

(19) World Intellectual Property Organization  
International Bureau



(43) International Publication Date  
12 July 2007 (12.07.2007)

PCT

(10) International Publication Number  
**WO 2007/077541 A2**

(51) International Patent Classification:  
A61K 8/49 (2006.01) A61K 31/47 (2006.01)  
A61Q 19/06 (2006.01)

(21) International Application Number:  
PCT/IB2007/050024

(22) International Filing Date: 4 January 2007 (04.01.2007)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:  
Fr 0600068 4 January 2006 (04.01.2006) FR

(71) Applicant (for all designated States except US): SE-  
DERMA; 29 rue du Chemin Vert, Boîte postale 33,  
F-78610 Le Perray en Yvelines Cedex (FR).

(72) Inventors; and

(75) Inventors/Applicants (for US only): LINTNER, Karl  
[FR/FR]; 2 rue du Manège, F-78120 Rambouillet (FR).  
MAS CHAMBERLIN, Claire [FR/FR]; Les Chardon-  
nettes, 5 rue de Dampierre, F-78460 Chevreuse (FR).  
MONDON, Philippe [FR/FR]; 16 rue Rémy Dumoncel,  
F-75014 Paris (FR).

(81) Designated States (unless otherwise indicated, for every  
kind of national protection available): AE, AG, AL, AM,  
AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN,  
CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI,  
GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS,  
JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS,  
LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY,  
MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS,  
RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN,  
TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

(84) Designated States (unless otherwise indicated, for every  
kind of regional protection available): ARIPO (BW, GH,  
GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM,  
ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM),  
European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI,  
FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT,  
RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA,  
GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:

— without international search report and to be republished  
upon receipt of that report

For two-letter codes and other abbreviations, refer to the "Guid-  
ance Notes on Codes and Abbreviations" appearing at the begin-  
ning of each regular issue of the PCT Gazette.

(54) Title: COSMETIC COMPOSITION COMPRISING GLAUCINE AND ITS USE

(57) Abstract: The present invention concerns the use of glaucine or a plant extract containing it, as an active ingredient, alone or in association with at least another active ingredient usually used in cosmetic or dermatopharmaceutical field, for the preparation of a cosmetic or dermatopharmaceutical composition with a topical use for skin, integuments, and/or mucosae. The present invention relates also to the use of glaucine or a plant extract containing it as an agent inducing adipocyte reversion, for the preparation of cosmetic or dermatopharmaceutical compositions.



WO 2007/077541 A2

## COSMETIC COMPOSITION COMPRISING GLAUCINE AND ITS USE

## DESCRIPTION

5

## TECHNICAL FIELD

The present invention relates to the field of cosmetics and personal care products.

## BACKGROUND ART

10 The present invention concerns the use, as an active agent, of glaucine or plant extracts containing it, and a composition containing at least one such active, for cosmetic, dermatopharmaceutical or pharmaceutical applications.

The present invention relates also to a cosmetic and/or dermatopharmaceutical composition to regulate the proportion of fat in adipocytes and/or to regulate adipocyte differentiation to *in fine* prevent and/or regulate the greasy installation.

15 The fat tissue, dominating tissue in the energy balance to mammals, is constituted by an extracellular matrix, by a dense capillary network and by specific cells: the adipocytes.

Its development is characterized by modifications of all components of the hypodermic tissue with repercussions at the level of the more superficial layers. So, we observe an increase of thickness at the level of the dermis, probably owed to a liquidien clogging and to an infiltration  
20 of fat lobules deforming the connection dermis/hypodermis. This adiposis manifests itself with a change of the figure and the appearance of "spare tires" and fat deposits, more or less unsightly with sometimes an aspect of "orange peel skin".

The weight development of the fat tissue, the direct reflection of the reserves of lipidic energy, in which participate numerous mechanisms, is notably a function of the increase of the size and  
25 of the number of adipocytes.

The mature adipocyte is equipped to constitute a body energy reserve, strictly controlled by multiple systems, in particular hormonal. This differentiated cell which lost its division's capacity can enlarge its faculty of stocking by increasing the quantity of stored fat in the form of triglycerides (lipogenesis) or conversely mobilize these fats stored via a mechanism leading  
30 to the liberation of acids fat and of glycerol and/or mono-, diesters of glycerol (lipolysis).

In normal conditions, there is equilibrium between lipogenesis and lipolysis in order to ensure the stability of the fat mass. If, for various reasons, an imbalance arises between these two mechanisms, triglycerides accumulate themselves in adipocytes.

35 Cells precursors of adipocytes (pre-adipocytes) present at the level of the fat tissue, can under the influence of different stimuli multiply and differentiate themselves to adipocytes throughout the life. We speak about adipocyte differentiation or conversion.

A pre-adipocyte in the active growth phase must escape the cell cycle. Arresting growth is necessary in order for the cell to initiate the process of conversion to an adipocyte. Between the arrest of growth and the start of differentiation into an adipocyte, only a single and unique supplementary division occurs. This is known as “clonal expansion” and increases the pool of differentiation-competent pre-adipocytes.

This adipocyte differentiation is mainly characterized by a morphological modification of precursor cells, a phenotypic change, and the appearance of the specific markers of adipocyte. The genes most activated at the initiation of differentiation are C/EBP $\beta$  and  $\delta$  first, then CEBP $\alpha$  accompanied by PPAR $\gamma$  (transcription factors). During that early phase, the cell changes from an elongated fibroblastic shape to a spheroidal conformation and numerous associated changes affect the cytoskeletal proteins and the components of the extracellular matrix. It is known since some years that the morphotypic change is independent from the formation of lipid droplets because pre-adipocytes 3T3-L1 can maintain this new spheroidal conformation even if triglyceride synthesis is inhibited or if exposed to lipolytics.

Finally, during the terminal phase of differentiation, lipogenesis is strongly activated and all the enzymes involved in the formation of triglycerides increase: acetyl-CoA, glycerol-3-phosphate dehydrogenase (G3PDH), fatty acid synthase (FAS). The expression of receptors then begins: insulin-specific receptors, adrenergic receptors and, lastly, specialized proteins such as perilipin and vimentin (formation of lipid droplets) and secretion of agents promoting the development of fat mass (monobutylin, angiogenic factors, angiotensinogen II).

Among antiadipogenic compounds, we can quote TNF $\alpha$  described in literature as a differentiation inhibitor for human, rat and mouse adipocytes.

The first examples of that effect were reported by TORTI in 1989 [Torti et al., 1989, Modulation of adipocyte differentiation by TNF $\alpha$  and TGF $\beta$ , J Cell Biol, 108, p1105-1113]. The latter showed that, in the presence of TNF $\alpha$ , adipocytes lose the activity of the enzymes involved in lipid metabolism and display a reduction in lipid-droplet content.

In addition, the cells lose their adipocyte spheroidal morphology and return to a morphology closer to that of the pre-adipocyte, i.e. elongated with cytoplasmic extensions. The more recent studies by XING [Xing et al., 1997, TNF $\alpha$ -Mediated Inhibition and Reversal of adipocyte differentiation is accompanied by suppressed expression of PPAR $\gamma$  without effect on Pref-1 Expression., Endocrinology, 138, p2776-2783] showed that the adipocyte reversion occurred very fast, in a few hours and was associated with events affecting DNA transcription inactivation and that a marked decrease in PPAR $\gamma$  may be obtained in both the early and late phase of differentiation with, as a consequence, reduced expression of specific adipocyte genes.

Obesity is increasing constantly in developed countries and is a major concern for our public health institutes. In addition, each individual aspires to maintaining a youthful self-image and attributes increasing importance to his/her figure and skin quality. An external sign of good health, a well-defined figure without localized excesses of fat or steatomery is everyone's secret hope.

To answer to this expectancy, various slimming compositions targeted to the mature adipocytes and favoring the lipolysis and/or inhibiting the lipogenesis are on the market of cosmetics. We can notably quote the use of actives based on a direct activation of the lipolysis via the inhibition of the phosphodiesterase (as the caffeine), of cholesterol-like molecules and their capacity to inhibit the storage of the lipidic biochemical material in fatty tissue (FR 98 14753 SEDERMA), of diterpene (FR 2855057 SEDERMA).

There is still a need of identification of molecules adapted to a cosmetic use capable not only of inhibiting the expansion of the fat tissue, but also of regulating its installation.

We discovered in an unexpected way that glaucine possessed not only antilipogenic properties but also antiadipogenic properties. Indeed, our researches allowed us to highlight the fact that the glaucine was on the one hand capable of inhibiting the lipogenesis and favoring the lipolysis, and on the other hand that it had an opposing effect on the adipocyte differentiation and that it favored the reversion of the adipocyte morphotype.

Glaucine is an alkaloid known for its antithrombotic, analgesic and anti-inflammatory properties. With its bronchodilatator activity, this molecule is often used in pharmacology as antitussive.

The invention proposes a solution for a localized loss of weight based on :

- a control of the mechanisms of lipolysis/lipogenesis of adipocytes,
- an upstream control of the renewal of adipocytes by means of a decrease and/or an inhibition of the differentiation of preadipocytes to mature adipocytes,
- and the replacement of the fat tissue by mesenchymatous tissue to decrease *in fine* the thickness of the hypodermis and/or prevent its thickening and firm up the skin.

Thus, the principal object of the present invention consists of a use of glaucine or a plant extract containing it, as an active ingredient, alone or in association with at least another active usually used in the cosmetic or dermopharmaceutical field, for the preparation of a cosmetic or dermopharmaceutical composition with a topical use for skin, integuments, and/or mucosas.

According to a second embodiment of the invention, glaucine is intended to control the renewal and/or the number of adipocytes within the fat tissue.

5 According to a third embodiment, the invention concerns a cosmetic method intended to decrease expansion an/or prevent the installation of fat tissue within hypoderma, a cosmetic method intended to prevent and/or fight against cellulite or the orange peel skin and/or to refine the figure or the contours of the face and/or to fight against fat deposits and the “spare tires” and/or to decrease water retention in the fat deposits, and a cosmetic method to firm up the skin, and/or to stimulate the smoothing of the skin and/or to stretch out the skin.

10 We saw previously that the increase of the number of adipocytes, important element in the development of the fat tissue, is function of the adipocyte differentiation and reversion.

One of embodiment of the present invention is therefore to propose the use of glaucine or a plant extract containing it, for the preparation of a cosmetic or dermopharmaceutical composition, wherein said glaucine or said composition are intended to inhibit the formation of mature adipocytes.

15 According to another embodiment, the invention relates to the use of glaucine or a plant extract containing it, for the preparation of a cosmetic or dermopharmaceutical composition, glaucine or said composition being intended to stimulate the adipocyte reversion.

20 Within the framework of the present invention, « adipocyte maturation », « adipocyte conversion », « adipocyte transformation » or « adipocyte differentiation » as used herein, means formation of mature adipocytes from adipocytes precursor cells (such as preadipocyte or fibroblasts).

We shall use without distinction the terms «inhibitory effect on the adipocytes’formation” and «antiadipogenic effect”.

25 In the same way, within the framework of the present invention, the term “adipocyte reversion”, as used herein, means the involution of the morphotype of mature adipocytes towards a morphotype of adipocytes precursor cells (preadipocytes or fibroblasts).

30 Still according to another embodiment, the invention concerns the use of glaucine or a plant extract containing it, for the preparation of a cosmetic or dermopharmaceutical composition, wherein said glaucine or said composition are intended to regulate the fat proportion in the adipocytes.

The term “regulation of the proportion of fat in the adipocytes” means a modification of the balance between the mechanism of lipolysis and lipogenesis within the adipocytes, and more particularly a stimulation of the lipolysis and/or inhibition of the lipogenesis.

35 Another embodiment is the use of glaucine or a plant extract containing it for the preparation of a cosmetic or dermopharmaceutical composition, glaucine or said composition being

intended to decrease the thickness of the fat tissue within the hypoderma and/or to prevent its filling out.

Glaucine is also used to stimulate the decompression of vessels, microcirculation, blood drainage, densification of tissues, in order to prevent oedema.

5 Within the framework of the present invention, the term "glaucine" means its optical isomers, stereoisomers, enantiomers, diastereoisomers, tautomerics, under their free form, or under the form of a salt with an acid physiologically acceptable.

To obtain the effects described in this patent, glaucine usable in the cosmetic and dermopharmaceutical compositions, can be obtained from any source of supply, in particular  
10 by chemical hemisynthesis, chemical synthesis, enzymatic, by one of many methodologies of biotechnology, by plant extraction or any other means usable allowing its supply at reasonable costs in the finished product in order to be used industrially. In the case of obtention through vegetable origin, it is obvious that any plant species can be appropriate provided that the extract, from an unspecified part of the plant, contains glaucine.

15 As non-restricted examples, we can quote the extracts of d' *Annonaceae* (*Alphonsea* ; *Annona*, *Polyalthia*, *Schefferomitra*, *Uvaria*), *Berberidaceae* (*Berberis*, *Mahonia*), *Euphorbiaceae* (*Croton*), *Fumariaceae* (*Corydalis*, *Dicentra*), *Lauraceae* (*Beilshmedia*, *Ocotea*, *Litsea*), *Magnoliaceae* (*Liriodendron*, *Magnolia*), *Menispermaceae* (*Chasmanthera*), *Papaveraceae* (*Glaucium*, *Papaver*), *Ranunculaceae* (*Thalictrum*, *Aconitum*), *Rhamnaceae* (*Colubrina*),  
20 *Monimiaceae* (*Hedycaria*), *Poaceae*, *Hordeum vulgare*L., *Mahonia repens*, *Annona squamosa* L., *Eschscholzia californica* subsp. *Californica*.

The plant extraction can be realized through the usual technics, for example by phenolic extraction, from any part of the plant such as the seed, the fruit, the root, the tuber, the leaf, the pericarpe and preferably the rhizome. Extraction solvents can be chosen among water,  
25 propylene glycol, butylene glycol, glycerin, PEG-6 Caprylic/capric glycerides, polyethylene glycol, methylic and/or ethylic diglycol ethers, cyclic polyols, ethoxylated or propoxylated diglycols, alcohols (methanol, ethanol, propanol, butanol), or any mixture of those solvents. In addition, it is possible to make vegetable extracts of the present invention through other methods such as, for example, steeping, simple decoction, lixiviation, extraction under reflux,  
30 supercritical extraction, extraction with ultrasounds or micro-waves or finally with countercurrent technology, without this list being restrictive.

The amount of glaucine present in the composition according to the invention can vary on a big range, and will be preferably from about 0.00001% w/w to about 50% w/w, preferably from about 0.0001 % w/w to 2% w/w, and more preferably about 0,001% to 10% by weight of the  
35 composition.

All the percentages and the ratios used herein are by weight of the total composition and all the measures are made for 25 °C unless it is otherwise clarified.

It is known that it is possible to integrate in the composition of the present invention, products already known as presenting an activity in the slimming field.

5 Thus, according to a particular embodiment, the composition of the present invention can also contain at least one complementary active chosen among the lypolitic active ingredients and/or active ingredients inhibiting the lipogenesis, active ingredients draining or active ingredients acting on the microcirculation, slimming active ingredients, firming up active ingredients, and/or anti-glycan active ingredients, such as caffeine, holy box, Ruscus, Indian chestnut,  
10 Ginkgo bilboa, red vine.

In a known way, it is also possible to integrate in the composition of the present invention, products already known as presenting an activity in the field of anti-age. So, according to a particular embodiment, the composition of the present invention can contain at least one additional agent chosen among vitamins, phytosterols, flavonoids, DHEA or  
15 dehydroepiandrosterone and/or a chemical or biological precursor, a metalloproteinase inhibitor.

The present invention will be better understood from the following description. The terms "having" and "including" are to be construed as open-ended unless the context suggests otherwise.

20 The compositions of the present invention can comprise or consist essentially of the components of the present invention as well as other ingredients 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. Preferably, such additives will  
25 not be present at all or only in trace amounts.

"Adjuvants", "additives", and "optional components" are used synonymously with "additional ingredients". "Skin care actives", "actives" are used synonymously with "actives ingredients".

The term "dermatologically acceptable carrier" (without being restrictive) means an aqueous or hydroalcoholic solution, a water in oil emulsion, an oil in water emulsion, a microemulsion, an  
30 aqueous gel, an anhydrous gel, a serum or a vesicle dispersion.

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

The term "topical application" is used in the sense in which it is generally and widely used in  
35 the art of developing, testing and marketing cosmetic and personal care products.

The term "cosmetic composition" or more briefly just "composition" in accordance with the present invention relates to a formulation that can be used for cosmetic purposes, purposes of hygiene or as a basis for delivery of one or more dermatopharmaceutical ingredients. This includes cosmetics, personal care products and pharmaceutical preparations. It is also possible that these formulations are used for two or more of these same purposes at one time. A medicated dandruff shampoo, for example, has pharmacological properties and is used as a personal care product to provide clean hair.

Certain compositions of the present invention may also provide additional benefits, including stability, absence of significant (consumer-unacceptable) skin irritation, anti-inflammatory activity and good aesthetics.

In the cosmetic and dermatopharmaceutical compositions, it can be advantageous to associate glaucine, object of the present invention, with at least one additional ingredient selected from the group comprising

#### **I. Additives**

According to the invention, the dermatologically acceptable carrier can be an aqueous or hydroalcoholic solution, a water in oil emulsion, an oil in water emulsion, a microemulsion, an aqueous gel, an anhydrous gel, a serum or a vesicle dispersion.

The compositions of the invention may include various other and additional ingredients, which may be active, functional, conventionally used in cosmetic, personal care or topical/transdermal pharmaceutical products or otherwise. Of course, a decision to include an additional ingredient and the choice of specific additional ingredients depends on the specific application and product formulation. Also, the line of demarcation between an "active" ingredient and an "inactive ingredient" is artificial and dependent on the specific application and product type. A substance that is an "active" ingredient in one application or product may be a "functional" ingredient in another, and vice versa.

Thus, the compositions of the invention may include at least one skin care active. As used herein, "skin care actives" are additional ingredients, which provide some benefit to the object of the composition. Such additional ingredients may include one or more substances such as, without limitations, cleaning agents, hair conditioning agents, skin conditioning agents, hair styling agents, antidandruff agents, hair growth promoters, perfumes, sunscreen and/or sunblock compounds, pigments, moisturizers, film formers, hair colors, make-up agents, detergents, pharmaceuticals, thickening agents, emulsifiers, humectants, emollients, antiseptic agents, deodorant actives, dermatologically acceptable carriers and surfactants.

In any embodiment of the present invention, however, the actives useful herein can be categorized by the benefit they provide or by their postulated mode of action. However, it is to be understood that the actives useful herein can in some instances provide more than one



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 the active to that particular application or applications listed.

5 In a preferred embodiment, where the composition is to be in contact with human keratinous tissue, the additional ingredients should be suitable for application to keratinous tissue, that is, when incorporated into the composition they are suitable for use in contact with human keratinous tissue (hair, nails, skin, lips) without undue toxicity, incompatibility, instability, allergic response, and the like within the scope of sound medical judgment.

10 The CTFA Cosmetic Ingredient Handbook, Tenth Edition (published by the Cosmetic, Toiletry, and Fragrance Association, Inc., Washington, D.C.) (2004) describes a wide variety of nonlimiting materials that can be added to the composition herein. Examples of actives which may be added, include, but are not limited to: skin soothing and healing agents, skin anti-aging agents, skin moisturizing agents, anti-wrinkle agents, anti-atrophy agents, skin smoothing agents, antibacterial agents, antifungal agents, pesticides, anti parasitic agents, antimicrobial agents, anti-inflammatory agents, anti-pruriginous agents, external anaesthetic agents, antiviral agents, keratolytic agents, free radicals scavengers, antiseborrheic agents, antidandruff agents, the agents modulating the differentiation, proliferation or pigmentation of the skin and agents accelerating penetration, desquamating agents, depigmenting or propigmenting agents, antiglycation agents, tightening agents, agents stimulating the synthesis of dermal or epidermal macromolecules and/or preventing their degradation; agents stimulating the proliferation of fibroblasts and/or keratinocytes or stimulating the differentiation of keratinocytes; muscle relaxants; antipollution and/or anti-free radical agents; slimming agents, anticellulite agents, agents acting on the microcirculation; agents acting on the energy metabolism of the cells; cleaning agents, hair conditioning agents, hair styling agents, hair growth promoters, sunscreen and/or sunblock compounds, make-up agents, detergents, pharmaceutical drugs, emulsifiers, emollients, antiseptic agents, deodorant actives, dermatologically acceptable carriers, surfactants, abrasives, absorbents, aesthetic components such as fragrances, colorings/colorants, essential oils, skin sensates, cosmetic astringents, anti-acne agents, anti-caking agents, anti foaming agents, antioxidants, binders, biological additives, enzymes, enzymatic inhibitors, enzyme-inducing agents, coenzymes, plant extracts, plant derivatives, plant tissue extracts, plant seed extracts, plant oils, botanicals, botanical extracts, ceramides, peptides, buffering agents, bulking agents, chelating agents, chemical additives, colorants, cosmetic biocides, denaturants, drug astringents, external analgesics, film formers or materials, e.g., polymers, for aiding the film-forming properties and substantivity of the composition, quaternary derivatives, agents increasing the substantivity, opacifying agents, pH adjusters, pH regulator (e.g. triethanolamine), propellants, reducing agents, sequestrants, skin bleaching and

15  
20  
25  
30  
35

lightening agents, skin tanning agents, skin-conditioning agents (e.g., humectants, including miscellaneous and occlusive), skin soothing and/or healing agents and derivatives, skin treating agents, thickeners, lipid thickener (e.g. stearic acid), vitamins and derivatives thereof, peeling agents, moisturizing agents, curative agents, lignans, preservatives (e.g. phoxyethanol and parabens), UV absorbers, a cytotoxic, an anti-neoplastic agent, a fat-soluble active, suspending agents, viscosity modifiers, dyes, non-volatile solvents, diluents, pearlescent aids, foam boosters, a vaccine, a water-soluble sunscreen, antiperspirant, depilatory, perfumed water, fat soluble sunscreens substance intended to improve the state of dry or aged skin, skin restructuring agent (e.g. *Siegesbeckia orientalis* extract), emollient ( e.g. C12-15 alkyl benzoate), excipients, fillers, minerals, anti-mycobacterial agents, anti-allergenic agents, H1 or H2 antihistamines, anti-irritants, immune system boosting agents, immune system suppressing agents, insect repellents, lubricants, staining agents, hypopigmenting agents, preservatives, photostabilizing agents and their mixture.

Said additional ingredient is selected from the group consisting of sugar amines, glucosamine, D-glucosamine, N-acetyl glucosamine, N-acetyl-D-glucosamine, mannosamine, N-acetyl mannosamine, galactosamine, N-acetyl galactosamine, vitamin B3 and its derivatives, niacinamide, sodium dehydroacetate, dehydroacetic acid and its salts, phytosterols, salicylic acid compounds, hexamidines, dialkanoyl hydroxyproline compounds, soy extracts and derivatives, equol, isoflavones, flavonoids, phytantriol, farnesol, geraniol, peptides and their derivatives, di-, tri-, tetra-, penta-, and hexapeptides and their derivatives, lys-thr-thr-lys-ser, palmitoyl-lys-thr-thr-lys-ser, carnosine, N-acyl amino acid compounds, retinoids, retinyl propionate, retinol, retinyl palmitate, retinyl acetate, retinal, retinoic acid, water-soluble vitamins, ascorbates, vitamin C, ascorbic acid, ascorbyl glucoside, ascorbyl palmitate, magnesium ascorbyl phosphate, sodium ascorbyl phosphate, vitamins their salts and derivatives, provitamins and their salts and derivatives, ethyl panthenol, vitamin B, vitamin B derivatives, vitamin B1, vitamin B2, vitamin B6, vitamin B12, vitamin K, vitamin K derivatives, pantothenic acid and its derivatives, pantothenyl ethyl ether, panthenol and its derivatives, dexpanthenol, ethyl panthenol, biotin, amino acids and their salts and derivatives, water soluble amino acids, asparagine, alanine, indole, glutamic acid, water insoluble vitamins, vitamin A, vitamin E, vitamin F, vitamin D, mono-,di-, and tri-terpenoids, beta-ionol, cedrol, and their derivatives, water insoluble amino acids, tyrosine, tryptamine, butylated hydroxytoluene, butylated hydroxyanisole, allantoin, tocopherol nicotinate, tocopherol, tocopherol esters, palmitoyl-gly-his-lys, phytosterol, hydroxy acids, glycolic acid, lactic acid, lactobionic acid, keto acids, pyruvic acid, phytic acid, lysophosphatidic acid, stilbenes, cinnamates, resveratrol, kinetin, zeatin, dimethylaminoethanol, natural peptides, soy peptides, salts of sugar acids, Mn gluconate, Zn gluconate, particulate materials, pigment materials, natural colors, piroctone olamine, 3,4,4'- trichlorocarbanilide, triclocarban, zinc pyrithione,

hydroquinone, kojic acid, ascorbic acid, magnesium ascorbyl phosphate, ascorbyl glucoside, pyridoxine, aloe vera, terpene alcohols, allantoin, bisabolol, dipotassium glycyrrhizinate, glycerol acid, sorbitol acid, pentaerythritol acid, pyrrolidone acid and its salts, dihydroxyacetone, erythulose, glyceraldehyde, tartaraldehyde, clove oil, menthol, camphor, eucalyptus oil, eugenol, menthyl lactate, witch hazel distillate, eicosene and vinyl pyrrolidone copolymers, iodopropyl butylcarbamate, a polysaccharide, an essential fatty acid, salicylate, glycyrrhetic acid, carotenoids, ceramides and pseudo-ceramides, a lipid complex, oils in general of natural origin such as Shea butter, apricot oil, onagre oil, prunus oil, palm oil, monoi oil, HEPES; procysteine; O-octanoyl-6-D-maltose; the disodium salt of methylglycinediacetic acid, steroids such as diosgenin and derivatives of DHEA; N-ethyloxycarbonyl-4-para-aminophenol, bilberry extracts; phytohormones; extracts of the yeast *Saccharomyces cerevisiae*; extracts of algae; extracts of soybean, lupin, maize and/or pea; alverine and its salts, in particular alverine citrate, extract of butcher's broom and of horse chestnut, and mixtures thereof, without this list being limiting.

Further skin care and hair care active ingredients that are particularly useful in combination with the polypeptides can be found in SEDERMA commercial literature and on the website [www.sederma.fr](http://www.sederma.fr) (herewith incorporated in its entirety).

In any embodiment of the present invention, however, the additional ingredients useful herein can be categorized by the benefit they provide or by their postulated mode of action. However, it is to be understood that the additional ingredients useful herein can in some instances provide more than one 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 the additional ingredients to that particular application or applications listed.

1. Sugar Amines (Amino Sugars)

The compositions of the present invention can comprise a sugar amine, which is also known as amino sugar. Sugar amine compounds useful in the present invention can include those described in PCT Publication WO 02/076423 and US Patent No. 6,159,485.

In one embodiment, the composition comprises from about 0.01% to about 15%, more preferably from about 0.1% to about 10%, and even more preferably from about 0.5% to about 5% by weight of the composition, of sugar amine.

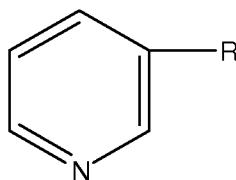
Sugar amines can be synthetic or natural in origin and can be used as pure compounds or mixtures of compounds (e.g., extracts from natural sources or mixtures of synthetic materials). For example, glucosamine is generally found in many shellfish and can also be derived from fungal sources. As used herein, "sugar amine" includes isomers and tautomers of such and its salts (e.g., HCl salt) and is commercially available from Sigma Chemical Co.

Examples of sugar amines that are useful herein include glucosamine, N-acetyl glucosamine, mannosamine, N-acetyl mannosamine, galactosamine, N-acetyl galactosamine, their isomers (e.g., stereoisomers), and their salts (e.g., HCl salt). Preferred for use herein are glucosamine, particularly D-glucosamine and N-acetyl glucosamine, particularly N-acetyl-D-glucosamine.

5           2.           Vitamin B3 Compounds

The compositions of the present invention can include a vitamin B3 compound. Vitamin B3 compounds are particularly useful for regulating skin conditions, as described in U.S. Patent No. 5,939,082. In one embodiment, the composition comprises from about 0.001% to about 50%, more preferably from about 0.01% to about 20%, even more preferably from about 10  
10           0.05% to about 10%, and still more preferably from about 0.1% to about 7%, even more preferably from about 0.5% to about 5%, by weight of the composition, of the vitamin B3 compound.

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



wherein R is - CONH<sub>2</sub> (i.e., niacinamide), - COOH (i.e., nicotinic acid) or - CH<sub>2</sub>OH (i.e., 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 (e.g, tocopherol nicotinate, myristyl  
20           nicotinate), 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 C<sub>1</sub>-C<sub>22</sub>, preferably C<sub>1</sub>-C<sub>16</sub>, more preferably C<sub>1</sub>-C<sub>6</sub> alcohols. Non-vasodilating esters of nicotinic acid include tocopherol nicotinate and inositol hexanicotinate; tocopherol nicotinate is preferred.

25           Other derivatives of the vitamin B3 compound are derivatives of niacinamide resulting from substitution of one or more hydrogens of the amide group. Specific examples of such derivatives include nicotinuric acid (C<sub>8</sub>H<sub>8</sub>N<sub>2</sub>O<sub>3</sub>) and nicotinyl hydroxamic acid (C<sub>6</sub>H<sub>6</sub>N<sub>2</sub>O<sub>2</sub>).

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  
30           examples of vitamin B3 compounds useful herein are 2-chloronicotinamide, 6-aminonicotinamide, 6-methylnicotinamide, n-methyl-nicotinamide, n,n-diethylnicotinamide, n-(hydroxymethyl)-nicotinamide, quinolinic acid imide, nicotinilide, n-benzylnicotinamide, n-

ethylnicotinamide, nifedazone, nicotinaldehyde, isonicotinic acid, methyl isonicotinic acid, thionicotinamide, nialamide, 1-(3-pyridylmethyl) urea, 2-mercaptonicotinic acid, nicomol, and niaprazine.

5 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; ICN Biomedicals, Inc. and Aldrich Chemical Company .

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

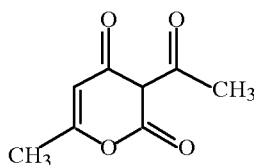
10 When used, salts, derivatives, and salt derivatives of niacinamide are preferably those having substantially the same efficacy as niacinamide.

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, 15 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 («The Reaction of L-Ascorbic and D-Iosascorbic Acid with Nicotinic Acid and Its Amide", J. Organic Chemistry, Vol. 14, 22-26 (1949)).

20 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.

### 3. Dehydroacetic Acid (DHA)

The composition of this invention can include dehydroacetic acid, having the structure:



25

or pharmaceutically acceptable salts, derivatives or tautomers thereof. The technical name for dehydroacetic acid is 3Acetyl-6-methyl-2H-pyran-2,4(3H)-dione and can be commercially purchased from Lonza.

30 Pharmaceutically acceptable salts include alkali metal salts, such as sodium and potassium; alkaline earth metal salts, such as calcium and magnesium; non-toxic heavy metal salts; ammonium salts; and trialkylammonium salts, such as trimethylammonium and triethylammonium. Sodium, potassium, and ammonium salts of dehydroacetic acid are

5 preferred. Highly preferred is sodium dehydroacetate which can be purchased from Tri-K, as Tristat SDHA. Derivatives of dehydroacetic acid include, but are not limited to, any compounds wherein the CH<sub>3</sub> groups are individually or in combination replaced by amides, esters, amino groups, alkyls, and alcohol esters. Tautomers of dehydroacetic acid can be described as having the chemical formula C<sub>8</sub>H<sub>8</sub>O<sub>4</sub> and generally having the structure above.

10 In one embodiment, the compositions of the present invention can comprise from about 0.001% to about 25% by weight of the composition, preferably from about 0.01% to about 10%, more preferably from about 0.05% to about 5%, and even more preferably from about 0.1% to about 1%, of dehydroacetic acid or pharmaceutically acceptable salts, derivatives or tautomers thereof.

#### 4. Phytosterol

15 The compositions of the present invention can comprise a phytosterol. For example, one or more phytosterols can be selected from the group consisting of  $\beta$ -sitosterol, campesterol, brassicasterol,  $\Delta^5$ -avenasterol, lupenol,  $\alpha$ -spinasterol, stigmasterol, their derivatives, analogs, and combinations thereof. More preferably, the phytosterol is selected from the group consisting of  $\beta$ -sitosterol, campesterol, brassicasterol, stigmasterol, their derivatives, and combinations thereof. More preferably, the phytosterol is stigmasterol.

20 Phytosterols can be synthetic or natural in origin and can be used as essentially pure compounds or mixtures of compounds (e.g., extracts from natural sources). Phytosterols are generally found in the unsaponifiable portion of vegetable oils and fats and are available as free sterols, acetylated derivatives, sterol esters, ethoxylated or glycosidic derivatives. More preferably, the phytosterols are free sterols. As used herein, "phytosterol" includes isomers and tautomers of such and is commercially available from Aldrich Chemical Company, Sigma Chemical Company and Cognis.

25 In one embodiment, the composition of the present invention comprises from about 0.0001% to about 25%, more preferably from about 0.001% to about 15%, even more preferably from about 0.01% to about 10%, still more preferably from about 0.1% to about 5%, and even more preferably from about 0.2% to about 2% of phytosterol, by weight of the composition.

#### 5. Salicylic Acid Compound

30 The compositions of the present invention may comprise a salicylic acid compound, its esters, its salts, or combinations thereof. In one embodiment of the compositions of the present invention, the composition preferably comprises from about 0.0001% to about 25%, more preferably from about 0.001% to about 15%, even more preferably from about 0.01% to about 10%, still more preferably from about 0.1% to about 5%, and even more preferably from about 0.2% to about 2%, by weight of the composition, of salicylic acid compound.

35

6. Hexamidine

The compositions of the present invention can include hexamidine compounds, its salts, and derivatives.

5 In one embodiment, the composition comprises from about 0.0001% to about 25%, more preferably from about 0.001% to about 10%, more preferably from about 0.01% to about 5%, and even more preferably from about 0.02% to about 2.5% of hexamidine by weight of the composition.

10 As used herein, hexamidine derivatives include any isomers and tautomers of hexamidine compounds including but not limited to organic acids and mineral acids, for example sulfonic acid, carboxylic acid, etc. Preferably, the hexamidine compounds include hexamidine diisethionate, commercially available as Eleastab® HP100 from Laboratoires Serobiologiques.

7. Dialkanoyl Hydroxyproline Compounds

The compositions of the present invention can comprise one or more dialkanoyl hydroxyproline compounds and their salts and derivatives.

15 In one embodiment, the dialkanoyl hydroxyproline compounds are preferably added to the composition from about 0.01% to about 10%, more preferably from about 0.1% to about 5%, even more preferably from about 0.1% to about 2% by weight of the composition

20 Suitable derivatives include but are not limited to esters, for example fatty esters, including, but not limited to tripalmitoyl hydroxyproline and dipalmitoyl acetyl hydroxyproline. A particularly useful compound is dipalmitoyl hydroxyproline. As used herein, dipalmitoyl hydroxyproline includes any isomers and tautomers of such and is commercially available under the tradename Sepilift DPHP® from Seppic, Inc. Further discussion of dipalmitoyl hydroxyproline appears in PCT Publication WO 93/23028. Preferably, the dipalmitoyl hydroxyproline is the triethanolamine salt of dipalmitoyl hydroxyproline.

25 8. Flavonoids

The compositions of the present invention can comprise a flavonoid compound. Flavonoids are broadly disclosed in U.S. Patents 5,686,082 and 5,686,367. As used herein, "flavonoid" means unsubstituted flavonoid or substituted flavonoid (i.e. mono-substituted flavonoid, or/and di-substituted flavonoid, or/and tri-substituted flavonoid). Examples of flavonoids particularly  
30 suitable for use in the present invention are one or more flavones, one or more flavanones, one or more isoflavones, one or more coumarins, one or more chromones, one or more dicoumarols, one or more chromanones, one or more chromanols, isomers (e.g., cis/trans isomers) thereof, and mixtures thereof.

35 Preferred for use herein are flavones and isoflavones, in particular daidzein (7,4'-dihydroxy isoflavone), genistein (5,7,4'-trihydroxy isoflavone), equol (7,4'-dihydroxy isoflavan), 5,7-

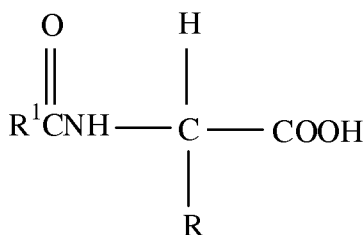
dihydroxy-4'-methoxy isoflavone, soy isoflavones (a mixture extracted from soy) and other plant sources of such mixtures (e.g., red clover), and mixtures thereof. Also preferred are flavanones such as hesperitin, hesperidin, and mixtures thereof.

5 Flavonoid compounds useful herein are commercially available from a number of sources, e.g., Indofine Chemical Company, Inc., Steraloids, Inc., and Aldrich Chemical Company, Inc. Suitable flavonoids are commercially available called Sterocare® offered by SEDERMA and described in WO 99/18927.

10 In one embodiment, the herein described flavonoid compounds may be added from about 0.01% to about 20%, more preferably from about 0.1% to about 10%, and even more preferably from about 0.5% to about 5%, by weight of the composition.

9. N-acyl Amino Acid Compound

The topical compositions of the present invention can comprise one or more N-acyl amino acid compounds. The amino acid can be one of any of the amino acids known in the art. The N-acyl amino acid compounds of the present invention can correspond to the formula:



15

wherein R can be a hydrogen, alkyl (substituted or unsubstituted, branched or straight chain), or a combination of alkyl and aromatic groups.

20 Preferably, the N-acyl amino acid compound is selected from the group comprising N-acyl Phenylalanine, N-acyl Tyrosine, their isomers, their salts, and derivatives thereof. The amino acid can be the D or L isomer or a mixture thereof

Among the broad class of N-acyl Phenylalanine derivatives, particularly useful is N-undecylenoyl-L-phenylalanine commercially available under the tradename Sepiwhite® from SEPPIC.

25 In one embodiment, the present invention preferably comprises from about 0.0001% to about 25%, more preferably from about 0.001% to about 10%, more preferably from about 0.01% to about 5%, and even more preferably from about 0.02% to about 2.5% of the N-acyl amino acid by weight of the composition.

10. Retinoid

30 The compositions of this invention can comprise a retinoid, preferably in a safe and effective amount such that the resultant composition is safe and effective for regulating keratinous tissue



condition, preferably for regulating visible and/or tactile discontinuities in keratinous tissue (e.g., regulating signs of skin aging). The compositions can comprise from about 0.001% to about 10%, more preferably from about 0.005% to about 2%, even more preferably from about 0.01% to about 1%, still more preferably from about 0.01% to about 0.5%, by weight of the composition, of the retinoid. The optimum concentration used in a composition will depend on the specific retinoid selected since their potency can vary considerably.

As used herein, "retinoid" includes all natural and/or synthetic analogs of Vitamin A or retinol-like compounds which possess the biological activity of Vitamin A in the skin as well as the geometric isomers and stereoisomers of these compounds. The retinoid is preferably selected from retinol, retinol esters (e.g., C2-C22 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), or mixtures thereof. More preferably the retinoid is a retinoid other than retinoic acid. These compounds are well known in the art and are commercially available from a number of sources, e.g., Sigma Chemical Company, and Boehringer Mannheim. Other retinoids which are useful herein are described in U.S. Patent Nos. 4,677,120, U.S. Patent No 4,885,311, U.S. Patent No 5,049,584, U.S. Patent No 5,124,356, and Reissue 34,075. Other suitable retinoids can include tocopheryl-retinoate [tocopherol ester of retinoic acid (trans- or cis-), adapalene {6-[3-(1-adamantyl)-4-methoxyphenyl]-2-naphthoic acid}, and tazarotene (ethyl 6-[2-(4,4-dimethylthiochroman-6-yl)-ethynyl]nicotinate). Preferred retinoids include retinol, retinyl palmitate, retinyl acetate, retinyl propionate, retinal and combinations thereof. More preferred is retinyl propionate, used most preferably from about 0.1% to about 0.3%.

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.

#### 11. Optional Peptide

The composition of the present invention can comprise an additional peptide. Suitable peptides can include, but are not limited to, di-, tri-, tetra-, penta-, and hexa- peptides and derivatives thereof. In one embodiment, the composition comprises from about  $1 \times 10^{-7}\%$  to about 20%, more preferably from about  $1 \times 10^{-6}\%$  to about 10%, even more preferably from about  $1 \times 10^{-5}\%$  to about 5%, by weight of additional peptide.

As used herein, "additional peptide" refers to peptides containing ten or fewer amino acids and their derivatives, isomers, and complexes with other species such as metal ions (e.g., copper, zinc, manganese, magnesium, and the like). As used herein, peptide refers to both naturally occurring and synthesized peptides. Also useful herein are naturally occurring and commercially available compositions that contain peptides.

Suitable additional dipeptides for use herein include but are not limited to Carnosine (beta-Ala-His), Tyr-Arg, Val-Trp (WO 0164178), Asn-Phe, Asp-Phe. Suitable additional tripeptides for use herein include, but are not limited to Arg-Lys-Arg (Peptide CK), His-Gly-Gly, Gly-His-Lys, Gly-Gly-His, Gly-His-Gly, Lys-Phe-Lys. Suitable additional tetrapeptides for use herein include but are not limited to, Peptide E, Arg-Ser-Arg-Lys, Gly-Gln-Pro-Arg. Suitable additional pentapeptides include, but are not limited to Lys-Thr-Thr-Lys-Ser. Suitable hexapeptides include but are not limited to Val-Gly-Val-Ala-Pro-Gly and such as those disclosed in Fr 2854897 and Us 2004/0120918.

Other suitable additional peptides for use herein include, but are not limited to lipophilic derivatives of peptides, preferably palmitoyl derivatives, and metal complexes of the aforementioned (e.g., copper complex of the tripeptide His-Gly-Gly). Preferred additional dipeptide derivatives include N-Palmitoyl-beta-Ala-His, N-Acetyl-Tyr-Arg-hexadecylester (CALMOSENSINE™ from SEDERMA, France, WO 9807744, Us 6,372,717). Preferred additional tripeptide derivatives include N-Palmitoyl-Gly-Lys-His, (Pal-GKH from SEDERMA, France, WO 0040611), a copper derivative of His-Gly-Gly sold commercially as lamin, from Sigma, lipospondin (N-Elaidoyl-Lys-Phe-Lys) and its analogs of conservative substitution, N-Acetyl-Arg-Lys-Arg-NH<sub>2</sub> (Peptide CK+), N-Biot-Gly-His-Lys (N-Biot-GHK from SEDERMA, WO 0058347) and derivatives thereof. Suitable additional tetrapeptide derivatives for use herein include, but are not limited to N-palmitoyl-Gly-Gln-Pro-Arg (from SEDERMA, France), suitable additional pentapeptide derivatives for use herein include, but are not limited to N-Palmitoyl-Lys-Thr-Thr-Lys-Ser (available as MATRIXYL™ from SEDERMA, France, WO 0015188 and Us 6,620, 419) N-Palmitoyl-Tyr-Gly-Gly-Phe-X with X Met or Leu or mixtures thereof. Suitable additional hexapeptide derivatives for use herein include, but are not limited to N-Palmitoyl-Val-Gly-Val-Ala-Pro-Gly and derivatives thereof.

The preferred compositions commercially available containing a additional tripeptide or a derivative include Biopeptide-CL™ by SEDERMA (WO 0143701), Maxilip™ by SEDERMA (WO 0143701), Biobustyl™ by SEDERMA. The compositions commercially available preferred sources of additional tetrapeptides include RIGIN™ (WO 0043417), EYELISS™ (WO 03068141), MATRIXYL™, and MATRIXYL3000™ which contain between 50 and 500 ppm of palmitoyl-Gly-Gln-Pro-Arg, and carrier, proposed by SEDERMA, France (Us 2004/0132667).

#### 12. Ascorbates and Other Vitamins

The compositions of the present invention may comprise one or more vitamins, such as ascorbates (e.g., vitamin C, vitamin C derivatives, ascorbic acid, ascorbyl glucoside, ascorbyl palmitate, magnesium ascorbyl phosphate, sodium ascorbyl phosphate). Such vitamins can include, but are not limited to, vitamin B, vitamin B derivatives, vitamin B1 to vitamin B12 and

theirs derivatives, vitamin K, vitamin K derivatives, vitamin H vitamin D, vitamin D derivatives, vitamin E, vitamin E derivatives, and provitamins thereof, such as panthenol and mixtures thereof. The vitamin compounds may be included as the substantially pure material, or as an extract obtained by suitable physical and/or chemical isolation from natural (e. g.,

5 plant) sources. In one embodiment, when vitamin compounds are present in the compositions of the instant invention, the compositions comprise from about 0.0001% to about 50%, more preferably from about 0.001% to about 10%, still more preferably from about 0.01% to about 8%, and still more preferably from about 0.1% to about 5%, by weight of the composition, of the vitamin compound.

10 13. Particulate Material

The compositions of the present invention can comprise one or more particulate materials. Non limiting examples of particulate materials useful in the present invention include colored and uncolored pigments, interference pigments, inorganic powders, organic powders, composite

15 powders, optical brightener particles, and combinations thereof. These particulates can, for instance, be platelet shaped, spherical, elongated or needle-shaped, or irregularly shaped, surface coated or uncoated, porous or non-porous, charged or uncharged, and can be added to the current compositions as a powder or as a pre-dispersion. In one embodiment, particulate materials are present in the composition in levels of from about 0.01% to about 20%, more preferably from about 0.05% to about 10%, still more preferably from about 0.1% to about 5%,

20 by weight of the composition. There are no specific limitations as to the pigment, colorant or filler powders used in the composition.

Particulate materials useful herein can include, but are not limited to, bismuth oxychloride, sericite, silica, mica, mica treated with barium sulfate or other materials, zeolite, kaolin, silica, boron nitride, lauroyl lysine, nylon, polyethylene, talc, styrene, polypropylene, polystyrene,

25 ethylene/acrylic acid copolymer, aluminum oxide, silicone resin, barium sulfate, calcium carbonate, cellulose acetate, PTFE, polymethyl methacrylate, starch, modified starches such as aluminum starch octenyl succinate, silk, glass, and mixtures thereof. Preferred organic powders/fillers include, but are not limited, to polymeric particles chosen from the methylsilsesquioxane resin microspheres such as, for example, those sold by Toshiba silicone

30 under the name Tospearl 145A, microspheres of polymethylmethacrylates such as those sold by Seppic under the name Micropearl M 100, the spherical particles of crosslinked polydimethylsiloxanes, especially such as those sold by Dow Corning Toray Silicone under the name Trefil E 506C or Trefil E 505C, spherical particles of polyamide and more specifically Nylon 12, especially such as those sold by Atochem under the name Orgasol 2002D Nat C05,

35 polystyrene microspheres such as for example those sold by Dyno Particles under the name Dynospheres, ethylene acrylate copolymer sold by Kobo under the name FloBead EA209,

PTFE, polypropylene, aluminium starch octenylsuccinate such as those sold by National Starch under the name Dry Flo, microspheres of polyethylene such as those sold by Equistar under the name of Microthene FN510-00, silicone resin, polymethylsilsesquioxane silicone polymer, platelet shaped powder made from L-lauroyl lysine, and mixtures thereof.

5 Also useful herein are interference pigments. The most common examples of interference pigments are micas layered with about 50 – 300 nm films of TiO<sub>2</sub>, Fe<sub>2</sub>O<sub>3</sub>, silica, tin oxide, and/or Cr<sub>2</sub>O<sub>3</sub>. Useful interference pigments are available commercially from a wide variety of suppliers, for example, Rona (Timiron™ and Dichrona™ ), Presperse (Flonac™ ), Englehard (Duochrome™ ), Kobo (SK-45-R and SK-45-G), BASF (Sicopearls) and Eckart  
10 (e.g. Prestige Silk Red).

Other pigments useful in the present invention can provide color primarily through selective absorption of specific wavelengths of visible light, and include inorganic pigments, organic pigments and combinations thereof. Examples of such useful inorganic pigments include iron oxides, ferric ammonium ferrocyanide, manganese violet, ultramarine blue, and Chrome oxide.  
15 Organic pigments can include natural colorants and synthetic monomeric and polymeric colorants. An example is phthalocyanine blue and green pigment. Also useful are lakes, primary FD&C or D&C lakes and blends thereof. Also useful are encapsulated soluble or insoluble dyes and other colorants. Inorganic white or uncolored pigments useful in the present invention, for example TiO<sub>2</sub>, ZnO, or ZrO<sub>2</sub>, are commercially available from a number of  
20 sources. One example of a suitable particulate material contains the material available from U.S. Cosmetics (TRONOX TiO<sub>2</sub> series, SAT-T CR837, a rutile TiO<sub>2</sub>), an other example is OPTISOL, proposed by Oxonica.

The pigments/powders of the current invention can be surface treated to provide added stability of color and/or for ease of formulation. Non-limiting examples of suitable coating materials  
25 include silicones, lecithin, amino acids, metal soaps, polyethylene and collagen. These surface treatments may be hydrophobic or hydrophilic, with hydrophobic treatments being preferred.

#### 14. Sunscreen Actives

The compositions of the subject invention may optionally contain a sunscreen active. As used herein, “sunscreen active” includes both sunscreen agents and physical sunblocks. Suitable  
30 sunscreen actives may be organic or inorganic.

A wide variety of conventional organic or inorganic sunscreen actives are suitable for use herein. In one embodiment, the composition comprises from about 0.1% to about 20%, more typically from about 0.5% to about 10% by weight of the composition, of the sun screen active. Exact amounts will vary depending upon the sunscreen chosen and the desired Sun Protection  
35 Factor (SPF).

As examples of organic screening agents which are active in UV-A and/or UV-B, there may be mentioned in particular those designated below by their CTFA name:

- 5 - para-aminobenzoic acid derivatives: PABA, Ethyl PABA, Ethyl Dihydroxypropyl PABA, Ethylhexyl Dimethyl PABA sold in particular under the name "ESCALOL 507" by ISP, Glyceryl PABA, PEG-25 PABA sold under the name "UVINUL P25" by BASF,
- 10 - salicyclic derivatives: Homosalate sold under the name "EUSOLEX HMS" by RONA/EM INDUSTRIES, Ethylhexyl Salicylate sold under the name "NEO HELIOPAN OS" by HAARMANN and REIMER, Dipropylenglycol Salicylate sold under the name "DIPSAL" by SCHER, TEA Salicylate, sold under the name "NEO HELIOPAN TS" by HAARMANN and REIMER,
- dibenzoylmethane derivatives: Butyl Methoxydibenzoylmethane sold in particular under the trademark "PARSOL 1789" by HOFFMANN LA ROCHE, Isopropyl Dibenzoylmethane,
- 15 - cinnamic derivatives: Ethylhexyl Methoxycinnamate sold in particular under the trademark "PARSOL MCX" by HOFFMANN LA ROCHE, Isopropyl Methoxy Cinnamate, Isoamyl Methoxy Cinnamate sold under the trademark "NEO HELIOPAN E 1000" by HAARMANN and REIMER, Cinoxate, DEA Methoxycinnamate, Diisopropyl Methylcinnamate, Glyceryl Ethylhexanoate Dimethoxycinnamate,
- 20 - ?? ?diphenylacrylate derivatives: Octocrylene sold in particular under the trademark "UVINUL N539" by BASF, Etocrylene, sold in particular under the trademark "UVINUL N35" by BASF,
- benzophenone derivatives: Benzophenone-1 sold under the trademark "UVINUL 400" by BASF, Benzophenone-2 sold under the trademark "UVINUL D50" by BASF, Benzophenone-3 or Oxybenzone, sold under the trademark "UVINUL M40" by BASF, Benzophenone-4 sold under the trademark "UVINUL MS40" by BASF, Benzophenone-5, Benzophenone-6 sold under the trademark "HELISORB 11 " by NORQUAY, Benzophenone-8 sold under the trademark "SPECTRA-SORB UV-24" by AMERICAN CYANAMID, Benzophenone-9 sold under the trademark "UVINUL DS-49" by BASF, Benzophenone-12,
- 25 - benzylidene camphor derivatives: 3-Benzylidene Camphor, 4Methylbenzylidene Camphor sold under the name "EUSOLEX 6300" by MERCK, Benzylidene Camphor Sulphonic Acid, Camphor Benzalkonium Methosulphate, Terephthalylidene Dicamphor Sulphonic Acid, Polyacrylamidomethyl Benzylidene Camphor,
- 30 - phenylbenzimidazole derivatives: Phenylbenzimidazole Sulphonic Acid sold in particular under the trademark "EUSOLEX 232" by MERCK, Benzimidazilate sold under the trademark "NEO HELIOPAN AP" by HAARMANN and REIMER,

- triazine derivatives: Anisotriazine sold under the trademark "TINOSORB S" by CIBA GEIGY, Ethylhexyl triazones sold in particular under the trademark "UVINUL T150" by BASF, Diethylhexyl Butamido Triazone sold under the trademark "UVASORB HEB" by SIGMA 3V,
- 5 - phenylbenzotriazole derivatives: Drometrizole Trisiloxane sold under the name "SILATRIZOLE" by RHODIA CHIMIE,
- anthranilic derivatives: Menthyl anthranilate sold under the trademark "NEO HELIOPAN MA" by HAARMANN and REIMER,
- imidazoline derivatives: Ethylhexyl Dimethoxybenzylidene Dioxoimidazoline Propionate,
- 10 - benzalmalonate derivatives: Polyorganosiloxane with benzalmalonate functional groups sold under the trademark "PARSOL SLX" by HOFFMANN LA ROCHE, and mixtures thereof.
- others: dihydroxycinnamic acid derivatives (umbelliferone, methylumbelliferone, methylaceto-umbelliferone); trihydroxy-cinnamic acid derivatives (esculetin, methylesculetin, daphnetin, and the glucosides, esculin and daphnin); hydrocarbons (diphenylbutadiene, 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 benzoxazole, methyl naphthoxazole, various aryl benzothiazoles); quinine salts (bisulfate, sulfate, chloride, oleate, and tannate);
- 15 quinoline derivatives (8-hydroxyquinoline salts, 2-phenylquinoline); uric and violuric acids; tannic acid and its derivatives (e.g., hexaethylether); (butyl carbotol) (6-propyl piperonyl) ether; hydroquinone;
- The organic UV-screening agents which are more particularly preferred are chosen from the following compounds: Ethylhexyl Salicylate, Butyl Methoxydibenzoylmethane, Ethylhexyl
- 25 Methoxycinnamate, Octocrylene, Phenylbenzimidazole Sulphonic Acid, Terephthalylidene Dicamphor Sulphonic, Benzophenone-3, Benzophenone-4, Benzophenone-5, 4-Methylbenzylidene camphor, Benzimidazilate, Anisotriazine, Ethylhexyl triazone, Diethylhexyl Butamido Triazone, Methylene bis-Benzotriazolyl Tetramethylbutylphenol, Drometrizole Trisiloxane, and mixtures thereof.
- 30 Also preferred are the compositions described in U.S. Patent No. 6,190,645 and in particular, sunscreen agents sold under the trademark INCROQUAT-UV-283 manufactured by Croda, Inc.
- The inorganic screening agents which may be used in the composition according to the invention are in particular nanopigments (mean size of the primary particles: generally between
- 35 5 nm and 100 nm, preferably between 10 nm and 50 nm) of coated or uncoated metal oxides

such as for example nanopigments of titanium oxide (amorphous or crystallized in the form of rutile and/or anatase), iron, zinc, zirconium or cerium oxides and mixtures thereof. Coating agents are moreover alumina and/or aluminum stearate. Such nanopigments of metal oxides, coated or uncoated, are in particular described in EP-A-0-518,772 and EP-A-0-518,773. One preferred TiO<sub>2</sub> / ZnO<sub>2</sub> sunscreen agent is OPTISOL, proposed by Oxonica

When used herein, the inorganic sunscreens are present in the amount of from about 0.1% to about 20%, preferably from about 0.5% to about 10%, more preferably from about 1% to about 5%, by weight of the composition.

15. Anti-Cellulite Agents

10 The compositions of the present invention may also comprise an anti-cellulite agent. Suitable agents may include, but are not limited to, xanthine compounds (e.g., caffeine, theophylline, theobromine, and aminophylline). In one embodiment, when anti-cellulite compounds are present in the compositions of the instant invention, the compositions comprise from about 0.0001% to about 50%, more preferably from about 0.001% to about 10%, still more preferably from about 0.01% to about 8%, and still more preferably from about 0.1% to about 5%, by weight of the composition, of the anti-cellulite compound.

Especially useful are combinations with the cellulite/slimming agents called Vexel™ (FR 2 654 619), Coaxel (FR 2 694 195), Cyclolipase™ (FR 2 733 149), Pleurimincyl™ and Lipocare™ (WO 98/43607), Redulite™ and Unislim™ (FR 0306063), all offered by SEDERMA.

16. Slimming, toning or draining actives

25 The compositions can include one or more lipolytic agent selected among : phosphodiesterase inhibitors (e. g., xanthine derivatives) , alpha-2 blockers compounds capable of blocking alpha-2 receptors at the adipocytes surface, beta-adrenergical agonists and antagonists (e.g. alverine and its organic or inorganic salts such as alverine citrate), agents inhibiting LDL and VLDL receptors synthesis, inhibitors of enzymes of fatty acid synthesis such as acetylCoA carboxylase, or fatty acid synthetase or cerulenine, compounds stimulating beta receptors and/or G proteins, glucose transport blockers such as serutine or rutine, neuropeptide Y (NPY) antagonists capable of blocking NPY receptors at the adipocytes surface, cAMP and its cosmetically acceptable derivatives, adenylate cyclase enzyme active agents such as forskolin, agents modifying fat acids transport, lipolytic peptides and lipolytic proteins, like peptides or proteins such as the peptides derived from the parathyroidal hormone, described in particular in the patents FR 2788058 and FR 2781231.

30 Others examples of usable lipolytic agents include botanical and marine extracts:

- among plant extracts, there may more particularly be mentioned the extract of English ivy (Hedera Helix), of Chinese thorowax (Bupleurum chinensis), of arnica (Arnica Montana L), of rosemary (Rosmarinus officinalis N), of marigold (Calendula officinalis), of sage (Salvia officinalis L), of ginseng (Panax ginseng), of ginko biloba , of St.-John's-Wort (Hypericum Perforatum), of butcher's-broom (Ruscus aculeatus L), of European meadowsweet (Filipendula ulmaria L), of big-flowered Jarva tea (Orthosiphon Stamincus Benth), of algae (Fucus Vesiculosus), of birch (Betula alba), of green tea, of cola nuts (Cola Nipida), of horse-chestnut, of bamboo, of spadeleaf (Centella asiatica), of heather, of fucus, of willow, of mouse-ear, extracts of escine, extracts of cangzhu, extracts of chrysanthellum indicum, extracts of the plants of the Armeniaceae genus, Atractylodis Platycodon, Sinnomenum, Pharbitidis, Flemingia, extracts of Coleus such as C. Forskohlii, C. blumei, C. esquirolii, C. scutellaroides, C. xanthantus and C. Barbatus, such as the extract of root of Coleus barbatus, extracts of Ballote, extracts of Guioa, of Davallia, of Terminalia, of Barringtonia, of Trema, of antirobia, cecropia, argania, dioscoreae such as Dioscorea opposita or Mexican,
- 15 - as extracted of marine origin: extracts of algae or phytoplankton such as an extract of Laminaria digitata, diatoms, rhodysterol. All these extracts being able of course to be taken in mixtures.

The compositions according to the invention can also contain in addition one or more additional active selected among: agents acting on the microcirculation (vasculoprotectors or vasodilators) such as the natural flavonoids, ruscogenines, esculosides, escine, nicotines, heperidine methyl chalcone, butcher's-broom, essential oils of lavender or rosemary, the extracts of Ammi visnaga; anti-glycation agents such as extracts of Centella asiatica and Siegesbeckia, silicium, amadorine, ergothioneine and its derivatives, hydroxystilbenes and their derivatives (e.g. resveratrol), vegetable extracts of the family of Ericaceae, in particular bilberry extracts (Vaccinium angustifolium), vitamin C and its derivatives , retinol and its derivatives.

17. Butylated Hydroxytoluene (BHT) and Butylated Hydroxyanisole (BHA)

The topical compositions of the present invention may comprise BHT or BHA.

In one embodiment, BHT and/or BHA is added from about 0.0001% to about 20% by weight of the composition, more preferably from about 0.001% to about 10%, even more preferably from about 0.01% to about 5%, and still more preferably from about 0.1% to about 0.5%.

18. Topical Anesthetics

The compositions of the present invention may also contain a safe and effective amount of a topical anesthetic. Examples of topical anesthetic drugs include benzocaine, lidocaine, bupivacaine, chlorprocaine, dibucaine, etidocaine, mepivacaine, tetracaine, dyclonine, hexylcaine, procaine, cocaine, ketamine, pramoxine, phenol, and pharmaceutically acceptable salts thereof.



19. Desquamating/ keratolytic Actives

A desquamating/keratolytic active may be added to the compositions of the present invention. In one embodiment, the composition comprises from about 0.01% to about 10%, preferably from about 0.1% to about 5%, more preferably from about 0.5% to about 2%, by weight of the composition, of a desquamating/keratolytic active.

Examples of useful keratolytic and/or desquamating agents include urea, salicylic acid and alkyl derivatives thereof, saturated and unsaturated monocarboxylic acids, saturated and unsaturated bicarboxylic acids, tricarboxylic acids, alpha hydroxyacids and beta hydroxyacids of monocarboxylic acids, alpha hydroxyacids and beta hydroxyacids of bicarboxylic acids, alpha hydroxyacids and beta hydroxyacids of tricarboxylic acids, ketoacids, alpha ketoacids, beta ketoacids, of the polycarboxylic acids, of the polyhydroxy monocarboxylic acids, of the polyhydroxy bicarboxylic acids, of the polyhydroxy tricarboxylic acids.

Illustrative of this group of materials are 2-hydroxyethanoic acid (glycolic acid); 2-hydroxypropanoic acid (lactic acid); 2-methyl 2-hydroxypropanoic acid (methyl lactic acid); 2-hydroxybutanoic acid; 2-hydroxypentanoic acid; 2-hydroxyhexanoic acid; 2-hydroxyheptanoic acid; 2-hydroxyoctanoic acid; 2-hydroxynonanoic acid; 2-hydroxydecanoic acid; 2-hydroxyundecanoic acid; 2-hydroxydodecanoic acid (alpha-hydroxy lauric acid); 2-hydroxytetradecanoic acid (alpha-hydroxy myristic acid); 2-hydroxyhexadecanoic acid (alpha-hydroxy palmitic acid); 2-hydroxyoctadecanoic acid (alpha-hydroxy stearic acid); 2-hydroxyeicosanoic acid (alpha-hydroxy arachidonic acid); 2-phenyl 2-hydroxyethanoic acid (mandelic acid); 2,2-diphenyl 2-hydroxyethanoic acid (benzilic acid); 3-phenyl 2-hydroxypropanoic acid (phenyl lactic acid); 2-phenyl 2-methyl 2-hydroxyethanoic acid (atrolactic acid); 2-(4'-hydroxyphenyl) 2-hydroxyethanoic acid; 2-(4'-chlorophenyl) 2-hydroxyethanoic acid; 2-(3'-hydroxy-4'-methoxyphenyl) 2-hydroxyethanoic acid; 2-(4'-hydroxy-3'-methoxyphenyl) 2-hydroxyethanoic acid; 3'-(2-hydroxyphenyl) 2-hydroxypropanoic acid; 3-(4'-hydroxyphenyl) 2-hydroxypropanoic acid; and 2-(3',4'-dihydroxyphenyl), and 2-hydroxyethanoic acid, 5-n-octanoylsalicylic acid, 5-n-dodecanoylsalicylic acid, 5-n-decanoylsalicylic acid, 5-n-octylsalicylic acid, 5-n-heptyloxysalicylic acid, 4n-heptyloxysalicylic acid and 2-hydroxy-3-methylbenzoic acid or alkoxy derivatives thereof, such as 2-hydroxy-3-methoxybenzoic acid.

Preferred keratolytic agents are selected from the group comprising glycolic acid, tartaric acid, salicylic acid, citric acid, lactic acid, pyruvic acid, gluconic acid, glucuronic acid, malic acid, mandelic acid, oxalic acid, malonic acid, succinic acid, acetic acid, phenol, resorcinol, retinoic acid, adapalene, trichloroacetic acid, 5-fluoro uracil, azelaic acid. Keratolytic agents are also the salts, esters, possible cis or trans forms, racemic mixtures and/or the relative dextrorotatory

or levorotatory forms of the above listed compounds. Such substances can be used singularly or in associations with each other.

Other keratolytic agents suitable for use herein can include enzymatic exfoliant based on a protease called Keratoline™ and offered by Sederma.

5 One desquamation system that is suitable for use herein comprises salicylic acid and zwitterionic surfactants and is described in U.S. Patent No. 5,652,228. Another desquamation system that is suitable for use herein contains sulfhydryl compounds and zwitterionic surfactants and is described in U.S. Patent No. 5,681,852. Zwitterionic surfactants such as those described in this referenced patent can also be useful as desquamatory agents herein, with cetyl  
10 betaine being particularly preferred.

#### 20. Anti-Acne Actives

The compositions of the present invention can comprise one or more anti-acne actives. Examples of useful anti-acne actives include resorcinol, sulfur, erythromycin, salicylic acid, benzoyl peroxide, dehydroacetic acid and zinc. Further examples of suitable anti-acne actives  
15 are described in U. S. Patent No. 5,607,980. Especially useful are combinations with the anti-acne ingredient called Ac.net™ offered by SEDERMA (WO 03/028692 A2).

In one embodiment, when anti-acne compounds are present in the compositions of the instant invention, the compositions comprise from about 0.0001% to about 50%, more preferably from about 0.001% to about 10%, still more preferably from about 0.01% to about 8%, and still  
20 more preferably from about 0.1% to about 5%, by weight of the composition, of the anti-acne compound.

#### 21. Anti-Wrinkle Actives/Anti-Atrophy Actives

The compositions of the present invention can comprise a one or more anti-wrinkle actives or anti-atrophy actives. Exemplary anti-wrinkle/anti-atrophy actives suitable for use in the  
25 compositions of the present invention include sulfur-containing D and L amino acids and their derivatives and salts, particularly the N-acetyl derivatives, a preferred example of which is N-acetyl-L-cysteine; thiols, e.g. ethane thiol, hydroxy acids (e.g., alpha-hydroxy acids such as lactic acid and glycolic acid or beta-hydroxy acids such as salicylic acid and salicylic acid derivatives such as the octanoyl derivative, lactobionic acid), keto acids (e.g., pyruvic acid),  
30 phytic acid, ascorbic acid (vitamin C), stilbenes, cinnamates, resveratrol, kinetin, zeatin, dimethylaminoethanol, peptides from natural sources (e.g., soy peptides), and salts of sugar acids (e.g., Mn gluconate, Zn gluconate), lipoic acid; lysophosphatidic acid, skin peel agents (e.g., phenol and the like), vitamin B3 compounds and retinoids and other vitamin B compounds (e.g., thiamine (vitamin B1), pantothenic acid (vitamin B5), riboflavin (vitamin  
35 B2), and their derivatives and salts (e.g., HCL salts or calcium salts). Especially useful are

combinations with the wrinkle agents called Dermolectine™ and Sterocare™ offered by SEDERMA (WO99/18927).

In one embodiment, when anti-wrinkle/anti-atrophy compounds are present in the compositions of the instant invention, the compositions comprise from about 0.0001% to about 50%, more preferably from about 0.001% to about 10%, still more preferably from about 0.01% to about 8%, and still more preferably from about 0.1% to about 5%, by weight of the composition, of the anti-wrinkle/anti-atrophy compound.

## 22. Anti-Oxidants/Racial Scavengers

The compositions of the present invention can include an anti-oxidant/radical scavenger. In one embodiment, the composition comprises from about 0.01% to about 10%, more preferably from about 0.1% to about 5%, of an anti-oxidant/radical scavenger.

Anti-oxidants/radical scavengers such as retinyl palmitate, ascorbic acid (vitamin C) and its salts, ascorbyl esters of fatty acids, ascorbic acid derivatives (e.g., magnesium ascorbyl phosphate, sodium ascorbyl phosphate, ascorbyl sorbate), tocopherol (vitamin E), tocopherol sorbate, tocopherol acetate, other esters of tocopherol, butylated hydroxy benzoic acids and their salts, peroxides including hydrogen peroxide, perborate, thioglycolates, persulfate 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, amines (e.g., N,N-diethylhydroxylamine, amino-guanidine), nordihydroguaiaretic acid, bioflavonoids, sulfhydryl compounds (e.g., glutathione), dihydroxy fumaric acid and its salts, lysine pidolate, arginine pilolate, amino acids, silymarin, lysine, l-methionine, proline, superoxide dismutase, sorbic acids and its salts, lipoic acid, olive extracts, tea extracts, polyphenols such as proanthocyanidine from pine bark, carotenoids, curcumin compounds such as tetrahydrocurcumin, OCTA (L-2-oxo-4-thiazolidine carboxylic acid), glutathione, melanin, rosemary extracts and grape skin/seed extracts may be used. Preferred anti-oxidants/radical scavengers can be selected from esters of tocopherol, more preferably tocopherol acetate and tocopherol sorbate (U.S. Pat. No. 4,847,071)

## 23. Humectants, Moisturizers and Conditioning Agents

The compositions of the present invention can contain a safe and effective amount of a conditioning agent selected from, for example, humectants, moisturizers, and skin conditioners. A variety of these materials can be employed and in one embodiment can be present at a level of from about 0.01% to about 20%, more preferably from about 0.1% to about 10%, and still more preferably from about 0.5% to about 7%, by weight of the composition. These materials can include, but are not limited to, guanidine, urea, glycolic acid, glycolate salts (e.g. ammonium and quaternary alkyl ammonium), salicylic acid, lactic acid, 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, mannitol, xylitol, erythritol, glycerol, hexanetriol, butanetriol, propylene glycol, butylene glycol, hexylene glycol and the like, polyethylene glycols, sugars (e.g., melibiose), starches, sugar and starch derivatives (e.g., alkoxyated glucose, fructose, glucosamine), hyaluronic acid, lactamide monoethanolamine, acetamide monoethanolamine, panthenol, allantoin, petroleum and mixtures thereof. Also  
5 useful herein are the propoxylated glycerols described in U.S. Patent No. 4,976,953.

Also useful are various C1-C30 monoesters and polyesters of sugars and related materials. These esters are derived from a sugar or polyol moiety and one or more carboxylic acid moieties.

10 Preferably, the conditioning agent is selected from urea, guanidine, sucrose polyester, panthenol, dexpanthenol, allantoin, glycerol, and combinations thereof.

Humectants can be selected from the group consisting of polyhydric alcohols, water soluble alkoxyated nonionic polymers, and mixtures thereof. Polyhydric alcohols useful herein include polyhydroxy alcohols aforementioned and glycerin, hexylene glycol, ethoxyated glucose, 1, 2-  
15 hexane diol, dipropylene glycol, trehalose, diglycerin, maltitol, maltose, glucose, fructose, sodium chondroitin sulfate, sodium hyaluronate, sodium adenosine phosphate, sodium lactate, pyrrolidone carbonate, glucosamine, cyclodextrin, and mixtures thereof. Water soluble alkoxyated nonionic polymers useful herein include polyethylene glycols and polypropylene glycols having a molecular weight of up to about 1000 such as those with CTFA names PEG-  
20 200, PEG-400, PEG-600, PEG-1000, PPG-12/SMDI copolymer and mixtures thereof.

#### 24. Active oxygen generation inhibitors

The compositions of the present invention may also comprise a an active oxygen generation inhibitor selected from the group comprising quercetin, rutin, taxifolin, kaempferol, myricetin, curcumin, resveratrol, arecoline, apigenin, wogonin, luteolin, tectorigenin, and a mixture  
25 thereof.

This active oxygen generation inhibitor may be contained in an amount of about 0.001% to about 5%, more preferably in an amount of about 0.01% to about 3% %, by weight of the composition.

#### 25. Chelators

30 The compositions of the present invention may also comprise a chelator or chelating agent. As used herein, "chelator" or "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 oxygen radical formation. In one embodiment, a chelating agent is added to a composition of the present invention, preferably from about 0.00001% to about 10%, more  
35 preferably from about 0.001% to about 5%, by weight of the composition. Exemplary

chelators that are useful herein include those that are disclosed in U.S. Patent No. 5,487,884, WO 91/16035 and WO 91/16034. Examples of chelating agents include N-hydroxysuccinimide, EDTA, Disodium EDTA, NTA, deferoxamine, hydroxamic acids and their salts, phytic acid, phytate, gluconic acid and its salts, transferrin, lactoferrin; furildioxime and derivatives thereof.

26. Anti-Inflammatory Agents

An anti-inflammatory agent may be added to the compositions of the present invention. In one embodiment, an anti-inflammatory agent is added at a level of from about 0.01% to about 10%, preferably from about 0.5% to about 5%, by weight of the composition. The exact amount of anti-inflammatory agent to be used in the compositions will depend on the particular anti-inflammatory agent utilized since such agents vary widely in potency

Steroidal anti-inflammatory agents can include, but are not limited to, corticosteroids such as hydrocortisone. In addition, nonsteroidal anti-inflammatory agents can be useful herein. The varieties of compounds encompassed by this group are well known to those skilled in the art.

Specific non-steroidal anti-inflammatory agents that can be useful in the composition of the present invention include, but are not limited to, oxicams such as piroxicam, salicylates such as aspirin; acetic acid derivatives, such as felbinac, fenamates, such as etofenamate, flufenamic, mefenamic, meclofenamic, acids ; propionic acid derivatives, such as ibuprofen, naproxen, pyrazoles, and mixtures thereof. Mixtures of these non-steroidal anti-inflammatory agents may also be employed, as well as the dermatologically acceptable salts and esters of these agents.

Finally, so-called "natural" anti-inflammatory agents are useful in methods of the present 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) or can be synthetically prepared. For example, candelilla wax, bisabolol (e.g., alpha bisabolol), aloe vera, plant sterols (e.g., phytosterol), 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, red clover extract, Piper methysticum extract (Kava Kava from SEDERMA (FR 2 771 002 and WO 99 / 25369), Bacopa monieri extract (Bacocalmine™ from SEDERMA, WO 99/40897) and sea whip extract, may be used. Anti-inflammatory agents useful herein include allantoin and 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-C24 saturated or unsaturated esters of the acids, preferably C10 C24, more preferably C16-C24. 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-glycyrrhetic acid, and disodium 3-succinyloxy-beta-glycyrrhetinate. Stearyl glycyrrhetinate is preferred. Additional anti inflammatory agents include diosgenol, saponines, sapogenines, lignanes, triterpenes saponosides and genines.

5 27. Tanning Actives

The compositions of the present invention can comprise a tanning active. In one embodiment, the composition comprises from about 0.1% to about 20%, more preferably from about 2% to about 7%, and even more preferably from about 3% to about 6%, by weight of the composition, of a tanning active. A preferred tanning active is dihydroxyacetone, which is also  
10 known as DHA or 1,3-dihydroxy-2-propanone. Especially useful are combinations with the tanning agents called Tyr-ol™ and Tyr-excel™ offered by SEDERMA and described in Fr 2 702 766 and WO 03/017966 respectively.

28. Skin Lightening Agents

The compositions of the present invention may contain a skin lightening agent. When used, the  
15 compositions preferably contain from about 0.001% to about 10%, more preferably from about 0.02% to about 5%, also preferably from about 0.05% to about 2%, by weight of the composition, of a skin lightening agent. Suitable skin lightening agents include those known in the art, including kojic acid, hydroquinone, aminophenol derivatives, N-cholesteryloxycarbonyl-para-aminophenol and N-ethyloxycarbonyl-para-aminophenol;  
20 iminophenol derivatives, L-2-oxothiazolidine-4-carboxylic acid or procysteine, and also its salts and esters, arbutin, tranexamic acid, ascorbic acid and derivatives thereof (e.g., magnesium ascorbyl phosphate or sodium ascorbyl phosphate, ascorbyl glucoside and the like (such as AA2G from Hayashibara)), and extracts (e.g., mulberry extract, placental extract, skullcap extract broussonetia extract, oil soluble liquorice extract (such as these available from  
25 Maruzen), oil soluble liquorice extract (glycyrrhiza, chamomile extract (such as these available from Kao)), m-Tranexamic acid/vitamin C ethyl (such as these available from Shiseido), adenosine monophosphate disodium (APM offered by Otsuka), ellagic acid (Lion), rucinol (Pola), ethyl ascorbyl ether). Skin lightening agents suitable for use herein also include those described in WO95/34280, PCT/US 95/07432, co-pending. US 08/390,152 and PCT/US  
30 95/23780. Especially useful are combinations with the skin lightening agents called Melaclear™, Etioline™, Melaslow™ and Lumiskin™ offered by SEDERMA and described respectively in FR 2 732 215, WO 98/05299, WO 02/15871 and PCT/FR 03/02400. Other skin lightening materials suitable for use herein can include Actiwhite® (Cognis), Emblica® (Rona), Azeloglicina (Sinerga) and Sepiwhite® (Seppic). A preferred skin lightening agent is  
35 ascorbyl glucoside.

29. Antimicrobial, Antibacterial and Antifungal Actives

The compositions of the present invention can comprise one or more anti-fungal or anti-microbial actives. A safe and effective amount of an antimicrobial or antifungal active can be added to the present compositions. In one embodiment, the composition comprises from about 0.001% to about 10%, preferably from about 0.01% to about 5%, and more preferably from about 0.05% to about 2%, by weight of the composition, of an antimicrobial or antifungal active.

Suitable anti-microbial actives include coal tar, sulfur, whitfield's ointment, castellani's paint, aluminum chloride, gentian violet, octopirox (piroctone olamine), 3,4,4'-trichlorocarbanilide (trichlosan), triclocarban, ciclopirox olamine, undecylenic acid and its metal salts, potassium permanganate, selenium sulphide, sodium thiosulfate, propylene glycol, oil of bitter orange, urea preparations, griseofulvin, 8-Hydroxyquinoline ciloquinol, thiobendazole, thiocarbamates, haloprogin, polyenes, hydroxypyridone, morpholine, benzylamine, allylamines (such as terbinafine), tea tree oil, clove leaf oil, coriander, palmarosa, berberine, thyme red, cinnamon oil, cinnamic aldehyde, citronellic acid, hinokitol, ichthyol pale, Sensiva SC-50, Elestab HP-100, azelaic acid, lyticase, iodopropynyl butylcarbamate (IPBC), isothiazalinones such as octyl isothiazolinone and azoles, and combinations thereof. Preferred anti-microbials include itraconazole, ketoconazole, selenium sulphide and coal tar. In one embodiment, one or more anti-fungal or anti-microbial active is combined with an anti-dandruff active selected from polyvalent metal salts of pyrithione.

20 a. Azoles

Azole anti-microbials include imidazoles such as benzimidazole, benzothiazole, bifonazole, butoconazole nitrate, climbazole, clotrimazole, croconazole, eberconazole, econazole, elubiol, fenticonazole, fluconazole, flutimazole, isoconazole, ketoconazole, lanconazole, metronidazole, miconazole, neticonazole, omoconazole, oxiconazole nitrate, sertaconazole, sulconazole nitrate, tioconazole, thiazole, and triazoles such as terconazole and itraconazole, and combinations thereof. When present in the composition, the azole anti-microbial active is included in an amount from about 0.01% to about 5%, preferably from about 0.1% to about 3%, and more preferably from about 0.3% to about 2%, by weight of the composition. Especially preferred herein are ketoconazole and climbazole.

30 b. Selenium Sulfide

Selenium sulfide is a particulate anti-dandruff agent suitable for use in the anti-microbial compositions of the present invention, effective concentrations of which range from about 0.1% to about 4%, by weight of the composition, preferably from about 0.3% to about 2.5%, more preferably from about 0.5% to about 1.5

35 c. Sulfur

Sulfur may also be used as a particulate anti-microbial/anti-dandruff agent in the anti-microbial compositions of the present invention. Effective concentrations of the particulate sulfur are typically from about 1% to about 4%, by weight of the composition, preferably from about 2% to about 4%.

5 d. Additional Anti-microbial Actives

Additional anti-microbial actives of the present invention may include one or more keratolytic agents such as salicylic acid, extracts of melaleuca (tea tree) and charcoal. The present invention may also comprise combinations of anti-microbial actives. Such combinations may include octopirox and zinc pyrithione combinations, pine tar and sulfur combinations, salicylic acid and zinc pyrithione combinations, octopirox and climbazole combinations, and salicylic acid and octopirox combinations, and mixtures thereof.

Preferred examples of actives useful herein include those selected from the group consisting of benzoyl peroxide, 3-hydroxy benzoic acid, glycolic acid, lactic acid, 4-hydroxy benzoic acid, 2-hydroxybutanoic acid, 2-hydroxypentanoic acid, 2-hydroxyhexanoic acid, phytic acid, lipoic acid, azelaic acid, arachidonic acid, benzoylperoxide, tetracycline, ibuprofen, naproxen, hydrocortisone, acetaminophen, resorcinol, phenoxyethanol, phenoxypropanol, phenoxyisopropanol, 2,4,4'-trichloro-2'-hydroxy diphenyl ether, 3,4,4'-trichlorocarbanilide, octopirox, ciclopirox, lidocaine hydrochloride, clotrimazole, miconazole, ketoconazole, neomycin sulfate, and mixtures thereof.

Especially useful are combinations with the ingredient range called OSMOCIDE™ offered by SEDERMA (WO 97/05856).

30. Thickening Agents (including thickeners and gelling agents)

The compositions of the present invention can comprise one or more thickening agents. In one embodiment, a thickening agent is present at a level of from about 0.05% to about 10%, preferably from about 0.1% to about 5%, and more preferably from about 0.25% to about 4%, by weight of the composition. Nonlimiting classes of thickening agents include those selected from the following:

a. Carboxylic Acid Polymers

These polymers are crosslinked compounds containing one or more monomers derived from acrylic acid, substituted acrylic acids, and salts and esters of these acrylic acids and the substituted acrylic acids, wherein the crosslinking agent contains two or more carbon-carbon double bonds and is derived from a polyhydric alcohol. Polymers useful in the present invention are more fully described in U.S. Pat. No. 5,087,445, U.S. Pat. No. 4,509,949, U.S. Pat. No. 2,798,053, and in CTFI International Cosmetic Ingredient Dictionary, Tenth Edition, 2004.



Examples of commercially available carboxylic acid polymers useful herein include the carbomers, which are homopolymers of acrylic acid crosslinked with allyl ethers of sucrose or pentaerythritol. The carbomers are available as the Carbopol® 900 series from B.F. Goodrich (e.g., Carbopol® 954). In addition, other suitable carboxylic acid polymeric agents include  
5 Ultrez® 10 (B.F. Godrich) and copolymers of C10-30 alkyl acrylates with one or more monomers of acrylic acid, methacrylic acid, or one of their short chain (i.e., C1-4 alcohol) esters, wherein the crosslinking agent is an allyl ether of sucrose or pentaerythritol. These copolymers are known as acrylates/C10 C30 alkyl acrylate crosspolymers and are commercially available as Carbopol® 1342, Carbopol® 1382, Pemulen TR-1, and Pemulen TR  
10 2, from B.F. Goodrich. In other words, examples of carboxylic acid polymer thickeners useful herein are those selected from carbomers, acrylates/C10-C30 alkyl acrylate crosspolymers, and mixtures thereof.

b. Crosslinked Polyacrylate Polymers

The compositions of the present invention can optionally contain crosslinked polyacrylate  
15 polymers useful as thickeners or gelling agents including both cationic and nonionic polymers, with the cationics being generally preferred. Examples of useful crosslinked nonionic polyacrylate polymers and crosslinked cationic polyacrylate polymers are those described in U.S. Pat. No. 5,100,660, U.S. Pat. No. 4,849,484, U.S. Pat. No. 4,835,206, U.S. Pat. No. 4,628,078 U.S. Pat. No. 4,599,379 and EP 228,868.

20 c. Polyacrylamide Polymers

The compositions of the present invention can optionally contain polyacrylamide polymers, especially nonionic polyacrylamide polymers including substituted branched or unbranched polymers. Preferred among these polyacrylamide polymers is the nonionic polymer given the CTF A designation polyacrylamide and isoparaffin and laureth-7, available under the  
25 Tradename Sepigel 305 from Seppic Corporation.

Other polyacrylamide polymers useful herein include multi-block copolymers of acrylamides and substituted acrylamides with acrylic acids and substituted acrylic acids. Commercially available examples of these multi-block copolymers include Hypan SR150H, SS500V, SS500W, SSSA100H, from Lipo Chemicals, Inc.

30 The compositions may also contain thickening and texturising gels of the type as exemplified by the product range called Lubrajel® from United Guardian. These gels have moisturizing, viscosifying, stabilizing properties and may be used in concentration ranges between 1 and 99%, most advantageously between 5 and 15%.

d. Polysaccharides

A wide variety of polysaccharides can be useful herein. "Polysaccharides" refer to gelling agents that contain a backbone of repeating sugar (i.e., carbohydrate) units. Nonlimiting examples of polysaccharide gelling agents 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. Preferred among the alkyl hydroxyalkyl 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<sup>®</sup> CS Plus from Aqualon Corporation.

Other useful polysaccharides include scleroglucans comprising a linear chain of (1-3) linked glucose units with a (1-6) linked glucose every three units, a commercially available example of which is Clearogel<sup>™</sup> CS11 from Michel Mercier Products Inc.

e. Gums

Other thickening and gelling agents useful herein include materials which are primarily derived from natural sources. Nonlimiting examples of these gelling agent gums include acacia, agar, algin, alginic acid, ammonium alginate, amylopectin, calcium alginate, calcium carrageenan, carnitine, 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.

31. Antiperspirant Actives

Antiperspirant actives may also be included in the compositions of the present invention. Suitable antiperspirant actives include astringent metallic salts, especially the inorganic and organic salts of aluminum zirconium and zinc, as well as mixtures thereof. Particularly preferred are the aluminum containing and/or zirconium-containing materials or salts, such as aluminum halides, aluminum chlorohydrate, aluminum hydroxyhalides, zirconyl oxyhalides, zirconyl hydroxyhalides, and mixtures thereof. In one embodiment, when antiperspirant actives are present in the compositions of the instant invention, the compositions comprise from about 0.01% to about 50%, more preferably from about 0.1% to about 40%, and still more preferably from about 1% to about 30%, by weight of the composition, of the antiperspirant compound.

32. Detersive Surfactants

The compositions of the present invention can include detersive surfactant from about 1% to about 90%, more preferably from about 5% to about 10%. The detersive surfactant component

can be included to provide cleaning performance to the composition. The deterative surfactant component in turn can comprise anionic deterative surfactant, zwitterionic or amphoteric deterative surfactant, or a combination thereof. Suitable anionic deterative surfactant components for use in the composition herein include those which are known for use in hair care or other personal care cleansing compositions. When included, the concentration of the anionic surfactant component in the composition can preferably be sufficient to provide the desired cleaning and lather performance, and generally can range from about 5% to about 50%, preferably from about 8% to about 30%, more preferably from about 10% to about 25%, even more preferably from about 12% to about 22%.

Preferred anionic surfactants suitable for use in the compositions are the alkyl and alkyl ether sulfates. Other suitable anionic deterative surfactants are the water-soluble salts of organic, sulfuric acid reaction products, alkoyl isethionates, sodium or potassium salts of fatty acid amides of methyl tauride, olefin sulfonates, and beta-alkyloxy alkane sulfonates.

Preferred anionic deterative surfactants for use in the compositions include ammonium lauryl sulfate, ammonium laureth sulfate, triethylamine lauryl sulfate, triethylamine laureth sulfate, triethanolamine lauryl sulfate, triethanolamine laureth sulfate, monoethanolamine lauryl sulfate, monoethanolamine laureth sulfate, diethanolamine lauryl sulfate, diethanolamine laureth sulfate, lauric monoglyceride sodium sulfate, sodium lauryl sulfate, sodium laureth sulfate, potassium lauryl sulfate, potassium laureth sulfate, sodium lauryl sarcosinate, sodium lauroyl sarcosinate, lauryl sarcosine, cocoyl sarcosine, ammonium cocoyl sulfate, ammonium lauroyl sulfate, sodium cocoyl sulfate, sodium lauroyl sulfate, potassium cocoyl sulfate, potassium lauryl sulfate, triethanolamine lauryl sulfate, triethanolamine lauryl sulfate, monoethanolamine cocoyl sulfate, monoethanolamine lauryl sulfate, sodium tridecyl benzene sulfonate, sodium dodecyl benzene sulfonate, sodium cocoyl isethionate and combinations thereof.

Suitable amphoteric or zwitterionic deterative surfactants for use in the composition herein include those which are known for use in hair care or other personal care cleansing. Concentration of such amphoteric deterative surfactants preferably ranges from about 0.5% to about 20%, preferably from about 1% to about 10%. Non limiting examples of suitable zwitterionic or amphoteric surfactants are described in U.S. Pat. Nos. 5,104,646 and 5,106,609.

Amphoteric deterative surfactants include derivatives of aliphatic secondary and tertiary amines. The compositions of the present invention may further comprise additional surfactants for use in combination with the anionic deterative surfactant component described hereinbefore. Suitable optional surfactants include nonionic and cationic surfactants. Any such surfactant known in the art for use in hair or personal care products may be used, provided that the optional additional surfactant is also chemically and physically compatible with the essential

components of the composition, or does not otherwise unduly impair product performance, aesthetics or stability. The concentration of the optional additional surfactants in the composition may vary with the cleansing or lather performance desired, the optional surfactant selected, the desired product concentration, the presence of other components in the composition, and other factors well known in the art.

Non limiting examples of other anionic, zwitterionic, amphoteric or optional additional surfactants suitable for use in the compositions are described in McCutcheon's, Emulsifiers and Detergents, 1989 Annual, published by M. C. Publishing Co., and U.S. Pat. Nos. 3,929,678, 2,658,072; 2,438,091; 2,528,378.

10 33. Cationic, anionic and amphoteric polymers

The compositions of the present invention can comprise polymers which may be homopolymers, copolymers, terpolymers, etc. For convenience in describing the polymers hereof, monomeric units present in the polymers may be referred to as the monomers from which they can be derived. The monomers can be ionic (e.g., anionic, cationic, amphoteric, zwitterionic) or non-ionic.

When included, concentrations of the cationic polymer in the composition can typically range from about 0.05% to about 3%, preferably from about 0.075% to about 2.0%, more preferably from about 0.1% to about 1.0

a. Cationic polymers

20 Suitable cationic polymers for use in the compositions of the present invention contain cationic nitrogen-containing moieties such as quaternary ammonium or cationic protonated amino moieties. Any anionic counterions can be used in association with the cationic polymers so long as the polymers remain soluble in water, in the composition, or in a coacervate phase of the composition, and so long as the counterions are physically and chemically compatible with the essential components of the composition or do not otherwise unduly impair product performance, stability or aesthetics. Non limiting examples of such counterions include halides (e.g., chloride, fluoride, bromide, iodide), sulfate and methylsulfate. Non limiting examples of such polymers are described in the CTFA.

30 Non limiting examples of suitable cationic polymers include copolymers of vinyl monomers having cationic protonated amine or quaternary ammonium functionalities with water soluble spacer monomers such as acrylamide, methacrylamide, alkyl and dialkyl acrylamides, alkyl and dialkyl methacrylamides, alkyl acrylate, alkyl methacrylate, vinyl caprolactone or vinyl pyrrolidone.

35 Examples of cationic monomers include monomers derived from acrylic acid or methacrylic acid, and a quaternarized epihalohydrin product of a trialkylamine having 1 to 5 carbon atoms

in the alkyl such as (meth)acryloxypropyltrimethylammonium chloride and (meth)acryloxypropyltriethylammonium bromide; amine derivatives of methacrylic acid or amine derivatives of methacrylamide derived from methacrylic acid or methacrylamide and a dialkylalkanolamine having C1–C6 alkyl groups such as dimethylaminoethyl (meth)acrylate, diethylaminoethyl (meth)acrylate, dimethylaminopropyl (meth)acrylate, or dimethylaminopropyl (meth)acrylamide.

Suitable cationic protonated amino and quaternary ammonium monomers, for inclusion in the cationic polymers of the composition herein, include vinyl compounds substituted with dialkylaminoalkyl acrylate, dialkylaminoalkyl methacrylate, monoalkylaminoalkyl acrylate, monoalkylaminoalkyl methacrylate, trialkyl methacryloxyalkyl ammonium salt, trialkyl acryloxyalkyl ammonium salt, diallyl quaternary ammonium salts, and vinyl quaternary ammonium monomers having cyclic cationic nitrogen-containing rings such as pyridinium, imidazolium, and quaternized pyrrolidone, e.g., alkyl vinyl imidazolium, alkyl vinyl pyridinium, alkyl vinyl pyrrolidone salts.

Other suitable cationic polymers for use in the compositions include copolymers of 1-vinyl-2-pyrrolidone and 1-vinyl-3-methylimidazolium salt (e.g., chloride salt) (referred to in the industry by the Cosmetic, Toiletry, and Fragrance Association, "CTFA", as Polyquaternium-16); copolymers of 1-vinyl-2-pyrrolidone and dimethylaminoethyl methacrylate (referred to in the industry by CTFA as Polyquaternium-11); cationic diallyl quaternary ammonium-containing polymers, including, for example, dimethyldiallylammonium chloride homopolymer, copolymers of acrylamide and dimethyldiallylammonium chloride (referred to in the industry by CTFA as Polyquaternium 6 and Polyquaternium 7, respectively); amphoteric copolymers of acrylic acid including copolymers of acrylic acid and dimethyldiallylammonium chloride (referred to in the industry by CTFA as Polyquaternium 22), terpolymers of acrylic acid with dimethyldiallylammonium chloride and acrylamide (referred to in the industry by CTFA as Polyquaternium 39), and terpolymers of acrylic acid with methacrylamidopropyl trimethylammonium chloride and methylacrylate (referred to in the industry by CTFA as Polyquaternium 47). Preferred cationic substituted monomers are the cationic substituted dialkylaminoalkyl acrylamides, dialkylaminoalkyl methacrylamides, and combinations thereof. A non limiting example is polymethacrylamidopropyl trimonium chloride, available under the tradename Polycare 133, from Rhone-Poulenc.

Other suitable cationic polymers for use in the composition include polysaccharide polymers, such as cationic cellulose derivatives and cationic starch derivatives.

Preferred cationic cellulose polymers are salts of hydroxyethyl cellulose reacted with trimethyl ammonium substituted epoxide, referred to in the industry (CTFA) as Polyquaternium 10 and available from Amerchol Corp. in their Polymer LR, JR, and KG series of polymers. Other

suitable types of cationic cellulose include the polymeric quaternary ammonium salts of hydroxyethyl cellulose reacted with lauryl dimethyl ammonium-substituted epoxide referred to in the industry (CTFA) as Polyquaternium 24. These materials are available from Amerchol Corp. under the tradename Polymer LM-200.

5 Other suitable cationic polymers include cationic guar gum derivatives, such as guar hydroxypropyltrimonium chloride, specific examples of which include the Jaguar series commercially available from Rhone-Poulenc Incorporated and the N-Hance series commercially available from Aqualon Division of Hercules, Inc. Other suitable cationic  
10 polymers include quaternary nitrogen-containing cellulose ethers, some examples of which are described in U.S. Pat. No. 3,962,418. Other suitable cationic polymers include copolymers of etherified cellulose, guar and starch, some examples of which are described in U.S. Pat. No. 3,958,581. When used, the cationic polymers herein are either soluble in the composition or are soluble in a complex coacervate phase in the composition formed by the cationic polymer and the anionic, amphoteric and/or zwitterionic detergent surfactant component described  
15 hereinbefore. Complex coacervates of the cationic polymer can also be formed with other charged materials in the composition.

b. anionic polymers

Examples of anionic polymers are copolymers of vinyl acetate and crotonic acid, terpolymers of vinyl acetate, crotonic acid and a vinyl ester of an alpha-branched saturated aliphatic  
20 monocarboxylic acid such as vinyl neodecanoate; and copolymers of methyl vinyl ether and maleic anhydride, acrylic copolymers and terpolymers containing acrylic acid or methacrylic acid.

Examples of anionic monomers include unsaturated carboxylic acid monomers such as acrylic acid, methacrylic acid, maleic acid, maleic acid half ester, itaconic acid, fumaric acid, and  
25 crotonic acid; half esters of an unsaturated polybasic acid anhydride such as succinic anhydride, phthalic anhydride or the like with a hydroxyl group-containing acrylate and/or methacrylate such as hydroxyethyl acrylate and, hydroxyethyl methacrylate, hydroxypropyl acrylate and the like; monomers having a sulfonic acid group such as styrenesulfonic acid, sulfoethyl acrylate and methacrylate, and the like; and monomers having a phosphoric acid  
30 group such as acid phosphoxyethyl acrylate and methacrylate, 3-chloro-2-acid phosphoxypropyl acrylate and methacrylate, and the like.

c. amphoteric monomers

Examples of the amphoteric monomers include zwitterionized derivatives of the  
aforementioned amine derivatives of (meth)acrylic acids or the amine derivatives of  
35 (meth)acrylamide such as dimethylaminoethyl (meth)acrylate, dimethylaminopropyl(meth)acrylamide by a halogenated fatty acid salt such as potassium

monochloroacetate, sodium monobromopropionate, aminomethylpropanol salt of monochloroacetic acid, triethanolamine salts of monochloroacetic acid and the like; and amine derivatives of (meth)acrylic acid or (meth)acrylamide, as discussed above, modified with propanesultone.

5 34. Nonionic polymers

The compositions herein can comprise nonionic polymers. For instance, polyalkylene glycols having a molecular weight of more than about 1000 can be used. Preferred polyethylene glycol polymers can include PEG-2M (also known as Polyox WSR® N-10, which is available from Union Carbide and as PEG-2,000); PEG-5M (also known as Polyox WSR® N-35 and Polyox  
10 WSR® N-80, available from Union Carbide and as PEG-5,000 and Polyethylene Glycol 300,000); PEG-7M (also known as Polyox WSR® N-750 available from Union Carbide); PEG-9M (also known as Polyox WSR® N-3333 available from Union Carbide); and PEG-14 M (also known as Polyox WSR® N-3000 available from Union Carbide).

Examples of nonionic monomers are acrylic or methacrylic acid esters of C1-C24 alcohols,  
15 such as methanol, ethanol, 1-propanol, 2-propanol, 1-butanol, 2-methyl-1-propanol, 1-pentanol, 2-pentanol, 3-pentanol, 2-methyl-1-butanol, 1-methyl-1-butanol, 3-methyl-1-butanol, 1-methyl-1-pentanol, 2-methyl-1-pentanol, 3-methyl-1-pentanol, t-butanol, cyclohexanol, 2-ethyl-1-butanol, 3heptanol, benzyl alcohol, 2octanol, 6methyl-1-heptanol, 2ethyl-1-hexanol, 3,5-dimethyl-1-hexanol, 3,5,5-trimethyl-1-hexanol, 1-decanol, 1-dodecanol, 1-hexadecanol, 1-  
20 octadecanol, styrene, chlorostyrene, vinyl esters such as vinyl acetate, vinyl chloride, vinylidene chloride, acrylonitrile, alpha-methylstyrene, t-butylstyrene, butadiene, cyclohexadiene, ethylene, propylene, vinyl toluene, alkoxyalkyl (meth)acrylate, methoxy ethyl (meth)acrylate, butoxyethyl (meth)acrylate, allyl acrylate, allyl methacrylate, cyclohexyl acrylate and methacrylate, oleyl acrylate and methacrylate, benzyl acrylate and methacrylate,  
25 tetrahydrofurfuryl acrylate and methacrylate, ethylene glycol di-acrylate and -methacrylate, 1,3-butyleneglycol di-acrylate and -methacrylate, diacetoneacrylamide, isobornyl (meth)acrylate, n-butyl methacrylate, isobutyl methacrylate, 2-ethylhexyl methacrylate, methyl methacrylate, t-butylacrylate, t-butylmethacrylate, and mixtures thereof.

35. Hair Conditioning agents

30 Conditioning agents include any material which is used to give a particular conditioning benefit to keratinous tissue. For instance, in hair treatment compositions, suitable conditioning agents include those which deliver one or more benefits relating to shine, softness, combability, antistatic properties, wet-handling, damage, manageability, body, and greasiness. Conditioning agents useful in the compositions of the present invention can comprise a water insoluble,  
35 water dispersible, non-volatile liquid that forms emulsified, liquid particles. Suitable conditioning agents for use in the composition include those conditioning agents characterized

generally as silicones (e.g., silicone oils, cationic silicones, silicone gums, high refractive silicones, and silicone resins), organic conditioning oils (e.g., hydrocarbon oils, polyolefins, and fatty esters) or combinations thereof, or those conditioning agents which otherwise form liquid, dispersed particles in the aqueous surfactant matrix herein.

5 When included, the concentration of the conditioning agent in the composition can be sufficient to provide the desired conditioning benefits, and as will be apparent to one of ordinary skill in the art. Such concentration can vary with the conditioning agent, the conditioning performance desired, the average size of the conditioning agent particles, the type and concentration of other components, and other like factors.

10 a. Silicones

The conditioning agent of the compositions of the present invention is preferably an insoluble silicone conditioning agent. The silicone conditioning agent particles may comprise volatile silicone, non-volatile silicone, or combinations thereof. Preferred are non-volatile silicone conditioning agents. If volatile silicones are present, it will typically be incidental to their use  
15 as a solvent or carrier for commercially available forms of non-volatile silicone materials ingredients, such as silicone gums and resins. The silicone conditioning agent particles may comprise a silicone fluid conditioning agent and may also comprise other ingredients, such as a silicone resin to improve silicone fluid deposition efficiency or enhance glossiness of the hair.

The concentration of the silicone conditioning agent typically ranges from about 0.01% to  
20 about 10%, preferably from about 0.1% to about 8%, more preferably from about 0.1% to about 5%, more preferably from about 0.2% to about 3%. Non-limiting examples of suitable silicone conditioning agents, and optional suspending agents for the silicone, are described in U.S. Reissue Pat. No. 34,584, U.S. Pat. No. 5,104,646, and U.S. Pat. No. 5,106,609.

Background material on silicones including sections discussing silicone fluids, gums, and  
25 resins, as well as manufacture of silicones, are found in Encyclopedia of Polymer Science and Engineering, vol. 15, 2d ed., pp 204 308, John Wiley & Sons, Inc. (1989).

b. Silicone oils

Silicone fluids include silicone oils, which are flowable silicone materials having a viscosity, as  
30 measured at 25°C, less than 1,000,000 csk, preferably from about 5 csk to about 1,000,000 csk, more preferably from about 100 csk to about 600,000 csk. Suitable silicone oils for use in the compositions of the present invention include polyalkyl siloxanes, polyaryl siloxanes, polyalkylaryl siloxanes, polyether siloxane copolymers, and mixtures thereof. Other insoluble, non-volatile silicone fluids having hair conditioning properties may also be used.

c. Amino and Cationic silicones



Cationic silicone fluids suitable for use in the compositions of the present invention include, but are not limited to, the polymer known as "trimethyl-silylamodimethicone".

Other silicone cationic polymers which may be used in the compositions of the present invention may be UCARE SILICONE ALE 56? , available from Union Carbide.

5 d. Silicone gums

Other silicone fluids suitable for use in the compositions of the present invention are the insoluble silicone gums. These gums are polyorganosiloxane materials having a viscosity, as measured at 25°C, of greater than or equal to 1,000,000 csk. Silicone gums are described in U.S. Pat. No. 4,152,416; Noll and Walter, Chemistry and Technology of Silicones, New York: Academic Press (1968); and in General Electric Silicone Rubber Product Data Sheets SE 30, SE 33, SE 54 and SE 76. Specific non-limiting examples of silicone gums for use in the compositions of the present invention include polydimethylsiloxane, (polydimethylsiloxane) (methylvinylsiloxane) copolymer, poly(dimethylsiloxane) (diphenyl siloxane)(methylvinylsiloxane) copolymer and mixtures thereof.

15 e. High refractive index silicones

Other non-volatile, insoluble silicone fluid conditioning agents that are suitable for use in the compositions of the present invention are those known as "high refractive index silicones," having a refractive index of at least about 1.46, preferably at least about 1.48, more preferably at least about 1.52, more preferably at least about 1.55. The refractive index of the polysiloxane fluid will generally be less than about 1.70, typically less than about 1.60. In this context, polysiloxane "fluid" includes oils as well as gums.

When high refractive index silicones are used in the compositions of the present invention, they are preferably used in solution with a spreading agent, such as a silicone resin or a surfactant, to reduce the surface tension by a sufficient amount to enhance spreading and thereby enhance the glossiness (subsequent to drying) of hair treated with the compositions.

Silicone fluids suitable for use in the compositions of the present invention are disclosed in U.S. Pat. No. 2,826,551, U.S. Pat. No. 3,964,500, U.S. Pat. No. 4,364,837, British Pat. No. 849,433, and Silicon Compounds, Petrarch Systems, Inc. (1984).

f. Silicone resins

30 Silicone resins may be included in the silicone conditioning agent of the compositions of the present invention. These resins are highly cross-linked polymeric siloxane systems. The cross-linking is introduced through the incorporation of trifunctional and tetrafunctional silanes with monofunctional or difunctional, or both, silanes during manufacture of the silicone resin.

36. Organic conditioning oils

Compositions of the present invention may also comprise organic conditioning oil. In one embodiment, from about 0.05% to about 20%, preferably from about 0.08% to about 1.5%, more preferably from about 0.1% to about 1%, of at least one organic conditioning oil is included as a conditioning agent, either alone or in combination with other conditioning agents, such as the silicones (described herein).

a. Hydrocarbon oils

Suitable organic conditioning oils for use as conditioning agents in the compositions of the present invention include, but are not limited to, hydrocarbon oils having at least about 10 carbon atoms, such as cyclic hydrocarbons, straight chain aliphatic hydrocarbons (saturated or unsaturated), and branched chain aliphatic hydrocarbons (saturated or unsaturated), including polymers and mixtures thereof. Straight chain hydrocarbon oils preferably are from about C12 to about C19. Branched chain hydrocarbon oils, including hydrocarbon polymers, typically will contain more than 19 carbon atoms.

Specific non-limiting examples of these hydrocarbon oils include paraffin oil, mineral oil, saturated and unsaturated dodecane, saturated and unsaturated tridecane, saturated and unsaturated tetradecane, saturated and unsaturated pentadecane, saturated and unsaturated hexadecane, polybutene, polydecene, and mixtures thereof. Branched-chain isomers of these compounds, as well as of higher chain length hydrocarbons, can also be used, examples of which include highly branched, saturated or unsaturated, alkanes such as the permethyl-substituted isomers, e.g., the permethyl-substituted isomers of hexadecane and eicosane, such as 2, 2, 4, 4, 6, 6, 8, 8-dimethyl-10-methylundecane and 2, 2, 4, 4, 6, 6-dimethyl-8-methylnonane, available from Permethyl Corporation, hydrocarbon polymers such as polybutene and polydecene. A preferred hydrocarbon polymer is polybutene, such as the copolymer of isobutylene and butene. A commercially available material of this type is L-14 polybutene from Amoco Chemical Corporation. Another example is hydrogenated polyisobutene or liquid isoparaffine.

b. Polyolefins

Organic conditioning oils for use in the compositions of the present invention can also include liquid polyolefins, more preferably liquid poly- $\alpha$ -olefins, more preferably hydrogenated liquid poly- $\alpha$ -olefins. Polyolefins for use herein are prepared by polymerization of C4 to about C14 olefinic monomers, preferably from about C6 to about C12.

Preferred non-limiting examples of olefinic monomers for use in preparing the polyolefin liquids herein include ethylene, propylene, 1-butene, 1-pentene, 1-hexene to 1-hexadecenes, 1-octene, 1-decene, 1-dodecene, 1-tetradecene, branched chain isomers such as 4-methyl-1-pentene, and mixtures thereof. Also suitable for preparing the polyolefin liquids are olefin-containing refinery feedstocks or effluents.

c. Fatty Esters

Other suitable organic conditioning oils for use as the conditioning agent in the compositions of the present invention include, but are not limited to, fatty esters having at least 10 carbon atoms. These fatty esters include esters with hydrocarbyl chains derived from fatty acids or alcohols (e.g. mono-esters, polyhydric alcohol esters, and di- and tri-carboxylic acid esters). The hydrocarbyl radicals of the fatty esters hereof may include or have covalently bonded thereto other compatible functionalities, such as amides and alkoxy moieties (e.g., ethoxy or ether linkages, etc.).

Specific examples of preferred fatty esters include, but are not limited to: isopropyl isostearate, hexyl laurate, isohexyl laurate, isohexyl palmitate, isopropyl palmitate, decyl oleate, isodecyl oleate, hexadecyl stearate, decyl stearate, isopropyl isostearate, dihexyldecyl adipate, lauryl lactate, myristyl lactate, cetyl lactate, oleyl stearate, oleyl oleate, oleyl myristate, lauryl acetate, cetyl propionate, and oleyl adipate.

Other fatty esters suitable for use in the compositions of the present invention are mono-carboxylic acid esters of the general formula  $R'COOR$ , wherein  $R'$  and  $R$  are alkyl or alkenyl radicals, and the sum of carbon atoms in  $R'$  and  $R$  is at least 10, preferably at least 22.

Still other fatty esters suitable for use in the compositions of the present invention are di- and tri-alkyl and alkenyl esters of carboxylic acids, such as esters of C4 to C8 dicarboxylic acids (e.g. C1 to C22 esters, preferably C1 to C6, of succinic acid, glutaric acid, and adipic acid). Specific non-limiting examples of di- and tri-alkyl and alkenyl esters of carboxylic acids include isocetyl stearyl stearate, diisopropyl adipate, and tristearyl citrate.

Other fatty esters suitable for use in the compositions of the present invention are those known as polyhydric alcohol esters. Such polyhydric alcohol esters include alkylene glycol esters, such as ethylene glycol mono and di-fatty acid esters, diethylene glycol mono- and di-fatty acid esters, polyethylene glycol mono- and di-fatty acid esters, propylene glycol mono- and di-fatty acid esters, polypropylene glycol monooleate, polypropylene glycol 2000 monostearate, ethoxylated propylene glycol monostearate, glyceryl mono- and di-fatty acid esters, polyglycerol poly-fatty acid esters, ethoxylated glyceryl monostearate, 1,3-butylene glycol monostearate, 1,3-butylene glycol distearate, polyoxyethylene polyol fatty acid ester, sorbitan fatty acid esters, and polyoxyethylene sorbitan fatty acid esters.

Still other fatty esters suitable for use in the compositions of the present invention are glycerides, including, but not limited to, mono-, di-, and tri-glycerides, preferably di- and tri-glycerides, more preferably triglycerides. For use in the compositions described herein, the glycerides are preferably the mono-, di-, and tri-esters of glycerol and long chain carboxylic acids, such as C10 to C22 carboxylic acids. A variety of these types of materials can be obtained from vegetable and animal fats and oils, such as castor oil, safflower oil, cottonseed

oil, corn oil, olive oil, cod liver oil, almond oil, avocado oil, palm oil, sesame oil, lanolin and soybean oil. Synthetic oils include, but are not limited to, triolein and tristearin glyceryl dilaurate.

5 Other fatty esters suitable for use in the compositions of the present invention are water insoluble synthetic fatty esters.

Specific non-limiting examples of suitable synthetic fatty esters for use in the compositions of the present invention include: P-43 (C8-C10 triester of trimethylolpropane), MCP-684 (tetraester of 3,3 diethanol-1,5 pentadiol), MCP 121 (C8-C10 diester of adipic acid), all of which are available from Mobil Chemical Company.

10 37. Anti-dandruff Actives

The compositions of the present invention may also contain an anti-dandruff agent. Suitable, non-limiting examples of anti-dandruff particulates include: pyridinethione salts, azoles, selenium sulfide, particulate sulfur, and mixtures thereof. Preferred are pyridinethione salts, especially 1-hydroxy-2-pyridinethione salts. The concentration of pyridinethione anti-dandruff particulate typically ranges from about 0.1% to about 4%, by weight of the composition, preferably from about 0.1% to about 3%, more preferably from about 0.3% to about 2%. Preferred pyridinethione salts include those formed from heavy metals such as zinc, tin, cadmium, magnesium, aluminum and zirconium, preferably zinc, more preferably the zinc salt of 1-hydroxy-2-pyridinethione (known as "zinc pyridinethione" or "ZPT"). Pyridinethione anti-dandruff agents are described, for example, in U.S. Pat. No. 2,809,971; U.S. Pat. No. 3,236,733; U.S. Pat. No. 3,753,196; U.S. Pat. No. 3,761,418; U.S. Pat. No. 4,345,080; U.S. Pat. No. 4,323,683; U.S. Pat. No. 4,379,753; and U.S. Pat. No. 4,470,982.

20 38. Humectant

The compositions of the present invention may contain a humectant. Humectants can be selected from the group consisting of polyhydric alcohols, water soluble alkoxyated nonionic polymers, and mixtures thereof. Humectants, when used herein, are preferably used at levels of from about 0.1% to about 20%, more preferably from about 0.5% to about 5%.

Polyhydric alcohols useful herein include glycerin, sorbitol, propylene glycol, butylene glycol, hexylene glycol, ethoxylated glucose, 1, 2-hexane diol, hexanetriol, dipropylene glycol, erythritol, trehalose, diglycerin, xylitol, maltitol, maltose, glucose, fructose, sodium chondroitin sulfate, sodium hyaluronate, sodium adenosine phosphate, sodium lactate, pyrrolidone carbonate, glucosamine, cyclodextrin, and mixtures thereof.

Water soluble alkoxyated nonionic polymers useful herein include polyethylene glycols and polypropylene glycols having a molecular weight of up to about 1000 such as PEG-200, PEG-400, PEG-600, PEG-1000 (CTFA names), and mixtures thereof.

39. Suspending Agent

The compositions of the present invention may further comprise a suspending agent, preferably at concentrations effective for suspending water-insoluble material in dispersed form in the compositions or for modifying the viscosity of the composition. Such concentrations can preferably range from about 0.1% to about 10%, more preferably from about 0.3% to about 5.0%.

Suspending agents useful herein include anionic polymers and nonionic polymers. Useful herein are vinyl polymers such as cross linked acrylic acid polymers with the CTFA name Carbomer, cellulose derivatives and modified cellulose polymers such as methyl cellulose, ethyl cellulose, nitro cellulose, sodium carboxymethyl cellulose, crystalline cellulose, cellulose powder, polyvinylpyrrolidone, polyvinyl alcohol, guar gum, hydroxypropyl guar gum, arabia gum, galactan, carob gum, pectin, agar, quince seed (*Cydonia oblonga* Mill), starch (rice, corn, potato, wheat), algae colloids (algae extract), microbiological polymers such as dextran, succinoglucon, pulleran, starch-based polymers such as carboxymethyl starch, methylhydroxypropyl starch, alginic acid-based polymers such as sodium alginate, alginic acid propylene glycol esters, acrylate polymers such as sodium polyacrylate, polyethylacrylate, polyacrylamide, polyethyleneimine, and inorganic water soluble material such as bentonite, aluminum magnesium silicate, laponite, hectonite, and anhydrous silicic acid. Actives aforementioned as thickening agents can also be used herein as suspending agents.

Commercially available viscosity modifiers highly useful herein include Carbomers with tradenames Carbopol 934, Carbopol 940, Carbopol 950, Carbopol 980, and Carbopol 981, all available from B. F. Goodrich Company, acrylates/stearath-20 methacrylate copolymer with tradename ACRY SOL 22 available from Rohm and Hass, nonoxynyl hydroxyethylcellulose with tradename AMERCELL POLYMER HM-1500 available from Amerchol, methylcellulose with tradename BENECEL, hydroxyethyl cellulose with tradename NATROSOL, hydroxypropyl cellulose with tradename KLUCEL, cetyl hydroxyethyl cellulose with tradename POLYSURF 67, all supplied by Hercules, ethylene oxide and/or propylene oxide based polymers with tradenames CARBOWAX PEGs, POLYOX WASRs, and UCON FLUIDS, all supplied by Amerchol.

Other optional suspending agents include crystalline suspending agents which can be categorized as acyl derivatives, long chain amine oxides, long chain acyl derivatives and mixtures thereof. These suspending agents are described in U.S. Pat. No. 4,741,855. These preferred suspending agents include ethylene glycol esters of fatty acids, alkanol amides of fatty acids, long chain esters of long chain fatty acids (e.g., stearyl stearate, cetyl palmitate, etc.); long chain esters of long chain alkanol amides (e.g., stearamide diethanolamide distearate, stearamide monoethanolamide stearate); and glyceryl esters (e.g., glyceryl distearate,

trihydroxystearin, tribehenin) a commercial example of which is Thixin® available from Rheox, Inc.

Other suitable suspending agents include primary amines having a fatty alkyl moiety having at least about 16 carbon atoms, examples of which include palmitamine or stearamine, and  
5 secondary amines having two fatty alkyl moieties each having at least about 12 carbon atoms, examples of which include dipalmitoylamine or di(hydrogenated tallow)amine. Still other suitable suspending agents include di(hydrogenated tallow)phthalic acid amide, and crosslinked maleic anhydride-methyl vinyl ether copolymer.

40. Terpene Alcohol

10 The compositions of the present invention may comprise a terpene alcohol or combinations of terpene alcohols. As used herein, "terpene alcohol" refers to organic compounds composed of two or more 5-carbon isoprene units  $[\text{CH}_2=\text{C}(\text{CH}_3)-\text{CH}=\text{CH}_2]$  with a terminal hydroxyl group. Preferably, the composition can comprise from about 0.001% to about 50%, preferably from about 0.01% to about 20%, more preferably from about 0.1% to about 15%, even more  
15 preferably from about 0.1% to about 10%, still more preferably from about 0.5% to about 5%, and still more preferably from about 1% to about 5%, by weight of the composition, of the terpene alcohol.

Examples of terpene alcohols that can be useful herein include farnesol, derivatives of farnesol, isomers of farnesol, geraniol, derivatives of geraniol, isomers of geraniol, phytantriol, derivatives of phytantriol, isomers of phytantriol, and mixtures thereof. A preferred terpene  
20 alcohol for use herein is farnesol.

a. Farnesol and Derivatives thereof

Farnesol is a naturally occurring substance which is believed to act as a precursor and/or intermediate in the biosynthesis of squalene and sterols, especially cholesterol. Farnesol is also  
25 involved in protein modification and regulation (e.g., farnesylation of proteins), and there is a cell nuclear receptor which is responsive to farnesol.

Chemically, farnesol is [2E,6E]-3,7,11-trimethyl-2,6,10-dodecatrien-1-ol and as used herein "farnesol" includes isomers and tautomers of such. Farnesol is commercially available, e.g.,  
30 under the names farnesol (a mixture of isomers from Dragoco) and trans-trans-farnesol (Sigma Chemical Company). A suitable derivative of farnesol is farnesyl acetate which is commercially available from Aldrich Chemical Company.

b. Geraniol and derivatives thereof

Geraniol is the common name for the chemical known as 3,7-dimethyl-2,6-octadien-1-ol. As used herein, "geraniol" includes isomers and tautomers of such. Geraniol is commercially  
35 available from Aldrich Chemical Company. Suitable derivatives of geraniol include geranyl

acetate, geranylgeraniol, geranyl pyrophosphate, and geranylgeranyl pyrophosphate, all of which are commercially available from Sigma Chemical Company. For example, geraniol is useful as a spider vessel/ red blotchiness repair agent, a dark circle/puffy eye repair agent, sallowness repair agent, a sagging repair agent, an anti-itch agent, a skin thickening agent, a pore reduction agent, oil/shine reduction agent, a post-inflammatory hyperpigmentation repair agent, wound treating agent, an anti-cellulite agent, and regulating skin texture, including wrinkles and fine lines.

c. Phytantriol and derivatives thereof

Phytantriol is the common name for the chemical known as 3,7,11,15 tetramethylhexadecane-1,2,3,-triol. Phytantriol is commercially available from BASF. For example, phytantriol is useful as a spider vessel/ red blotchiness repair agent, a dark circle/puffy eye repair agent, sallowness repair agent, a sagging repair agent, an anti-itch agent, a skin thickening agent, a pore reduction agent, oil/shine reduction agent, a post-inflammatory hyperpigmentation repair agent, wound treating agent, an anti-cellulite agent, and regulating skin texture, including wrinkles and fine lines.

41. Enzymes, Enzyme Inhibitors and Enzyme activators (Coenzymes)

The compositions of the present invention may contain a safe and effective amount of one or more enzymes, enzyme inhibitors or enzyme activators (coenzymes). Examples of enzymes are lipases, proteases, catalase, superoxide-dismutase, amylases, glucuronidases, peroxidases, in particular glutathione peroxidase or lactoperoxidase, ceramidases, hyaluronidases. All of these enzymes may be obtained by extraction or by fermentation biotechnology processes. Examples of enzyme inhibitors include trypsin inhibitors, Bowman Birk inhibitor, chymotrypsin inhibitors, botanical extracts with or without tannins, flavonoids, quercetin which inhibit enzymatic activity. Enzyme preparations can be found, for instance, in the product named VENUCEANE proposed by SEDERMA, France (WO 02/066668). Enzyme activators and coenzymes include Coenzyme A, coenzyme Q10 (ubiquinone), glycyrrhizidine, berberine, chrysine.

## **II Carrier**

The compositions of the present invention can comprise an orally or a dermatologically acceptable carrier, or injectible liquid, depending upon the desired product form.

### **A. Dermatologically acceptable carrier**

The topical compositions of the present invention can also comprise a dermatologically acceptable carrier for the composition. In one embodiment, the carrier is present at a level of from about 50% to about 99.99%, preferably from about 60% to about 99.9%, more preferably

from about 70% to about 98%, and even more preferably from about 80% to about 95%, by weight of the composition.

The carrier can be in a wide variety of forms. Non-limiting examples include simple solutions (water or oil based), emulsions, and solid forms (gels, sticks). For example, emulsion carriers  
5 can include, but are not limited to, oil-in-water, water-in-oil, water-in-silicone, water-in-oil-in-water, and oil-in-water-in-silicone emulsions.

Depending upon the desired product form, preferred carriers can comprise an emulsion such as oil-in-water emulsions (e.g., silicone in water) and water-in-oil emulsions, (e.g., water-in-silicone emulsions). As will be understood by the skilled artisan, a given component will  
10 distribute primarily into either the water or oil phase, depending on the water solubility/dispersability of the component in the composition. In one embodiment, oil-in-water emulsions are especially preferred.

Emulsions according to the present invention can contain an aqueous phase and a lipid or oil. Lipids and oils may be derived from animals, plants, or petroleum and may be natural or  
15 synthetic (i.e., man-made). Preferred emulsions can also contain a humectant, such as glycerin. Emulsions can further comprise from about 0.1% to about 10%, more preferably from about 0.2% to about 5%, of an emulsifier, based on the weight of the composition. Emulsifiers may be nonionic, anionic or cationic. Suitable emulsifiers are disclosed in, for example, U.S. Patent 3,755,560, U.S. Patent 4,421,769, and McCutcheon's Detergents and Emulsifiers, North  
20 American Edition, pages 317 324 (1986). Suitable emulsions may have a wide range of viscosities, depending on the desired product form.

The compositions of the present invention can be in the form of pourable liquids (under ambient conditions). The compositions can therefore comprise an aqueous carrier, which is typically present at a level of from about 20% to about 95%, preferably from about 60% to  
25 about 85%. The aqueous carrier may comprise water, or a miscible mixture of water and organic solvent, but preferably comprises water with minimal or no significant concentrations of organic solvent, except as otherwise incidentally incorporated into the composition as minor ingredients of other essential or optional components.

The emulsion may also contain an anti-foaming agent to minimize foaming upon application to  
30 the keratinous tissue. Anti-foaming agents include high molecular weight silicones and other materials well known in the art for such use.

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

1. Water-in-silicone emulsion

Water-in-silicone emulsions can contain a continuous silicone phase and a dispersed aqueous  
35 phase.



a. Continuous silicone phase

Preferred water-in-silicone emulsions of the present invention can contain 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.

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 active ingredients of the present invention. The continuous silicone phase of these preferred emulsions contain 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 contains 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 even more preferably less than about 2%, by weight of the continuous silicone phase.

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 atmospheric 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 organopolysiloxane oils include polyalkylsiloxanes, cyclic polyalkylsiloxanes, and polyalkylarylsiloxanes.

Polyalkylsiloxanes useful in the composition herein include polyalkylsiloxanes with viscosities of from about 0.5 to about 1,000,000 centistokes at 25°C. 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, Dow Corning® 225 fluid, and Dow Corning® 200 fluids. Examples of suitable alkyl-substituted dimethicones include cetyl dimethicone and lauryl dimethicone.

Cyclic polyalkylsiloxanes suitable for use in the composition include commercially available cyclomethicones such as Dow Corning® 244 fluid, Dow Corning® 344 fluid, Dow Corning® 245 fluid and Dow Corning® 345 fluid.

Also useful are materials such as trimethylsiloxysilicate. A commercially available trimethylsiloxysilicate is sold as a mixture with dimethicone as Dow Corning® 593 fluid.

Dimethiconols are also suitable for use in the composition. Commercially available dimethiconols are typically sold as mixtures with dimethicone or cyclomethicone (e.g. Dow Corning® 1401, 1402, and 1403 fluids).

Polyalkylaryl 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.

Preferred for use herein are organopolysiloxanes selected from polyalkylsiloxanes, alkyl substituted dimethicones, cyclomethicones, trimethylsiloxysilicates, dimethiconols, polyalkylaryl siloxanes, and mixtures thereof. More preferred for use herein are polyalkylsiloxanes and cyclomethicones. Preferred among the polyalkylsiloxanes are dimethicones.

As stated above, the continuous silicone phase may contain one or more non-silicone oils. 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.

b. Dispersed aqueous phase

The topical compositions of the present invention can contain from about 30% to about 90%, more preferably from about 50% to about 85%, and still more 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.

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

The topical compositions of the present invention will typically contain 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.

c. Emulsifier for dispersing the aqueous phase

The water-in-silicone emulsions of the present invention may preferably contain 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%, still more 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.

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 components of the composition of the present invention, 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 still more 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.

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 copolyols. 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 copolyols, i.e., compounds which contain C2-C30 pendant side chains. Still other useful dimethicone copolyols include materials having various cationic, anionic, amphoteric, and zwitterionic pendant moieties.

Nonlimiting examples of dimethicone copolyols and other silicone surfactants useful as emulsifiers herein include polydimethylsiloxane polyether copolymers with pendant polyethylene oxide side chains, polydimethylsiloxane polyether copolymers with pendant polypropylene oxide side chains, polydimethylsiloxane polyether copolymers with pendant mixed polyethylene oxide and polypropylene oxide side chains, polydimethylsiloxane polyether copolymers with pendant mixed poly(ethylene)(propylene)oxide side chains, 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, 25324 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 copolyolamine, 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.

Dimethicone copolyol emulsifiers useful herein are described, for example, in U.S. Patent No. 4,960,764, EP 330,369. Among the non-silicone-containing emulsifiers useful herein are various non-ionic and anionic emulsifying agents such as sugar esters and polyesters, alkoxyated sugar esters and polyesters, C1-C30 fatty acid esters of C1-C30 fatty alcohols, alkoxyated derivatives of C1-C30 fatty acid esters of C1-C30 fatty alcohols, alkoxyated ethers of C1-C30 fatty alcohols, polyglyceryl esters of C1-C30 fatty acids, C1-C30 esters of polyols, C1-C30 ethers 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; U.S. Patent No. 4,421,769; and U.S. Patent No. 3,755,560.

Nonlimiting examples of these non-silicon-containing emulsifiers include: polyethylene glycol sorbitan monolaurate (Polysorbate 20), polyethylene glycol 5 soya sterol, Steareth-20, Cetareth-20, PPG-2 methyl glucose ether distearate, 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, cetareth-20, PPG-2 methyl glucose ether distearate, ceteth-10, diethanolamine cetyl phosphate, glyceryl stearate, PEG-100 stearate, and mixtures thereof.

d. Silicone Elastomer

The compositions of the present invention may also include from about 0.1% to about 30%, by weight of the composition, of a silicone elastomer component. Preferably, the composition includes from about 1% to about 30%, more preferably from about 2% to about 20%, by weight of the composition, of the silicone elastomer component.

5 Suitable for use herein are silicone elastomers, which can be emulsifying or non-emulsifying crosslinked siloxane elastomers or mixtures thereof. No specific restriction exists as to the type of curable organopolysiloxane composition that can serve as starting material for the crosslinked organopolysiloxane elastomer. Examples in this respect are addition reaction-curing organopolysiloxane compositions which cure under platinum metal catalysis by the  
10 addition reaction between SiH-containing diorganopolysiloxane and organopolysiloxane having silicon-bonded vinyl groups; condensation-curing organopolysiloxane compositions which cure in the presence of an organotin compound by a dehydrogenation reaction between hydroxyl-terminated diorganopolysiloxane and SiH-containing diorganopolysiloxane and  
15 condensation-curing organopolysiloxane compositions which cure in the presence of an organotin compound or a titanate ester.

Addition reaction-curing organopolysiloxane compositions are preferred for their rapid curing rates and excellent uniformity of curing. A particularly preferred addition reaction-curing organopolysiloxane composition is prepared from: a) an organopolysiloxane having at least 2  
20 lower alkenyl groups in each molecule; b) an organopolysiloxane having at least 2 silicon-bonded hydrogen atoms in each molecule; and c) a platinum-type catalyst.

The compositions of the present invention may include an emulsifying crosslinked organopolysiloxane elastomer, a non-emulsifying crosslinked organopolysiloxane elastomer, or a mixture thereof. The term "non-emulsifying," as used herein, defines crosslinked organopolysiloxane elastomers from which polyoxyalkylene units are absent. The term  
25 "emulsifying," as used herein, means crosslinked organopolysiloxane elastomers having at least one polyoxyalkylene (e.g., polyoxyethylene or polyoxypropylene) unit. Preferred emulsifying elastomers herein include polyoxyalkylene modified elastomers formed from divinyl compounds, particularly siloxane polymers with at least two free vinyl groups, reacting with Si-H linkages on a polysiloxane backbone. Preferably, the elastomers are dimethyl polysiloxanes crosslinked by Si-H sites on a molecularly spherical MQ resin. Emulsifying crosslinked  
30 organopolysiloxane elastomers can notably be chosen from the crosslinked polymers described in U.S. Pat. Nos. 5,412,004, 5,837,793, and 5,811,487. In addition, an emulsifying elastomer comprised of dimethicone copolyol crosspolymer (and) dimethicone is available from Shin Etsu under the tradename KSG-21.

35 Advantageously, the non-emulsifying elastomers are dimethicone/vinyl dimethicone crosspolymers. Such dimethicone/vinyl dimethicone crosspolymers are supplied by a variety of

suppliers including Dow Corning (DC 9040 and DC 9041), General Electric (SFE 839), Shin Etsu (KSG-15, 16, 18 [dimethicone/phenyl vinyl dimethicone crosspolymer]), and Grant Industries (GRANSIL(TM) line of elastomers). Cross-linked organopolysiloxane elastomers useful in the present invention and processes for making them are further described in U.S. Pat. No. 4,970,252, U.S. Pat. No. 5,760,116, and U.S. Pat. No. 5,654,362.

Commercially available elastomers preferred for use herein are Dow Corning's 9040 silicone elastomer blend, Shin Etsu's KSG-21, and mixtures thereof.

e. Carrier for Silicone Elastomer

The topical compositions of the present invention may include from about 1% to about 80%, by weight of the composition, of a suitable carrier for the for the crosslinked organopolysiloxane elastomer component described above. The carrier, when combined with the cross-linked organopolysiloxane elastomer particles of the present invention, serves to suspend and swell the elastomer particles to provide an elastic, gel-like network or matrix. The carrier for the cross-linked siloxane elastomer is liquid under ambient conditions, and preferably has a low viscosity to provide for improved spreading on the skin.

Concentrations of the carrier in the cosmetic compositions of the present invention will vary primarily with the type and amount of carrier and the cross-linked siloxane elastomer employed. Preferred concentrations of the carrier are from about 5% to about 50%, more preferably from about 5% to about 40%, by weight of the composition.

The carrier for the cross-linked siloxane elastomer includes one or more liquid carriers suitable for topical application to human skin. These liquid carriers may be organic, silicone-containing or fluorine-containing, volatile or non-volatile, polar or non-polar, provided that the liquid carrier forms a solution or other homogenous liquid or liquid dispersion with the selected cross-linked siloxane elastomer at the selected siloxane elastomer concentration at a temperature of from about 28°C to about 250°C, preferably from about 28°C to about 100°C, preferably from about 28°C to about 78°C. The term "volatile" as used herein refers to all materials that are not "non-volatile" as previously defined herein. The phrase "relatively polar" as used herein means more polar than another material in terms of solubility parameter; i.e., the higher the solubility parameter the more polar the liquid. The term "non-polar" typically means that the material has a solubility parameter below about 6.5 (cal/cm<sup>3</sup>)<sup>0.5</sup>.

f. Non-polar, Volatile Oils

The composition of the present invention may include non-polar, volatile oils. The non-polar, volatile oil tends to impart highly desirable aesthetic properties to the compositions of the present invention. Consequently, the non-polar, volatile oils are preferably utilized at a fairly high level. Non-polar, volatile oils particularly useful in the present invention are silicone oils; hydrocarbons; and mixtures thereof. Such non-polar, volatile oils are disclosed, for example, in

Cosmetics, Science, and Technology, Vol. 1, 27-104 edited by Balsam and Sagarin, 1972. Examples of preferred non-polar, volatile hydrocarbons include polydecenes such as isododecane and isodecane (e.g., Permethy1-99A which is available from Presperse Inc.) and the C7-C8 through C12-C15 isoparaffins (such as the Isopar Series available from Exxon  
5 Chemicals). Linear volatile silicones generally have a viscosity of less than about 5 centistokes at 25°C, whereas the cyclic silicones have viscosities of less than about 10 centistokes at 25°C. Highly preferred examples of volatile silicone oils include cyclomethicones of varying viscosities, e.g., Dow Corning 200, Dow Corning 244, Dow Corning 245, Dow Corning 344, and Dow Corning 345, (commercially available from Dow Corning Corp.); SF-1204 and SF-  
10 1202 Silicone Fluids (commercially available from G.E. Silicones), GE 7207 and 7158 (commercially available from General Electric Co.); and SWS-03314 (commercially available from SWS Silicones Corp.).

g. Relatively Polar, Non-volatile oils

The composition of the present invention may include relatively polar, non-volatile oils. The  
15 non-volatile oil is "relatively polar" as compared to the non-polar, volatile oil discussed above. Therefore, the non-volatile co-carrier is more polar (i.e., has a higher solubility parameter) than at least one of the non-polar, volatile oils. Relatively polar, non-volatile oils potentially useful in the present invention are disclosed, for example, in Cosmetics, Science, and Technology, Vol. 1, 27-104 edited by Balsam and Sagarin, 1972; U.S. Pat. Nos. 4,202,879 and 4,816,261.  
20 Relatively polar, non-volatile oils useful in the present invention are preferably selected from silicone oils; hydrocarbon oils; fatty alcohols; fatty acids; esters of mono and dibasic carboxylic acids with mono and polyhydric alcohols; polyoxyethylenes; polyoxypropylenes; mixtures of polyoxyethylene and polyoxypropylene ethers of fatty alcohols; and mixtures thereof.

h. Non-polar, Non-volatile oils

In addition to the liquids discussed above, the carrier for the cross-linked siloxane elastomer  
25 may optionally include non-volatile, non-polar oils. Typical non-volatile, non-polar emollients are disclosed, for example, in Cosmetics, Science, and Technology, Vol. 1, 27-104 edited by Balsam and Sagarin, 1972; U.S. Pat. Nos. 4,202,879 and 4,816,261. The non-volatile oils useful in the present invention are essentially non-volatile polysiloxanes, paraffinic  
30 hydrocarbon oils, and mixtures thereof.

2. 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. The "oil phase"  
can contain oil, silicone or mixtures thereof, and includes but is not limited to the oils and  
35 silicones described above in the section on water-in-oil emulsions. The distinction of whether the emulsion is characterized as an oil-in-water or silicone-in-water emulsions is a function of

whether the oil phase is composed of primarily oil or silicone. The water phase of these emulsions consists primarily of water, but can also contain various other ingredients such as those water phase ingredients listed in the above section on water-in-oil emulsion. The preferred oil-in-water emulsions 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 total composition.

In addition to a continuous water phase and dispersed oil or silicone phase, these oil-in-water compositions also comprise an emulsifier to stabilize the emulsion. Emulsifiers useful herein are well known in the art, and include nonionic, anionic, cationic, and amphoteric emulsifiers. Non-limiting examples of emulsifiers useful in the oil-in-water emulsions of this invention are given in McCutcheon's, Detergents and Emulsifiers, North American Edition (1986), U.S. Pat. No. 5,011,681; U.S. Pat. No. 4,421,769; and U.S. Pat. No. 3,755,560. Examples of suitable oil-in-water emulsion carriers are described in U.S. Pat. No. 5,073,371, and U.S. Pat. No. 5,073,372. An especially preferred oil-in-water emulsion, containing a structuring agent, hydrophilic surfactant and water, is described in detail hereinafter.

a. Structuring Agent

A preferred oil-in-water emulsion contains a structuring agent to assist in the formation of a liquid crystalline gel network structure. Without being limited by theory, it is believed that the structuring agent assists in providing rheological characteristics to the composition which contribute to the stability of the composition. The structuring agent may also function as an emulsifier or surfactant. Preferred compositions of this invention contain from about 0.5% to about 20%, more preferably from about 1% to about 10%, even more preferably from about 1% to about 5%, by weight of the composition, of a structuring agent.

The preferred structuring agents of the present invention include stearic acid, palmitic acid, stearyl alcohol, cetyl alcohol, behenyl alcohol, the polyethylene glycol ether of stearyl alcohol having an average of about 1 to about 21 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 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 stearyl alcohol having an average of about 21 ethylene oxide units (steareth-21), 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 stearic acid, palmitic acid, stearyl alcohol, cetyl alcohol, behenyl alcohol, steareth-2, steareth-21, and mixtures thereof.

b. Hydrophilic surfactant



The preferred oil-in-water emulsions contain 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.

Preferred hydrophilic surfactants are selected from nonionic surfactants. Among the nonionic surfactants that are useful herein are those that can be broadly defined as condensation products of long chain alcohols, e.g. C8-30 alcohols, with sugar or starch polymers, i.e., glycosides. These compounds can be represented by the formula (S)<sub>n</sub> O R wherein S is a sugar moiety such as glucose, fructose, mannose, and galactose; n is an integer of from about 1 to about 1000, and R is a C8-30 alkyl group. Examples of long chain alcohols from which the alkyl group can be derived include decyl alcohol, cetyl alcohol, stearyl alcohol, lauryl alcohol, myristyl alcohol, oleyl alcohol, and the like. Preferred examples of these surfactants include those wherein S is a glucose moiety, R is a C8-20 alkyl group, and n is an integer of from about 1 to about 9. Commercially available examples of these surfactants include decyl polyglucoside (available as APG 325 CS from Henkel) and lauryl polyglucoside (available as APG 600 CS and 625 CS from Henkel).

Other useful nonionic surfactants include the condensation products of alkylene oxides with fatty acids (i.e. alkylene oxide esters of fatty acids), the condensation products of alkylene oxides with 2 moles of fatty acids (i.e. alkylene oxide diesters of fatty acids), the condensation products of alkylene oxides with fatty alcohols (i.e. alkylene oxide ethers of fatty alcohols), the condensation products of alkylene oxides with both fatty acids and fatty alcohols [i.e. wherein the polyalkylene oxide portion is esterified on one end with a fatty acid and etherified (i.e. connected via an ether linkage) on the other end with a fatty alcohol]. Nonlimiting examples of these alkylene oxide derived nonionic surfactants include ceteth 6, ceteth 10, ceteth 12, cetareth 6, cetareth 10, cetareth 12, steareth 6, steareth 10, steareth 12, steareth-21, PEG 6 stearate, PEG 10 stearate, PEG 100 stearate, PEG 12 stearate, PEG 20 glyceryl stearate, PEG 80 glyceryl tallowate, PEG 10 glyceryl stearate, PEG 30 glyceryl cocoate, PEG 80 glyceryl cocoate, PEG 200 glyceryl tallowate, PEG 8 dilaurate, PEG 10 distearate, and mixtures thereof.

Still other useful nonionic surfactants include polyhydroxy fatty acid amide surfactants. An especially preferred surfactant corresponding to the above structure is coconut alkyl N methyl glucoside amide. Processes for making compositions containing polyhydroxy fatty acid amides are disclosed, for example in U.S. Patent No. 2,965,576; U.S. Patent No. 2,703,798, and U.S. Patent No. 1,985,424.

Preferred among the nonionic surfactants are those selected from the group consisting of steareth-21, cetareth-20, cetareth-12, sucrose cocoate, steareth-100, PEG-100 stearate, and mixtures thereof.

Other nonionic surfactants suitable for use herein include sugar esters and polyesters, 5 alkoxyated sugar esters and polyesters, C1-C30 fatty acid esters of C1-C30 fatty alcohols, alkoxyated derivatives of C1-C30 fatty acid esters of C1-C30 fatty alcohols, alkoxyated ethers of C1-C30 fatty alcohols, polyglyceryl esters of C1-C30 fatty acids, C1-C30 esters of polyols, C1-C30 ethers of polyols, alkyl phosphates, polyoxyalkylene fatty ether phosphates, fatty acid amides, acyl lactylates, and mixtures thereof. Nonlimiting examples of these emulsifiers 10 include: polyethylene glycol 20 sorbitan monolaurate (Polysorbate 20), polyethylene glycol 5 soya sterol, Steareth-20, Cetareth-20, PPG-2 methyl glucose ether distearate, Ceteth-10, Polysorbate 80, cetyl phosphate, potassium cetyl phosphate, diethanolamine cetyl phosphate, Polysorbate 60, glyceryl stearate, polyoxyethylene 20 sorbitan trioleate (Polysorbate 85), sorbitan monolaurate, polyoxyethylene 4 lauryl ether sodium stearate, polyglyceryl-4 15 isostearate, hexyl laurate, PPG-2 methyl glucose ether distearate, PEG-100 stearate, and mixtures thereof.

Another group of non-ionic surfactants useful herein are fatty acid ester blends based on a mixture of sorbitan or sorbitol fatty acid ester and sucrose fatty acid ester, the fatty acid in each instance being preferably C8-C24, more preferably C10-C20. The preferred fatty acid ester 20 emulsifier is a blend of sorbitan or sorbitol C16-C20 fatty acid ester with sucrose C10-C16 fatty acid ester, especially sorbitan stearate and sucrose cocoate. This is commercially available from ICI under the tradename Arlatone 2121.

Other suitable surfactants useful herein include a wide variety of cationic, anionic, zwitterionic, and amphoteric surfactants such as are known in the art and discussed more fully below. The 25 hydrophilic surfactants useful herein can contain a single surfactant, or any combination of suitable surfactants. The exact surfactant (or surfactants) chosen will depend upon the pH of the composition and the other components present.

Also useful herein are cationic surfactants, especially dialkyl quaternary ammonium compounds, examples of which are described in U.S. Patent 5,151,209; U.S. Patent 5,151,210; 30 U.S. Patent 5,120,532; U.S. Patent 4,387,090; U.S. Patent 3,155,591; U.S. Patent 3,929,678; U.S. Patent 3,959,461; McCutcheon's, Detergents & Emulsifiers, (North American edition 1979) M.C. Publishing Co.; and Schwartz, et al., Surface Active Agents, Their Chemistry and Technology, New York: Interscience Publishers, 1949.

Nonlimiting examples of these cationic emulsifiers include cetearyl olivate, sorbitan olivate, 35 stearamidopropyl PG-dimonium chloride phosphate, behenamidopropyl PG dimonium chloride, stearamidopropyl ethyldimonium ethosulfate, stearamidopropyl dimethyl (myristyl

acetate) ammonium chloride, stearamidopropyl dimethyl ceteryl ammonium tosylate, stearamidopropyl dimethyl ammonium chloride, stearamidopropyl dimethyl ammonium lactate, and mixtures thereof. Especially preferred is behenamidopropyl PG dimonium chloride.

5 Nonlimiting examples of quaternary ammonium salt cationic surfactants include those selected from cetyl ammonium chloride, cetyl ammonium bromide, 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, cetyl trimethyl ammonium chloride, cetyl trimethyl 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 ditallow dimethyl ammonium chloride, dicetyl ammonium chloride, dicetyl ammonium bromide, dilauryl ammonium chloride, dilauryl ammonium bromide, distearyl ammonium chloride, distearyl ammonium bromide, dicetyl methyl ammonium chloride, dicetyl methyl ammonium bromide, dilauryl methyl ammonium chloride, dilauryl methyl ammonium bromide, distearyl methyl ammonium chloride, distearyl methyl 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 C16 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 methyl sulfate, di(hydrogenated tallow) dimethyl ammonium chloride, di(hydrogenated tallow) dimethyl ammonium acetate, ditallow dipropyl ammonium phosphate, ditallow dimethyl ammonium nitrate, di(coconutalkyl)dimethyl ammonium chloride, di(coconutalkyl)dimethyl ammonium bromide, tallow ammonium chloride, coconut ammonium chloride, 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 behenamidopropyl PG dimonium chloride, dilauryl dimethyl ammonium chloride, distearyl dimethyl ammonium chloride, dimyristyl dimethyl ammonium chloride, dipalmityl dimethyl ammonium chloride, distearyl dimethyl ammonium chloride, stearamidopropyl PG-dimonium chloride phosphate, stearamidopropyl ethyldiammonium ethosulfate, stearamidopropyl dimethyl (myristyl acetate)

ammonium chloride, stearamidopropyl dimethyl cetearyl ammonium tosylate, stearamidopropyl dimethyl ammonium chloride, stearamidopropyl dimethyl ammonium lactate, and mixtures thereof.

5 Still more preferred cationic surfactants are those selected from behenamidopropyl PG dimonium chloride, dilauryl dimethyl ammonium chloride, distearyl dimethyl ammonium chloride, dimyristyl dimethyl ammonium chloride, dipalmityl dimethyl ammonium chloride, and mixtures thereof.

10 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 maintain to enhance physical and chemical stability, especially when such a combination contains ionic and/or highly polar solvents.

15 A wide variety of anionic surfactants can also be useful herein. Nonlimiting examples of anionic surfactants include the alkoyl isethionates, and the alkyl and alkyl ether sulfates. The reaction products of fatty acids esterified with isethianonic acid and neutralized, i.e. the alkoyl isethionates typically have the formula  $\text{RCO OCH}_2\text{CH}_2\text{SO}_3\text{M}$  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. For example, the fatty acids are derivated from coconut or palm kernel oil. Nonlimiting examples of these isethionates include those alkoyl isethionates selected from ammonium cocoyl isethionate, sodium cocoyl isethionate, sodium lauroyl isethionate, sodium stearyl isethionate, and mixtures thereof. Also suitable are salts of fatty acids, amids of methyl taurides. Other similar anionic surfactants are described in U.S. Pat. Nos 2,486,921; 2,486,922 and 2,396,278.

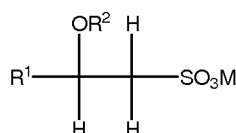
25 The alkyl and alkyl ether sulfates typically have the respective formulae  $\text{ROSO}_3\text{M}$  and  $\text{RO}(\text{C}_2\text{H}_4\text{O})_x\text{SO}_3\text{M}$ , wherein R is alkyl or alkenyl of from about 10 to about 30 carbon atoms, x is from about 1 to about 10, and M is a water soluble cation such as ammonium, alkanolamines such as triethanolamine, monovalent metals, such as sodium and potassium, and polyvalent metal cations such as magnesium and calcium. Preferably, R has from about 8 to about 18 carbon atoms, more preferably from about 10 to about 16 carbon atoms, even more preferably from about 12 to about 14 carbon atoms, in both the alkyl and alkyl ether sulfates.

30 The alkyl ether sulfates are typically made as condensation products of ethylene oxide and monohydric alcohols having from about 8 to about 24 carbon atoms. The alcohols can be synthetic or they can be derived from fats, e.g., coconut oil, palm kernel oil, tallow. Lauryl alcohol and straight chain alcohols derived from coconut oil or palm kernel oil are preferred. Such alcohols are reacted with between about 0 and about 10, preferably from about 2 to about 35 5, more preferably about 3, molar proportions of ethylene oxide, and the resulting mixture of

molecular species having, for example, an average of 3 moles of ethylene oxide per mole of alcohol, is sulfated and neutralized

Another suitable class of anionic surfactants are the water soluble salts of the organic, sulfuric acid reaction products of the general formula:  $R_1 SO_3 -M$  wherein  $R_1$  is chosen from the group including 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 described hereinbefore. 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 surfactants suitable for use in the compositions are the succinates, examples of which include disodium N-octadecylsulfosuccinate; disodium lauryl sulfosuccinate; diammonium lauryl sulfosuccinate; tetrasodium N-(1,2-dicarboxyethyl)-N-octadecylsulfosuccinate; diamyl ester of sodium sulfosuccinic acid; dihexyl ester of sodium sulfosuccinic acid; and dioctyl esters of sodium sulfosuccinic acid. Other suitable anionic surfactants include olefin sulfonates having about 10 to about 24 carbon atoms. In addition to the true alkene sulfonates and a proportion of hydroxy alkanesulfonates, the olefin sulfonates can contain minor amounts of other materials, such as alkene disulfonates depending upon the reaction conditions, proportion of reactants, the nature of the starting olefins and impurities in the olefin stock and side reactions during the sulfonation process. A non limiting example of such an alpha olefin sulfonate mixture is described in U.S. Patent 3,332,880.

Another class of anionic surfactants suitable for use in the compositions are the beta-alkyloxy alkane sulfonates. These surfactants conform to the formula



where  $R_1$  is a straight chain alkyl group having from about 6 to about 20 carbon atoms,  $R_2$  is a lower alkyl group having from about 1 to about 3 carbon atoms, preferably 1 carbon atom, and  $M$  is a water soluble cation as described hereinbefore. 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.

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 C8 - C18) 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  $RN[CH_2]_mCO_2M]_2$  and  $RNH(CH_2)_mCO_2M$  wherein m is from 1 to 4, R is a C8 C22 alkyl or alkenyl, and M is H, alkali metal, alkaline earth metal ammonium, or alkanolammonium. Preferred amphoteric surfactants for use in the present invention include cocoamphoacetate, cocoamphodiacetate, lauroamphoacetate, lauroamphodiacetate, and mixtures thereof. Also included are imidazolinium and ammonium derivatives. Specific examples of suitable amphoteric surfactants include sodium 3 dodecyl aminopropionate, sodium 3 dodecylaminopropane 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 U.S. Patent 2,438,091; and the products sold under the tradename "Miranol" and described in U.S. Patent 2,528,378. Other examples of useful amphoteric surfactants include phosphates, such as coamidopropyl PG dimonium chloride phosphate (commercially available as Monaquat PTC, from Mona Corp.).

Zwitterionic surfactants suitable for use in the composition are well known in the art, and include those surfactants broadly described as derivatives of aliphatic quaternary ammonium, phosphonium, and sulfonium compounds, in which the aliphatic radicals can be straight or branched chain, and wherein one of the aliphatic substituents contains from about 8 to about 18 carbon atoms and one contains an anionic group such as carboxy, sulfonate, sulfate, phosphate or phosphonate. Zwitterionics such as betaines are preferred. Examples of betaines include the higher alkyl betaines, such as coco dimethyl carboxymethyl betaine, lauryl dimethyl carboxymethyl betaine, lauryl dimethyl  $\alpha$ -carboxyethyl betaine, cetyl dimethyl carboxymethyl betaine, cetyl dimethyl betaine (available as Lonzaine 16SP from Lonza Corp.), lauryl bis (2 hydroxyethyl) carboxymethyl betaine, stearyl bis (2 hydroxypropyl) carboxymethyl betaine, oleyl dimethyl  $\gamma$ -carboxypropyl betaine, lauryl bis (2 hydroxypropyl) $\alpha$ -carboxyethyl betaine, coco dimethyl sulfopropyl betaine, stearyl dimethyl sulfopropyl betaine, lauryl dimethyl sulfoethyl betaine, lauryl bis (2 hydroxyethyl) sulfopropyl betaine, and amidobetaines and amidosulfobetaines (wherein the  $RCONH(CH_2)_3$  radical is attached to the nitrogen atom of the betaine), oleyl betaine (available as amphoteric Velvetex OLB 50 from Henkel), and cocamidopropyl betaine (available as Velvetex BK 35 and BA 35 from Henkel).

Other useful amphoteric and zwitterionic surfactants include the sultaines and hydroxysultaines such as cocamidopropyl hydroxysultaine (available as Mirataine CBS from Rhone Poulenc), and the alkanoyl sarcosinates corresponding to the formula  $RCON(CH_3)CH_2CH_2CO_2M$  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.

c. Water Emollient

The preferred oil-in-water emulsion contains 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 contain a dermatologically acceptable emollient. Such compositions preferably contain from about 1% 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 is 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 about 0.001 to about 30%, more preferably from about 0.01 to about 20%, still more preferably from about 0.1 to about 10%, e.g., 5%.

Lotions and creams according to the present invention generally contain a solution carrier system and one or more emollients. Lotions and creams typically contain from about 1% to about 50%, preferably from about 1% to about 20%, of emollient; from about 50% to about 90%, preferably from about 60% to about 80%, water; the polypeptides, according to the invention, and the additional skin care active (or actives) in the above described amounts. Creams are generally thicker than lotions due to higher levels of emollients or higher levels of thickeners.

Ointments of the present invention may contain 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 contain 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 contain from about 2% to about 10% of an emollient; from about 0.1% to about

2% of a thickening agent; and the polypeptide and the additional skin care active (or actives) in the above described amounts.

Compositions of this invention useful for cleansing ("cleansers") can be formulated with a suitable carrier, e.g., as described above, and preferably comprise from about 1% to about 90%,  
5 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 detergency art. Nonlimiting examples of possible surfactants include isoceteth 20, sodium methyl cocoyl taurate, sodium methyl oleoyl taurate, and sodium lauryl sulfate.  
10 See U.S. Patent No. 4,800,197 for exemplary surfactants useful herein. 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. The cleansing compositions can optionally contain, at their art-established levels, other materials which are conventionally used in cleansing compositions.

15 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  
20 smooth, even appearance to the skin. Foundations of the present invention include a dermatologically acceptable carrier 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 WO96/33689, and GB 2274585.

### 25 **B. Orally Acceptable Carrier**

The compositions of the present invention can also comprise an orally acceptable carrier if they are to be ingested. Any suitable orally ingestible carrier or carrier form, as known in the art or otherwise, can be used. Non-limiting examples of oral personal care compositions can include, but are not limited to, tablets, pills, capsules, drinks, beverages, syrups, granules, powders,  
30 vitamins, supplements, health bars, candies, chews, and drops.

### **C. Injectable Liquid**

The compositions of the present invention can also comprise a liquid that is acceptable for injection in and/or under the skin if the composition is to be injected. Any suitable acceptable liquid as known in the art or otherwise can be used.

## 35 **III COMPOSITION PREPARATION**



The compositions useful for the methods of the present invention are generally prepared by conventional methods such as are known in the art of making topical and oral compositions and compositions for injection. Such methods typically can 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.

The physical form of the compositions according to the invention is not important: creams, lotions, ointments, milks, gels, emulsions, dispersions, solutions, suspensions, cleansers, foundations, anhydrous preparations (sticks, in particular lipsticks, body and bath oils), shower and bath gels, shampoos and scalp treatment lotions, cream or lotion for care of the skin or hair, sun-screen lotions, milks or creams, artificial suntan lotions, creams or milks, shaving creams or foams, aftershave lotions, make-up, mascaras or nail varnishes, lipsticks, skin "essences," serums, adhesive or absorbent materials, transdermal patches, powders, emollient lotion, emollient milk, emollient cream, sprays, oils for the body and the bath, foundation tint bases, pomade, emulsion, colloid, compact or solid suspension, pencil, sprayable formulation, crossable, rouge, blush, eyeliner, lipliner, lip gloss, facial or body powder, mousse, styling gels, nail conditioner, brush on formulation, lip balms, skin conditioners, cold creams, moisturizers, hair sprays, soaps, body scrubs, exfoliants, astringents, depilatories and permanent waving solutions, antidandruff formulations, anti-sweat and antiperspirant compositions, shaving, pre-shaving and after-shaving products, moisturizers, deodorants, cold creams, cleansers, skin gels, rinses, nose sprays and so on. These compositions can also be presented in the form of lipsticks intended to apply colour or to protect the lips from cracking, or of make-up products for the eyes or tints and tint bases for the face. Compositions in accordance with the invention include cosmetics, personal care products and pharmaceutical preparations. One can also consider a composition in the shape of foam or in the form of compositions for aerosol also including a propellant agent under pressure.

Cosmetic compositions may also be for orodental use, for example, toothpaste. In that case, the compositions may contain the usual adjuvants and additives for compositions for oral use and, in particular, surfactants, thickening agents, moisturizing agents, polishing agents such as silica, various active substances such as fluorides, particularly sodium fluoride, and, possibly, sweetening agents such as saccharin sodium.

The compositions according to the present invention may be in the form of solution, dispersion, emulsion, paste, or powder. They may be included individually or as a premix in vehicles such as macro-, micro-, or nanocapsules, macro-, micro- or , nanospheres, liposomes, oleosomes or chylomicrons, macro-, micro-, or nanoparticles or macro-, micro or nanosponges. They may also be adsorbed on organic polymer powders, talcs, bentonites, or other inorganic or organic supports.

5 Glaucine or plant extract containing it, and composition according to the invention may be used in any form whatsoever, or in a form bound to or incorporated in or absorbed in or adsorbed on macro-, micro-, and nanoparticles, or macro-, micro-, and nanocapsules, for the treatment of textiles, natural or synthetic fibres, wools, and any materials that may be used for clothing or underwear for day or night intended to come into contact with the skin, such as tights, underclothes, handkerchiefs, or cloths, to exert their cosmetic effect via this skin/textile contact and to permit continuous topical delivery.

**IV METHODS FOR TREATING ADIPOCYTE TISSUE CONDITION**

10 The present invention covers a cosmetic method of stimulating adipocyte reversion, said cosmetic method comprising the step of topically applying to the skin of mammal in need of treatment, a safe and effective amount of glaucine, at least once a day for a period of time at least sufficient to provide adipocyte reversion of that portion of human skin.

15 The present invention also relates to the use of glaucine or a plant extract containing it, to manufacture a medicament stimulating the adipocyte reversion, particularly for a slimming treatment of weight overloads of the thighs, the hips and the belly skin firming, and particularly to prevent and/or to treat cellulite or orange peel and/or to refine contours of the face, and/or to treat fat deposits and “spare tires”.

**INDUSTRIAL APPLICABILITY**

The present invention relates to the chemical, medical, cosmetic and personal care industries.

20 **V 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. As an illustration of the invention, several cosmetic formulae will be cited. The formulae are representative of, but do not restrict, the invention.

**A. Formulae examples**

1) Slimming cream

Ingredients	% by weight
<b>Part A</b>	
Demineralized water	Qs 100.0000
Carbopol Ultrez 10	0.4000
<b>Part B</b>	
Glycerin	10.0000
Preservatives	Qs

<b>Part C</b>	
Hydroxyethyl cellulose	0.2000
<b>Part D</b>	
Crillet 1	2.0000
Crodamol OP	4.0000
DC 200	3.0000
Pemulen TR2	0.2000
<b>Part E</b>	
Potassium Sorbate	0.1000
<b>Part F</b>	
Demineralized water	6.0000
NaOH 30%	0.6000
<b>Part G</b>	
Ethanol	3.0000
<b>Part H</b>	
Glaucine	0.0025
<b>Part I</b>	
Fragrance	qs

- Method:** Let inflate Ultrez 10 in the water 30 mn. Heat the part B mixed in 60°C until dissolution. Add the part C in the part B and mix. Then add the part B+C in the part A under agitation. Let inflate 1 hour. Add the part D under agitation. At the same moment, add the part E, under agitation. Neutralize with the part F, then homogenize well. Add the part G and homogenize. Then, add the part H and the part I. Homogenize.

2) Slimming and firming up cream

<b>Ingredients</b>	<b>% by weight</b>
<b>Part A</b>	
Demineralized water	qsp 100%
Ultrez 10	0.40
<b>Part B</b>	
Glycerin	5.00
Phenova	0.80
<b>Part C</b>	
Crodamol OP	4.00
Crodacol CS90	0.50

Crodamol ML	0.30
Crillet 1	1.00
<b>Part D</b>	
Pemulen TR2	0.20
DC 345	2.00
<b>Part E</b>	
Potassium Sorbate	0.10
<b>Part F</b>	
NaOH 38%	0.60
Demineralized water	6.00
<b>Part G</b>	
Glaucine	0.01
<b>Part H</b>	
Matrixyl 3000®	3.00
<b>Part I</b>	
Fragance	qs

Matrixyl 3000® is a product sold by SEDERMA (US 2004/013667) stimulating the neosynthesis of macromolecules involved in the extracellular matrix.

**Method:** Part A: disperse Ultrez 10 in the water and let swell 20 minutes. Mix the Part B and heat it to 60°C until dissolution. Add the Part B to the Part A by shaking. Heat the Part (A+B). Weigh the Part C and heat it at 75°C. Add the Part C to the Part (A+B) by shaking. Homogenize carefully, then add the Part D. Add the Part E in approximately 50°C; neutralize with the Part F. Add the Parts G and H at approximately 35°C; then add the Part I. pH ~6,30.

3) Slimming gel against « orange peel skin »

Ingredients	% by weight
<b>Part A</b>	
Demineralized water	qs 100%
Ultrez 10	0.400
<b>Part B</b>	
Butylene glycol	5.000
Phenova	0.800
<b>Part C</b>	
Crill 3	1.200
Crillet 3	3.000
DC 200	2.000

Crodamol IPM	5.000
Crodamol W	0.300
CrodamolGTCC	5.000
Crodacol CS90	2.000
<b>Part D</b>	
Carbopol 980 2%	10.000
DC 345	2.000
<b>Part E</b>	
Potassium sorbate	0.100
<b>Part F</b>	
NaOH 38%	0.200
Demineralized water	2.000
<b>Part G</b>	
Lipocare®	3.000
<b>Part H</b>	
Glaucine	0.005
<b>Part I</b>	
Fragrance	qs

Lipocare® is a product sold by SEDERMA particularly used to the orange peel skin treatment.

- Method** : Homogenize the Part B and pour it into the Part A. Disperse Ultrez 10 in the water and let swell 20 minutes. Mix the Part B and heat it to 60°C until dissolution. Add the Part B to the Part A by shaking. Heat the Part (A+B). Weigh the Part C and heat it at 75°C. Add the Part C to the Part (A+B) by shaking. Homogenize carefully, then add the Part D. Add the Part E in approximately 50°C; neutralize with the Part F. Add the Parts G and H at approximately 35°C. Then, add the Part I.

4) Lifting for face and neck

<b>Ingredients</b>	<b>% by weight</b>
<b>Part A</b>	
Demineralized water	qs 100%
Ultrez 10	0.30
<b>Part B</b>	
Glycerin	5.00
Phenova	0.80
<b>Part C</b>	

Potassium sorbate	0.10
<b>Part D</b>	
Crodamol GTCC	4.00
Crodacol CS90	0.50
Crodamol ML	0.30
Crillet 1	1.00
<b>Part E</b>	
Pemulen TR2	0.20
DC 345	2.00
<b>Part F</b>	
NaOH 38%	0.50
Demineralized water	5.00
<b>Part G</b>	
Pleuymincyl®	3.00
<b>Part H</b>	
Glaucine	0.005
<b>Part I</b>	
Fragrance	qs

Pleuymincyl® is a product sold by SEDERMA which firms up the tissue and moisturizes the skin.

- Method:** Part A: disperse Ultrez 10 in the water and let swell 10 minutes. Mix. Add the Part B to the Part A in the bain-marie to 75°C. Heat the Part D to 75°C, then add the Part E to the Part D, then add to the Part (A+B). Add the Part C. Homogenize and add the Part F. Add the Part G, then the Part H at about 40°C. Add the Part I.

5) Slimming cream against stretch marks

Ingredients	% by weight
<b>Part A</b>	
Demineralized water	qs 100%
Ultrez 10	0.40
<b>Part B</b>	
Glycerin	5.00
Phenova	0.80
<b>Part C</b>	
Crodamol OP	4.00
Crodacol CS90	0.50

Crodamol ML	0.30
Crillet 1	1.00
<b>Part D</b>	
Pemulen TR2	0.20
DC 345	2.00
<b>Part E</b>	
Potassium sorbate	0.10
<b>Part F</b>	
NaOH 38%	0.60
Demineralized water	6.00
<b>Part G</b>	
Glaucine	0.50
<b>Part H</b>	
Darutoside®	3.00
<b>Part I</b>	
Matrixyl 3000®	3.00
<b>Part J</b>	
Fragrance	qs

Matrixyl 3000 is a product sold by SEDERMA (US 2004/013667) stimulating the neosynthesis of macromolecules involved in the extracellular matrix.

Darutoside® is a product sold by SEDERMA (FR 2723314) particularly used to the stretch mark treatment.

- 5 **Method:** Part A: disperse Ultrez 10 in the water and let swell 20 minutes. Mix the Part B and heat it at 60°C until dissolution. Add the Part B to the Part A by shaking. Heat the Part (A+B). Weigh the Part C and heat it at 75°C. Add the Part C to the Part (A+B) by shaking. Homogenize carefully, and then add the Part D. Add the Part E at approximately 50°C; neutralize with the Part F. Add the Parts G, H and I at approximately 35°C; pH 6,30. Add the Part J.

10

6) Tonic body milk

<b>Ingredients</b>	<b>% by weight</b>
<b>Part A</b>	
Demineralized water	qsp 100%
Ultrez 10	0.40
<b>Part B</b>	
Crodafos CS 20 acid	3.00

Crodamol AB	5.00
Crodamol GTCC	10.00
<b>Part C</b>	
Glycerin	5.00
Mixed Parabens	0.20
<b>Part D</b>	
Potassium sorbate	0.10
<b>Part E</b>	
NaOH 38%	0.50
Demineralized water	3.00
<b>Phase F</b>	
Glaucine	0.50
<b>Part G</b>	
Vexel ®	3.00
<b>Part H</b>	
Fragance	qs

Vexel ® is a tonic and firming up product sold by SEDERMA (FR 2654619).

**Method:** Part A: disperse Ultrez 10 in the water and let swell 15 minutes. Mix the Part B and heat it at 75°C. Add the Part C to the Part A by heating in the bain-marie. Pour the Part (A+C) into the Part B under agitation. Add the Parts D and E at approximately 50°C. Add the Parts F and G at approximately 35°C. Homogenize carefully, and then add the Part H.

5

7) Firming up tonic for the body

<b>Ingredient</b>	<b>% by weight</b>
<b>Part A</b>	
Demineralized water	Qs 100
Citric Acid	0.1150
Citrate Trisodique	0.6000
<b>Part B</b>	
Methyl paraben	0.2000
Procetyl AWS	2.0000
<b>Part C</b>	
Ethanol	10.0000
Fragance	0.3000
PEG-60 Almond glycerid	1.0000
<b>Part D</b>	



Birch sap™	3.0000
<b>Part E</b>	
Glaucine	0.0001
Caffeine	1.0000

Birch sap is a tonic and firming up product sold by SEDERMA (FR 0111967).

**Method** : Part A: weigh and mix by shaking. Add the Part B to the Part A. Add the Part C to the Part (A+B). Add the Part D then the Part E. Homogenise carefully.

8) Slimming Fluid for the body

<b>Ingred ients</b>	<b>% by weight</b>
<b>Part A</b>	
Demineralized water	qsp 100%
Ultrez 10	0.40
<b>Part B</b>	
Crill 3	2.40
Crillet 3	2.00
DC 200	2.00
Crodamol GTCC	4.00
<b>Part C</b>	
Butylene glycol	5.00
Methyl Paraben	0.20
<b>Part D</b>	
Potassium sorbate	0.10
<b>Part E</b>	
Osmocide®	2.00
<b>Part F</b>	
NaOH 30%	0.19
Demineralized water	2.00
<b>Part G</b>	
Lipocare™	3.00
<b>Part H</b>	
Glaucine	2.50
<b>Part I</b>	
Fragance	qs

- 5 Osmocide® is an antibacterial product sold by SEDERMA (WO 97/47310) having osmotic proprieties.

Lipocare® is a product sold by SEDERMA (WO 98/43607) having a lipolytic action thanks to the activation of proteins G.

- Method:** Part A: disperse Ultrez 10 in the water and let swell 30 minutes. Heat the Part B at 75°C in the bain-marie. Heat the Part A at 75°C in the bain-marie. Heat the Part C at 60°C.
- 5 Add the Part B to the Part A under agitation. At this moment add the Parts C and D to the Part (A+B). Homogenise. At approximately 40°C, add the Parts E then F. At approximately 35°C, add the Parts G and H. Homogenise then add the Part I.

9) Spray effect « smoothing Flash »

Ingredients	% by weight
<b>Part A</b>	
Demineralized water	Qs100
NaOH 30%	0.20
Potassium sorbate	0.10
<b>Part B</b>	
Volpo CS 20	3.00
Crodafos CS 20 acid	3.00
Crodamol GTCC	3.00
DC 345	2.00
<b>Part C</b>	
Glycerin	5.00
Preservatives	2.00
<b>Part D</b>	
Sorbitol 60%	3.00
VEXEL®	3.00
<b>Part E</b>	
Glucine	0.30
<b>Part F</b>	
Fragrance	qs

Vexel ® is a tonic and firming up product sold by SEDERMA (FR 2654619).

- 10 **Method:** Heat the Part B at 75°C. Melt the Part C until dissolution, then add the part A. Heat the Part (A+C) at 75°C in the bain-marie. Mix. Add the Part B to the Part (A+C) under agitation. Add the Parts D, E then F at approximately 35°C.

**B. In vitro tests:**

- 1) Stimulation of lipolysis :

Lipolytic effect, i.e the degradation of triglycerides in glycerol and fatty acids has been studied on classical Cells 3T3-L1.

5 These cells are seeded (multiplication) then differentiated in classical way (differentiation cocktail, followed by a medium allowing maturation); at this step, the pre-adipocytes assume an adipocyte morphotype presenting numerous lipid vesicles.

At the differentiated stage, these cells are incubated in the presence of glaucine at various concentrations. A positive control is conducted using 1  $\mu$ M isoproterenol.

10 After incubation for 3 hours 30, the quantity of glycerol was determined by spectrophotometry ( $\lambda = 340$  nm), using an enzymatic method, and compared with the values of the untreated control cells.

The percentages reported in table 1 were determined relative to untreated control cells and the test was validated by comparison with the positive control in the presence of isoproterenol.

15 Table 1 : Change vs. control in the quantity of glycerol in differentiated adipocytes 3T3-L1 in the presence of glaucine.

Glaucine concentration ( $\mu$ M)	% glycerol released by adipocytes 3T3-L1	Significance vs. control
24	+25.33	$p < 0.01$
30	+35.80	$p < 0.01$
45	+65.20	$p < 0.01$
75	+86.50	$p < 0.01$
Positive control (1 $\mu$ M IP)	+343	$p < 0.01$

As expected, the positive control (1  $\mu$ M isoproterenol) shows marked stimulation with the observed value of +343%.

20 In presence of glaucine, a dose-dependent effect of the glycerol release is observed. With a glaucine concentration of 24 $\mu$ M, the glycerol release is low (+25.3%) but significant, it increases to achieve, with a glaucine concentration of 75 $\mu$ M, a stimulation of lipolysis of 86,5 % with regard to the untreated control cells.

During a similar test realised on human pre-adipocytes (culture, differentiation induction by a differentiation cocktail, then incubation with glaucine for 3 hours), we also observe a lipolytic activity of the glaucine by glycerol release on human adipocytes.

25 2) Inhibition of the adipocyte differentiation

To estimate the capacity of the glaucine to inhibit the adipocyte differentiation, and thus the formation of the mature adipocytes, we measure the accumulation of neutral lipids by using the specific coloration Oil Red O.

5 3T3-L1 cells are seeded and cultivated during 4 days (multiplication). Follow a differentiation phase (incubation with a differentiation cocktail) in presence of glaucine at different concentrations, then a maturation phase still in presence of glaucine (maturation cocktail). At the end of this period, cells are washed, fixed and stained with red oil. Quantification was conducted by image analysis of the area of the cell layer stained in red.

10 The percentages of surface occupied by the red oil, as reported in table 2, have been established with regard to control cells untreated with the glaucine and the essay validated by comparison to a positive control of antidifferentiation (1.2. 10<sup>-2</sup>%).

Table 2 : Change of the quantity of accumulated lipids in 3T3-L1 cells in presence of glaucine.

Glaucine Concentration (10 <sup>-3</sup> %)	% change of the area of the cell layer stained red	Significance vs. control
1	- 44	p< 0.01
1.5	- 65	p< 0.01
2.5	- 96	p< 0.01
Antidifferenciation control	positive - 88	p< 0.01

15 We observe a decrease of coloring by the red oil of neutral lipids of lipidic droplets. The results show a significant decrease of the quantity of lipids (-44 %) as from the concentration of glaucine at 10<sup>-3</sup> %. The glaucine restricts the accumulation of lipids within adipocytes and inhibits the formation of the mature adipocytes in a dose-dependent manner.

3) Reversion of the adipocyte morphotype

a) Lost in adipocytes on a 3T3-L1 differentiated culture.

20 3T3-L1 cells have been seeded and differentiated according a classical way (multiplication, differentiation and maturation), then incubated in presence of glaucine at various concentrations during 6 days. After this period of incubation of 6 days, the cells are washed, fixed and stained with red oil. Cells are numerically photographed then the red coloring quantified by analysis of image.

25 Quantification of red oil's incorporation in the cell layer was reported in the table 3, a control was established with regard to 3T3-L1 differentiated control cells but untreated the glaucine.

Table 3 : Quantification of red oil incorporated in the cell layer

Glaucine Concentration ( $10^{-3}\%$ )	% of the area of the cell layer stained red
0 (control)	37.46
1	32.24
1.5	19.56
2.5	6.06

We observe a dose-dependent decrease of the incorporation of the red oil in the layer. Glaucine can reduce the proportion of differentiated cells.

5 b) Evolution of the morphotype of 3T3-L1 differentiated: observations in the microscope.

3T3-L1 cells have been seeded and differentiated according a classical way (multiplication, differentiation and maturation), then incubated or not (control) in presence of glaucine ( $2.5 \cdot 10^{-3}\%$ ). The cells are observed under the microscope for 72 hours.

10 The images obtained show that the mature adipocytes in the control culture continued to grow and store lipids: polyhedral appearance with a clearly visible central nucleus; the cell swell with lipid vesicles. The nucleus becomes invisible and the cell acquired a spheroidal shape at time point 72 hours.

15 In the presence of glaucine, cells are still loaded with lipids at time point 24h, then gradually “shrink” to time point 48h, a very marked retraction is observed and, at time point 72 h only one cell membrane remained visible. The remainder of the cell layer consists in flattened, scarcely visible cells.

4) Involution of adipose tissue and reconstruction of mesenchymatous tissue

a) Appearance of a fibroblastic basement layer: observations in the microscope.

20 3T3-L1 cells have been seeded and differentiated according a classical way (multiplication, differentiation and maturation), then incubated or not (control) in presence of glaucine ( $2.5 \cdot 10^{-3}\%$ ), at various concentrations during 6 days. After 6 days, the control cell layer shows confluent adipocytes that are highly differentiated and loaded with lipid droplets. The cell layers formed in the presence of glaucine have a different appearance and are composed of cells with mixed adipocytes fibroblast-like morphology (glaucine  $1.5 \cdot 10^{-3}\%$ ), or a fully fibroblast-like morphotype (glaucine  $2.5 \cdot 10^{-3}\%$ ). Thus, in the presence of glaucine, a complete change in morphotype was observed: 100% of the adipocytes became a cell layer consisting in 100% fibroblast-like cells which is not a storage tissue.

25 b) fibroblastic phenotype neoformed tissu in presence of glaucine

In a collagen raft contraction test, cells with the adipocyte morphotype are not able to generate tensile fibers as do cells with a fibroblast-like morphotype. The collagen support is therefore not deformed.

3T3-L1 cells have been seeded, brought in contact with a differentiation cocktail then in contact with a medium allowing maturation. Glaucine is brought in contact with the cells in these two last steps. The cells were trypsinized, counted, and integrated in a collagen gel. The contraction of the gel is followed macroscopically.

Contraction of the collagen gels is reported in table 4 below. A control is established with respect to 3T3-L1 differentiated control cells but untreated with glaucine.

Table 4 : Contraction of the collagen gels by 3T3-L1 differentiated cells treated with glaucine

Glaucine Concentration $\times 10^{-3}\%$	% contraction of the collagen gels
0 (control)	0
2.25	27
2.50	30

The cell layers derived from the control culture induced do not present any change in the size of the collagen raft. By contrast, a dose-dependent contraction is obtained with glaucine. The maximum effect (-30%) is obtained with a concentration of  $2.5 \cdot 10^{-3}\%$  glaucine.

Thus, thanks to these different in vitro tests, we could observed the effects of glaucine on: the inhibition (measured and displayed) of the differentiation of pre-adipocytes into mature adipocytes, the lipolysis (measured and displayed), accentuated over time, accompanied by reversion of the adipocyte phenotype and on a selective pressure (measured and displayed) in favor of the replacement of the adipose tissue by a mesenchymatous tissue whose fibroblasts are able to contract a collagen support.

**C. In vivo tests**

1) In vivo test: anti fat deposits effect

These clinical tests were realised with the slimming cream formulae presented in example 1.

The *in vivo* efficacy studies of PA1 were conducted on a panel of 17 female subjects.

The analysis of the skin surface was conducted using interference fringe topometry consisting of an analysis of the optical deformation of the fringe projection by the skin surface under laser illumination (FOITS method).

a) Principle

The thighs of the subjects are pinched by a contention system with a spring that applied a constant force. A measurement zone is delimited precisely in order to enable repositioning at each measurement time point. Thus, the macro-relief of the skin can be assessed visually by taking photographs under acute-incidence-angle light and quantitatively analyzed by fringe

projection (FOITS). The FOITS method thus enables investigation of the deformation of the skin surface without direct contact with the subject.

b) Protocol

*Inclusion criteria:* Age between 18 and 50 years, Caucasian subjects, presenting steatomery of the thighs, body mass index (BMI) between 20 and 26 kg/m<sup>2</sup>, stable weight for at least 3 months, no slimming diet in the 3 months preceding the study.

The 17 volunteers apply twice daily on only one thigh the glaucine product formulated in a fluid cream (example 1) during 56 days.

The treated thigh is either the left one or the right one, depending on randomization. Each subject thus acts as his own control thanks to the untreated thigh.

c) Results

The product was perfectly well tolerated by all the subjects.

Twenty volunteers took part in this study. The surface of the fat deposits was investigated in terms of two parameters: mean roughness (which reflects all the deformations in bumps and hollows on the analyzed surface) and maximum amplitude of the most marked fat deposits.

At T<sub>0</sub>, there was no significant difference between the left and right thighs.

Table 5 : Mean change in roughness after 28 and 56 days

	Thigh treated with glaucine			Untreated thigh		
	J0	J28	J56	J0	J28	J56
Roughness (x 10 <sup>-4</sup> )	1058**	1047**	874**	1032	1061	1048
Mean change %		-1.1	-17.4		+2.8	+1.5
Maximum change %, in n = 3 subjects		-11%	-43%			
Significance vs. D0		ns	p< 0.01		ns	ns

(\*\*) : n=17

While the control thigh was unchanged or showed a tendency to increased roughness, the treated thigh showed a very significant decrease in roughness. The improvement was progressive and became highly significant after 56 days (p < 0.01).

The decrease in roughness, the parameter reflecting the hollows and bumps related to the steatomery, was, on average, -17.4% after 56 days. For certains responders, roughness decreased by -11% after 28 days and -43% after 56 days.

Table 6 : change of the maximum amplitude of the most marked fat deposits

	Thigh treated with glaucine			Untreated thigh		
	J0	J28	J56	J0	J28	J56

Amplitude (x 10 <sup>-4</sup> )	4265**	4145**	3659**	4194	4401	4263
Mean change %		-2.8	-14.2		+4.9	+1.6
Maximum change		-16	-35			
Significance vs. D0		ns	p < 0.01		ns	ns

(\*\*) : n=15

For the untreated thigh, a tendency to the increase of the fat deposits at 28 days and 56 days was observed, but it is not significant in either cases.

The thighs treated with glaucine showed a 2.8% mean decrease in the amplitude of the fat deposits at 28 days. The decrease attained -14.2% at 56 days. For certain subjects, the reduction was -16% at 28 days and -35% at 56 days.

## 2) In vivo test : decrease in water retention by the fat deposits

### a) Principle

In parallel, the water retention in the adipose tissue was measured using a dual-probe operating at a frequency of 300 MHz (Moister Meter D).

The interaction between the high frequency waves (300 MHz) propagated toward the skin and reemitted and the tissues involve water molecules: the reflection of the frequency wave thus contains information on the water content of the investigated tissue.

Using 2 probes with different geometries, applied to the skin surface, it is possible to investigate from 2.5 to 5 mm in depth, i.e. in the hypodermal zone where the adipocyte clumps are located.

The system used was a Moister-Meter D (Delfin Technologies).

This is a new approach to the concept of water retention by steatomery sites.

### b) Results

20 Table 7 : decrease in water retention by the fat deposits after 28 days of treatment

Decrease in water retention by fat deposits				
	Zone >2.5 mm (dermis)		Zone >5 mm (hypodermis)	
	Control	Treated	Control	Treated
<b>% change vs. D0</b>	<b>0.2</b>	<b>+6.4</b>	<b>0.1</b>	<b>+7.5</b>
Significance	NS	p < 0.01	NS	p < 0.01

While the untreated thighs (control) showed no change in the water content of the deep or intermediate-depth tissues, a 6.4% increase in the lower dermis and a 7.5% increase in the hypodermis were observed after treatment with glaucine.

25 This increase is to be interpreted as a release of captive water initially located between the fat deposits and between those deposits and the superficial dermis by compression.

## 3) In vivo test: decrease in water retention

### a) Principle



A thigh firmness study was conducted on a panel of 13 female subjects by Laboratoires An SEM 575R cutometer, conventionally used to study the elastic properties of the skin, enables the determination of the cutaneous extensibility parameters under the effect of vertical aspiration.

5 The curve for cutaneous response to forced extension may be broken down into 4 parameters:

- Uf: maximum extension
- Ue: immediate elastic extension
- Uv: viscoelastic extension involving dermal proteoglycans
- Ur: immediate elastic retraction after aspiration

10 The 4 parameters interact and reflect the deformability status of the skin.

A product increasing skin firmness would be expected to decrease the maximum extension, Uf, which is related to a smaller immediate extension, Ue, and a decrease in the viscoelastic contribution, which decreases the parameter Uv.

The immediate retraction parameter, Ur, decreases if the maximum extension decreases.

15 b) Protocol

*Inclusion criteria:* Age between 18 and 50 years, Caucasian subjects, presenting steatomery of the thighs, BMI between 20 and 26 kg/m<sup>2</sup>, body weight stable for at least 3 months, no dieting in the 3 months preceding the study.

20 The 13 volunteers apply twice daily on only one thigh the glaucine product formulated in a fluid cream (example n°1), during 28 days.

The treated thigh is either the left one or the right one depending on randomization. Each subject acts as his own control thanks to the untreated thigh.

c) Results

The product was perfectly well tolerated by all the subjects.

25 The determinations were conducted on the back of each thigh. The test sites were precisely delimited.

The probe used was 6 mm in diameter. Suction was exerted by a negative pressure of 300 mbar applied for a duration of 2 seconds.

30 The determinations were conducted after a 20-minute resting time in a room whose temperature was between 20 and 22°C and whose relative humidity was between 45 and 55%.

At T0, there was no statistically significant difference between the left and right thighs.

Table 8 : the cutometry parameters were recorded after 28 days of treatment

	CHANGE (%) vs. T0			
	Uf	Ue	Uv	Ur
T 14 days 2.5% Thigh treated (Glaucine)	-2.08	-2.26	-1.30	-2.11

T14 days Control thigh	+0.04	-2.84	+12.18	+0.39
Significance at D14 Glaucine vs. control	NS	NS	p<0.05	NS
T 28 days (Glaucine)	-6.45	-4.44	-14.85	-6.13
T 28 days Control thigh	+2.67	+3.71	-1.79	+3.45
Significance at D28 Glaucine vs. control	p < 0.05	p < 0.05	p < 0.05	p < 0.01

The 4 measured parameters decreased as of the 14th day of application while they increased for the control thighs. After 28 days, the decreasing trend was confirmed and strengthened for the glaucine-treated thighs, while, for the control thighs, the opposite trend was very slightly accentuated: the difference was very significant for all parameters at D28, in favor of glaucine.

Thus, as of day 14, glaucine demonstrated its efficacy with regard to cutaneous extensibility, which decreased under the joint action of immediate elastic extension,  $U_e$ , and viscoelastic extensibility,  $U_v$ , related to the matrix tissue (collagen).

After 28 days, the gain was very significant since, for the certain subjects, the skin had gained firmness and enhanced resistance to induced stretching.

The parameter,  $U_v$ , was the most modified, reflecting strengthening of the dermis and its connective tissue, as shown in the table below:

Table 9: Change of the descriptor parameters of the cutaneous extensibility after 28 days of treatment

	CHANGE (%) vs. T0			
	$U_f$	$U_e$	$U_v$	$U_r$
9 volunteers	-12%	-11%	-16%	-12%
1st quartile	-19%	-20%	-17%	-20%

We observe that parameter,  $U_v$  increases for the control thighs, reflecting loss of firmness. By contrast, this parameter decreases for the treated thigh demonstrating an increase in the viscoelastic component of the skin related to a denser connective tissue

## CLAIMS

- 1) Use of glaucine or a plant extract containing it, as an active ingredient, alone or in association with at least another active usually used in cosmetic or dermopharmaceutical field, for the preparation of a cosmetical or dermopharmaceutical composition with a topical use for skin, integuments, and/or mucosas.  
5
- 2) Use in a cosmetic composition of glaucine or a plant extract containing it according to claim 1, wherein said glaucine is intended to stimulate the adipocyte reversion.
- 3) Use of glaucine according to claims 1 or 2, wherein said glaucine is intended to control the renewal and/or the number of adipocytes within the fat tissue.
- 10 4) Use of glaucine according to any of claims 1 to 3, wherein said glaucine is intended to inhibit the formation of mature adipocytes.
- 5) Use of glaucine according to any of claims 1 to 4, wherein said glaucine is intended to regulate the proportion of fat in the adipocytes.
- 15 6) Use of glaucine according to any of claims 1 to 5, wherein said glaucine is intended to decrease the thickness of the fat tissue within the hypoderma and/or to prevent its filling out.
- 7) Use of glaucine according to any of claims 1 to 6, wherein said glaucine is present from about 0.00001% w/w to about 50% w/w, preferably from about 0.0001 % w/w to 2% w/w, and more preferably from about 0.001% to 10% by weight of the composition.  
20
- 8) Use of glaucine according to any of claims 1 to 7, wherein said glaucine is combined with at least one complementary active chosen among the lypolitic active ingredients and/or active ingredients inhibiting the lipogenesis, draining active ingredients or active ingredients acting on the microcirculation, slimming active ingredients, firming up active ingredients, and/or anti-glycan active ingredients as well as their mixtures.  
25
- 9) Use of glaucine according to any of claims 1 to 8, wherein at least one of the active ingredients is used under the form of solution, dispersion, emulsion, paste, or powder, individually or as a premix, or in vehicles such as macrocapsules, microcapsules, or nanocapsules, microspheres, microspheres or nanospheres, liposomes, oleosomes or chylomicrons, macroparticles, microparticles, or nanoparticles or macrosponges, microsponges or nanosponges, or adsorbed on organic polymer powders, talcs, bentonites, or other inorganic or organic supports.  
30
- 10) Use of glaucine according to any of claims 1 to 9, wherein said composition is used in any cosmetic form, namely : creams, lotions, ointments, milks, gels, emulsions,

- dispersions, solutions, suspensions, cleansers, foundations, anhydrous preparations (sticks, in particular lipsticks, body and bath oils), shower and bath gels, shampoos and scalp treatment lotions, cream or lotion for care of the skin or hair, sun-screen lotions, milks or creams, artificial suntan lotions, creams or milks, shaving creams or foams, 5 aftershave lotions, make-up, mascaras or nail varnishes, lipsticks, skin "essences," serums, adhesive or absorbent materials, transdermal patches, powders, emollient lotion, emollient milk, emollient cream, sprays, oils for the body and the bath, foundation tint bases, pomade, emulsion, colloid, compact or solid suspension, pencil, sprayable formulation, brossable.
- 10 11) A cosmetic method of stimulating adipocyte reversion, said cosmetic method comprising the step of topically applying to the skin of mammal in need of treatment, a safe and effective amount of glaucine according to any of claims 1 to 10, at least once a day for a period of time at least sufficient to provide adipocyte reversion of that portion of human skin.
- 15 12) Use of glaucine or a plant extract containing it according to any of claims 1 to 10, to manufacture a medicament stimulating the adipocyte reversion, particularly for a slimming treatment of weight overloads of the thighs, the hips and the belly skin firming, and particularly to prevent and/or to treat cellulite or orange peel and/or to refine contours of the face, and/or to treat fat deposits and "spare tires".
- 20