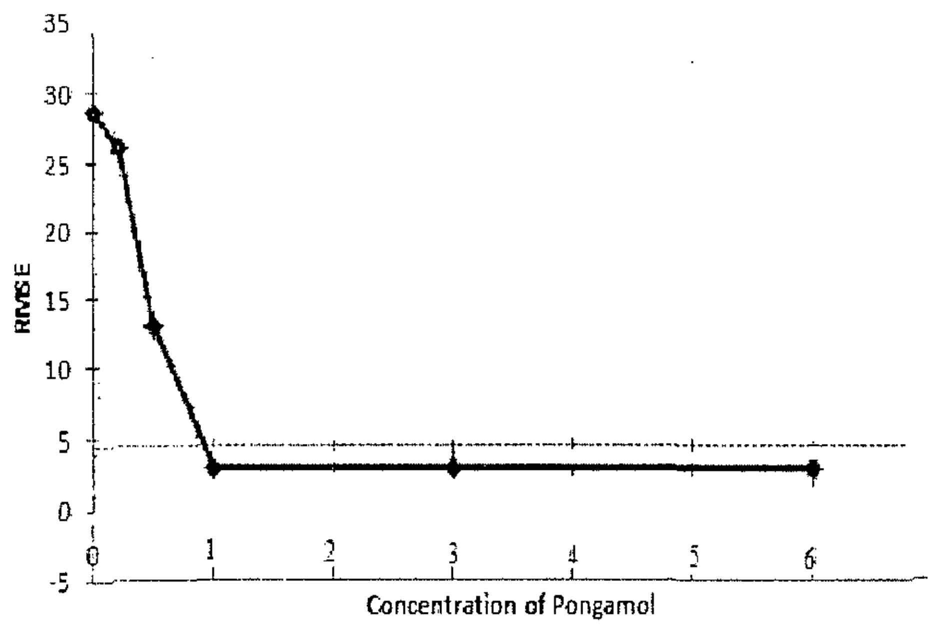

Fig 3

It is found from Fig 3 that the effective concentration of pongamol required to stabilize the product mixture is >0.9% by wt (to get the RMSE value ≤ 5).

Example 3

Experiment was conducted to determine the photostability of product mixtures of avobenzone, octyl-methoxycinnamate and other commercial UV filters (3% by wt avobenzone + 8% by wt octyl-methoxycinnamate + 14% by wt other UV filters) with and without pongamol (1% by wt) and the results were as shown in the following Table 2 :

Other UV filters used :

Tinosorb M (methylene bis-benzotriazolyl tetramethylbutylphenol),

Ethyl hexyl triazone

Octyl dimethyl PABA (para-aminobenzoate)

TiO_2

and

ZnO.

Table 2

comparison of spectrum curve	without pongamol	with pongamol at 1% by wt
Tolerance threshold of RMSE	5%	5%
RMSE percent calculated	8.7%	4.63%

It is quite clear from the Table 2 that pongamol at 1% by wt concentration *photostabilizes the product mixture comprising avobenzone, octyl-methodycinnamate* and the other UV filters.

Dated this 26th day of March 2014.

Kancor Ingredients Ltd
By their Agent & Attorney

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