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METHOD FOR STIMULATING CELLULAR BETA DEFENSINS

CROSS-REFERENCE TO RELATED APPLICATIONS

The present application claims priority from U.S. Provisional Applications
5 No. 61/663,909, filed June 25, 2012 and No. 61/671,137, filed July 13, 2012.

Field of the Invention

The invention relates to the field of topical compositions and uses thereof. In particular, the invention relates to topical compositions that can be used to stimulate
10 production of beta defensins in cells of keratinous surfaces such as skin, hair, or nails.

Background of the Invention

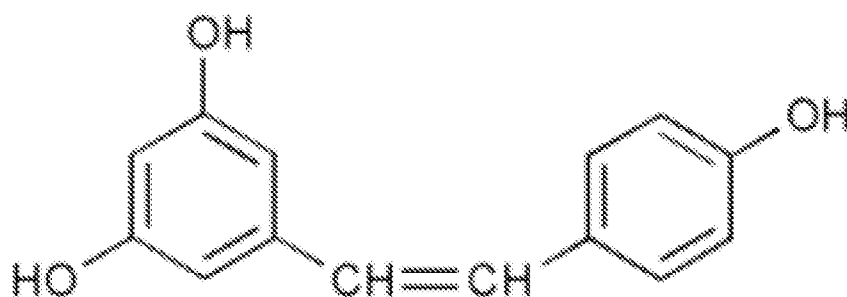
Antimicrobial peptides are a naturally occurring defense system that is widespread throughout a number of plant and animal species. One type of antimicrobial peptide found in
15 vertebrates is the group of molecules known as defensins. Structurally, these molecules are united by the presence of six invariant cysteines and three intramolecular cystine disulfide bonds. (Lehrer et al., *Cell* 64: 229-230, 1997; *Ann. Rev. Immunol.* 11: 105-128, 1993). Two different classes of defensins have been observed. The first are classic defensins, that are stored in neutrophils and macrophages, and which are used to inactivate microbes that these
20 cells have phagocytosed. The second class comprises beta defensins, which have been isolated from mammalian lung and skin cells. These molecules are known to exhibit a wide range of antibiotic activity against pathogens, such as bacteria, fungi, and viruses (Porter et al., *Infect. Immun.* 65(6): 2396-2401, 1997).

It is known that skin cells in particular, produce beta defensins. It has also been shown
25 that the exposure of skin cells to bacterial cells, in particular *Pseudomonas*, even in an inactivated state, can induce the production of beta defensin-2 in keratinocytes. Presumably

this response is present in the skin to protect it from the onslaught of noxious stimuli, particularly in the form of microbes.

It is now known that beta defensins 1, 2, and 3, a class of epithelial antimicrobial small cationic peptides, are secreted by cells when in contact with microbes in order to stimulate cellular defense mechanisms.

Resveratrol, also referred to as 3,5,4'-trihydroxystilbene, is a polyhydroxy-substituted compound having the general formula:



It is present in red grapes, raspberries, blueberries, and certain other plant berries or extracts. It has been reported that resveratrol has anti-aging, anti-cancer, and antiviral effects in addition to its ability to provide benefits to organisms that are associated with calorie restricted diets. Because of its perceived fountain-of-youth properties, resveratrol has been incorporated into a variety of cosmetic formulations, such as skin creams. It is also known that resveratrol is produced naturally by plants when under attack by pathogens such as bacteria and fungi.

U.S. Patent No. 7,510,073 teaches that extracts of *Lactobacillus*, in particular, fermented extracts, are effective in stimulating beta defensins in skin cells. However, there is interest in finding other ingredients that have similar activity and are easier to manufacture and do not require fermentation.

It has been discovered that resveratrol will stimulate beta defensin production in skin cells.

Summary of the Invention

The invention is directed to a method for stimulating the production of beta defensins
5 in skin cells comprising applying to the skin cells in need thereof a stimulatory effective amount of resveratrol.

The invention is also directed to a method for treating acne by applying to skin having a need for such treatment an effective amount of resveratrol.

The invention is further directed to a method for inhibiting microbial growth,
10 specifically undesired microbial growth on cells of keratinous surfaces by applying to the surfaces in need of such inhibition an effective amount of resveratrol.

The invention is also directed to a method for improving skin barrier repair by stimulating beta defensin production in keratinous cells by treating with resveratrol.

Brief Description of the Figures

Figure 1: Shows NHEK treated with resveratrol show presence of beta defensins within the cells when compared to untreated cells when beta defensin measured by expression of cellular beta defensin protein.

Figure 2: shows the presence of beta defensin in NHEK treated with resveratrol measured by
20 transcription.

Figure 3: shows presence of beta defensins in NHEK treated with resveratrol by measuring peptide excretion in cells treated with resveratrol.

Figure 4: shows presence of beta defensins in NHEK treated with resveratrol ferulate (the ferulic acid ester of resveratrol) when measured by transcription.

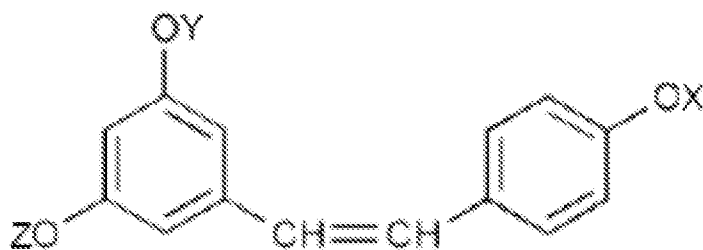
Figure 5: shows the presence of beta defensins in NHEK treated with resveratrol ferulate when measured by cellular excretion.

Detailed Description of the Invention

5 The invention is a method for stimulating beta defensins, treating acne, or inhibiting growth of microbial flora in cells of keratinous surfaces by treating such cells with an effective amount of resveratrol.

 The term “resveratrol” when used herein means 3,5,4’-trihydroxy trans stilbene and also includes derivatives thereof including but not limited to those set forth herein.

10 Suitable resveratrol derivatives include those having the general formula:



 wherein X, Y, and Z are either hydrogen or a protective group, provided that at least one of X, Y, and Z is the protective group.

 Resveratrol and/or such derivatives may be present ranging from about 0.0001 to 95%, preferably from about 0.005 to 90%, more preferably from about 0.1 to 20% by weight of the total composition. Examples of resveratrol derivatives within the scope of this invention include, but are not limited to, the following.

20 Resveratrol Esters of Inorganic or Organic Acids

 Resveratrol esters of inorganic acids, in which one or more of the X, Y, and Z are inorganic acid functional groups such as phosphates, nitrates, sulfonates, and carbonates, can

be used in the present invention. Following is a list of exemplary inorganic acid esters that are particularly suitable for practice of the present invention:

3-phosphate-5,4'-dihydroxystilbene;

5-phosphate-3,4'-dihydroxystilbene;

5 4'-phosphate-3,5-dihydroxystilbene;

3,5-diphosphate-4'-hydroxystilbene;

3,4'-diphosphate-5-hydroxystilbene;

4',5-diphosphate-3-hydroxystilbene;

3,5,4'-triphosphate stilbene;

10 3-nitrate-5,4'-dihydroxystilbene;

5-nitrate-3,4'-dihydroxystilbene;

4'-nitrate-3,5-dihydroxystilbene;

3,5-dinitrate-4'-hydroxystilbene;

3,4'-dinitrate-5-hydroxystilbene;

15 4',5-dinitrate-3-hydroxystilbene;

3,5,4'-trinitrate stilbene;

3-sulfonate-5,4'-dihydroxystilbene;

5-sulfonate-3,4'-dihydroxystilbene;

4'-sulfonate-3,5-dihydroxystilbene;

20 3,5-disulfonate-4'-hydroxystilbene;

3,4'-disulfonate-5-hydroxystilbene;

4',5-disulfonate-3-hydroxystilbene;

3,5,4'-trisulfonate stilbene;

3-carbonate-5,4'-dihydroxystilbene;

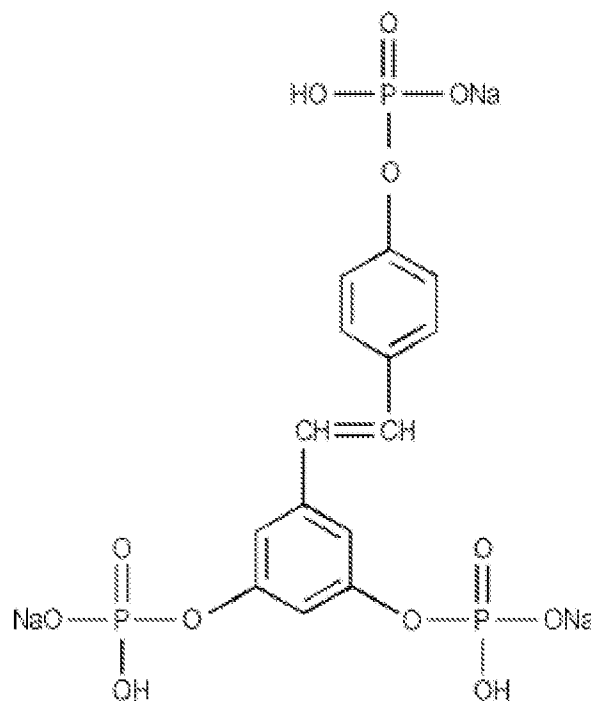
25 5-carbonate-3,4'-dihydroxystilbene;

4'-carbonate-3,5-dihydroxystilbene;
3,5-dicarbonate-4'-hydroxystilbene;
3,4'-dicarbonate-5-hydroxystilbene;
4',5-dicarbonate-3-hydroxystilbene; and
5 3,5,4'-tricarboxylate stilbene.

Pharmaceutically acceptable salts of the above-listed resveratrol esters can also be used in the cosmetic compositions of the present invention. Such salts may include one or more monovalent or divalent cations selected from the group consisting of Na, K, Mg, Ca, Fe, and NH₄. The salts can be formed by adding corresponding bases, such as sodium hydroxide,
10 potassium hydroxide, and the like, into a solution containing the resveratrol esters.

Such inorganic acid esters of resveratrol may be readily formed by well known chemical processes that substitute the hydroxyl groups of phenols or polyphenols with the phosphate, sulfonates, and carbonate functional groups. For example, U.S. Patent No. 4003966 describes a one-step process for selectively phosphorylating phenols to form
15 phosphate esters thereof, the contents of which are hereby incorporated herein by reference in their entireties for all purposes.

One specific example of a suitable derivative is the 3, 4', 5 – triphosphate stilbene, also referred to as a resveratrol triphosphate ester having the formula (resveratrol triphosphate):



Phosphate esters of resveratrol, including resveratrol triphosphate, are disclosed in International Patent Application Publication No. WO 2006/029484A1, which is hereby

5 incorporated by reference in its entirety. Resveratrol triphosphate may be synthesized by the method as set forth in Example 2 of WO 2006/029484A1. More specifically, a solution of resveratrol (3,4,5-trihydroxystilbene) (25 mmols, 5.7 grams) and dimethylaminopyridine (7.5 mmols, 0.93 grams) in 100 ml acetonitrile is cooled under nitrogen up to -10o C. After 10 minutes, carbon tetrachloride (375 mmol, 36.2 ml) and DIEA (159 mmol; 27.7 ml) and the

10 mixture maintained under stirring for 30 minutes. Dibenzylphosphate (113 mmols, 25.0 ml) is added and the mixture stirred for an additional 12 hours at room temperature. The course of the reaction is monitored by TLC (silica F254, eluent ethyl acetate/n-hexane 80/20 v/v). One liter of 0.5 M KH₂PO₄ is added, and the mixture then extract with ethyl acetate. The resulting product, tri(dibenzylphosphate) resveratrol, is purified by filtration on a silica gel, washing

15 first with a mixture of ethyl acetate/n-hexane (80/20 v/v) to remove any remaining unreacted resveratrol, and then with methanol, to obtain a yellow oil.

To the tri(dibenzylphosphate) resveratrol (12.5 mmol) in 200 mL of anhydrous DCM at 0°C, is added bromomethylsilane (79 mmols, 10.4 mL). After 2 hours, 300 mL of H₂O is added, and the reaction mixture is stirred for 1 hour. The water phase is washed again with ethyl acetate, then lyophilized to obtain an orange oil.

5 To the product obtained above, solubilized in 400 mL of ethanol, is added CH₃ONa (37 mmol; 2.03 g) and the reaction stirred for 12 hours at room temperature. The ethanol is evaporated in a rotavapor, and the residue solubilized in H₂O. The water phase is washed with ethyl acetate and lyophilized. The mass spectrum of the resulting white solid shows the presence of resveratrol triphosphate (PM = 468.1), with a total yield of > 90% with respect to
10 resveratrol.

If desired the resveratrol triphosphate may be neutralized with organic or inorganic bases such as sodium hydroxide, potassium hydroxide and the like. Particularly preferred is where the resveratrol triphosphate is neutralized with sodium hydroxide to form trisodium resveratrol triphosphate. Resveratrol triphosphate may also be purchased from Ajinomoto in
15 the neutralized form, having the CTFA trisodium resveratrol triphosphate.

Carboxylic Acid Esters of Resveratrol

Esters of resveratrol and aliphatic or aromatic carboxylic acids, in which one or more of X, Y, and Z is a -C(O)-R₁ group, wherein R₁ is selected from the group consisting of linear, branched, saturated or unsaturated, or cyclic C₁-C₄₀ alkyl, substituted C₁-C₄₀ alkyl, C₁-C₄₀
20 alkenyl, substituted C₁-C₄₀ alkenyl, C₁-C₄₀ alkynyl, substituted C₁-C₄₀ alkynyl, aryl, C₁-C₄₀ aryl, and C₁-C₄₀ substituted aryl. In one preferred embodiment, the R₁ group is a straight or branched chain fatty, or C₆₋₃₀, saturated or unsaturated alkyl group. The substituents may be selected from C₁₋₄₀ straight or branched chain, saturated or unsaturated alkyl, halogen (such as fluoro), hydrogen, alkoxy, hydroxyl, and the like.

25 Exemplary carboxylic acids that can be used to form ester of resveratrol include, but

are not limited to: substituted or unsubstituted saturated monocarboxylic acids, such as acetic acid, propionic acid, butyric acid (C4), valeric acid, hexanoic acid, caprylic acid (C8), lauric acid, stearic acid (C18), isostearic acid (branched C18), linoleic acid, linolenic acid, myristic acid (C14), arachidic acid (C20), arichidonic acid, erucic acid, behenic acid (C22), lauric acid
5 (C12), capric acid (C10), caproic (C6), and palmitic acid (C16); unsaturated monocarboxylic acids, such as acrylic acid, methacrylic acid, sorbic acid, oleic acid, linoleic acid, linolenic acid, docosaheptaenoic acid, and eicosapentaenoic acid; amino acids, such as arginine, glutamine, and tyrosine; keto acids, such as pyruvic acid and acetoacetic acid; aromatic carboxylic acids, such as ascorbic acid, benzoic acid, salicylic acid, and ferulic acid; di- and
10 tri-carboxylic acids, such as oxalic acid, malonic acid, malic acid, succinic acid, and glutaric acid. Also suitable are carboxylic acids substituted with cyclic disulfide groups, e.g. lipoic acid. The designation "C" followed by a number indicates the number of carbon atoms in the alkyl chain.

Following is a list of exemplary carboxylic acid esters of resveratrol that are
15 particularly suitable for practice of the present invention:

3-acetate-5,4'-dihydroxystilbene;
5-acetate-3,4'-dihydroxystilbene;
4'-acetate-3,5-dihydroxystilbene;
3,5-diacetate-4'-hydroxystilbene;
20 3,4'-diacetate-5-hydroxystilbene;
4',5-diacetate-3-hydroxystilbene;
3,5,4'-triacetate stilbene;
3-propionate-5,4'-dihydroxystilbene;
5-propionate-3,4'-dihydroxystilbene;
25 4'-propionate-3,5-dihydroxystilbene;

- 3,5-dipropionate-4'-hydroxystilbene;
3,4'-dipropionate-5-hydroxystilbene;
4',5-dipropionate-3-hydroxystilbene;
3,5,4'-tripropionate stilbene;
5 3-butyrate-5,4'-dihydroxystilbene;
5-butyrate-3,4'-dihydroxystilbene;
4'-butyrate-3,5-dihydroxystilbene;
3,5-dibutyrate-4'-hydroxystilbene;
3,4'-dibutyrate-5-hydroxystilbene;
10 4',5-dibutyrate-3-hydroxystilbene;
3,5,4'-tributyrate stilbene;
3-valerate-5,4'-dihydroxystilbene;
5-valerate-3,4'-dihydroxystilbene;
4'-valerate-3,5-dihydroxystilbene;
15 3,5-divalerate-4'-hydroxystilbene;
3,4'-divalerate-5-hydroxystilbene;
4',5-divalerate-3-hydroxystilbene;
3,5,4'-trivalerate stilbene;
3-hexanoate-5,4'-dihydroxystilbene;
20 5-hexanoate -3,4'-dihydroxystilbene;
4'-hexanoate-3,5-dihydroxystilbene;
3,5-dihexanoate-4'-hydroxystilbene;
3,4'-dihexanoate-5-hydroxystilbene;
4',5-dihexanoate-3-hydroxystilbene;
25 3,5,4'-trihexanoate stilbene;

- 3-caprylate-5,4'-dihydroxystilbene;
5-caprylate-3,4'-dihydroxystilbene;
4'-caprylate-3,5-dihydroxystilbene;
3,5-dicaprylate-4'-hydroxystilbene;
5 3,4'-dicaprylate-5-hydroxystilbene;
4',5-dicaprylate-3-hydroxystilbene;
3,5,4'-tricaprylate stilbene;
3-laurate-5,4'-dihydroxystilbene;
5-laurate-3,4'-dihydroxystilbene;
10 4'-laurate-3,5-dihydroxystilbene;
3,5-dilaurate-4'-hydroxystilbene;
3,4'-dilaurate-5-hydroxystilbene;
4',5-dilaurate-3-hydroxystilbene;
3,5,4'-trilaurate stilbene;
15 3-stearate-5,4'-dihydroxystilbene;
5-stearate-3,4'-dihydroxystilbene;
4'-stearate-3,5-dihydroxystilbene;
3,5-distearate-4'-hydroxystilbene;
3,4'-distearate-5-hydroxystilbene;
20 4',5-distearate-3-hydroxystilbene;
3,5,4'-tristearate stilbene;
3-palmitate-5,4'-dihydroxystilbene;
5-palmitate-3,4'-dihydroxystilbene;
4'-palmitate-3,5-dihydroxystilbene;
25 3,5-dipalmitate-4'-hydroxystilbene;

- 3,4'-dipalmitate-5-hydroxystilbene;
- 4',5-dipalmitate-3-hydroxystilbene;
- 3,5,4'-tripalmitate stilbene;
- 3-acrylate-5,4'-dihydroxystilbene;
- 5 5-acrylate-3,4'-dihydroxystilbene;
- 4'-acrylate-3,5-dihydroxystilbene;
- 3,5-diacrylate-4'-hydroxystilbene;
- 3,4'-diacrylate-5-hydroxystilbene;
- 4',5-diacrylate-3-hydroxystilbene;
- 10 3,5,4'-triacylate stilbene;
- 3-methacrylate-5,4'-dihydroxystilbene;
- 5-methacrylate-3,4'-dihydroxystilbene;
- 4'-methacrylate-3,5-dihydroxystilbene;
- 3,5-dimethacrylate-4'-hydroxystilbene;
- 15 3,4'-dimethacrylate-5-hydroxystilbene;
- 4',5-dimethacrylate-3-hydroxystilbene;
- 3,5,4'-trimethacrylate stilbene;
- 3-sorbate-5,4'-dihydroxystilbene;
- 5-sorbate-3,4'-dihydroxystilbene;
- 20 4'-sorbate-3,5-dihydroxystilbene;
- 3,5-disorbate-4'-hydroxystilbene;
- 3,4'-disorbate-5-hydroxystilbene;
- 4',5-disorbate-3-hydroxystilbene;
- 3,5,4'-trisorbate stilbene;
- 25 3-oleate-5,4'-dihydroxystilbene;

- 5-oleate-3,4'-dihydroxystilbene;
4'-oleate-3,5-dihydroxystilbene;
3,5-dioleate-4'-hydroxystilbene;
3,4'-dioleate-5-hydroxystilbene;
5 4',5-dioleate-3-hydroxystilbene;
3,5,4'-trioleate stilbene;
3-linoleate-5,4'-dihydroxystilbene;
5-linoleate-3,4'-dihydroxystilbene;
4'-linoleate-3,5-dihydroxystilbene;
10 3,5-dilinoleate-4'-hydroxystilbene;
3,4'-dilinoate-5-hydroxystilbene;
4',5-dilinoleate-3-hydroxystilbene;
3,5,4'-trilinoleate stilbene;
3-linolenate-5,4'-dihydroxystilbene;
15 5-linolenate-3,4'-dihydroxystilbene;
4'-linolenate-3,5-dihydroxystilbene;
3,5-dilinolenate-4'-hydroxystilbene;
3,4'-dilinenate-5-hydroxystilbene;
4',5-dilinolenate-3-hydroxystilbene;
20 3,5,4'-trilinolenate stilbene;
3-docosaheptaenoate-5,4'-dihydroxystilbene;
5-docosaheptaenoate-3,4'-dihydroxystilbene;
4'-docosaheptaenoate-3,5-dihydroxystilbene;
3,5-didocosaheptaenoate-4'-hydroxystilbene;
25 3,4'-didocosaheptaenoate-5-hydroxystilbene;

- 4',5-didocosahexaenoate-3-hydroxystilbene;
3,5,4'-tridocosahexaenoate stilbene;
3-eicosapentaenoic-5,4'-dihydroxystilbene;
5-eicosapentaenoic-3,4'-dihydroxystilbene;
5 4'-eicosapentaenoic-3,5-dihydroxystilbene;
3,5-dieicosapentaenoic-4'-hydroxystilbene;
3,4'-dieicosapentaenoic-5-hydroxystilbene;
4',5-dieicosapentaenoic-3-hydroxystilbene;
3,5,4'-trieicosapentaenoic stilbene;
10 3-arginate-5,4'-dihydroxystilbene;
5-arginate-3,4'-dihydroxystilbene;
4'-arginate-3,5-dihydroxystilbene;
3,5-diarginate-4'-hydroxystilbene;
3,4'-diarginate-5-hydroxystilbene;
15 4',5-diarginate-3-hydroxystilbene;
3,5,4'-triarginate stilbene;
3-glutamate-5,4'-dihydroxystilbene;
5-glutamate-3,4'-dihydroxystilbene;
4'-glutamate-3,5-dihydroxystilbene;
20 3,5-diglutamate-4'-hydroxystilbene;
3,4'-diglutamate-5-hydroxystilbene;
4',5-diglutamate-3-hydroxystilbene;
3,5,4'-triglutamate stilbene;
3-tyrosate-5,4'-dihydroxystilbene;
25 5-tyrosate-3,4'-dihydroxystilbene;

- 4'-tyrosate-3,5-dihydroxystilbene;
3,5-dityrosate-4'-hydroxystilbene;
3,4'-dityrosate-5-hydroxystilbene;
4',5-dityrosate-3-hydroxystilbene;
5 3,5,4'-trityrosate stilbene;
3-pyruvate-5,4'-dihydroxystilbene;
5-pyruvate-3,4'-dihydroxystilbene;
4'-pyruvate-3,5-dihydroxystilbene;
3,5-dipyruvate-4'-hydroxystilbene;
10 3,4'-dipyruvate-5-hydroxystilbene;
4',5-dipyruvate-3-hydroxystilbene;
3,5,4'-tripyruvate stilbene;
3-acetoacetate-5,4'-dihydroxystilbene;
5-acetoacetate-3,4'-dihydroxystilbene;
15 4'-acetoacetate-3,5-dihydroxystilbene;
3,5-diacetoacetate-4'-hydroxystilbene;
3,4'-diacetoacetate-5-hydroxystilbene;
4',5-diacetoacetate-3-hydroxystilbene;
3,5,4'-triacetoacetate stilbene;
20 3-ascorbate-5,4'-dihydroxystilbene;
5-ascorbate-3,4'-dihydroxystilbene;
4'-ascorbate-3,5-dihydroxystilbene;
3,5-diascorbate-4'-hydroxystilbene;
3,4'-diascorbate-5-hydroxystilbene;
25 4',5-diascorbate-3-hydroxystilbene;

- 3,5,4'-triascorbate stilbene;
- 3-benzoate-5,4'-dihydroxystilbene;
- 5-benzoate-3,4'-dihydroxystilbene;
- 4'-benzoate-3,5-dihydroxystilbene;
- 5 3,5-dibenzoate-4'-hydroxystilbene;
- 3,4'-dibenzoate-5-hydroxystilbene;
- 4',5-dibenzoate-3-hydroxystilbene;
- 3,5,4'-tribenzoate stilbene;
- 3-salicylate-5,4'-dihydroxystilbene;
- 10 5-salicylate-3,4'-dihydroxystilbene;
- 4'-salicylate-3,5-dihydroxystilbene;
- 3,5-disalicylate-4'-hydroxystilbene;
- 3,4'-disalicylate-5-hydroxystilbene;
- 4',5-disalicylate-3-hydroxystilbene;
- 15 3,5,4'-trisalicylate stilbene;
- 3-ferulate-5,4'-dihydroxystilbene;
- 5-ferulate-3,4'-dihydroxystilbene;
- 4'-ferulate-3,5-dihydroxystilbene;
- 3,5-diferulate-4'-hydroxystilbene;
- 20 3,4'-diferulate-5-hydroxystilbene;
- 4',5-diferulate-3-hydroxystilbene;
- 3,5,4'-triferulate stilbene;
- 3-oxalate-5,4'-dihydroxystilbene;
- 5-oxalate-3,4'-dihydroxystilbene;
- 25 4'-oxalate-3,5-dihydroxystilbene;

- 3,5-dioxalate-4'-hydroxystilbene;
- 3,4'-dioxalate-5-hydroxystilbene;
- 4',5-dioxalate-3-hydroxystilbene;
- 3,5,4'-trioxalate stilbene;
- 5 3-malonate-5,4'-dihydroxystilbene;
- 5-malonate-3,4'-dihydroxystilbene;
- 4'-malonate-3,5-dihydroxystilbene;
- 3,5-dimalonate-4'-hydroxystilbene;
- 3,4'-dimalonate-5-hydroxystilbene;
- 10 4',5-dimalonate-3-hydroxystilbene;
- 3,5,4'-trimalonate stilbene;
- 3-malate-5,4'-dihydroxystilbene;
- 5-malate-3,4'-dihydroxystilbene;
- 4'-malate-3,5-dihydroxystilbene;
- 15 3,5-dimalate-4'-hydroxystilbene;
- 3,4'-dimalate-5-hydroxystilbene;
- 4',5-dimalate-3-hydroxystilbene;
- 3,5,4'-trimalate stilbene;
- 3-succinate-5,4'-dihydroxystilbene;
- 20 5-succinate-3,4'-dihydroxystilbene;
- 4'-succinate-3,5-dihydroxystilbene;
- 3,5-disuccinate-4'-hydroxystilbene;
- 3,4'-disuccinate-5-hydroxystilbene;
- 4',5-disuccinate-3-hydroxystilbene;
- 25 3,5,4'-trisuccinate stilbene;

3-glutarate-5,4'-dihydroxystilbene;

5-glutarate-3,4'-dihydroxystilbene;

4'-glutarate-3,5-dihydroxystilbene;

3,5-diglutarate-4'-hydroxystilbene;

5 3,4'-diglutamate-5-hydroxystilbene;

4',5-diglutarate-3-hydroxystilbene;

3,5,4'-triglutarate stilbene;

3-glutarate-5,4'-dihydroxystilbene;

5-glutarate-3,4'-dihydroxystilbene;

10 4'-glutarate-3,5-dihydroxystilbene;

3,5-diglutarate-4'-hydroxystilbene;

3,4'-diglutamate-5-hydroxystilbene;

4',5-diglutarate-3-hydroxystilbene; and

3,5,4'-triglutarate stilbene;

15 Further specific examples include carboxylic acid esters of resveratrol that are either saturated or unsaturated fatty acid esters of resveratrol, such as resveratrol butyrates, resveratrol valerates, resveratrol hexanoates, resveratrol sorbates, resveratrol laurates, resveratrol stearates, resveratrol palmitates, resveratrol oleates, resveratrol lipoates, resveratrol linoleates, resveratrol linolenates, resveratrol eicosapentaenoates, and resveratrol
20 docosahehexanoates. Such fatty acid esters of resveratrol can be readily formed by esterification of resveratrol with acid derivatives according to the Schotten-Baumann reaction in alkaline aqueous medium, as described by U.S. Patent No. 6,572,882, the content of which is incorporated herein by reference in its entirety for all purposes.

Another particularly preferred group of carboxylic acid esters of resveratrol are the
25 aromatic carboxylic acid esters of resveratrol, such as resveratrol ferulates, which can be

formed by reacting resveratrol with ferulic acid in aqueous medium.

Resveratrol Ether Derivatives

Yet another group of suitable resveratrol derivatives are resveratrol ethers, in which one or more of X, Y, and Z is -R₂, wherein R₂ is selected from the group consisting of linear, 5 branched or cyclic C₁-C₄₀ alkyl, substituted C₁-C₄₀ alkyl, C₁-C₄₀ alkenyl, substituted C₁-C₄₀ alkenyl, C₁-C₄₀ alkynyl, substituted C₁-C₄₀ alkynyl, C₁-C₄₀ aryl, substituted C₁-C₄₀ aryl, and mono-, di-, oligo-, and polysaccharides. Following is a list of exemplary resveratrol ethers that are particularly suitable for practice of the present invention:

3-methoxy-5,4'-dihydroxystilbene;

10 5-methoxy-3,4'-dihydroxystilbene;

4'-methoxy-3,5-dihydroxystilbene;

3,5-dimethoxy-4'-hydroxystilbene;

3,4'-dimethoxy-5-hydroxystilbene;

4',5-dimethoxy-3-hydroxystilbene;

15 3,5,4'-trimethoxy stilbene;

3-ethoxy-5,4'-dihydroxystilbene;

5-ethoxy-3,4'-dihydroxystilbene;

4'-ethoxy-3,5-dihydroxystilbene;

3,5-diethoxy-4'-hydroxystilbene;

20 3,4'-diethoxy-5-hydroxystilbene;

4',5-diethoxy-3-hydroxystilbene;

3,5,4'-triethoxy stilbene;

3-propyloxy-5,4'-dihydroxystilbene;

5-propyloxy-3,4'-dihydroxystilbene;

25 4'-propyloxy-3,5-dihydroxystilbene;

3,5-dipropoxy-4'-hydroxystilbene;
 3,4'-dipropoxy-5-hydroxystilbene;
 4',5-dipropoxy-3-hydroxystilbene;
 3,5,4'-tripropoxy stilbene;
 5 3-phenyloxy-5,4'-dihydroxystilbene;
 5-phenyloxy-3,4'-dihydroxystilbene;
 4'-phenyloxy-3,5-dihydroxystilbene;
 3,5-diphenyloxy-4'-hydroxystilbene;
 3,4'-diphenyloxy-5-hydroxystilbene;
 10 4',5-diphenyloxy-3-hydroxystilbene;
 3,5,4'-triphenyloxy stilbene;
 3-glucoside-5,4'-dihydroxystilbene;
 5-glucoside-3,4'-dihydroxystilbene;
 4'-glucoside-3,5-dihydroxystilbene;
 15 3,5-diglucoside-4'-hydroxystilbene;
 3,4'-diglucoside-5-hydroxystilbene;
 4',5-diglucoside-3-hydroxystilbene; and
 3,5,4'-triglucoside stilbene.

One specific example includes a methoxy-substituted resveratrol derivative. For
 20 example, the compositions of the present invention may comprise 3,5-dimethoxy-4'-
 hydroxystilbene, which can be extracted from the Indian Kino Tree (*Pterocarpus marsupium*)
 and is commercially available under the trade name "Pterostilbene" from Sigma-Aldrich at St.
 Louis, MO.

In another specific example, the resveratrol derivative contains one or more
 25 saccharide-containing protective groups, such as glucose, galactose, mannose, fructose,

sucrose, lactose, maltose, trehalose, and the like. For example, resveratrol glucoside, which can be obtained by extraction from plants or plant material such as *polygonum cuspidatum* tissue or in vitro cultures of *vitis vinifera* cells, is used in the cosmetic compositions of the present invention.

5 Nitrogen-Containing Derivatives of Resveratrol

The resveratrol derivatives used in the compositions of the present invention may also contain one or more nitrogen-containing functional groups, i.e., one or more of X, Y, and Z in the above formula are selected from the group consisting of amides, amines, imines, amidines, and carboxamidines. Following is a list of exemplary resveratrol ethers that are particularly

10 suitable for practice of the present invention:

3-amide-5,4'-dihydroxystilbene;

5-amide-3,4'-dihydroxystilbene;

4'-amide-3,5-dihydroxystilbene;

3,5-diamide-4'-hydroxystilbene;

15 3,4'-diamide-5-hydroxystilbene;

4',5-diamide-3-hydroxystilbene;

3,5,4'-triamide stilbene;

3-amino-5,4'-dihydroxystilbene;

5-amino-3,4'-dihydroxystilbene;

20 4'-amino-3,5-dihydroxystilbene;

3,5-diamino-4'-hydroxystilbene;

3,4'-diamino-5-hydroxystilbene;

4',5-diamino-3-hydroxystilbene;

3,5,4'-triamino stilbene;

25 3-imino-5,4'-dihydroxystilbene;

5-imino-3,4'-dihydroxystilbene;
4'-imino-3,5-dihydroxystilbene;
3,5-diimino-4'-hydroxystilbene;
3,4'-diimino-5-hydroxystilbene;
5
4',5-diimino-3-hydroxystilbene;
3,5,4'-triimino stilbene;
3-amidino-5,4'-dihydroxystilbene;
5-amidino-3,4'-dihydroxystilbene;
4'-amidino-3,5-dihydroxystilbene;
10
3,5-diamidino-4'-hydroxystilbene;
3,4'-diamidino-5-hydroxystilbene;
4',5-diamidino-3-hydroxystilbene; and
3,5,4'-triamidino stilbene.

15 The Compositions

The compositions used to treat keratinous surfaces with resveratrol to stimulate beta defensins may be aqueous or anhydrous and in the solid, liquid, or semi-solid form. Suitable compositions including skin care products such as creams, lotions, cleansers, toners; color cosmetic products such as foundations, concealers, lipsticks, lip glosses, lip balms, eye
20 shadows, mascara, eyeliner, and so on.

When the composition is in the emulsion form it contains water and oil, for example, from about 0.01 to 99% water and 0.1 to 99% oil.

Suitable oils include silicones, esters, vegetable oils, synthetic oils, including but not limited to those set forth herein. The oils may be volatile or nonvolatile, and are in the form of
25 a pourable liquid at room temperature. The term "volatile" means that the oil has a measurable

vapor pressure, or a vapor pressure of at least about 2 mm. of mercury at 20° C. The term "nonvolatile" means that the oil has a vapor pressure of less than about 2 mm. of mercury at 20° C.

Volatile Oils

5 Suitable volatile oils generally have a viscosity ranging from about 0.5 to 5 centistokes 25° C. and include linear silicones, cyclic silicones, paraffinic hydrocarbons, or mixtures thereof.

Linear and cyclic volatile silicones are available from various commercial sources including Dow Corning Corporation and General Electric. The Dow Corning volatile silicones
10 are sold under the tradenames Dow Corning 244, 245, 344, and 200 fluids. These fluids comprise octamethylcyclotetrasiloxane, decamethylcyclopentasiloxane, dodecamethylcyclohexasiloxane and the like. Also suitable are linear volatile silicones such as hexamethyldisiloxane (viscosity 0.65 centistokes (abbreviated cst)), octamethyltrisiloxane (1.0 cst), decamethyltetrasiloxane (1.5 cst), dodecamethylpentasiloxane (2 cst) and mixtures
15 thereof.

Also suitable as the volatile oils are various straight or branched chain paraffinic hydrocarbons having 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20 carbon atoms, more preferably 8 to 16 carbon atoms. Suitable hydrocarbons include pentane, hexane, heptane, decane, dodecane, tetradecane, tridecane, and C₈₋₂₀ isoparaffins as disclosed in U.S.
20 Pat. Nos. 3,439,088 and 3,818,105, both of which are hereby incorporated by reference. Preferred volatile paraffinic hydrocarbons have a molecular weight of 70-225, preferably 160 to 190 and a boiling point range of 30 to 320, preferably 60 to 260° C., and a viscosity of less than about 10 cst. at 25° C. Such paraffinic hydrocarbons are available from EXXON under the ISOPARS trademark, and from the Permethyl Corporation. Suitable C₁₂ isoparaffins are
25 manufactured by Permethyl Corporation under the tradename Permethyl 99A. Various C₁₆ isoparaffins commercially available, such as isohexadecane (having the tradename Permethyl

R), are also suitable.

Non-Volatile Oils

A variety of nonvolatile oils are also suitable for use in the cosmetic compositions of the invention. The nonvolatile oils generally have a viscosity of greater than about 5 to 10 centistokes at 25° C., and may range in viscosity up to about 1,000,000 centipoise at 25° C. Examples of nonvolatile oils include, but are not limited to:

Suitable esters are mono-, di-, and triesters. The composition may comprise one or more esters selected from the group, or mixtures thereof.

Monoesters are defined as esters formed by the reaction of a monocarboxylic acid having the formula R-COOH, wherein R is a straight or branched chain saturated or unsaturated alkyl having 2 to 45 carbon atoms, or phenyl; and an alcohol having the formula R-OH wherein R is a straight or branched chain saturated or unsaturated alkyl having 2-30 carbon atoms, or phenyl. Both the alcohol and the acid may be substituted with one or more hydroxyl groups. Either one or both of the acid or alcohol may be a "fatty" acid or alcohol, and may have from about 6 to 30 carbon atoms, more preferably 12, 14, 16, 18, or 22 carbon atoms in straight or branched chain, saturated or unsaturated form. Examples of monoester oils that may be used in the compositions of the invention include hexyl laurate, butyl isostearate, hexadecyl isostearate, cetyl palmitate, isostearyl neopentanoate, stearyl heptanoate, isostearyl isononanoate, stearyl lactate, stearyl octanoate, stearyl stearate, isononyl isononanoate, and so on.

Suitable diesters are the reaction product of a dicarboxylic acid and an aliphatic or aromatic alcohol or an aliphatic or aromatic alcohol having at least two substituted hydroxyl groups and a monocarboxylic acid. The dicarboxylic acid may contain from 2 to 30 carbon atoms, and may be in the straight or branched chain, saturated or unsaturated form. The dicarboxylic acid may be substituted with one or more hydroxyl groups. The aliphatic or

aromatic alcohol may also contain 2 to 30 carbon atoms, and may be in the straight or branched chain, saturated, or unsaturated form. Preferably, one or more of the acid or alcohol is a fatty acid or alcohol, i.e. contains 12-22 carbon atoms. The dicarboxylic acid may also be an alpha hydroxy acid. The ester may be in the dimer or trimer form. Examples of diester
5 oils that may be used in the compositions of the invention include diisostearyl malate, neopentyl glycol dioctanoate, dibutyl sebacate, dicetearyl dimer dilinoleate, dicetyl adipate, diisocetyl adipate, diisononyl adipate, diisostearyl dimer dilinoleate, diisostearyl fumarate, diisostearyl malate, dioctyl malate, and so on.

Suitable triesters comprise the reaction product of a tricarboxylic acid and an aliphatic
10 or aromatic alcohol or alternatively the reaction product of an aliphatic or aromatic alcohol having three or more substituted hydroxyl groups with a monocarboxylic acid. As with the mono- and diesters mentioned above, the acid and alcohol contain 2 to 30 carbon atoms, and may be saturated or unsaturated, straight or branched chain, and may be substituted with one or more hydroxyl groups. Preferably, one or more of the acid or alcohol is a fatty acid or
15 alcohol containing 12 to 22 carbon atoms. Examples of triesters include esters of arachidonic, citric, or behenic acids, such as triarachidin, tributyl citrate, triisostearyl citrate, tri C₁₂₋₁₃ alkyl citrate, tricaprylin, tricaprylyl citrate, tridecyl behenate, trioctyldodecyl citrate, tridecyl behenate; or tridecyl cocoate, tridecyl isononanoate, and so on.

Esters suitable for use in the composition are further described on pages 2679-2688 of
20 the C.T.F.A. Cosmetic Ingredient Dictionary and Handbook, Eleventh Edition, 2006, which is hereby incorporated by reference in its entirety.

It may be desirable to incorporate one or more nonvolatile hydrocarbon oils into the composition. Suitable nonvolatile hydrocarbon oils include paraffinic hydrocarbons and olefins, preferably those having greater than about 20 carbon atoms. Examples of such
25 hydrocarbon oils include C₂₄₋₂₈ olefins, C₃₀₋₄₅ olefins, C₂₀₋₄₀ isoparaffins, hydrogenated

polyisobutene, polyisobutene, polydecene, hydrogenated polydecene, mineral oil, pentahydrosqualene, squalene, squalane, and mixtures thereof. In one preferred embodiment such hydrocarbons have a molecular weight ranging from about 300 to 1000 Daltons.

Synthetic or naturally occurring glyceryl esters of fatty acids, or triglycerides, are also suitable for use in the compositions. Both vegetable and animal sources may be used. Examples of such oils include castor oil, lanolin oil, C₁₀₋₁₈ triglycerides, caprylic/capric/triglycerides, sweet almond oil, apricot kernel oil, sesame oil, camelina sativa oil, tamanu seed oil, coconut oil, corn oil, cottonseed oil, linseed oil, ink oil, olive oil, palm oil, illipe butter, rapeseed oil, soybean oil, grapeseed oil, sunflower seed oil, walnut oil, and the like.

Also suitable are synthetic or semi-synthetic glyceryl esters, such as fatty acid mono-, di-, and triglycerides which are natural fats or oils that have been modified, for example, mono-, di- or triesters of polyols such as glycerin. In an example, a fatty (C₁₂₋₂₂) carboxylic acid is reacted with one or more repeating glyceryl groups. glyceryl stearate, diglyceryl diiosostearate, polyglyceryl-3 isostearate, polyglyceryl-4 isostearate, polyglyceryl-6 ricinoleate, glyceryl dioleate, glyceryl diisostearate, glyceryl tetraisostearate, glyceryl trioctanoate, diglyceryl distearate, glyceryl linoleate, glyceryl myristate, glyceryl isostearate, PEG castor oils, PEG glyceryl oleates, PEG glyceryl stearates, PEG glyceryl tallowates, and so on.

Nonvolatile silicone oils, both water soluble and water insoluble, are also suitable for use in the composition. Such silicones preferably have a viscosity ranging from about 10 to 800,000 cst, preferably 20 to 200,000 cst at 25° C. Suitable water insoluble silicones include amine functional silicones such as amodimethicone; phenyl substituted silicones such as bisphenylhexamethicone, trimethylsiloxyphenyl dimethicone, phenyl trimethicone, or polyphenylmethylsiloxane; dimethicone, dimethicone substituted with C₂₋₃₀ alkyl groups such

cetyl dimethicone. Further examples of such silicones include dimethicone, phenyl dimethicone, diphenyl dimethicone, phenyl trimethicone, or trimethylsiloxyphenyl dimethicone.

Other examples include alkyl dimethicones such as cetyl dimethicone, stearyl dimethicone. Phenyl trimethicone can be purchased from Dow Corning Corporation under the tradename 556 Fluid. Trimethylsiloxyphenyl dimethicone can be purchased from Wacker-Chemie under the tradename PDM-1000. Cetyl dimethicone, also referred to as a liquid silicone wax, may be purchased from Dow Corning as Fluid 2502, or from DeGussa Care & Surface Specialties under the trade names Abil Wax 9801, or 9814.

Various types of fluorinated oils may also be suitable for use in the compositions including but not limited to fluorinated silicones, fluorinated esters, or perfluoropolyethers. Particularly suitable are fluorosilicones such as trimethylsilyl endcapped fluorosilicone oil, polytrifluoropropylmethylsiloxanes, and similar silicones such as those disclosed in U.S. Pat. No. 5,118,496 which is hereby incorporated by reference. Perfluoropolyethers include those disclosed in U.S. Pat. Nos. 5,183,589, 4,803,067, 5,183,588 all of which are hereby incorporated by reference, which are commercially available from Montefluos under the trademark Fomblin.

Oil Phase Structuring Agents

A variety of oil phase structuring agents may be present. The term “oil phase structuring agent” means an ingredient or combination of ingredients, soluble or dispersible in the oil phase, which will increase the viscosity, or structure, the oil phase. The oil phase structuring agent is compatible with the resveratrol derivative and the rest of the formulation ingredients. The term “compatible” means that the oil phase structuring agent and resveratrol derivative are capable of being formulated into a cosmetic product that is generally stable.

The structuring agent may be present in an amount sufficient to provide a liquid composition

with increased viscosity, a semi-solid, or in some cases a solid composition that may be self-supporting. The structuring agent itself may be present in the liquid, semi-solid, or solid form. Suggested ranges of structuring agent are from about 0.01 to 70%, preferably from about 0.05 to 50%, more preferably from about 0.1-35% by weight of the total composition. Suitable oil
5 phase structuring agents include those that are silicone based or organic based. They may be polymers or non-polymers, synthetic, natural, or a combination of both.

A variety of oil phase structuring agents may be silicone based, such as silicone elastomers, silicone gums, silicone waxes, linear silicones having a degree of polymerization that provides the silicone with a degree of viscosity such that when incorporated into the
10 cosmetic composition it is capable of increasing the viscosity of the oil phase. Examples of silicone structuring agents include, but are not limited to:

Silicone elastomers suitable for use in the compositions of the invention include those that are formed by addition reaction-curing, by reacting an SiH-containing diorganosiloxane and an organopolysiloxane having terminal olefinic unsaturation, or an alpha-omega diene
15 hydrocarbon, in the presence of a platinum metal catalyst. Such elastomers may also be formed by other reaction methods such as condensation-curing organopolysiloxane compositions in the presence of an organotin compound via a dehydrogenation reaction between hydroxyl-terminated diorganopolysiloxane and SiH-containing diorganopolysiloxane or alpha omega diene; or by condensation-curing organopolysiloxane compositions in the
20 presence of an organotin compound or a titanate ester using a condensation reaction between an hydroxyl-terminated diorganopolysiloxane and a hydrolysable organosiloxane; peroxide-curing organopolysiloxane compositions which thermally cure in the presence of an organoperoxide catalyst.

One type of elastomer that may be suitable is prepared by addition reaction-curing an
25 organopolysiloxane having at least 2 lower alkenyl groups in each molecule or an alpha-

omega diene; and an organopolysiloxane having at least 2 silicon-bonded hydrogen atoms in each molecule; and a platinum-type catalyst. While the lower alkenyl groups such as vinyl, can be present at any position in the molecule, terminal olefinic unsaturation on one or both molecular terminals is preferred. The molecular structure of this component may be straight
5 chain, branched straight chain, cyclic, or network. These organopolysiloxanes are exemplified by methylvinylsiloxanes, methylvinylsiloxane-dimethylsiloxane copolymers, dimethylvinylsiloxyl-terminated dimethylpolysiloxanes, dimethylvinylsiloxyl-terminated dimethylsiloxane-methylphenylsiloxane copolymers, dimethylvinylsiloxyl-terminated dimethylsiloxane-diphenylsiloxane-methylvinylsiloxane copolymers, trimethylsiloxyl-
10 terminated dimethylsiloxane-methylvinylsiloxane copolymers, trimethylsiloxyl-terminated dimethylsiloxane-methylphenylsiloxane-methylvinylsiloxane copolymers, dimethylvinylsiloxyl-terminated methyl(3,3,3-trifluoropropyl) polysiloxanes, and dimethylvinylsiloxyl-terminated dimethylsiloxane-methyl(3,3,3-trifluoropropyl)siloxane copolymers, decadiene, octadiene, heptadiene, hexadiene, pentadiene, or tetradene, or
15 tridiene.

Curing proceeds by the addition reaction of the silicon-bonded hydrogen atoms in the dimethyl methylhydrogen siloxane, with the siloxane or alpha-omega diene under catalysis using the catalyst mentioned herein. To form a highly crosslinked structure, the methyl hydrogen siloxane must contain at least 2 silicon-bonded hydrogen atoms in each molecule in
20 order to optimize function as a crosslinker.

The catalyst used in the addition reaction of silicon-bonded hydrogen atoms and alkenyl groups, and is concretely exemplified by chloroplatinic acid, possibly dissolved in an alcohol or ketone and this solution optionally aged, chloroplatinic acid-olefin complexes, chloroplatinic acid-alkenylsiloxane complexes, chloroplatinic acid-diketone complexes,
25 platinum black, and carrier-supported platinum.

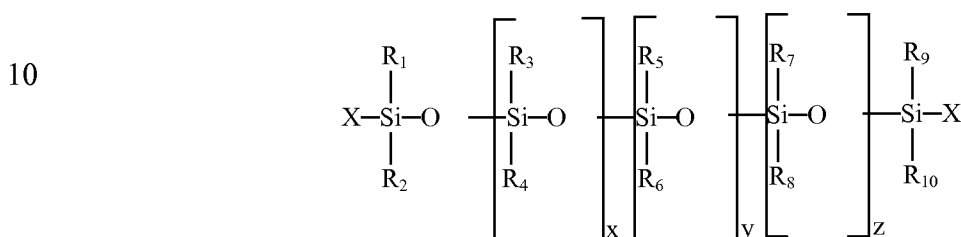
Examples of suitable silicone elastomers for use in the compositions of the invention may be in the powder form, or dispersed or solubilized in solvents such as volatile or non-volatile silicones, or silicone compatible vehicles such as paraffinic hydrocarbons or esters. Examples of silicone elastomer powders include vinyl dimethicone/methicone silsesquioxane crosspolymers like Shin-Etsu's KSP-100, KSP-101, KSP-102, KSP-103, KSP-104, KSP-105, hybrid silicone powders that contain a fluoroalkyl group like Shin-Etsu's KSP-200 which is a fluoro-silicone elastomer, and hybrid silicone powders that contain a phenyl group such as Shin-Etsu's KSP-300, which is a phenyl substituted silicone elastomer; and Dow Coming's DC 9506. Examples of silicone elastomer powders dispersed in a silicone compatible vehicle include dimethicone/vinyl dimethicone crosspolymers supplied by a variety of suppliers including Dow Corning Corporation under the tradenames 9040 or 9041, GE Silicones under the tradename SFE 839, or Shin-Etsu Silicones under the tradenames KSG-15, 16, 18. KSG-15 has the CTFA name cyclopentasiloxane/dimethicone/vinyl dimethicone crosspolymer. KSG-18 has the INCI name phenyl trimethicone/dimethicone/phenyl vinyl dimethicone crosspolymer. Silicone elastomers may also be purchased from Grant Industries under the Gransil trademark. Also suitable are silicone elastomers having long chain alkyl substitutions such as lauryl dimethicone/vinyl dimethicone crosspolymers supplied by Shin Etsu under the tradenames KSG-31, KSG-32, KSG-41, KSG-42, KSG-43, and KSG-44. 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 to Sakuta et al., issued Nov. 13, 1990; U.S. Pat. No. 5,760,116 to Kilgour et al., issued Jun. 2, 1998; U.S. Pat. No. 5,654,362 to Schulz, Jr. et al. issued Aug. 5, 1997; and Japanese Patent Application JP 61-18708, assigned to Pola Kasei Kogyo KK, each of which are herein incorporated by reference in its entirety.

Also suitable for use as an oil phase structuring agent are one or more silicone gums.

The term "gum" means a silicone polymer having a degree of polymerization sufficient to

provide a silicone having a gum-like texture. In certain cases the silicone polymer forming the gum may be crosslinked. The silicone gum typically has a viscosity ranging from about 500,000 to 100 million cst at 25° C., preferably from about 600,000 to 20 million, more preferably from about 600,000 to 12 million cst. All ranges mentioned herein include all subranges, e.g. 550,000; 925,000; 3.5 million.

The silicone gums that are used in the compositions include, but are not limited to, those of the general formula wherein:



R₁ to R₉ are each independently an alkyl having 1 to 30 carbon atoms, aryl, or aralkyl; and X is OH or a C₁₋₃₀ alkyl, or vinyl; and wherein x, y, or z may be zero with the proviso that no more than two of x, y, or z are zero at any one time, and further that x, y, and z are such that the silicone gum has a viscosity of at least about 500,000 cst, ranging up to about 100 million centistokes at 25° C. Preferred is where R is methyl or OH.

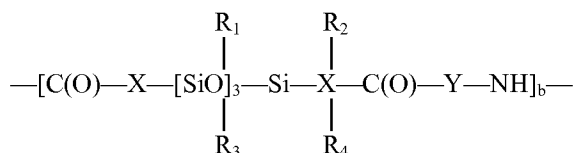
Such silicone gums may be purchased in pure form from a variety of silicone manufacturers including Wacker-Chemie or Dow Corning, and the like. Such silicone gums include those sold by Wacker-Belsil under the trade names CM3092, Wacker-Belsil 1000, or Wacker-Belsil DM 3096. A silicone gum where X is OH, also referred to as dimethiconol, is available from Dow Corning Corporation under the trade name 1401. The silicone gum may also be purchased in the form of a solution or dispersion in a silicone compatible vehicle such as volatile or nonvolatile silicone. An example of such a mixture may be purchased from

Barnet Silicones under the HL-88 trade name, having the INCI name dimethicone.

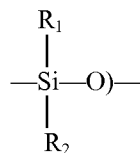
Another type of oily phase structuring agent includes silicone waxes that are typically referred to as alkyl silicone waxes which are semi-solids or solids at room temperature. The term “alkyl silicone wax” means a polydimethylsiloxane having a substituted long chain alkyl (such as C16 to 30) that confers a semi-solid or solid property to the siloxane. Examples of such silicone waxes include stearyl dimethicone, which may be purchased from DeGussa Care & Surface Specialties under the trade name Abil Wax 9800 or from Dow Corning under the trade name 2503. Another example is bis-stearyl dimethicone, which may be purchased from Gransil Industries under the trade name Gransil A-18, or behenyl dimethicone, behenoxy dimethicone.

Also suitable as oil phase structuring agents are various types of polymeric compounds such as polyamides or silicone polyamides.

The term silicone polyamide means a polymer comprised of silicone monomers and monomers containing amide groups as further described herein. The silicone polyamide preferably comprises moieties of the general formula:



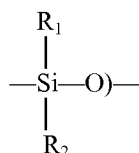
X is a linear or branched alkylene having from about 1-30 carbon atoms; R₁, R₂, R₃, and R₄ are each independently C₁₋₃₀ straight or branched chain alkyl which may be substituted with one or more hydroxyl or halogen groups; phenyl which may be substituted with one or more C₁₋₃₀ alkyl groups, halogen, hydroxyl, or alkoxy groups; or a siloxane chain having the general formula:



5 and Y is:

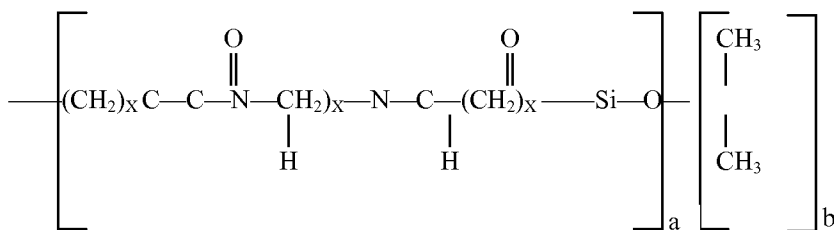
- (a) a linear or branched alkylene having from about 1-40 carbon atoms which may be substituted with (i) one or more amide groups having the general formula R_1CONR_1 , or (ii) C_{5-6} cyclic ring, or (iii) phenylene which may be substituted with one or more C_{1-10} alkyl groups, or (iv) hydroxy, or (v) C_{3-8} cycloalkane, or (vi) C_{1-20} alkyl which
 10 may be substituted with one or more hydroxy groups, or (vii) C_{1-10} alkyl amines; or
 (b) $\text{TR}_5\text{R}_6\text{R}_7$.

wherein R_5 , R_6 , and R_7 , are each independently a C_{1-10} linear or branched alkylenes, and T is CR_8 wherein R_8 is hydrogen, a trivalent atom N, P, or Al, or a C_{1-30} straight or branched chain alkyl which may be substituted with one or more hydroxyl or halogen groups; phenyl which
 15 may be substituted with one or more C_{1-30} alkyl groups, halogen, hydroxyl, or alkoxy groups; or a siloxane chain having the general formula:



20

Preferred is where R_1 , R_2 , R_3 , and R_4 are C_{1-10} , preferably methyl; and X and Y is a linear or branched alkylene. Preferred are silicone polyamides having the general formula:



5

wherein a and b are each independently sufficient to provide a silicone polyamide polymer having a melting point ranging from about 60 to 120° C., and a molecular weight ranging from about 40,000 to 500,000 Daltons. One type of silicone polyamide that may be used in the compositions of the invention may be purchased from Dow Corning Corporation under the tradename Dow Corning 2-8178 gellant which has the CTFA name nylon-611/dimethicone copolymer which is sold in a composition containing PPG-3 myristyl ether.

10

Also suitable are polyamides such as those purchased from Arizona Chemical under the trade names Uniclear and Sylvaclear. Such polyamides may be ester terminated or amide terminated.

15

General examples of ester and amide terminated polyamides that may be used as oil phase gelling agents include those sold by Arizona Chemical under the tradenames Sylvaclear A200V or A2614V, both having the CTFA name ethylenediamine/hydrogenated dimer dilinoleate copolymer/bis-di-C₁₄₋₁₈ alkyl amide; Sylvaclear AF1900V; Sylvaclear C75V having the CTFA name bis-stearyl ethylenediamine/neopentyl glycol/stearyl hydrogenated dimer dilinoleate copolymer; Sylvaclear PA1200V having the CTFA name Polyamide-3; Sylvaclear PE400V; Sylvaclear WF1500V; or Uniclear, such as Uniclear 100VG having the INCI name ethylenediamine/stearyl dimer dilinoleate copolymer; or ethylenediamine/stearyl dimer ditallate copolymer. Other examples of suitable polyamides include those sold by Henkel under the Versamid trademark (such as Versamid 930, 744, 1655), or by Olin Mathieson Chemical Corp. under the brand name Onamid S or Onamid C.

20

25

Also suitable as the oil phase structuring agent may be one or more natural or synthetic waxes such as animal, vegetable, or mineral waxes. Preferably such waxes will have a higher melting point such as from about 60 to 150° C., more preferably from about 65 to 100° C.

Examples of such waxes include waxes made by Fischer-Tropsch synthesis, such as

5 polyethylene or synthetic wax; or various vegetable waxes such as bayberry, candelilla, ozokerite, acacia, beeswax, ceresin, cetyl esters, flower wax, citrus wax, carnauba wax, jojoba wax, japan wax, polyethylene, microcrystalline, rice bran, lanolin wax, mink, montan, bayberry, ouricury, ozokerite, palm kernel wax, paraffin, avocado wax, apple wax, shellac wax, clary wax, spent grain wax, grape wax, and polyalkylene glycol derivatives thereof such
10 as PEG6-20 beeswax, or PEG-12 carnauba wax; or fatty acids or fatty alcohols, including esters thereof, such as hydroxystearic acids (for example 12-hydroxy stearic acid), tristearin, tribehenin, and so on.

One type of structuring agent that may be used in the composition comprises natural or synthetic montmorillonite minerals such as hectorite, bentonite, and quaternized derivatives
15 thereof, which are obtained by reacting the minerals with a quaternary ammonium compound, such as stearylalkonium bentonite, hectorites, quaternized hectorites such as Quaternium-18 hectorite, attapulgite, carbonates such as propylene carbonate, bentones, and the like.

Another type of structuring agent that may be used in the compositions are silicas, silicates, silica silylate, and alkali metal or alkaline earth metal derivatives thereof. These
20 silicas and silicates are generally found in the particulate form and include silica, silica silylate, magnesium aluminum silicate, and the like.

Other Ingredients

The compositions of the invention may contain a variety of other ingredients including, but not limited to, surfactants, botanicals, sugars, humectants, preservatives, peptides, and the
25 like, including but not limited to those mentioned herein.

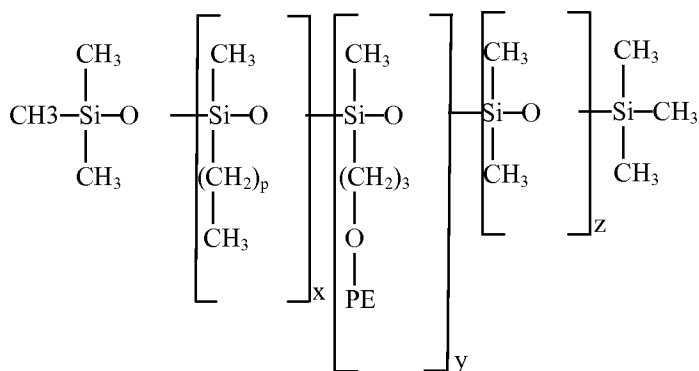
Surfactants

The composition preferably contains one or more surfactants, which may be silicone or organic. The surfactants will aid in the formation of stable emulsions of either the water-in-oil or oil-in-water form. If present, the surfactant may range from about 0.001 to 30%, preferably
5 from about 0.005 to 25%, more preferably from about 0.1 to 20% by weight of the total composition.

Suitable silicone surfactants include polyorganosiloxane polymers that have amphiphilic properties, for example contain hydrophilic radicals and lipophilic radicals. These silicone surfactants may be liquids or solids at room temperature.

10 One type of silicone surfactant that may be used is generally referred to as dimethicone copolyol or alkyl dimethicone copolyol. This surfactant is either a water-in-oil or oil-in-water surfactant having an Hydrophile/Lipophile Balance (HLB) ranging from about 2 to 18. Preferably the silicone surfactant is a nonionic surfactant having an HLB ranging from about 2 to 12, preferably about 2 to 10, most preferably about 4 to 6. The term "hydrophilic radical"
15 means a radical that, when substituted onto the organosiloxane polymer backbone, confers hydrophilic properties to the substituted portion of the polymer. Examples of radicals that will confer hydrophilicity are hydroxy-polyethyleneoxy, hydroxyl, carboxylates, and mixtures thereof. The term "lipophilic radical" means an organic radical that, when substituted onto the organosiloxane polymer backbone, confers lipophilic properties to the substituted portion
20 of the polymer. Examples of organic radicals that will confer lipophilicity are C₁₋₄₀ straight or branched chain alkyl, fluoro, aryl, aryloxy, C₁₋₄₀ hydrocarbyl acyl, hydroxy-polypropyleneoxy, or mixtures thereof.

One type of suitable silicone surfactant has the general formula:



wherein p is 0-40 (the range including all numbers between and subranges such as 2, 3, 4, 13, 14, 15, 16, 17, 18, etc.), and PE is $(-\text{C}_2\text{H}_4\text{O})_a(-\text{C}_3\text{H}_6\text{O})_b\text{H}$ wherein a is 0 to 25, b is 0-25 with the proviso that both a and b cannot be 0 simultaneously, x and y are each independently ranging from 0 to 1 million with the proviso that they both cannot be 0 simultaneously. In one preferred embodiment, x, y, z, a, and b are such that the molecular weight of the polymer ranges from about 5,000 to about 500,000, more preferably from about 10,000 to 100,000, and is most preferably approximately about 50,000 and the polymer is generically referred to as dimethicone copolyol.

One type of silicone surfactant is wherein p is such that the long chain alkyl is cetyl or lauryl, and the surfactant is called, generically, cetyl dimethicone copolyol or lauryl dimethicone copolyol respectively.

In some cases the number of repeating ethylene oxide or propylene oxide units in the polymer are also specified, such as a dimethicone copolyol that is also referred to as PEG-15/PPG-10 dimethicone, which refers to a dimethicone having substituents containing 15 ethylene glycol units and 10 propylene glycol units on the siloxane backbone. It is also possible for one or more of the methyl groups in the above general structure to be substituted with a longer chain alkyl (e.g. ethyl, propyl, butyl, etc.) or an ether such as methyl ether, ethyl ether, propyl ether, butyl ether, and the like.

Examples of silicone surfactants are those sold by Dow Corning under the tradename Dow Corning 3225C Formulation Aid having the CTFA name cyclotetrasiloxane (and) cyclopentasiloxane (and) PEG/PPG-18 dimethicone; or 5225C Formulation Aid, having the CTFA name cyclopentasiloxane (and) PEG/PPG-18/18 dimethicone; or Dow Coming 190

5 Surfactant having the CTFA name PEG/PPG-18/18 dimethicone; or Dow Corning 193 Fluid, Dow Corning 5200 having the CTFA name lauryl PEG/PPG-18/18 methicone; or Abil EM 90 having the CTFA name cetyl PEG/PPG-14/14 dimethicone sold by Goldschmidt; or Abil EM 97 having the CTFA name bis-cetyl PEG/PPG-14/14 dimethicone sold by Goldschmidt; or Abil WE 09 having the CTFA name cetyl PEG/PPG-10/1 dimethicone in a mixture also

10 containing polyglyceryl-4 isostearate and hexyl laurate; or KF-6011 sold by Shin-Etsu Silicones having the CTFA name PEG-11 methyl ether dimethicone; KF-6012 sold by Shin-Etsu Silicones having the CTFA name PEG/PPG-20/22 butyl ether dimethicone; or KF-6013 sold by Shin-Etsu Silicones having the CTFA name PEG-9 dimethicone; or KF-6015 sold by Shin-Etsu Silicones having the CTFA name PEG-3 dimethicone; or KF-6016 sold by Shin-

15 Etsu Silicones having the CTFA name PEG-9 methyl ether dimethicone; or KF-6017 sold by Shin-Etsu Silicones having the CTFA name PEG-10 dimethicone; or KF-6038 sold by Shin-Etsu Silicones having the CTFA name lauryl PEG-9 polydimethylsiloxyethyl dimethicone.

Also suitable are various types of crosslinked silicone surfactants are referred to as emulsifying elastomers. They are typically prepared as set forth above with respect to the

20 section "silicone elastomers" except that the silicone elastomers will contain at least one hydrophilic moiety such as polyoxyalkylenated groups. Typically these polyoxyalkylenated silicone elastomers are crosslinked organopolysiloxanes that may be obtained by a crosslinking addition reaction of diorganopolysiloxane comprising at least one hydrogen bonded to silicon and of a polyoxyalkylene comprising at least two ethylenically unsaturated

25 groups. In at least one embodiment, the polyoxyalkylenated crosslinked organo-polysiloxanes

are obtained by a crosslinking addition reaction of a diorganopolysiloxane comprising at least two hydrogens each bonded to a silicon, and a polyoxyalkylene comprising at least two ethylenically unsaturated groups, optionally in the presence of a platinum catalyst, as described, for example, in U.S. Pat. No. 5,236,986 and U.S. Pat. No. 5,412,004, U.S. Pat. No. 5,837,793 and U.S. Pat. No. 5,811,487, the contents of which are incorporated by reference.

Polyoxyalkylenated silicone elastomers that may be used in at least one embodiment of the invention include those sold by Shin-Etsu Silicones under the names KSG-21, KSG-20, KSG-30, KSG-31, KSG-32, KSG-33; KSG-210 which is dimethicone/PEG-10/15 crosspolymer dispersed in dimethicone; KSG-310 which is PEG-15 lauryl dimethicone crosspolymer; KSG-320 which is PEG-15 lauryl dimethicone crosspolymer dispersed in isododecane; KSG-330 (the former dispersed in triethylhexanoin), KSG-340 which is a mixture of PEG-10 lauryl dimethicone crosspolymer and PEG-15 lauryl dimethicone crosspolymer.

Also suitable are polyglycerolated silicone elastomers like those disclosed in PCT/WO 2004/024798, which is hereby incorporated by reference in its entirety. Such elastomers include Shin-Etsu's KSG series, such as KSG-710 which is dimethicone/polyglycerin-3 crosspolymer dispersed in dimethicone; or lauryl dimethicone/polyglycerin-3 crosspolymer dispersed in a variety of solvent such as isododecane, dimethicone, triethylhexanoin, sold under the Shin-Etsu tradenames KSG-810, KSG-820, KSG-830, or KSG-840. Also suitable are silicones sold by Dow Corning under the tradenames 9010 and DC9011.

One preferred crosslinked silicone elastomer emulsifier is dimethicone/PEG-10/15 crosspolymer.

The composition may comprise one or more nonionic organic surfactants. Suitable nonionic surfactants include alkoxylated alcohols, or ethers, formed by the reaction of an alcohol with an alkylene oxide, usually ethylene or propylene oxide. Preferably the alcohol is

either a fatty alcohol having 6 to 30 carbon atoms. Examples of such ingredients include Steareth 2-100, which is formed by the reaction of stearyl alcohol and ethylene oxide and the number of ethylene oxide units ranges from 2 to 100; Beheneth 5-30 which is formed by the reaction of behenyl alcohol and ethylene oxide where the number of repeating ethylene oxide units is 5 to 30; Cetareth 2-100, formed by the reaction of a mixture of cetyl and stearyl alcohol with ethylene oxide, where the number of repeating ethylene oxide units in the molecule is 2 to 100; Ceteth 1-45 which is formed by the reaction of cetyl alcohol and ethylene oxide, and the number of repeating ethylene oxide units is 1 to 45, and so on.

Other alkoxyated alcohols are formed by the reaction of fatty acids and mono-, di- or polyhydric alcohols with an alkylene oxide. For example, the reaction products of C₆₋₃₀ fatty carboxylic acids and polyhydric alcohols which are monosaccharides such as glucose, galactose, methyl glucose, and the like, with an alkoxyated alcohol. Examples include polymeric alkylene glycols reacted with glyceryl fatty acid esters such as PEG glyceryl oleates, PEG glyceryl stearate; or PEG polyhydroxyalkanotes such as PEG dipolyhydroxystearate wherein the number of repeating ethylene glycol units ranges from 3 to 1000.

Also suitable as nonionic surfactants are formed by the reaction of a carboxylic acid with an alkylene oxide or with a polymeric ether. The resulting products have the general formula: where RCO is the carboxylic ester radical, X is hydrogen or lower alkyl, and n is the number of polymerized alkoxy groups. In the case of the diesters, the two RCO-groups do not need to be identical. Preferably, R is a C₆₋₃₀ straight or branched chain, saturated or unsaturated alkyl, and n is from 1-100.

Monomeric, homopolymeric, or block copolymeric ethers are also suitable as nonionic surfactants. Typically, such ethers are formed by the polymerization of monomeric alkylene oxides, generally ethylene or propylene oxide. Such polymeric ethers have the following

general formula: wherein R is H or lower alkyl and n is the number of repeating monomer units, and ranges from 1 to 500.

Other suitable nonionic surfactants include alkoxyated sorbitan and alkoxyated sorbitan derivatives. For example, alkoxylation, in particular ethoxylation of sorbitan provides polyalkoxyated sorbitan derivatives. Esterification of polyalkoxyated sorbitan provides sorbitan esters such as the polysorbates. For example, the polyalkoxyated sorbitan can be esterified with C6-30, preferably C12-22 fatty acids. Examples of such ingredients include Polysorbates 20-85, sorbitan oleate, sorbitan sesquioleate, sorbitan palmitate, sorbitan sesquiossearate, sorbitan searate, and so on.

Certain types of amphoteric, zwitterionic, or cationic surfactants may also be used in the compositions. Descriptions of such surfactants are set forth in U.S. Pat. No. 5,843,193, which is hereby incorporated by reference in its entirety.

It may also be desirable to include one or more humectants in the composition. If present, such humectants may range from about 0.001 to 25%, preferably from about 0.005 to 20%, more preferably from about 0.1 to 15% by weight of the total composition. Examples of suitable humectants include glycols, sugars, and the like. Suitable glycols are in monomeric or polymeric form and include polyethylene and polypropylene glycols such as PEG 4-200, which are polyethylene glycols having from 4 to 200 repeating ethylene oxide units; as well as C₁₋₆ alkylene glycols such as propylene glycol, butylene glycol, pentylene glycol, and the like.

Suitable sugars, some of which are also polyhydric alcohols, are also suitable humectants. Examples of such sugars include glucose, fructose, honey, hydrogenated honey, inositol, maltose, mannitol, maltitol, sorbitol, sucrose, xylitol, xylose, and so on. Preferably, the humectants used in the composition of the invention are C₁₋₆, preferably C₂₋₄ alkylene glycols, most particularly butylene glycol.

It may be desirable to include one or more aqueous phase structuring agents in the

composition. Such agents will typically thicken or increase the viscosity of the aqueous phase of the emulsion. If present, suggested ranges are from about 0.01 to 30%, preferably from about 0.1 to 20%, more preferably from about 0.5 to 15% by weight of the total composition. Examples of such agents include various acrylate based thickening agents, natural or synthetic
5 gums, polysaccharides, and the like.

A variety of polysaccharides in various forms may be suitable aqueous phase thickening agents. Examples of such polysaccharides include naturally derived materials such as agar, agarose, algal polysaccharides, algin, alginic acid, amylopectin, chitin, dextran, cassia gum, cellulose gum, gelatin, gellan gum, hyaluronic acid, hydroxyethyl cellulose,
10 methyl cellulose, ethyl cellulose, pectin, sclerotium gum, xanthan gum, pectin, trehalose, gelatin, and so on.

For example, acrylic polymeric thickeners comprised of monomers A and B wherein A is selected from the group consisting of acrylic acid, methacrylic acid, and mixtures thereof; and B is selected from the group consisting of a C₁₋₂₂ alkyl acrylate, a C₁₋₂₂ alkyl methacrylate, and mixtures thereof are suitable. In one embodiment the A monomer comprises one or more
15 of acrylic acid or methacrylic acid, and the B monomer is selected from the group consisting of a C₁₋₁₀, most preferably C₁₋₄ alkyl acrylate, a C₁₋₁₀, most preferably C₁₋₄ alkyl methacrylate, and mixtures thereof. Most preferably the B monomer is one or more of methyl or ethyl acrylate or methacrylate. The acrylic copolymer may be supplied in an aqueous solution
20 having a solids content ranging from about 10-60%, preferably 20-50%, more preferably 25-45% by weight of the polymer, with the remainder water. The composition of the acrylic copolymer may contain from about 0.1-99 parts of the A monomer, and about 0.1-99 parts of the B monomer. Acrylic polymer solutions include those sold by Seppic, Inc., under the tradename Capigel.

25 Examples of such secondary thickening agents include acrylates/stearate-

methacrylate copolymer, which is sold by Rohm & Haas under the tradename Acrysol ICS-1.

Also suitable are acrylate based anionic amphiphilic polymers containing at least one hydrophilic unit and at least one allyl ether unit containing a fatty chain. Examples of polymers are crosslinked terpolymers of methacrylic acid, of ethyl acrylate, of polyethylene glycol (having 10 EO units) ether of stearyl alcohol or steareth-10, in particular those sold by the company Allied Colloids under the names **SALCARE** SC80 and **SALCARE** SC90, which are aqueous emulsions

containing 30% of a crosslinked terpolymer of methacrylic acid, of ethyl acrylate and of steareth-10 allyl ether (40/50/10).

Also suitable are acrylate copolymers such as Polyacrylate-3 which is a copolymer of methacrylic acid, methylmethacrylate, methylstyrene isopropylisocyanate, and PEG-40 behenate monomers; Polyacrylate-10 which is a copolymer of sodium acryloyldimethyltaurate, sodium acrylate, acrylamide and vinyl pyrrolidone monomers; or Polyacrylate-11, which is a copolymer of sodium acryloyldimethylacryloyldimethyl taurate, sodium acrylate, hydroxyethyl acrylate, lauryl acrylate, butyl acrylate, and acrylamide monomers.

Also suitable are crosslinked acrylate based polymers where one or more of the acrylic groups may have substituted long chain alkyl (such as 6-40, 10-30, and the like) groups, for example acrylates/C₁₀₋₃₀ alkyl acrylate crosspolymer which is a copolymer of C₁₀₋₃₀ alkyl acrylate and one or more monomers of acrylic acid, methacrylic acid, or one of their simple esters crosslinked with the allyl ether of sucrose or the allyl ether of pentaerythritol. Such polymers are commonly sold under the Carbopol or Pemulen tradenames.

Also suitable are acrylate based polymeric thickeners sold by Clariant under the Aristoflex trademark such as Aristoflex AVC, which is ammonium

acryloyldimethyltaurate/VP copolymer; Aristoflex AVL which is the same polymer has found

in AVC dispersed in mixture containing caprylic/capric triglyceride, trilaureth-4, and polyglyceryl-2 sesquiisostearate; or Aristoflex HMB which is ammonium acryloyldimethyltaurate/behent-25 methacrylate crosspolymer, and the like.

Also suitable as the aqueous phase thickening agents are various polyethylene glycols (PEG) derivatives where the degree of polymerization ranges from 1,000 to 200,000. Such ingredients are indicated by the designation "PEG" followed by the degree of polymerization in thousands, such as PEG-45M, which means PEG having 45,000 repeating ethylene oxide units. Examples of suitable PEG derivatives include PEG 2M, 5M, 7M, 9M, 14M, 20M, 23M, 25M, 45M, 65M, 90M, 115M, 160M, 180M, and the like.

Also suitable are polyglycerins which are repeating glycerin moieties where the number of repeating moieties ranges from 15 to 200, preferably from about 20-100. Examples of suitable polyglycerins include those having the CFTA names polyglycerin-20, polyglycerin-40, and the like.

Botanical Extracts

It may be desirable to include one or more botanical extracts in the compositions. If so, suggested ranges are from about 0.0001 to 10%, preferably about 0.0005 to 8%, more preferably about 0.001 to 5% by weight of the total composition. Suitable botanical extracts include extracts from plants (herbs, roots, flowers, fruits, seeds) such as flowers, fruits, vegetables, and so on, including yeast ferment extract, padica pavonica extract, thermus thermophilis ferment extract, camelina sativa seed oil, boswellia serrata extract, olive extract, aribodopsis thaliana extract, acacia dealbata extract, acer saccharinum (sugar maple), acidopholus, acorus, aesculus, agaricus, agave, agrimonia, algae, aloe, citrus, brassica, cinnamon, orange, apple, blueberry, cranberry, peach, pear, lemon, lime, pea, seaweed, caffeine, green tea, chamomile, willowbark, mulberry, poppy, and those set forth on pages 1646 through 1660 of the CTFA Cosmetic Ingredient Handbook, Eighth Edition, Volume 2.

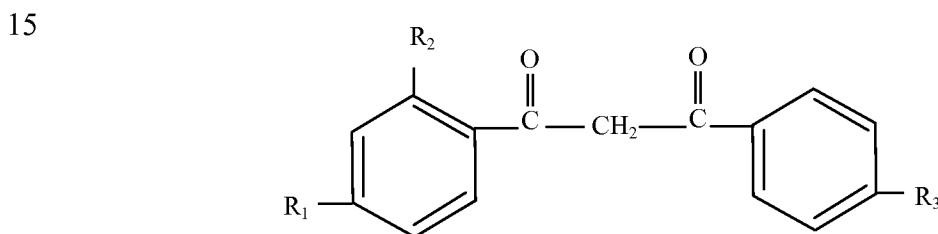
Further specific examples include, but are not limited to, Glycyrrhiza Glabra, Salix Nigra, Macrocyctis Pyrifera, Pyrus Malus, Saxifraga Sarmentosa, Vilis Vinifera, Morus Nigra, Scutellaria Baicalensis, Anthemis Nobilis, Salvia Sclarea, Rosmarinus Officianalis, Citrus Medica Limonum, Panax Ginseng, and mixtures thereof.

5 Sunscreens

It may also be desirable to include one or more sunscreens in the compositions of the invention. Such sunscreens include chemical UVA or UVB sunscreens or physical sunscreens in the particulate form.

UVA Chemical Sunscreens

10 If desired, the composition may comprise one or more UVA sunscreens. The term "UVA sunscreen" means a chemical compound that blocks UV radiation in the wavelength range of about 320 to 400 nm. Preferred UVA sunscreens are dibenzoylmethane compounds having the general formula:



20 wherein R₁ is H, OR and NRR wherein each R is independently H, C₁₋₂₀ straight or branched chain alkyl; R₂ is H or OH; and R₃ is H, C₁₋₂₀ straight or branched chain alkyl.

Preferred is where R₁ is OR where R is a C₁₋₂₀ straight or branched alkyl, preferably methyl; R₂ is H; and R₃ is a C₁₋₂₀ straight or branched chain alkyl, more preferably, butyl.

25 Examples of suitable UVA sunscreen compounds of this general formula include 4-methyldibenzoylmethane, 2-methyldibenzoylmethane, 4-isopropyldibenzoylmethane, 4-tert-butyldibenzoylmethane, 2,4-dimethyldibenzoylmethane, 2,5-dimethyldibenzoylmethane,

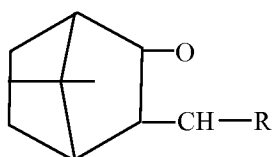
4,4'-diisopropylbenzoylmethane, 4-tert-butyl-4'-methoxydibenzoylmethane, 4,4'-
diisopropylbenzoylmethane, 2-methyl-5-isopropyl-4'-methoxydibenzoylmethane, 2-methyl-5-
tert-butyl-4'-methoxydibenzoylmethane, and so on. Particularly preferred is 4-tert-butyl-4'-
methoxydibenzoylmethane, also referred to as Avobenzone. Avobenzone is commercial
5 available from Givaudan-Roure under the trademark Parsol 1789, and Merck & Co. under the
tradename Eusolex 9020.

The composition may contain from about 0.001-20%, preferably 0.005-5%, more
preferably about 0.005-3% by weight of the composition of UVA sunscreen. In the preferred
embodiment of the invention the UVA sunscreen is Avobenzone, and it is present at not
10 greater than about 3% by weight of the total composition.

UVB Chemical Sunscreens

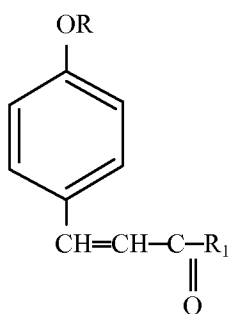
The term "UVB sunscreen" means a compound that blocks UV radiation in the
wavelength range of from about 290 to 320 nm. A variety of UVB chemical sunscreens exist
including alpha-cyano-beta,beta-diphenyl acrylic acid esters as set forth in U.S. Pat. No.
15 3,215,724, which is hereby incorporated by reference in its entirety. One particular example of
an alpha-cyano-beta,beta-diphenyl acrylic acid ester is Octocrylene, which is 2-ethylhexyl 2-
cyano-3,3-diphenylacrylate. In certain cases the composition may contain no more than about
110% by weight of the total composition of octocrylene. Suitable amounts range from about
0.001-10% by weight. Octocrylene may be purchased from BASF under the tradename Uvinul
20 N-539.

Other suitable sunscreens include benzylidene camphor derivatives as set forth in U.S.
Pat. No. 3,781,417, which is hereby incorporated by reference in its entirety. Such benzylidene
camphor derivatives have the general formula:



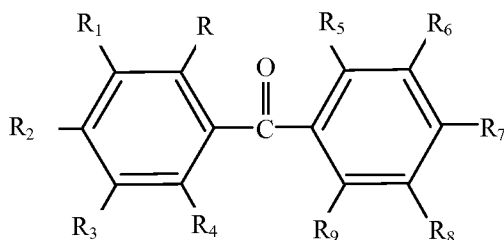
wherein R is p-tolyl or styryl, preferably styryl. Particularly preferred is 4-methylbenzylidene camphor, which is a lipid soluble UVB sunscreen compound sold under the tradename Eusolex 6300 by Merck.

Also suitable are cinnamate derivatives having the general formula:



wherein R and R₁ are each independently a C₁₋₂₀ straight or branched chain alkyl. Preferred is where R is methyl and R₁ is a branched chain C₁₋₁₀, preferably C₈ alkyl. The preferred compound is ethylhexyl methoxycinnamate, also referred to as Octoxinate or octyl methoxycinnamate. The compound may be purchased from Givaudan Corporation under the tradename Parsol MCX, or BASF under the tradename Uvinul MC 80. Also suitable are mono-, di-, and triethanolamine derivatives of such methoxy cinnamates including diethanolamine methoxycinnamate. Cinoxate, the aromatic ether derivative of the above compound is also acceptable. If present, the Cinoxate should be found at no more than about 3% by weight of the total composition.

Also suitable as UVB screening agents are various benzophenone derivatives having the general formula:



5

wherein R through R₉ are each independently H, OH, NaO₃S, SO₃H, SO₃Na, Cl, R", OR"

where R" is C₁₋₂₀ straight or branched chain alkyl. Examples of such compounds include

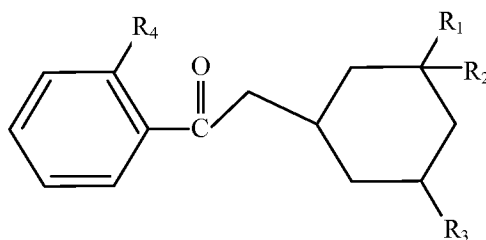
Benzophenone 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, and 12. Particularly preferred is where the

10 benzophenone derivative is Benzophenone 3 (also referred to as Oxybenzone), Benzophenone

4 (also referred to as Sulisobenzzone), Benzophenone 5 (Sulisobenzzone Sodium), and the like.

Most preferred is Benzophenone 3.

Also suitable are certain menthyl salicylate derivatives having the general formula:

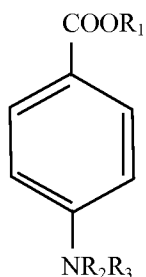


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20 wherein R₁, R₂, R₃, and R₄ are each independently H, OH, NH₂, or C₁₋₂₀ straight or branched chain alkyl. Particularly preferred is where R₁, R₂, and R₃ are methyl and R₄ is hydroxyl or NH₂, the compound having the name homomenthyl salicylate (also known as Homosalate) or menthyl anthranilate. Homosalate is available commercially from Merck under the tradename Eusolex HMS and menthyl anthranilate is commercially available from Haarmann & Reimer

25 under the tradename Heliopan. If present, the Homosalate should be found at no more than about 15% by weight of the total composition.

Various amino benzoic acid derivatives are suitable UVB absorbers including those



5

wherein R_1 , R_2 , and R_3 are each independently H, C_{1-20} straight or branched chain alkyl which may be substituted with one or more hydroxy groups. Particularly preferred is wherein R_1 is H or C_{1-8} straight or branched alkyl, and R_2 and R_3 are H, or C_{1-8} straight or branched chain alkyl.

10 Particularly preferred are PABA, ethyl hexyl dimethyl PABA (Padimate O), ethyldihydroxypropyl PABA, and the like. If present Padimate O should be found at no more than about 8% by weight of the total composition.

Salicylate derivatives are also acceptable UVB absorbers. Such compounds have the general formula: wherein R is a straight or branched chain alkyl, including derivatives of the
15 above compound formed from mono-, di-, or triethanolamines. Particular preferred are octyl salicylate, TEA-salicylate, DEA-salicylate, and mixtures thereof.

Generally, the amount of the UVB chemical sunscreen present may range from about 0.001-45%, preferably 0.005-40%, more preferably about 0.01-35% by weight of the total composition.

20 If desired, the compositions of the invention may be formulated to have a certain SPF (sun protective factor) values ranging from about 1-50, preferably about 2-45, most preferably about 5-30. Calculation of SPF values is well known in the art. Preferably, the claimed compositions have SPF values greater than 4.

Particulate Materials

25 The compositions of the invention may contain particulate materials in the form of pigments, inert particulates, or mixtures thereof. If present, suggested ranges are from about

0.1-75%, preferably about 0.5-70%, more preferably about 0.1-65% by weight of the total composition. In the case where the composition may comprise mixtures of pigments and powders, suitable ranges include about 0.01-75% pigment and 0.1-75% powder, such weights by weight of the total composition.

5 The particulate matter may be colored or non-colored (for example white) non-pigmentatious powders. Suitable non-pigmentatious powders include bismuth oxychloride, titanated mica, fumed silica, spherical silica, polymethylmethacrylate, micronized teflon, boron nitride, acrylate copolymers, aluminum silicate, aluminum starch octenylsuccinate, bentonite, calcium silicate, cellulose, chalk, corn starch, diatomaceous earth, fuller's earth,
10 glyceryl starch, hectorite, hydrated silica, kaolin, magnesium aluminum silicate, magnesium trisilicate, maltodextrin, montmorillonite, microcrystalline cellulose, rice starch, silica, talc, mica, titanium dioxide, zinc laurate, zinc myristate, zinc rosinate, alumina, attapulgite, calcium carbonate, calcium silicate, dextran, kaolin, nylon, silica silylate, silk powder, sericite, soy flour, tin oxide, titanium hydroxide, trimagnesium phosphate, walnut shell powder, or
15 mixtures thereof. The above mentioned powders may be surface treated with lecithin, amino acids, mineral oil, silicone, or various other agents either alone or in combination, which coat the powder surface and render the particles more lipophilic in nature.

 The particulate materials may comprise various organic and/or inorganic pigments. The organic pigments are generally various aromatic types including azo, indigoid,
20 triphenylmethane, anthroquinone, and xanthine dyes which are designated as D&C and FD&C blues, browns, greens, oranges, reds, yellows, etc. Organic pigments generally consist of insoluble metallic salts of certified color additives, referred to as the Lakes. Inorganic pigments include iron oxides, ultramarines, chromium, chromium hydroxide colors, and mixtures thereof. Iron oxides of red, blue, yellow, brown, black, and mixtures thereof are
25 suitable.

Preservatives

The composition may contain 0.001-8%, preferably 0.01-6%, more preferably 0.05-5% by weight of the total composition of preservatives. A variety of preservatives are suitable, including such as benzoic acid, benzyl alcohol, benzylhemiformal, benzylparaben, 5-bromo-5-nitro-1,3-dioxane, 2-bromo-2-nitropropane-1,3-diol, butyl paraben, phenoxyethanol, methyl paraben, propyl paraben, diazolidinyl urea, calcium benzoate, calcium propionate, caprylyl glycol, biguanide derivatives, phenoxyethanol, captan, chlorhexidine diacetate, chlorhexidine digluconate, chlorhexidine dihydrochloride, chloroacetamide, chlorobutanol, p-chloro-m-cresol, chlorophene, chlorothymol, chloroxylenol, m-cresol, o-cresol, DEDM Hydantoin, DEDM Hydantoin dilaurate, dehydroacetic acid, diazolidinyl urea, dibromopropamide diisethionate, DMDM Hydantoin, and the like. In one preferred embodiment the composition is free of parabens.

Vitamins and Antioxidants

The compositions of the invention, may contain vitamins and/or coenzymes, as well as antioxidants. If so, 0.001-10%, preferably 0.01-8%, more preferably 0.05-5% by weight of the total composition are suggested. Suitable vitamins include ascorbic acid and derivatives thereof, the B vitamins such as thiamine, riboflavin, pyridoxin, and so on, as well as coenzymes such as thiamine pyrophosphate, flavin adenin dinucleotide, folic acid, pyridoxal phosphate, tetrahydrofolic acid, and so on. Also Vitamin A and derivatives thereof are suitable. Examples are Vitamin A palmitate, acetate, or other esters thereof, as well as Vitamin A in the form of beta carotene. Also suitable is Vitamin E and derivatives thereof such as Vitamin E acetate, nicotinate, or other esters thereof. In addition, Vitamins D and K are suitable.

Suitable antioxidants are ingredients which assist in preventing or retarding spoilage. Examples of antioxidants suitable for use in the compositions of the invention are potassium

sulfite, sodium bisulfite, sodium erythrobate, sodium metabisulfite, sodium sulfite, propyl gallate, cysteine hydrochloride, butylated hydroxytoluene, butylated hydroxyanisole, and so on.

Typical skin creams or lotions comprise from about 5-98% water, 1-85% oil, and from about 0.1 to 20% of one or more surfactants. Preferably the surfactants are nonionic and may be in the form of silicones or organic nonionic surfactants.

Typical color cosmetic compositions such as foundations, blush, eyeshadow and the like will preferably contain from about 5-98% water, 1-85% oil, and from about 0.1 to 20% of one or more surfactants in addition to from about 0.1 to 65% of particulates that are pigments or a combination of pigments and powders.

Typical mascara compositions generally contain from about 5-98% water, 1-85% oil, and from about 0.1 to 20% surfactant in addition to natural or synthetic polymers that are film forming, such as aqueous dispersions of acrylic copolymers, aqueous dispersions of polyurethane, or silicone resins.

The emulsion compositions of the invention may be found in a wide variety of other forms.

The invention will be further described in connection with the following examples which are set forth for the purposes of illustration only.

The invention is further illustrated by the following examples that are set forth for the purpose of illustration only:

EXAMPLE 1

Stimulation of β -defensin production by resveratrol was determined by measuring cellular expression of β -defensin protein. The following materials were used:

- NHEK, passage 4, Cambrex

- Rabbit Anti-human, β defensin-2 pAb: Santa Cruz Biotechnology Inc.
- Donkey Anti-rabbit IgG (H+L) Alexa Fluor®488: Invitrogen Molecular Probes
- Vectashield® Mounting Medium with DAPI Vector Laboratories
- Triton X-100 BP-151-100
- 5 • FBS HyClone
- PBS, Cellgro
- 10% Formalin Sigma

Normal Human Epidermal Keratinocytes (NHEK) in Epilife media were plated in the 8-well chamber slides at 2×10^4 concentration. Wells were treated with $10 \mu\text{g/ml}$ resveratrol, $25 \mu\text{g/ml}$ $\text{TNF}\alpha$, and 1.3mM CaCl_2 . Wells containing *Pseudomonas aeruginosa* and well containing heat inactivated lysates from 100% DMSO were included as positive and negative controls respectively. The plates were incubated at 37°C . for 24 hours. The medium was aspirated off and the cells washed with PBS and fixed with 4% formalin for 10 min at room temperature. The formalin was washed off with 3 washes of PBS-T (PBS with 0.1% Triton x-100) and nonspecific binding was blocked by treatment with 10 % FBS. Rabbit Anti-Human antibody was diluted in 1:250 in blocking buffer PBS-D (Phosphate buffered saline with 10% FBS (fetal bovine serum)), and cells were incubated overnight. The next morning the unbound antibody was washed off with PBS-T (PBS with 0.1% Triton X-100). Donkey Anti-Rabbit antibody was diluted at 1 mg/ml in blocking buffer (PBS-D) and incubated for 1 hour. After washing with PBS-T, the cells were mounted with Vectrashield mounting medium, and picture taken with Olympus microscope equipped with Nikon camera at 300x. The results are set forth in Figure 1. The presence of β -defensin is noted by presence of green. The untreated cells appeared blue. The cells treated with resveratrol showed increase in presence of β -defensin. Cells treated with $25 \mu\text{g/ml}$ $\text{TNF}\alpha$ and 1.3mM CaCl_2 separately also showed presence of β -defensin in the cytoplasm. The

untreated and negative controls showed no presence of β -defensin.

EXAMPLE 2

Ability to stimulate β -defensin production in cells was tested by measuring cellular transcription levels. The following materials were used:

Materials for determination of transcription levels:

- RNA extraction kit(RNeasy Qiagen)
- NEHK pass 4 cells grown in complete Epilife medium
- Resveratrol
- TNF α
- Primer/probe (for GAPDH)
- Primer/probe (for β -Defensin 2)
- I Script CDNA Kit Bio-Rad
- TaqMan Fast Universal PCR Master Mix (2X)
- RNase-free water
- Invitrogen – Quant it RNA assay kit
- Bapta AM Oregon green
 - Dissolve in 700 μ l DMSO for 40 mM
- Calbochem
 - Compound C stock at cat # 10 mM

NHEK p3 were plated in Epilife medium at 1×10^6 cells per 100x100mm plate. The next day the medium was replaced with new volume of Epilife medium (10 ml) and incubated for another 24 hours at 37° C. The inhibitors (Bapta and Compound C) were added in concentrations as set forth below.

Inhibitor	Final concentration
Bapta AM (Ca chelator)	30 μ M
Compound C cAMPK inhibitor	10 and 20 μ M

Sixty minutes later wells which were treated with inhibitors received resveratrol at final concentration of 5 μ g/ml as did the wells that were untreated with inhibitors. Here again the (TNF- α) at 10 mg/ml, was used as a positive control for induction of β defesins transcription. Cells were incubated for 6 and 24 hours, then washed twice with PBS, scraped and stored at -80o C. prior to RNA extraction.

The RNA was extracted with RNeasy [®] kit and 500 ng of each RNA was reverse transcribed using high capacity cDNA RT-kit. Real time PCR was performed using Taq-man primer probe set. The house keeping gene GAPDH was used as a reference. The transcripts levels were established by using comparative C_T method ($\Delta\Delta C_T$) and measured with Fast PCR 7500, Applied Bioscience. The results are set forth in Figure 2 and show that when resveratrol is applied to cells the transcription of β -defensin protein increases. This induction of transcription can be specifically inhibited by both inhibitors used ;Bapta AM and Compound C.

EXAMPLE 3

The effect of resveratrol on β -defensin secretion in medium was measured. The following materials were used:

Materials for determination of protein secretion levels

- Resveratrol Sigma cat#R5010 lot111k5206
- ELISA kit from Adipo Bioscience, cat#SK00044-01, lot#20110236
- NHEK p4

NHEK were plated in Epilife medium in the 6 well plate at 1 million cells per well.

Resveratrol at 2 and 10 µg/ml was added to the wells to a final volume of 1 ml. TNFα was added as a positive control, and cells alone as the negative control. The plate was incubated for 48 hours at 37° C. At the end of the incubation, the medium was centrifuged for 2 minutes at 12,000 rpm. The ELISA for β-defensin 2 test was performed using the ELISA kit and
 5 supplied protocol and standards. The results are set forth in Figure 3 and show that treatment of cells with resveratrol caused secretion of β-defensin in the medium.

EXAMPLE 4

10 Resveratrol ferulate, the triester of ferulic acid and resveratrol, was tested for ability to stimulate beta defensins in keratinocytes by repeating the procedures of Examples 2 and 3, except for substitution resveratrol ferulate for resveratrol. The results depicted in Figures 4 and 5. Resveratrol ferulate at 5 µg/ml concentration shows an increase in transcription of beta defensin protein as set forth in Figure 4. Resveratrol ferulate at 2 and 10 µg/ml concentration
 15 shows stimulatory activity for beta defensins when compared to untreated cells and the positive control when measured according to the transcription test.

EXAMPLE 5

20 Skin treatment oil-in-water (1), and oil-in-water-in-silicone oil (2), creams may be prepared as follows:

Ingredient	w/w%	
	1	2
Water	QS	QS
Hydroxyethyl urea	0.50	
Hyaluronic acid	9.00	9.00
Disodium EDTA	0.12	
Creatine	0.05	
Sucrose	0.50	

Caffeine	0.20	
Caprylyl glycol	0.40	0.28
Caprylic/capric triglyceride/cetyl alcohol/C12-20 acid PEG-8 ester	4.00	
PEG-100 stearate	1.20	
C12-20 acid PEG-8 ester	4.96	
Caprylic/capric triglyceride	0.55	
Behenyl alcohol	0.50	
Coco caprylate caprate	5.10	
Sweet almond oil	0.10	
Dimethicone, 100 cst.	2.50	
Dimethicone, 6 cst		5.00
Dimethicone (silicone gum/20 cst dimethicone blend)		8.00
Dimethicone/polysilicone 11		6.00
Dimethicone/dimethicone PEG-10/15 crosspolymer		1.00
Lauryl PEG-9 polydimethylsiloxylethyl dimethicone		1.00
Sesame oil	0.10	
Potassium cetyl phosphate	0.50	
Apricot kernel oil	0.10	
Wheat bran extract/olive extract	0.20	0.20
Cholesterol	0.20	
Linoleic acid	0.20	
Cholesterol/potassium sulfate	0.20	
Theobroma grandiflorum seed butter	1.40	
Lauryl PCA	0.01	1.00
Dimethicone	1.50	
Phenoxyethanol	0.70	0.60
Water/polyaminopropyl biguanide	0.40	
Glycerin	2.00	
Butylene glycol	1.00	
Hexylene glycol		0.05
Mica/titanium dioxide	1.00	0.75
Mica/titanium dioxide/triethoxycaprylyl silane		0.50
Pearl powder	0.001	
Silica	0.50	
30% aqueous sodium hydroxide	0.35	
Trehalose	0.50	
N-acetyl glucosamine	1.00	1.00
Water/purified aribodopsis thaliana extract/lecithin	0.50	1.00
Aqueous solution acetyl hexapeptide-8	1.00	1.00
Yeast ferment extract	1.00	1.00
Water/lecithin/micrococcus lysate	0.50	0.50
Milk protein/lactose/glucose/fructose	0.50	0.50
Saccharide isomerate	0.50	
Whey protein	0.50	0.560
Water/butylene glycol/lecithin/lauryldimonium hydroxypropyl hydrolyzed soy protein/lecithin/xanthan gum/ascorbyl tocopheryl maleate	1.00	1.00

Glycerin/padina povonica extract	0.10	0.10
Thermus thermophilus ferment/glycerin	0.05	
Camelina sativa seed oil	0.05	
Water/gold/hydrolyzed wheat protein	0.001	
Sorbitol/water/ascophyllum nodosum extract/asparagopsis armata extract	0.25	
Butylene glycol	0.50	
Boswellia serrata extract	0.05	
Calophyllum inophyllum (tamanu) seed oil	0.05	
Fragrance	0.20	
FD&C yellow No. 5 (1% aqueous solution)	0.05	
Aminomethyl propanol		0.03
Sodim phosphate dibasic (10% aqueous solution)		0.75
Citric acid (10% aqueous solution)		0.008
Sodium acrylate/sodium acryloyldimethyl taurate copolymer/hydrogenated polydecene/laureth-8	1.00	1.00
Ammonium acrylodimethyltaurate/VP copolymer		0.70
Water/butylene glycol/decarboxy carnosine HCl		0.50
Resveratrol	0.50	0.50

The composition was prepared by combining the water phase and oil phase ingredients separately, then emulsifying to form an emulsion. The above compositions are suitable vehicles for topical application to skin to stimulate beta defensin production in keratinocytes.

5

EXAMPLE 6

A water in silicone oil emulsion skin serum is prepared as follows:

Ingredient	w/w%
Dimethicone/dimethicone PEG-10/15 crosspolymer	4.00
Dimethicone/dimethiconol	1.00
Dimethicone, 6 cst.	6.00
Trisiloxane (1.0 cst)	16.00
Water	QS
Phenoxyethanol	0.50
Caprylyl glycol/phenoxyethanol/hexylene glycol/iodopropynyl butylcarbamate	0.50
Water/polyaminobiguanide	0.20
Trisodium resveratrol triphosphate	0.50
Butylene glycol	2.00
Glycerin	10.00
Sodium citrate	0.50

The composition was prepared by combining the oil phase ingredients and water phase ingredients separately, then mixing well to emulsify. The above composition is suitable for topical application to skin to induce stimulation of beta defensins in skin cells.

5

EXAMPLE 7

Oil-in-water (O/W) and water-in-oil (W/O) emulsion mascaras are prepared as follows:

Ingredient	w/w%	
	O/W	W/O
Ethylenediamine/Stearyl Dimer Tallate Copolymer – Uniclear 100VG, Arizona Chemical	10.	12.00
PEG-30 Dipolyhydroxystearate		3.00
Sorbitan tristearate	1.00	--
Glyceryl stearate/PEG-100 stearate	1.00	--
Stearic acid	4.00	3.00
Cetyl acetate/Acetylated lanolin alcohol		1.00
Diethyl adipate/octyl stearate/octyl palmitate	1.00	--
Stearamide MEA stearate	3.00	--
Glyceryl olivate	--	0.50
Diethyl malate	--	1.00
Dimethicone	2.50	--
Cyclomethicone	5.00	--
Isododecane	11.00	38.00
Ethanol	0.50	--
Water	QS	QS
Silica	1.00	--
Polysorbate 20	2.00	--
Acacia gum	0.25	--
Black iron oxide	8.00	10.00
Polyvinylpyrrolidone	1.00	--
Resveratrol ferulate	0.50	--
Shellac	2.00	--
Acrylic copolymer solids dispersed in aqueous solution	5.00	7.00
Preservatives	0.80	--

The mascaras were made by combining the oily phase ingredients except for the cyclomethicone and dimethicone and heating to about 90° C. until solids melted. The cyclomethicone and dimethicone were added to the mixture and the heat maintained at about 60° C. The water phase ingredients were combined and heated to about 60° C. and combined

with the mixture. The phases were emulsified to form the final mixture.

EXAMPLE 8

5 Emulsion foundation makeup compositions are prepared as follows:

Ingredient	w/w%
Cyclomethicone	16.90
Polysilicone-11	5.00
Cyclomethicone/dimethiconol	1.00
Dimethicone copolyol	1.50
Sorbitan sesquioleate	1.50
Phenyl trimethicone	10.00
Dimethicone	10.00
Resveratrol tripalmitate	0.50
Red Iron Oxide treated with methicone	0.50
Yellow iron oxide treated with methicone	1.22
Black iron oxide treated with methicone	0.13
Titanium dioxide coated with methicone	8.06
Water	QS
Butylene glycol	5.00
Xanthan gum	0.10
Magnesium sulfate	1.00
Laureth-7	0.25

The water, oil and pigment phases were separately prepared by low shear mixing. The phases were combined with high shear blending to form a foundation makeup composition which is suitable for application to skin to stimulate beta defensins.

10 While the invention has been described in connection with the preferred embodiment, it is not intended to limit the scope of the invention to the particular form set forth but, on the contrary, it is intended to cover such alternatives, modifications, and equivalents as may be included within the spirit and scope of the invention as defined by the appended claims.

What we claimed is:

1. A method of stimulating beta-defensins in skin cells which comprises applying to the skin cells an effective amount of resveratrol.

5

2. A method of reducing the amount of microflora on the skin comprising applying to the skin an effective amount of resveratrol.

3. A method for the treatment of acne comprising applying to skin affected with acne an effective amount of resveratrol.

10

4. A method for reducing skin sensitivity comprising applying to sensitive skin an effective amount of resveratrol.

15

5. A method of improving the barrier function of the skin comprising applying to the skin an effective amount of resveratrol.

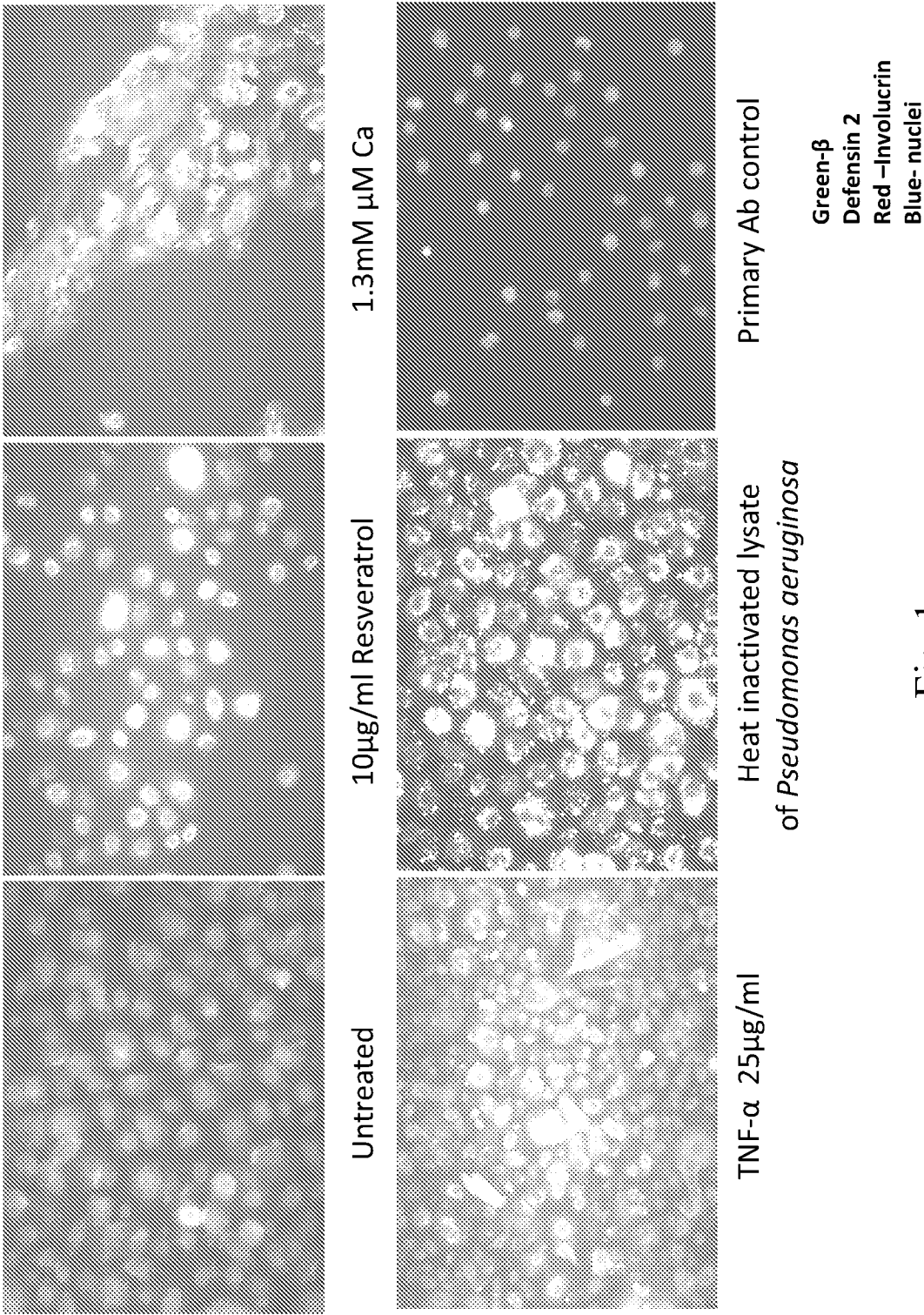


Fig. 1

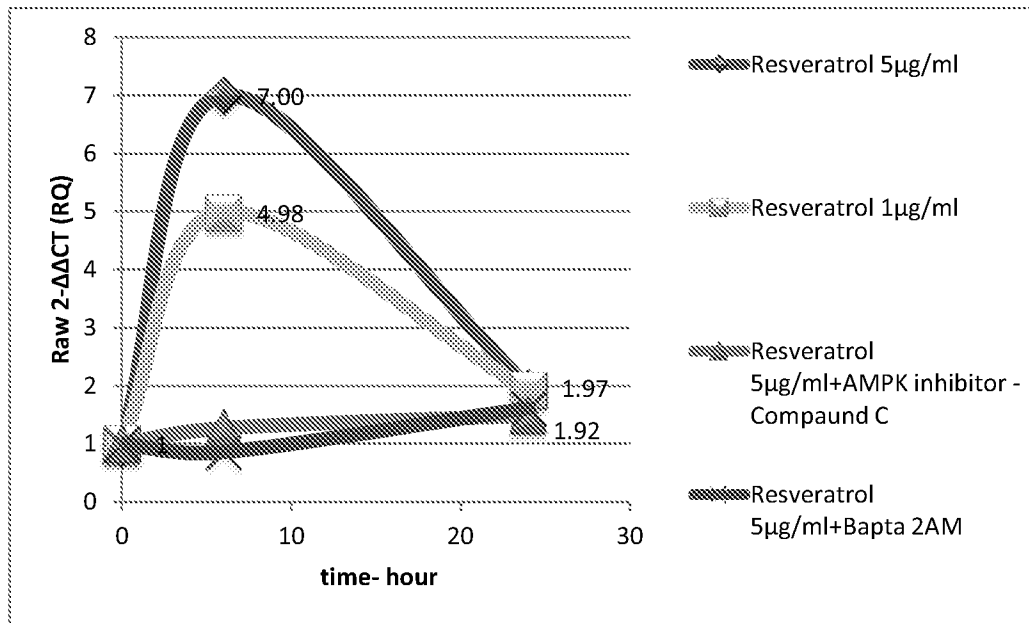


Fig. 2

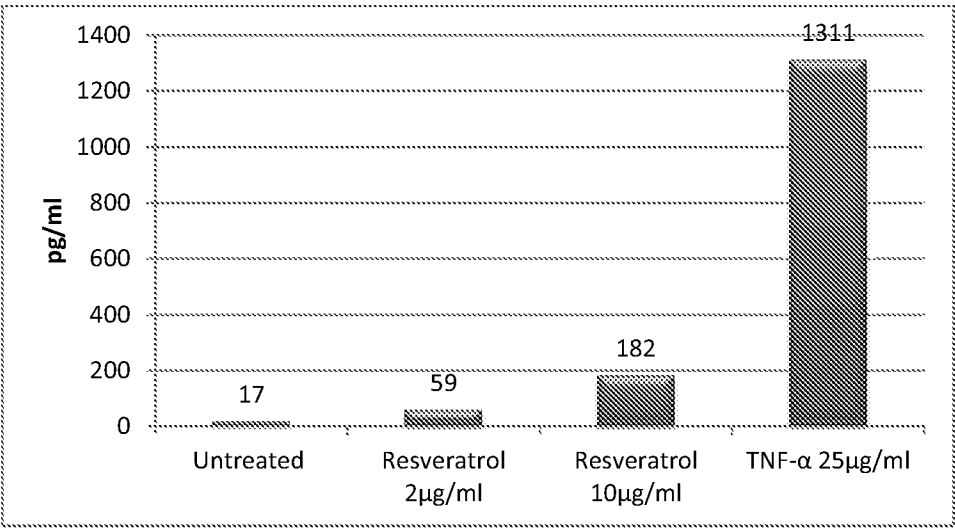


Fig. 3

RT-PCR

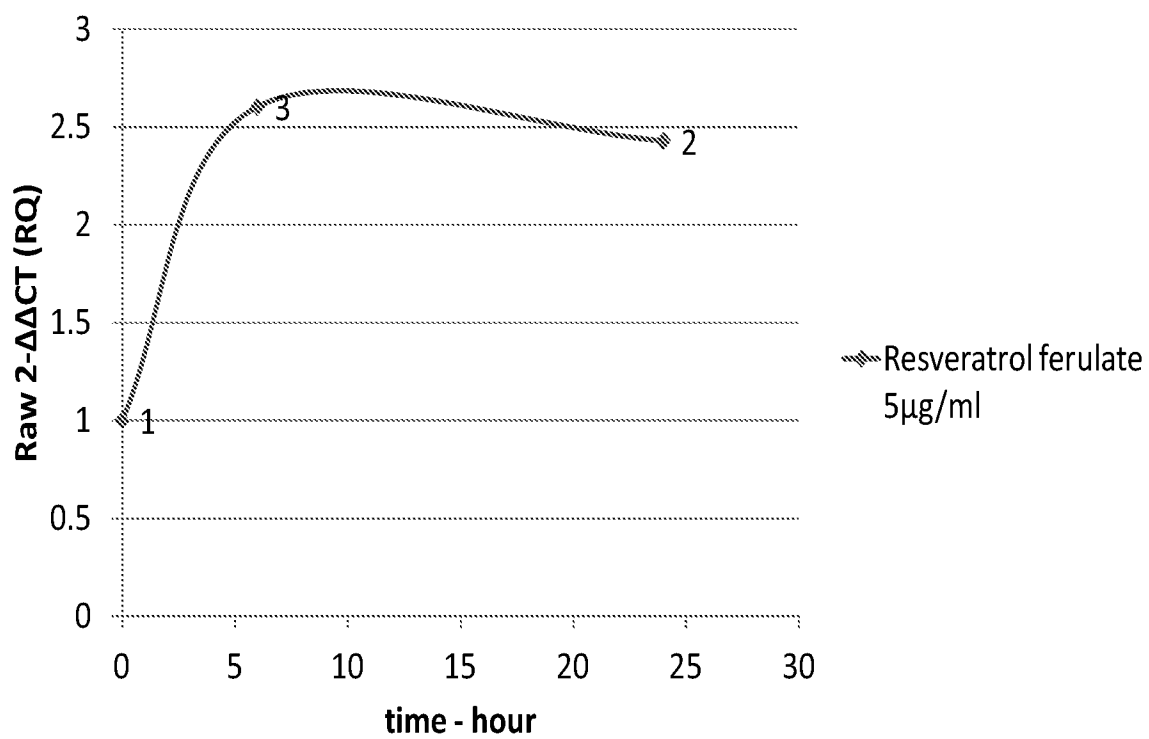


Fig. 4

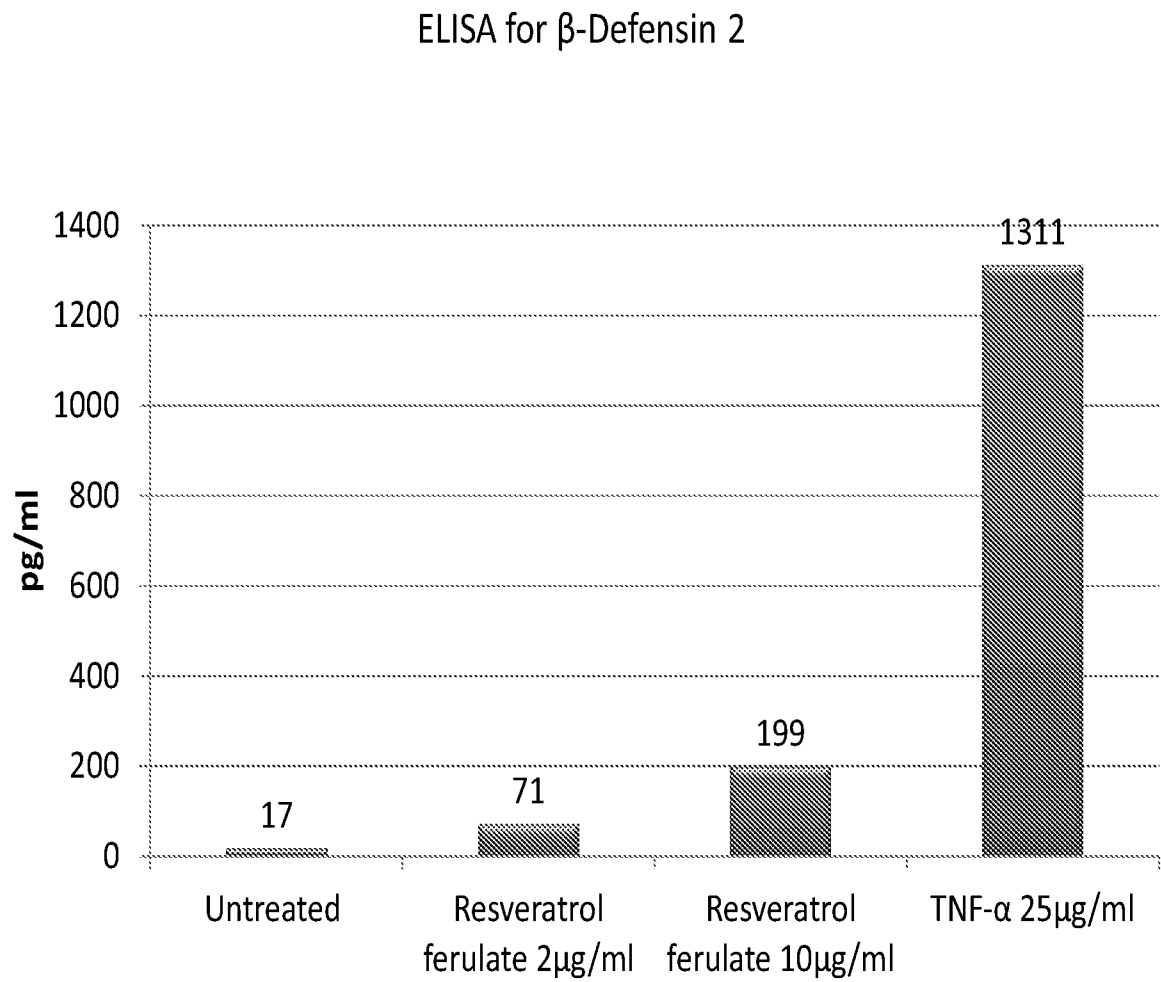


Fig. 5

PATENT COOPERATION TREATY

PCT

DECLARATION OF NON-ESTABLISHMENT OF INTERNATIONAL SEARCH REPORT (PCT Article 17(2)(a), Rules 13ter.1(c) and (d) and 39)

Applicant's or agent's file reference 12-26	IMPORTANT DECLARATION	Date of mailing (<i>day/month/year</i>) 25 September 2013 (25.09.2013)
International application No. PCT/US2013/047239	International filing date (<i>day/month/year</i>) 24 June 2013 (24.06.2013)	(Earliest) Priority date (<i>day/month/year</i>) 25 June 2012 (25.06.2012)
International Patent Classification (IPC) or both national classification and IPC A61K 31/05(2006.01)i, A61P 17/00(2006.01)i		
Applicant ELC MANAGEMENT LLC		

This International Searching Authority hereby declares, according to Article 17(2)(a), that **no international search report will be established** on the international application for the reasons indicated below.

1. ☒ The subject matter of the international application relates to:
 - a. ☐ scientific theories.
 - b. ☐ mathematical theories.
 - c. ☐ plant varieties.
 - d. ☐ animal varieties.
 - e. ☐ essentially biological processes for the production of plants and animals, other than microbiological processes and the products of such processes.
 - f. ☐ schemes, rules or methods of doing business.
 - g. ☐ schemes, rules or methods of performing purely mental acts.
 - h. ☐ schemes, rules or methods of playing games.
 - i. ☒ methods for treatment of the human body by surgery or therapy.
 - j. ☐ methods for treatment of the animal body by surgery or therapy.
 - k. ☐ diagnostic methods practised on the human or animal body.
 - l. ☐ mere presentation of information.
 - m. ☐ computer programs for which this International Searching Authority is not equipped to search prior art.
2. ☐ The failure of the following parts of the international application to comply with prescribed requirements prevents a meaningful search from being carried out:

☐ the description
☐ the claims
☐ the drawings
3. ☐ A meaningful search could not be carried out without the sequence listing; the applicant did not, within the prescribed time limit:

☐ furnish a sequence listing on paper complying with the standard provided for in Annex C of the Administrative Instructions, and such listing was not available to the International Searching Authority in a form and manner acceptable to it.
☐ furnish a sequence listing in electronic form complying with the standard provided for in Annex C of the Administrative Instructions, and such listing was not available to the International Searching Authority in a form and manner acceptable to it.
☐ pay the required late furnishing fee for the furnishing of a sequence listing in response to an invitation under Rule 13ter.1(a) or (b)

4. Further comments:

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