Title: AN OIL-IN-WATER EMULSION CONTAINING AN ASCORBIC ACID COMPOUND

Abstract

Disclosed is an oil-in-water emulsion comprising: (a) a water-soluble ascorbic acid compound; (b) a metallic oxide; (c) a structuring compound; (d) a hydrophobic component; and (e) a hydrophilic liquid carrier, wherein the emulsion has a pH of from about 6 to about 10.
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AN OIL-IN-WATER EMULSION CONTAINING
AN ASCORBIC ACID COMPOUND

FIELD

The present invention relates to a topical composition. In particular, it relates to a topical skin lightening emulsion.

BACKGROUND

Consumers frequently use cosmetic products to care for their skin as well as to improve the health and/or physical appearance of their skin. Rough and/or broken skin and hyperpigmentations (such as age spots, freckles, and brown patches associated with skin aging or environmental damage to the human skin) are areas consumers typically seek to treat. Skin lightening is of particular interest in certain Asian populations.

Irradiation of ultra-violet (UV) rays tends to cause sun-burning, resulting in skin darkening and/or hyperpigmentation. It is generally known that conditions which result in defective or missing tyrosinase, an enzyme involved in the formation of melanin, lead to hyperpigmentation, e.g. albinism. The irradiation of UV rays as a consequence of exposure to sunlight promotes a melanin complex formation in melanocytes located in the basal layer of the epidermis. Melanin is subsequently released from the dendrites of the melanocytes, then diffused to keratinocytes, resulting in hyperpigmentation of the skin. Such hyperpigmentation may take the form of spots, freckles, blotches, unwelcome general darkening and/or unevenness of the basal skin.

A wide variety of compounds and/or ingredients, e.g., ascorbic acid and derivatives thereof, kojic acid and derivatives thereof, hydroquinone, arbutine, and a variety of extracts such as glycyrrhiza, are known and are commonly-available for skin-lightening use. In recent years, hi-tech synthetic ingredients
useful for skin-lightening are also available in a wide variety and array of product forms.

L-ascorbic acids (e.g., Vitamin C) are useful ingredients as skin lightening and/or evenness agents as well as a reductant, UV-absorbent and melanin-information inhibitor in cosmetics. GB 2259014-A, Hadas et al., issued March 3, 1998, discloses a composition for skin lightening containing oil-soluble ascorbic acid derivatives such as ascorbic palmitate with sun screening agents such as titanium dioxide.

However, it is also known that L-ascorbic acid tends to be unstable in formulation. Particularly, increasing the level of L-ascorbic acid in an emulsion-type composition can result in an unstable emulsion. For example, increased levels of L-ascorbic acids tend to cause e.g., decomposition of L-ascorbic acid in the emulsion, imparting a yellowish and/or brownish color to the composition. It would be desired to stabilize the composition containing ascorbic acids, particularly while increasing the levels in emulsion.

Certain combinations have been designed to stabilize compositions containing ascorbic acids. Japanese Laid-open (Kokai) H1-213212, Imamura et al., issued August 28, 1989, discloses stable cosmetic compositions containing ascorbic acid derivatives and gluconic acids. Japanese Laid-open H1-305009, Yamada et al., issued December 8, 1989, discloses stable cosmetic compositions containing ascorbic acid derivatives and cyclodextrin. Japanese Laid-open H3-63208, Sato, issued March 19, 1991, discloses compositions containing ascorbic acid and phenoxyethanol. Such combinations tend to provide acceptable stability of the compositions, but the product appearance change to yellow or brown is still observed, especially in storage.

Based on the foregoing, there is a need for a stable skin lightening emulsion having increased levels of ascorbic acid compound as well as sustained pleasant product aesthetics. None of the existing art provides all the advantages and benefits of the present invention.

**SUMMARY**

The present invention is directed to an oil-in-water emulsion comprising:

(a) a water-soluble ascorbic acid compound;
(b) a metallic oxide;
(c) a structuring compound;
(d) a hydrophobic component; and
(e) a hydrophilic liquid carrier,
wherein the emulsion has a pH of from about 6 to about 10.

These and other features, aspects, and advantages of the present
invention will become better understood from a reading of the following
description, and appended claims.

DETAILED DESCRIPTION

While the specification concludes with claims particularly pointing out and
distinctly claiming the invention, it is believed that the present invention will be
better understood from the following description.

All percentages, ratios, and levels of ingredients referred to herein are
based on the actually total amount of the composition, unless otherwise indicated.

All measurements referred to herein are made at 25°C unless otherwise
specified.

All publications, patent applications, and issued patents mentioned herein
are hereby incorporated in their entirety by reference. Citation of any reference
is not an admission regarding any determination as to its availability as prior art
to the claimed invention.

Herein, "comprising" means that other steps and other ingredients which
do not affect the end result can be added. This term encompasses the terms
"consisting of" and "consisting essentially of."

Herein, "topical application" means to apply or spread a material onto the
surface of the skin.

Herein, "skin lightening" refers altering the appearance of the skin to a
brighter, lighter, and/or whiter appearance, and improving hyperpigmentation as
compared to pre-treatment.

Herein, "cosmetically-acceptable" 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.

Herein, "safe and effective amount," 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, e.g., to provide a
reasonable benefit to risk ratio, within the scope of sound judgment of the skilled artisan.

Herein, "mixtures" is meant to include a simple combination of materials and any compounds that may result from their combination.

All ingredients such as actives and other ingredients useful herein may be categorized or described by their cosmetic and/or therapeutic benefit or their postulated mode of action. However, it is to be understood that the active and other ingredients useful herein can, in some instances, provide more than one cosmetic and/or therapeutic benefit or operate via more than one mode of action. Therefore, classifications herein are made for the sake of convenience and are not intended to limit an ingredient to the particularly stated application or applications listed.

The present invention is directed to an oil-in-water emulsion comprising: (a) a water-soluble ascorbic acid compound; (b) a metallic oxide; (c) a structuring compound; (d) a hydrophobic component; and (e) a hydrophilic liquid carrier. Preferably, the pH of the emulsion of the present invention is from about 6 to about 10, more preferably from about 7 to about 9.

Without being bound by theory, it is believed that a high reduction capability of the water-soluble ascorbic acid compound provides promotion of cell respiration, enzyme activation and anti-oxidation. It is further believed topical application of the ascorbic acid compound tends to reduce oxidized melanin complex itself and its precursors, as well as inhibit tyrosinase activity in the melanosome. Consequently, it is also believed that compositions containing the ascorbic acid compound can provide skin benefits such as the prevention of melanin production and the reduction of age spots, blotches and/or freckles associated with skin hyperpigmentation.

Increasing the concentration of ascorbic acid in compositions will typically improve the efficacy of the composition. For example, increasing the level of ascorbic acid in a skin lightening composition will result in improved lightening of the skin. Unfortunately, in the past it has been difficult to increase these levels because compositions having such increased levels of ascorbic acid, particularly those in emulsion from, tend to be unstable, particularly in physical properties, such as product appearance changing to yellow or brown. However, we have discovered that including a structuring compound in emulsion can sustain the original physical properties of a water-soluble ascorbic acid compound and the
emulsion thereof, even when the composition contains relatively high levels of the water-soluble ascorbic acid compound.

A. Water-Soluble Ascorbic Acid Compound

The oil-in-water emulsion of the present invention includes a water-soluble ascorbic acid compound. The water-soluble ascorbic acid compound is selected depending upon its compatibility with the other ingredients. The water-soluble ascorbic acid compound may be included as a substantially pure material, for example, which may be an extract obtained by suitable physical and/or chemical isolation from natural (e.g., plant) sources.

The oil-in-water emulsion of the present invention preferably contains from about 1.0% to about 10.0% of a water-soluble ascorbic acid compound, more preferably from about 2.0% to about 5.0%.

Herein, "water-soluble ascorbic acid compound," means ascorbic acid or derivatives thereof which have the formula (I):

![Chemical Structure](image)

(I)

wherein V and W are independently -OH; R¹ is -CH(OH)-CH₂OH; and salts thereof.

Preferably, the water-soluble ascorbic acid compound useful herein is an ascorbic acid salt or derivative thereof, such as the non-toxic alkali metal, alkaline earth metal and ammonium salts commonly known by those skilled in the art including, but not limited to, the sodium, potassium, lithium, calcium, magnesium, barium, ammonium and protamine salts which are prepared by methods well known in the art.

More preferably, the water-soluble ascorbic acid salt useful herein is a metal ascorbate having the following formula (II):

![Chemical Structure](image)

xM¹ (II)
wherein \( R^2 \) and \( R^3 \) are independently selected from hydrogen and linear or branched alkyl of 1 to about 8 carbons; \( M^1 \) is a metal; and \( x \) is an integer of from 1 to about 3. More preferably, \( R^2 \) and \( R^3 \) are independently selected from hydrogen and linear or branched alkyl of 1 to about 3 carbons; \( M^1 \) is sodium, potassium, magnesium, or calcium.

Examples of other preferred water-soluble ascorbic acid salts having formula (II) include monovalent metal salts (e.g., sodium ascorbate, potassium ascorbate), divalent metal salts (e.g., magnesium ascorbate, calcium ascorbate) and trivalent metal salts (e.g., aluminum ascorbate) of ascorbic acid.

Preferably, the water-soluble ascorbic acid salt useful herein is a water soluble ascorbyl ester having the following formula (III):

\[
\begin{align*}
\text{O} & \text{H} \\
\text{O} & \text{CH-CH}_2\text{OR}^5 \\
\text{O} & \text{OR}^4 \\
\text{A} & \\
\end{align*}
\]

\[
yM^2
\] (III)

wherein \( A \) is sulfate or phosphate; \( R^4 \) and \( R^5 \) are independently selected from hydrogen and linear or branched alkyl of 1 to about 8 carbons; \( M^2 \) is a metal; and \( y \) is an integer of 1 to about 3. More preferably, \( R^4 \) and \( R^5 \) are independently selected from hydrogen and linear or branched alkyl of 1 to about 3 carbons; \( M^2 \) is sodium, potassium, magnesium, or calcium.

Exemplary water soluble salt derivatives include, but are not limited to, L-ascorbil phosphate ester salts such as sodium L-ascorbil phosphate, potassium L-ascorbil phosphate, magnesium L-ascorbil phosphate, calcium L-ascorbil phosphate, aluminum L-ascorbil phosphate. L-ascorbil sulfate ester salts can also be used. Examples are sodium L-ascorbil sulfate, potassium L-ascorbil sulfate, magnesium L-ascorbil sulfate, calcium L-ascorbil sulfate and aluminum L-ascorbil sulfate.

B. Metallic Oxide

The oil-in-water emulsion of the present invention includes a metallic oxide. The metallic oxide useful herein present in the emulsion from about 0.1% to about 5.0%, more preferably from about 0.5% to about 2.0%.

Preferably, the metallic oxide is selected from the group consisting of titanium dioxide, zinc oxide, zirconium dioxide, aluminum oxide, and combinations thereof (combinations are intended to include particles which
comprise one or more of these materials, as well as mixtures of these particulate materials), more preferably, titanium dioxide.

The metallic oxides useful herein are commercially available from a number of sources. For example, a suitable metallic oxides are Tronox™ (titanium dioxide series) and SAT-T CR837 (rutile Titanium dioxide) available from U. S. Cosmetics, titanium dioxide CR-50 available from Ishihara Sangyo Kaisha, and titanium dioxide JA-1 available from Tayca Corporation.

C. Structuring Compound

The oil-in-water emulsion of the present invention comprises a structuring compound. Herein, "structuring compound" refers to a compound which forms an organized structure, a gel network system, such that the system can exist in hydrophobic or hydrophilic components. It is believed that the structuring compound assists in providing good rheological characteristics to the composition which contribute to the stability of the emulsion. Preferably, the structuring compound is present from about 1.0% to about 10.0%, more preferably from about 2.0% to about 8.0% in the composition.

Preferably, the structuring compound comprises a fatty alcohol and an amphiphilic surfactant. While not wishing to be bound by theory, it is believed that the fatty alcohol, together with the amphiphilic surfactant, is oriented in order to form a lamellar structure, resulting in sustaining oil and water phases. It is also believed such an organized structure, called "fatty alcohol gel network system," contribute to stability of the emulsion.

The fatty alcohols useful herein are a saturated, linear or branched fatty alcohol, selected from the group consisting of a saturated, linear or branched C_{12-30} fatty alcohols, a saturated, linear or branched C_{12-30} diols, and mixtures thereof. Preferred fatty alcohols are cetyl alcohol, stearyl alcohol, and mixtures thereof. Preferably, the fatty alcohols useful herein present from about 1.0% to 10.0% in the composition, more preferably from about 1.0% to about 5.0%.

The amphiphilic surfactant useful herein includes surfactants, any of a wide variety of nonionic, cationic, anionic, zwitterionic, amphoteric as well as mixtures of these surfactants. Examples of a broad variety of additional surfactants useful herein are described in McCutcheon's Detergents and Emulsifiers, North American Edition (1986), published by Allured Publishing Corporation, which is incorporated herein by reference in its entirety. Also see U.S. Patent No. 4,800,197, to Kowcz et al., issued January 24, 1989, which is
incorporated herein by reference in its entirety, for exemplary surfactants useful herein. Preferably, the amphiphilic surfactants useful herein present from about 1.0% to 10.0% in the composition, more preferably from about 2.0% to about 6.0%.

Preferably, the amphiphilic surfactant of the present invention is nonionic surfactants. Preferred nonionic surfactants useful herein are the condensation products of alkylene oxides with both fatty acids and fatty alcohols (e.g., wherein the polyalkylene oxide portion is esterified on one end with a fatty acid and etherified (e.g., connected via an ether linkage) on the other end with a fatty alcohol). These materials have the general formula \( R^2CO(X^1)_2OR^3 \) wherein \( R^2 \) and \( R^3 \) are independently alkyl of from about 10 to about 30 carbons; \( X^1 \) is \(-OCH_2CH_2\) derived from, for example ethylene glycol or oxide or \(-OCH_2CH(CH_3)\) derived from propylene glycol or oxide; and \( z \) is an integer from about 6 to about 100.

Other examples of such alkylene oxide derived nonionic surfactants include ceteth-6, ceteth-10, ceteth-12, ceteareth-6, ceteareth-10, ceteareth-12, ceteareth-20, steareth-6, steareth-10, steareth-12, steareth-20, steareth-21, steareth-100, PEG-6 stearate, PEG-10 stearate, PEG-12 stearate, PEG-100 stearate, PEG-10 glyceryl stearate, PEG-20 glyceryl stearate, PEG-30 glyceryl cocoate, PEG-80 glyceryl cocoate, PEG-80 glyceryl tallowate, PEG-200 glyceryl tallowate, PEG-8 dilaurate, PEG-10 distearate, glyceryl monostearate, glyceryl distearate, glyceryl monolaurate, glyceryl dilaurate and mixtures thereof.

The structuring compound may further contain a co-thickener. Exemplary co-thickeners useful herein are polysaccharides and materials which are primarily derived from natural sources such as gums.

A wide variety of the polysaccharides known in the art may be used. "Polysaccharides" as used herein means an ingredient containing a backbone of repeating sugar (i.e., carbohydrate) units. Nonlimiting examples of polysaccharide include those selected from the group consisting of cellulose, carboxymethyl hydroxyethylcellulose, cellulose acetate propionate carboxylate, hydroxyethylcellulose, hydroxyethyl ethylcellulose, hydroxypropylcellulose, hydroxypropyl methylcellulose, methyl hydroxyethylcellulose, microcrystalline cellulose, sodium cellulose sulfate, and mixtures thereof.

Also useful herein are the alkyl substituted celluloses. In these polymers, the hydroxy groups of the cellulose polymer is hydroxyalkylated (preferably
hydroxyethylated or hydroxypropylated) to form a hydroxylalkylated cellulose which is then further modified with a C₁₀₋₃₀ straight chain or branched chain alkyl group through an ether linkage. Typically these polymers are ethers of C₁₀₋₃₀ straight or branched chain alcohols with hydroxylalkylcelluloses. Examples of alkyl groups useful herein include those selected from the group consisting of stearyl, isostearyl, lauryl, myristyl, cetyl, isocetyl, cocoyl (i.e. alkyl groups derived from the alcohols of coconut oil), palmityl, oleyl, linoleyl, linolenyl, ricinoleyl, behenyl, and mixtures thereof. Preferred among the alkyl hydroxylalkyl cellulose ethers is the material given the CTFA designation cetyl hydroxyethylcellulose, which is the ether of cetyl alcohol and hydroxyethylcellulose. This material is sold under the tradename Natrosol® CS Plus from Aqualon Corporation.

Other useful polysaccharides include scleroglucans comprising a linear chain of (less than 3) linked glucose units with a less than 6 linked glucose every three units, a commercially available example of which is Clearogel™ CS11 from Michel Mercier Products Inc. (Mountainside, NJ).

Nonlimiting examples of the gums include materials selected from the group consisting of acacia, agar, algin, alginic acid, ammonium alginate, amylopectin, calcium alginate, calcium carrageenan, carrtine, carrageenan, dextrin, gelatin, gellan gum, guar gum, guar hydroxypropyltrimonium chloride, hectorite, hyaluronic acid, hydrated silica, hydroxypropyl chitosan, hydroxypropyl guar, karaya gum, kelp, locust bean gum, natto gum, potassium alginate, potassium carrageenan, propylene glycol alginate, sclerotium gum, sodium carboxymethyl dextran, sodium carrageenan, tragacanth gum, xanthan gum, and mixtures thereof.

D. Hydrophobic Component

Hydrophobic components useful in the present invention include a lipid, oil, oily or other hydrophobic component. The hydrophobic component is used as an emollient.

A wide variety of suitable hydrophobic components are known and may be used herein and numerous examples can be found in Sagarin, Cosmetics, Science and Technology, 2nd Edition, Vol. 1, pp. 32-43 (1972). Nonlimiting examples of suitable hydrophobic components include mineral oil, petrolatum, C₇₋₄₀ straight and branched hydrocarbons, C₁₋₃₀ alcohol esters, glycerides, alkylene glycol esters, propoxylated and ethoxylated derivatives, sugar ester,

A fatty acid sugar ester useful herein is C₁₃-3₀ monoester or polyester of sugars and one or more carboxylic acid moieties, 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.

Preferably, the oil-in-water emulsion contains from about 2% to about 20% of the hydrophobic component, more preferably from about 3% to about 10%. The hydrophobic component may include an ingredient derived from animals, plants, or petroleum and which is natural or synthetic (e.g., man-made).

E. Hydrophilic Liquid Carrier

The oil-in-water emulsion of the present invention contains a hydrophilic liquid carrier (HLC). Preferred HLC can contain a dermatologically acceptable, non-aqueous hydrophilic diluent. Nonlimiting examples of hydrophilic diluents are polyhydric alcohols such as low molecular weight monovalent alcohols (i.e., C₁₂;₆) and low molecular weight glycols and polyols including propylene glycol, butylene glycol, hexylene glycol, dipropylene glycol, polyethylene glycol (e.g., Molecular Weight 200-1000 g/mole), polypropylene glycol (e.g., Molecular Weight 425-2025 g/mole), glycerol, 1,2,4-butanetriol, 1,2,6-hexanetriol, and combinations thereof.

Preferably, the oil-in-water emulsion contains from about 60.0% to about 95.0% of HLC, more preferably from about 70.0% to about 85.0%. The HLC includes water and one or more water soluble or dispersible ingredients. The exact amount of water in the formulation will vary with the ranges of the required and optional components chosen.

The HLC may further contain a pH adjuster. Herein, “pH adjuster” refers to any component which is employed to increase or decrease the overall pH of
the composition to an optimum pH, thereby preventing decomposition of ingredients (particularly the ascorbic acid compound). An optimum pH is subject to the selection of the ascorbic acid compound. For example, when the composition includes magnesium L-ascorbyl phosphate (MAP), the optimum pH is around 7.0 to about 8.0. Suitable pH adjusters herein include acetate, phosphate, citrate, triethanolamine and carbonate. A combination of the foregoing are often employed to adjust to a specific optimal pH for the emulsion. The total level by weight of emulsion of the pH adjuster is from about 0.01% to about 5.0%, preferably, from about 0.5% to about 2.0%.

F. Other Actives

The oil-in-water emulsion of the present invention may further comprise other actives capable of functioning in different ways to enhance the benefits of the ascorbic acid compound and/or to provide other benefits. Examples of such substances include, but are not limited to, vitamin B3 compound, antioxidants/radical scavengers, anti-inflammatory agents, antimicrobial agents, sunscreens and sunblocks, and chelators.

(i) Vitamin B3 Compounds: The vitamin B3 compound enhances the skin appearance benefits of the present invention, especially in regulating skin condition, including regulating signs of skin aging, more especially wrinkles, lines, and pores. The vitamin B3 compound preferably present 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%.

Herein, "vitamin B3 compound" means a compound having the formula:

```
\[
\text{R}
\]
```

wherein R is -CONH₂ (e.g., niacinamide), -COOH (e.g., nicotinic acid) or -CH₂OH (e.g., nicotinyl alcohol); derivatives thereof; and salts of any of the foregoing.

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.
Suitable esters of nicotinic acid include nicotinic acid esters of from 1 to about 22 carbons, preferably 1 to about 16 carbons, more preferably alcohols from about 1 to about 6 carbons. 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, i.e., the ester is non-rubifacient). Non-vasodilating esters of nicotinic acid include tocopherol nicotinate and inositol hexanicotinate; tocopherol nicotinate is preferred.

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., 1 to about 18 carbons). Specific examples of such derivatives include nicotinuric acid (C_8H_6N_2O_3) and nicotinyl hydroxamic acid (C_6H_6N_2O_2), which have the following chemical structures:

nicotinuric acid:

\[
\text{C-\text{NH-CH}_{2}-\text{COH}}
\]

nicotinyl hydroxamic acid:

\[
\text{C-\text{NH-OH}}
\]

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-
icotinamide, n,n-diethyl nicotinamide, n-(hydroxymethyl)-nicotinamide, quinolinic
acid imide, nicotinanilide, n-benzyl nicotinamide, n-ethyl nicotinamide, nifenazone,
nicotinaldehyde, isonicotinic acid, methyl isonicotinic acid, thionicotinamide,
nialamide, 1-(3-pyridylmethyl) urea, 2-mercaptopnicotinic acid, nicomol, and
niaprazine.

Nonlimiting 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).

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

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.

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-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
synthesis of the ascorbic acid salt of niacinamide.

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.

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.

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.

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.

(ii) Anti-Oxidants and Radical Scavengers Anti-oxidant and radical scavengers are 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.

Anti-oxidants and radical scavengers such as tocopherol (vitamin E), tocopherol sorbate, tocopherol acetate, 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 (i.e., N,N-diethylhydroxylamine, aminoguanidine), sulfhydryl compounds (i.e., glutathione), dihydroxy fumaric acid and its salts, lycine pidolate, 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 4,847,071, Bissett et al, issued on July 11, 1989.

(iii) Anti-Inflammatory Agents Anti-inflammatory agents enhance the skin appearance benefits, by for example, contribution of uniformity and acceptable skin tone and/or color.

Preferably, the anti-inflammatory agent includes a steroidal anti-inflammatory agent and an non-steroidal anti-inflammatory agent. Preferred steroidal anti-inflammatory for use is hydrocortisone.

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 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), each incorporated herein by reference.

So-called "natural" anti-inflammatory agents are also useful. Such agents may suitably be obtained as an extract by suitable physical and/or chemical isolation from natural sources (i.e., plants, fungi, by-products of microorganisms). For example, 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 C2-24 saturated or unsaturated esters of the acids, preferably C10-24, more preferably C16-24.

(iv) Antimicrobial Agent As used herein, "antimicrobial agents" 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. Preferred antimicrobial agents useful
in the present invention are benzoyl peroxide, erythromycin, tetracycline, clindamycin, azelaic acid, sulfur resorcinol phenoxyethanol, and Irgasan™ DP 300 (Ciba Geigy Corp., U.S.A.). A safe and effective amount of an antimicrobial agent may be added to compositions of the present invention, preferably from about 0.001% to about 10%, more preferably from about 0.01% to about 5%, still more preferably from about 0.05% to about 2%.

(v) Sunscreens and Sunblocks. Sunscreens and sunblocks generally prevent excessive scaling and texture changes of the stratum corneum by exposure of ultraviolet light and may be added to the composition of the present invention. Suitable sunscreens and sunblocks may be organic or inorganic.

A wide variety of conventional sunscreens and sunblocks are suitable for use herein. See, U.S. Patent 5,087,445, Haffey et al, issued February 11, 1992; U.S. Patent 5,073,372, Turner et al, issued December 17, 1991; U.S. Patent 5,073,371, Turner et al., issued December 17, 1991; and Segarin, et al, at Chapter VIII, pages 189 et seq., of Cosmetics Science and Technology (1972), which discloses numerous suitable sunscreens and sunblocks. Preferred among those sunscreens and sunblocks which are useful in the compositions are those selected from 2-ethylhexyl-p-methoxy cinnamate (commercially available as PARSOL MCX), butylmethoxy dibenzoyl-methane, 2-hydroxy-4-methoxybenzophenone, 2-phenylbenzimidazole-5-sulfonic acid, octyldimethyl-p-aminobenzoic acid, octocrylene, 2-ethylhexyl N,N-dimethyl-p-aminobenzoate, p-aminobenzoic acid, 2-phenylbenzimidazole-5-sulfonic acid, octocrylene, oxybenzone, homomethyl salicylate, octyl salicylate, 4,4'-methoxy-t-butyl dibenzoylmethane, 4-isopropyl dibenzoylmethane, 3-benzylidene camphor, 3-(4-methylbenzylidene) camphor, titanium dioxide, zinc oxide, silica, iron oxide, Eusolex™ 6300, Octocrylene, Parsol 1789, and mixtures thereof.

Also particularly useful in the compositions are sunscreens and sunblocks such as those disclosed in U.S. Patent 4,937,370, Sabatelli, issued on June 26, 1990, and U.S. Patent 4,999,186, Sabatelli, issued on March 12, 1991. The sunscreens and sunblocks disclosed therein have, in a single molecular, two distinct chromophore moieties which exhibit different ultraviolet radiation absorption spectra. One of the chromophore moieties absorbs predominantly in the UVB radiation range and the other absorbs strongly in the UVA radiation range. These sunscreens and sunblocks provide higher efficacy, broader UV
absorption, lower skin penetration and longer lasting efficacy relative to conventional sunscreens and sunblocks.

Exact amounts will vary depending upon the sunscreen chosen and the desired Sun Protection Factor (SPF). SPF is a commonly used measure of photoprotection of a sunscreen against erythema. See Federal Register, Vol. 43, No. 166, pp. 38206-38269, August 25, 1978.

A sunscreen or sunblock herein may also be added to improve the skin, particularly to enhance their resistance to being washed off by water, or rubbed off. Preferred sunscreens and sunblocks which will provide this benefit are 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.

(vi) Chelators. As used herein, "chelator" refers to a compound that reacts for 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 chelator 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.


G. Other components

In addition to the above described other actives components, the composition of the present invention may further include preservatives and preservative enhancers such as water-soluble or solubilizable preservatives including Germall 115, methyl, ethyl, propyl and butyl esters of hydroxybenzoic acid, benzyl alcohol, EDTA, Bronopol (2-bromo-2-nitropropane-1,3-diol) and phenoxypropanol; other skin lightening/evenness agents including kojic acid, arbutin; WO95/23780, Kvalnes et al, published September 8, 1995; skin-conditioning agents; skin penetration enhancing agents; skin protectants; skin soothing agents; skin healing agents; ultraviolet light absorbers or scattering agents; sequestrants; anti-acne agents; anti-androgens; depilation agents; keratolytic agents/ desquamation agents/ exfoliants such as salicylic acid; panthenol moisturizer such as D-pantenol; soluble or colloidally-soluble moisturizing agents such as hyaluronic acid and starch-grafted sodium
polyacrylates such as Sanwet™ IM-1000, IM-1500 and IM-2500 available from Celanese Superabsorbent Materials, Portsmouth, VA, USA and described in US Patent 4,076,663; proteins and polypeptides and derivatives thereof; organic hydroxy acids; drug astringents; external analgesics; film formers; absorbents including oil absorbents such as clays and polymeric absorbents; abrasives; anticaking agents; antifoaming agents; binders; biological additives; bulking agents; coloring agents; perfumes, essential oils, and solubilizers thereof; natural extracts; compounds which stimulate collagen production.

H. Method for Making Composition

The oil-in-water emulsions of the present invention are generally prepared by any method conventionally used for providing skin care compositions, particularly for skin lotions, that are known in the art. Such methods typically involve mixing of the ingredients in one or more steps to a relatively uniform state, with or without heating, cooling, and the like. Typical methods are described in, for example are described in Harry’s Cosmetology, 7th Ed., Harry & Wilkinson (Hill Publishers, London 1982).

EXAMPLES

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. Where applicable, ingredients are identified by chemical or CTFA name, or otherwise defined below.
The compositions shown below can be prepared by any conventional method known in the art. Suitable methods and formulations are as follows:

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<th>Chemical Name</th>
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<th>B</th>
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<tbody>
<tr>
<td>Magnesium Ascorbyl Phosphate</td>
<td>3.000</td>
<td>-</td>
<td>2.000</td>
</tr>
<tr>
<td>Sodium Ascorbyl Phosphate</td>
<td>-</td>
<td>4.000</td>
<td>-</td>
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<tr>
<td>Titanium Dioxide</td>
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<td>1.000</td>
</tr>
<tr>
<td>Stearyl Alcohol</td>
<td>2.000</td>
<td>1.000</td>
<td>-</td>
</tr>
<tr>
<td>Cetyl Alcohol</td>
<td>0.500</td>
<td>1.000</td>
<td>2.000</td>
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<tr>
<td>Xanthan gum</td>
<td>0.100</td>
<td>0.020</td>
<td>-</td>
</tr>
<tr>
<td>Fatty acid ester of sugar</td>
<td>-</td>
<td>2.000</td>
<td>1.000</td>
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<tr>
<td>Glycerol</td>
<td>5.000</td>
<td>7.000</td>
<td>9.000</td>
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<tr>
<td>Glyceryl monostearate</td>
<td>3.000</td>
<td>2.000</td>
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<tr>
<td>Ceteareth-10</td>
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<td>Steareth-21</td>
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<td>Isohexadecane</td>
<td>-</td>
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</tr>
<tr>
<td>Sodium Citrate</td>
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</tr>
<tr>
<td>Water</td>
<td>up to 100%</td>
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The oil-in-water emulsion above described are suitably made as follows:

1. Dissolve water-soluble contents except for a water-soluble ascorbic acid and sodium citrate and heat the solution to about 75 °C;

2. Mix a separate water solution of the water-soluble ascorbic acid compound and sodium citrate and cool the mixture to below about 40° C;

3. Mix (1) and (2) and keep the temperature at about 75 °C;

4. Heat a mixture of the structuring compounds and the oil components to about 80 °C;

5. Add the mixture (4) into the water phase (3) followed by high pressure homogenizing; and

6. Add the titanium dioxide and glycerin to the mixture (2) at about 30 °C.
The embodiments disclosed and represented by the previous examples have many advantages. For example, the composition herein contains increased levels of ascorbic acid compound for skin lightening, while exhibiting improved product aesthetic such as product appearance unchanging to yellow or brown, even if maintained in storage for extended periods of time.

It is understood that the foregoing detailed description of examples and embodiments of the present invention are given merely by way of illustration, and that numerous modifications and variations may become apparent to those skilled in the art without departing from the spirit and scope of the invention; and such apparent modifications and variations are to be included in the scope of the appended claims.
What is claimed is:

1. A oil-in-water emulsion comprising:
   (a) a water-soluble ascorbic acid compound;
   (b) a metallic oxide;
   (c) a structuring compound;
   (d) a hydrophobic component; and
   (e) a hydrophilic liquid carrier,
   wherein the emulsion has a pH of from about 6 to about 10.

2. The oil-in-water emulsion of Claim 1, wherein the emulsion contains from about 1.0% to about 10.0% of the water-soluble ascorbic acid compound.

3. The oil-in-water emulsion of Claim 2, wherein the emulsion contains from about 1.0% to about 10.0% of a structuring compound.

4. The oil-in-water emulsion of Claim 3, wherein the structuring compound comprises a fatty alcohol and an amphiphilic surfactant.

5. The oil-in-water emulsion of Claim 4, wherein the emulsion contains from about 0.1% to about 5.0% of the metallic oxide.

6. The oil-in-water emulsion of Claim 5, wherein the metallic oxide is selected from the group consisting of titanium dioxide, zinc oxide, zirconium dioxide, aluminum oxide, and mixtures thereof.

7. The oil-in-water emulsion of 6, wherein the structuring compound further comprises a co-thickener selected from the group consisting of gums and polysaccharides.

8. The oil-in-water emulsion of Claim 6, wherein the emulsion comprises at least one other active selected from the group consisting of vitamin B3 compounds, anti-oxidants/radical scavengers, anti-inflammatory agents, antimicrobial agents, sunscreens and sunblocks, and chelators.
9. A oil-in-water emulsion comprising:
   (a) from about 2.0% to about 5.0% of an water-soluble ascorbic acid compound;
   (b) from about 0.5% to about 2.0% of a metallic oxide;
   (c) from about 2.0% to about 8.0% of a structuring compound;
   (d) from about 2.0% to about 20.0% a hydrophobic component; and
   (e) from about 60.0% to about 95.0% of a hydrophilic liquid carrier,
   wherein the emulsion has a pH of from about 6 to about 10.

10. The oil-in water emulsion of Claim 9, wherein the structuring compound comprises from about 1.0% to 5.0% of a fatty alcohol and from about 2.0% to about 6.0% of an amphiphilic surfactant.
INTERNATIONAL SEARCH REPORT

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 A61K7/48

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

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 A61K

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

Electronic database consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

<table>
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<th>Citation of document, with indication, where appropriate, of the relevant passages</th>
<th>Relevant to claim No.</th>
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<td>GB 2 259 014 A (FISCHER PHARMACEUTICALS LIMITED) 3 March 1993 (1993-03-03) cited in the application abstract; examples 19,12,19</td>
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<td>EP 0 669 126 A (L'OREAL) 30 August 1995 (1995-08-30) abstract; claim 1; examples 1,3</td>
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Further documents are listed in the continuation of box C.

Date of the actual completion of the international search

9 July 1999

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2 NL-2280 HV Rijswijk Tel: (+31-70) 340-3040, Tx: 31 651 apo nl, Fax: (+31-70) 340-3016

Date of mailing of the international search report

23/07/1999

Authorized officer

Alvarez Alvarez, C

Form PCT/ISA210 (second sheet) (July 1992)
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