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(54) Title: NON-IRRITATING, NON-BLURRING, PHOTOSTABLE OPHTHALMIC SUNSCREEN COMPOSITION

(57) Abstract: A non-irritation, non-blurring, photostable ophthalmic sunscreen composition contains at least one of the following: bemotrizinol; bisoctrizole; tris-biphenyl triazine; and/or octyl methoxycinnamate. A liquid vehicle base is then a remainder of the solution by weight. The composition is an artificial tear formulation or an ophthalmic suspension or ointment. The composition may include at least one inorganic and/or at least one organic active ingredient. The inorganic active ingredients may include, but not be limited to zinc oxide, titanium dioxide, iron oxide, zirconium oxide, and cerium oxide. The organic active ingredients may include, but not be limited to dioxybenzone, octinoxate, octisalate, homosalate, avobenzone, octocrylene, para-aminobenzoic acid, cinoxate, methyl anthranilate, octocrylene, padimate O, ensulizole, sulisobenzone, trolamine salicylate, and ecamsule.

NON-IRRITATING, NON-BLURRING, PHOTOSTABLE OPHTHALMIC SUNSCREEN COMPOSITION

CROSS-REFERENCE TO RELATED APPLICATIONS

[Para 1] This International patent application claims priority to U.S. Patent Application No. 15/648,107 filed on July 12, 2017 and U.S. Provisional Patent Application No. 62/361,189 filed on July 12, 2016. The entire contents of all the priority applications (non-provisional and provisional) are hereby incorporated in full by these references.

DESCRIPTION:

FIELD OF THE INVENTION

[Para 2] The present invention generally relates to a sunscreen formulation designed for protecting the eyes including the conjunctiva, cornea, lens, and retina. More particularly, the present invention relates to a non-irritating sunscreen that is applied directly onto the ocular surface of the eye for protection from ultraviolet radiation.

BACKGROUND OF THE INVENTION

[Para 3] Ultraviolet radiation is part of the electromagnetic spectrum that reaches the earth from the sun. It has wavelengths shorter than visible light, making it invisible to the naked eye. These wavelengths are classified as UVA, UVB, or UVC. UVA has the longest of the three at 320-400 nanometers. UVA is further divided into two wave ranges, UVA I, which measures 340-400 nanometers (nm, or billionths of a meter), and UVA II which extends from 320-340 nanometers. UVB ranges from 290 to 320 nm. With even shorter rays, most UVC is fortunately absorbed by the ozone layer and does not reach the earth.

[Para 4] Both UVA and UVB penetrate the Earth's atmosphere and play an important role in conditions such as premature skin aging, eye damage, hair damage, and certain skin cancers.

[Para 5] Photoconjunctivitis and Photokeratitis describe conditions where ultraviolet radiation inflames and/or damages the delicate structures of the ocular surface (the conjunctiva and the cornea, respectively). UV exposure to the eyes (either direct or indirect) can cause severe redness, dryness, irritation, tearing, photosensitivity, and pain. This pain can be so severe as to cause chemosis and sloughing of the corneal epithelium with resultant scarring and even permanent vision loss.

[Para 6] Long-term ophthalmic exposure to UV radiation has been associated with permanent thickening of the conjunctiva (called a pingueculum), vascular proliferation and tissue growth over the cornea (called a pterygium), conjunctival discoloration (melanosis), even cancer (e.g., conjunctival/uveal melanoma).

[Para 7] Long-standing UV exposure to the eyes has also been associated with damage to the internal structures of the eyes, e.g., the natural lens and the retina. Certain forms of cataracts (e.g., nuclear sclerosis), as well as macular degeneration have been linked to the damage caused by oxidative damage from UV exposure.

[Para 8] Accordingly, protecting the ocular structures form UV radiation may be beneficial in preventing such oxidative damage that leads to all of these very common ophthalmic conditions. Until recently, the only proposed mechanism to protect the eyes from UV radiation has been the use of glasses with UV protection, sunglasses, and tinted contact lenses.

[Para 9] There is a plethora of prior art suggesting the use of different physical and/or chemical sunscreen compositions for just the skin and formulations that won't damage the eye should any formulation get within the eye, but these patents and prior art did not envision and/or describe the use of such formulations for protecting the ocular structures in any way. For example, Dueva-Koganov et al. (Pub. No.: US 2010/0226867 A1) proposed a "cosmetic and/or dermatological" composition that are non-irritating to mammalian eyes. While this is a significant advantage for a dermatological composition not to burn the eyes in case of inadvertent contact, it does not describe the application of a solution that is designed for "ophthalmic" use per se.

[Para 10] There have been inventions that have proposed formulations specifically for the purpose of protecting the human eye from UV radiation, but such prior art has suggested formulations that are very different than what is proposed

herein with potential side-effects that may render them impractical for frequent use. Such prior art has proposed compositions that would make vision extremely blurry and/or be extremely irritating to the eyes, thus making them less suitable for frequent use by the general population.

[Para 11] For example Michalos (Patent Number 4,923,693) proposed the use of 0.3-0.4% hydroxypropylmethylcellulose in the form of an eyedrop or ointment applied to the eyes prior to exposure to UV radiation). This formulation, while effective against UV radiation, would affect vision tremendously and make it difficult for the user to see clearly for hours.

[Para 12] Baron (Patent Number 5,041,244) described an ophthalmic liquid sunglass that is composed of dosages of chromophores in aqueous gel to block transmission of all or various spectrums of UV from the eyes. He has described the use of high molecular weight polymers which form viscous dispersions and can be used to prolong the curation of the chromophore when the gel is applied to the eye. This alone would cause significant blurring of the users' vision. Further, there is no mention of the irritation that's caused once this mixture is directly applied to the eye. This makes Baron's invention not entirely practical for frequent use by the public.

[Para 13] Smith (U.S. Publication Number 2013/0331362 A1) has described an Ophthalmic Solution For Absorbing Ultraviolet Radiation and Method For Absorbing Ultraviolet Radiation, where he proposed two active organic ingredients to protect the eyes from UVA and UVB radiation, respectively. This formulation, while effective in theory, would cause significant irritation to the users' eyes to the point that it would render the formulation unusable due to its severe side effects. These ingredients, used as described, would also cause severe blurring of the users's vision due to the size of the molecules proposed. This would also render the Smith formulation a poor candidate for regular use. Last, when it comes to an ophthalmic preparation, the formulation must take into effect the fact that the ingredients used must be photostable (i.e., that the UV filters don't break down or degrade once exposed to UV light). The Smith patent proposes the use of avobenzone or octisalate, two of the most unstable sunscreen agents. This would further render this formulation ineffective for its proposed use.

[Para 14] From another standpoint, it is very important to consider how to dissolve or disperse the proposed ingredients in a mixture, which could be utilized as

an eye drop/suspension/ointment. The Smith patent publication has not described a method with which the proposed ingredients could be mixed into a vehicle that could be utilized for ophthalmic use. The present invention fulfills needs for a new form of UV radiation ophthalmic protection and provides other related advantages addressing all of the challenges aforementioned.

[Para 15] This present disclosure describes the composition of a sunscreen solution, suspension, emulsion, and/or an ointment that is designed to be directly applied to the eye itself to protect it from UV damage without causing significant irritation to the eye or affecting the users' vision. The present invention fulfills these needs for a new form of UV radiation protection and provides other related advantages.

SUMMARY OF THE INVENTION

[Para 16] Advances in our understanding of the sun protective effects of organic and inorganic ingredients has lead to the development of sunscreen preparations with very effective protection against the ultraviolet rays of the sun. Until now, the effects of these ingredients has only been described for the skin, and the prior art has warned against the use of such ingredients on the ocular surface. In fact, people are asked to rinse their eyes thoroughly in case such ingredients get into their eyes. The present invention describes the specific use of such ingredients onto the ocular surface itself. The present invention proposes formulations that provide very high SPF for the eyes, while causing minimal irritation without making vision blurry.

[Para 17] Examples of embodiments of the present invention include compositions that are manufactured as ophthalmic solutions, emollients, creams, or ointments that can be instilled directly on the eyes. It is understood that the use of the term “ophthalmic solution” shall include emollients, creams and ointments that can be instilled directly on the eyes.

[Para 18] An embodiment of the present invention of an ophthalmic sunscreen solution, comprises: a first portion comprising 0.25 percent to 15 percent by weight, wherein the first portion comprises at least one of the following: bemotrizinol; bisoctrizole; tris-biphenyl triazine; and/or octyl methoxycinnamate; and a second portion comprising a liquid vehicle base comprising a remainder of the solution by weight.

[Para 19] Other embodiments may include a third portion comprising an inorganic active ingredient comprising 0.25 percent to 15 percent by weight. The inorganic active ingredient may be selected from the group consisting of titanium dioxide, zinc oxide, iron oxide, zirconium oxide, cerium oxide and mixtures thereof and wherein the inorganic active ingredient is in micronized form or nanoparticle form.

[Para 20] Other embodiments may include a third portion comprising an organic active ingredient comprising 0.25 percent to 15 percent by weight and wherein the organic active ingredient is in micronized form or nanoparticle form. The organic active ingredient may be selected from the group consisting of dioxybenzone, octinoxate, octisalate, homosalate, avobenzone, octocrylene, para-aminobenzoic

acid, cinoxate, methyl anthranilate, octocrylene, padimate O, ensulizole, sulisobenzone, trolamine salicylate and ecamsule.

[Para 21] The first portion may comprise 0.25 percent to 10 percent by weight. The first portion may comprise 0.25 percent to 5 percent by weight. The liquid vehicle base may be water-based or oil-based.

[Para 22] Other embodiments may include an emulsifier. The emulsifier may be selected from the group consisting of a silicone-based emulsifier, a polyethylene glycol emulsifier, a polysiloxane emulsifier, a glyscoside emulsifier, an acrylic-based emulsifier and combinations thereof. The emulsifier may comprise polysorbate, carbomer and/or castor oil.

[Para 23] Other embodiments may include an emollient. The emollient may be selected from the group consisting of aloe extracts, oleaginous esters, ethers and combinations thereof. The emollient may comprises an anhydrous lanolin and/or an oleaginous ingredient.

[Para 24] Other embodiments may include a preservative, wherein the preservative is an ionic-buffered preservative, a detergent or an oxidizing detergent.

[Para 25] Other embodiments may include a chelating agent or an antioxidant.

[Para 26] The ophthalmic sunscreen solution may be in the form of an eye drop, a suspension, an emulsion, or an ointment, all of which are synthesized specifically to be applied onto the ocular surface.

[Para 27] Other embodiments may include an ophthalmic demulcent, wherein the ophthalmic demulcent is a cellulose derivative demulcent or a liquid polyol.

[Para 28] Other embodiments may include a hypertonicity agent, wherein the hypertonicity agent is sodium chloride.

[Para 29] Other embodiments may include an ophthalmic lubricant or an ophthalmic astringent.

[Para 30] The first portion may be in micronized or nanoparticle form.

[Para 31] Another embodiment of the present invention includes an ophthalmic solution comprised of diluted forms of an inorganic active ingredient such as titanium dioxide, zinc oxide, iron oxide, zirconium oxide, cerium oxide, or mixtures thereof. This composition may also contain a weak concentration of an organic active ingredient such as avobenzone, octinoxate, octisalate, homosalate, octocrylene, para- aminobenzoic acid, cinoxate, dioxybenzone, methyl anthranilate, octocrylene,

padimate O, ensulizole, sulisobenzone, trolamine salicylate, ecamsule, and mixtures thereof.

[Para 32] An example embodiment of the present invention includes an ophthalmic sunscreen composition which is comprised of anywhere from 0.25% to up to 15% zinc oxide by weight.

[Para 33] Another example of this invention includes embodiments comprised of octinoxate and/or octisalate.

[Para 34] Another example of this invention includes embodiments comprised of an emulsifier, silicone- or acrylic-based, glycosides, polyethylene glycols, or a mixture thereof.

[Para 35] Another example of this invention includes embodiments comprised of sunscreen composition comprising an emulsifier selected from the group consisting of Arlacel P 135, DC 9011 silicone elastomer, Abil WE 09, Abil EM-90, Emulgade 68/50, Simulgel A, Simulgel EG, and mixtures thereof.

[Para 36] Another example of this invention includes embodiments comprised of an emollient. Said emollient may be selected from the group consisting of Aloe extracts, ethers, oleaginous esters, and mixtures thereof.

[Para 37] Another example of this invention includes embodiments comprised of an emollient selected from the group consisting of actiphyte of aloe vera, Cetiol OE, Lexol IPL, octyl palmitate, neopentyl glycol heptanoate, neopentyl glycol diheptanoate, Trivent NP-13, CJ2- is alkyl benzoate, and mixtures thereof.

[Para 38] Other features and advantages of the present invention will become apparent from the following more detailed description, when taken in conjunction with the accompanying drawings, which illustrate, by way of example, the principles of the invention.

DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENTS

[Para 39] Examples of ophthalmic sunscreen compositions of the present invention provide an SPF of up to 50 or higher. As the eyes are usually not in direct exposure to UV radiation as opposed to the skin, such high SPF ratings may not be necessary for the present invention, and as such, the concentration of the active (and inactive) ingredients may be much lower than those proposed for dermal use.

[Para 40] The application of much lower concentrations of these ingredients will lead to much lower incidences of ophthalmic irritation/stinging when applied, and will lessen the known side-effects of such ingredients. Further, by reducing the concentrations of these ingredients, possible absorption of these ingredients into the eye (i.e., through the Cornea) will be reduced as to prevent possible intra-ocular effects (e.g., cataract formation).

[Para 41] Compositions of the present invention are now described, but are not limited to these embodiments.

[Para 42] Ophthalmic sunscreen compositions according to the present invention may contain a liquid vehicle base, such as an artificial tear formulation, which may be water and/or oil-based, or an ophthalmic suspension or ointment and include at least one inorganic and at least one organic active ingredient.

[Para 43] Inorganic active ingredients may include, but not be limited to zinc oxide, titanium dioxide, iron oxide, zirconium oxide, and cerium oxide, optionally in micronized form as to prevent blurred vision when applied.

[Para 44] Organic active ingredients may include, but not be limited to dioxybenzone, octinoxate, octisalate, homosalate, avobenzone, octocrylene, para-aminobenzoic acid, cinoxate, methyl anthranilate, octocrylene, padimate O, ensulizole, sulisobenzone, trolamine salicylate, and ecamsule.

[Para 45] The inactive ingredients of the present invention shall also include emulsifier(s) and/or emollient(s). Silicone-based emulsifiers like polyethylene glycols, polysiloxanes, glycosides are excellent choices. Acrylic-based emulsifiers, and mixtures thereof may also be used safely for the present preparation. Emollients may include, but not be limited to aloe extracts, oleaginous esters, and ethers, or a combination thereof.

[Para 46] The composition of the present invention shall also include, but not be limited to preservatives, chelating agents, and/or antioxidants.

[Para 47] The following examples describe a composition of the present invention, but it is obviously not intended to limit the scope of the invention.

[Para 48] Example 1:

[Para 49] An ophthalmic sunscreen solution can be synthesized by mixing 5% micronized zinc oxide and 3% octinoxate in an ophthalmic artificial tear formulation. This solution may contain carboxymethylcellulose sodium 0.1%; glycerin 0.25%; boric acid; calcium chloride dihydrate; erythritol; levocarnitine; magnesium chloride hexahydrate; potassium chloride; purified water; sodium borate decahydrate; and sodium citrate dihydrate.

[Para 50] Example 2:

[Para 51] An ophthalmic sunscreen solution can be synthesized by mixing a range of 5% micronized titanium dioxide and 3% octisalate in an ophthalmic artificial tear solution.

[Para 52] Example 3:

[Para 53] An ophthalmic sunscreen ointment can be synthesized by mixing a range of 5% micronized zinc oxide and 3% octinoxate in an ophthalmic ointment consisting of hypromellose, boric acid, sodium perborate, phosphonic acid, potassium chloride, purified water, and sodium chloride.

[Para 54] The present disclosure describes the composition of an ophthalmic sunscreen utilizing Tinosorb® (preferably Tinosorb M, IUPAC name 2,2′-methanediylbis[6-(2H-benzotriazol-2-yl)-4-(2,4,4-trimethylpentan-2-yl)phenol]) as its active ingredient. Tinosorb® is the trade name of a number of UV absorbers including the following: bemotrizinol (Tinosorb® S); bisoctrizole (Tinosorb® M); tris-biphenyl triazine (Tinosorb® A2B); and octyl methoxycinnamate (Tinosorb® OMC). Tinosorb® M is a photostable sunscreen composition that possesses multiple chemical characteristics over all other sunscreen agents currently available, that render it as an ideal candidate for use in a sunscreen formulation that is designed specifically to be directly applied to the ocular surface.

[Para 55] Bisoctrizole (marketed by BASF as Tinosorb® M and by MPI as Milestab 360, INCI methylene bis-benzotriazolyl tetramethylbutylphenol) is a benzotriazole-based organic compound that is added to sunscreens to absorb UV

rays. Bisoctrizole is a broad-spectrum ultraviolet radiation absorber, absorbing UVB as well as UVA rays, which makes it an ideal active ingredient for an ophthalmic sunscreen composition. It also reflects and scatters UV adding to its SPF capability for this specific application. Bisoctrizole is a hybrid UV absorber, the only organic UV filter produced and microfine organic particles (< 200 nm), like microfine zinc oxide and titanium dioxide. Where other organic UV absorbers need to be dissolved in either the oil or water phase, bisoctrizole dissolves poorly in both. Bisoctrizole is added to the water phase of a sunscreen as a 50% suspension, whereas mineral micropigments are usually added to the oil phase. The bisoctrizole particles are stabilized by the surfactant decyl glucoside. This allows for an ideal ophthalmic preparation that could be used in suspension form.

[Para 56] Bisoctrizole shows very little photodegradation and has a stabilizing effect on other UV absorbers, octyl methoxycinnamate (octinoxate) in particular. This is an extremely important factor when considering the very low concentration of the active ingredient that can be used in a formulation that is to be applied directly on the ocular surface. When formulated into a dermatologic sunscreen, bisoctrizole has minimal skin penetration. Work is still in progress by our laboratory to study its penetration into the Conjunctival or Corneal Tissues, but as an Ophthalmic Sunscreens, it should impregnate the surface layers of the Conjunctiva & Cornea so that its not washed out by blinking or the natural tears constantly irrigating the ocular surface. Bisoctrizole may penetrate the Conjunctiva and build a concentration in the episcleral connective tissue, and permeate through the Cornea and build an effective concentration in the eye's anterior chamber (aqueous humour) and serve as an effective barrier for UVA & UVB light that enters the eye, potentially preventing cataract formation and/or macular degeneration.

[Para 57] Unlike some other organic sunscreen actives, Tinosorb® has shown no estrogenic effects in vitro. Although there is very little systemic absorption of such agents when used on the ocular surface, it is a positive finding that this agent is safe in this regard. Tinosorb® one of the first UV filters that have been made available in micronized "nano" form, and used in this format, it will minimize significant irritation to the eye or affecting the users' vision. Further, Tinosorb® used in Particulate form (smaller than 100 nanometers) causes significantly less/no blurring for the user.

From a preparation standpoint, Nanoparticle easily dispersible in oil or glycol systems, making it an ideal preparation for an ophthalmic emulsion.

[Para 58] Advances in our understanding of the sun protective effects of organic and inorganic ingredients has lead to the development of sunscreen preparations with very effective protection against the ultraviolet rays of the sun. Until now, the effects of these ingredients has only been described for the skin, and the prior art has warned against the use of such ingredients directly on the ocular surface. In fact, people are asked to rinse their eyes thoroughly in case such ingredients get into their eyes. The present invention describes the specific use of such ingredients, particularly Tinosorb®, onto the ocular surface itself. The present invention proposes formulations that provide UV protection for the eyes, while causing minimal irritation without making vision blurry.

[Para 59] Examples of embodiments of the present invention include compositions that are manufactured as ophthalmic solutions, emollients, creams, or ointments that can be instilled directly on the eyes. It is understood that the use of the term "ophthalmic solution" shall include emollients, creams and ointments that can be instilled directly on the eyes.

[Para 60] An embodiment of the present invention includes an ophthalmic solution comprised of diluted forms of Tinosorb® an inorganic active ingredient by itself, or mixed with a weak concentration of another organic active ingredient.

[Para 61] An example embodiment of the present invention includes an ophthalmic sunscreen composition, which is comprised of Tinosorb® in an artificial tear vehicle.

[Para 62] Another example embodiment of the present invention includes an ophthalmic sunscreen composition, which is comprised of Tinosorb® with an organic sunscreen (e.g., Avobenzone) in an artificial tear vehicle.

[Para 63] Another example embodiment of the present invention includes an ophthalmic sunscreen composition, which is comprised of Tinosorb® with an inorganic sunscreen (e.g., Zinc Oxide) in an artificial tear vehicle.

[Para 64] Another example embodiment of the present invention includes an ophthalmic sunscreen composition, which is comprised of Tinosorb® with an organic, as well as an inorganic sunscreen an artificial tear

[Para 65] vehicle.

[Para 66] Another example of this invention includes said solution containing embodiments comprised of an emulsifier, silicone- or acrylic-based, glycosides, polyethylene glycols, or a mixture thereof.

[Para 67] Another example of this invention includes embodiments comprised of sunscreen composition comprising an emulsifier selected from the group consisting of Arlacel P 135, DC 9011 silicone elastomer, Abil WE 09, Abil EM-90, Emulgade 68/50, Simulgel A, Simulgel EG, and mixtures thereof.

[Para 68] Another example of this invention includes embodiments comprised of an emollient. Said emollient may be selected from the group consisting of Aloe extracts, ethers, oleaginous esters, and mixtures thereof.

[Para 69] Another example of this invention includes embodiments comprised of an emollient selected from the group consisting of actiphyte of aloe vera, Cetiol OE, Lexol IPL, octyl palmitate, neopentyl glycol heptanoate, neopentyl glycol diheptanoate, Trivent NP-13, CJ2- is alkyl benzoate, and mixtures thereof.

[Para 70] Compositions of the present invention are now described, but are not limited to these embodiments.

[Para 71] Ophthalmic sunscreen compositions according to the present invention may contain a liquid vehicle base, such as an artificial tear formulation, which may be water and/or oil-based, or an ophthalmic suspension or ointment and include at least one form of Tinosorb® (e.g., Tinosorb® M) by itself, or mixed with an organic- and/or an inorganic molecule with UV protecting features. Tinosorb® can be used in nano form, and refers to a number of UV absorbers: Bemotrizinol (Tinosorb® S), Bisoctrizole (Tinosorb® M), Tris-Biphenyl Triazine (Tinosorb® A2B), Octyl methoxycinnamate (Tinosorb® OMC).

[Para 72] Inorganic active ingredients may include, but not be limited to zinc oxide, titanium dioxide, iron oxide, zirconium oxide, and cerium oxide, optionally in micronized form as to prevent blurred vision when applied.

[Para 73] Organic active ingredients may include, but not be limited to dioxybenzone, octinoxate, octisalate, homosalate, avobenzone, octocrylene, para-aminobenzoic acid, cinoxate, methyl anthranilate, octocrylene, padimate O, ensulizole, sulisobenzone, trolamine salicylate, and ecamsule.

[Para 74] The inactive ingredients of the present invention shall also include emulsifier(s) and/or emollient(s). Silicone-based emulsifiers like polyethylene glycols, polysiloxanes, glycosides are excellent choices.

[Para 75] Acrylic-based emulsifiers, and mixtures thereof may also be used safely for the present preparation. Emollients may include, but not be limited to aloe extracts, oleaginous esters, and ethers, or a combination thereof.

[Para 76] The composition of the present invention shall also include, but not be limited to preservatives, chelating agents, and/or antioxidants.

[Para 77] The following examples describe a composition of the present invention, but it is obviously not intended to limit the scope of the invention.

[Para 78] Example 1: An ophthalmic sunscreen solution can be synthesized by mixing 5% micronized Tinosorb® M in an ophthalmic artificial tear formulation. This solution may contain carboxymethylcellulose sodium 0.1%; glycerin 0.25%; boric acid; calcium chloride dihydrate; erythritol; levocarnitine; magnesium chloride hexahydrate; potassium chloride; purified water; sodium borate decahydrate; and sodium citrate dihydrate.

[Para 79] Example 2: An ophthalmic sunscreen solution can be synthesized by mixing a range of 5% Tinosorb® with micronized titanium dioxide and 3% octisalate in an ophthalmic artificial tear solution. This solution may contain carboxymethylcellulose sodium 0.1%; glycerin 0.25%; boric acid; calcium chloride dihydrate; erythritol; levocarnitine; magnesium chloride hexahydrate; potassium chloride; purified water; sodium borate decahydrate; and sodium citrate dihydrate.

[Para 80] Example 3: An ophthalmic sunscreen ointment can be synthesized by mixing 5% micronized Tinosorb® M in an ophthalmic ointment consisting of hypromellose , boric acid, sodium perborate, phosphonic acid, potassium chloride, purified water, and sodium chloride.

[Para 81] Although several embodiments have been described in detail for purposes of illustration, various modifications may be made to each without departing from the scope and spirit of the invention. Accordingly, the invention is not to be limited, except as by the appended claims.

What is claimed is:

[Claim 1] An ophthalmic sunscreen solution, comprising:

a first portion comprising 0.25 percent to 15 percent by weight, wherein the first portion comprises at least one of the following:

bemotrizinol;

bisoctrizole;

tris-biphenyl triazine; and/or

octyl methoxycinnamate;

a second portion comprising a liquid vehicle base comprising a remainder of the solution by weight.

[Claim 2] The solution of claim 1, including a third portion comprising an inorganic active ingredient comprising 0.25 percent to 15 percent by weight.

[Claim 3] The solution of claim 2, wherein the inorganic active ingredient is selected from the group consisting of titanium dioxide, zinc oxide, iron oxide, zirconium oxide, cerium oxide and mixtures thereof and wherein the inorganic active ingredient is in micronized form or nanoparticle form.

[Claim 4] The solution of claim 3, including a third portion comprising an organic active ingredient comprising 0.25 percent to 15 percent by weight and wherein the organic active ingredient is in micronized form or nanoparticle form.

[Claim 5] The solution of claim 4, wherein the organic active ingredient is selected from the group consisting of dioxybenzone, octinoxate, octisalate, homosalate, avobenzone, octocrylene, para-aminobenzoic acid, cinoxate, methyl anthranilate, octocrylene, padimate O, ensulizole, sulisobenzone, trolamine salicylate and ecamsule.

[Claim 6] The solution of claim 5, wherein the first portion comprises 0.25 percent to 10 percent by weight.

[Claim 7] The solution of claim 5, wherein the first portion comprises 0.25 percent to 5 percent by weight.

[Claim 8] The solution of claim 5, wherein the liquid vehicle base is water-based or oil-based.

[Claim 9] The solution of claim 1, including an emulsifier.

[Claim 10] The solution of claim 9, wherein the emulsifier is selected from the group consisting of a silicone-based emulsifier, a polyethylene glycol emulsifier, a polysiloxane emulsifier, a glyscoside emulsifier, an acrylic-based emulsifier and combinations thereof.

[Claim 11] The solution of claim 9, wherein the emulsifier comprises polysorbate, carbomer and/or castor oil.

[Claim 12] The solution of claim 1, including an emollient.

[Claim 13] The solution of claim 12, wherein the emollient is selected from the group consisting of aloe extracts, oleaginous esters, ethers and combinations thereof.

[Claim 14] The solution of claim 12, wherein the emollient is comprises an anhydrous lanolin and/or an oleaginous ingredient.

[Claim 15] The solution of claim 1, including a preservative.

[Claim 16] The solution of claim 15, wherein the preservative is an ionic-buffered preservative, a detergent or an oxidizing detergent.

[Claim 17] The solution of claim 1, including a chelating agent.

[Claim 18] The solution of claim 1, including an antioxidant.

[Claim 19] The solution of claim 1, wherein the ophthalmic sunscreen solution is in the form of an eye drop, a suspension, an emulsion, or an ointment, all of which are synthesized specifically to be applied onto the ocular surface.

[Claim 20] The solution of claim 1, including an ophthalmic demulcent.

[Claim 21] The solution of claim 20, wherein the ophthalmic demulcent is a cellulose derivative demulcent or a liquid polyol.

[Claim 22] The solution of claim 1, including a hypertonicity agent.

[Claim 23] The solution of claim 1, wherein the hypertonicity agent is sodium chloride.

[Claim 24] The solution of claim 1, including an ophthalmic lubricant.

[Claim 25] The solution of claim 1, including an ophthalmic astringent.

[Claim 26] The solution of claim 1, wherein the first portion is in micronized or nanoparticle form.

[Claim 27] An ophthalmic sunscreen solution, comprising:

a first portion comprising 0.25 percent to 15 percent by weight, wherein the first portion is in micronized form or nanoparticle form, and wherein the first portion comprises at least one of the following:

bemotrizinol;

bisoctrizole;

tris-biphenyl triazine; and/or

octyl methoxycinnamate;

a second portion comprising an inorganic active ingredient comprising 0.25 percent to 15 percent by weight, wherein the inorganic active ingredient is selected from the group consisting of titanium dioxide, zinc oxide, iron oxide, zirconium oxide, cerium oxide and mixtures thereof, wherein the inorganic active ingredient is in micronized form or nanoparticle form;

a third portion comprising an organic active ingredient comprising 0.25 percent to 15 percent by weight, wherein the organic active ingredient is selected from the group consisting of dioxybenzone, octinoxate, octisalate, homosalate, avobenzone, octocrylene, para-aminobenzoic acid, cinoxate, methyl anthranilate, octocrylene, padimate O, ensulizole, sulisobenzone, trolamine salicylate and ecamsule; and

a fourth portion comprising a liquid vehicle base comprising a remainder of the solution by weight, wherein the liquid vehicle base is water-based or oil-based;

wherein the ophthalmic sunscreen solution is in the form of an eye drop, a suspension, an emulsion, or an ointment, all of which are synthesized specifically to be applied onto the ocular surface.

[Claim 28] An ophthalmic sunscreen solution, consisting essentially of:

a first portion comprising 0.25 percent to 15 percent by weight, wherein the first portion is in micronized form or nanoparticle form, and wherein the first portion consists essentially of:

bemotrizinol;

bisoctrizole;

tris-biphenyl triazine; and/or

octyl methoxycinnamate;

a second portion comprising an inorganic active ingredient comprising 0.25 percent to 15 percent by weight, wherein the inorganic active ingredient is selected from the group consisting of titanium dioxide, zinc oxide, iron oxide, zirconium oxide, cerium oxide and mixtures thereof, wherein the inorganic active ingredient is in micronized form or nanoparticle form;

a third portion comprising an organic active ingredient comprising 0.25 percent to 15 percent by weight, wherein the organic active ingredient is selected from the group consisting of dioxybenzone, octinoxate, octisalate, homosalate,

avobenzone, octocrylene, para-aminobenzoic acid, cinoxate, methyl anthranilate, octocrylene, padimate O, ensulizole, sulisobenzone, trolamine salicylate and ecamsule; and

a fourth portion comprising a liquid vehicle base comprising a remainder of the solution by weight, wherein the liquid vehicle base is water-based or oil-based;

wherein the ophthalmic sunscreen solution is in the form of an eye drop, a suspension, an emulsion, or an ointment, all of which are synthesized specifically to be applied onto the ocular surface.

INTERNATIONAL SEARCH REPORT

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A. CLASSIFICATION OF SUBJECT MATTER
IPC(8) - A61P 17/00, A61K 8/00 (2017.01)
CPC - A61Q 17/04, A61K 8/347

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
See Search History Document

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched
See Search History Document

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
See Search History Document

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 2015/0328148 A1 (Smith) 19 November 2015 (19.11.2015) para [0010]; [0046]; [0049]; [0055]; [0057]	1, 9-11, 15-16
X --- Y	US 2015/0272848 A1 (Holyfield) 01 October 2015 (01.10.2015) para [0002]; [0014]; [0018]-[0030]; [0041]-[0045]	1-8, 19, 26-28 --- 12-14, 17-18, 20-25
Y --- A	US 2015/0328098 A1 (Soroudi) 19 November 2015 (19.11.2015) para [0027]-[0028]; [0030]-[0031]; [0033]; Claim 1, 14-15	12-14, 17-18, 20-25 --- 3-8, 26-28
A	US 4,603,046 A (Georgalas et al.) 29 July 1986 (29.07.1986) whole document	1-28
A	US 2013/0028853 A1 (Nurse et al.) 31 January 2013 (31.01.2013) whole document	1-28
A	US 2016/0008237 A1 (Tagra Biotechnologies Ltd.) 14 January 2016 (14.01.2016) whole document	1-28
A	US 4,765,977 A (Baron) 23 August 1988 (23.08.1988) whole document	1-28

☐ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

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Date of the actual completion of the international search	Date of mailing of the international search report
07 September 2017	28 SEP 2017
Name and mailing address of the ISA/US Mail Stop PCT, Attn: ISA/US, Commissioner for Patents P.O. Box 1450, Alexandria, Virginia 22313-1450 Facsimile No. 571-273-8300	Authorized officer: Lee W. Young PCT Helpdesk: 571-272-4300 PCT OSP: 571-272-7774

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