

FORMULATIONS OF PECTOLINARIGENIN

I. FIELD OF THE INVENTION

The invention is related to formulations of pectolinarigenin and methods of using the formulations for topical conditions in a subject.

5 II. BACKGROUND OF THE INVENTION

Mammalian epidermis and its appendages (e.g., hair, nail, sebaceous and sweat glands) provide a barrier to keep harmful elements out of the body and essential body fluids in. As the first line of defense against the various physical traumas of the environment, the epidermis must protect itself as well as the underlying tissues. The epidermis is also exposed to mutagenic
10 ultraviolet radiation. In nonhaired or sparsely haired regions such as most human skin, the epidermis is thicker than that of furred skin, and in these locations the skin functions primarily in a protective role. The constant assaults on the epidermis necessitate self-renewal, making the epidermis a prime example of an adult tissue that undergoes continual and rapid flux.

Aged skin differs from youthful skin both in appearance and in function. The aged
15 epidermis demonstrates decreased keratinocyte proliferation and is physically thinner, but mostly from decline of the rete ridges. In addition to thinning, aging slows wound healing, prolongs epidermal turnover, and impairs barrier formation. The skin appears thin, wrinkled, bruised, and rough. Wrinkling and bruising can also result from aging-related changes in the dermis. The dermis, too, is characteristically thinner in aged persons. Aged fibroblasts are less
20 likely to synthesize normal amounts of collagen, elastin, laminin glycosaminoglycans, and fibronectin. The dermis can, in such cases, lack elasticity, strength, vessel support, remodeling abilities, and ground substances. For example, rete ridges can be effaced, and basal cells can no longer display villous projections into the dermis. Epidermal cell turnover is reduced up to 50% in the aged as compared to youth.

25 For example, melanocyte numbers can decrease 8-20% per decade. There are fewer Langerhans cells in the aged, and those present are often functionally impaired. Collagen synthesis decreases, for example, up to 30% within 4 years of menopause in women. The numbers of collagen and elastic fibers are also decreased. The dermis can also become less echogenic to ultrasounds, consistent with changes in collagen and elastic tissues.

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III. SUMMARY OF THE INVENTION

The invention relates to compositions of pectolinarigenin, and methods of using the compositions for treating, protecting, and/or altering (e.g., improving) the condition and/or aesthetic appearance of skin, including, for example, treating, preventing, ameliorating, reducing and/or eliminating fine lines and/or wrinkles of skin and/or improving the aesthetic appearance of fine lines and/or wrinkles of skin. In certain embodiments, the compositions of the invention lead to increase in skin and/or hair resiliency. In certain embodiments, the compositions of the invention lead to increase in elasticity of the skin. In certain embodiments, the compositions of the invention prevent skin damage.

Topical administration of pectolinarigenin was not known in the field. Beneficially, the invention recognizes, for the first time, that topical compositions comprising pectolinarigenin may be used for improving the condition of the skin or for treatment of any ailment related to the skin of a subject. In one aspect, the invention includes a composition for topical administration comprising an effective amount of pectolinarigenin. The effective amount of pectolinarigenin is an amount of pectolinarigenin that would be effective in treating, ameliorating, or otherwise impacting the underlying condition of the skin. The invention recognizes that pectolinarigenin is poorly soluble or insoluble in water. The invention also recognizes that pectolinarigenin is also poorly soluble or insoluble in oil, for example, the pectolinarigenin is insoluble in Helianthus Annuus (Sunflower) Seed Oil. In certain embodiments of the invention, pectolinarigenin is dissolved in a solvent selected from a group consisting of: dimethyl isosorbide, ethoxydiglycol, isopropyl lauryl sarcosinate, pentylene glycol, propanediol, 1,2-hexanediol, and/or butylene glycol. In certain preferred embodiments, pectolinarigenin is dissolved in dimethyl isosorbide.

In certain embodiments, pectolinarigenin is dissolved in a solvent selected from a group consisting of: 1,2 heptanediol, 1,2 hexanediol, 1,2 propanediol, butylene glycol, C₁₅₋₁₉ alkane, capric/caprylic triglyceride, dibutyl adipate, diisopropyl adipate, dimethyl isosorbide, dipropylene glycol, ethanol, ethoxydiglycol, isoamyl laurate, isohexadecane, isopentyldiol, isopropyl myristate, isopropyl lauryl sarcosinate, jojoba oil, meadowfoam seed oil, mineral oil, neopentyl glycol diethylhexanoate, octyldodecanol, oleyl alcohol, pentylene glycol, phenylpropanol, polysorbate 20, propanediol, safflower seed oil, squalene, sunflower oil, t-butyl alcohol, tributyl

citrate, tributyl-O-acetylcitrate, tri-C₁₅₋₁₉ alkyl citrate, triethyl citrate, triethyl O-acetylcitrate, and triisostearin.

Thus, in certain embodiments, the composition comprises an emulsion. Preferably, the emulsion is oil/water emulsion. In certain embodiments, the composition further comprises
5 dimethyl isosorbide. In certain embodiments, the pectolinarigenin is dissolved in dimethyl isosorbide. The compositions of the invention are wherein the composition is stable under storage for at least 3 months. This is beneficial because the compositions of the invention may be stored prior to administration to the subjects. In certain embodiments, wherein the compositions of the invention have less than about 20% degradation when stored at 4 °C or 25 °C for 3 months. In
10 certain embodiments, the compositions of the invention have less than about 30% degradation when stored at 40 °C or 50 °C for 3 months.

In certain embodiments, the composition comprises pectolinarigenin in a concentration of about 5 nM to about 2500 nM. In certain embodiments, in the compositions of the invention, pectolinarigenin is present in a concentration of about 0.0001% to about 5.0% w/w. In certain other
15 embodiments, pectolinarigenin is present in a concentration of 0.0005% to about 2.0% w/w. In certain other embodiments, pectolinarigenin is present in a concentration of 0.0007% to about 1.0% w/w. In certain other embodiments, pectolinarigenin is present in a concentration of 0.001% to about 0.75% w/w. In certain other embodiments, pectolinarigenin is present in a concentration of 0.001% to about 0.75% w/w. In certain other embodiments, pectolinarigenin is present in a
20 concentration of about 0.5% w/w.

In certain aspects, the compositions of the invention may be administered as a topical composition on the skin of the subject. The compositions of the invention may be included in any formulation suitable for topical administration. In certain embodiments, the composition of the invention is a fluid, emulsion, encapsulation, suspension, solid, semi-solid, jelly, paste, gel,
25 hydrogel, ointment, lotion, emulsion, cream, foam, mousse, liquid, spray, suspension, dispersion, powder, aerosol, color cosmetic, and/or hair treatment. In certain embodiments, the compositions of the invention also include excipients. These excipients may be selected from a group consisting of: solvent, emulsifier, preservative, antioxidant, emollient, thickening agent, penetration enhancer, surfactant, diluent, filler, carrier, and/or pH control agent. In certain embodiments, the

preservative in the composition is an antimicrobial preservative or chelating agent. In certain embodiments, the solvent of the invention is dimethyl isosorbide.

The compositions of the invention may be prepared by various methods. As an example, the compositions may be prepared by dissolving, dispersing, etc. pectolinarigenin as provided
5 herein and optional excipients in a carrier (e.g., water, saline, aqueous dextrose, glycerol, glycols, ethanol or the like) or a solvent to form a solution, colloid, liposome, emulsion, complexes (including inclusion complexes), coacervate, or suspension. In certain embodiments, the compositions of the current invention can also contain additional excipients such as wetting agents, emulsifying agents, co-solvents, solubilizing agents, pH buffering agents, and the like (e.g.,
10 sodium acetate, sodium citrate, cyclodextrins and derivatives, sorbitan monolaurate, triethanolamine acetate, triethanolamine oleate, hydroxyethylpiperazine and the like). In certain embodiments, the compositions of the invention may further include one or more additional excipients selected from a group consisting of: carriers, excipients, or diluents including, but not limited to, absorbents, anti-irritants, antibacterials, anti-acne agents, antioxidants, coloring
15 agents/pigments, emollients (moisturizers), emulsifiers, film-forming/holding agents, fragrances, leave-on exfoliants, prescription drugs, preservatives, scrub agents, silicones, skin-identical/repairing agents, slip agents, sunscreen actives, surfactants/detergent cleansing agents, penetration enhancers, and thickeners.

In certain embodiments, the compositions of the invention comprise: pectolinarigenin, in
20 an oil/water emulsion, and a preservative.

In certain embodiments, the compositions of the invention comprise: pectolinarigenin, in an oil/water emulsion, a solvent for solubilizing pectolinarigenin, and a preservative.

In certain embodiments, the compositions of the invention comprise: pectolinarigenin, in an oil/water emulsion, a solvent for solubilizing pectolinarigenin, a diluent, and a preservative.

25 In certain embodiments, the compositions of the invention comprise: pectolinarigenin, in an oil/water emulsion, a solvent for solubilizing pectolinarigenin, a thickener, optionally a diluent, and a preservative.

In certain embodiments, the compositions of the invention comprise: pectolinarigenin, in an oil/water emulsion, a solvent for solubilizing pectolinarigenin, and one or more excipients

selected from the group consisting of: diluents, absorbents, antioxidants, emollients, emulsifiers, thickeners, surfactants, and/or preservatives.

In certain embodiments, the excipients included in the composition are water, dimethyl isosorbide, glycerin, caprylic/capric triglyceride, propanediol, sunflower seed oil, ethoxydiglycol, squalane, sodium acrylate copolymer, cetearyl alcohol, phenoxyethanol, glyceryl stearate, capryloyl glycerin/sebacic acid copolymer, diheptyl succinate, naringenin, lecithin, decylene glycol, pentylene glycol, cetearyl glucoside, shea butter, palmitic acid, arachidyl alcohol, behenyl alcohol, arachidyl glucoside, phenethyl alcohol, 1,2-hexanediol, hydrogenated olive oil, olea europaea (olive) fruit oil, olea europaea (olive) oil unsaponifiables, hydroxyethyl acrylate/sodium acryloyldimethyl taurate copolymer, citric acid, sodium acetylated hyaluronate, sodium hyaluronate crosspolymer, sodium phytate, hydrolyzed sodium hyaluronate, and/or ethylhexylglycerin.

In certain aspects, the invention provides that the compositions of the inventions are synergistic. The compositions provided in the invention are beneficial because of their enhanced stability due to the synergistic effects of the ingredients in the composition and the resulting stability and efficacy. In certain embodiments, the invention provides that the compositions of the invention are more efficacious and stable as compared to when they are administered or stored as individual ingredients. The compositions of the invention may also act synergistically when administered along with other therapies for treatment of the conditions described herein.

In certain aspects of the invention, the compositions comprising pectolinarigenin demonstrate antioxidant activity. In certain embodiments, the compositions of the invention, the antioxidant activity of pectolinarigenin is demonstrated at concentrations of about 0.00005% w/w or higher. Advantageously, the compositions of the invention comprising pectolinarigenin, demonstrating antioxidant activity, are effective for treating and/or preventing oxidation damage. In certain embodiments, the compositions of the invention comprising pectolinarigenin, demonstrating antioxidant activity, are effective for treatment of skin and/or hair damaged by reactive oxygen species and protection from other environmental aggressors that may damage the skin of the subject. In certain other embodiments, the compositions of the invention comprising pectolinarigenin, demonstrating antioxidant activity, are effective for prevention of skin and/or

hair damage by reactive oxygen species, including the damage caused by environmental aggressors.

In certain aspects of the invention, the compositions comprising pectolinarigenin demonstrate elastase enzyme inhibition. In certain embodiments, the compositions of the invention, the elastase enzyme inhibition activity of pectolinarigenin is demonstrated at concentrations of about 0.005% w/w or higher. Advantageously, the compositions comprising pectolinarigenin, demonstrating elastase enzyme inhibition activity, are effective for promoting the elasticity of the skin. In certain embodiments, the compositions of the invention comprising pectolinarigenin, demonstrating elastase enzyme inhibition, are effective in reduction of fine lines and/or wrinkles in the skin. In certain embodiments, the compositions of the invention comprising pectolinarigenin, demonstrating elastase enzyme inhibition, are effective in prevention of formation of fine lines and/or wrinkles in the skin.

In certain aspects of the invention, the compositions comprising pectolinarigenin demonstrate inhibition of glycation. In certain embodiments, the compositions of the invention, the glycation inhibition activity of pectolinarigenin is demonstrated at concentrations of about 0.0005% w/w or higher. Advantageously, the compositions comprising pectolinarigenin, demonstrating glycation inhibition activity, are effective for supporting and promoting skin and/or hair resiliency.

In certain aspects of the invention, the compositions comprising pectolinarigenin promote skin lightening and/or brightening. In certain embodiments, the compositions comprising pectolinarigenin at least a concentration of 0.01% w/w, have at least about 10% higher L value (reflecting the lightening of the skin), as compared to skin treated with a corresponding composition lacking pectolinarigenin. In certain embodiments, the compositions comprising pectolinarigenin at least a concentration of 0.1% w/w, have about 4.6 units higher L value as compared to skin treated with a corresponding composition lacking pectolinarigenin.

In certain aspects of the invention, a composition comprising pectolinarigenin modulates expression of one more genes that is related to a topical condition. In certain embodiments, the one or more genes are selected from a group consisting of: (i) VCAN, (ii) COL1A2, (iii) MMP1, (iv) IL6, (v) IL23A, (vi) TLR2, and (vii) MMP3. In certain embodiments, administration of a

composition comprising pectolinarigenin leads to up-regulation of VCAN, and/or COL1A2. In certain embodiments, administration of a composition comprising pectolinarigenin leads to down-regulation of MMP1, MMP3, IL6, TLR2, and/or IL23A.

VCAN gene plays a role in maintenance of skin barrier through interaction with
5 extracellular matrix proteins. COL1A2 gene is involved in regulation of collagen expression. An increase in collagen expression reduces wrinkles and sagging. MMP1 gene is involved in regulation of collagen degradation. Reduction in collagen degradation improves appearance of the skin. IL6 gene plays a role in regulation of inflammation, tissue atrophy, muscle loss, and/or melanogenesis. Decrease in expression of IL6 reduces inflammation, decreases tissue atrophy,
10 decreases muscle loss, and downregulates melanogenesis. IL23A gene plays a role in inflammation.

In certain embodiments, administration of a composition comprising pectolinarigenin causes upregulation of one or more genes related to barrier and extracellular matrix proteins proteoglycan and collagens. In certain embodiments of the invention, the administration of the
15 composition comprising pectolinarigenin leads to at least about ten (10) fold up regulation of one or more genes related to barrier and extracellular matrix proteins proteoglycan and collagens.

In certain embodiments, administration of a composition comprising pectolinarigenin causes downregulation of collagenase. In certain embodiments, administration of a composition comprising pectolinarigenin leads to at least about five (5) fold down regulation of one or more
20 genes related to barrier and extracellular matrix proteins proteoglycan and collagens.

In certain embodiments, administration of a composition comprising pectolinarigenin downregulates the expression of inflammatory genes. In certain embodiments, administration of a composition comprising pectolinarigenin leads to at least about two hundred (200) fold down regulation of the expression of inflammatory genes.

25 In certain embodiments, administration of a composition comprising pectolinarigenin downregulates the proteins involved in melanogenesis signaling pathway. In certain embodiments, administration of a composition comprising pectolinarigenin to a subject leads to the treatment of prevention of a topical condition of the subject through the modulation of levels of expression or activity of one or genes that may be involved in the topical condition. In certain embodiments,

administration of a composition comprising pectolinarigenin alters one or more of a function related with the modulated genes, wherein the one or more function is selected from the group consisting of: (i) maintenance of skin barrier, (ii) collagen expression, (iii) collagen degradation, (iv) inflammation, (v) tissue atrophy, (vi) muscle loss, and (vii) melanin production.

5 IV. BRIEF DESCRIPTION OF DRAWINGS

FIG. 1A is a picture of the solution with 0.5% w/w pectolinarigenin in oil/water emulsion.

FIG. 1B is a picture of 1.03% w/w pectolinarigenin solubilized in dimethyl isosorbide.

FIG. 2 is a chart of stability of pectolinarigenin in dimethyl isosorbide.

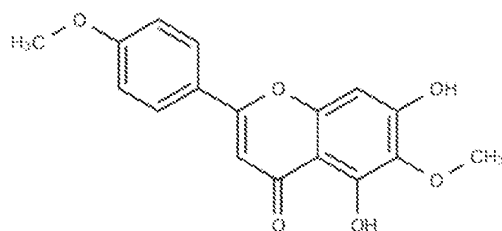
FIG. 3 provides the data pertaining to gene modulation expression.

10 V. DETAILED DESCRIPTION

Pectolinarigenin

Pectolinarigenin as a flavone isolated from *Cirsium* thistles. Pectolinarigenin is commonly used as an anti-inflammatory agent as a COX-2 inhibitor and/or Nf-kB/Nrf2 pathway inhibitor. Feng et al., Pectolinarigenin Suppresses LPS-Induced Inflammatory Response in Macrophages and Attenuates DSS-Induced Colitis by Modulating the NF-κB/Nrf2 Signaling Pathway, *Inflammation*, 2022 Dec;45(6):2529-2543.

The chemical structure of pectolinarigenin is provided below:



Pectolinarigenin may also be referred to as: 5,7-Dihydroxy-6-methoxy-2-(4-methoxyphenyl)-4H-chromen-4-one.

The anti-inflammatory properties of pectolinarigenin have been evaluated with results indicating potential use as treatment in edema, allergic inflammation, and passive cutaneous anaphylaxis. Lim, et al. Anti-inflammatory activity of pectolinarigenin and pectolinarin isolated from *Cirsium chanroenicum*, *Biol Pharm Bull.* 2008 Nov;31(11):2063-2067.

5 Pectolinarigenin also exhibits protective properties in the nervous system. Pectolinarigenin functions as a neuroprotective agent to defend astrocytes from inflammatory toxicity. Heimfarth, et al., Neuroprotective and anti-inflammatory effect of pectolinarigenin, a flavonoid from Amazonian *Aegiphila integrifolia* (Jacq.), against lipopolysaccharide-induced inflammation in astrocytes via NFκB and MAPK pathways, *Food Chem Toxicol.* 2021 Nov; 157:112538.

10 Further, pectolinarigenin also induces melanoma cell apoptosis and decrease melanoma metastasis by altering mitochondria potential and altering expression of apoptosis associated proteins. Kumkarnjana et al., Anti-adipogenic effect of flavonoids from *Chromolaena odorata* leaves in 3T3-L1 adipocytes. *J Integr Med.*, 2018 Nov;16(6):427-434. Pectolinarigenin also inhibits tumor progression in osteosarcoma tumor via inhibition of STAT3. Zhang et al.,
15 Pectolinarigenin acts as a potential anti-osteosarcoma agent via mediating SHP-1/JAK2/STAT3 signaling. *Biomed Pharmacother.* 2022 Sep;153:113323.

Pectolinarigenin also inhibits melanin synthesis and reduction of SREBP induced lipogenesis to prevent lipid accumulation in adipocytes and hepatoma cells. Lee et al., Pectolinarigenin, an aglycone of pectolinarin, has more potent inhibitory activities on
20 melanogenesis than pectolinarin, *Biochem Biophys Res Commun.* 2017 Nov 4;493(1):765-772.

Compositions of pectolinarigenin

In one aspect, the invention provides compositions comprising pectolinarigenin. In certain embodiments, the invention provides compositions comprising pectolinarigenin that are suitable for administration on the skin of the subject.

25 The invention recognizes that pectolinarigenin is poorly soluble or insoluble in water. The invention also recognizes that pectolinarigenin is also poorly soluble or insoluble in oil, for example, the pectolinarigenin is insoluble in *Helianthus Annuus* (Sunflower) Seed Oil. The invention recognizes that the solvent used for preparing pectolinarigenin compositions should be any solvent acceptable to be used in cosmetic formulations.

In certain embodiments, pectolinarigenin is dissolved in a solvent selected from a group consisting of: 1,2 heptanediol, 1,2 hexanediol, 1,2 propanediol, butylene glycol, C₁₅₋₁₉ alkane, capric/caprylic triglyceride, dibutyl adipate, diisopropyl adipate, dimethyl isosorbide, dipropylene glycol, ethanol, ethoxydiglycol, isoamyl laurate, isohexadecane, isopentyldiol, isopropyl myristate, isoproyl lauryl sarcosinate, jojoba oil, meadowfoam seed oil, mineral oil, neopentyl glycol diethylhexanoate, octyldodecanol, oleyl alcohol, pentylene glycol, phenylpropanol, polysorbate 20, propanediol, safflower seed oil, squalene, sunflower oil, t-butyl alcohol, tributyl citrate, tributyl-O-acetylcitrate, tri-C₁₅₋₁₉ alkyl citrate, triethyl citrate, triethyl O-acetylcitrate, and triisostearin.

10 In certain embodiments of the invention, pectolinarigenin is dissolved in a solvent selected from a group consisting of: dimethyl isosorbide, ethoxydiglycol, isopropyl lauryl sarcosinate, pentylene glycol, propanediol, 1,2-hexanediol, and/or butylene glycol. In certain preferred embodiments, pectolinarigenin is dissolved in dimethyl isosorbide. Table 1 provides the solubility data for pectolinarigenin in several solvents.

15 **Table 1: Solubility of Pectolinarigenin**

Solvent	Solubility (%w/w)
Deionized Water	Not soluble
Dimethyl Isosorbide	1.03
Helianthus Annuus (Sunflower) Seed Oil	Not soluble

As evident from the data provided above, pectolinarigenin is soluble in dimethyl isosorbide. FIG. 1B provides a picture of a solution of pectolinarigenin dissolved in dimethyl isosorbide.

20 Thus, in certain embodiments, the composition comprises an emulsion. Preferably, the emulsion is oil/water emulsion. FIG. 1B provides a picture of pectolinarigenin formulated in oil/water emulsion.

In certain embodiments, the composition further comprises dimethyl isosorbide. In certain embodiments, the pectolinarigenin is dissolved in dimethyl isosorbide. The compositions of the invention are wherein the composition is stable under storage for at least 3 months. This is beneficial because the compositions of the invention may be stored prior to administration to the subjects. In certain embodiments, wherein the compositions of the invention have less than about 20% degradation when stored at 4 °C or 25 °C for 3 months. In certain embodiments, the compositions of the invention have less than about 30% degradation when stored at 40 °C or 50 °C for 3 months. FIG. 2 provides the data for stability of pectolinarigenin dissolved in dimethyl isosorbide. The invention beneficially provides that solutions of pectolinarigenin dissolved in dimethyl isosorbide have increased solubility and are shelf stable. Since pectolinarigenin is not soluble in sunflower oil and other commonly used solvents, the increased solubility in dimethyl isosorbide is surprising and unexpected.

In certain embodiments, the composition comprises pectolinarigenin in a concentration of about 5 nM to about 2500 nM. In certain embodiments, in the compositions of the invention, pectolinarigenin is present in a concentration of about 0.0001% to about 5.0% w/w. In certain other embodiments, pectolinarigenin is present in a concentration of 0.0005% to about 2.0% w/w. In certain other embodiments, pectolinarigenin is present in a concentration of 0.0007% to about 1.0% w/w. In certain other embodiments, pectolinarigenin is present in a concentration of 0.001% to about 0.75% w/w. In certain other embodiments, pectolinarigenin is present in a concentration of 0.001% to about 0.75% w/w. In certain other embodiments, pectolinarigenin is present in a concentration of about 0.5% w/w.

In certain aspects, the compositions of the invention may be administered as a topical composition on the skin of the subject. The compositions of the invention may be included in any formulation suitable for topical administration. In certain embodiments, the composition of the invention is a fluid, emulsion, encapsulation, suspension, solid, semi-solid, jelly, paste, gel, hydrogel, ointment, lotion, emulsion, cream, foam, mousse, liquid, spray, suspension, dispersion, powder, aerosol, color cosmetic, and/or hair treatment. In certain embodiments, the compositions of the invention also include excipients. These excipients may be selected from a group consisting of: solvent, emulsifier, preservative, antioxidant, emollient, thickening agent, penetration enhancer, surfactant, diluent, filler, carrier, and/or pH control agent. In certain embodiments, the

preservative in the composition is an antimicrobial preservative or chelating agent. In certain embodiments, the solvent of the invention is dimethyl isosorbide.

The compositions of the invention may be prepared by various methods. As an example, the compositions may be prepared by dissolving, dispersing, etc. pectolinarigenin as provided herein and optional excipients in a carrier (e.g., water, saline, aqueous dextrose, glycerol, glycols, ethanol or the like) or a solvent to form a solution, colloid, liposome, emulsion, complexes (including inclusion complexes), coacervate, or suspension. In certain embodiments, the compositions of the current invention can also contain auxiliary substances such as wetting agents, emulsifying agents, co-solvents, solubilizing agents, pH buffering agents, and the like (e.g., sodium acetate, sodium citrate, cyclodextrins and derivatives, sorbitan monolaurate, triethanolamine acetate, triethanolamine oleate, hydroxyethylpiperazine and the like). In certain embodiments, the compositions of the invention may further include one or more additional excipients selected from a group consisting of: carriers, excipients, or diluents including, but not limited to, absorbents, anti-irritants, antibacterials, anti-acne agents, antioxidants, coloring agents/pigments, emollients (moisturizers), emulsifiers, film-forming/holding agents, fragrances, leave-on exfoliants, prescription drugs, preservatives, scrub agents, silicones, skin-identical/repairing agents, slip agents, sunscreen actives, surfactants/detergent cleansing agents, penetration enhancers, and thickeners.

Absorbents are substances which are added to topical products to take up water and oil-soluble dissolved or finely dispersed substances. Topical absorbents can also be used as thickeners in a wide variety of formulations including facial creams, lipsticks, shampoos and calamine lotions. In some embodiments, absorbents may include, but are not limited to, alcohol (ethyl alcohol, methanol, isopropyl alcohol, SD alcohol [especially denatured alcohol] and benzyl alcohol), alumina (aluminum oxide), aluminum chlorohydrate, aluminum hydroxide, aluminum magnesium silicate, aluminum silicate, aluminum starch octenylsuccinate, aluminum sulfate, ammonium chloride, bentonite, bismuth oxychloride, boron nitride, calcium carbonate, carnauba wax, charcoal, China clay, clay, Copernicia cerifera wax, cornstarch, fuller's earth, hydrolyzed corn starch, iron powder, kaolin, lithium magnesium sodium silicate, magnesium, magnesium carbonate, magnesium hydroxide, montmorillonite, nylon-12, rice starch, silica, silicate, silk powder, silt, sodium carbonate, sodium polyacrylates, and zeolite.

Anti-Irritants are substances which are added to topical products to reduce inflammation, especially, the inflammation resulting from the application of the product itself. The excipients included as anti-irritants that perform the function of anti-irritants or anti-inflammatories may have more than one function. For example, many antioxidants also function as anti-irritants. In some
5 embodiments, anti-irritants and/or antioxidants may include, but are not limited to, Acacia senegal, acetylsalicylic acid, *Achillea millefolium*, adenosine, citric acid, adenosine triphosphate, Aloe barbadensis, aloe barbadensis leaf juice extract, aloe extract, aloe juice, hydrogenated olive oil, hydrogenated palm glycerides, hydrolyzed silk, hydroquinone, aloe vera, and/or alpha bisabolol.

In certain embodiments, the compositions of the invention may further include humectants.
10 Humectants (or moisturizers) are important cosmetic ingredients that prevent loss of moisture thereby retaining the skin's natural moisture. Some humectants also can actively attract moisture. In certain embodiments, the humectants may be selected from a group consisting of sodium hyaluronate, sodium acetylated hyaluronate, hydrolyzed sodium hyaluronate, propylene glycol, hexylene glycol, and butylene glycol.

In certain embodiments, the compositions of the invention may further include slip agents. The term "slip agent" is used to describe a range of ingredients which can help other ingredients spread over the skin and penetrate into the skin. Slip agents can also have humectant (hygroscopic) properties. In some embodiments, slip agents may include, but are not limited to, amodimethicone, bis-PEG-18 methyl ether dimethyl silane, bis-phenylpropyl dimethicone, butylene glycol, cetyl
20 dimethicone, cetyl dimethicone copolyol, cetyl PEG/PPG-10/1-dimethicone, cyclohexasiloxane, cyclomethicone, cyclopentasiloxane, cyclotetrasiloxane, decylene glycol, diisostearyl trimethylolpropane siloxy silicate, dimethicone, dimethicone copolyol, dimethicone crosspolymer, dimethiconol, dipropylene glycol, hexylene glycol, hydrolyzed silk, isododecane, methicone, methyl trimethicone, methylsilanol mannuronate, methylsilanol PEG-7 glyceryl cocoate, Good,
25 PEG-10 dimethicone, PEG-10 dimethicone/vinyl dimethicone crosspolymer, PEG-12 dimethicone, PEG/PPG-18/18 dimethicone, PEG/PPG-20/15 dimethicone, pentylene glycol, phenyl trimethicone, polymethylsiloxane, PPG-3 benzyl ether myristate, silica dimethyl silylate, silk powder, siloxane, simethicone, sorbitol, stearyl dimethicone, stearyl methicone, triethoxycaprylsilane, trimethylsiloxysilicate, xylitol, and zinc stearate.

In certain embodiments, the compositions of the invention may further include diluents, and/or carriers. Diluents and/or carriers may include, but are not limited to, polyethylene glycols (such as PEG200, PEG300, PEG400, PEG540, PEG600, PEG1450 or mixtures thereof) and coconut oils (such as propylene glycol dicaprate, coco-caprylate/caprate, propylene glycol dicaprylate/dicaprate, caprylic/capric triglyceride, caprylic/capric/lauric triglyceride, caprylic/capric/linoleic triglyceride, tricaprin, tricaprylin, glyceryl trioleate, neopentyl glycol dicaprylate/dicaprate, caprylic/capric/palmitic/stearic triglyceride, or mixtures thereof).

In certain embodiments, the compositions of the invention may further include emollients. Emollients are supple, waxlike, lubricating, thickening substances which are added to cosmetic/dermatological products to prevent water loss and have a softening and soothing effect on the skin. In some embodiments, emollients may include, but are not limited to, 10-hydroxydecanoic acid, acetyl glyceryl ricinoleate, acetylated castor oil, acetylated hydrogenated cottonseed glyceride, acetylated lanolin, acetylated lanolin alcohol, acetylated palm kernel glycerides, agar, algae extract, algin, almond oil, squalane, squalene, α -glucan oligosaccharide, amodimethicone, *Anacystis nidulans* extract, apricot kernel oil, arachidic acid, arachidonic acid, arachidyl alcohol, arachidyl propionate, C₁₀₋₃₀ cholesterol/lanosterol esters, C₁₂₋₁₅ alkyl benzoate, C₁₂₋₁₈ acid triglyceride, C₁₈₋₃₆ acid triglyceride, candelilla wax, *Cannabis sativa* L. oil, caprylic/capric triglyceride, caprylyl methicone, carrot oil, *Carthamus tinctorius* oil, *Carya illinoensis* oil, castor isostearate succinate, castor oil, *Caulerpa taxifolia* extract, and/or cephalin.

In certain embodiments, the compositions of the invention may further include film-forming/holding agents. Film-Forming/Holding agents are substances which are added to cosmetic/dermatological products to help leave a pliable, cohesive, and continuous covering over the skin. This film has water-binding properties and leaves a smooth feel on skin. In some embodiments, film-forming/holding agents may include, but are not limited to, acrylate, acrylates copolymer, acrylates/C₁₀₋₃₀ alkyl acrylate crosspolymer, acrylates/dimethicone copolymer, adipic acid/neopentyl glycol/trimellitic anhydride copolymer, allyl methacrylates crosspolymer, carnauba wax, cellulose gum, *Copernicia cerifera* wax, dextrin, diisopropyl adipate, glyceryl polymethacrylate, hydrolyzed wheat protein, hydroxyethylcellulose, locust bean, neopentyl glycol diheptanoate, PEG-40 hydrogenated castor oil, polyacrylamide, polyacrylate-17, polyglucuronic

acid, polyglyceryl methacrylate, polyisobutene, polymethyl methacrylate, polyquaternium-10, polyquaterniums, polyvinyl alcohol, polyvinylpyrrolidone, propylene carbonate, PVM/MA (polyvinyl methyl ether/maleic acid) decadiene crosspolymer, PVP [poly(vinylpyrrolidone)] copolymer, PVP/dimethylaminoethyl-methacrylate, sodium carbomer, sodium polyacrylate, 5 styrene/acrylates copolymer, triethoxycaprylylsilane crosspolymer, VA (vinyl acetate)/crotonates, VA/crotonates copolymer, VP (vinylpyrrolidone)/eicosene copolymer, and VP/hexadecene copolymer.

In certain embodiments, the compositions of the invention may further include excipients related to the fragrance of the formulation. Fragrance ingredients are a single or a blend of volatile 10 and/or fragrant plant oils (or synthetically derived oils) that impart aroma and odor to cosmetic/dermatological products. The level of fragrance to use varies according to the product type. In some embodiments, the composition of the formulation may contain up to about 0.01% fragrance by weight. In some embodiments, fragrances (e.g., synthetic and fragrant plant extracts) may include, but are not limited to, *Acacia farnesiana* extract, *Aerocarpus santalinus*, amyl 15 cinnamate, amyl salicylate, amyris oil, *Anethum graveolens*, *Angelica archangelica* root oil, anisaldehyde, anise, balm mint extract, balsam peru, bay leaf oil, bergamot oil, bitter orange flower, bois de rose oil, bois oil, *Boswellia carterii*, butylphenyl methylpropional, *cananga* extract, *Cananga odorata*, cardamom, cedarwood, cherry extract, *Citrus aurantifolia*, *Citrus aurantium*, *Citrus aurantium* extract, *Citrus medica limonium*, 20 clary oil, *Commiphora myrrha* extract, coriander, *Cucurbita pepo*, cyclamen aldehyde, dill extract, ethyl vanillin, eugenol, farnesol, farnesyl acetate, *Ferula galbaniflua*, fir needle oil, floralozone, *Foeniculum vulgare* extract, frankincense extract, *galbanum*, *Gardenia florida* extract, grapefruit oil, guaiac wood, *Guaiacum officinale*, hedione, hexyl cinnamal, hyssop, *Illicium verum*, Iris florentina extract, jasmine oil, *Jasminium grandiflorum*, jonquil 25 extract, *Laurus nobilis*, lauryl lactate, lavandin oil, *Lavandula angustifolia*, *Lavandula officinalis*, lavender extract and oil, lemon, lemon balm, lemongrass oil, *Levisticum officinale* root extract, lime oil and extract, limonene, linalool, *Litsea cubeba*, mandarin orange oil or extract, marjoram, *Melissa officinalis*, *Mentha piperita*, *Mentha spicata*, *Mentha viridis*, menthol, menthone, menthoxypropanediol, and menthyl lactate.

In certain embodiments, the composition of the invention may further include preservatives. Preservatives are substances which prevent bacterial, microbial or fungal contamination of cosmetic/dermatological products thereby increasing the product's shelf life and consumer safety. Some of these agents also have stabilizing effects able to preserve the function of various active ingredients including anti-oxidants (vitamins), emulsifiers and surfactants. In some embodiments, preservatives may include, but are not limited to, 1,2-hexanediol, benzoic acid, benzothonium chloride, borax, bronopol, butylparaben, caprylyl glycol, chlorophene, chloroxylenol, chlorphenesin, decylene glycol, dehydroacetic acid, diazolidinyl urea, DMDM hydantoin, hydroxyacetophenone, ethylhexylglycerin, ethylparaben, formaldehyde-releasing preservative, Germaben II, hoelen, imidazolidinyl urea, iodopropynyl butylcarbamate, isobutylparaben, methylchloroisothiazolinone, methyldibromo glutaronitrile, Methylisothiazolinone, methylparaben, o-cymen-5-ol, phenoxyethanol, phenoxyisopropanol, phytosphingosine, polyaminopropyl biguanide, potassium sorbate, propylparaben, quaternium-15, sodium benzoate, sodium citrate, sodium dehydroacetate, sodium hexametaphosphate, sodium hydroxymethylglycinate, phenethyl alcohol, sodium lactobionate, sodium metabisulfite, sodium sulfite, sorbic acid, and *styrax benzoin*.

In certain aspects of the invention, the pharmaceutical composition is an emulsion. The emulsion compositions of the invention may further include emulsifiers. Emulsifiers are substances which are added to cosmetic/dermatological products to help keep unlike ingredients (such as oil and water) from separating in an emulsion. There are 2 types of emulsifiers. Oil-in-water (o/w) emulsifiers keep oil drops packed in water, while water-in-oil (w/o) emulsifiers keep water drops packed in oil. W/O emulsifiers are used for a fatty feel (e.g. night & sun protection creams). O/W emulsifiers are used more in moisturizing products (e.g. body lotions, day creams).

In certain embodiments, the compositions of the invention may further include surfactants. Surfactants are compounds that lower surface tension or interfacial tension. Reducing the surface tension allows a liquid to spread easier while reducing the interfacial tension (interfacial meaning between two faces) between water and an oil/lipid allows them to mix. Surfactants may have a be anionic, amphoteric, non-ionic, and/or quaternary agents. Surfactants form the base of all personal cleansing products and can also have wetting, conditioning, defatting, emulsifying, & thickening effects. In some embodiments, emulsifiers, surfactants, and detergents may include, but are not

limited to, ammonium laureth sulfate, ammonium lauryl sulfate, arachidyl glucoside, behenic acid, bis-PEG-18 methyl ether dimethyl silane, C₂₀₋₄₀ pareth-40, cocamidopropyl betaine, cocamidopropyl dimethylamine, cocamidopropyl hydroxysultaine, coco-glucoside, coconut oil, decyl glucoside, dicetyl phosphate, dihydrocholeth-30, disodium cocoamphodiacetate, disodium

5 cocoyl glutamate, disodium lauraminopropionate, glyceryl behenate, hydrogenated vegetable glycerides citrate, isohexadecane, isostearamide DEA, lauramphocarboxyglycinate, laureth-23, laureth-4, laureth-7, lauryl PEG-9 polydimethylsiloxyethyl dimethicone, lauryl alcohol, lauryl glucoside, magnesium laureth sulfate, magnesium oleth sulfate, myristic acid, nonoxynols, oleic acid, oleth 10, palm kernel acid, palmitic acid, PEG-60 almond glycerides, PEG-75 shea butter

10 glycerides, PEG 90M, PEG-10 dimethicone, PEG-10 dimethicone/vinyl dimethicone crosspolymer, PEG-10 rapeseed sterol, PEG-100 stearate, PEG-12 dimethicone, PEG-120 methyl glucose dioleate, PEG-20 methyl glucose sesquistearate, PEG-40 stearate, PEG-60 hydrogenated castor oil, PEG-7 glyceryl cocoate, PEG-8, PEG-80 sorbitan laurate, PEG/PPG-17/6 copolymer (polyethylene glycol/polypropylene glycol-17/6 copolymer), PEG/PPG-18/18 dimethicone,

15 PEG/PPG-20/15 dimethicone, poloxamer 184, Poloxamer 407, poloxamers, polyglyceryl-3 beeswax, polyglyceryl-4 isostearate, polyglyceryl-6 isostearate, polysorbate 20, polysorbate 60, polysorbate 80, potassium cetyl phosphate, potassium hydroxide, potassium myristate, PPG-12 buteth-16, PPG-26-Buteth-26, *Salvia officinalis*, *Saponaria officinalis* extract, soapwort, sodium C₁₄₋₁₆ olefin sulfonate, sodium cetearyl sulfate, sodium cocoamphoacetate, sodium cocoate,

20 sodium cocoyl glutamate, sodium cocoyl isethionate, sodium dilauramidoglutamide lysine, sodium hexametaphosphate, sodium hydroxide, sodium laureth sulfate, sodium laureth-13 carboxylate, sodium lauroamphoacetate, sodium lauroyl lactylate, sodium lauroyl sarcosinate, sodium lauryl glucose carboxylate, sodium lauryl sulfate, sodium methyl cocoyl taurate, sodium methyl taurate, sodium myreth sulfate, sodium palm kernelate, sodium palmate, sodium PEG-7

25 olive oil carboxylate, sodium trideceth sulfate, steareth-20, TEA-lauryl sulfate (triethanolamine-lauryl sulfate), and tribehenin PEG-20 esters.

In certain embodiments, the compositions of the invention may further include one or more thickeners. Thickeners are substances which are added to cosmetic/dermatological products to enhance the consistency, volume and viscosity of cosmetic products, thereby providing more

30 stability and better performance. While some thickeners have also emulsifying or gelling

properties, the majority of thickeners have the ability to retain water on the skin and act therefore as moisturizers. Thickeners can be completely natural like waxes but also synthetic or semi-synthetic. In some embodiments, thickeners may include, but are not limited to, Acacia senegal, acetyl glyceryl ricinoleate, acetylated castor oil, acetylated hydrogenated cottonseed glyceride, acetylated palm kernel glycerides, acrylates/steareth-20 methacrylate copolymer, agar, *Ahnfeltia* 5 *concinna* extract, *ahnfeltia* extract, *Alaria esculenta*, algae, algae extract, algin, alkyloamides, *Althaea rosea*, *Althea officinalis*, alumina, aluminum hydroxide, aluminum stearate, ammonium acryloyldimethyltaurate/VP copolymer, *Anacystis nidulans* extract, arachidic acid, arachidonic acid, arachidyl alcohol, arachidyl propionate, arrowroot, artemia extract, *Ascophyllum* 10 *nodosum*, ascorbyl methylsilanol pectinate, Asparagopsis armata extract, beeswax, behenic acid, behentrimonium chloride, behenyl alcohol, bis-diglyceryl polyacyladipate, bismuth oxychloride, C₁₂₋₁₅ alkyl benzoate, C₁₂₋₁₈ acid triglyceride, C₁₃₋₁₄ isoparaffin, C₁₈₋₃₆ acid triglyceride, candelilla wax, caprylic/capric triglyceride, carbomer, carbopol, carnauba wax, carrageenan, Caulerpa taxifolia extract, cellulose, Cellulose gum, cephalin, Cera alba, ceresin, ceteareth-20, cetearyl 15 alcohol, cetearyl ethylhexanoate, cetearyl glucoside, cetearyl octanoate, cetyl alcohol, cetyl dimethicone copolyol, cetyl hydroxyethylcellulose, cetyl palmitate, cetyl PEG/PPG-10/1-dimethicone, *chlorella*, *Chondrus crispus*, cocamide DEA and MEA, cocoglycerides, *Codium tomentosum* extract, Copernicia cerifera wax, *Corallina officinalis* extract, *Corallina*, DEA oleth-10 phosphate, diethanolamine (DEA), di-PPG-3 myristyl ether adipate, dimethicone crosspolymer, 20 dimethicone/vinyl dimethicone crosspolymer, polyacrylate crosspolymer, and/or dimer dilinoleyl dimer dilinoleate.

In certain embodiments, the compositions of the invention may further include one or more chelators. Chelating agents are any of numerous ingredients that bind with metal ions or metallic compounds, preventing them from adhering to a surface (such as skin, hair, or clothing) or causing 25 contamination, such as in the case of trace amounts of iron. In some embodiments, chelators may include, but are not limited to tetrasodium EDTA, sodium phytate, and/or teathydroxypropyl ethylenediamine.

In certain embodiments, the excipients included in the composition are water, dimethyl isosorbide, glycerin, caprylic/capric triglyceride, propanediol, sunflower seed oil, ethoxydiglycol, 30 squalane, sodium acrylate copolymer, cetearyl alcohol, phenoxyethanol, glyceryl stearate,

capryloyl glycerin/sebacic acid copolymer, diheptyl succinate, naringenin, lecithin, decylene glycol, pentylene glycol, cetearyl glucoside, shea butter, palmitic acid, arachidyl alcohol, behenyl alcohol, arachidyl glucoside, phenethyl alcohol, 1,2-hexanediol, hydrogenated olive oil, olea europaea (olive) fruit oil, olea europaea (olive) oil unsaponifiables, hydroxyethyl acrylate/sodium acryloyldimethyl taurate copolymer, citric acid, sodium acetylated hyaluronate, sodium hyaluronate crosspolymer, sodium phytate, hydrolyzed sodium hyaluronate, and/or ethylhexylglycerin.

Table 2 provides a list of excipients, along with their approximate concentrations, that may be used in the exemplary compositions of the invention. is provided below:

Table 2: Excipients in an exemplary composition:

Ingredient	%w/w
Water	40 - 80
Dimethyl Isosorbide	10 - 30
Glycerin	1 - 10
Caprylic/Capric Triglyceride	0 - 5
Propanediol	0 - 5
Helianthus Annuus (Sunflower) Seed Oil	0 - 5
Ethoxydiglycol	0 - 5
Squalane	0 - 2
Sodium Arcylates Copolymer	0 - 2
Cetearyl Alcohol	0 - 2
Phenoxyethanol	0 - 2
Pectolinarigenin	0.0001-5.00
Glyceryl Stearate	0 - 2
Capryloyl Glycerin/Sebacic Acid Copolymer	0 - 2
Diheptyl Succinate	0 - 2
Naringenin	0 - 2
Lecithin	0 - 2
Decylene Glycol	0 - 2
Pentylene Glycol	0 - 1
Cetearyl Glucoside	0 - 1
Butyrospermum Parkii (Shea) Butter	0 - 1
Palmitic Acid	0 - 1
Arachidyl Alcohol	0 - 1
Behenyl Alcohol	0 - 1
Arachidyl Glucoside	0 - 1
Phenethyl Alcohol	0 - 1
1,2-Hexanediol	0 - 1

Hydrogenated Olive Oil	0 - 1
Olea Europaea (Olive) Fruit oil	0 - 1
Olea Europaea (Olive) Oil Unsaponifiables	0 - 1
Hydroxyethyl Acrylate/Sodium Acryloyldimethyl Taurate Copolymer	0 - 1
Citric Acid	0 - 1
Sodium Acetylated Hyaluronate	0 - 1
Sodium Hyaluronate	0 - 1
Sodium Hyaluronate Crosspolymer	0 - 1
Sodium Phytate	0 - 1
Hydrolyzed Sodium Hyaluronate	0 - 1
Ethylhexylglycerin	0 - 1

Pectolinarigenin for treatment of topical conditions:

Advantageously, it was discovered that pectolinarigenin impacts the genes and signaling pathways involved in several topical conditions. In one aspect, the invention provides methods of using the compositions for treating, protecting, and/or altering (e.g., improving) the condition and/or aesthetic appearance of skin, including, for example, treating, preventing, ameliorating, reducing and/or eliminating fine lines and/or wrinkles of skin and/or improving the aesthetic appearance of fine lines and/or wrinkles of skin. In certain embodiments, the compositions of the invention lead to increase in skin and/or hair resiliency. In certain embodiments, the compositions of the invention lead to increase in elasticity of the skin. In certain embodiments, the compositions of the invention prevent skin damage.

In one aspect, the invention includes a composition for topical administration comprising an effective amount of pectolinarigenin. The effective amount of pectolinarigenin is an amount of pectolinarigenin that would be effective in treating, ameliorating, or otherwise impacting the underlying condition of the skin.

In certain aspects of the invention, the compositions comprising pectolinarigenin promote skin lightening and/or brightening. In certain embodiments, the compositions comprising pectolinarigenin at least a concentration of 0.01% w/w, have at least about 10% higher L value (reflecting the lightening of the skin), as compared to skin treated with a corresponding composition lacking pectolinarigenin. In certain embodiments, the compositions comprising

pectolinarigenin at least a concentration of 0.1% w/w, have about 4.6 units higher L value as compared to skin treated with a corresponding composition lacking pectolinarigenin.

In an embodiment, the invention provides a method of skin lightening and/or brightening by administration of compositions comprising pectolinarigenin. As demonstrated in the data provided in Example 2, skin tissues treated with compositions comprising 0.1% (w/w) and 0.01% (w/w) pectolinarigenin are 4.65 and 4.01 respectively, as compared to the solvent treated tissues. Thus, the compositions comprising pectolinarigenin are beneficial for lightening and/or brightening of the skin.

In certain aspects of the invention, the compositions comprising pectolinarigenin demonstrate antioxidant activity. In certain embodiments, the compositions of the invention, the antioxidant activity of pectolinarigenin is demonstrated at concentrations of about 0.00005% w/w or higher. Advantageously, the compositions of the invention comprising pectolinarigenin, demonstrating antioxidant activity, are effective for treating and/or preventing oxidation damage. In certain embodiments, the compositions of the invention comprising pectolinarigenin, demonstrating antioxidant activity, are effective for treatment of skin and/or hair damaged by reactive oxygen species and protection from other environmental aggressors that may damage the skin of the subject. In certain other embodiments, the compositions of the invention comprising pectolinarigenin, demonstrating antioxidant activity, are effective for prevention of skin and/or hair damage by reactive oxygen species, including the damage caused by environmental aggressors.

As demonstrated from the data provided in Examples 3 and 4, compositions comprising pectolinarigenin are effective in demonstrating robust antioxidant activity in both aqueous and organic solvent systems. The IC₅₀ values for antioxidant activity calculated in aqueous and organic solvent systems was 0.00027% w/w and 0.044% system. These results demonstrate that compositions comprising pectolinarigenin have robust antioxidant activity.

In certain aspects of the invention, the compositions comprising pectolinarigenin demonstrate elastase enzyme inhibition. In certain embodiments, the compositions of the invention, the elastase enzyme inhibition activity of pectolinarigenin is demonstrated at concentrations of about 0.005% w/w or higher. As evident from the data provided in Example 4,

compositions comprising pectolinarigenin have robust elastase enzyme inhibition activity. Indeed, the IC₅₀ value calculated for elastase enzyme inhibition activity of pectolinarigenin was 0.016%.

Advantageously, the compositions comprising pectolinarigenin, demonstrating elastase enzyme inhibition activity, are effective for promoting the elasticity of the skin. In certain embodiments, the compositions of the invention comprising pectolinarigenin, demonstrating elastase enzyme inhibition, are effective in reduction of fine lines and/or wrinkles in the skin. In certain embodiments, the compositions of the invention comprising pectolinarigenin, demonstrating elastase enzyme inhibition, are effective in prevention of formation of fine lines and/or wrinkles in the skin.

In certain aspects of the invention, the compositions comprising pectolinarigenin demonstrate inhibition of glycation. In certain embodiments, the compositions of the invention, the glycation inhibition activity of pectolinarigenin is demonstrated at concentrations of about 0.0005% w/w or higher. As evident from the data provided in Example 5, compositions comprising pectolinarigenin have robust glycation inhibition. Indeed, the calculated IC₅₀ value for glycation inhibition by compositions comprising pectolinarigenin is 0.002%. Advantageously, the compositions comprising pectolinarigenin, demonstrating glycation inhibition activity, are effective for supporting and promoting skin and/or hair resiliency.

Genetic expression and/or activity modulation

In certain aspects of the invention, a composition comprising pectolinarigenin modulates expression of one or more genes that is related to a topical condition. In certain embodiments, the one or more genes are selected from a group consisting of: (i) VCAN, (ii) COL1A2, (iii) MMP1, (iv) IL6, (v) IL23A, (vi) TLR2, and (vii) MMP3. In certain embodiments, administration of a composition comprising pectolinarigenin leads to up-regulation of VCAN, and/or COL1A2. In certain embodiments, administration of a composition comprising pectolinarigenin leads to down-regulation of MMP1, MMP3, IL6, TLR2, and/or IL23A.

Advantageously, it has been determined that compositions comprising pectolinarigenin impact the expression and/or activity of genes that are involved in pathways responsible maintaining the condition of the skin. In certain embodiments, the administration of compositions comprising pectolinarigenin impact the expression and/or activity of genes selected from a group

consisting of: (i) VCAN, (ii) COL1A2, (iii) MMP1, (iv) IL6, (v) IL23A, (vi) TLR2, and (vii) MMP3.

VCAN (versican) gene plays a role in maintenance of skin barrier through interaction with extracellular matrix proteins. The VCAN gene is responsible for versican protein expression. Versican is a type of protein known as a proteoglycan, which means it has several sugar molecules attached to it. Versican is found in the extracellular matrix of many different tissues and organs. The extracellular matrix is the intricate lattice of proteins and other molecules that forms in the spaces between cells. Versican interacts with many proteins and molecules to facilitate the assembly of the extracellular matrix and ensure its stability. As demonstrated in the data provided in FIG. 3, pectolarigenin administration caused an approximately ten (10) fold increase in expression of VCAN. This upregulation of VCAN results in increased strength in the skin barrier, which is indicative of anti-aging effect of pectolarigenin.

COL1A2 (collagen type I alpha 2 chain) gene encodes the pro-alpha2 chain of type I collagen whose triple helix comprises two alpha1 chains and one alpha2 chain. Type I is a fibril-forming collagen found in most connective tissues and is abundant in bone, cornea, dermis and tendon. COL1A2 gene is involved in regulation of collagen expression. An increase in collagen expression reduces wrinkles and sagging. As demonstrated in the data provided in FIG. 3, pectolarigenin administration caused an approximately fourteen (14) fold increase in expression of COL1A2. This upregulation of COL1A2 results in increased production of collagen, which is responsible for maintaining strength and integrity of the skin.

MMP1 (matrix metalloproteinase 1) encodes a member of the peptidase M10 family of matrix metalloproteinases (MMPs). Proteins in this family are involved in the breakdown of extracellular matrix in normal physiological processes, such as embryonic development, reproduction, and tissue remodeling, as well as in disease processes, such as arthritis and metastasis. The encoded preproprotein is proteolytically processed to generate the mature protease. This secreted protease breaks down the interstitial collagens, including types I, II, and III. The gene is part of a cluster of MMP genes on chromosome 11. Thus, MMP1 is involved in collagen degradation. Reduction in collagen degradation improves appearance of the skin. As demonstrated in the data provided in FIG. 3, pectolarigenin administration caused an approximately five (5) fold decrease in expression of MMP1. This decrease in expression of MMP1 results in decrease in

the rate of degradation of collagen, which is responsible for maintaining strength and integrity of the skin.

MMP3 (matrix metalloproteinase 3) encodes for matrix metalloproteinase-3, an enzyme responsible for degradation of collagen types II, III, IV, IX, and X, proteoglycans, fibronectin, laminin, and elastin. This is also a protein in the family of matrix metalloproteinases (MMPs). Proteins in this family are involved in the breakdown of extracellular matrix in normal physiological processes, such as embryonic development, reproduction, and tissue remodeling, as well as in disease processes, such as arthritis and metastasis. The encoded preproprotein is proteolytically processed to generate the mature protease. This secreted protease breaks down the interstitial collagens, including types I, II, and III. The gene is part of a cluster of MMP genes on chromosome 11. Thus, MMP3 is also involved in collagen degradation. As demonstrated in the data provided in FIG. 3, pectolinarigenin administration caused an approximately twenty (20) fold decrease in expression of MMP3. This decrease in expression of MMP3 results in decrease in the rate of degradation of collagen, which is responsible for maintaining strength and integrity of the skin.

IL6 (interleukin 6) gene encodes a cytokine that functions in inflammation and the maturation of B cells. In addition, the encoded protein has been shown to be an endogenous pyrogen capable of inducing fever in people with autoimmune diseases or infections. The protein is primarily produced at sites of acute and chronic inflammation, where it is secreted into the serum and induces a transcriptional inflammatory response through interleukin 6 receptor, alpha. This gene plays a role in regulation of inflammation, tissue atrophy, muscle loss, and/or melanogenesis. Decrease in expression of IL6 reduces inflammation, decreases tissue atrophy, decreases muscle loss, and downregulates melanogenesis. As demonstrated in the data provided in FIG. 3, pectolinarigenin administration caused an approximately two hundred (200) fold decrease in expression of IL6. This decrease in expression of IL6 results in decrease in the inflammatory activity of this gene. These results indicate that pectolinarigenin has a strong anti-inflammatory activity.

IL23A (interleukin 23 subunit alpha) gene also plays a role in inflammation. This gene encodes a subunit of the heterodimeric cytokine interleukin 23 (IL23). IL23 is composed of this protein and the p40 subunit of interleukin 12 (IL12B). The receptor of IL23 is formed by the beta

1 subunit of IL12 (IL12RB1) and an IL23 specific subunit, IL23R. Both IL23 and IL12 can activate the transcription activator STAT4, and stimulate the production of interferon-gamma (IFNG). In contrast to IL12, which acts mainly on naive CD4(+) T cells. As demonstrated in the data provided in FIG. 3, pectolarigenin administration caused an approximately four (4) fold decrease in expression of IL23A. This decrease in expression of IL23A results in decrease in the inflammatory activity of this gene. These results indicate that pectolarigenin has a strong anti-inflammatory activity.

TLR2 (toll like receptor 2) gene encodes for protein which is a member of the Toll-like receptor (TLR) family, which plays a fundamental role in pathogen recognition and activation of innate immunity. TLRs are highly conserved from Drosophila to humans and share structural and functional similarities. This protein is a cell-surface protein that can form heterodimers with other TLR family members to recognize conserved molecules derived from microorganisms known as pathogen-associated molecular patterns (PAMPs). Activation of TLRs by PAMPs leads to an up-regulation of signaling pathways to modulate the host's inflammatory response. Thus, TLR2 is also involved in the inflammatory pathway. As demonstrated in the data provided in FIG. 3, pectolarigenin administration caused an approximately five (5) fold decrease in expression of TLR2. This decrease in expression of TLR2 results in decrease in the inflammatory activity of this gene. These results indicate that pectolarigenin has a strong anti-inflammatory activity.

In certain embodiments, administration of a composition comprising pectolarigenin causes upregulation of one or more genes related to barrier and extracellular matrix proteins proteoglycan and collagens. In certain embodiments of the invention, the administration of the composition comprising pectolarigenin leads to at least about ten (10) fold up regulation of one or more genes related to barrier and extracellular matrix proteins proteoglycan and collagens.

In certain embodiments, administration of a composition comprising pectolarigenin causes downregulation of collagenase. In certain embodiments, administration of a composition comprising pectolarigenin leads to at least about five (5) fold down regulation of one or more genes related to barrier and extracellular matrix proteins proteoglycan and collagens.

In certain embodiments, administration of a composition comprising pectolarigenin downregulates the expression of inflammatory genes. In certain embodiments, administration of a

composition comprising pectolinarigenin leads to at least about two hundred (200) fold down regulation of the expression of inflammatory genes.

In certain embodiments, administration of a composition comprising pectolinarigenin downregulates the proteins involved in melanogenesis signaling pathway. In certain embodiments, administration of a composition comprising pectolinarigenin to a subject leads to the treatment of prevention of a topical condition of the subject through the modulation of levels of expression or activity of one or genes that may be involved in the topical condition. In certain embodiments, administration of a composition comprising pectolinarigenin alters one or more of a function related with the modulated genes, wherein the one or more function is selected from the group consisting of: (i) maintenance of skin barrier, (ii) collagen expression, (iii) collagen degradation, (iv) inflammation, (v) tissue atrophy, (vi) muscle loss, and (vii) melanin production.

Treatment of topical conditions

The current invention recognizes that the compositions comprising pectolinarigenin is beneficial for treating, protecting and/or improving the condition and/or aesthetic appearance of skin. For example, the compositions of the invention may be effective for altering the aesthetic appearance of skin associated with or affected by, or for treating or preventing, fine lines and/or wrinkles of skin caused by, for example, cellular senescence, environmental damage or dermatoheliosis. The invention also provides methods for stimulating skin cell renewal, increasing cell or tissue regeneration, promoting fibroblast proliferation and synthesizing elastin, collagen, proteoglycans, and/or new connective tissue, thereby reducing or improving the appearance of wrinkles, restoring elasticity, resiliency, and/or suppleness to the skin.

The compositions of the invention provided herein can be useful for improving the aesthetic appearance of skin. Such improvements can include, but are not limited to, all outward visibly and tactilely perceptible manifestations as well as any other macro or micro effects due to skin aging and damage. Such manifestations and effects can be induced or caused by intrinsic factors and/or extrinsic factors, e.g., chronological aging, environmental damage, climate, sun (UV) exposure, smoking, drugs, alcohol consumption, jetlag, night work, changes in circadian rhythm, pregnancy, menopause, genetic factors, nutritional factors and/or deficiencies, dehydration, stress, allergies (e.g., to plants, animals, medications, and other substances), exposure

to industrial and/or household chemicals, indoor heating and cooling, various disorders and diseases such as arteriosclerosis, diabetes, heart disease, liver disease, and obesity, thinning of the outer layer of skin, decreases in the number of pigment-containing cells, increases in the size of pigment-containing cells, changes in the connective tissue, and reduction in the strength and elasticity of the skin.

The aesthetic appearance of skin can be improved, for example, by improving the appearance of skin associated with or affected by one or more of wrinkles, dry skin, sensitive skin; wrinkling and sagging; acne; vitiligo (skin condition in which there is a loss of brown color (pigment) from areas of skin); fine lines, wizened skin, thinning of the dermis, the degradation of collagen fibers, flaccid skin, thinned skin, and skin exposed to ultraviolet radiation. In some embodiments, the compositions of the invention can improve the aesthetic appearance of skin by decreasing the appearance of fine lines in the skin; creating a more youthful appearance of the skin; decreasing bags and/or rings around the eyes; increasing or restoring the elasticity, resiliency, and/or suppleness of the skin; increasing the apparent thickness, elasticity, flexibility, radiance, glow, and plumpness of the skin; improving the fineness of the skin texture; improving the appearance of wrinkles, lined, dry, flaky, aged, and/or photodamaged skin; treating or preventing photodamaged skin; reducing the signs of skin aging; reducing the appearance of hyperpigmentation; treating or preventing hyperpigmentation; treating or preventing pigment deposition in the skin (e.g., that caused by UV exposure); reducing the appearance of skin discolorations; and whitening, lightening, and/or bleaching the skin.

In certain embodiments, the compositions may be used for care, treatment, cleansing, and/or protective products for facial or body skin; anti-wrinkle or anti-aging compositions; skin firming compositions; skin lightening compositions; compositions for irritated skin; sunscreen compositions, artificial tanning (self-tanning) compositions or after-sun care compositions; scalp care compositions; shaving preparation compositions; depilatory compositions; or make-up products for the skin of the face or body.

In certain embodiments, the compositions comprising pectolinarigenin are administered for altering the aesthetic appearance of skin associated with or affected by, or treating or preventing, a skin condition/disorder (e.g., a skin condition/disorder accompanied with a loss of skin elasticity).

In certain embodiments, the compositions comprising pectolinarigenin are administered for improving the barrier function and viability of the skin.

In certain embodiments, the compositions comprising pectolinarigenin are administered for altering the aesthetic appearance of skin associated with or affected by wrinkling, sagging,
5 and/or a loss of skin elasticity.

In certain embodiments, the compositions comprising pectolinarigenin are administered for altering the aesthetic appearance of skin associated with or affected by deteriorations in skin viscoelasticity.

In certain embodiments, the compositions comprising pectolinarigenin are administered
10 for altering the aesthetic appearance of skin associated with or affected by one or more of wrinkles and/or fine lines, wizened skin, a lack of elasticity and/or of tonus of the skin, thinning of the dermis, degradation of collagen fibers, flaccid skin, thinned skin, and the internal degradation of the skin following exposure to ultraviolet radiation.

In certain embodiments, the compositions comprising pectolinarigenin are administered
15 for decreasing the appearance of fine lines and/or wrinkles in the skin.

In certain embodiments, the compositions comprising pectolinarigenin are administered for decreasing the appearance of bags and/or rings around the eyes.

In certain embodiments, the compositions comprising pectolinarigenin are administered for reducing the appearance of hyperpigmentation.

20 In certain embodiments, the compositions comprising pectolinarigenin are administered for improving or increasing one or more of the thickness, elasticity, flexibility, radiance, glow, and plumpness of the skin.

In certain embodiments, the compositions comprising pectolinarigenin are administered for improving the fineness of skin texture.

25 In certain embodiments, the compositions comprising pectolinarigenin are administered for improving the appearance of wrinkled, lined, dry, flaky, aged or photodamaged skin.

In certain embodiments, the compositions comprising pectolinarigenin are administered for altering the aesthetic appearance of skin associated with or affected by skin discolorations.

Methods of Administration:

5 In one aspect, the invention provides methods of administration of the compositions comprising pectolinarigenin. In certain embodiments, the invention the compositions of the invention are designed for topical administration.

In certain embodiments, the compositions of the invention may be administered as a topical composition on the skin of the subject. The compositions of the invention may be included in any
10 formulation suitable for topical administration. In certain embodiments, the composition of the invention is a fluid, emulsion, encapsulation, suspension, solid, semi-solid, jelly, paste, gel, hydrogel, ointment, lotion, emulsion, cream, foam, mousse, liquid, spray, suspension, dispersion, powder, aerosol, color cosmetic, and/or hair treatment.

In certain other embodiments, the compositions comprising pectolinarigenin may be
15 prepared and used in the form of an aerosol spray, cream, emulsion, solid, liquid, dispersion, foam, oil, gel, lotion, mousse, ointment, powder, patch, pomade, solution, pump spray, stick, towelette, soap, or other forms commonly employed in the art of topical administration and/or cosmetic and skin care formulation. The compositions can be in an emulsion form. In addition, compounds provided herein used in the compositions provided herein can be used in color cosmetic
20 compositions such as foundation makeups, blushes, eyeshadows, mascaras, concealers, eyeliners, lip colors, nail colors, and so on. Other cosmetic compositions can include perfumes, lipsticks, fingernail and toenail polish, eye and facial makeup, towelettes, deodorants, hand sanitizer, baby products, bath oils, bubble baths, and butters.

In certain embodiments, the compositions comprising pectolinarigenin are administered
25 over an area of about $1.0 \mu\text{g}/\text{cm}^2$ to about $100 \mu\text{g}/\text{cm}^2$.

In certain embodiments, the compositions comprising pectolinarigenin are administered for a duration till the desired impact in amelioration or prevention of a topical condition is realized. In certain embodiments, the composition comprising pectolinarigenin comprises an effective

amount of pectolinarigenin. The effective amount of pectolinarigenin is an amount of pectolinarigenin that results in the desired result in the condition of the skin. In certain embodiments, the composition comprising pectolinarigenin is administered once a day. In certain embodiments, the composition comprising pectolinarigenin is administered twice a day. In certain
5 embodiments, the composition comprising pectolinarigenin is administered thrice a day. In certain
embodiments, the composition comprising pectolinarigenin is administered once every two days. In certain embodiments, the composition comprising pectolinarigenin is administered once every three days.

Examples:

10 **Example 1:** Exemplary composition comprising pectolinarigenin:

Table 3 provides an exemplary formulation of pectolinarigenin:

Table 3: Exemplary composition comprising pectolinarigenin:

Ingredient	%w/w
Water	61.7528
Dimethyl Isosorbide	19.5000
Glycerin	4.0000
Caprylic/Capric Triglyceride	2.6064
Propanediol	2.4387
Helianthus Annuus (Sunflower) Seed Oil	2.4000
Ethoxydiglycol	1.1868
Squalane	0.8000
Sodium Arcylates Copolymer	0.7500
Cetearyl Alcohol	0.6214
Phenoxyethanol	0.5400
Pectolinarigenin	0.5000
Glyceryl Stearate	0.4400
Capryloyl Glycerin/Sebacic Acid Copolymer	0.4400
Diheptyl Succinate	0.4400
Naringenin	0.3612
Lecithin	0.2500
Decylene Glycol	0.2000
Pentylene Glycol	0.0707
Cetearyl Glucoside	0.0774
Butyrospermum Parkii (Shea) Butter	0.0645
Palmitic Acid	0.0645
Arachidyl Alcohol	0.0645

Behenyl Alcohol	0.0645
Arachidyl Glucoside	0.0645
Phenethyl Alcohol	0.0645
1,2-Hexanediol	0.0600
Hydrogenated Olive Oil	0.0387
Olea Europaea (Olive) Fruit oil	0.0387
Olea Europaea (Olive) Oil Unsaponifiables	0.0387
Hydroxyethyl Acrylate/Sodium Acryloyldimethyl Taurate Copolymer	0.0335
Citric Acid	0.0080
Sodium Acetylated Hyaluronate	0.0068
Sodium Hyaluronate	0.0060
Sodium Hyaluronate Crosspolymer	0.0028
Sodium Phytate	0.0026
Hydrolyzed Sodium Hyaluronate	0.0012
Ethylhexylglycerin	0.0006

Example 2: Preclinical analysis of lightening and/or brightening effects of compositions comprising pectolinarigenin:

5 The experiment was designed to evaluate the impact of compositions comprising pectolinarigenin on skin lightening and/or brightening. In preclinical analysis, conducted on in vitro skin tissues, the compositions comprising pectolinarigenin resulted in lightening and/or brightening of the skin.

Table 4: Lightening and/or Brightening of skin tissues

Pectolinarigenin Concentration (%w/w)	L value
0.10	48.84
0.01	48.20
Solvent control	44.19

10 As evident from the data provided in Table 4, skin tissues treated with compositions comprising 0.1% and 0.01% pectolinarigenin are 4.65 and 4.01 respectively, as compared to the skin tissue samples treated with solvent.

Example 3: ABTS antioxidant assay:

The 2,2'-Azinobis [3-ethylbenzothiazoline-6-sulfonic acid]-diammonium salt (ABTS) antioxidant assay is designed to evaluate the antioxidant activity of compositions comprising pectolinarigenin in an aqueous medium.

- 5 ABTS⁺ solution is generated as a free radical and used to measure relative ability of a compound to scavenge free radicals. Reduction of the absorbance at 734 nm was standardized to solvent control as an indication of ABTS⁺ scavenging.

Table 5, provided below, demonstrates the results from these experiments:

Table 5: ABTS (aqueous antioxidant assay) radical inhibition

Concentration (%w/w)	% Radical Inhibition
0.002	93.36
0.0004	66.25
0.00008	19.13

10

As evident from the results provided in Table 5 above, compositions comprising pectolinarigenin demonstrates antioxidant activity at concentrations as low as 0.00008% w/w in aqueous systems. The calculated IC₅₀ value is: 0.00027% w/w.

Example 4: DPPH Antioxidant Activity assay

- 15 The 2,2-diphenyl-1-picrylhydrazyl (DPPH) antioxidant assay is designed to evaluate the antioxidant activity of compositions comprising pectolinarigenin in an organic medium.

2,2-diphenyl-1-picrylhydrazyl (DPPH) is a stable free radical used to evaluate free radical scavenging capacity of a material. In the presence of an antioxidant DPPH is reduced, resulting in the formation of a colorless solution. Reduction of absorbance at 517 nm is standardized to solvent control as an indication of DPPH scavenging.

20

Table 6, provided below, provides the antioxidant activity data.

Table 6: DPPH Radical Inhibition

Pectolinarigenin concentration (%w/w)	% Radical Inhibition
0.083	63.64
0.042	48.69
0.007	19.91

As evident from the results provided in Table 6 above, compositions comprising pectolinarigenin demonstrates antioxidant activity at concentrations at low as 0.007% w/w in organic solvent systems. The calculated IC₅₀ value is: 0.0044% w/w.

Example 5: Elastase enzyme inhibition:

The assay was conducted to evaluate the elastase enzyme inhibition activity of compositions comprising pectolinarigenin.

Neutrophil infiltration and neutrophil elastase are both increased in the skin in response to UV stress. Neutrophil elastase has been shown to activate MMP-1 and MMP-2 collagenase in response to low dose UV exposure, harming the extracellular matrix and contributing to photoaging and wrinkle formation. The activity of elastase can be further upregulated in the presence of reactive oxygen species. Therefore, inhibition of this enzyme, particularly in combination with antioxidant activity, is effective in delaying wrinkle development and aiding in maintaining skin integrity. This assay is measures release of 4-nitroaniline from an Me-Suc-Ala-Ala-Pro-Val-pNA by human neutrophil elastase and can be quantified at 405 nm by comparing to solvent control.

Table 7 provides the elastase inhibition activity of compositions comprising pectolinarigenin:

Table 7: Elastase enzyme inhibition

Pectolinarigenin concentration (%w/w)	% Enzyme Inhibition
---------------------------------------	---------------------

0.031	74.21
0.016	48.99
0.008	36.00

As evident from the data provide in Table 7, compositions comprising pectolinarigenin inhibits elastase enzyme activity as low at 0.008% w/w. The IC50 calculated for elastase inhibition activity was 0.016%.

5 **Example 6:** Glycation inhibition assay:

The assay was conducted to evaluate the glycation inhibition activity of compositions comprising pectolinarigenin.

10 Nonenzymatic glycation can occur when glucose reacts with proteins, forming a Schiff base intermediate that subsequently undergoes Amadori rearrangement to form glycosylated proteins, when they react with skin proteins to form Advanced Glycation End products (AGE). AGE formation can result in loss of skin elasticity and impaired cellular function. The glycation inhibition ability of a compound is measured by change in fluorescence at excitation/emission of 360nm/420 nm relative to solvent control.

Table 8 provides the data for glycation inhibition.

15

Table 8: Glycation Inhibition

Pectolinarigenin concentration (%w/w)	% Enzyme Inhibition
0.019	92.75
0.006	79.22
0.002	58.50
0.0007	44.06

As evident from the data provided in Table 8, compositions comprising pectolinarigenin inhibits glycation as low as 0.0007% w/w. The IC₅₀ value calculated for glycation inhibition is 0.002%.

5

Incorporation by Reference

References and citations to other documents, such as patents, patent applications, patent publications, journals, books, papers, web contents, publicly accessible databases, have been made throughout this disclosure. All such documents are hereby incorporated herein by reference in their
10 entirety for all purposes.

Equivalents

Various modifications of the invention and many further embodiments thereof, in addition to those shown and described herein, will become apparent to those skilled in the art from the full contents of this document, including references to the scientific and patent literature cited herein.
15 The subject matter herein contains important information, exemplification and guidance that can be adapted to the practice of this invention in its various embodiments and equivalents thereof.

CLAIMS:

1. A composition for topical administration comprising an effective amount of pectolinarigenin.
2. The composition of claim 1, wherein the composition comprises an emulsion.
3. The composition of claim 2, wherein the emulsion is an oil/water emulsion.
4. The composition of claim 1, wherein the composition further comprises dimethyl isosorbide.
5. The composition of claim 1, wherein the pectolinarigenin is dissolved in dimethyl isosorbide.
6. The composition of claim 5, wherein the composition is stable under storage for at least 3 months.
7. The composition of claim 5, wherein the composition has less than about 20% degradation when stored at 4 °C or 25 °C for 3 months.
8. The composition of claim 5, wherein the composition has less than about 30% degradation when stored at 40 °C or 50 °C for 3 months.
9. The composition of claim 1, wherein the pectolinarigenin is present in a concentration of about 0.0001% to about 5.0% w/w.
10. The composition of claim 1, wherein the pectolinarigenin is present in a concentration of about 0.0005% to about 2.0% w/w.
11. The composition of claim 1, wherein the pectolinarigenin is present in a concentration of 0.0007% to about 1.0% w/w.

12. The composition of claim 1, wherein the pectolinarigenin is present in a concentration of about 0.001% to about 0.75% w/w.
13. The composition of claim 1, wherein pectolinarigenin is present in a concentration of about 0.5% w/w.
14. The composition of claim 1, wherein the composition is selected from a group consisting of: fluid, emulsion, encapsulation, suspension, solid, semi-solid, jelly, paste, gel, hydrogel, ointment, lotion, emulsion, cream, foam, mousse, liquid, spray, suspension, dispersion, powder, aerosol, color cosmetic, hair treatment, and any combination thereof.
15. The composition of claim 1, wherein the composition further comprises one or more excipients selected from a group consisting of: solvent, emulsifier, preservative, antioxidant, emollient, thickening agent, penetration enhancer, surfactant, diluent, filler, carrier, and/or pH control agent.
16. The composition of claim 15, wherein the preservative is an antimicrobial preservative or chelating agent.
17. The composition of claim 15, wherein the solvent is dimethyl isosorbide.
18. The composition of claim 1, wherein the composition further comprises one or more excipients selected from a group consisting of: water, dimethyl isosorbide, glycerin, caprylic/capric triglyceride, propanediol, sunflower seed oil, ethoxydiglycol, squalane, sodium acrylate copolymer, cetearyl alcohol, phenoxyethanol, glyceryl stearate, capryloyl glycerin/sebacic acid copolymer, diheptyl succinate, naringenin, lecithin, decylene glycol, pentylene glycol, cetearyl glucoside, shea butter, palmitic acid, arachidyl alcohol, behenyl alcohol, arachidyl glucoside, phenethyl alcohol, 1,2-hexanediol, hydrogenated olive oil, olea europaea (olive) fruit oil, olea europaea (olive) oil unsaponifiables, hydroxyethyl acrylate/sodium acryloyldimethyl taurate copolymer, citric acid, sodium acetylated hyaluronate, sodium hyaluronate crosspolymer, sodium phytate, hydrolyzed sodium hyaluronate, and ethylhexylglycerin.

19. The composition of claim 1, wherein the composition comprises about 50% to about 70% water (w/w) and about 10% to about 30% (w/w) dimethyl isosorbide.

20. The composition of claim 1, wherein the composition is:

Ingredient	%w/w
Water	40 - 80
Dimethyl Isosorbide	10 - 30
Glycerin	1 - 10
Caprylic/Capric Triglyceride	0 - 5
Propanediol	0 - 5
Helianthus Annuus (Sunflower) Seed Oil	0 - 5
Ethoxydiglycol	0 - 5
Squalane	0 - 2
Sodium Arcylates Copolymer	0 - 2
Cetearyl Alcohol	0 - 2
Phenoxyethanol	0 - 2
Pectolinarigenin	0.0001-5.00
Glyceryl Stearate	0 - 2
Capryloyl Glycerin/Sebacic Acid Copolymer	0 - 2
Diheptyl Succinate	0 - 2
Naringenin	0 - 2
Lecithin	0 - 2
Decylene Glycol	0 - 2
Pentylene Glycol	0 - 1
Cetearyl Glucoside	0 - 1
Butyrospermum Parkii (Shea) Butter	0 - 1
Palmitic Acid	0 - 1
Arachidyl Alcohol	0 - 1
Behenyl Alcohol	0 - 1
Arachidyl Glucoside	0 - 1
Phenethyl Alcohol	0 - 1
1,2-Hexanediol	0 - 1
Hydrogenated Olive Oil	0 - 1
Olea Europaea (Olive) Fruit oil	0 - 1
Olea Europaea (Olive) Oil Unsaponifiables	0 - 1
Hydroxyethyl Acrylate/Sodium Acryloyldimethyl Taurate Copolymer	0 - 1
Citric Acid	0 - 1
Sodium Acetylated Hyaluronate	0 - 1
Sodium Hyaluronate	0 - 1
Sodium Hyaluronate Crosspolymer	0 - 1
Sodium Phytate	0 - 1

Hydrolyzed Sodium Hyaluronate	0 - 1
Ethylhexylglycerin	0 - 1

21. A method of treating or preventing a topical condition in a subject by administration of a composition comprising an effective amount of pectolinarigenin.
22. The method of claim 21, wherein the administration of the composition prevents lines or wrinkles on skin of the subject.
23. The method of claim 21, wherein the administration of the composition leads to supporting firmness and elasticity of skin of the subject.
24. The method of claim 21, wherein the administration of the composition leads to the prevention of skin and hair damaged by reaction oxygen species.
25. The method of claim 21, wherein the administration of the composition leads to protection from environment aggressors on skin.
26. The method of claim 21, wherein the administration of the composition leads to supporting skin elasticity.
27. The method of claim 21, wherein the topical condition is glycation.
28. The method of claim 21, wherein the administration of the composition leads increase in skin and/or hair resiliency.
29. The method of claim 21, wherein the administration of the composition leads to increase in elasticity of skin.
30. The method of claim 21, wherein the administration of the composition leads to prevention of skin damage.
31. The method of claim 21, wherein the composition is administered topically.

32. The method of claim 21, wherein the composition comprises an emulsion.
33. The method of claim 32, wherein the emulsion is an oil/water emulsion.
34. The method of claim 21, wherein the composition further comprises dimethyl isosorbide.
35. The method of claim 21, wherein the pectolinarigenin is dissolved in dimethyl isosorbide.
36. The method of claim 35, wherein the composition is stable under storage for at least 3 months.
37. The method of claim 35, wherein the composition has less than about 20% degradation when stored at 4 °C or 25 °C for 3 months.
38. The method of claim 35, wherein the composition has less than about 30% degradation when stored at 40 °C or 50 °C for 3 months.
39. The method of claim 21, wherein the pectolinarigenin is present in a concentration of about 0.0001% to about 5.0% w/w.
40. The method of claim 21, wherein the pectolinarigenin is present in a concentration of about 0.0005% to about 2.0% w/w.
41. The method of claim 21, wherein the pectolinarigenin is present in a concentration of 0.0007% to about 1.0% w/w.
42. The method of claim 21, wherein the pectolinarigenin is present in a concentration of about 0.001% to about 0.75% w/w.
43. The method of claim 21, wherein pectolinarigenin is present in a concentration of about 0.5% w/w.
44. The method of claim 21, wherein the composition is selected from a group consisting of: fluid, emulsion, encapsulation, suspension, solid, semi-solid, jelly, paste, gel, hydrogel,

ointment, lotion, emulsion, cream, foam, mousse, liquid, spray, suspension, dispersion, powder, aerosol, color cosmetic, and any combination thereof.

45. The method of claim 21, wherein the composition further comprises one or more excipients selected from a group consisting of: solvent, emulsifier, preservative, antioxidant, emollient, thickening agent, penetration enhancer, surfactant, diluent, filler, carrier and/or pH control agent.
46. The method of claim 45, wherein the preservative is an antimicrobial preservative.
47. The method of claim 45, wherein the solvent is dimethyl isosorbide.
48. The method of claim 21, wherein the composition further comprises one or more excipients selected from a group consisting of: water, dimethyl isosorbide, glycerin, caprylic/capric triglyceride, propanediol, sunflower seed oil, ethoxydiglycol, squalane, sodium acrylate copolymer, cetearyl alcohol, phenoxyethanol, glyceryl stearate, capryloyl glycerin/sebacic acid copolymer, diheptyl succinate, naringenin, lecithin, decylene glycol, pentylene glycol, cetearyl glucoside, shea butter, palmitic acid, arachidyl alcohol, behenyl alcohol, arachidyl glucoside, phenethyl alcohol, 1,2-hexanediol, hydrogenated olive oil, olea europaea (olive) fruit oil, olea europaea (olive) oil unsaponifiables, hydroxyethyl acrylate/sodium acryloyldimethyl taurate copolymer, citric acid, sodium acetylated hyaluronate, sodium hyaluronate crosspolymer, sodium phytate, hydrolyzed sodium hyaluronate, and ethylhexylglycerin.
49. The method of claim 21, wherein the composition comprises about 50% to about 70% water (w/w) and about 10% to about 30% (w/w) dimethyl isosorbide.

50. The method of claim 21, wherein the composition is:

Ingredient	%w/w
Water	40 - 80
Dimethyl Isosorbide	10 - 30
Glycerin	1 - 10
Caprylic/Capric Triglyceride	0 - 5
Propanediol	0 - 5

Helianthus Annuus (Sunflower) Seed Oil	0 - 5
Ethoxydiglycol	0 - 5
Squalane	0 - 2
Sodium Arcylates Copolymer	0 - 2
Cetearyl Alcohol	0 - 2
Phenoxyethanol	0 - 2
Pectolinarigenin	0.0001-5.00
Glyceryl Stearate	0 - 2
Capryloyl Glycerin/Sebacic Acid Copolymer	0 - 2
Diheptyl Succinate	0 - 2
Naringenin	0 - 2
Lecithin	0 - 2
Decylene Glycol	0 - 2
Pentylene Glycol	0 - 1
Cetearyl Glucoside	0 - 1
Butyrospermum Parkii (Shea) Butter	0 - 1
Palmitic Acid	0 - 1
Arachidyl Alcohol	0 - 1
Behenyl Alcohol	0 - 1
Arachidyl Glucoside	0 - 1
Phenethyl Alcohol	0 - 1
1,2-Hexanediol	0 - 1
Hydrogenated Olive Oil	0 - 1
Olea Europaea (Olive) Fruit oil	0 - 1
Olea Europaea (Olive) Oil Unsaponifiables	0 - 1
Hydroxyethyl Acrylate/Sodium Acryloyldimethyl Taurate Copolymer	0 - 1
Citric Acid	0 - 1
Sodium Acetylated Hyaluronate	0 - 1
Sodium Hyaluronate	0 - 1
Sodium Hyaluronate Crosspolymer	0 - 1
Sodium Phytate	0 - 1
Hydrolyzed Sodium Hyaluronate	0 - 1
Ethylhexylglycerin	0 - 1

51. The composition of claim 1, wherein the composition is anhydrous.

52. The composition of claim 1, wherein the composition comprises oil as the only solvent.

53. The method of claim 21, wherein the composition is anhydrous.

54. The method of claim 21, wherein the composition comprises oil as the only solvent.

55. The method of claim 21, wherein the administration of the composition results in lightening of skin of the subject.
56. The method of claim 55, wherein the lightening is about two (2) units to about ten (10) units higher as compared to skin treated with placebo.
57. The method of claim 55, wherein the administration of a composition comprising about 0.1% pectolinarigenin is more than about four (4) units as compared to skin treated with placebo.
58. The method of claim 55, wherein the administration of a composition comprising about 0.1% pectolinarigenin is more than about 4.65 units as compared to skin treated with placebo.
59. The method of claim 55, wherein the administration of a composition comprising about 0.01% pectolinarigenin is more than about three (3) units as compared to skin treated with placebo.
60. The method of claim 55, wherein the administration of a composition comprising about 0.01% pectolinarigenin is more than about 4.01 units as compared to skin treated with placebo.
61. A method of modulating expression of one or more genes by administration of a composition comprising pectolinarigenin, wherein at least one of the genes is related to a topical condition.
62. The method of claim 61, wherein the one or more genes are selected from a group consisting of: (i) VCAN, (ii) COL1A2, (iii) MMP1, (iv) IL6, (v) IL23A, (vi) TLR2, and (vii) MMP3
63. The method of claim 61, wherein the administration of the composition leads to up-regulation of VCAN, and/or COL1A2.

64. The method of claim 61, wherein the administration of the composition leads to down-regulation of MMP1, MMP3, IL6, TLR2, and/or IL23A.
65. The method of claim 61, wherein the administration of composition causes upregulation of one or more genes related to barrier and extracellular matrix proteins proteoglycan and collagens.
66. The method of claim 65, wherein the administration of composition further causes downregulation of collagenase.
67. The method of claim 61, wherein the administration of the composition downregulates the expression of inflammatory genes.
68. The method of claim 61, wherein the administration of the composition downregulates the proteins involved in melanogenesis signaling pathway.
69. The method of claim 61, wherein the administration of the composition to a subject leads to the treatment of prevention of a topical condition of the subject.
70. The method of claim 65, wherein the administration of the composition leads to at least about ten (10) fold up regulation of one or more genes related to barrier and extracellular matrix proteins proteoglycan and collagens.
71. The method of claim 66, wherein the administration of the composition leads to at least about five (5) fold down regulation of one or more genes related to barrier and extracellular matrix proteins proteoglycan and collagens.
72. The method of claim 67, wherein the wherein the administration of the composition leads to at least about two hundred (200) fold down regulation of the expression of inflammatory genes.
73. The method of claim 61, wherein the administration of composition alters one or more of a function related with the modulated genes, wherein the one or more function is selected

from the group consisting of: (i) maintenance of skin barrier, (ii) collagen expression, (iii) collagen degradation, (iv) inflammation, (v) tissue atrophy, (vi) muscle loss, and (vii) melanin production.

74. The method of claim 62, wherein the VCAN gene maintains skin barrier through interaction with extracellular matrix proteins.
75. The method of claim 62, wherein the COL1A2 gene regulated collagen expression.
76. The method of claim 75, wherein increase in the collagen expression reduces wrinkles and sagging.
77. The method of claim 62, wherein the MMP1 gene regulates collagen degradation.
78. The method of claim 77, wherein reducing the collagen degradation improves appearance of skin.
79. The method of claim 62, wherein the IL6 gene plays a role in regulation of inflammation, tissue atrophy, muscle loss, and/or melanogenesis.
80. The method of claim 62, wherein the IL23A gene plays a role in inflammation.
81. The method of claim 61, wherein the composition comprises from about 5 nM to about 2500 nM pectolinarigenin.
82. The method of claim 61, wherein the composition further comprises a solvent.
83. The method of claim 61, wherein the solvent is selected from a group consisting of: dimethyl isosorbide, ethoxydiglycol, isopropyl lauryl sarcosinate, pentylene glycol, propanediol, 1,2-hexanediol, and/or butylene glycol.