METHODS OF REGULATING SKIN APPEARANCE WITH VITAMIN B3 COMPOUND

VERFAHREN UND REGELUNG DES HAUTAUSSEHENS MIT VITAMIN - B3 - VERBINDUNGEN

METHODES DE TRAITEMENT ET D’AMELIORATION DE L’ASPECT DE LA PEAU AU MOYEN D’UN COMPOSÉ A LA VITAMINE B3

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References cited:
EP-A- 0 052 705
WO-A-91/14431
WO-A-94/09756
FR-A- 1 351 454
FR-A- 2 592 790
GB-A- 2 210 789
US-A- 5 496 827

• DATABASE WPI Week 9011 Derwent
  Publications Ltd., London, GB; AN 90-079175
  XP002041710 "Agent for topical application to
  skin - contains N-(2-hydroxyethyl)nicotinic acid
  amide nitrate or its salt" & JP 02 032 006 A
  (SHISEIDO) , 1 February 1990

• DATABASE WPI Week 9250 Derwent
  Publications Ltd., London, GB; AN 92-410107
  XP002041711 "Novel skin external agent,
  preventing rough skin and ageing effectively -
  contains extract from Mellisa plant (s), Labiatae
  and one or more vitamin(s) e. g. vitamin A oil"
  & JP 04 305 512 A (SHISEIDO) , 28 October 1992

• DATABASE WPI Week 9621 Derwent
  Publications Ltd., London, GB; AN 96-205427
  XP002041731 "Dermatological prepn. contg.
  water soluble deriv. of retinol - useful for treating
  hyper-keratosis and preventing wrinkles is safe
  and stable" & JP 08 073 338 A (NOEVIR) , 19
  March 1996

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TECHNICAL FIELD

[0001] The present invention relates to a cosmetic method involving the application of topical compositions containing a vitamin B3 compound for regulating the condition of skin, especially for regulating visible and/or tactile discontinuities in skin associated, e.g., with skin aging. Preferred compositions contain niacinamide.

CROSS REFERENCE

[0002] This application claims priority under Title 35, United States Code 119(e) from Provisional Application Serial No. 60/016,043, filed April 23, 1996, Provisional Application Serial No. 60/025,242, filed September 16, 1996, and Provisional Application Serial No. 60/028,902, filed October 21, 1996. This application is a continuation-in-part of U.S. Application Serial No. 08/554,067, filed November 6, 1995.

BACKGROUND OF THE INVENTION

[0003] Many personal care products currently available to consumers are directed primarily to improving the health and/or physical appearance of the skin. Among these skin care products, many are directed to delaying, minimizing or even eliminating skin wrinkling and other histological changes typically associated with the aging of skin or environmental damage to human skin.

[0004] Skin is subject to insults by many extrinsic and intrinsic factors. Extrinsic factors include ultraviolet radiation (e.g., from sun exposure), environmental pollution, wind, heat, low humidity, harsh surfactants, abrasives, and the like. Intrinsic factors include chronological aging and other biochemical changes from within the skin. Whether extrinsic or intrinsic, these factors result in visible signs of skin aging and environmental damage, such as wrinkling and other forms of roughness (including increased pore size, flaking and skin lines), and other histological changes associated with skin aging or damage. To many people, skin wrinkles are a reminder of the disappearance of youth. As a result, the elimination of wrinkles has become a booming business in youth-conscious societies. Treatments range from cosmetic creams and moisturizers to various forms of cosmetic surgery.

[0005] Extrinsic or intrinsic factors may result in the thinning and general degradation of the skin. For example, as the skin naturally ages, there is a reduction in the cells and blood vessels that supply the skin. There is also a flattening of the dermal-epidermal junction which results in weaker mechanical resistance of this junction. See, for example, Oikarinen, "The Aging of Skin: Chronoaging Versus Photoaging," Photodermatol. Photomed. Photobiol., vol. 7, pp. 3-4, 1990.

[0006] It has now been found that vitamin B3 compounds, including niacinamide, provide benefits in regulating skin condition previously unrecognized in the art of which the present inventors are aware. For example, topical niacinamide can regulate the signs of skin aging, e.g., reduce or efface the visibility of the fine lines, wrinkles, and other forms of uneven or rough surface texture associated with aged or photodamaged skin. It has also now been found that topical compositions containing a vitamin B3 compound and a retinoid provide benefits in regulating skin condition previously unrecognized in the art of which the present inventors are aware. For example, such compositions enable the regulation of signs of skin aging with decreased potential for retinoid dermatitis. In addition, the vitamin B3 compound in combination with certain retinoids synergistically regulates signs of skin aging, especially visible and/or tactile discontinuities in skin texture associated with aged skin, including fine lines and wrinkles.

[0007] It is therefore an object of the present invention to provide topical compositions for cosmecically regulating skin pore size containing a vitamin B3 compound, especially niacinamide.

[0008] Other objects of the present invention are to provide such topical compositions further comprising a retinoid.

[0009] The present invention also relates to methods of providing such regulation using the subject compositions.

[0010] These and other objects of this invention will become apparent in light of the following disclosure.

SUMMARY OF THE INVENTION

[0011] The present invention relates to regulation of skin condition involving the topical application of a composition containing a vitamin B3 compound, especially niacinamide. The present invention also relates to regulation of skin condition involving topical application of a composition containing a vitamin B3 compound, especially niacinamide, and a retinoid. The invention especially relates to regulation of signs of skin aging, more especially regulating visible and/or tactile discontinuities in mammalian skin texture, including discontinuities associated with aged skin, involving the topical application of such compositions. The present invention relates to cosmetic regulation of skin condition.

[0012] In preferred embodiments, the vitamin B3 compound is substantially free of the salt form and is uncomplexed,
the vitamin B₃ compound is niacinamide, and the carrier contains a hydrophilic diluent.

DETAILED DESCRIPTION OF THE INVENTION

All percentages and ratios used herein are by weight of the total composition and all measurements made are at 25°C, unless otherwise designated.

The compositions of the present invention can comprise, consist essentially of, or consist of, the essential as well as optional ingredients and components described herein. As used herein, "consisting essentially of" means that the composition or component may include additional ingredients, but only if the additional ingredients do not materially alter the basic and novel characteristics of the claimed compositions or methods.

All publications cited herein are hereby incorporated by reference in their entirety.

The term "topical application", as used herein, means to apply or spread the compositions of the present invention onto the surface of the skin.

The term "dermatologically-acceptable," as used herein, means that the compositions or components thereof so described are suitable for use in contact with human skin without undue toxicity, incompatibility, instability, allergic response, and the like.

The term "safe and effective amount" as used herein means an amount of a compound or composition sufficient to significantly induce a positive benefit, preferably a positive skin appearance or feel benefit, including independently the benefits disclosed herein, but low enough to avoid serious side effects, i.e., to provide a reasonable benefit to risk ratio, within the scope of sound judgment of the skilled artisan.

The compositions of the present invention are useful for topical application and for regulating skin condition, including visible and/or tactile discontinuities in skin (especially the skin surface; such discontinuities are generally undesired). Such discontinuities may be induced or caused by internal and/or external factors, and include the signs of skin aging described herein. "Regulating skin condition" includes cosmetically regulating skin condition, including visible and/or tactile discontinuities in skin. Regulating skin condition involves improving skin appearance and/or feel.

The compositions of the present invention are useful for regulating signs of skin aging, more especially visible and/or tactile discontinuities in skin texture associated with aging. "Regulating the signs of skin aging" includes cosmetically regulating one or more of such signs (similarly, regulating a given sign of skin aging, e.g., lines, wrinkles or pores, includes cosmetically regulating that sign).

"Signs of skin aging" include, but are not limited to, all outward visibly and tactilely perceptible manifestations as well as any other macro or micro effects due to skin aging. Such signs may be induced or caused by intrinsic factors or extrinsic factors, e.g., chronological aging and/or environmental damage. These signs may result from processes which include, but are not limited to, the development of textural discontinuities such as wrinkles, including both fine superficial wrinkles and coarse deep wrinkles, skin lines, crevices, bumps, large pores (e.g., associated with adnexal structures such as sweat gland ducts, sebaceous glands, or hair follicles), scaliness, flakiness and/or other forms of skin unevenness or roughness, loss of skin elasticity (loss and/or inactivation of functional skin elastin), sagging (including puffiness in the eye area and jowls), loss of skin firmness, loss of skin tightness, loss of skin recoil from deformation, discoloration (including undereye circles), blotching, sallowness, hyperpigmented skin regions such as age spots and freckles, keratoses, abnormal differentiation, hyperkeratinization, elastosis, collagen breakdown, and other histological changes in the stratum corneum, dermis, epidermis, the skin vascular system (e.g., telangiectasia or spider vessels), and underlying tissues, especially those proximate to the skin.

It is to be understood that the present invention is not to be limited to regulation of the above mentioned "signs of skin aging" which arise due to mechanisms associated with skin aging, but is intended to include regulation of said signs irrespective of the mechanism of origin. As used herein, "regulating skin condition" is intended to include regulation of such signs irrespective of the mechanism of origin.

The present invention is especially useful for cosmetically regulating visible and/or tactile discontinuities in mammalian skin texture, including texture discontinuities associated with skin aging. As used herein, cosmetically regulating such discontinuities includes ameliorating, e.g., diminishing, minimizing and/or effacing visible and/or tactile discontinuities in the texture of mammalian skin, to thereby provide improved skin appearance and/or feel, e.g., a smoother, more even appearance and/or feel. Such visible and/or tactile discontinuities in skin texture include crevices, bumps, pores, fine lines, wrinkles, scales, flakes and/or other forms of textural unevenness or roughness associated with skin aging. For example, the length, depth, and/or other dimension of lines and/or wrinkles are decreased, the apparent diameter of pores decreases, or the apparent height of tissue immediately proximate to pore openings approaches that of the interadnexal skin.

The compositions of the present invention are also useful for promoting exfoliation of the skin. Without intending to be bound or limited by theory, it is believed that the compositions containing the vitamin B₃ compound, particularly niacinamide, strengthen the energy state of cells regulating exfoliation, resulting in normalization of epidermal differentiation and keratinization.
Vitamin B₃ component

[0025] The compositions of the present invention comprise a safe and effective amount of a vitamin B₃ compound. The compositions of the present invention preferably comprise from about 0.01% to about 50%, more preferably from about 0.1% to about 10%, even more preferably from about 0.5% to about 10%, and still more preferably from about 1% to about 5%, most preferably from about 2% to about 5%, of the vitamin B₃ compound.

[0026] As used herein, "vitamin B₃ compound" means a compound having the formula:

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\begin{align*}
\text{R} &\quad \text{(i.e., niacinamide), - COOH (i.e., nicotinic acid) or - CH₂OH (i.e., nicotinyl alcohol); derivatives thereof, and salts of any of the foregoing.} \\
\text{[0027]} \quad \text{Exemplary derivatives of the foregoing vitamin B₃ compounds include nicotinic acid esters, including non-vasodilating esters of nicotinic acid, nicotinyl amino acids, nicotinyl alcohol esters of carboxylic acids, nicotinic acid N-oxide and niacinamide N-oxide.} \\
\text{[0028]} \quad \text{Suitable esters of nicotinic acid include nicotinic acid esters of C₁-C₂₂, preferably C₁-C₁₆, more preferably C₁-C₆ alcohols. The alcohols are suitably straight-chain or branched chain, cyclic or acyclic, saturated or unsaturated (including aromatic), and substituted or unsubstituted. The esters are preferably non-vasodilating. As used herein, "non-vasodilating" means that the ester does not commonly yield a visible flushing response after application to the skin in the subject compositions (the majority of the general population would not experience a visible flushing response, although such compounds may cause vasodilation not visible to the naked eye). Non-vasodilating esters of nicotinic acid include tocopherol nicotinate and inositol hexanicotinate; tocopherol nicatinate is preferred.} \\
\text{[0029]} \quad \text{Other derivatives of the vitamin B₃ compound are derivatives of niacinamide resulting from substitution of one or more of the amide group hydrogens. Nonlimiting examples of derivatives of niacinamide useful herein include nicotinyl amino acids, derived, for example, from the reaction of an activated nicotinic acid compound (e.g., nicotinic acid azide or nicotinyl chloride) with an amino acid, and nicotinyl alcohol esters of organic carboxylic acids (e.g., C₁ - C₁₈). Specific examples of such derivatives include nicotinuric acid (C₈H₈N₂O₃) and nicotinyl hydroxamic acid (C₈H₉N₃O₂), which have the following chemical structures:} \\
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\text{nicotinuric acid:} \\
\begin{align*}
\text{O} &\quad \text{O} \\
\text{C-\text{NH-CH₂-COH}} &\quad \text{nicotinyl hydroxamic acid:} \\
\end{align*}
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\begin{align*}
\text{nicotinyl hydroxamic acid:} \\
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[0030] Exemplary nicotinyl alcohol esters include nicotinyl alcohol esters of the carboxylic acids salicylic acid, acetic
acid, glycolic acid, palmitic acid and the like. Other non-limiting examples of vitamin B₃ compounds useful herein are 2-chloronicotinamide, 6-aminonicotinamide, 6-methylnicotinamide, n-methyl-nicotinamide, n,n-diethylnicotinamide, n-(hydroxyethyl)-nicotinamide, quinolinic acid imide, nicotinanilide, n-benzynicotinamide, n-ethylnicotinamide, nifenazone, nicotinaldehyde, isonicotinic acid, methyl isonicotinic acid, thionicotinamide, nialamide, 1-(3-pyridylmethyl) urea, 2-mercaptonicotinic acid, nicomol, and niaprazine.

[0031] Examples of the above vitamin B₃ compounds are well known in the art and are commercially available from a number of sources, e.g., the Sigma Chemical Company (St. Louis, MO); ICN Biomedicals, Inc. (Irvin, CA) and Aldrich Chemical Company (Milwaukee, WI).

[0032] One or more vitamin B₃ compounds may be used herein. Preferred vitamin B₃ compounds are niacinamide and tocopherol nicotinate. Niacinamide is more preferred.

[0033] When used, salts, derivatives, and salt derivatives of niacinamide are preferably those having substantially the same efficacy as niacinamide in the methods of regulating skin condition described herein.

[0034] Salts of the vitamin B₃ compound are also useful herein. Nonlimiting examples of salts of the vitamin B₃ compound useful herein include organic or inorganic salts, such as inorganic salts with anionic inorganic species (e.g., chloride, bromide, iodide, carbonate, preferably chloride), and organic carboxylic acid salts (including mono-, di- and tri-C₁-C₁₈ carboxylic acid salts, e.g., acetate, salicylate, glycolate, lactate, malate, citrate, preferably monocarboxylic acid salts such as acetate). These and other salts of the vitamin B₃ compound can be readily prepared by the skilled artisan, for example, as described by W. Wenner, "The Reaction of L-Ascorbic and D-Iosascorbic Acid with Nicotinic Acid and Its Amide", J. Organic Chemistry, VOL. 14. 22-26 (1949). Wenner describes the synthesis of the ascorbic acid salt of niacinamide.

[0035] In a preferred embodiment, the ring nitrogen of the vitamin B₃ compound is substantially chemically free (e.g., unbound and/or unhindered), or after delivery to the skin becomes substantially chemically free ("chemically free" is hereinafter alternatively referred to as "uncomplexed"). More preferably, the vitamin B₃ compound is essentially uncomplexed. Therefore, if the composition contains the vitamin B₃ compound in a salt or otherwise complexed form, such complex is preferably substantially reversible, more preferably essentially reversible, upon delivery of the composition to the skin. For example, such complex should be substantially reversible at a pH of from about 5.0 to about 6.0. Such reversibility can be readily determined by one having ordinary skill in the art.

[0036] More preferably the vitamin B₃ compound is substantially uncomplexed in the composition prior to delivery to the skin. Exemplary approaches to minimizing or preventing the formation of undesirable complexes include omission of materials which form substantially irreversible or other complexes with the vitamin B₃ compound, pH adjustment, ionic strength adjustment, the use of surfactants, and formulating wherein the vitamin B₃ compound and materials which complex therewith are in different phases. Such approaches are well within the level of ordinary skill in the art.

[0037] Thus, in a preferred embodiment, the vitamin B₃ compound contains a limited amount of the salt form and is more preferably substantially free of salts of a vitamin B₃ compound. Preferably the vitamin B₃ compound contains less than about 50% of such salt, and is more preferably essentially free of the salt form. The vitamin B₃ compound in the compositions hereof having a pH of from about 4 to about 7 typically contain less than about 50% of the salt form. The vitamin B₃ compound may be included as the substantially pure material, or as an extract obtained by suitable physical and/or chemical isolation from natural (e.g., plant) sources. The vitamin B₃ compound is preferably substantially pure, more preferably essentially pure.

Carrier

[0039] The compositions of the present invention comprise a dermatologically acceptable carrier within which the vitamin B₃ compound is incorporated to enable the vitamin B₃ compound and optional other actives to be delivered to the skin at an appropriate concentration. The carrier can thus act as a diluent, dispersant, solvent, or the like for the active(s) which ensures that it can be applied to and distributed evenly over the selected target at an appropriate concentration.

[0040] The carrier may contain one or more dermatologically acceptable solid, semi-solid or liquid fillers, diluents, solvents, extenders and the like. The carrier may be solid, semi-solid or liquid. The carrier can itself be inert or it can possess dermatological benefits of its own. Concentrations of the carrier can vary with the carrier selected and the intended concentrations of the essential and optional components.

[0041] Suitable carriers include conventional or otherwise known carriers that are dermatologically acceptable. The carrier should also be physically and chemically compatible with the essential components described herein, and should not unduly impair stability, efficacy or other use benefits associated with the compositions of the present invention. Preferred components of the compositions of this invention should be capable of being comingled in a manner such that there is no interaction which would substantially reduce the efficacy of the composition under ordinary use situations.

[0042] The type of carrier utilized in the present invention depends on the type of product form desired for the com-
position. The topical compositions useful in the subject invention may be made into a wide variety of product forms such as are known in the art. These include, but are not limited to, lotions, creams, gels, sticks, sprays, ointments, pastes, mousses and cosmetics (e.g., solid, semi-solid, or liquid make-up, including foundations, eye-make-up, pigmented or non-pigmented lip treatments, e.g., lipsticks, and the like). These product forms may comprise several types of carriers including, but not limited to, solutions, aerosols, emulsions, gels, solids, and liposomes.

[0043] Preferred carriers contain a dermatologically acceptable, hydrophilic diluent. As used herein, “diluent” includes materials in which the vitamin B₃ compound can be dispersed, dissolved, or otherwise incorporated. Hydrophilic diluents include water, organic hydrophilic diluents such as lower monovalent alcohols (e.g., C₁ - C₄) and low molecular weight glycols and polyols, including propylene glycol, polyethylene glycol (e.g., Molecular Weight 200-600 g/mole), polypropylene glycol (e.g., Molecular Weight 425-2025 g/mole), glycerol, butylene glycol, 1,2,4-butanetriol, sorbitol esters, 1,2,6-hexanetriol, ethanol, isopropanol, sorbitol esters, butanediol, ether propanol, ethoxylated ethers, propoxylated ethers and combinations thereof. Water is a preferred diluent. The composition preferably comprises from about 80% to about 99.99% of the hydrophilic diluent and the vitamin B₃ compound in the above described amounts.

[0044] Solutions according to the subject invention typically include a dermatologically acceptable hydrophilic diluent. Solutions useful in the subject invention preferably contain from about 80% to about 99.99% of the hydrophilic diluent and the vitamin B₃ compound in the above described amounts.

[0045] Aerosols according to the subject invention can be formed by adding a propellant to a solution such as described above. Exemplary propellants include chloro-fluorinated lower molecular weight hydrocarbons. Additional propellants that are useful herein are described in Sagarin, Cosmetics Science and Technology, 2nd Edition, Vol. 2, pp. 443-465 (1972). Aerosols are typically applied to the skin as a spray-on product.

[0046] Preferred carriers comprise an emulsion such as oil-in-water emulsions, water-in-oil emulsions, and water-in-silicone emulsions. As will be understood by the skilled artisan, a given component will distribute primarily into either the water or oil/silicone phase, depending on the water solubility/dispersibility of the component in the composition. Preferred vitamin B₃ compounds distribute primarily into the aqueous phase. Oil-in-water emulsions are especially preferred.

[0047] Emulsions according to the present invention generally contain a solution as described above and a lipid or oil. Lipids and oils may be derived from animals, plants, or petroleum and may be natural or synthetic (i.e., man-made). Preferred emulsions also contain a humectant, such as glycerin. Emulsions will preferably further contain from about 1% to about 10%, more preferably from about 2% to about 5%, of an emulsifier, based on the weight of the carrier.


[0049] Preferred emulsions may have a wide range of viscosities, depending on the desired product form. Exemplary low viscosity emulsions, which are preferred, have a viscosity of about 50 centistokes or less, more preferably about 10 centistokes or less, most preferably about 5 centistokes or less.

[0050] Preferred water-in-silicone and oil-in-water emulsions are described in greater detail below.

a) Water-in-silicone emulsion

[0051] Water-in-silicone emulsions contain a continuous silicone phase and a dispersed aqueous phase.

(i) Continuous silicone phase

[0052] Preferred water-in-silicone emulsions of the present invention comprise from about 1% to about 60%, preferably from about 5% to about 40%, more preferably from about 10% to about 20%, by weight of a continuous silicone phase. The continuous silicone phase exists as an external phase that contains or surrounds the discontinuous aqueous phase described hereinafter.

[0053] The continuous silicone phase contains a polyorganosiloxane oil. A preferred water-in-silicone emulsion system is formulated to provide an oxidatively stable vehicle for the optional retinoid. The continuous silicone phase of these preferred emulsions comprises between about 50% and about 99.9% by weight of organopolysiloxane oil and less than about 50% by weight of a non-silicone oil. In an especially preferred embodiment, the continuous silicone phase comprises at least about 50%, preferably from about 60% to about 99.9%, more preferably from about 70% to about 99.9%, and even more preferably from about 80% to about 99.9%, polyorganosiloxane oil by weight of the continuous silicone phase, and up to about 50% non-silicone oils, preferably less about 40%, more preferably less than about 30%, even more preferably less than about 10%, and most preferably less than about 2%, by weight of the continuous silicone phase. These preferred emulsion systems provide more oxidative stability to the retinoid over
extended periods of time than comparable water-in-oil emulsions containing lower concentrations of the polyorganosiloxane oil. Concentrations of non-silicone oils in the continuous silicone phase are minimized or avoided altogether so as to further enhance oxidative stability of the selected retinoid in the compositions. Water-in-silicone emulsions of this type are described in copending U.S. Patent Application Serial No. 08/570,275, filed December 11, 1995, in the names of Joseph Michael Zukowski, Brent William Mason, Larry Richard Robinson and Greg George Hillebrand.

[0054] The organopolysiloxane oil for use in the composition may be volatile, non-volatile, or a mixture of volatile and non-volatile silicones. The term "nonvolatile" as used in this context refers to those silicones that are liquid under ambient conditions and have a flash point (under one atmosphere of pressure) of or greater than about 100°C. The term "volatile" as used in this context refers to all other silicone oils. Suitable organopolysiloxanes can be selected from a wide variety of silicones spanning a broad range of volatilities and viscosities. Examples of suitable organosiloxane oils include polyalkylsiloxanes, cyclic polyalkylsiloxanes, and polyalkyaryl siloxanes.

[0055] Polyalkylsiloxanes useful in the composition herein include polyalkylsiloxanes with viscosities of from about 0.5 to about 1,000,000 centistokes at 25°C. Such polyalkylsiloxanes can be represented by the general chemical formula R₃SiO[R₂SiO]ₓSi₃ wherein R is an alkyl group having from one to about 30 carbon atoms (preferably R is methyl or ethyl, more preferably methyl; also mixed alkyl groups can be used in the same molecule), and x is an integer from 0 to about 10,000, chosen to achieve the desired molecular weight which can range to over about 10,000,000. Commercially available polyalkylsiloxanes include the polydimethylsiloxanes, which are also known as dimethicones, examples of which include the Vicasil® series sold by General Electric Company and the Dow Corning® 200 series sold by Dow Corning Corporation. Specific examples of suitable polydimethylsiloxanes include Dow Corning® 200 fluid having a viscosity of 0.65 centistokes and a boiling point of 100°C, Dow Corning® 225 fluid having a viscosity of 10 centistokes and a boiling point greater than 200°C, Dow Corning® 255 fluids having viscosities of 50, 350, and 1,250 centistokes, respectively, and boiling points greater than 200°C. Suitable dimethicones include those represented by the chemical formula (CH₃)₃SiO[(CH₂)₄SiO]ₓSi(CH₃)₃ wherein R is straight or branched chain alkyl having from two to about 30 carbon atoms and x and y are each integers of 1 or greater selected to achieve the desired molecular weight which can range to over about 10,000,000. Examples of these alkyl-substituted dimethicones include cetyl dimethicone and lauryl dimethicone.

[0056] Cyclic polyalkylsiloxanes suitable for use in the composition include those represented by the chemical formula [SiR₂-O]ₓ wherein R is an alkyl group (preferably R is methyl or ethyl, more preferably methyl) and n is an integer from about 3 to 5, more preferably n is an integer from about 3 to 7, and most preferably n is an integer from about 4 to about 6. When R is methyl, these materials are typically referred to as cyclomethicones. Commercially available cyclomethicones include Dow Corning® 244 fluid having a viscosity of 2.5 centistokes, and a boiling point of 172°C, which primarily contains the cyclomethicone tetramer (i.e. n=4), Dow Corning® 344 fluid having a viscosity of 2.5 centistokes and a boiling point of 178°C, which primarily contains the cyclomethicone pentamer (i.e. n=5), Dow Corning® 245 fluid having a viscosity of 4.2 centistokes and a boiling point of 205°C, which primarily contains a mixture of the cyclomethicone tetramer and pentamer (i.e. n=4 and 5), and Dow Corning® 345 fluid having a viscosity of 4.5 centistokes and a boiling point of 217°C, which primarily contains a mixture of the cyclomethicone tetramer, pentamer, and hexamer (i.e. n=4, 5, and 6).

[0057] Also useful are materials such as trimethylsilyloxilicate, which is a polymeric material corresponding to the general chemical formula [(CH₂)₃SiO₁/₂]x[SiO₂]y wherein x is an integer from about 1 to about 500 and y is an integer from about 1 to about 500. A commercially available trimethylsiloxy silicate is sold as a mixture with dimethicone as Dow Corning® 593 fluid.

[0058] Dimethiconols are also suitable for use in the composition. These compounds can be represented by the chemical formulas R₃SiO[R₂SiO]ₓSi₂OH and HOR₂SiO[R₂SiO]ₓSi₂OH wherein R is an alkyl group (preferably R is methyl or ethyl, more preferably methyl) and x is an integer from 0 to about 500, chosen to achieve the desired molecular weight. Commercially available dimethiconols are typically sold as mixtures with dimethicone or cyclomethicone (e.g. Dow Corning® 1401, 1402, and 1403 fluids).

[0059] Polyalkyaryl siloxanes are also suitable for use in the composition. Polymethylphenyl siloxanes having viscosities from about 15 to about 65 centistokes at 25°C are especially useful.

[0060] Preferred for use herein are organopolysiloxanes selected from the group consisting of polyalkylsiloxanes, alkyl substituted dimethicones, cyclomethicones, trimethylsiloxy silicates, dimethiconols, polyalkylaryl siloxanes, and mixtures thereof. More preferred for use herein are polyalkylsiloxanes and cyclomethicones. Preferred among the polyalkylsiloxanes are dimethicones.

[0061] As stated above, the continuous silicone phase may contain one or more non-silicone oils. Concentrations of non-silicone oils in the continuous silicone phase are preferably minimized or avoided altogether so as to further enhance oxidative stability of the selected retinoid in the compositions. Suitable non-silicone oils have a melting point of about 25°C or less under about one atmosphere of pressure. Examples of non-silicone oils suitable for use in the continuous silicone phase are those well known in the chemical arts in topical personal care products in the form of water-in-oil emulsions, e.g., mineral oil, vegetable oils, synthetic oils, semisynthetic oils, etc.
(ii) Dispersed aqueous phase

[0062] The topical compositions of the present invention comprise from about 30% to about 90%, more preferably from about 50% to about 85%, and most preferably from about 70% to about 80% of a dispersed aqueous phase. In emulsion technology, the term "dispersed phase" is a term well-known to one skilled in the art which means that the phase exists as small particles or droplets that are suspended in and surrounded by a continuous phase. The dispersed phase is also known as the internal or discontinuous phase. The dispersed aqueous phase is a dispersion of small aqueous particles or droplets suspended in and surrounded by the continuous silicone phase described hereinbefore.

[0063] The aqueous phase can be water, or a combination of water and one or more water soluble or dispersible ingredients. Nonlimiting examples of such optional ingredients include thickeners, acids, bases, salts, chelants, gums, water-soluble or dispersible alcohols and polyols, buffers, preservatives, sunscreening agents, colorings, and the like.

[0064] The topical compositions of the present invention will typically comprise from about 25% to about 90%, preferably from about 40% to about 80%, more preferably from about 60% to about 80%, water in the dispersed aqueous phase by weight of the composition.

(iii) Emulsifier for dispersing the aqueous phase

[0065] The water-in-silicone emulsions of the present invention preferably comprise an emulsifier. In a preferred embodiment, the composition contains from about 0.1% to about 10% emulsifier, more preferably from about 0.5% to about 7.5%, most preferably from about 1% to about 5%, emulsifier by weight of the composition. The emulsifier helps disperse and suspend the aqueous phase within the continuous silicone phase.

[0066] A wide variety of emulsifying agents can be employed herein to form the preferred water-in-silicone emulsion. Known or conventional emulsifying agents can be used in the composition, provided that the selected emulsifying agent is chemically and physically compatible with essential components of the composition, and provides the desired dispersion characteristics. Suitable emulsifiers include silicone emulsifiers, non-silicon-containing emulsifiers, and mixtures thereof, known by those skilled in the art for use in topical personal care products. Preferably these emulsifiers have an HLB value of or less than about 14, more preferably from about 2 to about 14, and most preferably from about 4 to about 14. Emulsifiers having an HLB value outside of these ranges can be used in combination with other emulsifiers to achieve an effective weighted average HLB for the combination that falls within these ranges.

[0067] Silicone emulsifiers are preferred. A wide variety of silicone emulsifiers are useful herein. These silicone emulsifiers are typically organically modified organopolysiloxanes, also known to those skilled in the art as silicone surfactants. Useful silicone emulsifiers include dimethicone copolyls. These materials are polydimethyl siloxanes which have been modified to include polyether side chains such as polyethylene oxide chains, polypropylene oxide chains, mixtures of these chains, and polyether chains containing moieties derived from both ethylene oxide and propylene oxide. Other examples include alkyl-modified dimethicone copolyls, i.e., compounds which contain C2-C30 pendant side chains. Still other useful dimethicone copolyls include materials having various cationic, anionic, amphoteric, and zwitterionic pendant moieties.

[0068] The dimethicone copolyl emulsifiers useful herein can be described by the following general structure:

\[
\text{CH}_3 \quad -\text{Si}-O-\left(\text{CH}_2\right)_n-O-\left(\text{CH}_2\text{CHR}_3^0\right)_m-O-\text{H},
\]

wherein R is C1-C30 straight, branched, or cyclic alkyl and R\(^2\) is selected from the group consisting of

\[
\text{and}
\]

\[
\text{CH}_3 \quad -\text{Si}-O-\left(\text{CH}_2\right)_n-O-\left(\text{CH}_2\text{CHR}_3^0\right)_m-O-\left(\text{CH}_2\text{CHR}_4^0\right)_o-O-\text{H},
\]

wherein n is an integer from 3 to about 10; R\(^3\) and R\(^4\) are selected from the group consisting of H and C1-C6 straight.
or branched chain alkyl such that \( R^3 \) and \( R^4 \) are not simultaneously the same; and \( m, o, x, \) and \( y \) are selected such that the molecule has an overall molecular weight from about 200 to about 10,000,000, with \( m, o, x, \) and \( y \) being independently selected from integers of zero or greater such that \( m \) and \( o \) are not both simultaneously zero, and \( z \) being independently selected from integers of 1 or greater. It is recognized that positional isomers of these copolymers can be achieved. The chemical representations depicted above for the \( R^2 \) moieties containing the \( R^3 \) and \( R^4 \) groups are not meant to be limiting but are shown as such for convenience.

**[0069]** Also useful herein, although not strictly classified as dimethicone copolyols, are silicone surfactants as depicted in the structures in the previous paragraph wherein \( R^2 \) is:

\[
\begin{align*}
\text{--(CH}_2\text{)}_n\text{--O--R}^5,
\end{align*}
\]

wherein \( R^5 \) is a cationic, anionic, amphoteric, or zwitterionic moiety.

**[0070]** Nonlimiting examples of dimethicone copolyols and other silicone surfactants useful as emulsifiers herein include polydimethylsiloxane polyether copolymers with pendant polyethylene oxide sidechains, polydimethylsiloxane polyether copolymers with pendant polypropylene oxide sidechains, polydimethylsiloxane polyether copolymers with pendant mixed polyethylene oxide and polypropylene oxide sidechains, polydimethylsiloxane polyether copolymers with pendant mixed poly(ethylene)(propylene)oxide sidechains, polydimethylsiloxane polyether copolymers with pendant organobetaine sidechains, polydimethylsiloxane polyether copolymers with pendant carboxylate sidechains, polydimethylsiloxane polyether copolymers with pendant quaternary ammonium sidechains; and also further modifications of the preceding copolymers containing pendant C2-C30 straight, branched, or cyclic alkyl moieties. Examples of commercially available dimethicone copolyols useful herein sold by Dow Corning Corporation are Dow Corning® 190, 193, Q2-5220, 2501 Wax, 2-5324 fluid, and 3225C (this later material being sold as a mixture with cyclomethicone). Cetyl dimethicone copolyol is commercially available as a mixture with polyglyceryl-4 isostearate (and) hexyl laurate and is sold under the tradename ABIL® WE-09 (available from Goldschmidt). Cetyl dimethicone copolyol is also commercially available as a mixture with hexyl laurate (and) polyglyceryl-3 oleate (and) cetyl dimethicone and is sold under the tradename ABIL® WS-08 (also available from Goldschmidt). Other nonlimiting examples of dimethicone copolyols also include lauryl dimethicone copolyol, dimethicone copolyol acetate, dimethicone copolyol adipate, dimethicone copolyol behenate, dimethicone copolyol butyl ether, dimethicone copolyol hydroxy stearate, dimethicone copolyol isostearate, dimethicone copolyol laurate, dimethicone copolyol methyl ether, dimethicone copolyol phosphate, and dimethicone copolyol stearate. See International Cosmetic Ingredient Dictionary, Fifth Edition, 1993.


**[0072]** Among the non-silicon-containing emulsifiers useful herein are various nonionic and anionic emulsifying agents such as sugar esters and polyesters, alkoxylated sugar esters and polyesters, C1-C30 fatty acid esters of C1-C30 fatty acids, alkoxylated derivatives of C1-C30 fatty acid esters of C1-C30 fatty acids, alkoxylated ethers of C1-C30 fatty acids, polyglycerol esters of C1-C30 fatty acids, C1-C30 esters of polysiloxanes, C1-C30 esters of polyols, alkyl phosphates, polyoxyalkylene fatty ether phosphates, fatty acid amides, acyl lactylates, soaps, and mixtures thereof. Other suitable emulsifiers are described, for example, in McCutcheon’s, Detergents and Emulsifiers, North American Edition (1986), published by Allured Publishing Corporation; U.S. Patent No. 5,011,681 to Ciotti et al., issued April 30, 1991; U.S. Patent No. 4,421,769 to Dixon et al., issued December 20, 1983; and U.S. Patent No. 3,755,560 to Dickert et al., issued August 28, 1973.

**[0073]** Nonlimiting examples of these non-silicon-containing emulsifiers include: polyethylene glycol 20 sorbitan monolaurate (Polysorbate 20), polyethylene glycol 5 soya sterol, Steareth-20, Ceteareth-20, PPG-2 methyl glucose ether distearteate, Ceteth-10, Polysorbate 80, cetyl phosphate, potassium cetyl phosphate, diethanolamine cetyl phosphate, Polysorbate 60, glyceryl stearate, PEG-100 stearate, polyoxyethylene 20 sorbitan trioleate (Polysorbate 85), sorbitan monolaurate, polyoxyethylene 4 lauryl ether sodium stearate, polyglyceryl-4 isostearate, hexyl laurate, steareth-20, ceteareth-20, PPG-2 methyl glucose ether distearteate, cethet-10, diethanolamine cetyl phosphate, glyceryl stearate,
b) Oil-in-Water Emulsions

Other preferred topical carriers include oil-in-water emulsions, having a continuous aqueous phase and a hydrophobic, water-insoluble phase ("oil phase") dispersed therein. An especially preferred oil-in-water emulsion, containing a structuring agent, hydrophilic surfactant and water, is described in detail hereinafter.

(i) Structuring Agent

A preferred oil-in-water emulsion comprises a structuring agent to assist in the formation of a liquid crystalline gel network structure. Concentrations of such structuring agents are from about 1% to about 20%, preferably from about 1% to about 10%, more preferably from about 3% to about 9% by weight of the topical carrier.

Suitable structuring agents are those selected from the group consisting of saturated C_{16} to C_{30} fatty alcohols, saturated C_{16} to C_{30} fatty alcohols containing from about 1 to about 5 moles of ethylene oxide, saturated C_{16} to C_{30} diols, saturated C_{16} to C_{30} monoglycerol ethers, saturated C_{16} to C_{30} hydroxy fatty acids, and mixtures thereof, having a melting point of at least about 45°C.

Preferred structuring agents include stearyl alcohol, cetyl alcohol, behenyl alcohol, stearic acid, palmitic acid, the polyethylene glycol ether of stearyl alcohol having an average of about 1 to about 5 ethylene oxide units, the polyethylene glycol ether of cetyl alcohol having an average of about 1 to about 5 ethylene oxide units, and mixtures thereof. More preferred structuring agents of the present invention are selected from the group consisting of stearyl alcohol, cetyl alcohol, behenyl alcohol, the polyethylene glycol ether of stearyl alcohol having an average of about 2 ethylene oxide units (steareth-2), the polyethylene glycol ether of cetyl alcohol having an average of about 2 ethylene oxide units, and mixtures thereof. Even more preferred structuring agents are selected from the group consisting of stearyl alcohol, cetyl alcohol, behenyl alcohol, steareth-2, and mixtures thereof. Most preferred is steareth-2, available under the tradename of Brij® 72 from ICI Americas.

(ii) Hydrophilic surfactant

The preferred oil-in-water emulsions comprise from about 0.05% to about 10%, preferably from about 1% to about 6%, and more preferably from about 1% to about 3% of at least one hydrophilic surfactant which can disperse the hydrophobic materials in the water phase (percentages by weight of the topical carrier). The surfactant, at a minimum, must be hydrophilic enough to disperse in water.


\[
[R_1\text{N}^+\text{R}_2\text{R}_3\text{N}^-\text{R}_4^-] + \\
X^-
\]

wherein \(R_1\) is an alkyl group having from about 12 to about 30 carbon atoms, or an aromatic, aryl or alkaryl group having from about 12 to about 30 carbon atoms; \(R_2, R_3, \) and \(R_4\) are independently selected from hydrogen, an alkyl group having from about 1 to about 22 carbon atoms, or aromatic, aryl or alkaryl groups having from about 12 to about 22 carbon atoms; and \(X\) is any compatible anion, preferably selected from the group consisting of chloride, bromide, iodide, acetate, phosphate, nitrate, sulfate, methyl sulfate, ethyl sulfate, tosylate, lactate, citrate, glycolate, and mixtures thereof.
thereof. Additionally, the allyl groups of R₁, R₂, R₃, and R₄ can also contain ester and/or ether linkages, or hydroxy or amino group substituents (e.g., the alkyl groups can contain polyethylene glycol and polypropylene glycol moieties).

More preferably, R₁ is an alkyl group having from about 12 to about 22 carbon atoms; R₂ is selected from H or an alkyl group having from about 1 to about 3 carbon atoms; and X is as described previously.

Most preferably, R₁ is an alkyl group having from about 12 to about 22 carbon atoms; R₂, R₃, and R₄ are selected from H or an alkyl group having from about 1 to about 3 carbon atoms; and X is as described previously.

Alternatively, other useful cationic emulsifiers include amino-amides, wherein in the above structure R₁ is alternatively R₂CONH-(CH₂)ₙ, wherein R₂ is an alkyl group having from about 12 to about 22 carbon atoms, and n is an integer from about 2 to about 6, more preferably from about 2 to about 4, and most preferably from about 2 to about 4. Nonlimiting examples of these cationic emulsifiers include stearamidopropyl PG-dimonium chloride phosphate, behenamidopropyl PG dimonium chloride, stearamidopropyl ethyldimonium ethosulfate, stearamidopropyl dimethyl (myristyl acetate) ammonium chloride, stearamidopropyl dimethyl cetearyl ammonium tosylate, stearamidopropyl dimethyl ammonium chloride, stearamidopropyl dimethyl ammonium lactate, and mixtures thereof. Especially preferred is behenamidopropyl PG dimonium chloride.

Nonlimiting examples of quaternary ammonium salt cationic surfactants include those selected from the group consisting of cetyl ammonium chloride, cetyl ammonium lactate, lauryl ammonium chloride, lauryl ammonium bromide, stearyl ammonium chloride, stearyl ammonium bromide, cetyl dimethyl ammonium chloride, cetyl dimethyl ammonium bromide, lauryl dimethyl ammonium chloride, lauryl dimethyl ammonium bromide, stearyl dimethyl ammonium chloride, stearyl dimethyl ammonium bromide, lauryl trimethyl ammonium chloride, lauryl trimethyl ammonium bromide, stearyl trimethyl ammonium chloride, stearyl trimethyl ammonium bromide, lauryl dimethyl ammonium chloride, stearyl dimethyl cetyl dimethyl ammonium chloride, dicetyl ammonium chloride, dicetyl ammonium bromide, di lauryl ammonium chloride, di lauryl ammonium bromide, distearyl ammonium chloride, distearyl ammonium bromide, di cetyl ammonium chloride, di cetyl ammonium bromide, ditallow dimethyl ammonium chloride, ditallow dimethyl ammonium bromide, and mixtures thereof.

Additional quaternary ammonium salts include those wherein the C₁₂ to C₃₀ alkyl carbon chain is derived from a tallow fatty acid or from a coconut fatty acid. The term "tallow" refers to an alkyl group derived from tallow fatty acids (usually hydrogenated tallow fatty acids), which generally have mixtures of alkyl chains in the C₁₂ to C₁₈ range. The term "coconut" refers to an alkyl group derived from a coconut fatty acid, which generally have mixtures of alkyl chains in the C₁₂ to C₁₄ range. Examples of quaternary ammonium salts derived from these tallow and coconut sources include ditallow dimethyl ammonium chloride, ditallow dimethyl ammonium sulfate, di(hydrogenated tallow) dimethyl ammonium chloride, di(hydrogenated tallow) dimethyl ammonium acetate, ditallow dimethyl ammonium phosphate, ditallow dimethyl ammonium nitrate, di(coconutalkyl)dimethyl ammonium chloride, di(coconutalkyl)dimethyl ammonium bromide, ditallow dimethyl ammonium chloride, stearamidopropyl PG-dimonium chloride phosphate, stearamidopropyl ethyldimonium ethosulfate, stearamidopropyl dimethyl (myristyl acetate) ammonium chloride, stearamidopropyl dimethyl cetearyl ammonium tosylate, stearamidopropyl dimethyl ammonium chloride, stearamidopropyl dimethyl ammonium lactate, and mixtures thereof. An example of a quaternary ammonium compound having an alkyl group with an ester linkage is ditallowyl oxyethyl dimethyl ammonium chloride.

More preferred cationic surfactants are those selected from the group consisting of behenamidopropyl PG dimonium chloride, dilauryl dimethyl ammonium chloride, distearyl dimethyl ammonium chloride, dimyristyl dimethyl ammonium chloride, dipalmityl dimethyl ammonium chloride, distearoyl dimethyl ammonium chloride, stearamidopropyl PG-dimonium chloride phosphate, stearamidopropyl ethyldimonium ethosulfate, stearamidopropyl dimethyl (myristyl acetate) ammonium chloride, stearamidopropyl dimethyl cetearyl ammonium tosylate, stearamidopropyl dimethyl ammonium chloride, stearamidopropyl dimethyl ammonium lactate, and mixtures thereof.

Most preferred cationic surfactants are those selected from the group consisting of behenamidopropyl PG dimonium chloride, dilauryl dimethyl ammonium chloride, distearyl dimethyl ammonium chloride, dimyristyl dimethyl ammonium chloride, dipalmityl dimethyl ammonium chloride, distearoyl dimethyl ammonium chloride, stearamidopropyl PG-dimonium chloride phosphate, stearamidopropyl ethyldimonium ethosulfate, stearamidopropyl dimethyl (myristyl acetate) ammonium chloride, stearamidopropyl dimethyl cetearyl ammonium tosylate, stearamidopropyl dimethyl ammonium chloride, stearamidopropyl dimethyl ammonium lactate, and mixtures thereof.

A preferred combination of cationic surfactant and structuring agent is behenamidopropyl PG dimonium chloride and/or behenyl alcohol, wherein the ratio is preferably optimized to maintained to enhance physical and chemical stability, especially when such a combination contains ionic and/or highly polar solvents. This combination is especially useful for delivery of sun-screening agents such as zinc oxide and octyl methoxycinnamate.

A wide variety of anionic surfactants are also useful herein. See, e.g., U.S. Patent No. 3,929,678, to Laughlin et al., issued December 30, 1975. Nonlimiting examples of anionic surfactants include the alkoyl isethionates, and the alkyl and alkyl ether sulfates. The alkoyl isethionates typically have the formula RCO-OCH₂ CH₂ SO₃ M wherein R is alkyl or alkenyl of from about 10 to about 30 carbon atoms, and M is a water-soluble cation such as ammonium, sodium, potassium and triethanolamine. Nonlimiting examples of these isethionates include those alkoyl isethionates selected from the group consisting of ammonium cocoyl isethionate, sodium cocoyl isethionate, sodium lauryl isethionate,
sodium stearoyl isethionate, and mixtures thereof.

The alkyl and alkyl ether sulfates typically have the respective formulae RO\textsubscript{SO\textsubscript{3}}M and RO(C\textsubscript{2}H\textsubscript{4}O)\textsubscript{x}SO\textsubscript{3}M, wherein R is alkyl or alkenyl of from about 10 to about 30 carbon atoms, x is from about 1 to about 10, and M is a water-soluble cation such as ammonium, sodium, potassium and triethanolamine. Another suitable class of anionic surfactants are the water-soluble salts of the organic, sulfuric acid reaction products of the general formula:

\[ R_1-\text{SO}_3^-M \]

wherein \( R_1 \) is chosen from the group consisting of a straight or branched chain, saturated aliphatic hydrocarbon radical having from about 8 to about 24, preferably about 10 to about 16, carbon atoms; and M is a cation. Still other anionic synthetic surfactants include the class designated as succinamates, olefin sulfonates having about 12 to about 24 carbon atoms, and \( \beta \)-alkyloxy alkane sulfonates. Examples of these materials are sodium lauryl sulfate and ammonium lauryl sulfate.

Other anionic materials useful herein are soaps (i.e. alkali metal salts, e.g., sodium or potassium salts) of fatty acids, typically having from about 8 to about 24 carbon atoms, preferably from about 10 to about 20 carbon atoms. The fatty acids used in making the soaps can be obtained from natural sources such as, for instance, plant or animal-derived glycerides (e.g., palm oil, coconut oil, soybean oil, castor oil, tallow, lard, etc.) The fatty acids can also be synthetically prepared. Soaps are described in more detail in U.S. Patent No. 4,557,853, cited above.

Amphoteric and zwitterionic surfactants are also useful herein. Examples of amphoteric and zwitterionic surfactants which can be used in the compositions of the present invention are those which are broadly described as derivatives of aliphatic secondary and tertiary amines in which the aliphatic radical can be straight or branched chain and wherein one of the aliphatic substituents contains from about 8 to about 22 carbon atoms (preferably C\textsubscript{8} - C\textsubscript{18}) and one contains an anionic water solubilizing group, e.g., carboxy, sulfonate, sulfate, phosphate, or phosphonate.

Examples are alkyl imino acetates, and iminodialkanoates and aminoalkanoates of the formulas RN(\text{CH}_2)_m\text{CO}_2\text{M} and RNH(\text{CH}_2)_m\text{CO}_2\text{M} wherein m is from 1 to 4, R is a C\textsubscript{8}-C\textsubscript{22} alkyl or alkenyl, and M is H, alkali metal, alkaline earth metal ammonium, or alkanolammonium. Also included are imidazolinium and ammonium derivatives. Specific examples of suitable amphoteric surfactants include sodium 3-dodecylaminopropanoate, sodium 3-dodecylaminopropanoate sulfonate, N-alkyltaurines such as the one prepared by reacting dodecylamine with sodium isethionate according to the teaching of U.S. Patent 2,658,072 N-higher alkyl aspartic acids such as those produced according to the teaching of this invention. Other examples of useful amphoteric surfactants include the class designated as succinamates, olefin sulfonates having about 12 to about 24 carbon atoms, and \( \beta \)-alkyloxy alkane sulfonates. Examples of these materials are sodium lauryl sulfate and ammonium lauryl sulfate.

Other useful anionic surfactants include the sulfates and hydroxysultaines such as cocamidopropyl PG-dimonium chloride phosphate (commercially available as Monaquat PTC, from Mona Corp.). Also useful herein as amphoteric or zwitterionic surfactants are the betaines. Examples of betaines include the higher alkyl betaines, such as coco dimethyl carboxymethyl betaine, lauryl dimethyl carboxymethyl betaine, lauryl dimethyl alphacarboxyethyl betaine, cetyl dimethyl carboxymethyl betaine, cetyl dimethyl betaine (available as Lonza-INE 16SP from Lonza Corp.), lauryl bis-(2-hydroxyethyl) carboxymethyl betaine, stearyl bis-(2-hydroxypropyly) carboxymethyl betaine, oleyl dimethyl gamma-carboxypropyl betaine, lauryl bis-(2-hydroxypropyl)alpha-carboxyethyl betaine, coco dimethyl sulfopropyl betaine, stearyl dimethyl sulfopropyl betaine, lauryl dimethyl sulfopolyethyl betaine, lauryl bis-(2-hydroxyethyl) sulfopropyl betaine, and amidobetaines and amidosulfobetaines (wherein the RCONH(CH\textsubscript{2})\textsubscript{3} radical is attached to the nitrogen atom of the betaine), oleyl betaine (available as amphoteric Velvex BK-35 and BA-35 from Henkel), and cocamidopropyl betaine (available as Velvex BK-35 and BA-35 from Henkel).

Other useful amphoteric and zwitterionic surfactants include the sulfates and hydroxysultaines such as cocamidopropyl hydroxysultaine (available as Mirataine CBS from Rhone-Poulenc), and the alkanoyl sarcosinates corresponding to the formula RCON(H\text{CH}_2)\text{CH}_2\text{CH}_2\text{CO}_2\text{M} wherein R is alkyl or alkenyl of about 10 to about 20 carbon atoms, and M is a water-soluble cation such as ammonium, sodium, potassium and trialkanolamine (e.g., triethanolamine), a preferred example of which is sodium lauroyl sarcosinate.

### (iii) Water

The preferred oil-in-water emulsion comprises from about 25% to about 98%, preferably from about 65% to about 95%, more preferably from about 70% to about 90% water by weight of the topical carrier. The hydrophobic phase is dispersed in the continuous aqueous phase. The hydrophobic phase may contain water insoluble or partially soluble materials such as are known in the art, including but not limited to the silicones described herein in reference to silicone-in-water emulsions, and other oils and lipids such as described above in reference to emulsions.

The topical compositions of the subject invention, including but not limited to lotions and creams, may comprise...
a dermatologically acceptable emollient. Such compositions preferably contain from about 2% to about 50% of the emollient. As used herein, "emollient" refers to a material useful for the prevention or relief of dryness, as well as for the protection of the skin. A wide variety of suitable emollients are known and may be used herein. Sagarin, Cosmetics, Science and Technology, 2nd Edition, Vol. 1, pp. 32-43 (1972), contains numerous examples of materials suitable as an emollient. A preferred emollient is glycerin. Glycerin is preferably used in an amount of from or about 0.01% to or about 20%, more preferably from or about 0.01% to or about 10%, most preferably from or about 0.1% to or about 5%, e. g., 3%.

Lotions and creams according to the present invention generally comprise a solution carrier system and one or more emollients. Lotions typically comprise from about 1% to about 20%, preferably from about 5% to about 10%, of emollient; from about 50% to about 90%, preferably from about 60% to about 80%, water; and the vitamin B₃ compound in the above described amounts. A cream typically comprises from about 5% to about 50%, preferably from about 10% to about 20%, of emollient; from about 45% to about 85%, preferably from about 50% to about 75%, water; and the vitamin B₃ compound in the above described amounts.

Ointments of the present invention may comprise a simple carrier base of animal or vegetable oils or semi-solid hydrocarbons (oleaginous); absorption ointment bases which absorb water to form emulsions; or water soluble carriers, e.g., a water soluble solution carrier. Ointments may further comprise a thickening agent, such as described in Sagarin, Cosmetics, Science and Technology, 2nd Edition, Vol. 1, pp. 72-73 (1972), and/or an emollient. For example, an ointment may comprise from about 2% to about 10% of an emollient; from about 0.1% to about 2%, from about 45% to about 85%, preferably from about 50% to about 75%, water; and the vitamin B₃ compound in the above described amounts.

Compositions of this invention useful for cleansing ("cleansers") are formulated with a suitable carrier, e.g., as described above, and preferably contain, in addition to the vitamin B₃ compound in the above described amounts, from about 1% to about 90%, more preferably from about 5% to about 10%, of a dermatologically acceptable surfactant. The surfactant is suitably selected from anionic, nonionic, zwitterionic, amphoteric and ampholytic surfactants, as well as mixtures of these surfactants. Such surfactants are well known to those skilled in the detergent art. Nonlimiting examples of possible surfactants include isoceteth-20, sodium methyl cocoyl taurate, sodium methyl oleoyl taurate, and sodium lauryl sulfate. See U.S. Patent No. 4,800,197, to Kowcz et al., issued January 24, 1989, for exemplary surfactants useful herein. Examples of a broad variety of additional surfactants useful herein are described in McCutch-eon's Detergents and Emulsifiers, North American Edition (1986), published by Allured Publishing Corporation. The cleansing compositions can optionally contain, at their art-established levels, other materials which are conventionally used in cleansing compositions.

The physical form of the cleansing compositions is not critical. The compositions can be, for example, formulated as toilet bars, liquids, shampoos, bath gels, hair conditioners, hair tonics, pastes, or mousses. Toilet bars are most preferred since this is the form of cleansing agent most commonly used to wash the skin. Rinse-off cleansing compositions, such as shampoos, require a delivery system adequate to deposit sufficient levels of actives on the skin and scalp. A preferred delivery system involves the use of insoluble complexes. For a more complete disclosure of such delivery systems, see U.S. Patent 4,835,148, Barford et al., issued May 30, 1989.

As used herein, the term "foundation" refers to a liquid, semi-liquid, semi-solid, or solid skin cosmetic which includes, but is not limited to lotions, creams, gels, pastes, cakes, and the like. Typically the foundation is used over a large area of the skin, such as over the face, to provide a particular look. Foundations are typically used to provide an adherent base for color cosmetics such as rouge, blusher, powder and the like, and tend to hide skin imperfections and impart a smooth, even appearance to the skin. Foundations of the present invention include a dermatologically acceptable carrier for the vitamin B₃ compound and may include conventional ingredients such as oils, colorants, pigments, emollients, fragrances, waxes, stabilizers, and the like. Exemplary carriers and such other ingredients which are suitable for use herein are described, for example, in copending patent application Serial No. 08/430,961, filed on April 28, 1995 in the names of Marcia L. Canter, Brain D. Barford, and Brian D. Hofrichter.

The compositions of the present invention are preferably formulated to have a pH of 10.5 or below. The pH values of these compositions preferably range from about 2 to about 10.5, more preferably from about 3 to about 8, even more preferably from about 4 to about 7, and also from about 4.5 to about 5.5.

Optional Components

The topical compositions of the present invention may comprise a wide variety of optional components, provided that such optional components are physically and chemically compatible with the essential components described herein, and do not unduly impair stability, efficacy or other use benefits associated with the compositions of the present invention. Any optional ingredients should be compatible with the vitamin B₃ compound such that its activity does not decrease unacceptably, preferably not to any significant extent, over a useful period (preferably at least about two years under normal storage conditions). For example, strong oxidizing agents may be incompatible with the vitamin B₃ compound such that such agents are preferably avoided. Optional components may be dispersed, dissolved or the
Steroidal anti-inflammatory agents, including but not limited to, corticosteroids such as hydrocortisone, hydroxytiramcinolone, alpha-methyl dexamethasone, dexamethasone-phosphate, beclomethasone dipropionates, clobetasol valerate, desonide, desoxymethasone, desoxycorticosterone acetate, dexamethasone, dichlorsoine, diflorasone diacetate, difluradrolone valerate, fluadrenolone, fludronolone acetonide, flurodroncione, flumethasone pivalate, flusinolone acetonide, flucinonide, fluocortolone, flupredniolone (fluprednylidene) acetate, fluvardrenolone, halcinolone, hydrocortisone acetate, hydrocortisone butyrate, methylprednisolone, triamcinolone acetonide, cortisone, cortodoxone, flucortolone, fludrocortisone, flurnasone diacetate, fluadrenolone, fludronolone acetonide, medrysone, amcinafel, amcinafide, betamethasone and the balance of its esters, chloroprednisone, chlorprednisone acetate, clocortelone, clescinolone, dichlorisone, difluprednate, flucronide, flumisolide, fluoromethalone, fluporolone, fluprednisolone, hydrocortisone valerate, hydrocortisone cyclopentylpropionate, hydrocortamate, meprednisone, paramethasone, prednisolone, prednisone, beclomethasone dipropionate, triamdnolone, and mixtures thereof may be used. The preferred steroidal anti-inflammatory for use is hydrocortisone.
A second class of anti-inflammatory agents which is useful in the compositions includes the nonsteroidal anti-inflammatory agents. The variety of compounds encompassed by this group are well-known to those skilled in the art. For detailed disclosure of the chemical structure, synthesis, side effects, etc. of non-steroidal and anti-inflammatory agents, reference may be had to standard texts, including Anti-inflammatory and Anti-Rheumatic Drugs, K.D. Rainsford, Vol. I-III, CRC Press, Boca Raton, (1985), and Anti-inflammatory Agents, Chemistry and Pharmacology, 1, R.A. Scherrer, et al., Academic Press, New York (1974).

Specific non-steroidal anti-inflammatory agents useful in the composition invention include, but are not limited to:

1. the oxicams, such as piroxicam, isoxicam, tenoxicam, sudoxicam, and CP-14,304;
2. the salicylates, such as aspirin, disalcid, benorylate, trilisate, safapryn, solprin, diflunisal, and fendosal;
3. the acetic acid derivatives, such as didofenac, fenclofenac, indomethacin, sulindac, tometin, isoxefac, furofenac, tiopinac, zidometacin, acetamin, fentiazac, zomepirac, clindanac, oxepinac, felbinac, and ketorolac;
4. the fenamates, such as mfenamic acid, meclofenamic acid, flufenamic acid, niflumic acid, and tolenamic acids;
5. the propionic acid derivatives, such as ibuprofen, naproxen, benoxaprofen, flurbiprofen, ketoprofen, fenoprofen, fenbufen, indoprofen, pirprofen, carprofen, oxaproxin, pranoprofen, miroprofen, tenoxicam, suprofen, alminoprofen, and tiaprofenic;
6. the pyrazoles, such as phenylbutazone, oxyphenbutazone, feprazone, azapropazone, and trimethazone.

Mixtures of these non-steroidal anti-inflammatory agents may also be employed, as well as the dermatologically acceptable salts and esters of these agents. For example, etofenamate, a flufenamic acid derivative, is particularly useful for topical application. Of the nonsteroidal anti-inflammatory agents, ibuprofen, naproxen, flufenamic acid, etofenamate, aspirin, mfenamic acid, meclofenamic acid, piroxicam and felbinac are preferred; ibuprofen, naproxen, etofenamate, aspirin and flufenamic acid are most preferred.

Finally, so-called "natural" anti-inflammatory agents are useful in methods of the subject invention. Such agents may suitably be obtained as an extract by suitable physical and/or chemical isolation from natural sources (e.g., plants, fungi, by-products of microorganisms). For example, candelilla wax, alpha bisabolol, aloe vera, Manjistha (extracted from plants in the genus Rubia, particularly Rubia Cordifolia), and Guggal (extracted from plants in the genus Commiphora, particularly Commiphora Mukul), kola extract, chamomile, and sea whip extract, may be used.

Additional anti-inflammatory agents useful herein include compounds of the Licorice (the plant genus/species Glycyrrhiza glabra) family, including glycyrrhetic acid, glycyrrhizic acid, and derivatives thereof (e.g., salts and esters). Suitable salts of the foregoing compounds include metal and ammonium salts. Suitable esters include C-2 -C-24 saturated or unsaturated esters of the acids, preferably C-10 - C-24, more preferably C-16 - C-24. Specific examples of the foregoing include oil soluble licorice extract, the glycyrrhizic and glycyrrhetic acids themselves, monoammonium glycyrrhizinate, monopotassium glycyrrhizinate, dipotassium glycyrrhizinate, 1-beta-glycyrrhetic acid, stearyl glycyrrhetinate, and 3-stearyloxy-glycyrrhetinic acid, and disodium 3-succinylloxy-beta-glycyrrhetinate. Stearyl glycyrrhetinate is preferred.

In a preferred embodiment, the compositions of the present invention also contain a retinoid. The vitamin B-3 compound and retinoid provide unexpected benefits in regulating skin condition, especially in combetically regulating signs of skin aging, more especially wrinkles, lines, and pores. Without intending to be bound or otherwise limited by theory, it is believed that the vitamin B-3 compound increases the conversion of certain retinoids to trans-retinoic acid, which is believed to be the biologically active form of the retinoid, to provide synergistic regulation of skin condition (namely, increased conversion for retinol, retinol esters, and retinal). In addition, the vitamin B-3 compound unexpectedly mitigates redness, inflammation, dermatitis and the like which may otherwise be associated with topical application of retinoid (often referred to, and hereinafter alternatively referred to as "retinoid dermatitis"). Furthermore, the combined vitamin B-3 compound and retinoid tend to increase the amount and activity of thioredoxin, which tends to increase collagen expression levels via the protein AP-1. Therefore, the present invention enables reduced active levels, and therefore reduced potential for retinoid dermatitis, while retaining significant positive skin conditioning benefits. In addition, higher levels of retinoid may still be used to obtain greater skin conditioning efficacy, without undesirable retinoid dermatitis occurring.

As used herein, "retinoid" includes all natural and/or synthetic analogs of Vitamin A or retinol-like compounds which possess the biochemical activity of Vitamin A in the skin as well as the geometric isomers and stereoisomers of these compounds. The retinoid is preferably retinol, retinol esters (e.g., C-2 - C-22 alkyl esters of retinol, including retinyl palmitate, retinyl acetate, retinyl propionate), retinal, and/or retinoic acid (including all-trans retinoic acid and/or 13-cis-retinoic acid), more preferably retinoids other than retinolic acid. These compounds are well known in the art and are commercially available from a number of sources, e.g., Sigma Chemical Company (St. Louis, MO), and Boehringer.
Mannheim (Indianapolis, IN). Other retinoids which are useful herein are described in U.S. Patent Nos. 4,677,120, issued Jun. 30, 1987 to Parish et al.; 4,885,311, issued Dec. 5, 1989 to Parish et al.; 5,049,584, issued Sep. 17, 1991 to Purcell et al.; 5,124,356, issued Jun. 23, 1992 to Purcell et al.; and Reissue 34,075, issued Sep. 22, 1992 to Purcell et al. Other suitable retinoids are tocopherol-retinoid [tocopherol ester of retinoic acid (trans- or cis-), adapalene {6-[3-(1-adamantyl)-4-methoxyphenyl]-2-naphthoic acid}, and tazarotene (ethyl 6-[(4,4-dimethylthiochroman-6-yl)-ethyl]nicotinate). One or more retinoids may be used herein. Preferred retinoids are retinol, retinyl palmitate, retinyl acetate, retinyl propionate, retinal and combinations thereof. More preferred are retinol and retinyl palmitate.

The retinoid may be included as the substantially pure material, or as an extract obtained by suitable physical and/or chemical isolation from natural (e.g., plant) sources. The retinoid is preferably substantially pure, more preferably essentially pure.

The compositions of this invention may contain a safe and effective amount of the retinoid, thus that the resultant composition is safe and effective for regulating skin condition, preferably for regulating visible and/or tactile discontinuities in skin, more preferably for regulating signs of skin aging, even more preferably for regulating visible and/or tactile discontinuities in skin texture associated with skin aging. The compositions preferably contain from or about 0.005% to or about 2%, more preferably 0.01% to or about 2%, retinoid. Retinol is most preferably used in an amount of from or about 0.01% to or about 15%; retinol esters are most preferably used in an amount of from or about 0.01% to or about 2% (e.g., about 1%); retinoic acids are most preferably used in an amount of from or about 0.01% to or about 25%; tocopherol-retinoid [tocopherol ester of retinoic acid (trans- or cis), adapalene {6-[3-(1-adamantyl)-4-methoxyphenyl]-2-naphthoic acid}, and tazarotene are most preferably used in an amount of from or about 0.01% to or about 2%. When the composition contains a retinoid, the vitamin B3 compound is preferably used in an amount of from or about 0.1% to or about 10%, more preferably from or about 2% to or about 5%.

**C. Antimicrobial Agents**

As used herein, “antimicrobial agent” means a compound capable of destroying microbes, preventing the development of microbes or preventing the pathogenic action of microbes. Antimicrobial agents are useful, for example, in controlling acne. A safe and effective amount of an antimicrobial agent may be added to compositions of the subject invention, preferably from about 0.001% to about 10%, more preferably from about 0.01% to about 5%, also from about 0.05% to about 2% or from about 0.05% to about 1% of the compositions. Preferred antimicrobial agents useful in the subject invention are benzoyl peroxide, erythromycin, tetracycline, clindamycin, azelaic acid, and sulfon resorcinol.

**D. Antiandrogens**

As used herein, “anti-androgen” means a compound capable of correcting androgen-related disorders by interfering with the action of androgens at their target organs. The target organ for the subject invention is mammalian skin. Exemplary antiandrogens include pregnesnaionc (and its derivatives), hops extract, oxygenated alkyl substituted bicyclo alkanes (e.g., ethoxyhexyl-bicyclo octanones such as marketed by Chantal Pharmaceutical of Los Angeles, CA under the trade names ETHOCYN and CYOCTOL, and 2-(5-ethoxy hept-1-yl)bicyclo[3.3.0]octanone), and oleanolic acid. Suitable antiandrogens are disclosed in U.S. Patent Nos. 4,689,345 and 4,855,322, both issued to Kasha et al.

**E. Sunscreens and Sunblocks**

Exposure to ultraviolet light can result in excessive scaling and texture changes of the stratum corneum. Therefore, the compositions of the subject invention preferably contain a sunscreen or sunblock. Suitable sunscreens or sunblocks may be organic or inorganic.

A wide variety of conventional sunscreening agents are suitable for use herein. Sagarin, et al., at Chapter VIII, pages 189 et seq., of Cosmetics Science and Technology (1972), discloses numerous suitable agents. Specific suitable sunscreening agents include, for example: p-aminobenzoic acid, its salts and its derivatives (ethyl, isobutyl, glyceryl esters; p-dimethylaminobenzoic acid); anthranilates (i.e., o-amino-benzoates; methyl, menthyl, phenyl, benzyl, phenylethyl, linanyl, terpinyl, and cyclohexenyl esters); salicylates (amyl, phenyl, octyl, benzyl, menthyl, glyceryl, and di-pro-pyleneglycol esters); cinnamic acid derivatives (menthyl and benzyl esters, a-phenyl cinnamnone; butyl cinnamoyl pyvivate); dihydroxycinnamic acid derivatives (umbelliferone, methylumbelliferone, methylaceto-umbellifer-one); trihydroxy-cinnamic acid derivatives (esculetin, methylesculetine, daphnetin, and the glucosides, esculin and daphnin); hydrocarbons (diphenylebutadiene, stilbene); dibenzalacetone and benzalacetophenone; naphtholsulfonates (sodium salts of 2-naphthol-3,6-disulfonic and of 2-naphthol-6,8-disulfonic acids); di-hydroxynaphthoic acid and its salts; o- and p-hydroxybiphenyldisulfonates; coumarin derivatives (7-hydroxy, 7-methyl, 3-phenyl); diazoles (2-acetyl-3-bromoindazole, phenyl benzoaxazole, methyl naphthoxazole, various aryl benzothiazoles); quinine salts (bisulfate,
sulfate, chloride, oleate, and tannate); quinoline derivatives (8-hydroxyquinoline salts, 2-phenylquinoline); hydroxy- or methoxy-substituted benzophenones; uric and violuric acids; tannic acid and its derivatives (e.g., hexaethylyther); (butyl carbitol) (6-propyl piperonyl) ether, hydroquinone; benzophenones (oxybenzene, sulisobenzone, dioxyberizone, benzorescorcinol, 2,2',4,4'-tetrahydroxybenzophenone, 2,2'-dihydroxy-4,4'-dimethoxybenzophenone, octabenzone; 4-isopropylidibenzoylmethane; butylmethoxydibenzoylmethane; etocrylene; octocrylene; [3-(4'-methylbenzylidene bar- man-2-one) and 4-isopropyl-di-benzoylmethane.

Of these, 2-ethylhexyl-p-methoxycinnamate (commercially available as PARSOL MCX), 4,4’-butyl methoxy-dibenzoyl-methane (commercially available as PARSOL 1789), 2-hydroxy-4-methoxybenzophenone, octyldimethyl-p-aminobenzoic acid, digalloyltrioleate, 2,2-dihydroxy-4-methoxybenzophenone, ethyl-4-(bis(hydroxy-propyl))amino benzoonate, 2-ethylhexyl-2-cyano-3,3-diphenylacrylate, 2-ethylhexyl-salicylate, glyceryl-p-aminobenzoate, 3,3,5-tri-methylcyclohexylsalicylate, methilranthranilate, p-dimethyl-aminobenzoic acid or aminobenzoate, 2-ethylhexyl-p-dimethyl-amino-benzoate, 2-phenylbenzimidazole-5-sulfonic acid, 2-(p-dimethylaminophenyl)-5-sulfonicbenzoxazoic acid, octocrylene and mixtures of these compounds, are preferred.

More preferred organic sunscreens useful in the compositions useful in the subject invention are 2-ethylhexyl-p-methoxycinnamate, butylmethoxydibenzoylmethane, 2-hydroxy-4-methoxybenzo-phenone, 2-phenylbenzimida zole-5-sulfonic acid, octyldimethyl-p-aminobenzoic acid, octocrylene and mixtures thereof.

Also particularly useful in the compositions are sunscreens such as those disclosed in U.S. Patent No. 4,937,370 issued to Sabatelli on June 26, 1990, and U.S. Patent No. 4,999,186 issued to Sabatelli & Spirnak on March 12, 1991. The sunscreening agents disclosed therein have, in a single molecule, two distinct chromophore moieties which exhibit different ultra-violet radiation absorption spectra. One of the chromophore moieties absorbs predominently in the UVB radiation range and the other absorbes strongly in the UVA radiation range.

Preferred members of this class of sunscreening agents are 4-N,N-(2-ethylhexyl)methyl-aminobenzoic acid ester of 2,4-dihydroxybenzophenone; N,N-di-(2-ethylhexyl)-4-aminobenzoic acid ester with 4-hydroxydibenzoylmethane; 4-N,N-(2-ethylhexyl)methyl-aminobenzoic acid ester of 4-hydroxydibenzoylmethane; 4-N,N-(2-ethylhexyl)methyl-aminobenzoic acid ester of 2-hydroxy-4-(2-hydroxyethoxy)benzophenone; 4,N,N-(2-ethylhexyl)-methylaminobenzoic acid ester of 4-(2-hydroxyethoxy) dibenzoylmethane; N,N-di-(2-ethylhexyl)-4-aminobenzoic acid ester of 2-hydroxy-4-(2-hydroxyethoxy)benzophenone; and N,N-di-(2-ethylhexyl)-4-aminobenzoic acid ester of 4-(2-hydrox yethoxy)dibenzoylmethane and mixtures thereof.

Suitable inorganic sunscreens or sunblocks include metal oxides, e.g., zinc oxide and titanium dioxide. For example, the use of a titanium dioxide in topical sunscreen compositions that is applicable to the present invention is described in copending application Serial No. 08/448,942, filed on May 24, 1995, in the names of Jiang Yue, Lisa R. Dew and Donald L. Bissett.

Especially preferred sunscreens or sunblocks include the metal oxides such as zinc oxide and titanium dioxide, butylmethoxydibenzoylmethane, 2-ethylhexyl-p-methoxycinnamate, phenyl benzimidazole sulfonic acid, and octoc rylene.

A safe and effective amount of the sunscreen or sunblock is used, typically from about 1% to about 20%, more typically from about 2% to about 10%. Exact amounts will vary depending upon the sunscreen chosen and the desired Sun Protection Factor (SPF).

An agent may also be added to any of the compositions useful in the subject invention to improve the skin substantivity of those compositions, particularly to enhance their resistance to being washed off by water, or rubbed off. A preferred agent which will provide this benefit is a copolymer of ethylene and acrylic acid. Compositions comprising this copolymer are disclosed in U.S. Patent 4,663,157, Brock, issued May 5, 1987.

F. Anti-Oxidants/Radical Scavengers

Preferred compositions of the subject invention include an anti-oxidant/radical scavenger as an active in addition to the primary active agents. The anti-oxidant/radical scavenger is especially useful for providing protection against UV radiation which can cause increased scaling or texture changes in the stratum corneum and against other environmental agents which can cause skin damage.

A safe and effective amount of an anti-oxidant/radical scavenger may be added to the compositions of the subject invention, preferably from about 0.1% to about 10%, more preferably from about 1% to about 5%, of the composition.

Anti-oxidants/radical scavengers such as ascorbic acid (vitamin C) and its salts, ascorbyl esters of fatty acids, ascorbic acid derivatives (e.g., magnesium ascorbyl phosphate), tocopherol (vitamin E), tocopherol sorbate, other esters of tocopherol, butylated hydroxy benzoic acids and their salts, 6-hydroxy-2,5,7,8-tetramethylchroman-2-carboxylic acid (commercially available under the tradename Trolox®), gallic acid and its alkyl esters, especially propyl gallate, uric acid and its salts and alkyl esters, sorbic acid and its salts, amines (e.g., N,N-diethylhydroxylamine, amino-guanidine), sulfhydryl compounds (e.g., glutathione), dihydroxy fumaric acid and its salts, lycine pilolate, arginine pilolate,
nordihydroguaiaretic acid, bioflavonoids, lysine, methionine, proline, superoxide dismutase, silymarin, tea extracts, grape skin/seed extracts, melanin, and rosemary extracts may be used. Preferred anti-oxidants/radical scavengers are selected from tocopherol sorbate and other esters of tocopherol, more preferably tocopherol sorbate. For example, the use of tocopherol sorbate in topical compositions and applicable to the present invention is described in U.S. Patent No. 4,847,071, issued on July 11, 1989 to Donald L. Bissett, Rodney D. Bush and Ranjit Chatterjee.

G. Chelators

[0135] As used herein, "chelating agent" means an active agent capable of removing a metal ion from a system by forming a complex so that the metal ion cannot readily participate in or catalyze chemical reactions. The inclusion of a chelating agent is especially useful for providing protection against UV radiation which can contribute to excessive scaling or skin texture changes and against other environmental agents which can cause skin damage.

[0136] A safe and effective amount of a chelating agent may be added to the compositions of the subject invention, preferably from about 0.1% to about 10%, more preferably from about 1% to about 5%, of the composition. Exemplary chelators that are useful herein are disclosed in U.S. Patent No. 5,487,884, issued 1/30/96 to Bissett et al.; International Publication No. 91/16035, Bush et al., published 10/31/95; and International Publication No. 91/16034, Bush et al., published 10/31/95; Preferred chelators useful in compositions of the subject invention are furildioxime and derivatives thereof.

H. Organic Hydroxy Acids

[0137] Compositions of the present invention preferably comprise an organic hydroxy acid. Suitable hydroxy acids include C_{1}-C_{18} hydroxy acids, preferably C_{8} or below. The hydroxy acids can be substituted or unsubstituted, straight chain, branched chain or cyclic (preferably straight chain), and saturated or unsaturated (mono- or poly- unsaturated) (preferably saturated). Non-limiting examples of suitable hydroxy acids include salicylic acid, glycolic acid, lactic acid, 5 octanoyl salicylic acid, hydroxyoctanoic acid, hydroxycaprylic acid, and lanolin fatty acids. Preferred concentrations of the organic hydroxy acid range from about 0.1% to about 10%, more preferably from about 0.2% to about 5%, also preferably from about 0.5% to about 2%. Salicylic acid is preferred. The organic hydroxy acids enhance the skin appearance benefits of the present invention. For example, the organic hydroxy acids tend to improve the texture of the skin.

I. Desquamation Agents/Exfoliants

[0138] A safe and effective amount of a desquamation agent is preferably added to the compositions of the subject invention, more preferably from about 0.1% to about 10%, even more preferably from about 0.2% to about 5%, also preferably from about 0.5% to about 4% of the composition. Desquamation agents enhance the skin appearance benefits of the present invention. For example, the desquamation agents tend to improve the texture of the skin (e.g., smoothness). A variety of desquamation agents are known in the art and are suitable for use herein, including but not limited to the organic hydroxy agents described above. One desquamation system that is suitable for use herein comprises sulfhydryl compounds and zwitterionic surfactants and is described in copending application Serial No. 08/480,632, filed on June 7, 1995 in the name of Donald L. Bissett, corresponding to PCT Application No. U.S. 95/08136, filed 6/30/95. Another desquamation system that is suitable for use herein comprises salicylic acid and zwitterionic surfactants and is described in copending patent application Serial No. 08/554,944, filed on November 13, 1995 as a continuation of Serial No.08/209,401, filed on March 9, 1994 in the name of Bissett, corresponding to PCT Application No. 94/12745, filed 11/4/94, published 5/18/95. Zwitterionic surfactants such as described in these applications are also useful as desquamatory agents herein, with cetyl betaine being particularly preferred.

J. Depilation Agents

[0139] The compositions of the present invention may include a safe and effective amount of a depilation agent. When used, the composition preferably contains from about 0.1% to about 10%, more preferably from about 0.2% to about 5%, also preferably from about 0.5% to about 2% of depilation agent A depilation agent preferred for use herein comprises a sulfhydryl compound, e.g., N-acetyl-L-cysteine. The use of such depilation agents is described in more detail in copending application Serial No. 08/479,878, filed on June 7, 1995, in the name of Greg G. Hillebrand and Vladimir Gartstein, corresponding to PCT Application No. U.S. 95/07311, filed 6/8/95.
K. Skin Lightening Agents

[0140] The compositions of the present invention may comprise a skin lightening agent. When used, the compositions preferably comprise from about 0.1% to about 10%, more preferably from about 0.2% to about 5%, also preferably from about 0.5% to about 2%, of a skin lightening agent. Suitable skin lightening agents include those known in the art, including kojic acid, arbutin, ascorbic acid and derivatives thereof, e.g., magnesium ascorbyl phosphate. Skin lightening agents suitable for use herein also include those described in copending patent application Serial No. 08/479,935, filed on June 7, 1995 in the name of Hillebrand, corresponding to PCT Application No. U.S. 95/07432, filed 6/12/95; and copending patent application Serial No.08/390,152, filed on February 24, 1995 in the names of Kalla L. Kvalnes, Mitchell A. DeLong, Barton J. Bradbury, Curtis B. Motley, and John D. Carter, corresponding to PCT Application No. U.S. 95/02809, filed 3/1/95, published 9/8/95;

L. Zinc Salts

[0141] The compositions of the present invention may further comprise a zinc salt. Zinc salts are especially preferred where the composition contains a sulfhydryl compound, e.g., N-acetyl-L-cysteine. Without intending to be limited or bound by theory, it is believed that the zinc salt acts as a chelating agent capable of complexing with the sulfhydryl compound prior to topical application, stabilizes the sulfhydryl compound and/or controls odor associated with the sulfhydryl compound. Concentrations of the zinc salt can range from about 0.001% to about 10%, more preferably from about 0.01% to about 5%, most preferably from about 0.1% to about 0.5% by weight of the composition.

[0142] Preferred zinc salts include zinc acetate, zinc acetate hydrates such as zinc acetate-2-water, zinc aluminum oxide complexes such as galnate, zinc diamine, zinc antimonide, zinc bromide hydrates such as zinc bromide-6-water, zinc bromide, zinc carbonates such as zincspar and smithsonite, zinc chloride hydrates such as zinc chloride-4-water, zinc chloride, zinc diamine dichloride, zinc citrate, zinc chromate, zinc dichromate, zinc diphosphate, zinc hexacyanoferrate (II), zinc fluorite, zinc oxide hydrates such as zinc fluoride-4-water, zinc formate, zinc formate hydrates such as zinc formate-2-water, zinc hydroxide, zinc iodate, zinc iodate hydrates such as zinc iodate-2-water, zinc iodide, zinc iron oxide complexes, zinc nitrate hydrates such as zinc nitrate-6-water, zinc nitride, zinc oxalate hydrates such as zinc oxalate-2-water, zinc oxides such as zincite, zinc perchlorate hydrates such as zinc perchlorate-6-water, zinc permanganate hydrates such as zinc permanganate-6-water, zinc peroxide, zinc p-phenolsulfonate hydrates such as zinc p-phenolsulfonate-8-water, zinc phosphate, zinc phosphate hydrates such as zinc phosphate-4-water, zinc phosphide, zinc propionate, zinc selenate hydrates such as zinc selenate-5-water, zinc selenide, zinc silicates such as zinc silicate (2) and zinc silicate (4), zinc silicon oxide water complexes such as hemimorphite, zinc hexafluorosilicate hydrates such as zinc hexafluorosilicate-6-water, zinc stearate, zinc sulfate, zinc sulfate hydrates such as zinc sulfate-7-water, zinc sulfide, zinc sulfite hydrates such as zinc sulfite-2-water, zinc telluride, zinc thiocyanate, zinc (II) salts of N-acetyl L-cysteine, and mixtures thereof.

[0143] Especially preferred zinc salts include zinc citrate, zinc oxide, zinc chloride, zinc acetate, zinc stearate, zinc sulfate, and mixtures thereof. Zinc citrate is especially preferred.

M. Humectants, Moisturizers, and Skin Conditioners

[0144] The compositions of the present invention may further comprise a humectant, moisturizing agent or other skin conditioning agent. A variety of these materials can be employed and each can be present at a level of from or about 0.1% to or about 20%, more preferably from or about 1% to or about 10%, and most preferably from or about 2% to or about 5%. These materials include guanidine; glycolic acid and glycolate salts (e.g. ammonium and quaternary alkyl ammonium); lactic acid and lactate salts (e.g. ammonium and quaternary alkyl ammonium); aloe vera in any of its variety of forms (e.g., aloe vera gel); polyhydroxy alcohols such as sorbitol, glycerol, hexanetriol, propylene glycol, butylene glycol, hexylene glycol and the like; polyethylene glycols; sugars and starches; sugar and starch derivatives (e.g., alkoxylated glucose); hyaluronic acid; lactamide monoethanolamine; acetamide monooethanolamine; and mixtures thereof.

[0145] Also useful herein are the propoxylated glycerols described in U.S. Patent No. 4,976,953.

[0146] Also useful are various C1-C30 monesters and polyesters of sugars and related materials. These esters are derived from a sugar or polyol moiety and one or more carboxylic acid moieties. Depending on the constituent acid and sugar, these esters can be in either liquid or solid form at room temperature. Examples of liquid esters include: glucose tetraoleate, the glucose tetraesters of soybean oil fatty acids (unsaturated), the mannose tetraesters of mixed soybean oil fatty acids, the galactose tetraesters of oleic acid, the arabinose tetraesters of linoleic acid, xylose tetraolinate, galactose pentaoaleate, sorbitol tetraoleate, the sorbitol hexaesters of unsaturated soybean oil fatty acids, xylitol pentaoaleate, sucrose tetroaleate, sucrose pentaoaleate, sucrase hexaoaleate, sucrose hepatoleate, sucrose octaoaleate, and mixtures thereof. Examples of solid esters include: sorbitol hexaester in which the carboxylic acid ester...
moieties are palmitoleate and arachidate in a 1:2 molar ratio; the octaester of raffinose in which the carboxylic acid ester moieties are linoleate and behenate in a 1:3 molar ratio; the heptaester of maltose wherein the esterifying carboxylic acid moieties are sunflower seed oil fatty acids and lignocerate in a 3:4 molar ratio; the octaester of sucrose wherein the esterifying carboxylic acid moieties are oleate and behenate in a 2:6 molar ratio; and the octaester of sucrose wherein the esterifying carboxylic acid moieties are laurate, linoleate and behenic in a 1:3:4 molar ratio. A preferred solid ester polymer in which the degree of esterification is 7-8, and in which the fatty acid moieties are C18 mono- and/or di-unsaturated and behenic, in a molar ratio of unsaturates:behenic of 1:7 to 3:5. A particularly preferred solid sugar polyester is the octaester of sucrose in which there are about 7 behenic fatty acid moieties and about 1 oleic acid moiety in the molecule. The ester materials are further described in, U.S. Patent No. 2,831,854, U.S. Patent No. 4,005,196, to Jandacek, issued January 25, 1977; U.S. Patent No. 4,005,195, to Jandacek, issued January 25, 1977, U.S. Patent No. 5,306,516, to Letton et al., issued April 26, 1994; U.S. Patent No. 5,306,515, to Letton et al., issued April 26, 1994; U.S. Patent No. 5,305,514, to Letton et al., issued April 26, 1994; U.S. Patent No. 4,797,300, to Jandacek et al., issued January 10, 1989; U.S. Patent No. 3,963,699, to Rizzi et al. issued June 15, 1976; U.S. Patent No. 4,518,772, to Volpenhein, issued May 21, 1985; and U.S. Patent No. 4,517,360, to Volpenhein, issued May 21, 1985.

N. Other Optional Components

[0147] The compositions of the present invention may also include an extract obtained by suitable physical and/or chemical isolation from natural sources (e.g., plants, fungi, by-products of microorganisms), including those known in the topical personal care art. Preferred extracts are those which enhance the skin appearance benefits of the present invention, and which are preferably used in a safe and effective amount, more preferably an amount of from 0.1% to about 20%, even more preferably 0.5% to about 10%, also from 1% to about 5%. Such extracts include plant and fungal extracts such as extracts of yeast, rice bran, and of the plant Centella Asiatica. Natural extracts of Centella Asiatica are preferred and are commercially available from MMP, Inc. of Plainfield, New Jersey under the trade name (s) Centella Asiatica E.P.C.A. ("Extract Purified of Centella asiatica") and Genines amel. Genines amel is the purer form of the extract.

[0148] Compounds which are known to stimulate the production of collagen can also be used in the present invention. Such compounds include Factor X (kinetin), Factor Z (zeatin), n-methyl taurine, dipalmityl hydroxyproline, palmitoyl hydroxy wheat protein, biopeptide CL (palmitoyl glycy1-histidyl-lysine), ASC III (Amplifier of Synthesis of Collagen III, E. Merck, Germany), and beta glucan.

[0149] The compositions hereof can also include natural ceramides or the like, for example, ceramide 1 - 6.

[0150] The compositions can also contain an oil absorbent such as are known in the art, e.g. clays (e.g. bentonite) and polymeric absorbents (e.g., MICROSPONGES 5647 and POLYTRAP, both commercially available from Advanced Polymer Systems, Inc. of Redwood City, California, USA., MICROSPONGES 5647 is a polymer mixture derived from styrene, methyl methacrylate, and hydrogel acrylate/methacrylate.

[0151] Other examples of additional components usefull herein include the following: water-soluble vitamins and derivatives thereof (e.g., vitamin C); polyethylene glycols and polypropylene glycols; polymers for aiding the film-forming properties and substantivity of the composition (such as a copolymer of eicosene and vinyl pyrrolidone, an example of which is available from GAF Chemical Corporation as Ganex® V-220). Also useful are crosslinked and non-crosslinked nonionic and cationic polyacrylamides [e.g., Salcare SC92 which has the CTFA designation polyquaternium 37 (and) mineral oil (and) polyquaternium (e.g., vitamin C); polyethyleneglycols and polypropyleneglycols; polymers for aiding the film-forming properties and substantivity of the composition (such as a copolymer of eicosene and vinyl pyrrolidone, an example of which is available from GAF Chemical Corporation as Ganex® V-220). Also useful are crosslinked and non-crosslinked carboxylic acid polymers and copolymers such as those containing one or more monomers derived from acrylic acid, substituted acrylic acids, and salts and esters of these acrylic acids and the substituted acrylates, wherein the crosslinking agent contains two or more carbon-carbon double bonds and is derived from a polyhydric alcohol (examples useful herein include the carboxylic acids homopolymers of acrylic acid crosslinked with allyl ethers of sucrose or pentaerytrol and which are available as the Carbopol® 900 series from B.F. Goodrich, and copolymers of C10-30 alkyl acrylates with one or more monomers of acrylic acid, methacrylic acid, or one or their short chain (i.e., C1-4 alkyl) esters, wherein the crosslinking agent is an allyl ether of sucrose or pentaerytrol, these copolymers being known as acrylates/C10-30 alkyl acrylate copolymers and are commercially available as Carbopol® 1342, Pemulen TR-1, and Pemulen TR-2, from B.F. Goodrich). These carboxylic acid polymers and copolymers are more fully described in U.S. Patent No. 5,087,445, to Haffey et al., issued September 11, 1992; U.S. Patent No. 4,590,949, to Huang et al., issued April 5, 1985; U.S. Patent No. 2,798,053, to Brown, issued July 2, 1957; which are incorporated by reference herein. See also, CTFA International Cosmetic Ingredient Dictionary, fourth edition, 1991, pp. 12 and 80;

[0152] Also useful herein are aesthetic components such as fragrances, pigments, colorings, essential oils, skin sensates, astringents, skin soothing agents, skin healing agents and the like, nonlimiting examples of these aesthetic
components include clove oil, menthol, camphor, eucalyptus oil, eugenol, menthyl lactate, witch hazel distillate, bisabolol, dipotassium glycyrrhizinate and the like.

Preparation of Compositions

[0153] The compositions of the present invention are generally prepared by conventional methods such as are known in the art of making topical compositions. Such methods typically involve mixing of the ingredients in one or more steps to a relatively uniform state, with or without heating, cooling, application of vacuum, and the like.

Methods for Regulating Skin Condition

[0154] The compositions of the present invention are useful for regulating mammalian skin condition (especially human skin, more especially human facial skin), including visible and/or tactile discontinuities in skin, signs of skin aging, and visible and/or tactile discontinuities in skin associated with skin aging (including fine lines, wrinkles, large pores, surface roughness and other texture discontinuities associated with aged skin). Such regulation includes cosmetic regulation.

[0155] Regulating skin condition involves topically applying to the skin a safe and effective amount of a composition of the present invention. The amount of the composition which is applied, the frequency of application and the period of use will vary widely depending upon the level of vitamin B3 compound and/or other components of a given composition and the level of regulation desired, e.g., in light of the level of skin aging present in the subject and the rate of further skin aging.

[0156] In a preferred embodiment, the composition is chronically applied to the skin. By "chronic topical application" is meant continued topical application of the composition over an extended period during the subject's lifetime, preferably for a period of at least about one week, more preferably for a period of at least about one month, even more preferably for at least about three months, even more preferably for at least about six months, and more preferably still for at least about one year. While benefits are obtainable after various maximum periods of use (e.g., five, ten or twenty years), it is preferred that chronic application continue throughout the subject's lifetime. Typically applications would be on the order of about once per day over such extended periods, however application rates can vary from about once per week up to about three times per day or more.

[0157] A wide range of quantities of the compositions of the present invention can be employed to provide a skin appearance and/or feel benefit. Quantities of the present compositions which are typically applied per application are, in mg composition/cm² skin, from about 0.1 mg/cm² to about 10 mg/cm². A particularly useful application amount is about 2 mg/cm².

[0158] Regulating skin condition is preferably practiced by applying a composition in the form of a skin lotion, cream, cosmetic, or the like which is intended to be left on the skin for some esthetic, cosmetic or other benefit (i.e., a "leave-on" composition). After applying the composition to the skin, it is preferably left on the skin for a period of at least about 15 minutes, more preferably at least about 30 minutes, even more preferably at least about 1 hour, most preferably for at least several hours, e.g., up to about 12 hours.

EXAMPLES

[0159] The following examples further describe and demonstrate embodiments within the scope of the present invention. The examples are given solely for the purpose of illustration and are not to be construed as limitations of the present invention, as many variations thereof are possible without departing from the spirit and scope of the invention.

Example 1

[0160] A skin cream is prepared by conventional methods from the following components.

<table>
<thead>
<tr>
<th>Ingredient (CTFA Name)</th>
<th>Weight %</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>PHASE A</strong></td>
<td></td>
</tr>
<tr>
<td>Water U.S.P.</td>
<td>57.31</td>
</tr>
<tr>
<td>Disodium EDTA</td>
<td>0.13</td>
</tr>
<tr>
<td>Methyl Paraben</td>
<td>0.25</td>
</tr>
<tr>
<td>Glycerin</td>
<td>3.00</td>
</tr>
<tr>
<td>Zinc Citrate</td>
<td>1.00</td>
</tr>
</tbody>
</table>
Blend the A phase components with a suitable mixer (e.g., Tekmar model RW20DZM), heating while stirring to a temperature of 70-80°C. Separately, blend the B phase components with a suitable mixer and heat with mixing to melt the components. Separately, blend the C phase components and mill to obtain an acceptably smooth mixture (e.g., using a Tekmar T50 Mill).

Add the C phase mixture to the B phase mixture and mix. Then add the resulting mix to the A phase mixture with mixing, cool with a cold water bath and mill, then continue stirring. Remove the combination from the bath, with continued stirring, once the temperature reaches 40°C.

Separately, blend the D phase components by stirring until dissolved, then add this to the combination of A-C materials.

Separately, blend the E phase components by mixing until smooth and continuous, then add this to the combination of the A-D materials. Add and mix the fragrance, then the NaOH. Adjust the pH as necessary to 5.5.

Example 2

An emulsion is prepared by conventional methods from the following components:

<table>
<thead>
<tr>
<th>Ingredient (CTFA Name)</th>
<th>Weight %</th>
</tr>
</thead>
<tbody>
<tr>
<td>PHASE B</td>
<td></td>
</tr>
<tr>
<td>Cetyl Alcohol</td>
<td>0.56</td>
</tr>
<tr>
<td>Stearyl Alcohol</td>
<td>2.03</td>
</tr>
<tr>
<td>Behenyl Alcohol</td>
<td>0.22</td>
</tr>
<tr>
<td>Steareth-21 (Brij 721)</td>
<td>0.37</td>
</tr>
<tr>
<td>Steareth-2 (Brij 72)</td>
<td>1.10</td>
</tr>
<tr>
<td>Distearyl dimonium chloride (Varisoft TA-100)</td>
<td>0.95</td>
</tr>
<tr>
<td>Propyl Paraben</td>
<td>0.10</td>
</tr>
<tr>
<td>Polypropylene glycol-15 stearyl ether (Arlamol E)</td>
<td>3.25</td>
</tr>
<tr>
<td>PHASE C</td>
<td></td>
</tr>
<tr>
<td>Polypropylene glycol-15 stearyl ether (Arlamol E)</td>
<td>2.17</td>
</tr>
<tr>
<td>titanium dioxide</td>
<td>0.75</td>
</tr>
<tr>
<td>PHASE D</td>
<td></td>
</tr>
<tr>
<td>Niacinamide</td>
<td>5.00</td>
</tr>
<tr>
<td>Citric acid</td>
<td>0.19</td>
</tr>
<tr>
<td>water U.S.P.</td>
<td>17.00</td>
</tr>
<tr>
<td>50% NaOH</td>
<td>0.94</td>
</tr>
<tr>
<td>PHASE E</td>
<td></td>
</tr>
<tr>
<td>Benzyl Alcohol</td>
<td>0.50</td>
</tr>
<tr>
<td>Silicone fluid (DC Q2 - 1401; cyclomethicone/dimethiconol - 50/50 blend</td>
<td>0.75</td>
</tr>
<tr>
<td>dimethicone 10 cst</td>
<td>1.00</td>
</tr>
<tr>
<td>polyethylene Low Density Beads</td>
<td>1.00</td>
</tr>
<tr>
<td>PHASE F</td>
<td></td>
</tr>
<tr>
<td>Fragrance</td>
<td>0.10</td>
</tr>
<tr>
<td>PHASE G</td>
<td></td>
</tr>
<tr>
<td>50% NaOH</td>
<td>0.33</td>
</tr>
</tbody>
</table>
Form the water phase in a suitable vessel charged with the water as follows: add the glycerin and then niacinamide to the water with stirring. Add to this mixture with stirring the methyl paraben dissolved in the benzyl alcohol. Add to this mixture with stirring the EDTA.

Form the silicone phase in a separate suitable vessel by adding and stirring together the silicone fluids. Add the water phase to the silicone phase slowly with stirring to form the emulsion.

Apply the resulting composition to a subject's wrinkled, aged, or photodamaged facial skin at the rate of 2 mg composition/cm² skin once or twice daily for a period of at least 3-6 months to reduce fine lines and wrinkles and improve skin surface texture.

Example 3

A skin cream is prepared by conventional methods from the following components.

<table>
<thead>
<tr>
<th>Ingredient (CTFA Name)</th>
<th>Weight %</th>
</tr>
</thead>
<tbody>
<tr>
<td>PHASE A</td>
<td></td>
</tr>
<tr>
<td>Water U.S.P.</td>
<td>63.96</td>
</tr>
<tr>
<td>Disodium EDTA</td>
<td>0.15</td>
</tr>
<tr>
<td>Glycerin</td>
<td>5</td>
</tr>
<tr>
<td>PHASE B</td>
<td></td>
</tr>
<tr>
<td>Cetyl hydroxy ethyl cellulose</td>
<td>0.15</td>
</tr>
<tr>
<td>Methyl Paraben</td>
<td>0.25</td>
</tr>
<tr>
<td>PHASE C</td>
<td></td>
</tr>
<tr>
<td>Cetyl Alcohol</td>
<td>0.5</td>
</tr>
<tr>
<td>Stearyl Alcohol</td>
<td>0.5</td>
</tr>
<tr>
<td>Behenyl Alcohol</td>
<td>0.5</td>
</tr>
<tr>
<td>Cetyl ricinoleate</td>
<td>3</td>
</tr>
<tr>
<td>Steareth-2 (Brij 72)</td>
<td>1.05</td>
</tr>
<tr>
<td>Distearyldimonium chloride (Varisoft TA-100)</td>
<td>0.25</td>
</tr>
<tr>
<td>Propyl Paraben</td>
<td>0.10</td>
</tr>
<tr>
<td>Myristyl myristate</td>
<td>1.5</td>
</tr>
<tr>
<td>Capiylcaprylylglycerides</td>
<td>1.5</td>
</tr>
<tr>
<td>MINERAL OIL</td>
<td>2</td>
</tr>
<tr>
<td>Fatty acid ester of sugar*</td>
<td>1</td>
</tr>
<tr>
<td>Polypropylene glycol-15 stearyl ether (Arlamol E)</td>
<td>1.05</td>
</tr>
</tbody>
</table>

* A C1-C30 monoester or polyester of sugars and one or more carboxylic acid moieties as described herein, preferably a sucrose polyester in which the degree of esterification is 7-8, and in which the fatty acid moieties are C18 mono- and/or di-unsaturated and behenic, in a molar ratio of unsaturates: behenic of 1.7 to 3.5, more preferably the octaester of sucrose in which there are about 7 behenic fatty acid moieties and about 1 oleic acid moiety in the molecule, e.g., sucrose ester of cottonseed oil fatty acids.
Blend the A phase components with a suitable mixer (e.g., Tekmar model RW20DZM), heating while stirring to a temperature of about 70-80°C. Add the cetyl hydroxy ethyl cellulose and methyl paraben with mixing at about 70-80°C to melt the components. Separately, blend the C phase components and mill to obtain an acceptably smooth mixture (e.g., using a Tekmar T50 Mill).

Add the C phase mixture to the above mixture and mix. Remove the combination from the bath, with continued stirring, once the temperature reaches about 45°C. Add the dimethicone and mix.

Separately, blend the E phase components by mixing until smooth and continuous, then add this to the above mixture. Add and mix in the benzyl alcohol, then the NaOH. Adjust the pH as necessary to 7.

Apply the composition to a subject's wrinkled, aged, or photodamaged facial skin at the rate of 2 mg composition/cm² skin once or twice daily for a period of at least 3-6 months to reduce fine lines and wrinkles and improve skin surface texture.

Example 4

A skin cream is prepared by conventional methods from the following components.

<table>
<thead>
<tr>
<th>Component</th>
<th>Weight %</th>
</tr>
</thead>
<tbody>
<tr>
<td>PHASE A</td>
<td></td>
</tr>
<tr>
<td>benzyl alcohol</td>
<td>0.30</td>
</tr>
<tr>
<td>methyl p-hydroxybenzoate (a.k.a. methylparaben)</td>
<td>0.20</td>
</tr>
<tr>
<td>ethanol</td>
<td>3.00</td>
</tr>
<tr>
<td>water</td>
<td>60.60-61.35</td>
</tr>
<tr>
<td>PHASE B</td>
<td></td>
</tr>
<tr>
<td>disodium EDTA</td>
<td>0.50</td>
</tr>
<tr>
<td>glycerol</td>
<td>10.00</td>
</tr>
<tr>
<td>hexylene glycol</td>
<td>2.00</td>
</tr>
<tr>
<td>niacinamide</td>
<td>2.00</td>
</tr>
<tr>
<td>triethanol amine</td>
<td>0.05</td>
</tr>
<tr>
<td>butylated hydroxytoluene</td>
<td>0.10</td>
</tr>
<tr>
<td>PHASE C</td>
<td></td>
</tr>
<tr>
<td>Dow Corning 345 Fluid</td>
<td>12.50</td>
</tr>
<tr>
<td>Abil WE-09</td>
<td>2.50</td>
</tr>
<tr>
<td>Dow Corning -3225C</td>
<td>2.50</td>
</tr>
<tr>
<td>petrolatum</td>
<td>1.50</td>
</tr>
<tr>
<td>retinol (10% in soybean oil)</td>
<td>0.75-1.50</td>
</tr>
<tr>
<td>fatty acid ester of sugar*</td>
<td>1.00</td>
</tr>
</tbody>
</table>

* See Example 3

[0177] Blend the A phase components with a suitable mixer (e.g., Tekmar model RW20DZM). Blend the B phase components into the A phase with a suitable mixer. Separately, blend the C phase components until they are uniform. Add the C phase mixture to the A/B phase mixture, mix until uniform and emulsified, and then mill to obtain an acceptably smooth mixture (e.g., using a Tekmar T50 Mill).
[0178] Apply the composition to a subject's wrinkled, intrinsically aged, or photodamaged facial skin at the rate of 2 mg composition/cm² skin once or twice daily for a period of at least 3-6 months to improve skin surface texture, including diminishing fine lines and wrinkles.

[0179] An alternative skin cream having reduced retinol levels can be prepared in the same manner from the above components wherein the retinol is added in an amount of 0.025% (0.25% of 10% retinol in soybean oil), quo sine to 100% with water, the amounts of the other components being as shown.

[0180] While particular embodiments of the subject invention have been described, it will be obvious to those skilled in the art that various changes and modifications to the subject invention can be made without departing from the spirit and scope of the invention. It is intended to cover, in the appended claims, all such modifications that are within the scope of the subject invention.

Claims

1. A cosmetic method of regulating mammalian skin pore size, characterised in that it comprises applying to the skin of a mammal a safe and effective amount of a composition comprising:

   (a) a safe and effective amount of an active for regulating skin pore size, said active consisting essentially of a vitamin B₃ compound selected from niacinamide, nicotinic acid, nicotinyl alcohol, nicotinic acid esters, nicotinyl amino acids, nicotinyl alcohol esters of carboxylic acids, nicotinic acid N-oxide, nicotinyl hydroxamic acid, 2-chloronicotinamide, 6-aminonicotinamide, 6-methylnicotinamide, N-methyl-nicotinamide, N,N-diethylnicotinamide, N-(hydroxymethyl)-nicotinamide, quinolinic acid imide, nicotinanilide, N-benzynicotinamide, N-ethyl-nicotinamide, nipecoxone, nicotinaldehyde, isonicotinic acid, methyl isonicotinic acid, thionicotinamide, nialamide, 1-(3-pyridylmethyl) urea, 2-mercaptoptonicotonic acid, nicomol, niaprazine and salts thereof; and

   (b) a carrier for said vitamin B₃ compound.

2. A cosmetic method of regulating skin pore size, characterised in that it comprises applying to the skin of a mammal a safe and effective amount of a composition comprising:

   (a) a safe and effective amount, ranging from 2% to 5%, of a vitamin B₃ compound selected from niacinamide, nicotinyl alcohol, nicotinic acid esters, derivatives of niacinamide and salts thereof;

   (b) a safe and effective amount of a retinoid; and

   (c) a carrier for said vitamin B₃ compound and said retinoid.

3. The method of any of the preceding claims wherein said vitamin B₃ compound is selected from niacinamide, derivatives of niacinamide, non-vasodilating esters of nicotinic acid, and combinations thereof, preferably selected from niacinamide, tocopherol nicotinate, and combinations thereof, more preferably niacinamide.

4. The method of any of the preceding claims wherein said vitamin B₃ compound is substantially free of salts of the vitamin B₃ compound and/or is substantially uncomplexed.

5. The method of any of the preceding claims wherein said carrier comprises a hydrophilic diluent.

6. The method of any of the preceding claims wherein said composition further comprises a compound selected from the group consisting of:

   (a) hydroxy acids, preferably salicylic acid;

   (b) desquamatory agents, preferably selected from zwitterionic surfactants;

   (c) sunscreens, preferably selected from zinc oxide, titanium dioxide, phenyl benzimidazole sulfonic acid, octocrylene and combinations thereof;

   (d) anti-oxidants, preferably selected from esters of tocopherol; and combinations thereof.

7. A method according to claim 2 which comprises ameliorating visible and/or tactile discontinuities in the texture of mammalian skin.

8. A method according to claim 2 which comprises delaying, minimising and/or preventing visible and/or tactile discontinuities in the texture of mammalian skin.
9. A method according to claim 2 in which the retinoid is retinol propionate.

**Patentansprüche**

5. **Kosmetisches Verfahren zur Regulierung der Hautporengröße bei einem Säuger, dadurch gekennzeichnet, dass es das Aufbringen auf die Haut eines Säugers einer sicheren und wirksamen Menge einer Zusammensetzung umfasst, welche umfasst:**

   (a) eine sichere und wirksame Menge eines Wirkstoffs zur Regulierung der Hautporengröße, wobei der Wirkstoff im wesentlichen besteht aus einer Vitamin B₃-Verbindung, gewählt aus Niacinamid, Nicotinsäure, Nicotinylalkohol, Nicotinsäureestern, Nicotinylaminosäuren, Nicotinylalkoholestern von Carbonsäuren, Nicotinsäure-N-oxid, Nicotinylhydroxamsäure, 2-Chlornicotamid, 6-Aminonicotinamid, 6-Methylnicotinamid, N-Methylnicotinamid, N,N-Diethylnicotinamid, N-(Hydroxyethyl)-nicotinamid, Chinolin säure-amid, Nicotinimid, N-Benzylnicotinamid, N-Ethylnicotinamid, Nilazon, Nicotinaldehyd, Isonicotinsäure, Methylisonicotinsäure, Thionicotiamid, Nialamid, 1-(3-Pyridylmethyl)harnstoff, 2-Mercaptopnicotinsäure, Nicomol, Niaprazin und Salzen hiervon; und
   (b) einen Träger für die Vitamin B₃-Verbindung.

10. **Kosmetisches Verfahren zur Regulierung der Hautporengröße, dadurch gekennzeichnet, dass es das Aufbringen auf die Haut eines Säugers einer sicheren und wirksamen Menge einer Zusammensetzung umfasst, welche umfasst:**

   (a) eine sichere und wirksame Menge, im Bereich von 2 % bis 5 %, einer Vitamin B₃-Verbindung, gewählt aus Niacinamid, Nicotinylalkohol, Nicotinsäureester, Derivaten von Niacinamid und Salzen hiervon; (b) eine sichere und wirksame Menge eines Retinoids; und (c) einen Träger für die Vitamin B₃-Verbindung und das Retinoid.

15. **Verfahren nach mindestens einem der vorangehenden Ansprüche, wobei die Vitamin B₃-Verbindung gewählt wird aus Niacinamid, Derivaten von Niacinamid, nicht-vasodilatierenden Estern von Nicotinsäure und Kombinationen hiervon, vorzugsweise gewählt aus Niacinamid, Tocopherolnicotinat und Kombinationen hiervon, weiter vorzugsweise Niacinamid.**

20. **Verfahren nach mindestens einem der vorangehenden Ansprüche, wobei die Vitamin B₃-Verbindung im wesentlichen frei ist an Salzen der Vitamin B₃-Verbindung und/oder im wesentlichen unkomplexiert ist.**

25. **Verfahren nach mindestens einem der vorangehenden Ansprüche, wobei der Träger ein hydrophiles Verdünnungsmittel umfasst.**

30. **Verfahren nach mindestens einem der vorangehenden Ansprüche, wobei die Zusammensetzung weiterhin eine Verbindung umfasst, gewählt aus der Gruppe, bestehend aus:**

   (a) Hydroxsäuren, vorzugsweise Salicylsäure; (b) desquamatorischen Mitteln, vorzugsweise gewählt aus zwitterionischen Tensiden; (c) Sonnenschutzmitteln, vorzugsweise gewählt aus Zinkoxid, Titandioxid, Phenylbenzimidazolsulfonsäure, Oxyerylken und Kombinationen hier von; (d) Antioxidantien, vorzugsweise gewählt aus Estern von Tocopherol; und Kombinationen hiervon.

35. **Verfahren nach Anspruch 2, umfassend die Amelioration sichtbarer und/oder taktiler Diskontinuitäten in der Textur von Säugerhaut.**

40. **Verfahren nach Anspruch 2, umfassend die Verzögerung, Minimierung und/oder Verhinderung sichtbarer und/oder taktiler Diskontinuitäten in der Textur von Säugerhaut.**

45. **Verfahren nach Anspruch 2, wobei das Retinoid Retinolpropionat ist.**
Revendications

1. Procédé cosmétique de régulation de la taille des pores de la peau d'un mammifère, caractérisé en ce qu'il comprend l'application, sur la peau d'un mammifère, d'une quantité efficace et sans danger d'une composition comprenant :

(a) une quantité efficace et sans danger d'un principe actif pour réguler la taille des pores de la peau, ledit principe actif étant essentiellement constitué d'un composé de vitamine B₃ choisi parmi le niacinamide, l'acide nicotinique, l'alcool nicotinylique, les esters d'acide nicotinique, les nicotinylaminoacides, les esters d'alcool nicotinylique et d'acides carboxyliques, le N-oxyde d'acide nicotinique, l'acide nicotinyl-hydroxamique, le 2-chloronicotinamide, le 6-aminonicotinamide, le 6-méthylnicotinamide, le N,N-diéthyl-nicotinamide, le N-(hydroxyméthyl)nicotinamide, l'imide d'acide quinoléinique, l'nicotinanilide, le N-benzylnicotinamide, le N-éthylnicotinamide, la nifénazone, le nicotinaldéhyde, l'acide isonicotinique, l'acide méthylisonicotinique, le thionicotinamide, le nialamide, la 1-(3-pyridylméthyl)urée, l'acide 2-mercaptop nicotinique, le nicomol, la niaprazine et leurs sels ; et
(b) un véhicule pour ledit composé de vitamine B₃.

2. Procédé cosmétique de régulation de la taille des pores de la peau, caractérisé en ce qu'il comprend l'application sur la peau d'un mammifère d'une quantité efficace et sans danger d'une composition comprenant :

(a) une quantité efficace et sans danger, allant de 2% à 5%, d'un composé de vitamine B₃ choisi parmi le niacinamide, l'alcool nicotinylique, les esters d'acide nicotinique, les dérivés de niacinamide et leurs sels; (b) une quantité efficace et sans danger d'un rétinoïde; et (c) un véhicule pour ledit composé de vitamine B₃ et ledit rétinoïde.

3. Procédé selon l'une quelconque des revendications précédentes dans lequel ledit composé de vitamine B₃ est choisi parmi le niacinamide, les dérivés de niacinamide, les esters non vasodilatateurs de l'acide nicotinique, et leurs combinaisons, de préférence choisi parmi le niacinamide, le nicotide de tocophérol, et leurs combinaisons, en particulier le niacinamide.

4. Procédé selon l'une quelconque des revendications précédentes dans lequel ledit composé de vitamine B₃ est essentiellement exempt de sels du composé de vitamine B₃ et/ou est essentiellement non complexé.

5. Procédé selon l'une quelconque des revendications précédentes dans lequel ladite composition comprend un diluant hydrophile.

6. Procédé selon l'une quelconque des revendications précédentes dans lequel ladite composition comprend en outre un composé choisi dans le groupe constitué par:

(a) les hydroxyacides, de préférence l'acide salicylique; (b) les agents desquamants, de préférence choisis parmi les tensioactifs zwitterioniques; (c) les écrans solaires, de préférence choisis parmi l'oxyde de zinc, le dioxyde de titane, l’acide phénylbenzimidazolesulfonique, l’octocrylène, et leurs combinaisons; (d) les antioxydants, de préférence choisis parmi les esters de tocophérol; et leurs combinaisons.

7. Procédé selon la revendication 2 qui comprend le fait d'améliorer les discontinuités visibles et/ou tactiles dans la texture de la peau d'un mammifère.

8. Procédé selon la revendication 2 qui comprend le fait de retarder, de minimiser et/ou de prévenir les discontinuités visibles et/ou tactiles dans la texture de la peau d'un mammifère.

9. Procédé selon la revendication 2 dans lequel le rétinoïde est le propionate de rétanol.