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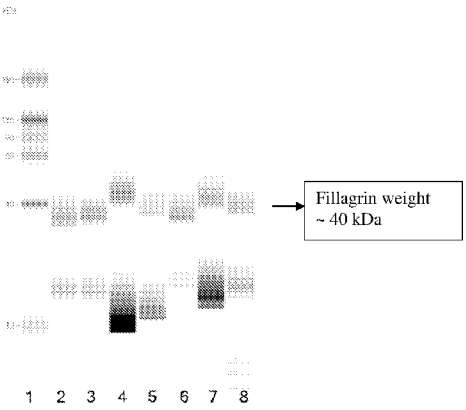

Column No.	Test Composition
1	Biotinylated Ladder
2	Control
3	Calcium
4	*Imperata cylindrical* extract
5	*Verbena officinalis* extract
6	*Laminaria saccharina* extract
7	marine plankton extract
8	*Opuntia ficua-indica* extract

THE FIGURE

(57) Abstract: The present invention relates generally to methods of use and compositions for enhancing skin hydration in a person, attracting and binding moisture in the air to the skin's outer layers, transporting surface moisture below the skin's stratum corneum, increasing skin moisture content, plumping and tightening the skin, protecting the skin from moisture loss to the environment, supporting optimal skin barrier function, and/or stimulating production of the skin's own Natural Moisturizing Factor. The composition includes a combination of the *Verbena officinalis* extract, hydrolyzed sodium hyaluronate, and ceramide.

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DESCRIPTION

TOPICAL COSMETIC COMPOSITIONS

CROSS-REFERENCE TO RELATED APPLICATIONS

[0001] This application claims the benefit of priority to U.S. Provisional Patent Application Serial No. 63/014,517, filed April 23, 2020, hereby incorporated by reference in its entirety.

BACKGROUND OF THE INVENTION

A. Field of the Invention

[0002] The present invention relates generally to cosmetic compositions and methods that can be used to increase skin moisture content, attract and bind moisture in the air to the skin's outer layers, transport surface moisture below the skin's stratum corneum, plump and tighten the skin, protect the skin from moisture loss to the environment, support optimal skin barrier function, and/or stimulate production of the skin's own Natural Moisturizing Factor, and/or increase the efficacy of cosmetic products to increase skin moisture content, attract and bind moisture in the air to the skin's outer layers, transport surface moisture below the skin's stratum corneum, plump and tighten the skin, protect the skin from moisture loss to the environment, support optimal skin barrier function, and/or stimulate production of the skin's own Natural Moisturizing Factor. In particular, the compositions can include *Verbena officinalis* extract, hydrolyzed sodium hyaluronate, and ceramide.

B. Description of Related Art

[0003] Various factors can lead to different stresses on skin, including ageing, chronic exposure to adverse environmental factors, malnutrition, fatigue, stress, changes in seasons, and other extrinsic and intrinsic factors which may damage skin, to name a few examples. These stresses can change the visual appearance, physical properties, or physiological functions of skin and tissue in ways that are considered visually undesirable. Notable and obvious changes include dry skin, coarse surface texture, the development of fine lines and wrinkles, loss of elasticity, decreased skin barrier function, loss of color evenness or tone, and mottled pigmentation. Many of these stressors are difficult or impossible to avoid.

[0004] Less obvious but measurable changes which occur as skin and tissue ages or endures chronic environmental insult include a general reduction in cellular and tissue vitality, reduction in cell replication rates, reduced cutaneous blood flow, reduced moisture content,

accumulated errors in structure and function, alterations in the normal regulation of common biochemical pathways, and a reduction in the skin's and tissue's ability to remodel and repair itself. Many of the alterations in appearance and function of the skin are caused by changes in the outer epidermal layer of the skin, while others are caused by changes in the lower dermis. Regardless of the stimulus for skin damage, when damage occurs, numerous natural and complex biochemical mechanisms are set into motion in attempts to repair the damage.

[0005] Normal healthy skin has a smooth epidermal layer that acts as a good barrier to water and environmental damage. Skin color and tone is even and unblemished. Natural firming and hydrating elements such as collagen (which provides skin firmness), elastin (which supplies skin elasticity and rebound) and glycosaminoglycans or GAGs (which keep the skin hydrated) are all abundant. However, age slows the natural production of collagen, elastin, and GAGs, which results in unwanted changes in skin such as dryness, itchiness, redness, shadows or dark areas, sagging, thinning, or more noticeable fine lines and wrinkles. Maintaining skin moisture helps overcome some of these changes. However, maintaining moisture of the skin can be difficult. This is especially true for subjects with skin that is more dry than average (dry skin type). Exposure to sun, wind, dry air, chemicals, solvents, washing, cosmetics, or fabrics are some of the many ways that skin can lose moisture. With so many factors compromising the skin's ability to stay hydrated, a moisturizer alone may not always be enough.

[0006] Others have attempted to create compositions and methods that hydrate skin and/or stimulate the skin's own natural hydration. However, many attempts have been ineffective, only addressed one or a few of the undesired outcomes, or caused unacceptable side effects themselves, such as skin irritation. Thus, there is a need for new products that are effective at hydrating and/or stimulating the skin's own natural hydration without causing skin irritation.

SUMMARY OF THE INVENTION

[0007] The inventors have identified a solution to the problems associated with current cosmetic products. The solution resides in a combination of ingredients including *Verbena officinalis* extract, hydrolyzed sodium hyaluronate, and ceramide. The combination can be used to increase skin moisture content, attract and bind moisture in the air to the skin's outer layers, transport surface moisture below the skin's stratum corneum, plump and tighten the skin, protect the skin from moisture loss to the environment, support optimal skin barrier function, and/or stimulate production of the skin's own Natural Moisturizing Factor. The combination can also be used to increase the efficacy of cosmetic products to increase skin

moisture content, attract and bind moisture in the air to the skin's outer layers, transport surface moisture below the skin's stratum corneum, plump and tighten the skin, protect the skin from moisture loss to the environment, support optimal skin barrier function, and/or stimulate production of the skin's own Natural Moisturizing Factor. Additional benefits can include reducing or mitigating unwanted side effects of current cosmetic products. In some aspects, an effective amount of a combination of *Verbena officinalis* extract, hydrolyzed sodium hyaluronate, and ceramide is combined with an effective amount of glycerin to boost skin moisture content and/or stimulate the skin's own natural hydration. In some aspects, an effective amount of a combination of *Verbena officinalis* extract, hydrolyzed sodium hyaluronate, and ceramide is combined with an effective amount of sodium hyaluronate to attract and bind moisture in the air to the skin's outer layers and protect the skin from moisture loss to the environment. In some aspects, the *Verbena officinalis* extract is provided as an aqueous extract.

[0008] In some aspects, there is disclosed a topical skin composition. In some instances, the composition includes an effective amount of *Verbena officinalis* extract, hydrolyzed sodium hyaluronate, and ceramide, wherein topical application of the composition enhances skin moisture content, attracts and binds moisture in the air to the skin's outer layers, transports surface moisture below the skin's stratum corneum, plumps and tightens the skin, protects the skin from moisture loss to the environment, supports optimal skin barrier function, and/or stimulates production of the skin's own Natural Moisturizing Factor. In some instances, the composition includes an effective amount of *Verbena officinalis* extract, hydrolyzed sodium hyaluronate, and ceramide, wherein topical application of the composition increases skin moisture content at least 10, 20, 30, 40, or 50% after a single application. In some instances, the composition includes an effective amount of *Verbena officinalis* extract, hydrolyzed sodium hyaluronate, and ceramide, wherein topical application of the composition stimulates production of the skin's own Natural Moisturizing Factor.

[0009] In some instances, the topical composition includes 0.001% to 1% w/w of *Verbena officinalis* extract, 0.01% to 10% w/w of hydrolyzed sodium hyaluronate, and 0.001% to 1% w/w of ceramide. In some aspects, the composition includes 0.001% to 1% w/w of *Verbena officinalis* extract. In some aspects, the composition includes 0.01% to 0.1% w/w of *Verbena officinalis* extract. In some aspects, the composition includes 0.01% to 10% w/w of hydrolyzed sodium hyaluronate. In some aspects, the composition includes 0.05 to 5% w/w of hydrolyzed

sodium hyaluronate. In some aspects, the composition includes 0.001% to 1% w/w of ceramide. In some aspects, the composition includes 0.005% to 0.5% w/w of ceramide.

[0010] In some instances, a second skin care composition is applied to the skin before application of the composition to the skin. In some instances, the composition is combined with the second composition prior to application to the skin. In some instances, the second skin care composition affects a hydrating effect on skin. In some instances, the second skin care composition does not affect a hydrating effect on skin. In some instances, more than one other skin care composition is applied to the skin before application of the composition to the skin. In some instances, the composition is combined with more than one other composition prior to application to the skin. In some instances, the more than one other skin care composition affects a hydrating effect on skin. In some instances, the more than one other composition does not affect a hydrating effect on skin.

[0011] In some instances, the composition further includes one or more of a humectant, an emollient, a skin conditioning agent, and/or a pH adjuster. In some instances, the composition further includes an effective amount of one or more of water, glycerin, pentylene glycol, betaine, and/or phenoxyethanol to moisturize and/or enhance a skin product's hydrating effect. In some instances, the composition includes one or more of 1 to 95% by weight water, 1 to 30% by weight glycerin, 0.1 to 15% by weight pentylene glycol, 0.1 to 15% by weight betaine, and/or 0.05 to 10% by weight phenoxyethanol. In some instances, the composition includes 40 to 85% by weight of water. In some aspects, the composition includes 1% to 30% w/w of glycerin. In some aspects, the composition includes 5% to 20% w/w of glycerin.

[0012] In some instances, the composition further includes one or more of xanthan gum and/or sodium hyaluronate. In some instances, the composition includes one or more of 0.01 to 5% by weight xanthan gum, and/or 0.01 to 1% by weight sodium hyaluronate. In some instances, the composition further includes *Opuntia tuna* (prickly pear) extract. In some instances, the composition includes 0.001 to 2% by weight of *Opuntia tuna* (prickly pear) extract.

[0013] In some instances, the composition is an enhancing composition capable of enhancing the activity of a skin care composition by combining the enhancing composition and the skin care composition, wherein the enhancing composition includes an effective amount of *Verbena officinalis* extract, hydrolyzed sodium hyaluronate, and ceramide to increase or

promote an ability of the cosmetic composition to increase skin moisture content, attract and bind moisture in the air to the skin's outer layers, transport surface moisture below the skin's stratum corneum, plump and tighten the skin, protect the skin from moisture loss to the environment, support optimal skin barrier function, and/or stimulate production of the skin's own Natural Moisturizing Factor. In some instances, the skin care composition affects a hydrating effect on skin. In some instances, the skin care composition does not affect a hydrating effect on skin.

[0014] In some aspects, the composition is applied to skin multiple times per week. In some instances, the composition can be applied to skin 2-3 times per week. In some instances, the composition can be applied to skin 2 times per week. In some instances, the composition can be applied to skin 3 times per week. In some instances, the composition can be applied to skin more than 3 times per week.

[0015] In some aspects, the composition can be combined with one or more other skin care compositions for treating skin. In some aspects, the one or more other skin care compositions for treating skin includes a moisturizer. In some aspects, the one or more other skin care compositions for treating skin includes a serum. In some aspects, the one or more other skin care compositions for treating skin includes retinol. In some aspects, the one or more other skin care compositions for treating skin includes an exfoliating composition. In some aspects, the one or more other skin care compositions for treating skin includes a smoothing composition. In some instances, the smoothing composition includes glycolic acid and gluconolactone. In some aspects, the one or more other skin care compositions for treating skin includes a brightening composition. In some instances, the brightening composition includes ferulic acid, niacinamide, and navy bean extract. In some aspects, the one or more other skin care compositions for treating skin includes an anti-aging composition. In some instances, the anti-aging composition includes vitamin C, resveratrol, and acetyl hexapeptide-8.

[0016] In some aspects, the composition is applied to clean skin. In some instances, the composition is left on the skin to be absorbed. In some instances, the application of the composition is preceded by application of the one or more other skin care compositions. In some instances, the composition is applied after the one or more other skin care compositions is absorbed into the skin. In some instances, a blend of the composition and the one or more other skin care compositions is applied to the skin.

[0017] In some aspects, the compositions of the present invention can further include a surfactant, a silicone containing compounds, a UV agent, an oil, and/or other ingredients identified in this specification or those known in the art. The composition can be a lotion, cream, body butter, mask, scrub, wash, gel, serum, emulsion (e.g., oil-in-water, water-in-oil, silicone-in-water, water-in-silicone, water-in-oil-in-water, oil-in-water-in-oil, oil-in-water-in-silicone, etc.), solutions (e.g., aqueous or hydro-alcoholic solutions), anhydrous bases (e.g., lipstick or a powder), ointments, milk, paste, aerosol, solid forms, eye jellies, gel serums, gel emulsions, etc. In some instances, the composition is a serum, a cream, a gel, a cream gel, an oil-in-water emulsion, a water-in-oil emulsion, or a liquid. In some instances, the composition is a liquid. In some instances, the composition is comprised in an ampule. The composition can be formulated for topical skin application at least 1, 2, 3, 4, 5, 6, 7, or more times a day during use. In some aspects of the present invention, compositions can be storage stable or color stable, or both. It is also contemplated that the viscosity of the composition can be selected to achieve a desired result, e.g., depending on the type of composition desired, the viscosity of such composition can be from about 1 cps to well over 1 million cps or any range or integer derivable therein (e.g., 2 cps, 3, 4, 5, 6, 7, 8, 9, 10, 20, 30, 40, 50, 60, 70, 80, 90, 100, 200, 300, 400, 500, 600, 700, 800, 900, 1000, 2000, 3000, 4000, 5000, 6000, 7000, 8000, 9000, 10000, 20000, 30000, 40000, 50000, 60000, 70000, 80000, 90000, 100000, 200000, 300000, 400000, 500000, 600000, 700000, 800000, 900000, 1000000, 2000000, 3000000, 4000000, 5000000, 10000000, cps, etc., as measured on a Brookfield Viscometer using a TC spindle at 2.5 rpm at 25°C).

[0018] The compositions, in non-limiting aspects, can have a pH of about 6 to about 9. In some aspects, the pH can be 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, or 14. The compositions can include a triglyceride. Non-limiting examples include small, medium, and large chain triglycerides. In certain aspects, the triglyceride is a medium chain triglyceride (e.g., caprylic capric triglyceride). The compositions can also include preservatives. Non-limiting examples of preservatives include phenoxyethanol, methylparaben, propylparaben, iodopropynyl butylcarbamate, potassium sorbate, sodium benzoate, or any mixture thereof. In some embodiments, the composition is paraben-free.

[0019] Compositions of the present invention can have UVA and UVB absorption properties. The compositions can have a sun protection factor (SPF) of 2, 3, 4, 5, 6, 7, 8, 9, 10,

11, 12, 13, 14, 15, 20, 25, 30, 35, 40, 45, 50, 55, 60, or more, or any integer or derivative therein. The compositions can be sunscreen lotions, sprays, or creams.

[0020] The compositions of the present invention can also include any one of, any combination of, or all of the following additional ingredients: a conditioning agent, a moisturizing agent, a pH adjuster, a structuring agent, inorganic salts, a preservative, a thickening agent, a silicone containing compound, an essential oil, a fragrance, a vitamin, a pharmaceutical ingredient, or an antioxidant, or any combination of such ingredients or mixtures of such ingredients. In certain aspects, the composition can include at least two, three, four, five, six, seven, eight, nine, ten, or more, or all of these additional ingredients identified in the previous sentence. Non-limiting examples of these additional ingredients are identified throughout this specification and are incorporated into this section by reference. The amounts of such ingredients can range from 0.0001% to 99.9% by weight or volume of the composition, or any integer or range in between as disclosed in other sections of this specification, which are incorporated into this paragraph by reference.

[0021] Methods of use for the compositions disclosed herein are also disclosed. In some aspects, a method is disclosed to increase skin moisture content, attract and bind moisture in the air to the skin's outer layers, transport surface moisture below the skin's stratum corneum, plump and tighten the skin, protect the skin from moisture loss to the environment, support optimal skin barrier function, and/or stimulate production of the skin's own Natural Moisturizing Factor. In some aspects, a method is disclosed to increase the efficacy of cosmetic products to increase skin moisture content, attract and bind moisture in the air to the skin's outer layers, transport surface moisture below the skin's stratum corneum, plump and tighten the skin, protect the skin from moisture loss to the environment, support optimal skin barrier function, and/or stimulate production of the skin's own Natural Moisturizing Factor. In some instances, the method comprises topically applying any one of the compositions disclosed herein to skin in need thereof. In one aspect, any one of the compositions disclosed herein are topically applied and the composition is left on the application area, removed from the application area after a period of time, and/or removed directly after application.

[0022] In some aspects, the compositions disclosed herein are used to increase skin moisture content. In some aspects, the compositions disclosed herein are used to attract and bind moisture in the air to the skin's outer layers. In some aspects, the compositions disclosed herein are used to transport surface moisture below the skin's stratum corneum. In some

aspects, the compositions disclosed herein are used to plump and tighten the skin. In some aspects, the compositions disclosed herein are used to protect the skin from moisture loss to the environment. In some aspects, the compositions disclosed herein are used to support optimal skin barrier function. In some aspects, the compositions disclosed herein are used to stimulate production of the skin's own Natural Moisturizing Factor. In some aspects, the compositions disclosed herein are used to increase skin moisture content at least 10, 20, 30, 40, or 50% after a single application.

[0023] It is also contemplated that the compositions disclosed throughout this specification can be used as a leave-on or rinse-off composition. By way of example, a leave-on composition can be one that is topically applied to skin and remains on the skin for a period of time (e.g., at least 5, 6, 7, 8, 9, 10, 20, or 30 minutes, or at least 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23 or 24 hours, or overnight or throughout the day). Alternatively, a rinse-off composition can be a product that is intended to be applied to the skin and then removed or rinsed from the skin (e.g., with water) within a period of time such as less than 5, 4, 3, 2, or 1 minute. In some instances, the composition is designed to be washed away after 30 seconds, 1 minutes, 2 minutes, 3 minutes, 4 minutes, 5 minutes, 6 minutes, 7 minutes, 8 minutes, 9 minutes, 10 minutes, 11 minutes, 12 minutes, 13 minutes, 14 minutes, 15 minutes, 20 minutes, 30 minutes, 40 minutes, 50 minutes, 60 minutes, or any amount or range therein. An example of a rinse off composition can be a skin cleanser, shampoo, conditioner, or soap. An example of a leave-on composition can be a skin moisturizer, sunscreen, mask, overnight cream, or a day cream.

[0024] Kits that include the compositions of the present invention are also contemplated. In certain embodiments, the composition is comprised in a container. The container can be a bottle, dispenser, or package. The container can dispense a pre-determined amount of the composition. In certain aspects, the compositions is dispensed in a spray, mist, dollop, or liquid. The container can include indicia on its surface. The indicia can be a word, an abbreviation, a picture, or a symbol.

[0025] It is contemplated that any embodiment discussed in this specification can be implemented with respect to any method or composition of the invention, and *vice versa*. Furthermore, compositions of the invention can be used to achieve methods of the invention.

[0026] In the context of the present invention, at least the following 47 aspects are described. Aspect 1 includes a method of enhancing skin hydration in a person. The method comprises topically applying to the skin of the person a composition comprising an effective amount of *Verbena officinalis* extract, hydrolyzed sodium hyaluronate, and ceramide, and topical application of the composition attracts and binds moisture in the air to the skin's outer layers, transports surface moisture below the skin's stratum corneum, increases skin moisture content, plumps and tightens the skin, protects the skin from moisture loss to the environment, supports optimal skin barrier function, and/or stimulates production of the skin's own Natural Moisturizing Factor. Aspect 2 depends on Aspect 1, wherein the composition comprises 0.001 to 1% by weight of *Verbena officinalis* extract, 0.01 to 10% by weight of hydrolyzed sodium hyaluronate, and 0.001 to 1% by weight of ceramide. Aspect 3 depends on any of Aspects 1 and 2, wherein one or more other skin care compositions are applied to the skin before application of the composition to the skin. Aspect 4 depends on any of Aspects 1 to 2, wherein the composition is combined with one or more other skin care compositions prior to application to the skin. Aspect 5 depends on any of Aspects 3 to 4, wherein the one or more other skin care compositions affects a hydrating effect on skin. Aspect 6 depends on any of Aspects 3 to 4, wherein the one or more other skin care compositions do not affect a hydrating effect on skin. Aspect 7 depends on any of Aspects 1 to 6, wherein the composition further comprises one or more of a humectant, an emollient, a skin conditioning agent, and/or a pH adjuster. Aspect 8 depends on any of Aspects 1 to 7, wherein the composition further comprises an effective amount of one or more of water, glycerin, pentylene glycol, betaine, and/or phenoxyethanol to increase skin moisture content and/or enhance a skin product's hydrating effect. Aspect 9 depends on Aspect 8, wherein the composition comprises 1 to 95% by weight water, 1 to 30% by weight glycerin, 0.1 to 15% by weight pentylene glycol, 0.1 to 15% by weight betaine, and/or 0.05 to 10% by weight phenoxyethanol. Aspect 10 depends on any of Aspects 1 to 9, wherein the composition further comprises one or more of xanthan gum and sodium hyaluronate. Aspect 11 depends on Aspect 10, wherein the composition comprises 0.01 to 5% by weight xanthan gum and 0.01 to 1% by weight sodium hyaluronate. Aspect 12 depends on Aspect 11, wherein the composition comprises 0.001 to 1% by weight of *Verbena officinalis* extract. Aspect 13 depends on Aspect 12, wherein the composition comprises 0.01 to 0.1% by weight of *Verbena officinalis* extract. Aspect 14 depends on any of Aspects 1 to 13, wherein the composition comprises 0.01 to 10% by weight of hydrolyzed sodium hyaluronate. Aspect 15 depends on Aspect 14, wherein the composition comprises 0.05 to 5% by weight of hydrolyzed sodium hyaluronate. Aspect 16 depends on any of Aspects 1 to 15,

wherein the composition comprises 0.001 to 1% by weight of ceramide. Aspect 17 depends on Aspect 16, wherein the composition comprises 0.005 to 0.5% by weight of ceramide. Aspect 18 depends on any of Aspects 1 to 17, wherein the composition comprises 1 to 30% by weight of glycerin. Aspect 19 depends on Aspect 18, wherein the composition comprises 5 to 20% by weight of glycerin. Aspect 20 depends on any of Aspects 1 to 19, wherein the composition further comprises 40 to 85% by weight of water. Aspect 21 depends on any of Aspects 1 to 20, wherein the composition comprises an effective amount of *Verbena officinalis* extract, hydrolyzed sodium hyaluronate, and ceramide, wherein topical application of the composition increases skin moisture content by at least 50% after a single application. Aspect 22 depends on any of Aspects 1 to 21, wherein the composition comprises an effective amount of *Verbena officinalis* extract, hydrolyzed sodium hyaluronate, and ceramide, wherein topical application of the composition stimulates production of the skin's own Natural Moisturizing Factor. Aspect 23 includes a method of enhancing the hydrating activity of a skin care composition. The method comprises combining an enhancing composition and the skin care composition, wherein the enhancing composition comprises an effective amount of *Verbena officinalis* extract, hydrolyzed sodium hyaluronate, and ceramide to increase or promote an ability of the cosmetic composition to attract and bind moisture in the air to the skin's outer layers, transport surface moisture below the skin's stratum corneum, increase skin moisture content, plump and tighten the skin, protect the skin from moisture loss to the environment, support optimal skin barrier function, and/or stimulate production of the skin's own Natural Moisturizing Factor. Aspect 24 depends on Aspect 23, wherein the skin care composition affects a hydrating effect on skin. Aspect 25 depends on Aspect 23, wherein the skin care composition does not affect a hydrating effect on skin. Aspect 26 depends on any of Aspects 23 to 25, wherein the enhancing composition comprises an effective amount of *Verbena officinalis* extract, hydrolyzed sodium hyaluronate, and ceramide to increase skin moisture content by at least 50% in a single application. Aspect 27 depends on any of Aspects 23 to 26, wherein the enhancing composition comprises an effective amount of *Verbena officinalis* extract, hydrolyzed sodium hyaluronate, and ceramide to stimulate production of the skin's own Natural Moisturizing Factor. Aspect 28 includes a product enhancing composition comprising an effective amount of a combination of *Verbena officinalis* extract, hydrolyzed sodium hyaluronate, and ceramide to attract and bind moisture in the air to the skin's outer layers, transport surface moisture below the skin's stratum corneum, increase skin moisture content, plump and tighten the skin, protect the skin from moisture loss to the environment, support optimal skin barrier function, and/or stimulate production of the skin's own Natural

Moisturizing Factor. Aspect 29 depends on Aspect 28, wherein the composition comprises 0.001 to 1% by weight of *Verbena officinalis* extract, 0.01 to 10% by weight of hydrolyzed sodium hyaluronate, and 0.001 to 1% by weight of ceramide. Aspect 30 depends on any of Aspects 28 or 29, further comprising one or more of a humectant, an emollient, a skin conditioning agent, and/or a pH adjuster. Aspect 31 depends on any of Aspects 28 to 30, further comprising an effective amount of one or more of: water, glycerin, pentylene glycol, betaine, and/or phenoxyethanol to increase skin moisture content and/or enhance a skin product's hydrating effect. Aspect 32 depends on Aspect 31, further comprising 1 to 95% by weight water, 1 to 30% by weight glycerin, 0.1 to 15% by weight pentylene glycol, 0.1 to 15% by weight betaine, and/or 0.05 to 10% by weight phenoxyethanol. Aspect 33 depends on any of Aspects 28 to 32, further comprising one or more of xanthan gum and sodium hyaluronate. Aspect 34 depends on Aspect 33, further comprising 0.01 to 5% by weight xanthan gum and 0.01 to 1% by weight sodium hyaluronate. Aspect 35 depends on any of Aspects 28 to 34, wherein the composition comprises 0.001 to 1% by weight of *Verbena officinalis* extract. Aspect 36 depends on Aspect 35, wherein the composition comprises 0.01 to 0.1% by weight of *Verbena officinalis* extract. Aspect 37 depends on any of Aspects 28 to 36, wherein the composition comprises 0.01 to 10% by weight of hydrolyzed sodium hyaluronate. Aspect 38 depends on Aspect 37, wherein the composition comprises 0.05 to 5% by weight of hydrolyzed sodium hyaluronate. Aspect 39 depends on any of Aspects 28 to 38, wherein the composition comprises 0.001 to 1% by weight of ceramide. Aspect 40 depends on Aspect 39, wherein the composition comprises 0.005 to 0.5% by weight of ceramide. Aspect 41 depends on any of Aspects 28 to 40, wherein the composition comprises 1 to 30% by weight of glycerin. Aspect 42 depends on Aspect 41, wherein the composition comprises 5 to 20% by weight of glycerin. Aspect 43 depends on any of Aspects 28 to 42, wherein the composition further comprises 40 to 85% by weight of water. Aspect 44 depends on any of Aspects 28 to 43, wherein the composition is a serum or a cream. Aspect 45 depends on any of Aspects 28 to 44, wherein the composition is comprised in an ampule. Aspect 46 depends on any of Aspects 28 to 45, wherein the effective amount of a combination of *Verbena officinalis* extract, hydrolyzed sodium hyaluronate, and ceramide increases skin moisture content by at least 50% in a single application. Aspect 47 depends on any of Aspects 28 to 46 wherein the enhancing composition comprises an effective amount of Verbena officinalis extract, hydrolyzed sodium hyaluronate, and ceramide to stimulate production of the skin's own Natural Moisturizing Factor.

[0027] In some embodiments, compositions of the present invention can be pharmaceutically or cosmetically elegant or can have pleasant tactile properties. "Pharmaceutically elegant," "cosmetically elegant," and/or "pleasant tactile properties" describes a composition that has particular tactile properties which feel pleasant on the skin (e.g., compositions that are not too watery or greasy, compositions that have a silky texture, compositions that are non-tacky or sticky, etc.). Pharmaceutically or cosmetically elegant can also relate to the creaminess or lubricity properties of the composition or to the moisture retaining properties of the composition.

[0028] Also contemplated is a product comprising a composition of the present invention. In non-limiting aspects, the product can be a cosmetic product. The cosmetic product can be those described in other sections of this specification or those known to a person of skill in the art. Non-limiting examples of products include a moisturizer, a cream, a lotion, a skin softener, a serum, a gel, a wash, a body butter, a scrub, a foundation, a night cream, a lipstick, a cleanser, a toner, a sunscreen, a mask, an anti-aging product, a deodorant, an antiperspirant, a perfume, a cologne, etc.

[0029] "Topical application" means to apply or spread a composition onto the surface of lips or keratinous tissue. "Topical skin composition" includes compositions suitable for topical application on skin and/or keratinous tissue. Such compositions are typically dermatologically-acceptable in that they do not have undue toxicity, incompatibility, instability, allergic response, and the like, when applied to skin and/or keratinous tissue. Topical skin care compositions of the present invention can have a selected viscosity to avoid significant dripping or pooling after application to skin and/or keratinous tissue.

[0030] "Keratinous tissue" includes keratin-containing layers disposed as the outermost protective covering of mammals and includes, but is not limited to, lips, skin, hair, and nails.

[0031] The term "about" or "approximately" are defined as being close to as understood by one of ordinary skill in the art. In one non-limiting embodiment the terms are defined to be within 10%, preferably within 5%, more preferably within 1%, and most preferably within 0.5%.

[0032] The term "substantially" and its variations are refers to ranges within 10%, within 5%, within 1%, or within 0.5%.

[0033] The terms "inhibiting" or "reducing" or any variation of these terms includes any measurable decrease or complete inhibition to achieve a desired result. The terms "promote" or "increase" or any variation of these terms includes any measurable increase, such as a measurable increase of a protein or molecule (*e.g.,* matrix proteins such as fibronectin, laminin, collagen, or elastin or molecules such as hyaluronic acid) to achieve a desired result.

[0034] The term "effective," as that term is used in the specification and/or claims, means adequate to accomplish a desired, expected, or intended result.

[0035] The use of the word "a" or "an" when used in conjunction with the terms "comprising," "including," "having," or "containing," or any variations of these terms, in the claims and/or the specification may mean "one," but it is also consistent with the meaning of "one or more," "at least one," and "one or more than one."

[0036] As used in this specification and claim(s), the words "comprising" (and any form of comprising, such as "comprise" and "comprises"), "having" (and any form of having, such as "have" and "has"), "including" (and any form of including, such as "includes" and "include") or "containing" (and any form of containing, such as "contains" and "contain") are inclusive or open-ended and do not exclude additional, unrecited elements or method steps.

[0037] The compositions and methods for their use can "comprise," "consist essentially of," or "consist of" any of the ingredients or steps disclosed throughout the specification. With respect to the phrase "consisting essentially of," a basic and novel property of the compositions and methods of the present invention is the ability to increase skin moisture content, attract and bind moisture in the air to the skin's outer layers, transport surface moisture below the skin's stratum corneum, plump and tighten the skin, protect the skin from moisture loss to the environment, support optimal skin barrier function, and/or stimulate production of the skin's own Natural Moisturizing Factor and/or increase the efficacy of cosmetic products to increase skin moisture content, attract and bind moisture in the air to the skin's outer layers, transport surface moisture below the skin's stratum corneum, plump and tighten the skin, protect the skin from moisture loss to the environment, support optimal skin barrier function, and/or stimulate production of the skin's own Natural Moisturizing Factor.

[0038] Other objects, features, and advantages of the present invention will become apparent from the following detailed description. It should be understood, however, that the detailed description and the examples, while indicating specific embodiments of the invention,

are given by way of illustration only. Additionally, it is contemplated that changes and modifications within the spirit and scope of the invention will become apparent to those skilled in the art from this detailed description.

BRIEF DESCRIPTION OF THE DRAWINGS

[0039] The following drawings form part of the present specification and are included to further demonstrate certain aspects of the present invention. The invention may be better understood by reference to one or more of these drawings in combination with the detailed description of specific embodiments presented herein.

[0040] **THE FIGURE** is a Western blot assay with results of filaggrin expression tests employing various test compositions. The biotinylated ladder in column 1 includes a mixture of purified reference proteins with molecular weights ranging from 9-200 kDa. The compositions in columns 2-8 were tested for their effects on expression of filaggrin protein, which appears at ~40 kDa. Quantification of the columns 2-8 test compositions showed that *Verbena officinalis* extract in column 5 provided the greatest increase in filaggrin protein expression (>66%).

DESCRIPTION OF ILLUSTRATIVE EMBODIMENTS

[0041] As noted above, the present invention provides a solution to the problems associated with current cosmetic products. In some embodiments, an effective amount of a composition that includes any one of, any combination of, or all of *Verbena officinalis* extract, hydrolyzed hyaluronic acid, and/or ceramide was found to increase skin moisture content. The combination of ingredients was also shown to retain skin's moisture and support optimal barrier function. The combination of ingredients was also shown to draw moisture from the air to hydrate skin from the outside. The combination of ingredients was further shown to penetrate the stratum corneum to deliver moisture and plump and tighten the skin from within. The combination of ingredients was additionally shown to stimulate production of skin's own Natural Moisturizing Factor to further improve skin hydration and barrier function. The combination of ingredients was additionally shown to increase skin moisture content at least 50% after a single application.

[0042] Ceramide was shown to retain skin's moisture and support optimal barrier function. Hydrolyzed hyaluronic acid was shown to penetrate the stratum corneum to deliver

moisture and plump and tighten the skin from within. *Verbena officinalis* extract was shown to stimulate production of skin's own Natural Moisturizing Factor to further improve skin moisture content and barrier function. Glycerin was shown to enhance the ability of the above ingredients to boost skin moisture content and/or stimulate the skin's own natural hydration. Hyaluronic acid was shown to enhance the ability of the above ingredients to draw moisture from the air to protect and hydrate skin from the outside.

[0043] A particular composition of the present invention is designed to work as a topical composition. The composition relies on a unique combination of any one of, any combination of, or all of *Verbena Officinalis* extract, hydrolyzed hyaluronic acid, and/or ceramide. The combination can be used to increase skin moisture content, attract and bind moisture in the air to the skin's outer layers, transport surface moisture below the skin's stratum corneum, plump and tighten the skin, protect the skin from moisture loss to the environment, support optimal skin barrier function, and/or stimulate production of the skin's own Natural Moisturizing Factor. The combination can also be used to increase the efficacy of cosmetic products to increase skin moisture content, attract and bind moisture in the air to the skin's outer layers, transport surface moisture below the skin's stratum corneum, plump and tighten the skin, protect the skin from moisture loss to the environment, support optimal skin barrier function, and/or stimulate production of the skin's own Natural Moisturizing Factor. Non-limiting examples of such compositions are provided in Table 1 of Example 1 below.

[0044] Some compositions disclosed herein can be applied to the skin and remain on the skin for a period of time (e.g., at least 1, 2, 3, 4, 5, 10, 20, 30, or 60 minutes or more). After which, the composition, if needed, can be rinsed from the skin or peeled from the skin. Some compositions disclosed herein can be applied to the skin and immediately rinsed from the skin. Some compositions disclosed herein can be applied to the skin and absorbed at least in part by the skin. Some compositions are designed to be left on skin.

[0045] These and other non-limiting aspects of the present invention are described in the following sections.

A. Active Ingredients

[0046] ***Verbena officinalis* extract** - *Verbena Officinalis* extract is an extract of the leaves of the *Verbena officinalis* plant. *Verbena Officinalis* extract functions in cosmetics as an emollient and skin-conditioning agent. *Verbena Officinalis* extract, containing iridoid,

phenylpropanoid, flavonoid, luteolin and terpenoid compounds, also displays antioxidant and antibacterial activities. *Verbena officinalis* extract has also been shown to stimulate production of the skin's own Natural Moisturizing Factor, a group of amino acids and water-soluble compounds. Natural Moisturizing Factor is produced in the skin as the natural breakdown products of filaggrin within the stratum corneum and act to preserve skin hydration, local immune response, and the barrier function. In some embodiments, the *Verbena officinalis* extract is an aqueous extract.

[0047] **Hyaluronic acid** - Hyaluronic acid is a naturally occurring glycosaminoglycan found throughout the body's connective tissue, including the skin, where it is involved in tissue repair. Both natural and synthetic hyaluronic acids are used in cosmetics as a humectant and are capable of binding up to 1000 times its weight in water. Hyaluronic acid keeps the surface of the skin hydrated by absorbing water from the air and by slowing the rate at which water evaporates from the skin. Hydrolyzed hyaluronic acid is the hydrolysate of hyaluronic acid derived by acid, enzyme or other method of hydrolysis. Hydrolyzed hyaluronic acid is also classified as a humectant and skin conditioning agent. Due to a lower molecular weight, hydrolyzed hyaluronic acid is able to penetrate the stratum corneum, carry bound water below the skin's surface, and plump and tighten the skin from within.

[0048] **Ceramides** - Ceramides are the major lipid constituent of the stratum corneum and are thought to function as a barrier for the epidermis, the outermost layer of the skin. As ceramide levels decline with normal aging, the skin barrier can be disrupted, leading to redness, dryness, and skin irritation. Synthetic ceramides are used in skin care products to maintain the skin's barrier, to lock in moisture and keep the skin hydrated, prevent and treat skin irritation from exposure to the environment, and reduce the appearance of fine lines and other signs of aging.

[0049] This combination of ingredients can be used in different product forms to treat various skin conditions. By way of non-limiting examples, the combination of ingredients can be formulated in an ampule, an emulsion (e.g., oil in water, water in oil), a gel, a serum, a gel emulsion, a gel serum, a lotion, a mask, a scrub, a wash, a cream, or a body butter.

[0050] The components described herein can be extracts made through extraction methods known in the art and combinations thereof. Non-limiting examples of extraction methods include the use of liquid-liquid extraction, solid phase extraction, aqueous extraction,

ethyl acetate, alcohol, acetone, oil, supercritical carbon dioxide, heat, pressure, pressure drop extraction, ultrasonic extraction, etc. Extracts can be a liquid, solid, dried liquid, re-suspended solid, etc.

B. Amounts of Ingredients

[0051] It is contemplated that the compositions of the present invention can include any amount of the ingredients discussed in this specification. The compositions can also include any number of combinations of additional ingredients described throughout this specification (e.g., pigments, or additional cosmetic or pharmaceutical ingredients). The concentrations of the any ingredient within the compositions can vary. In non-limiting embodiments, for example, the compositions can comprise, consisting essentially of, or consist of, in their final form, for example, at least about 0.0001%, 0.0002%, 0.0003%, 0.0004%, 0.0005%, 0.0006%, 0.0007%, 0.0008%, 0.0009%, 0.0010%, 0.0011%, 0.0012%, 0.0013%, 0.0014%, 0.0015%, 0.0016%, 0.0017%, 0.0018%, 0.0019%, 0.0020%, 0.0021%, 0.0022%, 0.0023%, 0.0024%, 0.0025%, 0.0026%, 0.0027%, 0.0028%, 0.0029%, 0.0030%, 0.0031%, 0.0032%, 0.0033%, 0.0034%, 0.0035%, 0.0036%, 0.0037%, 0.0038%, 0.0039%, 0.0040%, 0.0041%, 0.0042%, 0.0043%, 0.0044%, 0.0045%, 0.0046%, 0.0047%, 0.0048%, 0.0049%, 0.0050%, 0.0051%, 0.0052%, 0.0053%, 0.0054%, 0.0055%, 0.0056%, 0.0057%, 0.0058%, 0.0059%, 0.0060%, 0.0061%, 0.0062%, 0.0063%, 0.0064%, 0.0065%, 0.0066%, 0.0067%, 0.0068%, 0.0069%, 0.0070%, 0.0071%, 0.0072%, 0.0073%, 0.0074%, 0.0075%, 0.0076%, 0.0077%, 0.0078%, 0.0079%, 0.0080%, 0.0081%, 0.0082%, 0.0083%, 0.0084%, 0.0085%, 0.0086%, 0.0087%, 0.0088%, 0.0089%, 0.0090%, 0.0091%, 0.0092%, 0.0093%, 0.0094%, 0.0095%, 0.0096%, 0.0097%, 0.0098%, 0.0099%, 0.0100%, 0.0200%, 0.0250%, 0.0275%, 0.0300%, 0.0325%, 0.0350%, 0.0375%, 0.0400%, 0.0425%, 0.0450%, 0.0475%, 0.0500%, 0.0525%, 0.0550%, 0.0575%, 0.0600%, 0.0625%, 0.0650%, 0.0675%, 0.0700%, 0.0725%, 0.0750%, 0.0775%, 0.0800%, 0.0825%, 0.0850%, 0.0875%, 0.0900%, 0.0925%, 0.0950%, 0.0975%, 0.1000%, 0.1250%, 0.1500%, 0.1750%, 0.2000%, 0.2250%, 0.2500%, 0.2750%, 0.3000%, 0.3250%, 0.3500%, 0.3750%, 0.4000%, 0.4250%, 0.4500%, 0.4750%, 0.5000%, 0.5250%, 0.0550%, 0.5750%, 0.6000%, 0.6250%, 0.6500%, 0.6750%, 0.7000%, 0.7250%, 0.7500%, 0.7750%, 0.8000%, 0.8250%, 0.8500%, 0.8750%, 0.9000%, 0.9250%, 0.9500%, 0.9750%, 1.0%, 1.1%, 1.2%, 1.3%, 1.4%, 1.5%, 1.6%, 1.7%, 1.8%, 1.9%, 2.0%, 2.1%, 2.2%, 2.3%, 2.4%, 2.5%, 2.6%, 2.7%, 2.8%, 2.9%, 3.0%, 3.1%, 3.2%, 3.3%, 3.4%, 3.5%, 3.6%, 3.7%, 3.8%, 3.9%, 4.0%, 4.1%, 4.2%, 4.3%, 4.4%, 4.5%, 4.6%, 4.7%, 4.8%, 4.9%, 5.0%, 5.1%, 5.2%, 5.3%, 5.4%, 5.5%, 5.6%, 5.7%, 5.8%, 5.9%, 6.0%, 6.1%, 6.2%, 6.3%, 6.4%, 6.5%, 6.6%, 6.7%, 6.8%, 6.9%, 7.0%, 7.1%,

7.2%, 7.3%, 7.4%, 7.5%, 7.6%, 7.7%, 7.8%, 7.9%, 8.0%, 8.1%, 8.2%, 8.3%, 8.4%, 8.5%, 8.6%, 8.7%, 8.8%, 8.9%, 9.0%, 9.1%, 9.2%, 9.3%, 9.4%, 9.5%, 9.6%, 9.7%, 9.8%, 9.9%, 10%, 11%, 12%, 13%, 14%, 15%, 16%, 17%, 18%, 19%, 20%, 21%, 22%, 23%, 24%, 25%, 26%, 27%, 28%, 29%, 30%, 35%, 40%, 45%, 50%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, or 99% or any range derivable therein, of at least one of the ingredients that are mentioned throughout the specification and claims. In non-limiting aspects, the percentage can be calculated by weight or volume of the total composition. A person of ordinary skill in the art would understand that the concentrations can vary depending on the addition, substitution, and/or subtraction of ingredients in a given composition.

C. Vehicles

[0052] The compositions of the present invention can include or be incorporated into all types of vehicles and carriers. The vehicle or carrier can be a pharmaceutically or dermatologically acceptable vehicle or carrier. Non-limiting examples of vehicles or carriers include water, glycerin, alcohol, oil, a silicon containing compound, a silicone compound, and wax. Variations and other appropriate vehicles will be apparent to the skilled artisan and are appropriate for use in the present invention. In certain aspects, the concentrations and combinations of the compounds, ingredients, and agents can be selected in such a way that the combinations are chemically compatible and do not form complexes which precipitate from the finished product.

D. Structure

[0053] The compositions of the present invention can be structured or formulated into a variety of different forms. Non-limiting examples include emulsions (e.g., water-in-oil, water-in-oil-in-water, oil-in-water, silicone-in-water, water-in-silicone, oil-in-water-in-oil, oil-in-water-in-silicone emulsions), creams, lotions, solutions (both aqueous and hydro-alcoholic), anhydrous bases (such as lipsticks and powders), gels, masks, scrubs, body butters, peels, and ointments. Variations and other structures will be apparent to the skilled artisan and are appropriate for use in the present invention.

E. Additional Ingredients

[0054] In addition to the combination of ingredients disclosed by the inventors, the compositions can also include additional ingredients such as cosmetic ingredients and

pharmaceutical active ingredients. Non-limiting examples of these additional ingredients are described in the following subsections.

1. Cosmetic Ingredients

[0055] The CTFA International Cosmetic Ingredient Dictionary and Handbook (2004 and 2008) describes a wide variety of non-limiting cosmetic ingredients that can be used in the context of the present invention. Examples of these ingredient classes include: fragrance agents (artificial and natural; e.g., gluconic acid, phenoxyethanol, and triethanolamine), dyes and color ingredients (e.g., Blue 1, Blue 1 Lake, Red 40, titanium dioxide, D&C blue no. 4, D&C green no. 5, D&C orange no. 4, D&C red no. 17, D&C red no. 33, D&C violet no. 2, D&C yellow no. 10, and D&C yellow no. 11), flavoring agents / aroma agents (e.g., *Stevia rebaudiana* (sweetleaf) extract, and menthol), adsorbents, lubricants, solvents, moisturizers (including, e.g., emollients, humectants, film formers, occlusive agents, and agents that affect the natural moisturization mechanisms of the skin), water-repellants, UV absorbers (physical and chemical absorbers such as para-aminobenzoic acid ("PABA") and corresponding PABA derivatives, titanium dioxide, zinc oxide, etc.), essential oils, vitamins (e.g., A, B, C, D, E, and K), trace metals (e.g., zinc, calcium and selenium), anti-irritants (e.g., steroids and non-steroidal anti-inflammatories), botanical extracts (e.g., *Aloe vera*, chamomile, cucumber extract, *Ginkgo biloba*, ginseng, and rosemary), anti-microbial agents, antioxidants (e.g., BHT and tocopherol), chelating agents (e.g., disodium EDTA and tetrasodium EDTA), preservatives (e.g., methylparaben and propylparaben), pH adjusters (e.g., sodium hydroxide and citric acid), absorbents (e.g., aluminum starch octenylsuccinate, kaolin, corn starch, oat starch, cyclodextrin, talc, and zeolite), skin bleaching and lightening agents (e.g., hydroquinone and niacinamide lactate), humectants (e.g., sorbitol, urea, methyl gluceth-20, saccharide isomerate, and mannitol), exfoliants, waterproofing agents (e.g., magnesium/aluminum hydroxide stearate), skin conditioning agents (e.g., aloe extracts, allantoin, bisabolol, ceramides, dimethicone, hyaluronic acid, biosaccharide gum-1, ethylhexylglycerin, pentylene glycol, hydrogenated polydecene, octyldodecyl oleate, gluconolactone, calcium gluconate, cyclohexasiloxane, and dipotassium glycyrrhizate). Non-limiting examples of some of these ingredients are provided in the following subsections.

a. UV Absorption and/or Reflecting Agents

[0056] UV absorption and/or reflecting agents that can be used in combination with the compositions of the present invention include chemical and physical sunblocks. Non-limiting

examples of chemical sunblocks that can be used include para-aminobenzoic acid (PABA), PABA esters (glyceryl PABA, amyldimethyl PABA and octyldimethyl PABA), butyl PABA, ethyl PABA, ethyl dihydroxypropyl PABA, benzophenones (oxybenzone, sulisobenzone, benzophenone, and benzophenone-1 through 12), cinnamates (octyl methoxycinnamate (octinoxate), isoamyl p-methoxycinnamate, octylmethoxy cinnamate, cinoxate, diisopropyl methyl cinnamate, DEA-methoxycinnamate, ethyl diisopropylcinnamate, glyceryl octanoate dimethoxycinnamate and ethyl methoxycinnamate), cinnamate esters, salicylates (homomethyl salicylate, benzyl salicylate, glycol salicylate, isopropylbenzyl salicylate, etc.), anthranilates, ethyl urocanate, homosalate, octisalate, dibenzoylmethane derivatives (e.g., avobenzone), octocrylene, octyl triazone, digalloyl trioleate, glyceryl aminobenzoate, lawsone with dihydroxyacetone, ethylhexyl triazone, dioctyl butamido triazone, benzylidene malonate polysiloxane, terephthalylidene dicamphor sulfonic acid, disodium phenyl dibenzimidazole tetrasulfonate, diethylamino hydroxybenzoyl hexyl benzoate, bis diethylamino hydroxybenzoyl benzoate, bis benzoxazoylphenyl ethylhexylimino triazine, drometrizole trisiloxane, methylene bis-benzotriazolyl tetramethylbutylphenol, and bis-ethylhexyloxyphenol methoxyphenyltriazine, 4-methylbenzylidene camphor, and isopentyl 4-methoxycinnamate. Non-limiting examples of physical sunblocks include, kaolin, talc, petrolatum and metal oxides (e.g., titanium dioxide and zinc oxide).

b. Moisturizing Agents

[0057] Non-limiting examples of moisturizing agents that can be used with the compositions of the present invention include amino acids, chondroitin sulfate, diglycerin, erythritol, fructose, glucose, glycerin, glycerol polymers, glycol, 1,2,6-hexanetriol, honey, hyaluronic acid, hydrogenated honey, hydrogenated starch hydrolysate, inositol, lactitol, maltitol, maltose, mannitol, natural moisturizing factor, PEG-15 butanediol, polyglyceryl sorbitol, salts of pyrrolidone carboxylic acid, potassium PCA, propylene glycol, saccharide isomerate, sodium glucuronate, sodium PCA, sorbitol, sucrose, trehalose, urea, and xylitol.

[0058] Other examples include acetylated lanolin, acetylated lanolin alcohol, alanine, algae extract, *Aloe barbadensis*, *Aloe barbadensis* extract, *Aloe barbadensis* gel, *Althea officinalis* extract, apricot (*Prunus* armeniaca) kernel oil, arginine, arginine aspartate, *Arnica montana* extract, aspartic acid, avocado (*Persea gratissima*) oil, barrier sphingolipids, butyl alcohol, beeswax, behenyl alcohol, beta-sitosterol, birch (*Betula alba*) bark extract, borage (*Borago officinalis*) extract, butcherbroom (*Ruscus aculeatus*) extract, butylene glycol,

Calendula officinalis extract, *Calendula officinalis* oil, candelilla (*Euphorbia cerifera*) wax, canola oil, caprylic/capric triglyceride, cardamom (*Elettaria cardamomum*) oil, carnauba (*Copernicia cerifera*) wax, carrot (*Daucus carota sativa*) oil, castor (*Ricinus communis*) oil, ceramides, ceresin, ceteareth-5, ceteareth-12, ceteareth-20, cetearyl octanoate, ceteth-20, ceteth-24, cetyl acetate, cetyl octanoate, cetyl palmitate, chamomile (*Anthemis nobilis*) oil, cholesterol, cholesterol esters, cholesteryl hydroxystearate, citric acid, clary (*Salvia sclarea*) oil, cocoa (*Theobroma cacao*) butter, coco-caprylate/caprate, coconut (*Cocos nucifera*) oil, collagen, collagen amino acids, corn (*Zea mays*) oil, fatty acids, decyl oleate, dimethicone copolyol, dimethiconol, dioctyl adipate, dioctyl succinate, dipentaerythrityl hexacaprylate/hexacaprate, DNA, erythritol, ethoxydiglycol, ethyl linoleate, *Eucalyptus globulus* oil, evening primrose (*Oenothera biennis*) oil, fatty acids, *Geranium maculatum* oil, glucosamine, glucose glutamate, glutamic acid, glycereth-26, glycerin, glycerol, glyceryl distearate, glyceryl hydroxystearate, glyceryl laurate, glyceryl linoleate, glyceryl myristate, glyceryl oleate, glyceryl stearate, glyceryl stearate SE, glycine, glycol stearate, glycol stearate SE, glycosaminoglycans, grape (*Vitis vinifera*) seed oil, hazel (*Corylus americana*) nut oil, hazel (*Corylus avellana*) nut oil, hexylene glycol, hyaluronic acid, hybrid safflower (*Carthamus tinctorius*) oil, hydrogenated castor oil, hydrogenated coco-glycerides, hydrogenated coconut oil, hydrogenated lanolin, hydrogenated lecithin, hydrogenated palm glyceride, hydrogenated palm kernel oil, hydrogenated soybean oil, hydrogenated tallow glyceride, hydrogenated vegetable oil, hydrolyzed collagen, hydrolyzed elastin, hydrolyzed glycosaminoglycans, hydrolyzed keratin, hydrolyzed soy protein, hydroxylated lanolin, hydroxyproline, isocetyl stearate, isocetyl stearoyl stearate, isodecyl oleate, isopropyl isostearate, isopropyl lanolate, isopropyl myristate, isopropyl palmitate, isopropyl stearate, isostearamide DEA, isostearic acid, isostearyl lactate, isostearyl neopentanoate, jasmine (*Jasminum officinale*) oil, jojoba (*Buxus chinensis*) oil, kelp, kukui (*Aleurites moluccana*) nut oil, lactamide MEA, laneth-16, laneth-10 acetate, lanolin, lanolin acid, lanolin alcohol, lanolin oil, lanolin wax, lavender (*Lavandula angustifolia*) oil, lecithin, lemon (*Citrus medica limonum*) oil, linoleic acid, linolenic acid, *Macadamia ternifolia* nut oil, maltitol, matricaria (*Chamomilla recutita*) oil, methyl glucose sesquistearate, methylsilanol PCA, mineral oil, mink oil, mortierella oil, myristyl lactate, myristyl myristate, myristyl propionate, neopentyl glycol dicaprylate/dicaprate, octyldodecanol, octyldodecyl myristate, octyldodecyl stearoyl stearate, octyl hydroxystearate, octyl palmitate, octyl salicylate, octyl stearate, oleic acid, olive (*Olea europaea*) oil, orange (*Citrus aurantium dulcis*) oil, palm (*Elaeis guineensis*) oil, palmitic acid, pantethine, panthenol, panthenyl ethyl ether, paraffin, PCA, peach (*Prunus persica*) kernel oil,

peanut (*Arachis hypogaea*) oil, PEG-8 C12-18 ester, PEG-15 cocamine, PEG-150 distearate, PEG-60 glyceryl isostearate, PEG-5 glyceryl stearate, PEG-30 glyceryl stearate, PEG-7 hydrogenated castor oil, PEG-40 hydrogenated castor oil, PEG-60 hydrogenated castor oil, PEG-20 methyl glucose sesquistearate, PEG-40 sorbitan peroleate, PEG-5 soy sterol, PEG-10 soy sterol, PEG-2 stearate, PEG-8 stearate, PEG-20 stearate, PEG-32 stearate, PEG-40 stearate, PEG-50 stearate, PEG-100 stearate, PEG-150 stearate, pentadecalactone, peppermint (*Mentha piperita*) oil, petrolatum, phospholipids, plankton extract, polyamino sugar condensate, polyglyceryl-3 diisostearate, polyquaternium-24, polysorbate 20, polysorbate 40, polysorbate 60, polysorbate 80, polysorbate 85, potassium myristate, potassium palmitate, propylene glycol, propylene glycol dicaprylate/dicaprate, propylene glycol dioctanoate, propylene glycol dipelargonate, propylene glycol laurate, propylene glycol stearate, propylene glycol stearate SE, PVP, pyridoxine dipalmitate, retinol, retinyl palmitate, rice (*Oryza sativa*) bran oil, RNA, rosemary (*Rosmarinus officinalis*) oil, rose oil, safflower (*Carthamus tinctorius*) oil, sage (*Salvia officinalis*) oil, sandalwood (*Santalum album*) oil, serine, serum protein, sesame (*Sesamum indicum*) oil, shea butter (*Butyrospermum parkii*), silk powder, sodium chondroitin sulfate, sodium hyaluronate, sodium lactate, sodium palmitate, sodium PCA, sodium polyglutamate, soluble collagen, sorbitan laurate, sorbitan oleate, sorbitan palmitate, sorbitan sesquioleate, sorbitan stearate, sorbitol, soybean (*Glycine soja*) oil, sphingolipids, squalane, squalene, stearamide MEA-stearate, stearic acid, stearoxy dimethicone, stearoxytrimethylsilane, stearyl alcohol, stearyl glycyrrhetinate, stearyl heptanoate, stearyl stearate, sunflower (*Helianthus annuus*) seed oil, sweet almond (*Prunus amygdalus dulcis*) oil, synthetic beeswax, tocopherol, tocopheryl acetate, tocopheryl linoleate, tribehenin, tridecyl neopentanoate, tridecyl stearate, triethanolamine, tristearin, urea, vegetable oil, water, waxes, wheat (*Triticum vulgare*) germ oil, and ylang (*Cananga odorata*) oil.

c. Antioxidants

[0059] Non-limiting examples of antioxidants that can be used with the compositions of the present invention include acetyl cysteine, ascorbic acid polypeptide, ascorbyl dipalmitate, ascorbyl methylsilanol pectinate, ascorbyl palmitate, ascorbyl stearate, BHA, BHT, t-butyl hydroquinone, cysteine, cysteine HCI, diamylhydroquinone, di-t-butylhydroquinone, dicetyl thiodipropionate, dioleyl tocopheryl methylsilanol, disodium ascorbyl sulfate, distearyl thiodipropionate, ditridecyl thiodipropionate, dodecyl gallate, erythorbic acid, esters of ascorbic acid, ethyl ferulate, ferulic acid, gallic acid esters, hydroquinone, isooctyl thioglycolate, kojic acid, magnesium ascorbate, magnesium ascorbyl

phosphate, methylsilanol ascorbate, natural botanical anti-oxidants such as green tea or grape seed extracts, nordihydroguaiaretic acid, octyl gallate, phenylthioglycolic acid, potassium ascorbyl tocopheryl phosphate, potassium sulfite, propyl gallate, quinones, rosmarinic acid, sodium ascorbate, sodium bisulfite, sodium erythorbate, sodium metabisulfite, sodium sulfite, superoxide dismutase, sodium thioglycolate, sorbityl furfural, thiodiglycol, thiodiglycolamide, thiodiglycolic acid, thioglycolic acid, thiolactic acid, thiosalicylic acid, tocophereth-5, tocophereth-10, tocophereth-12, tocophereth-18, tocophereth-50, tocopherol, tocophersolan, tocopheryl acetate, tocopheryl linoleate, tocopheryl nicotinate, tocopheryl succinate, and tris(nonylphenyl)phosphite.

d. Structuring Agents

[0060] In other non-limiting aspects, the compositions of the present invention can include a structuring agent. Structuring agent, in certain aspects, assist in providing rheological characteristics to the composition to contribute to the composition's stability. In other aspects, structuring agents can also function as an emulsifier or surfactant. Non-limiting examples of structuring agents include sodium cocoyl glutamate, hydroxypropyl cyclodextrin, stearic acid, palmitic acid, stearyl alcohol, cetyl alcohol, behenyl alcohol, stearic acid, palmitic acid, the polyethylene glycol ether of stearyl alcohol having an average of about 1 to about 21 ethylene oxide units, the polyethylene glycol ether of cetyl alcohol having an average of about 1 to about 5 ethylene oxide units, and mixtures thereof.

e. Emulsifiers

[0061] In certain aspects of the present invention, the compositions do not include an emulsifier. In other aspects, however, the compositions can include one or more emulsifiers. Emulsifiers can reduce the interfacial tension between phases and improve the formulation and stability of an emulsion. The emulsifiers can be nonionic, cationic, anionic, and zwitterionic emulsifiers (*see* U.S. Pat. Nos. 5,011,681; 4,421,769; 3,755,560). Non-limiting examples include esters of glycerin, esters of propylene glycol, fatty acid esters of polyethylene glycol, fatty acid esters of polypropylene glycol, esters of sorbitol, esters of sorbitan anhydrides, carboxylic acid copolymers, esters and ethers of glucose, ethoxylated ethers, ethoxylated alcohols, alkyl phosphates, polyoxyethylene fatty ether phosphates, fatty acid amides, acyl lactylates, soaps, TEA stearate, DEA oleth-3 phosphate, polyethylene glycol 20 sorbitan monolaurate (polysorbate 20), polyethylene glycol 5 soya sterol, steareth-2, steareth-20, steareth-21, ceteareth-20, cetearyl glucoside, cetearyl alcohol, C12-13 pareth-3, PPG-2 methyl

glucose ether distearate, PPG-5-ceteth-20, bis-PEG/PPG-20/20 dimethicone, ceteth-10, polysorbate 80, cetyl phosphate, potassium cetyl phosphate, diethanolamine cetyl phosphate, polysorbate 60, glyceryl stearate, PEG-100 stearate, arachidyl alcohol, arachidyl glucoside, and mixtures thereof.

f. Silicone Containing Compounds

[0062] In non-limiting aspects, silicone containing compounds include any member of a family of polymeric products whose molecular backbone is made up of alternating silicon and oxygen atoms with side groups attached to the silicon atoms. By varying the -Si-O- chain lengths, side groups, and crosslinking, silicones can be synthesized into a wide variety of materials. They can vary in consistency from liquid to gel to solids.

[0063] The silicone containing compounds that can be used in the context of the present invention include those described in this specification or those known to a person of ordinary skill in the art. Non-limiting examples include silicone oils (e.g., volatile and non-volatile oils), gels, and solids. In certain aspects, the silicon containing compounds includes a silicone oils such as a polyorganosiloxane. Non-limiting examples of polyorganosiloxanes include dimethicone, cyclomethicone, cyclohexasiloxane, polysilicone-11, phenyl trimethicone, trimethylsilylamodimethicone, stearoxytrimethylsilane, or mixtures of these and other organosiloxane materials in any given ratio in order to achieve the desired consistency and application characteristics depending upon the intended application (e.g., to a particular area such as the skin, hair, or eyes). A "volatile silicone oil" includes a silicone oil have a low heat of vaporization, i.e., normally less than about 50 cal per gram of silicone oil. Non-limiting examples of volatile silicone oils include: cyclomethicones such as Dow Corning 344 Fluid, Dow Corning 345 Fluid, Dow Corning 244 Fluid, and Dow Corning 245 Fluid, Volatile Silicon 7207 (Union Carbide Corp., Danbury, Conn.); low viscosity dimethicones, i.e., dimethicones having a viscosity of about 50 cst or less (e.g., dimethicones such as Dow Corning 200-0.5 cst Fluid). The Dow Corning Fluids are available from Dow Corning Corporation, Midland, Michigan. Cyclomethicone and dimethicone are described in the Third Edition of the CTFA Cosmetic Ingredient Dictionary (incorporated by reference) as cyclic dimethyl polysiloxane compounds and a mixture of fully methylated linear siloxane polymers end-blocked with trimethylsiloxy units, respectively. Other non-limiting volatile silicone oils that can be used in the context of the present invention include those available from General Electric Co., Silicone

Products Div., Waterford, N.Y. and SWS Silicones Div. of Stauffer Chemical Co., Adrian, Michigan.

g. Exfoliating Agent

[0064] Exfoliating agents include ingredients that remove dead skin cells on the skin's outer surface. These agents may act through mechanical, chemical, and/or other means. Non-limiting examples of mechanical exfoliating agents include abrasives such as pumice, silica, cloth, paper, shells, beads, solid crystals, solid polymers, etc. Non-limiting examples of chemical exfoliating agents include acids and enzyme exfoliants. Acids that can be used as exfoliating agents include, but are not limited to, glycolic acid, lactic acid, citric acid, α hydroxy acids, beta hydroxy acids, etc. Other exfoliating agents known to those of skill in the art are also contemplated as being useful within the context of the present invention.

h. Essential Oils

[0065] Essential oils include oils derived from herbs, flowers, trees, and other plants. Such oils are typically present as tiny droplets between the plant's cells, and can be extracted by several method known to those of skill in the art (e.g., steam distilled, enfleurage (i.e., extraction by using fat), maceration, solvent extraction, or mechanical pressing). When these types of oils are exposed to air they tend to evaporate (i.e., a volatile oil). As a result, many essential oils are colorless, but with age they can oxidize and become darker. Essential oils are insoluble in water and are soluble in alcohol, ether, fixed oils (vegetal), and other organic solvents. Typical physical characteristics found in essential oils include boiling points that vary from about 160° to 240° C and densities ranging from about 0.759 to about 1.096.

[0066] Essential oils typically are named by the plant from which the oil is found. For example, rose oil or peppermint oil are derived from rose or peppermint plants, respectively. Non-limiting examples of essential oils that can be used in the context of the present invention include sesame oil, macadamia nut oil, tea tree oil, evening primrose oil, Spanish sage oil, Spanish rosemary oil, coriander oil, thyme oil, pimento berries oil, rose oil, anise oil, balsam oil, bergamot oil, rosewood oil, cedar oil, chamomile oil, sage oil, clary sage oil, clove oil, cypress oil, eucalyptus oil, fennel oil, sea fennel oil, frankincense oil, geranium oil, ginger oil, grapefruit oil, jasmine oil, juniper oil, lavender oil, lemon oil, lemongrass oil, lime oil, mandarin oil, marjoram oil, myrrh oil, neroli oil, orange oil, patchouli oil, pepper oil, black pepper oil, petitgrain oil, pine oil, rose otto oil, rosemary oil, sandalwood oil, spearmint oil,

spikenard oil, vetiver oil, wintergreen oil, or ylang. Other essential oils known to those of skill in the art are also contemplated as being useful within the context of the present invention.

i. Thickening Agents

[0067] Thickening agents, including thickener or gelling agents, include substances which that can increase the viscosity of a composition. Thickeners includes those that can increase the viscosity of a composition without substantially modifying the efficacy of the active ingredient within the composition. Thickeners can also increase the stability of the compositions of the present invention. In certain aspects of the present invention, thickeners include hydrogenated polyisobutene, trihydroxystearin, ammonium acryloyldimethyltaurate/VP copolymer, or a mixture of them.

[0068] Non-limiting examples of additional thickening agents that can be used in the context of the present invention include carboxylic acid polymers, crosslinked polyacrylate polymers, polyacrylamide polymers, polysaccharides, and gums. Examples of carboxylic acid polymers include crosslinked compounds containing one or more monomers derived from acrylic acid, substituted acrylic acids, and salts and esters of these acrylic acids and the substituted acrylic acids, wherein the crosslinking agent contains two or more carbon-carbon double bonds and is derived from a polyhydric alcohol (see U.S. Pat. Nos. 5,087,445; 4,509,949; 2,798,053; CTFA International Cosmetic Ingredient Dictionary, Fourth edition, 1991, pp. 12 and 80). Examples of commercially available carboxylic acid polymers include carbomers, which are homopolymers of acrylic acid crosslinked with allyl ethers of sucrose or pentaerytritol (e.g., CARBOPOL™ 900 series from B. F. Goodrich).

[0069] Non-limiting examples of crosslinked polyacrylate polymers include cationic and nonionic polymers. Examples are described in U.S. Pat. Nos. 5,100,660; 4,849,484; 4,835,206; 4,628,078; 4,599,379).

[0070] Non-limiting examples of polyacrylamide polymers (including nonionic polyacrylamide polymers including substituted branched or unbranched polymers) include polyacrylamide, isoparaffin and laureth-7, multi-block copolymers of acrylamides and substituted acrylamides with acrylic acids and substituted acrylic acids.

[0071] Non-limiting examples of polysaccharides include cellulose, carboxymethyl hydroxyethylcellulose, cellulose acetate propionate carboxylate, hydroxyethylcellulose,

hydroxyethyl ethylcellulose, hydroxypropylcellulose, hydroxypropyl methylcellulose, methyl hydroxyethylcellulose, microcrystalline cellulose, sodium cellulose sulfate, and mixtures thereof. Another example is an alkyl substituted cellulose where the hydroxy groups of the cellulose polymer is hydroxyalkylated (preferably hydroxy ethylated or hydroxypropylated) to form a hydroxyalkylated cellulose which is then further modified with a C10-C30 straight chain or branched chain alkyl group through an ether linkage. Typically these polymers are ethers of C10-C30 straight or branched chain alcohols with hydroxyalkylcelluloses. Other useful polysaccharides include scleroglucans comprising a linear chain of (1-3) linked glucose units with a (1-6) linked glucose every three unit.

[0072] Non-limiting examples of gums that can be used with the present invention include acacia, agar, algin, alginic acid, ammonium alginate, amylopectin, calcium alginate, calcium carrageenan, carnitine, carrageenan, dextrin, gelatin, gellan gum, guar gum, guar hydroxypropyltrimonium chloride, hectorite, hyaluronic acid, hydrated silica, hydroxypropyl chitosan, hydroxypropyl guar, karaya gum, kelp, locust bean gum, natto gum, potassium alginate, potassium carrageenan, propylene glycol alginate, sclerotium gum, sodium carboxymethyl dextran, sodium carrageenan, tragacanth gum, xanthan gum, and mixtures thereof.

j. Preservatives

[0073] Non-limiting examples of preservatives that can be used in the context of the present invention include quaternary ammonium preservatives such as polyquaternium-1 and benzalkonium halides (e.g., benzalkonium chloride ("BAC") and benzalkonium bromide), parabens (e.g., methylparabens and propylparabens), phenoxyethanol, benzyl alcohol, chlorobutanol, phenol, sorbic acid, thimerosal or combinations thereof.

2. Pharmaceutical Ingredients

[0074] Pharmaceutical active agents are also contemplated as being useful with the compositions of the present invention. Non-limiting examples of pharmaceutical active agents include anti-acne agents, agents used to treat rosacea, analgesics, anesthetics, anorectals, antihistamines, anti-inflammatory agents including non-steroidal anti-inflammatory drugs, antibiotics, antifungals, antivirals, antimicrobials, anti-cancer actives, scabicides, pediculicides, antineoplastics, antiperspirants, antipruritics, antipsoriatic agents, antiseborrheic agents, biologically active proteins and peptides, burn treatment agents, cauterizing agents,

depigmenting agents, depilatories, diaper rash treatment agents, enzymes, hair growth stimulants, hair growth retardants including DFMO and its salts and analogs, hemostatics, kerotolytics, canker sore treatment agents, cold sore treatment agents, dental and periodontal treatment agents, photosensitizing actives, skin protectant/barrier agents, steroids including hormones and corticosteroids, sunburn treatment agents, sunscreens, transdermal actives, nasal actives, vaginal actives, wart treatment agents, wound treatment agents, wound healing agents, etc.

F. Kits

[0075] Kits are also contemplated as being used in certain aspects of the present invention. For instance, compositions of the present invention can be included in a kit. A kit can include a container. Containers can include a bottle, a metal tube, a laminate tube, a plastic tube, a dispenser, a pressurized container, a barrier container, a package, a compartment, a lipstick container, a compact container, cosmetic pans that can hold cosmetic compositions, or other types of containers such as injection or blow-molded plastic containers into which the dispersions or compositions or desired bottles, dispensers, or packages are retained. The kit and/or container can include indicia on its surface. The indicia, for example, can be a word, a phrase, an abbreviation, a picture, or a symbol.

[0076] The containers can dispense a pre-determined amount of the composition. In other embodiments, the container can be squeezed (e.g., metal, laminate, or plastic tube) to dispense a desired amount of the composition. The composition can be dispensed as a spray, an aerosol, a liquid, a fluid, or a semi-solid. The containers can have spray, pump, or squeeze mechanisms. A kit can also include instructions for employing the kit components as well the use of any other compositions included in the container. Instructions can include an explanation use, and maintain the compositions.

EXAMPLES

[0077] The following examples are included to demonstrate preferred embodiments of the invention. It should be appreciated by those of skill in the art that the techniques disclosed in the examples which follow represent techniques discovered by the inventor to function well in the practice of the invention, and thus can be considered to constitute preferred modes for its practice. However, those of skill in the art should, in light of the present disclosure, appreciate

that many changes can be made in the specific embodiments which are disclosed and still obtain a like or similar result without departing from the spirit and scope of the invention.

[0078] All of the compositions and methods disclosed and claimed herein can be made and executed without undue experimentation in light of the present disclosure. While the compositions and methods of this invention have been described in terms of preferred embodiments, it will be apparent to those of skill in the art that variations may be applied to the compositions and methods and in the steps or in the sequence of steps of the method described herein without departing from the concept, spirit, and scope of the invention. More specifically, it will be apparent that certain agents which are both chemically and physiologically related may be substituted for the agents described herein while the same or similar results would be achieved. All such similar substitutes and modifications apparent to those skilled in the art are deemed to be within the spirit, scope and concept of the invention as defined by the appended claims.

EXAMPLE 1

(Exemplary Formulations)

[0079] Formulations having the ingredients disclosed herein were prepared as topical skin compositions. In some instances, the topical skin compositions can be prepared as an ampule, serum, cream, emulsion, gel, or gel emulsion. The formulation in Table 1 is an example of a topical skin composition prepared as an ampule.

TABLE 1^

Ingredient	% Concentration (by weight)
Water	78.5
Glycerin	14.9
Pentylene Glycol	3
Betaine	2
Phenoxyethanol	0.8
Xanthan Gum	0.4
Hydrolyzed Sodium Hyaluronate	0.2
Sodium Hyaluronate	0.1
Verbena Officinalis extract	0.04
Ceramide	0.01
Excipients*	q.s.

^ Formulation can be prepared by mixing the ingredients in a beaker under heat 70-75°C until homogenous. Subsequently, the formulation can be cooled to standing room temperature (20-25°C). Further, and if desired, additional ingredients can be added, for example, to modify the rheological properties of the composition or ingredients that provide benefits to skin.

* Excipients can be added, for example, to modify the rheological properties of the composition. Alternatively, the amount of water can be varied so long as the amount of water in the composition is at least 40% w/w, and preferably between 60 to 90% w/w.

EXAMPLE 2

(Materials Used)

[0080] The active ingredients in Table 2 were used to prepare the formulation in Table 1 above.

TABLE 2

Ingredient
Verbena officinalis, supplied by Silab under the tradename Vitalayer®
Hydrolyzed sodium hyaluronate, supplied by Tri-K under the trademane HyaClear® 10K
Ceramide NG, supplied by DKSH under the tradename DS-HydroCeramide

EXAMPLE 3

Effect on Filaggrin Protein Expression

[0081] Changes in the production of filaggrin in keratinocytes due to each of the active ingredients, any one of the combination of ingredients, or compositions having said combinations disclosed in the specification can be measured. Filaggrin is the precursor to Natural Moisturizing Factor (NMF) in the skin. Increased NMF increases the moisture content of the skin.

[0082] Filaggrin production in treated and non-treated keratinocytes was determined using the PROTEINSIMPLE® SIMON™ western blotting bioassay that employs an antibody specific for filaggrin to quantitatively detect filaggrin concentration in keratinocyte cell lysates. The treated group of keratinocytes was treated with 1% of calcium or an extract of *Laminaria saccharina*, marine plankton, *Opuntia ficus-indica*, *Imperata cylindrical*, or *Verbena officinalis* (1%).

[0083] For each sample, normal human epidermal keratinocytes (NHEK) were grown in EPI-200 –Mattek EPILIFE™ growth media with calcium from Life Technologies (M-EP-500-CA). NHEK were incubated in growth medium overnight at 37 °C in 5% CO_2 prior to treatment. NHEK were then incubated in growth medium with 1% test compound/extract or no compound/extract (negative control) for 24 to 36 hours. The NHEK were then washed, collected, and stored on ice or colder until lysed on ice using a lysis buffer and sonication. The protein concentrations of the samples were determined and used to normalize the samples. The lysates were stored at -80 °C until used in the quantification assay. Normalized samples and molecular weight standards were loaded and ran on a denatured protein separation gel using capillary electrophoresis (**THE FIGURE**). The proteins in the gel were immobilized and immunoprobed using a primary antibody specific for filaggrin. The immobilized proteins were then immunoprobed with an enzyme-linked detection antibody that binds the primary antibody. A chemiluminescent substrate solution was then be added to the immobilized proteins to allow chemiluminescent development in proportion to the amount of filaggrin bound in the immobilization. The chemiluminescent development was stopped at a specific time and the intensity of the chemiluminescent signal was measured (reported as Area Under Curve, AUC in Table 3 below) and compared to controls. As demonstrated in Table 3 below, *Verbena officinalis* extract provided the greatest increase in filaggrin expression (> 66%).

TABLE 3

Administered Composition	% Tested	AUC	% Ctrl
Control	1%	70848	-
Calcium	1%	81899	15.60
Extract of *Laminaria saccharina*	1%	99298	40.16
Extract of marine plankton	1%	90465	27.69
Extract of *Opuntia ficus-indica*	1%	74952	5.79
Extract of *Imperata cylindrica*	1%	93792	32.38
Extract of *Verbena officinalis*	1%	118267	66.93

EXAMPLE 4

Analysis of Skin Moisturization Efficacy

[0084] Skin moisture/hydration benefits can be measured by using impedance measurements with the Nova Dermal Phase Meter. The impedance meter measures changes in skin moisture content. The outer layer of the skin has distinct electrical properties. When skin is dry it conducts electricity very poorly. As it becomes more hydrated increasing conductivity results. Consequently, changes in skin impedance (related to conductivity) can be used to assess changes in skin hydration. The unit can be calibrated according to instrument instructions for each testing day. A notation of temperature and relative humidity can also be made. Each of the active ingredients, any one of the combination of ingredients, or compositions having said combinations disclosed in the specification can be assayed according to this process.

[0085] A clinical study was performed to evaluate the surface effects of a single use of a composition as disclosed herein. Thirty (30) subjects ranging in age from 21 to 63 years were enrolled, and twenty-one (21) completed the study. Subjects were acclimated to an

environmentally-controlled room (70 ± 3 °F; 45% + 15% relative humidity) for at least 15 minutes with their faces exposed prior to each set of measurements.

[0086] The study duration for each subject was approximately 1 hour the first day and 2 hours the second day. The first day visit involved wash-out instructions and preparation for the second day visit. The second day visit involved instrumental measurements at baseline and immediately (approximately 15 minutes) after application of the test composition. Pre-treatment measurements were taken on the subjects' forehead, eye, cheek, jaw, and nose regions using a Novameter Technologies DPM 9003 impedance meter. The test composition was then applied to the subjects' faces. Three post-treatment impedance measurements were taken at each of 10 sites in the forehead region, 4 sites in the eye region, 7 sites in the cheek region, 5 sites in the jaw region, and 5 sites in various regions around the nose.

[0087] Changes from baseline were assessed using a paired difference t-test, and the data was evaluated with the confidence interval placed at 95% ($p<0.05$). The Novameter Technologies DPM 9003 measures impedance, the resistance to the flow of alternating current. A higher impedance measurements corresponds to a higher skin moisturization value. The test composition provided a significant increase in moisturization in all examined regions, relative to baseline, at the immediate time point. The aggregate value across all measurements depicted in Table 3 below indicates that the test composition afforded a greater than 53% increase in skin moisturization, which represents a significant increase in moisture content.

TABLE 4

Descriptive Statistics	Baseline	Immediate (15 mins)
Mean	105.34	162.06
Percent Change*	--	53.84%
P-Value^	--	$p<0.05$

*Percent change when compared to baseline
^Represents a significant change when compared to baseline ($p \leq 0.05$)

EXAMPLE 5

(Additional Assays)

[0088] Assays that can be used to determine the efficacy of any one of the ingredients or any combination of ingredients or compositions having said combination of ingredients disclosed throughout the specification and claims can be determined by methods known to those of ordinary skill in the art. The following are non-limiting assays that can be used in the

context of the present invention. It should be recognized that other testing procedures can be used, including, for example, objective and subjective procedures.

[0089] Antioxidant (AO) Assay: An antioxidant assay can be performed on skin cells (e.g., epidermal keratinocytes, fibroblasts, and/or dermal endothelial cells) to determine the ability of any one of the active ingredients, combination of ingredients, or compositions having said combinations disclosed in the specification to provide anti-oxidant capacity (TEAC) by inhibiting the oxidation of ABTS® (2,2'-azino-di-[3-ethylbenzthiazoline sulphonate]) to ABTS®·+ by metmyoglobin. The antioxidant system of living organisms can include enzymes such as superoxide dismutase, catalase, and glutathione peroxidase; macromolecules such as albumin, ceruloplasmin, and ferritin; and an array of small molecules, including ascorbic acid, α-tocopherol, β-carotene, reduced glutathione, uric acid, and bilirubin. The sum of endogenous and food-derived antioxidants represents the total antioxidant activity of the extracellular fluid. Cooperation of all the different antioxidants can provide greater protection against attack by reactive oxygen or nitrogen radicals, than any single compound alone. Thus, the overall antioxidant capacity may give more relevant biological information compared to that obtained by the measurement of individual components, as it considers the cumulative effect of all antioxidants present in plasma and body fluids. The capacity of the ingredients in the composition to prevent ABTS oxidation can be compared with that of Trolox, a water-soluble tocopherol analogue, and was quantified as molar Trolox equivalents. Anti-Oxidant capacity kit # 709001 from Cayman Chemical (Ann Arbor, Michigan USA) can be used to measure the total anti-oxidant capacity.

[0090] Collagen Stimulation Assay: A collagen stimulation assay can be used to determine the ability of any one of the active ingredients, combination of ingredients, or compositions having said combinations disclosed in the specification to increase expression of procollagen-1, a precursor to collagen. Collagens (types I, II, III, IV and V) can be synthesized as precursor molecules called procollagens. These precursor molecules can contain additional peptide sequences, usually called "propeptides", at both the amino-terminal and the carboxy-terminal ends. During cellular expression and secretion, procollagens can be assembled in the trimeric form and then cleaved at specific N- and C-terminal sites by specific endopeptidases, generating three fragments: procollagen-1 N-terminal propeptide (PINP), Type I collagen, and procollagen-1 carboxy-terminal propeptide (PICP).

[0091] The function of the propeptides is to facilitate the winding of procollagen molecules into a triple-helical conformation within the endoplasmic reticulum. The propeptides can be cleaved off from the collagen triple helix molecule during its secretion, after which the triple helix collagens polymerize into extracellular collagen fibrils. Thus, the amount of the free propeptides reflects stoichiometrically the amount of collagen molecules synthesized (a relationship analogous to that between the carboxy-terminal peptide of proinsulin and the endogenously produced insulin). Collagen is an extracellular matrix protein critical for skin structure. Increased synthesis of collagen helps improve skin firmness and elasticity.

[0092] Quantitative detection of PICP in fibroblast cell extracts and culture supernatants can be performed with an enzyme immunoassay kit (e.g., Takara #MK101) to assess the effects of the ingredients on the synthesis of PICP in skin. This bioassay can be used to examine effects on the production of procollagen peptide (a precursor to collagen) by human epidermal fibroblasts. The endpoint of this assay can be a spectrophotometric measurement that reflects the presence of procollagen peptide and cellular viability. The assay employs the quantitative sandwich enzyme immunoassay technique whereby a monoclonal antibody specific for procollagen peptide was pre-coated onto a microplate. Standards and samples can be pipetted into the wells and any procollagen peptide present was bound by the immobilized antibody. After washing away any unbound substances, an enzyme-linked polyclonal antibody specific for procollagen peptide can be added to the wells. Following a wash to remove any unbound antibody-enzyme reagent, a substrate solution can be added to the wells and color was developed in proportion to the amount of procollagen peptide bound in the initial step. Color development was stopped and the intensity of the color at 450 nm was measured using a microplate reader.

[0093] For generation of samples and controls, subconfluent normal human adult epidermal fibroblasts (Cascade Biologics) can be cultivated in standard DMEM growth medium with 10% fetal bovine serum (Mediatech) at 37°C in 10% CO_2. The cells can be treated with each of the tested ingredients and controls for 3 days. Following incubation, cell culture medium can be collected and the amount of Type I procollagen peptide secretion was quantified using the sandwich enzyme linked immuno-sorbant assay (ELISA) from Takara (#MK101) as explained above.

[0094] **Elastin Stimulation Assay:** Elastin is a connective tissue protein that helps skin resume shape after stretching or contracting. Elastin is also an important load-bearing protein used in places where mechanical energy is required to be stored. Elastin is made by linking many soluble tropoelastin protein molecules, in a reaction catalyzed by lysyl oxidase. Elastin secretion and elastin fibers can be monitored in cultured human fibroblasts by staining of cultured human fibroblasts using immunofluorescent antibodies directed against elastin by a direct ELISA sandwich method. A Meso Scale Discovery system SECTOR 2400 Imaging system can be used to analyze the results. Changes in elastin secretion and elastin fibers caused by one or more ingredients in the composition can be determined by incubating cultured human fibroblasts with the active ingredient for a period of time before probing the cells or a lysate thereof with antibodies directed against elastin.

[0095] **Laminin Stimulation Assay**: Laminin is a major protein in the dermal-epidermal junction (DEJ) (also referred to as the basement membrane). The DEJ is located between the dermis and the epidermis interlocks forming fingerlike projections called rete ridges. The cells of the epidermis receive their nutrients from the blood vessels in the dermis. The rete ridges increase the surface area of the epidermis that is exposed to these blood vessels and the needed nutrients. The DEJ provides adhesion of the two tissue compartments and governs the structural integrity of the skin. Laminin is a structural glycoprotein located in the DEJ. Together with fibronectin, laminin is considered the glue that holds the cells together, and both are secreted by dermal fibroblasts to help facilitate intra- and inter-cellular adhesion of the epidermal calls to the DEJ.

[0096] Laminin secretion can be monitored by quantifying laminin in cell supernatants of cultured human fibroblasts treated for 3 days with culture medium with or without 1.0% final concentration of the test ingredient(s). Following incubation, laminin content can be measured using immunofluorescent antibodies directed against each protein in an enzyme linked immuno-sorbant assay (ELISA).

[0097] **Matrix Metalloproteinase 1 Enzyme Activity (MMP-1) Assay:** MMPs are extracellular proteases that play a role in many normal and disease states by virtue of their broad substrate specificity. MMP-1 substrates include collagen IV. The Molecular Probes Enz/Chek Gelatinase/ Collagenase Assay kit (#E12055), can be used to detect MMP-1 protease activity, and utilizes a fluorogenic gelatin substrate and tests proteolytic cleavage of the substrate by purified MMP-1 enzyme. Upon proteolytic cleavage of the substrate, bright green

fluorescence is revealed and can be monitored using a fluorescent microplate reader to measure enzymatic activity. Test materials can be incubated in the presence or absence of the purified enzyme and substrate to determine their protease inhibitor capacity.

[0098] **Matrix Metalloproteinase 3 and 9 Enzyme Activity (MMP-3; MMP-9) Assay:** MMPs are extracellular proteases that play a role in many normal and disease states by virtue of their broad substrate specificity. MMP-3 substrates include collagens, fibronectins, and laminin; while MMP-9 substrates include collagen VII, fibronectins and laminin. Colorimetric Drug Discovery kits from BioMol International for MMP-3 (AK-400) and MMP-9 (AK-410) can be used to measure protease activity of MMPs using a thiopeptide as a chromogenic substrate (Ac-PLG-[2-mercapto-4-methyl-pentanoyl]-LG-OC2H5)5,6. The MMP cleavage site peptide bond is replaced by a thioester bond in the thiopeptide. Hydrolysis of this bond by an MMP produces a sulfhydryl group, which reacts with DTNB [5,5'-dithiobis(2- nitrobenzoic acid), Ellman's reagent] to form 2-nitro-5- thiobenzoic acid, which can be detected by its absorbance at 412 nm (ε=13,600 M-1cm-1 at pH 6.0 and above 7).

[0099] **Lipoxygenase (LO) Assay:** A lipoxygenase assay can be used to determine the ability of any one of the active ingredients, combination of ingredients, or compositions having said combinations disclosed in the specification to inhibit lipoxygenase (LO) expression. LOs are non-heme iron-containing dioxygenases that catalyze the addition of molecular oxygen to fatty acids. Linoleate and arachidonate are the main substrates for LOs in plants and animals. Arachadonic acid may then be converted to hydroxyeicosotrienenoic (HETE) acid derivatives, that are subsequently converted to leukotrienes, potent inflammatory mediators. An accurate and convenient method for screening lipoxygenase inhibitors can be performed by measuring the hydroperoxides generated from the incubation of a lipoxygenase (5-, 12-, or 15-LO) with arachidonic acid. The Colorimetric LO Inhibitor screening kit (#760700, Cayman Chemical) can be used to determine the ability of ingredients of the composition to inhibit enzyme activity.

[0100] Purified 15-lipoxygenase and test ingredients can be mixed in assay buffer and incubated with shaking for 10 min at room temperature. Following incubation, arachidonic acid can be added to initiate the reaction and the mixtures were incubated for an additional 10 min at room temperature. Colorimetric substrate can be added to terminate catalysis and color progression was evaluated by fluorescence plate reading at 490 nm. The percent inhibition of lipoxyganse activity can be calculated compared to non-treated controls to determine the ability of ingredients of the composition to inhibit the activity of purified enzyme.

[0101] **Tumor Necrosis Factor Alpha (TNF-α) Assay:** The prototype ligand of the TNF superfamily, TNF-α, is a pleiotropic cytokine that plays a central role in inflammation. Increase in its expression is associated with an up regulation in pro-inflammatory activity. The bioassay can be used to analyze the effect of ingredients of the composition on the production of TNF-α by human epidermal keratinocytes. The endpoint of this assay can be a spectrophotometric measurement that reflects the presence of TNF-α and cellular viability. The assay can employ the quantitative sandwich enzyme immunoassay technique whereby a monoclonal antibody specific for TNF-α had been pre-coated onto a microplate.

[0102] Standards and samples can be pipetted into wells of the microplate and any TNF-α present was bound by the immobilized antibody. After washing away any unbound substances, an enzyme-linked polyclonal antibody specific for TNF-α can be added to the wells. Following a wash to remove any unbound antibody-enzyme reagent, a substrate solution can be added to the wells and color developed in proportion to the amount of TNF-α bound in the initial step using a microplate reader for detection at 450 nm. The color development can be stopped and the intensity of the color can be measured. Subconfluent normal human adult keratinocytes (Cascade Biologics) cultivated in EPILIFE™ standard growth medium (Cascade Biologics) at 37°C in 5% CO_2 can be treated with phorbol 12-myristate 13-acetate (PMA, 10 ng/ml, Sigma Chemical, #P1585-1MG) and of ingredients of the composition or no test ingredient (for negative control) for 6 hours. PMA can be shown to cause a dramatic increase in TNF-α secretion which peaks at 6 hours after treatment. Following incubation, cell culture medium can be collected and the amount of TNF-α secretion quantified using a sandwich enzyme linked immuno-sorbant assay (ELISA) from R&D Systems (#DTA00C).

[0103] **Elastase Assay:** ENZCHEK® Elastase Assay (Kit# E-12056) from Molecular Probes (Eugene, Oregon USA) can be used as an *in vitro* enzyme inhibition assay for measuring inhibition of elastase activity in the presence of ingredients of the composition. The EnzChek kit can contain soluble bovine neck ligament elastin that is labeled with dye such that the conjugate's fluorescence is quenched. The non-fluorescent substrate can be digested by elastase or other proteases to yield highly fluorescent fragments. The resulting increase in fluorescence can be monitored with a fluorescence microplate reader. Digestion products from the elastin substrate can have absorption maxima at ~505 nm and fluorescence emission maxima at ~515 nm. The peptide, N-methoxysuccinyl-Ala-Ala-Pro-Val- chloromethyl ketone,

can be used as a selective, collective inhibitor of elastase for a positive control when utilizing the EnzChek Elastase Assay Kit for screening for elastase inhibitors.

[0104] **Fibronectin Stimulation Assay**: Fibronectin is a major protein in the dermal-epidermal junction (DEJ) (also referred to as the basement membrane). The DEJ is located between the dermis and the epidermis interlocks forming fingerlike projections called rete ridges. The cells of the epidermis receive their nutrients from the blood vessels in the dermis. The rete ridges increase the surface area of the epidermis that is exposed to these blood vessels and the needed nutrients. The DEJ provides adhesion of the two tissue compartments and governs the structural integrity of the skin. Fibronectin is a structural glycoprotein located in the DEJ. Together with laminin, fibronectin is considered the glue that holds the cells together, and both are secreted by dermal fibroblasts to help facilitate intra- and inter-cellular adhesion of the epidermal calls to the DEJ.

[0105] Fibronectin secretion can be monitored by quantifying fibronectin in cell supernatants of cultured human fibroblasts treated for 3 days with culture medium with or without 1.0% final concentration of the test ingredient(s). Following incubation, fibronectin content can be measured using immunofluorescent antibodies directed against each protein in an enzyme linked immuno-sorbant assay (ELISA).

[0106] **Lysyl Oxidase Assay:** A lysyl oxidase assay can be performed on skin cells (e.g., epidermal keratinocytes, fibroblasts, and/or dermal endothelial cells) to determine the ability of any one of the active ingredients, combination of ingredients, or compositions having said combinations disclosed in the specification to stimulate expression of lysyl oxidase in skin. Lysyl oxidase can catalyze crosslinking of elastin and collagens, thereby providing for a more structurally rigid matrix for skin. By increasing expression of lysyl oxidase, increased cross-linking of elastin and collagens can occur, which can be beneficial in reducing the appearance of fine lines, wrinkles, sagging skin, and/or non-elastic skin.

[0107] **B16 Pigmentation Assay:** Melanogenesis is the process by which melanocytes produce melanin, a naturally produced pigment that imparts color to skin, hair, and eyes. Inhibiting melanogenesis is beneficial to prevent skin darkening and lighten dark spots associated with aging. This bioassay can utilize B16-F1 melanocytes (ATCC), an immortalized mouse melanoma cell line, to analyze the effect of compounds on melanogenesis. The endpoint of this assay can be a spectrophotometric measurement of melanin production

and cellular viability. B16-F1 melanocytes, can be cultivated in standard DMEM growth medium with 10% fetal bovine serum (Mediatech) at 37°C in 10% CO_2 and then treated with any one of the active ingredients, combination of ingredients, or compositions having said combinations disclosed in the specification for 6 days. Following incubation, melanin secretion can be measured by absorbance at 405 nm and cellular viability is quantified.

[0108] **ORAC Assay:** Oxygen Radical Absorption (or Absorbance) Capacity (ORAC) of any one of the active ingredients, combination of ingredients, or compositions having said combinations disclosed in the specification can also be assayed by measuring the antioxidant activity of such ingredients or compositions. Antioxidant activity indicates a capability to reduce oxidizing agents (oxidants). This assay quantifies the degree and length of time it takes to inhibit the action of an oxidizing agent, such as oxygen radicals, that are known to cause damage to cells (e.g., skin cells). The ORAC value of any one of the active ingredients, combination of ingredients, or compositions having said combinations disclosed in the specification can be determined by methods known to those of ordinary skill in the art (*see* U.S. Publication Nos. 2004/0109905 and 2005/0163880; and commercially available kits such as Zen-Bio ORAC Anti-oxidant Assay kit (#AOX-2)). The Zen-Bio ORAC Anti-oxidant Assay kit measures the loss of fluorescein fluorescence over time due to the peroxyl-radical formation by the breakdown of AAPH (2,2'-axobis-2-methyl propanimidamide, dihydrochloride). Trolox, a water soluble vitamin E analog, serves as positive control inhibition fluorescein decay in a dose dependent manner.

[0109] **Production of Hyaluronic Acid:** Changes in the production of hyaluronic acid (HA) in human dermal fibroblasts due to each of the active ingredients, any one of the combination of ingredients, or compositions having said combinations disclosed in the specification can be measured. HA is a polysaccharide involved in stabilization of the structure of the matrix and is involved in providing turgor pressure to tissue and cells. As one non-limiting example, HA production in treated and non-treated adult human dermal fibroblasts (HDFa) cells can be determined using the Hyaluronan DuoSet ELISA kit from R&D Systems (DY3614). In this assay, for production of samples, subconfluent HDFa cells from Cascade Biologics (C-13-5C) are incubated at 37 °C and 10% CO_2 in starvation medium (0.15% fetal bovine serum and 1% Penicillin Streptomycin solution in Dulbecco's Modified Eagle Medium) for 72 hours prior to treatment. The cells are then incubated with fresh starvation medium with either test compound, positive control (phorbol 12-myristate 13-acetate from Sigma-Aldrich

(P1585) and platelet derived growth factor from Sigma-Aldrich (P3201)), or no additive for 24 hours. Media is then collected and frozen at -80 °C until use in the ELISA assay.

[0110] Briefly, the ELISA assay employs a quantitative sandwich enzyme immunoassay technique whereby a capture antibody specific for HA can be pre-coated onto a microplate. Standards and media from treated and untreated cells are pipetted into the microplate wells to enable any HA present to be bound by the immobilized antibody. After washing away any unbound substances, an enzyme-linked detection antibody specific for HA is added to the wells. Following a wash to remove any unbound antibody-enzyme reagent, a substrate solution is added to the wells to allow color development in proportion to the amount of HA bound in the initial step. The color development is stopped at a specific time and the intensity of the color at 450nm can be measured using a microplate reader.

[0111] **Production of Occludin:** Changes in the production of occludin in keratinocytes due to each of the active ingredients, any one of the combination of ingredients, or compositions having said combinations disclosed in the specification can be measured. Occludin is a protein critical to the formulation of tight junctions and the skin's moisture barrier function. A non-limiting example of how occludin production in treated and non-treated keratinocytes can be determined is by the use of a bioassay that analyzes occludin concentration in keratinocyte cell lysates. The bioassay can be performed using PROTEINSIMPLE® SIMON™ western blotting protocol. For the samples, adult human epidermal keratinocytes (HEKa) from Life Technologies (C-005-5C) can be grown at 37 °C and 5% CO2 for 24 hours in EPILIFE™ growth media with calcium from Life Technologies (M-EP-500-CA) supplemented with Keratinocyte Growth Supplement (HKGS) from Life Technologies (S-101-5). HEKa are then incubated in growth medium with test compound/extract, no compound/extract for negative control, or with 1mM $CaCl_2$ for positive control for 24 to 48 hours. The HEKa are then washed, collected, and stored on ice or colder until lysed on ice using a lysis buffer and sonication. The protein concentrations of the samples can be determined and used to normalize the samples. The lysates are stored at -80 °C until use in the bioassay.

[0112] The PROTEINSIMPLE® SIMON™ western blotting bioassay assay employs a quantitative western blotting immunoassay technique using an antibody specific for occludin to quantitatively detect occludin in the test samples. Cell samples are lysed and normalized for protein concentration. Normalized samples and molecular weight standards are then loaded

and ran on a denatured protein separation gel using capillary electrophoresis. The proteins in the gel are then immobilized and immunoprobed using a primary antibody specific for occludin. The immobilized proteins are immunoprobed with an enzyme-linked detection antibody that binds the primary antibody. A chemiluminescent substrate solution is then added to the immobilized proteins to allow chemiluminescent development in proportion to the amount of occludin bound in the immobilization. The chemiluminescent development can be stopped at a specific time and the intensity of the chemiluminescent signal can be measured and compared to positive and negative controls.

[0113] Keratinocyte Monolayer Permeability: Changes in the permeability of a keratinocyte monolayer due to each of the active ingredients, any one of the combination of ingredients, or compositions having said combinations disclosed in the specification can be measured. Keratinocyte monolayer permeability is a measure of skin barrier integrity. Keratinocyte monolayer permeability in treated and non-treated keratinocytes can be determined using, as a non-limiting example, the *In Vitro* Vascular Permeability assay by Millipore (ECM642). This assay analyzes endothelial cell adsorption, transport, and permeability. Briefly, adult human epidermal keratinocytes from Life Technologies (C-005-5C) can be seeded onto a porous collagen-coated membrane within a collection well. The keratinocytes are then incubated for 24 hours at 37 °C and 5% CO_2 in Epilife growth media with calcium from Life Technologies (M-EP-500-CA) supplemented with Keratinocyte Growth Supplement (HKGS) from Life Technologies (S-101-5). This incubation time allows the cells to form a monolayer and occlude the membrane pores. The media is then replaced with fresh media with (test sample) or without (non-treated control) test compounds/extracts and the keratinocytes are incubated for an additional 48 hours at 37 °C and 5% CO_2. To determine permeability of the keratinocyte monolayer after incubation with/without the test compound/extract, the media is replaced with fresh media containing a high molecular weight Fluorescein isothiocyanate (FITC)-Dextran and the keratinocytes are incubated for 4 hours at 37 °C and 5% CO_2. During the 4 hours incubation, FITC can pass through the keratinocytes monolayer and porous membrane into the collection well at a rate proportional to the monolayer's permeability. After the 4 hour incubation, cell viability and the content of FITC in the collection wells can be determined. For the FITC content, the media in the collection well is collected and fluorescence of the media determined at 480nm (Em) when excited at 520nm. Percent permeability and percent change in comparison to the non-treated controls can be determined by the following equations: Percent Permeability = ((Mean Ex/Em of test

sample)/Mean Ex/Em untreated control)*100; Percent Change = Percent Permeability of test sample – Percent Permeability of untreated control.

[0114] **Mushroom tyrosinase activity assay:** In mammalian cells, tyrosinase catalyzes two steps in the multi-step biosynthesis of melanin pigments from tyrosine (and from the polymerization of dopachrome). Tyrosinase is localized in melanocytes and produces melanin (aromatic quinone compounds) that imparts color to skin, hair, and eyes. Purified mushroom tyrosinase (Sigma) can be incubated with its substrate L-Dopa (Fisher) in the presence or absence of each of the active ingredients, any one of the combination of ingredients, or compositions having said combinations disclosed in the specification. Pigment formation can be evaluated by colorimetric plate reading at 490nm. The percent inhibition of mushroom tyrosinase activity can be calculated compared to non-treated controls to determine the ability of test ingredients or combinations thereof to inhibit the activity of purified enzyme. Test extract inhibition was compared with that of kojic acid (Sigma).

[0115] **Cyclooxygenase (COX) Assay:** An *in vitro* cyclooxygenase-1 and -2 (COX-1, -2) inhibition assay. COX is a bifunctional enzyme exhibiting both cyclooxygenase and peroxidase activities. The cyclooxygenase activity converts arachidonic acid to a hydroperoxy endoperoxide (Prostaglandin G2; PGG2) and the peroxidase component reduces the endoperoxide (Prostaglandin H2; PGH2) to the corresponding alcohol, the precursor of prostaglandins, thromboxanes, and prostacyclins. This COX Inhibitor screening assay measures the peroxidase component of cyclooxygenases. The peroxidase activity is assayed colorimetrically by monitoring the appearance of oxidized N,N,N',N'-tetramethyl-p-phenylenediamine (TMPD). This inhibitor screening assay includes both COX-1 and COX-2 enzymes in order to screen isozyme-specific inhibitors. The Colormetric COX (ovine) Inhibitor screening assay (#760111, Cayman Chemical) can be used to analyze the effects of each of the active ingredients, any one of the combination of ingredients, or compositions having said combinations disclosed in the specification on the activity of purified cyclooxygnase enzyme (COX-1 or COX-2). According to manufacturer instructions, purified enzyme, heme and test extracts can be mixed in assay buffer and incubated with shaking for 15 min at room temperature. Following incubation, arachidonic acid and colorimetric substrate can be added to initiate the reaction. Color progression can be evaluated by colorimetric plate reading at 590nm. The percent inhibition of COX-1 or COX-2 activity can be calculated

compared to non-treated controls to determine the ability of test extracts to inhibit the activity of purified enzyme.

[0116] **Oil Control Assay:** An assay to measure reduction of sebum secretion from sebaceous glands and/or reduction of sebum production from sebaceous glands can be assayed by using standard techniques known to those having ordinary skill in the art. In one instance, the forehead can be used. Each of the active ingredients, any one of the combination of ingredients, or compositions having said combinations disclosed in the specification can be applied to one portion of the forehead once or twice daily for a set period of days (e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, or more days), while another portion of the forehead is not treated with the composition. After the set period of days expires, then sebum secretion can be assayed by application of fine blotting paper to the treated and untreated forehead skin. This is done by first removing any sebum from the treated and untreated areas with moist and dry cloths. Blotting paper can then be applied to the treated and untreated areas of the forehead, and an elastic band can be placed around the forehead to gently press the blotting paper onto the skin. After 2 hours the blotting papers can be removed, allowed to dry and then transilluminated. Darker blotting paper correlates with more sebum secretion (or lighter blotting paper correlates with reduced sebum secretion.

[0117] **Erythema Assay:** An assay to measure the reduction of skin redness can be evaluated using a Minolta Chromometer. Skin erythema may be induced by applying a 0.2% solution of sodium dodecyl sulfate on the forearm of a subject. The area is protected by an occlusive patch for 24hrs. After 24 hrs, the patch is removed and the irritation-induced redness can be assessed using the a* values of the Minolta Chroma Meter. The a* value measures changes in skin color in the red region. Immediately after reading, the area is treated with the active ingredients, any one of the combination of ingredients, or compositions having said combinations disclosed in the specification. Repeat measurements can be taken at regular intervals to determine the formula's ability to reduce redness and irritation.

[0118] **Skin Clarity and Reduction in Freckles and Age Spots Assay:** Skin clarity and the reduction in freckles and age spots can be evaluated using a Minolta Chromometer. Changes in skin color can be assessed to determine irritation potential due to product treatment using the a* values of the Minolta Chroma Meter. The a* value measures changes in skin color in the red region. This is used to determine whether each of the active ingredients, any one of the combination of ingredients, or compositions having said combinations disclosed in the

specification is inducing irritation. The measurements can be made on each side of the face and averaged, as left and right facial values. Skin clarity can also be measured using the Minolta Meter. The measurement is a combination of the a*, b, and L values of the Minolta Meter and is related to skin brightness, and correlates well with skin smoothness and hydration. Skin reading is taken as above. In one non-limiting aspect, skin clarity can be described as L/C where C is chroma and is defined as (a2+ b2)1/2.

[0119] Skin Dryness, Surface Fine Lines, Skin Smoothness, and Skin Tone Assay: Skin dryness, surface fine lines, skin smoothness, and skin tone can be evaluated with clinical grading techniques. For example, clinical grading of skin dryness can be determined by a five point standard Kligman Scale: (0) skin is soft and moist; (1) skin appears normal with no visible dryness; (2) skin feels slightly dry to the touch with no visible flaking; (3) skin feels dry, tough, and has a whitish appearance with some scaling; and (4) skin feels very dry, rough, and has a whitish appearance with scaling. Evaluations can be made independently by two clinicians and averaged.

[0120] Clinical Grading of Skin Tone Assay: Clinical grading of skin tone can be performed *via* a ten point analog numerical scale: (10) even skin of uniform, pinkish brown color. No dark, erythremic, or scaly patches upon examination with a hand held magnifying lens. Microtexture of the skin very uniform upon touch; (7) even skin tone observed without magnification. No scaly areas, but slight discolorations either due to pigmentation or erythema. No discolorations more than 1 cm in diameter; (4) both skin discoloration and uneven texture easily noticeable. Slight scaliness. Skin rough to the touch in some areas; and (1) uneven skin coloration and texture. Numerous areas of scaliness and discoloration, either hypopigmented, erythremic or dark spots. Large areas of uneven color more than 1 cm in diameter. Evaluations were made independently by two clinicians and averaged.

[0121] Clinical Grading of Skin Smoothness Assay: Clinical grading of skin smoothness can be analyzed *via* a ten point analog numerical scale: (10) smooth, skin is moist and glistening, no resistance upon dragging finger across surface; (7) somewhat smooth, slight resistance; (4) rough, visibly altered, friction upon rubbing; and (1) rough, flaky, uneven surface. Evaluations were made independently by two clinicians and averaged.

[0122] Skin Smoothness and Wrinkle Reduction Assay With Methods Disclosed in Packman *et al.* (1978): Skin smoothness and wrinkle reduction can also be assessed

visually by using the methods disclosed in Packman *et al.* (1978). For example, at each subject visit, the depth, shallowness and the total number of superficial facial lines (SFLs) of each subject can be carefully scored and recorded. A numerical score was obtained by multiplying a number factor times a depth/width/length factor. Scores are obtained for the eye area and mouth area (left and right sides) and added together as the total wrinkle score.

[0123] Appearance of Lines and Wrinkles Assay with Replicas: The appearance of lines and wrinkles on the skin can be evaluated using replicas, which is the impression of the skin's surface. Silicone rubber like material can be used. The replica can be analyzed by image analysis. Changes in the visibility of lines and wrinkles can be objectively quantified *via* the taking of silicon replicas form the subjects' face and analyzing the replicas image using a computer image analysis system. Replicas can be taken from the eye area and the neck area, and photographed with a digital camera using a low angle incidence lighting. The digital images can be analyzed with an image processing program and are of the replicas covered by wrinkles or fine lines was determined.

[0124] Skin Firmness Assay with a Hargens Ballistometer: Skin firmness can be measured using a Hargens ballistometer, a device that evaluates the elasticity and firmness of the skin by dropping a small body onto the skin and recording its first two rebound peaks. The ballistometry is a small lightweight probe with a relatively blunt tip (4 square mm-contact area) was used. The probe penetrates slightly into the skin and results in measurements that are dependent upon the properties of the outer layers of the skin, including the stratum corneum and outer epidermis and some of the dermal layers.

[0125] Skin Softness/Suppleness Assay with a Gas Bearing Electrodynamometer: Skin softness/suppleness can be evaluated using the Gas Bearing Electrodynamometer, an instrument that measures the stress/strain properties of the skin. The viscoelastic properties of skin correlate with skin moisturization. Measurements can be obtained on the predetermined site on the cheek area by attaching the probe to the skin surface with double-stick tape. A force of approximately 3.5 gm can be applied parallel to the skin surface and the skin displacement is accurately measured. Skin suppleness can then be calculated and is expressed as DSR (Dynamic Spring Rate in gm/mm).

[0126] Surface Contour of the Skin Assay with a Profilometer/Stylus Method: The surface contour of the skin can be measured by using the profilometer/Stylus method. This

includes either shining a light or dragging a stylus across the replica surface. The vertical displacement of the stylus can be fed into a computer *via* a distance transducer, and after scanning a fixed length of replica a cross-sectional analysis of skin profile can be generated as a two-dimensional curve. This scan can be repeated any number of times along a fix axis to generate a simulated 3-D picture of the skin. Ten random sections of the replicas using the stylus technique can be obtained and combined to generate average values. The values of interest include Ra which is the arithmetic mean of all roughness (height) values computed by integrating the profile height relative to the mean profile height. Rt which is the maximum vertical distance between the highest peak and lowest trough, and Rz which is the mean peak amplitude minus the mean peak height. Values are given as a calibrated value in mm. Equipment should be standardized prior to each use by scanning metal standards of know values. Ra Value can be computed by the following equation: Ra = Standardize roughness; *l*m = the traverse (scan) length; and y = the absolute value of the location of the profile relative to the mean profile height (x-axis).

[0127] MELANODERM™ Assay: In other non-limiting aspects, the efficacy of each of the active ingredients, any one of the combination of ingredients, or compositions having said combinations disclosed in the specification can be evaluated by using a skin analog, such as, for example, MELANODERMTM. Melanocytes, one of the cells in the skin analog, stain positively when exposed to L-dihydroxyphenyl alanine (L-DOPA), a precursor of melanin. The skin analog, MELANODERMTM, can be treated with a variety of bases containing each of the active ingredients, any one of the combination of ingredients, or compositions having said combinations disclosed in the specification or with the base alone as a control. Alternatively, an untreated sample of the skin analog can be used as a control.

[0128] Inhibition of Hyaluronidase Activity: Changes in the activity of hyaluronidase due to each of the active ingredients, any one of the combination of ingredients, or compositions having said combinations disclosed in the specification can be measured. Hyaluronidase is an enzyme that degrades HA. HA is a polysaccharide involved in stabilization of the structure of the matrix and is involved in providing turgor pressure to tissue and cells. As one non-limiting example, hyaluronidase activity can be determined using an *in vitro* protocol modified from Sigma-Aldrich protocol # EC 3.2.1.35. Briefly, hyaluronidase type 1-S from Sigma-Aldrich (H3506) is added to microplate reaction wells containing test compound or controls. Tannic acid can be used as a positive control inhibitor, no test

compound can be added for the control enzyme, and wells with test compound or positive control but without hyaluronidase can be used as a background negative control. The wells are incubated at 37 °C for 10 minutes before addition of substrate (HA). Substrate is added and the reactions incubated at 37 °C for 45 minutes. A portion of each reaction solution is then transferred to and gently mixed in a solution of sodium acetate and acetic acid pH 3.75 to stop that portion of the reaction (stopped wells). The stopped wells and the reaction wells should both contain the same volume of solution after addition of the portion of the reaction solution to the stopped wells. Both the reaction wells and the stopped wells are incubated for 10 minutes at room temperature. Absorbance at 600nm is then measured for both the reaction wells and the stopped wells. Inhibition can be calculated using the following formulas: Inhibitor (or control) activity = (Inhibitor stopped wells absorbance at 600nm – inhibitor reaction wells absorbance at 600nm); Initial activity = control enzyme absorbance at 600nm; Percent Inhibition = [(Initial activity/ Inhibitor Activity)*100]-100.

[0129] Peroxisome Proliferator-Activated Receptor Gamma (PPAR-γ) Activity: Changes in the activity of PPAR-γ due to each of the active ingredients, any one of the combination of ingredients, or compositions having said combinations disclosed in the specification can be measured. PPAR-γ is a receptor critical for the production of sebum. As one non-limiting example, the activity of PPAR-γ can be determined using a bioassay that analyzes the ability of a test compound or composition to inhibit binding of a ligand. Briefly, fluorescent small-molecule pan-PPAR ligand, FLUORMONE™ Pan-PPAR Green, available from Life Technologies (PV4894), can be used to determine if test compounds or compositions are able to inhibit binding of the ligand to PPAR-γ. The samples wells include PPAR-γ and fluorescent ligand and either: test compound or composition (test); a reference inhibitor, rosiglitazone (positive control); or no test compound (negative control). The wells are incubated for a set period of time to allow the ligand opportunity to bind the PPAR-γ. The fluorescence polarization of each sample well can then be measured and compared to the negative control well to determine the percentage of inhibition by the test compound or composition.

[0130] Cytokine Array: Human epidermal keratinocytes are cultured to 70-80% confluency. The media in the plate is aspirated and 0.025% trypsin/EDTA is added. When the cells became rounded, the culture dish is gently tapped to release the cells. The trypsin/EDTA containing cells are removed from the culture dish and neutralized. Cells are centrifuged for 5

min. at 180 x *g* to form a pellet of cells. The supernatant is aspirated. The resulting pellet is resuspended in EPILIFE™ media (Cascade Biologics). The cells are seeded in 6-well plates at approximately 10-20% confluency. After the cells became approximately 80% confluent, the media is aspirated and 1.0 ml of EPILIFE™, along with phorbol 13-Myristate 12-acetate ("PMA") (a known inducer of inflammation) and the test composition dilutions are added to two replicate wells (i.e., 1.0% (100µl of 100X stock) and 0.1% (10µl of 100X stock) test compositions are diluted into a final volume of 1 ml EpiLife Growth Medium). The media is gently swirled to ensure adequate mixing. In addition, 1.0 ml of EPILIFE™ is added to the control wells, with and without additional PMA. The plates are then incubated at 37±1°C and 5.0±1% CO_2 for approximately 5 hours after dosing. Following this 5-hour incubation, all media is collected in conical tubes and frozen at -70°C.

[0131] For analysis, a 16-pad hybridization chamber is attached to 16-pad FAST slides arrayed in triplicate with 16 anti-cytokine antibodies plus experimental controls (Whatman BioSciences), and the slides are placed into a FASTFrame (4 slides per frame) for processing. Arrays are blocked for 15 min. at room temp. using 70 ml S&S Protein Array Blocking buffer (Whatman Schleicher and Scheull). Blocking buffer is removed and 70 ml of each supernatant sample is added to each array. Arrays are incubated for 3 hours at room temp. with gentle agitation. Arrays are washed 3 times with TBS-T. Arrays are treated with 70 ml of an antibody cocktail, containing one biotinylated antibody corresponding to each of the arrayed capture antibodies. Arrays are incubated for 1 hour at room temp. with gentle agitation. Arrays are washed 3 times with TBS-T. Arrays are incubated with 70 ml of a solution containing streptavidin-Cy5 conjugate for 1 hour at room temp. with gentle agitation. Arrays are washed 3 times with TBS-T, quickly rinsed in de-ionized water, and dried.

[0132] Slides can be imaged in a Perkin-Elmer ScanArray 4000 confocal fluorescent imaging system. Array images can be saved and analyzed using Imaging Research ArrayVision software. Briefly, spot intensities are determined by subtracting background signal. Spot replicates from each sample condition can be averaged and then compared to the appropriate controls.

[0133] **Endothelial Tube Formation:** Endothelial tube formation is involved in angiogenesis and micro-vessel capillary formation. Capillary formation and angiogenesis may contribute to redness and rosacea of the skin. The ability for endothelial cells to form tubes in the presence or absence of test extracts and compounds may be determined using a capillary

tubule disruption assay with pre-formed primary human umbilical vein endothelial cells (HUVEC) in a cell culture system.

[0134] Briefly, HUVECs are cultured *in vitro* on Extracellular Matrix, which stimulates the attachment and tubular morphogenesis of endothelial cells to form capillary-like lumen structures. These *in vitro* formed capillary tubules are similar to human blood vessel capillaries in many aspects. The capillary tube assay is based on this phenomenon and is used for evaluation of potential vasculature targeting agents.

[0135] HUVEC cultures are grown in a 5% CO_2 37ºC cell incubator. The full growth medium for HUVECs is Endothelial Cell Basal Medium (EBM) supplemented with 2% fetal bovine serum (FBS), 12 μg /ml bovine brain extract, 1 μg/ml hydrocortisone, and 1 μg/ml GA-1000 (gentamicin-amphothericin). HUVEC cultures between passage 3 and 8 may be used for all assay experiments.

[0136] HUVECs are pre-labeled with fluorescent agent Calcein AM and seeded in Extracellular Matrix coated 96-well culture plate with their full growth medium. After about four hours of the morphogenesis process, the endothelial capillary tubes should be formed. Then, test agent in designed doses in 50μl volume is applied into the formed capillary tubule cultures as treatment conditions. The no-treatment controls can be added with vehicle of test agents. Sutent, a FDA approved anti-angiogenic drug one concentration can be included as assay performance control. After about six hours of treatment, the endothelial tubule morphology in each well is examined by microscopy, imaged, and the capillary disrupting activities under treatment conditions can be quantitatively analyzed. Each test conditions can be conducted in duplicate wells, including controls.

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[0137] All of the compositions and/or methods disclosed and claimed herein can be made and executed without undue experimentation in light of the present disclosure. While the compositions and methods of this invention have been described in terms of preferred embodiments, it will be apparent to those of skill in the art that variations may be applied to the compositions and/or methods and in the steps or in the sequence of steps of the method described herein without departing from the concept, spirit and scope of the invention. More specifically, it will be apparent that certain agents which are both chemically and

physiologically related may be substituted for the agents described herein while the same or similar results would be achieved. All such similar substitutes and modifications apparent to those skilled in the art are deemed to be within the spirit, scope and concept of the invention as defined by the appended claims.

CLAIMS

1. A method of enhancing skin hydration in a person, the method comprising topically applying to the skin of the person a composition comprising an effective amount of *Verbena officinalis* extract, hydrolyzed sodium hyaluronate, and ceramide, wherein topical application of the composition attracts and binds moisture in the air to the skin's outer layers, transports surface moisture below the skin's stratum corneum, increases skin moisture content, plumps and tightens the skin, protects the skin from moisture loss to the environment, supports optimal skin barrier function, and/or stimulates production of the skin's own Natural Moisturizing Factor.

2. The method of claim 1, wherein the composition comprises 0.001 to 1% by weight of *Verbena officinalis* extract, 0.01 to 10% by weight of hydrolyzed sodium hyaluronate, and 0.001 to 1% by weight of ceramide.

3. The method of claim 1, wherein the composition is combined with one or more other skin care compositions prior to application to the skin.

4. The method of claim 1, wherein the composition further comprises one or more of: a humectant, an emollient, a skin conditioning agent, and/or a pH adjuster.

5. The method of claim 1, wherein the composition further comprises an effective amount of one or more of: water, glycerin, pentylene glycol, betaine, and/or phenoxyethanol to increase skin moisture content and/or enhance a skin product's hydrating effect.

6. The method of claim 5, wherein the composition comprises:
   1 to 95% by weight water;
   1 to 30% by weight glycerin;
   0.1 to 15% by weight pentylene glycol;
   0.1 to 15% by weight betaine; and/or
   0.05 to 10% by weight phenoxyethanol.

7. The method of claim 1, wherein the composition further comprises one or more of xanthan gum and sodium hyaluronate.

8. The method of claim 7, wherein the composition comprises:
0.01 to 5% by weight xanthan gum;
0.01 to 1% by weight sodium hyaluronate.

9. The method of claim 1, wherein the composition comprises an effective amount of *Verbena officinalis* extract, hydrolyzed sodium hyaluronate, and ceramide, wherein topical application of the composition increases skin moisture content by at least 50% after a single application.

10. The method of claim 1, wherein the composition comprises an effective amount of *Verbena officinalis* extract, hydrolyzed sodium hyaluronate, and ceramide, wherein topical application of the composition stimulates production of the skin's own Natural Moisturizing Factor.

11. A method of enhancing the hydrating activity of a skin care composition, the method comprising combining an enhancing composition and the skin care composition, wherein the enhancing composition comprises an effective amount of *Verbena officinalis* extract, hydrolyzed sodium hyaluronate, and ceramide to increase or promote an ability of the cosmetic composition to attract and bind moisture in the air to the skin's outer layers, transport surface moisture below the skin's stratum corneum, increase skin moisture content, plump and tighten the skin, protect the skin from moisture loss to the environment, support optimal skin barrier function, and/or stimulate production of the skin's own Natural Moisturizing Factor.

12. The method of claim 11, wherein the enhancing composition comprises an effective amount of *Verbena officinalis* extract, hydrolyzed sodium hyaluronate, and ceramide to increase skin moisture content by at least 50% in a single application.

13. The method of claim 11, wherein the enhancing composition comprises an effective amount of *Verbena officinalis* extract, hydrolyzed sodium hyaluronate, and ceramide to stimulate production of the skin's own Natural Moisturizing Factor.

14. A product enhancing composition comprising an effective amount of a combination of *Verbena officinalis* extract, hydrolyzed sodium hyaluronate, and ceramide to attract and bind moisture in the air to the skin's outer layers, transport surface moisture below the skin's stratum

corneum, increase skin moisture content, plump and tighten the skin, protect the skin from moisture loss to the environment, support optimal skin barrier function, and/or stimulate production of the skin's own Natural Moisturizing Factor.

15. The composition of claim 14, comprising 0.001 to 1% by weight of *Verbena officinalis* extract, 0.01 to 10% by weight of hydrolyzed sodium hyaluronate, and 0.001 to 1% by weight of ceramide.

16. The composition of claim 14, further comprising one or more of: a humectant, an emollient, a skin conditioning agent, and/or a pH adjuster.

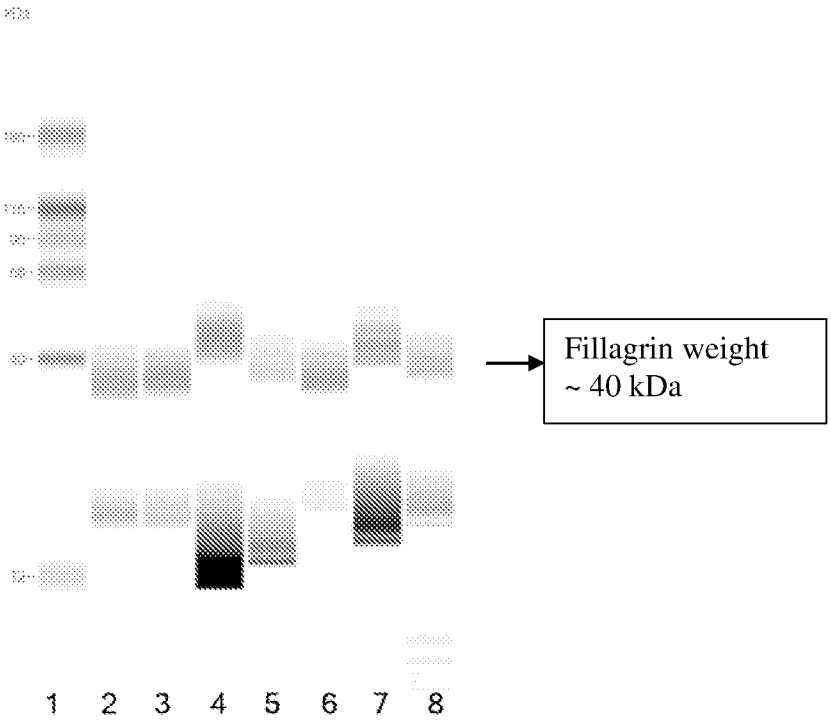
17. The composition of claim 14, further comprising an effective amount of one or more of: water, glycerin, pentylene glycol, betaine, and/or phenoxyethanol to increase skin moisture content and/or enhance a skin product's hydrating effect.

18. The composition of claim 17, comprising:
1 to 95% by weight water;
1 to 30% by weight glycerin;
0.1 to 15% by weight pentylene glycol;
0.1 to 15% by weight betaine; and/or
0.05 to 10% by weight phenoxyethanol.

19. The composition of claim 14, further comprising one or more of xanthan gum and sodium hyaluronate.

20. The composition of claim 19, comprising:
0.01 to 5% by weight xanthan gum;
0.01 to 1% by weight sodium hyaluronate.

DRAWING



Column No.	Test Composition
1	Biotinylated Ladder
2	Control
3	Calcium
4	*Imperata cylindrical* extract
5	*Verbena officinalis* extract
6	*Laminaria saccharina* extract
7	marine plankton extract
8	*Opuntia ficua-indica* extract

THE FIGURE

INTERNATIONAL SEARCH REPORT

International application No
PCT/US2021/070433

A. CLASSIFICATION OF SUBJECT MATTER
INV. A61K8/68 A61K8/73 A61K8/9789 A61Q19/00 A61Q19/08
ADD.

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

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
A61K A61Q

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

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

EPO-Internal, BIOSIS, CHEM ABS Data, COMPENDEX, EMBASE, EMBL, FSTA, INSPEC, IBM-TDB, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	CN 109 172 506 A (DALIAN OUMAISHA IND CORPORATION) 11 January 2019 (2019-01-11)	1,2,4,5, 7-17,19, 20
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Y	CN 109 464 342 B (GUANGZHOU BEST BEAUTY COSMETICS CO LTD) 8 November 2019 (2019-11-08) abstract	1-20

Y	FR 2 962 904 A1 (SILAB SA [FR]) 27 January 2012 (2012-01-27) the whole document	1-20

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[X] Further documents are listed in the continuation of Box C.

[X] See patent family annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent but published on or after the international filing date

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"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
6 August 2021	17/08/2021

Name and mailing address of the ISA/	Authorized officer
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Form PCT/ISA/210 (second sheet) (April 2005)

INTERNATIONAL SEARCH REPORT

International application No
PCT/US2021/070433

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	EP 3 498 259 A1 (YANG SHENG TANG SHANGHAI COSMETIC R&D CO LTD [CN]) 19 June 2019 (2019-06-19) paragraph [0002] paragraph [0005] - paragraph [0019] paragraph [0023] - paragraph [0024] examples claims	1-20
A	US 2018/185268 A1 (FRUSHOUR MICHAEL [US] ET AL) 5 July 2018 (2018-07-05) the whole document	1-20
A	WO 2017/048807 A1 (JRX BIOTECHNOLOGY INC [US]) 23 March 2017 (2017-03-23) the whole document	1-20

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INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
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