

TOPICAL ANTIOXIDANT COMPOSITIONS AND METHODS OF USING THE SAME

CROSS-REFERENCE TO RELATED APPLICATIONS

[0001] This application claims priority to (i) U.S. Provisional Patent Application No. 63/613,403, filed December 21, 2023; (ii) U.S. Provisional Patent Application No. 63/580,278, filed September 1, 2023; and (iii) U.S. Provisional Patent Application No. 63/526,911, filed July 14, 2023, the entire contents of all of which are hereby incorporated by reference herein.

FIELD

[0002] The present disclosure relates to antioxidant topical compositions for neutralizing reactive oxygen species (ROS) in the skin and stimulating collagenesis and elastogenesis.

BACKGROUND

[0003] The following description of the background of the present technology is provided simply as an aid in understanding the present technology and is not admitted to describe or constitute prior art to the present technology

[0004] The presence of reactive oxygen species (ROS) in the body causes oxidative stress, a major contributor to pathogenic processes of many diseases. In particular, the skin is constantly exposed to UV radiation, producing ROS and necessitating antioxidant production by the outer stratum corneum layer to neutralize these ROS. This protective mechanism mobilizes lipophilic and hydrophilic low-molecular-weight antioxidants, including vitamins (*e.g.*, A, C, D, and E), enzymes (*e.g.*, superoxide dismutase, catalase, and glutathione peroxidase), and other compounds (*e.g.*, melanin, flavonoids, lipoic acid, selenium, and coenzyme Q10), which work collectively to neutralize the ROS in the body. However, with time, aging, and external stresses, antioxidant levels in the skin are depleted, thereby diminishing this important protective system. Thus, there exists a need for topical antioxidant replacements.

[0005] Vitamin C, also known as ascorbic acid, is a potent antioxidant that neutralizes and removes oxidants after skin exposure to ultraviolet radiation. Additionally, Vitamin C is a known enhancer of collagen deposition, and has been reported to inhibit elastogenesis. Certain types of ascorbic acid are suspected of destabilizing tropoelastin mRNA and causing excess hydroxylation on prolyl/lysyl residues of tropoelastin molecules, thereby promoting their intracellular accumulation and inhibiting their secretion. However, sodium ascorbate (SA), a Vitamin C sodium salt, has been demonstrated to stimulate both collagenesis and elastogenesis, with investigators endorsing its use in the treatment of wrinkled and stretch-marked skin.

[0006] Thus, there exists great interest in Vitamin C antioxidant topical formulations. However, it has been found that UV light can degrade Vitamin C. For topical application, stabilizing Vitamin C against exposure to light and oxidation, and ensuring penetration into the skin are serious challenges. Indeed, very few topical Vitamin C formulations can effectively reduce ROS while increasing collagenesis, and elastogenesis. Moreover, applying high concentrations of Vitamin C to skin can lead to redness, irritation, inflammation and possibly collagen and elastin degradation. Accordingly, there is great interest in combatting the damage cause by ROS and increasing collagen and elastin synthesis, while minimizing the damage caused by high concentrations of certain antioxidants, such as Vitamin C, in skin. The present disclosure seeks to overcome some of these limitations with a combination of antioxidants and low concentrations of sodium ascorbate that can penetrate the skin and increase elastogenesis while effectively reducing ROS present in skin.

SUMMARY

[0007] In one aspect, which may be combined with any other aspect or embodiment, the present disclosure relates to a topical composition comprising: a hydrophilic antioxidant, wherein the hydrophilic antioxidant comprises sodium ascorbate; an enzymatic antioxidant; and a hydrophobic antioxidant.

[0008] In some embodiments, the sodium ascorbate is present at a concentration of about 0.01 wt.% to about 1.0 wt.%, relative to the total weight of the composition. In some

embodiments, the sodium ascorbate is present at a concentration of about 0.02 wt.% to about 0.10 wt.%, relative to the total weight of the composition.

[0009] In some embodiments, the hydrophilic antioxidant further comprises, lactoferrin, ergothioneine, oleuropein, *Punica granatum* extract, ectoine, *Centella asiatica* extract, carnosine, *Camellia sinensis* extract, or any combination thereof. In some embodiments, the hydrophilic antioxidant comprises lactoferrin. In some embodiments, the lactoferrin is present at a concentration of 0.01 wt.% to 0.1 wt.%.

[0010] In some embodiments, the enzymatic antioxidant comprises ubiquinone, betaine, superoxide dismutase, catalase, glutathione peroxidase, or any combination thereof. In some embodiments, the enzymatic antioxidant comprises ubiquinone. In some embodiments, the ubiquinone is present in the composition at a concentration of 0.001 wt.% to 0.1 wt.%, relative to the total weight of the composition. In some embodiments, the ubiquinone is present in the composition at a concentration of 0.005 wt.% to 0.05 wt.%, relative to the total weight of the composition.

[0011] In some embodiments, the hydrophobic antioxidant comprises bisabolol, phytoene, phytofluene and physalis angulate, or any combination thereof. In some embodiments, the hydrophobic antioxidant is present in the composition at a concentration of 0.1 wt.% to 1.2 wt.%, relative to the total weight of the composition.

[0012] In some embodiments, the sodium ascorbate is encapsulated in a first liposome. In some embodiments, the first liposome comprises phosphatidylcholine.

[0013] In some embodiments, the topical composition comprises a second hydrophilic antioxidant, wherein the second antioxidant is lactoferrin encapsulated in a second liposome. In some embodiments, the second liposome comprises propanediol, lecithin, or any combination thereof. In some embodiments, the second liposome is different from the first liposome.

[0014] In some embodiments, the total concentration of antioxidants in the composition is less than 15 wt.%, relative to the total weight of the composition. In some embodiments, the

total concentration of antioxidants in the composition is less than 10 wt.%, relative to the total weight of the composition.

[0015] In some embodiments, the hydrophilic antioxidant comprises sodium ascorbate and lactoferrin; the enzymatic antioxidant comprises ubiquinone; and the hydrophobic antioxidant comprises one or more of bisabolol, phytoene, phytofluene, *Physalis angulata* or a combination thereof. In some embodiments, the sodium ascorbate is present at a concentration of 0.02 wt.% to 0.1 wt.%; the lactoferrin is present at a concentration of 0.02 wt.% to 0.08 wt.%; and the ubiquinone is present at a concentration of 0.005 wt.% to 0.5 wt.%.

[0016] In some embodiments, the sodium ascorbate, the enzymatic antioxidant, and the hydrophobic antioxidant are present at concentrations sufficient to reduce reactive oxygen species in skin. In some embodiments, at least one of the following is achieved: the sodium ascorbate and the lactoferrin are present at concentrations sufficient to synergistically promote elastogenesis or collagenesis in skin or to synergistically reduce ROS in skin; or any combination of the sodium ascorbate, the lactoferrin, the enzymatic antioxidant, and the hydrophobic antioxidant are present at concentrations sufficient to synergistically promote at least one of elastogenesis or collagenesis in skin or to synergistically reduce ROS in skin.

[0017] In one aspect, which may be combined with any other aspect or embodiment, the present disclosure relates to a topical composition, comprising: sodium ascorbate; and lactoferrin, wherein the sodium ascorbate and lactoferrin synergistically enhance elastogenesis.

[0018] In some embodiments, the sodium ascorbate is present at a concentration of about 0.01 wt.% to about 1.0 wt.%, relative to the total weight of the composition. In some embodiments, the sodium ascorbate is present at a concentration of about 0.02 wt.% to about 0.10 wt.%, relative to the total weight of the composition. In some embodiments, the lactoferrin is present at a concentration of 0.01 wt.% to 0.1 wt.%.

[0019] In some embodiments, the composition enhances tropoelastin production or CD44 expression in skin. In some embodiments, the composition enhances tropoelastin production

relative to a composition comprising only one of lactoferrin or sodium ascorbate. In some embodiments, the composition preserves CD44 expression relative to a composition comprising sodium ascorbate but not comprising lactoferrin.

[0020] In one aspect, which may be combined with any other aspect or embodiment, the present disclosure relates to a method for stimulating production of collagen fibers and elastin fibers in skin, the method comprising: administering the topical composition according to any of the embodiments disclosed herein to the skin.

[0021] In one aspect, which may be combined with any other aspect or embodiment, the present disclosure relates to a method for reducing the effects of aging in skin, the method comprising: instructing the administration of the topical composition according to any of the embodiments disclosed herein to the skin.

[0022] In one aspect, which may be combined with any other aspect or embodiment, the present disclosure relates to a method for reducing the effects of aging in skin, the method comprising: administering the topical composition according to any of the embodiments disclosed herein to the skin.

[0023] In one aspect, which may be combined with any other aspect or embodiment, the present disclosure relates to a method for reducing the amount of ROS in skin, the method comprising: instructing the administration of the topical composition according to any of the embodiments disclosed herein to the skin.

[0024] In one aspect, which may be combined with any other aspect or embodiment, the present disclosure relates to a method for reducing the amount of ROS in skin, the method comprising: administering the topical composition according to any of the embodiments disclosed herein to the skin.

[0025] In one aspect, which may be combined with any other aspect or embodiment, the present disclosure relates to a method for improving the appearance of skin, the method comprising: instructing the administration of the topical composition according to any of the embodiments disclosed herein to the skin.

[0026] In one aspect, which may be combined with any other aspect or embodiment, the present disclosure relates to a method for improving the appearance of skin, the method comprising: administering the topical composition according to any of the embodiments disclosed herein to the skin.

[0027] In one aspect, which may be combined with any other aspect or embodiment, the present disclosure relates to a method for reducing the appearance of wrinkles or crepiness in skin, the method comprising: instructing the administration of the topical composition according to any of the embodiments disclosed herein to the skin.

[0028] In one aspect, which may be combined with any other aspect or embodiment, the present disclosure relates to a method for reducing the appearance of wrinkles or crepiness in skin, the method comprising: administering the topical composition according to any of the embodiments disclosed herein to the skin.

[0029] In one aspect, which may be combined with any other aspect or embodiment, the present disclosure relates to a method for increasing tropoelastin production in skin, the method comprising: instructing the administration of the topical composition according to any of the embodiments disclosed herein to the skin.

[0030] In one aspect, which may be combined with any other aspect or embodiment, the present disclosure relates to a method for increasing tropoelastin production in skin, the method comprising: administering the topical composition according to any of the embodiments disclosed herein to the skin.

[0031] In one aspect, which may be combined with any other aspect or embodiment, the present disclosure relates to a method for increasing CD44 expression in skin, the method comprising: instructing the administration of the topical composition according to any of the embodiments disclosed herein to the skin.

[0032] In one aspect, which may be combined with any other aspect or embodiment, the present disclosure relates to a method for increasing CD44 expression in skin, the method comprising: administering the topical composition according to any of the embodiments disclosed herein to the skin.

[0033] In one aspect, which may be combined with any other aspect or embodiment, the present disclosure relates to a composition according to any of the embodiments disclosed herein for use in stimulating elastogenesis in skin, stimulating production of collagen fibers and elastin fibers in skin, increasing tropoelastin production in skin, increasing CD44 expression in skin, reducing the effects of aging in skin, reducing the amount of ROS in skin, improving the appearance of skin, or reducing the appearance of wrinkles or crepiness in skin.

[0034] In one aspect, which may be combined with any other aspect or embodiment, the present disclosure relates to use of a composition according to any of the embodiments disclosed herein for stimulating elastogenesis in skin, stimulating production of collagen fibers and elastin fibers in skin, increasing tropoelastin production in skin, increasing CD44 expression in skin, reducing the effects of aging in skin, reducing the amount of ROS in skin, improving the appearance of skin, or reducing the appearance of wrinkles or crepiness in skin.

[0035] In one aspect, which may be combined with any other aspect or embodiment, the present disclosure relates to a composition according to any of the embodiments disclosed herein for use in the manufacture of a medicament for stimulating elastogenesis in skin, stimulating production of collagen fibers and elastin fibers in skin, increasing tropoelastin production in skin, increasing CD44 expression in skin, reducing the effects of aging in skin, reducing the amount of ROS in skin, improving the appearance of skin, or reducing the appearance of wrinkles or crepiness in skin.

[0036] Additional aspects and/or embodiments of the present technology will be provided, without limitation, in the detailed description of the present technology set forth below. The following detailed description is exemplary and explanatory, but it is not intended to be limiting.

BRIEF DESCRIPTION OF THE DRAWINGS

[0037] Various objects, aspects, features, and advantages of the disclosure will become more apparent and better understood by referring to the Detailed Description taken in conjunction with the accompanying Figures.

[0038] **FIGs. 1A-1F** are images of stained human skin specimens showing the antioxidant effect of Formulation A (**FIGs. 1A-1C**) and Formulation B (**FIGs. 1D-1F**) in human skin exposed to UV irradiation, using fluorescence of the DCFH-DA probe. The DCFH-DA probe undergoes deacetylation, producing DCHF. In the presence of ROS, DCHF is oxidized to DCF, which is highly fluorescent (green). Nuclei are detected by DAPI staining. The individual images show the effect of Formulation A (**FIG. 1C**) versus UV-treated (**FIG. 1B**) and untreated (**FIG. 1A**) samples and the effect of Formulation B (**FIG. 1F**) versus UV-treated (**FIG. 1E**) and untreated (**FIG. 1D**) samples. The scale bar in each image represents 20 μm .

[0039] **FIG. 2** shows quantitative evaluation of fluorescence (DCFH-DA probe) for human skin fragments exposed to UV radiation and treated with Formulation A and Formulation B, versus untreated human skin samples. The data represent the mean and standard deviation for six replicates. Statistical significance was determined by ANOVA followed by Bonferroni correction.

[0040] **FIGs. 3A-3C** show images of immunostained human skin explants cultured *ex vivo* and treated with Formulation A (**FIG. 3B**) or Formulation B (**FIG. 3C**) versus untreated samples (**FIG. 3A**). Skin samples were immunostained to detect tropoelastin (red) and CD44 (yellow). Nuclei were detected using DAPI staining.

[0041] **FIG. 4A** shows quantitative evaluation of signal intensity for tropoelastin in immunostained human skin explants cultured *ex vivo* and treated with Formulation A or Formulation B, versus untreated skin. Signal intensities were quantified using ImageJ.

[0042] **FIG. 4B** shows quantitative evaluation of signal intensity for CD44 in immunostained human skin explants cultured *ex vivo* and treated with Formulation A or Formulation B, versus untreated skin. Signal intensities were quantified using ImageJ.

[0043] **FIGs. 5A-B** show Movat-stained biopsies (10X) at baseline (**FIG. 5A**) and after 12 weeks (**FIG. 5B**) of applying a topical composition according to the present disclosure.

[0044] **FIGs. 6A-B** show Movat-stained biopsies (10X) at baseline (**FIG. 6A**) and after 12 weeks (**FIG. 6B**) of applying a topical composition according to the present disclosure.

[0045] **FIGs. 7A-B** show Movat-stained biopsies (10X) at baseline (**FIG. 7A**) and after 12 weeks (**FIG. 7B**) of applying a topical composition according to the present disclosure.

[0046] **FIGs. 8A-B** show Movat-stained biopsies (10X) at baseline (**FIG. 8A**) and after 12 weeks (**FIG. 8B**) of applying a topical composition according to the present disclosure.

[0047] **FIGs. 9A-B** show Movat-stained biopsies (10X) at baseline (**FIG. 9A**) and after 12 weeks (**FIG. 9B**) of applying a topical composition according to the present disclosure.

[0048] **FIGs. 10A-B** show H&E-stained biopsies (40X) at baseline (**FIG. 10A**) and after 12 weeks (**FIG. 10B**) of applying a topical composition according to the present disclosure.

[0049] **FIGs. 11A-B** show Herovici-stained biopsies (40X) at baseline (**FIG. 11A**) and after 12 weeks (**FIG. 11B**) of applying a topical composition according to the present disclosure.

[0050] **FIGs. 12A-12C** show images of immunostained human skin explants cultured *ex vivo* and treated with lactoferrin (**FIG. 12B**) or sodium ascorbate (**FIG. 12C**) versus an untreated sample (**FIG. 12A**). Skin samples were immunostained to detect tropoelastin (red) and CD44 (yellow). Nuclei were detected using DAPI staining.

[0051] **FIGs. 13A-13C** show images of immunostained human skin explants cultured *ex vivo* and treated with lactoferrin (**FIG. 13A**), sodium ascorbate (**FIG. 13B**), and a combination of lactoferrin and sodium ascorbate (**FIG. 13C**). Skin samples were immunostained to detect tropoelastin (red) and CD44 (yellow). Nuclei were detected using DAPI staining.

[0052] **FIGs. 14A-14C** show images of immunostained human skin explants cultured *ex vivo* and treated with the combination of lactoferrin and sodium ascorbate (**FIG. 14B**) or a commercial formulation (**FIG. 14C**), versus an untreated sample (**FIG. 14A**). Skin samples

were immunostained to detect tropoelastin (red) and CD44 (yellow). Nuclei were detected using DAPI staining.

[0053] FIG. 15 is a bar graph showing tropoelastin signal intensity derived from images of immunostained human skin explants cultured *ex vivo* and treated with lactoferrin, sodium ascorbate, a combination of lactoferrin and sodium ascorbate, and a commercial formulation, versus an untreated sample. * $p < 0.05$; *** $p, 0.001$.

[0054] FIG. 16 is a bar graph showing CD44 signal intensity derived from images of immunostained human skin explants cultured *ex vivo* and treated with lactoferrin, sodium ascorbate, a combination of lactoferrin and sodium ascorbate, and a commercial formulation, versus an untreated sample. ** $p < 0.01$; *** $p, 0.001$.

DETAILED DESCRIPTION

[0055] In the following description, numerous specific details are set forth in order to provide a thorough understanding of the present technology. Particular exemplary embodiments of the present technology may be implemented without some or all of these specific details. In other instances, well known process operations have not been described in detail in order not to unnecessarily obscure the present technologies.

[0056] In any of the aspects or embodiments disclosed herein, any ingredient discussed herein may be added in “dry” form or added as part of an active solution. As used herein, the term “active solution” refers to a solution containing the ingredient (*e.g.*, a plant extract) and a solvent (*e.g.*, water, glycerin, caprylic/capric triglyceride, etc.) and/or a carrier (*e.g.*, a liposome).

Hydrophilic Antioxidants

[0057] Compositions according to the present disclosure comprise at least one hydrophilic antioxidant. The hydrophilic antioxidants comprise water soluble compounds, such as sodium ascorbate. In some embodiments, the at least one hydrophilic antioxidant further comprises Vitamin C, a derivative of Vitamin C (*e.g.*, magnesium ascorbyl phosphate (MAP), sodium ascorbyl phosphate (SAP), ascorbyl glucoside, 3-O-ethyl ascorbic acid, etc.)

one or more Vitamin C-like compounds (*e.g.*, ferulic acid, calcium ascorbate, dehydroascorbic acid, ascorbic acid, ascorbyl glucoside), a B vitamin or derivative thereof, Vitamin E and derivatives thereof (*e.g.*, tocopherol and tocopheryl acetate), lactoferrin, green tea, ergothioneine, oleuropein, *Punica granatum* extract, ectoine, *Centella asiatica* extract, carnosine, or any combination thereof.

Sodium Ascorbate

[0058] The sodium ascorbate may be present at any suitable concentration for achieving a therapeutic benefit (*e.g.*, reducing ROS or enhancing collagenesis and/or elastogenesis). In some embodiments, the sodium ascorbate is present in the topical composition at a concentration, relative to the total weight of the topical composition, of at least about 0.001 wt.%, at least about 0.002 wt.%, at least about 0.003 wt.%, at least about 0.004 wt.%, at least about 0.005 wt.%, at least about 0.006 wt.%, at least about 0.007 wt.%, at least about 0.008 wt.%, at least about 0.009 wt.%, at least about 0.01 wt.%, at least about 0.02 wt.%, at least about 0.03 wt.%, at least about 0.04 wt.%, at least about 0.05 wt.%, at least about 0.06 wt.%, at least about 0.07 wt.%, at least about 0.08 wt.%, at least about 0.09 wt.%, at least about 0.10 wt.%, at least about 0.15 wt.%, at least about 0.20 wt.%, at least about 0.25 wt.%, at least about 0.30 wt.%, at least about 0.35 wt.%, at least about 0.40 wt.%, at least about 0.45 wt.%, at least about 0.50 wt.%, at least about 0.55 wt.%, at least about 0.60 wt.%, at least about 0.65 wt.%, at least about 0.70 wt.%, at least about 0.75 wt.%, at least about 0.80 wt.%, at least about 0.85 wt.%, at least about 0.90 wt.%, at least about 0.95 wt.%, at least about 1.0 wt.%, or any range or value therein between.

[0059] In some embodiments, the sodium ascorbate is present in the topical composition at a concentration, relative to the total weight of the topical composition, of less than or equal to about 1.0 wt.%, less than or equal to about 0.95 wt.%, less than or equal to about 0.90 wt.%, less than or equal to about 0.85 wt.%, less than or equal to about 0.80 wt.%, less than or equal to about 0.75 wt.%, less than or equal to about 0.70 wt.%, less than or equal to about 0.65 wt.%, less than or equal to about 0.60 wt.%, less than or equal to about 0.55 wt.%, less than or equal to about 0.50 wt.%, less than or equal to about 0.45 wt.%, less than or equal to about 0.40 wt.%, less than or equal to about 0.35 wt.%, less than or equal to about 0.30 wt.%, less

than or equal to about 0.25 wt.%, less than or equal to about 0.20 wt.%, less than or equal to about 0.15 wt.%, less than or equal to about 0.10 wt.%, less than or equal to about 0.09 wt.%, less than or equal to about 0.08 wt.%, less than or equal to about 0.07 wt.%, less than or equal to about 0.06 wt.%, less than or equal to about 0.05 wt.%, less than or equal to about 0.04 wt.%, less than or equal to about 0.03 wt.%, less than or equal to about 0.02 wt.%, less than or equal to about 0.01 wt.%, less than or equal to about 0.009 wt.%, less than or equal to about 0.008 wt.%, less than or equal to about 0.007 wt.%, less than or equal to about 0.006 wt.%, less than or equal to about 0.005 wt.%, less than or equal to about 0.004 wt.%, less than or equal to about 0.003 wt.%, less than or equal to about 0.002 wt.%, or any range or value therein between.

[0060] In some embodiments, the sodium ascorbate is present in the topical composition at a concentration, relative to the total weight of the topical composition, of 0.001 wt.% to 1.0 wt.%, 0.002 wt.% to 1.0 wt.%, 0.005 wt.% to 1.0 wt.%, 0.01 wt.% to 1.0 wt.%, 0.02 wt.% to 1.0 wt.%, 0.05 wt.% to 1.0 wt.%, 0.1 wt.% to 0.2 wt.%, 0.5 wt.% to 1.0 wt.%, 0.02 wt.% to 0.8 wt.%, 0.05 wt.% to 0.8 wt.%, 0.1 wt.% to 0.8 wt.%, 0.2 wt.% to 0.8 wt.%, 0.05 wt.% to 0.5 wt.%, 0.05 wt.% to 0.1 wt.%, or any range or value therein between.

[0061] In some embodiments, the sodium ascorbate is present in the composition at a concentration of greater than or equal to about 10 μM , greater than or equal to about 20 μM , greater than or equal to about 30 μM , greater than or equal to about 40 μM , greater than or equal to about 50 μM , greater than or equal to about 100 μM , greater than or equal to about 150 μM , greater than or equal to about 200 μM , greater than or equal to about 250 μM , greater than or equal to about 300 μM , greater than or equal to about 350 μM , greater than or equal to about 400 μM , greater than or equal to about 450 μM , greater than or equal to about 500 μM , or any range or value therein between. In some embodiments, the sodium ascorbate is present in the composition at a concentration of greater than 200 μM

[0062] In some embodiments, the sodium ascorbate is present in the composition at a concentration of less than or equal to about 500 μM , less than or equal to about 400 μM , less than or equal to about 300 μM , less than or equal to about 250 μM , less than or equal to about 200 μM , less than or equal to about 150 μM , less than or equal to about 100 μM , less than or

equal to about 50 μ M, less than or equal to about 20 μ M, or any range or value therein between. In some embodiments, the sodium ascorbate is present in the composition at a concentration of less than 50 μ M.

Additional Hydrophilic Antioxidants

[0063] In some embodiments, the at least one hydrophilic antioxidant further comprises Vitamin C, a derivative of Vitamin C (*e.g.*, magnesium ascorbyl phosphate (MAP), sodium ascorbyl phosphate (SAP), ascorbyl glucoside, 3-O-ethyl ascorbic acid, etc.) one or more Vitamin C-like compounds (*e.g.*, ferulic acid, calcium ascorbate, dehydroascorbic acid, ascorbic acid, ascorbyl glucoside), a B vitamin or derivative thereof, Vitamin E and derivatives thereof (*e.g.*, tocopherol and tocopheryl acetate), lactoferrin, green tea, ergothioneine, oleuropein, *Punica granatum* extract, ectoine, *Centella asiatica* extract, carnosine, or any combination thereof.

[0064] Any of the additional hydrophilic antioxidants may be present in the topical composition at a concentration, alone or in combination, suitable for achieving a therapeutic benefit (*e.g.*, reducing ROS or enhancing collagenesis and/or elastogenesis). In some embodiments, the additional hydrophilic antioxidants are present, alone or in combination, at a concentration, relative to the total weight of the topical composition, of at least about 0.001 wt.%, at least about 0.002 wt.%, at least about 0.003 wt.%, at least about 0.004 wt.%, at least about 0.005 wt.%, at least about 0.006 wt.%, at least about 0.007 wt.%, at least about 0.008 wt.%, at least about 0.009 wt.%, at least about 0.01 wt.%, at least about 0.02 wt.%, at least about 0.03 wt.%, at least about 0.04 wt.%, at least about 0.05 wt.%, at least about 0.06 wt.%, at least about 0.07 wt.%, at least about 0.08 wt.%, at least about 0.09 wt.%, at least about 0.10 wt.%, at least about 0.15 wt.%, at least about 0.20 wt.%, at least about 0.25 wt.%, at least about 0.30 wt.%, at least about 0.35 wt.%, at least about 0.40 wt.%, at least about 0.45 wt.%, at least about 0.50 wt.%, at least about 0.55 wt.%, at least about 0.60 wt.%, at least about 0.65 wt.%, at least about 0.70 wt.%, at least about 0.75 wt.%, at least about 0.80 wt.%, at least about 0.85 wt.%, at least about 0.90 wt.%, at least about 0.95 wt.%, at least about 1.0 wt.%, or any range or value therein between.

[0065] In some embodiments, the additional hydrophilic antioxidants are present, alone or in combination, at a concentration, relative to the total weight of the topical composition, of less than or equal to about 1.0 wt.%, less than or equal to about 0.95 wt.%, less than or equal to about 0.90 wt.%, less than or equal to about 0.85 wt.%, less than or equal to about 0.80 wt.%, less than or equal to about 0.75 wt.%, less than or equal to about 0.70 wt.%, less than or equal to about 0.65 wt.%, less than or equal to about 0.60 wt.%, less than or equal to about 0.55 wt.%, less than or equal to about 0.50 wt.%, less than or equal to about 0.45 wt.%, less than or equal to about 0.40 wt.%, less than or equal to about 0.35 wt.%, less than or equal to about 0.30 wt.%, less than or equal to about 0.25 wt.%, less than or equal to about 0.20 wt.%, less than or equal to about 0.15 wt.%, less than or equal to about 0.10 wt.%, less than or equal to about 0.09 wt.%, less than or equal to about 0.08 wt.%, less than or equal to about 0.07 wt.%, less than or equal to about 0.06 wt.%, less than or equal to about 0.05 wt.%, less than or equal to about 0.04 wt.%, less than or equal to about 0.03 wt.%, less than or equal to about 0.02 wt.%, less than or equal to about 0.01 wt.%, less than or equal to about 0.009 wt.%, less than or equal to about 0.008 wt.%, less than or equal to about 0.007 wt.%, less than or equal to about 0.006 wt.%, less than or equal to about 0.005 wt.%, less than or equal to about 0.004 wt.%, less than or equal to about 0.003 wt.%, less than or equal to about 0.002 wt.%, or any range or value therein between.

[0066] In some embodiments, the additional hydrophilic antioxidants are present, alone or in combination, at a concentration, relative to the total weight of the topical composition, relative to the total weight of the topical composition, of 0.001 wt.% to 1.0 wt.%, 0.002 wt.% to 1.0 wt.%, 0.005 wt.% to 1.0 wt.%, 0.01 wt.% to 1.0 wt.%, 0.02 wt.% to 1.0 wt.%, 0.05 wt.% to 1.0 wt.%, 0.1 wt.% to 0.2 wt.%, 0.5 wt.% to 1.0 wt.%, 0.02 wt.% to 0.8 wt.%, 0.05 wt.% to 0.8 wt.%, 0.1 wt.% to 0.8 wt.%, 0.2 wt.% to 0.8 wt.%, 0.05 wt.% to 0.5 wt.%, 0.05 wt.% to 0.1 wt.%, or any range or value therein between.

[0067] In some embodiments, the sodium ascorbate and one or more other hydrophilic antioxidants are present at concentrations suitable to achieve synergistic activity in one or more of: reducing ROS; enhancing elastogenesis; or enhancing collagenesis. For example, in some embodiments, the hydrophilic antioxidants comprise lactoferrin, and the sodium ascorbate and the lactoferrin are present at a weight ratio of about 100:1, about 90:1, about

80:1, about 70:1, about 60:1, about 50:1, about 40:1, about 30:1, about 20:1, about 10:1, about 8:1, about 6:1, about 5:1, about 4:1, about 3:1, about 2:1, about 1:1, about 0.8:1, about 0.6:1, about 0.5:1, about 0.4:1, about 0.3:1, about 0.2:1, about 0.1:1, about 0.09:1, about 0.08:1, about 0.07:1, about 0.06:1, about 0.05:1, about 0.04:1, about 0.03:1, about 0.02:1, about 0.01:1, or any range or value therein between.

[0068] In some embodiments, sodium ascorbate and lactoferrin are present in the composition at concentrations that achieve synergistic activity in enhancing elastogenesis or collagenesis in skin. In some embodiments, the sodium ascorbate and the lactoferrin are present in the composition at concentrations that synergistically increase the production of tropoelastin in skin. In some embodiments, the sodium ascorbate and the lactoferrin are present in the composition at concentrations that synergistically increase elastogenesis while maintaining or not significantly reducing the expression of CD44 in skin.

Enzymatic Antioxidants

[0069] Antioxidant enzymes can be used to protect the skin from the effects of ROS, but their inherent instability makes them difficult to formulate. Further, the skin's intrinsic enzymes can be rapidly overwhelmed by excessive sun exposure. To counteract this impact, compositions according to the present disclosure may comprise one or more organic or non-organic compounds that accelerate or facilitate chemical reactions. Such enzymatic antioxidants compounds can be protein-based catalysts or co-enzymes that reduce the levels of reactive oxygen (ROS) species in skin. Examples of enzymatic antioxidants include ubiquinone, betaine, and enzymes found in *Tremella fuciformis*, including but not limited to superoxide dismutase, glutathione peroxidase, and catalase.

[0070] In some embodiments, the enzymatic antioxidants comprise one or more selected from ubiquinone, superoxide dismutase, catalase, glutathione peroxidase, glutathione reductase, or any combination thereof. In some embodiments, the enzymatic antioxidant comprises ubiquinone (coenzyme Q10).

[0071] Any of the enzymatic antioxidants may be present in the topical composition at a concentration, alone or in combination, suitable for achieving a therapeutic benefit (*e.g.*,

reducing ROS or enhancing collagenesis and/or elastogenesis). In some embodiments, the one or more enzymatic antioxidants are present, alone or in combination, at a concentration, relative to the total weight of the topical composition, of at least about 0.001 wt.%, at least about 0.002 wt.%, at least about 0.003 wt.%, at least about 0.004 wt.%, at least about 0.005 wt.%, at least about 0.006 wt.%, at least about 0.007 wt.%, at least about 0.008 wt.%, at least about 0.009 wt.%, at least about 0.01 wt.%, at least about 0.02 wt.%, at least about 0.03 wt.%, at least about 0.04 wt.%, at least about 0.05 wt.%, at least about 0.06 wt.%, at least about 0.07 wt.%, at least about 0.08 wt.%, at least about 0.09 wt.%, at least about 0.10 wt.%, at least about 0.15 wt.%, at least about 0.20 wt.%, at least about 0.25 wt.%, at least about 0.30 wt.%, at least about 0.35 wt.%, at least about 0.40 wt.%, at least about 0.45 wt.%, at least about 0.50 wt.%, at least about 0.55 wt.%, at least about 0.60 wt.%, at least about 0.65 wt.%, at least about 0.70 wt.%, at least about 0.75 wt.%, at least about 0.80 wt.%, at least about 0.85 wt.%, at least about 0.90 wt.%, at least about 0.95 wt.%, at least about 1.0 wt.%, or any range or value therein between.

[0072] In some embodiments, the one or more enzymatic antioxidants are present, alone or in combination, at a concentration, relative to the total weight of the topical composition, of less than or equal to about 1.0 wt.%, less than or equal to about 0.95 wt.%, less than or equal to about 0.90 wt.%, less than or equal to about 0.85 wt.%, less than or equal to about 0.80 wt.%, less than or equal to about 0.75 wt.%, less than or equal to about 0.70 wt.%, less than or equal to about 0.65 wt.%, less than or equal to about 0.60 wt.%, less than or equal to about 0.55 wt.%, less than or equal to about 0.50 wt.%, less than or equal to about 0.45 wt.%, less than or equal to about 0.40 wt.%, less than or equal to about 0.35 wt.%, less than or equal to about 0.30 wt.%, less than or equal to about 0.25 wt.%, less than or equal to about 0.20 wt.%, less than or equal to about 0.15 wt.%, less than or equal to about 0.10 wt.%, less than or equal to about 0.09 wt.%, less than or equal to about 0.08 wt.%, less than or equal to about 0.07 wt.%, less than or equal to about 0.06 wt.%, less than or equal to about 0.05 wt.%, less than or equal to about 0.04 wt.%, less than or equal to about 0.03 wt.%, less than or equal to about 0.02 wt.%, less than or equal to about 0.01 wt.%, less than or equal to about 0.009 wt.%, less than or equal to about 0.008 wt.%, less than or equal to about 0.007 wt.%, less than or equal to about 0.006 wt.%, less than or equal to about 0.005 wt.%, less than or equal to about 0.004

wt.%, less than or equal to about 0.003 wt.%, less than or equal to about 0.002 wt.%, or any range or value therein between.

[0073] In some embodiments, the one or more enzymatic antioxidants are present, alone or in combination, at a concentration, relative to the total weight of the topical composition, of 0.001 wt.% to 1.0 wt.%, 0.002 wt.% to 1.0 wt.%, 0.005 wt.% to 1.0 wt.%, 0.01 wt.% to 1.0 wt.%, 0.02 wt.% to 1.0 wt.%, 0.05 wt.% to 1.0 wt.%, 0.1 wt.% to 0.2 wt.%, 0.5 wt.% to 1.0 wt.%, 0.02 wt.% to 0.8 wt.%, 0.05 wt.% to 0.8 wt.%, 0.1 wt.% to 0.8 wt.%, 0.2 wt.% to 0.8 wt.%, 0.05 wt.% to 0.5 wt.%, 0.05 wt.% to 0.1 wt.%, or any range or value therein between. In some embodiments, the one or more enzymatic antioxidants are present in a liposome. In some embodiments, the one or more enzymatic antioxidants are present without being encapsulated in a liposome.

[0074] In some embodiments, the one or more enzymatic antioxidants and the sodium ascorbate are present at concentrations suitable to achieve synergistic activity in one or more of: reducing ROS; enhancing elastogenesis; or enhancing collagenesis. For example, in some embodiments, the enzymatic antioxidants comprise ubiquinone, and the sodium ascorbate and the ubiquinone are present at a weight ratio of about 100:1, about 90:1, about 80:1, about 70:1, about 60:1, about 50:1, about 40:1, about 30:1, about 20:1, about 10:1, about 8:1, about 6:1, about 5:1, about 4:1, about 3:1, about 2:1, about 1:1, about 0.8:1, about 0.6:1, about 0.5:1, about 0.4:1, about 0.3:1, about 0.2:1, about 0.1:1, about 0.09:1, about 0.08:1, about 0.07:1, about 0.06:1, about 0.05:1, about 0.04:1, about 0.03:1, about 0.02:1, about 0.01:1, or any range or value therein between.

Hydrophobic Antioxidants

[0075] In some embodiments, compositions according to the present disclosure comprise one or more hydrophobic antioxidants (*e.g.*, lipophilic antioxidants). In some embodiments, the hydrophobic antioxidants are vitamin E-like compounds that are soluble in lipids. In some embodiments, the hydrophobic antioxidants are selected from bisabolol, phytoene, phytofluene, and *Physalis angulata*, or any combination thereof. In some embodiments, *Dunaliella salina* extract may comprise phytoene and phytofluene.

[0076] Any of the hydrophobic antioxidants may be present in the topical composition at a concentration, alone or in combination, suitable for achieving a therapeutic benefit (*e.g.*, reducing ROS or enhancing collagenesis and/or elastogenesis). In some embodiments, the one or more hydrophobic antioxidants are present, alone or in combination, at a concentration, relative to the total weight of the topical composition, of at least about 0.001 wt.%, at least about 0.002 wt.%, at least about 0.003 wt.%, at least about 0.004 wt.%, at least about 0.005 wt.%, at least about 0.006 wt.%, at least about 0.007 wt.%, at least about 0.008 wt.%, at least about 0.009 wt.%, at least about 0.01 wt.%, at least about 0.02 wt.%, at least about 0.03 wt.%, at least about 0.04 wt.%, at least about 0.05 wt.%, at least about 0.06 wt.%, at least about 0.07 wt.%, at least about 0.08 wt.%, at least about 0.09 wt.%, at least about 0.10 wt.%, at least about 0.15 wt.%, at least about 0.20 wt.%, at least about 0.25 wt.%, at least about 0.30 wt.%, at least about 0.35 wt.%, at least about 0.40 wt.%, at least about 0.45 wt.%, at least about 0.50 wt.%, at least about 0.55 wt.%, at least about 0.60 wt.%, at least about 0.65 wt.%, at least about 0.70 wt.%, at least about 0.75 wt.%, at least about 0.80 wt.%, at least about 0.85 wt.%, at least about 0.90 wt.%, at least about 0.95 wt.%, at least about 1.0 wt.%, or any range or value therein between.

[0077] In some embodiments, the one or more hydrophobic antioxidants are present, alone or in combination, at a concentration, relative to the total weight of the topical composition, of less than or equal to about 1.0 wt.%, less than or equal to about 0.95 wt.%, less than or equal to about 0.90 wt.%, less than or equal to about 0.85 wt.%, less than or equal to about 0.80 wt.%, less than or equal to about 0.75 wt.%, less than or equal to about 0.70 wt.%, less than or equal to about 0.65 wt.%, less than or equal to about 0.60 wt.%, less than or equal to about 0.55 wt.%, less than or equal to about 0.50 wt.%, less than or equal to about 0.45 wt.%, less than or equal to about 0.40 wt.%, less than or equal to about 0.35 wt.%, less than or equal to about 0.30 wt.%, less than or equal to about 0.25 wt.%, less than or equal to about 0.20 wt.%, less than or equal to about 0.15 wt.%, less than or equal to about 0.10 wt.%, less than or equal to about 0.09 wt.%, less than or equal to about 0.08 wt.%, less than or equal to about 0.07 wt.%, less than or equal to about 0.06 wt.%, less than or equal to about 0.05 wt.%, less than or equal to about 0.04 wt.%, less than or equal to about 0.03 wt.%, less than or equal to about 0.02 wt.%, less than or equal to about 0.01 wt.%, less than or equal to about 0.009 wt.%, less than or equal to about 0.008 wt.%, less than or equal to about 0.007 wt.%, less than or equal

to about 0.006 wt.%, less than or equal to about 0.005 wt.%, less than or equal to about 0.004 wt.%, less than or equal to about 0.003 wt.%, less than or equal to about 0.002 wt.%, or any range or value therein between.

[0078] In some embodiments, the one or more hydrophobic antioxidants are present, alone or in combination, at a concentration, relative to the total weight of the topical composition, relative to the total weight of the topical composition, of 0.001 wt.% to 1.0 wt.%, 0.002 wt.% to 1.0 wt.%, 0.005 wt.% to 1.0 wt.%, 0.01 wt.% to 1.0 wt.%, 0.02 wt.% to 1.0 wt.%, 0.05 wt.% to 1.0 wt.%, 0.1 wt.% to 0.2 wt.%, 0.5 wt.% to 1.0 wt.%, 0.02 wt.% to 0.8 wt.%, 0.05 wt.% to 0.8 wt.%, 0.1 wt.% to 0.8 wt.%, 0.2 wt.% to 0.8 wt.%, 0.05 wt.% to 0.5 wt.%, 0.05 wt.% to 0.1 wt.%, or any range or value therein between.

[0079] In some embodiments, the one or more hydrophobic antioxidants and the sodium ascorbate are present at concentrations suitable to achieve synergistic activity in one or more of: reducing ROS; enhancing elastogenesis; or enhancing collagenesis. For example, in some embodiments, one or more hydrophobic antioxidants and the sodium ascorbate are present at a weight ratio of about 100:1, about 90:1, about 80:1, about 70:1, about 60:1, about 50:1, about 40:1, about 30:1, about 20:1, about 10:1, about 8:1, about 6:1, about 5:1, about 4:1, about 3:1, about 2:1, about 1:1, about 0.8:1, about 0.6:1, about 0.5:1, about 0.4:1, about 0.3:1, about 0.2:1, about 0.1:1, about 0.09:1, about 0.08:1, about 0.07:1, about 0.06:1, about 0.05:1, about 0.04:1, about 0.03:1, about 0.02:1, about 0.01:1, or any range or value therein between.

[0080] In some embodiments, the total concentration of antioxidants (hydrophilic, enzymatic, and hydrophobic) in the composition is less than 15 wt.%, less than 12 wt.%, less than 10 wt.%, less than 8 wt.%, less than 6 wt.%, less than 5 wt.%, less than 4 wt.%, less than 3 wt.%, less than 2 wt.%, or less than 1 wt.%, relative to the total weight of the composition.

Liposomes

[0081] Since only a few active ingredients are effective after topical application due to the barrier function of the skin, lipid nanoparticles and liposomes have been explored as carriers to enhance the bioavailability, skin penetration, and retention of active ingredients. In particular, liposomes have been used as carriers for different applications in dermatology and

cosmetics. For example, due to its instability and low skin penetration, sodium ascorbate needs an appropriate carrier to obtain desirable efficacy.

Liposomes Encapsulating Hydrophilic Antioxidants, Including Sodium Ascorbate

[0082] Thus, in some embodiments, the sodium ascorbate is encapsulated in a liposome. The liposome encapsulating sodium ascorbate may be any suitable composition and size to allow penetration past the barrier of the stratum corneum and deliver the sodium ascorbate into the dermis to prevent photodamage.

[0083] In some embodiments, the liposome encapsulating sodium ascorbate comprises one or more of phosphatidylcholine, mannitol, glycerin, cetyl alcohol, decyl glucoside, or any combination thereof. In some embodiments, the liposome encapsulating sodium ascorbate comprises phosphatidylcholine, mannitol, glycerin, cetyl alcohol, and decyl glucoside. (See G. Serrano et al., *Phosphatidylcholine Liposomes as Carriers to Improve Topical Ascorbic Acid Treatment of Skin Disorders*, 8 CLIN. COSMET. & INVESTIG. DERMATOL. 8, 591–99 (2015).) A non-limiting example of such a liposome is Vegan DDS-Sodium Ascorbate by INdermal (Spain).

[0084] In some embodiments, the liposomes have any suitable size to improve delivery of sodium ascorbate into the skin. In some embodiments, the liposomes have an average diameter of greater than or equal to about 50 nm, greater than or equal to about 60 nm, greater than or equal to about 70 nm, greater than or equal to about 80 nm, greater than or equal to about 90 nm, greater than or equal to about 100 nm, greater than or equal to about 110 nm, greater than or equal to about 120 nm, greater than or equal to about 130 nm, greater than or equal to about 140 nm, greater than or equal to about 150 nm, greater than or equal to about 160 nm, greater than or equal to about 170 nm, greater than or equal to about 180 nm, greater than or equal to about 190 nm, greater than or equal to about 200 nm, greater than or equal to about 210 nm, greater than or equal to about 220 nm, greater than or equal to about 230 nm, greater than or equal to about 240 nm, greater than or equal to about 250 nm, greater than or equal to about 260 nm, greater than or equal to about 270 nm, greater than or equal to about 280 nm, greater than or equal to about 290 nm, greater than or equal to about 300 nm, greater than or equal to about 310 nm, greater than or equal to about 320 nm, greater than or

equal to about 330 nm, greater than or equal to about 340 nm, greater than or equal to about 350 nm, greater than or equal to about 360 nm, greater than or equal to about 370 nm, greater than or equal to about 380 nm, greater than or equal to about 390 nm, greater than or equal to about 400 nm, greater than or equal to about 410 nm, greater than or equal to about 420 nm, greater than or equal to about 430 nm, greater than or equal to about 440 nm, greater than or equal to about 450 nm, greater than or equal to about 500 nm, greater than or equal to about 500 nm, or any range or value therein between.

[0085] In some embodiments, the liposomes have an average diameter of about 50 nm to about 500 nm, about 50 nm to about 400 nm, about 50 nm to about 300 nm, about 50 nm to about 250 nm, about 100 nm to about 500 nm, about 100 nm to about 400 nm, about 100 nm to about 300 nm, 100 nm to about 250 nm, about 200 nm to about 500 nm, about 200 nm to about 400 nm, about 200 nm to about 300 nm, or any range or value therein. In some embodiments, the liposomes have an average diameter of about 250 nm.

[0086] In some embodiments, the hydrophilic antioxidants (*e.g.*, lactoferrin) are encapsulated in a liposome that is different in composition and/or size from the liposome encapsulating the sodium ascorbate. In some embodiments, one or more hydrophilic antioxidants are unencapsulated. In some embodiments, one or more hydrophilic antioxidants are present in a combination of unencapsulated and encapsulated forms.

[0087] In some embodiments, the liposome encapsulating one or more hydrophilic antioxidants (*e.g.*, lactoferrin) may be any suitable composition and size to allow penetration past the barrier of the stratum corneum and deliver the lactoferrin into the dermis to prevent photodamage.

[0088] In some embodiments, the liposomes encapsulating one or more hydrophilic antioxidants (*e.g.*, lactoferrin) have any suitable size to improve delivery of hydrophilic antioxidants (*e.g.*, lactoferrin) into the skin. In some embodiments, the liposomes have an average diameter of greater than or equal to about 50 nm, greater than or equal to about 60 nm, greater than or equal to about 70 nm, greater than or equal to about 80 nm, greater than or equal to about 90 nm, greater than or equal to about 100 nm, greater than or equal to about 110 nm, greater than or equal to about 120 nm, greater than or equal to about 130 nm, greater

than or equal to about 140 nm, greater than or equal to about 150 nm, greater than or equal to about 160 nm, greater than or equal to about 170 nm, greater than or equal to about 180 nm, greater than or equal to about 190 nm, greater than or equal to about 200 nm, greater than or equal to about 210 nm, greater than or equal to about 220 nm, greater than or equal to about 230 nm, greater than or equal to about 240 nm, greater than or equal to about 250 nm, greater than or equal to about 260 nm, greater than or equal to about 270 nm, greater than or equal to about 280 nm, greater than or equal to about 290 nm, greater than or equal to about 300 nm, greater than or equal to about 310 nm, greater than or equal to about 320 nm, greater than or equal to about 330 nm, greater than or equal to about 340 nm, greater than or equal to about 350 nm, greater than or equal to about 360 nm, greater than or equal to about 370 nm, greater than or equal to about 380 nm, greater than or equal to about 390 nm, greater than or equal to about 400 nm, greater than or equal to about 410 nm, greater than or equal to about 420 nm, greater than or equal to about 430 nm, greater than or equal to about 440 nm, greater than or equal to about 450 nm, greater than or equal to about 500 nm, greater than or equal to about 500 nm, or any range or value therein between.

[0089] In some embodiments, the liposomes encapsulating hydrophilic antioxidants (*e.g.*, lactoferrin) have an average diameter of about 50 nm to about 500 nm, about 50 nm to about 400 nm, about 50 nm to about 300 nm, about 50 nm to about 250 nm, about 100 nm to about 500 nm, about 100 nm to about 400 nm, about 100 nm to about 300 nm, 100 nm to about 250 nm, about 200 nm to about 500 nm, about 200 nm to about 400 nm, about 200 nm to about 300 nm, or any range or value therein. In some embodiments, the liposomes have an average diameter of about 250 nm. In some embodiments, the liposomes have an average diameter of 220 nm or less.

[0090] In some embodiments, the liposomes encapsulating hydrophilic antioxidants (*e.g.*, lactoferrin) have a polydispersity index (PDI) of 0 to about 0.2. In some embodiments, the polydispersity index is about 0.01, 0.025, 0.05, 0.1, 0.25, 0.3, 0.35, 0.4, 0.45, 0.5, 0.55, 0.6, 0.65, 0.7, 0.75, or 0.8. In some instances, the polydispersity index is in a range of about 0.01 to about 0.8, about 0.025 to about 0.75, about 0.05 to about 0.6, or about 0.1 to about 0.3.

[0091] In some embodiments, the liposomes encapsulating hydrophilic antioxidants (*e.g.*, lactoferrin) comprise propanediol, lecithin, or a combination thereof. In some embodiments, the propanediol is present in the liposomes at a concentration, by weight relative to the total weight of the liposomes, of greater than or equal to about 0.001 wt.%, greater than or equal to about 0.005 wt.%, greater than or equal to about 0.01 wt.%, greater than or equal to about 0.02 wt.%, greater than or equal to about 0.05 wt.%, greater than or equal to about 0.10 wt.%, greater than or equal to about 0.20 wt.%, greater than or equal to about 0.25 wt.%, greater than or equal to about 0.50 wt.%, greater than or equal to about 0.75 wt.%, greater than or equal to about 1.0 wt.%, greater than or equal to about 1.5 wt.%, greater than or equal to about 2.0 wt.%, greater than or equal to about 2.5 wt.%, greater than or equal to about 3.0 wt.%, greater than or equal to about 3.5 wt.%, greater than or equal to about 4.0 wt.%, greater than or equal to about 4.5 wt.%, greater than or equal to about 5.0 wt.%, greater than or equal to about 5.5 wt.%, greater than or equal to about 6.0 wt.%, greater than or equal to about 6.5 wt.%, greater than or equal to about 7.0 wt.%, greater than or equal to about 8 wt.%, greater than or equal to about 9 wt.%, greater than or equal to about 10 wt.%, or any range or value therein between.

[0092] In some embodiments, the propanediol is present in the liposomes encapsulating hydrophilic antioxidants (*e.g.*, lactoferrin) at a concentration, by weight relative to the total weight of the liposomes or relative to the total weight of the topical composition, of about 0.001 wt.% to about 6 wt.%, about 0.002 wt.% to about 4 wt.%, about 0.01 wt.% to about 3 wt.%, or about 0.02 wt.% to about 2 wt.% by weight.

[0093] In some embodiments, the lecithin is present in the liposomes encapsulating hydrophilic antioxidants (*e.g.*, lactoferrin) at a concentration, by weight relative to the total weight of the liposomes, of greater than or equal to about 0.001 wt.%, greater than or equal to about 0.005 wt.%, greater than or equal to about 0.01 wt.%, greater than or equal to about 0.02 wt.%, greater than or equal to about 0.05 wt.%, greater than or equal to about 0.10 wt.%, greater than or equal to about 0.20 wt.%, greater than or equal to about 0.25 wt.%, greater than or equal to about 0.50 wt.%, greater than or equal to about 0.75 wt.%, greater than or equal to about 1.0 wt.%, greater than or equal to about 1.5 wt.%, greater than or equal to about 2.0 wt.%, greater than or equal to about 2.5 wt.%, greater than or equal to

about 3.0 wt.%, greater than or equal to about 3.5 wt.%, greater than or equal to about 4.0 wt.%, greater than or equal to about 4.5 wt.%, greater than or equal to about 5.0 wt.%, greater than or equal to about 5.5 wt.%, greater than or equal to about 6.0 wt.%, greater than or equal to about 6.5 wt.%, greater than or equal to about 7.0 wt.%, greater than or equal to about 8 wt.%, greater than or equal to about 9 wt.%, greater than or equal to about 10 wt.%, or any range or value therein between.

[0094] In some embodiments, the lecithin is present in the liposomes encapsulating hydrophilic antioxidants (*e.g.*, lactoferrin) at a concentration, by weight relative to the total weight of the liposomes or relative to the total weight of the topical composition, of about 0.001 wt.% to about 6 wt.%, about 0.002 wt.% to about 4 wt.%, about 0.01 wt.% to about 3 wt.%, or about 0.02 wt.% to about 2 wt.% by weight.

[0095] In some embodiments, the liposomes encapsulating hydrophilic antioxidants (*e.g.*, lactoferrin) are commercially available (*e.g.*, PRO-LIPO™ NEO). In some embodiments, the liposomes comprise propanediol, lecithin, sunflower seed oil, and tocopherol. In some embodiments, hydrophilic antioxidants (*e.g.*, ergothioneine, oleuropein, *Punica Granatum* extract, ectoine, *Centella asiatica*, carnosine, or *Camellia sinensis*, etc.) are encapsulated in a liposome that is different in composition and/or size from the liposome encapsulating the sodium ascorbic and/or lactoferrin. In some embodiments, the one or more hydrophilic antioxidants are unencapsulated. In some embodiments, the one or more hydrophilic antioxidants are present in a combination of unencapsulated and encapsulated forms.

[0096] In some embodiments, the liposome encapsulating one or more hydrophilic antioxidants may be any suitable composition and size to allow penetration past the barrier of the stratum corneum and deliver the hydrophilic antioxidants into the dermis to prevent photodamage.

[0097] In some embodiments, the concentrations and compositions of the liposomes encapsulating the hydrophilic antioxidants are in accordance with the concentrations and compositions set forth in the embodiments disclosed herein.

Liposomes Encapsulating Enzymatic Antioxidants

[0098] In some embodiments, enzymatic antioxidants may be included into the disclosed compositions unencapsulated. In some embodiments, the enzymatic antioxidants (*e.g.*, ubiquinone) are encapsulated in a liposome. In some embodiments, enzymatic antioxidants may be present in a combination of encapsulated and unencapsulated forms. The liposome may be different in composition and/or size from the liposome encapsulating the sodium ascorbate and from liposomes encapsulating other antioxidants.

[0099] In some embodiments, the liposome encapsulating the enzymatic antioxidants (*e.g.*, ubiquinone) comprises one or more of cetyl palmitate, C12-15 alkyl benzoate, glycerin, lauryl glucoside, xanthan gum, phenoxyethanol, sodium lauroyl lactylate, lactic acid, or any combination thereof. In some embodiments, the liposome encapsulating enzymatic antioxidants (*e.g.*, ubiquinone) comprises cetyl palmitate, C12-15 alkyl benzoate, glycerin, lauryl glucoside, xanthan gum, phenoxyethanol, sodium lauroyl lactylate, lactic acid. A non-limiting example of such a liposome is VITISPHERES® Q10 (Clariant International Ltd.).

[0100] In some embodiments, the liposomes encapsulating the enzymatic antioxidants (*e.g.*, ubiquinone) have any suitable size to improve delivery of enzymatic antioxidants (*e.g.*, ubiquinone) into the skin. In some embodiments, the liposomes have an average diameter of greater than or equal to about 50 nm, greater than or equal to about 60 nm, greater than or equal to about 70 nm, greater than or equal to about 80 nm, greater than or equal to about 90 nm, greater than or equal to about 100 nm, greater than or equal to about 110 nm, greater than or equal to about 120 nm, greater than or equal to about 130 nm, greater than or equal to about 140 nm, greater than or equal to about 150 nm, greater than or equal to about 160 nm, greater than or equal to about 170 nm, greater than or equal to about 180 nm, greater than or equal to about 190 nm, greater than or equal to about 200 nm, greater than or equal to about 210 nm, greater than or equal to about 220 nm, greater than or equal to about 230 nm, greater than or equal to about 240 nm, greater than or equal to about 250 nm, greater than or equal to about 260 nm, greater than or equal to about 270 nm, greater than or equal to about 280 nm, greater than or equal to about 290 nm, greater than or equal to about 300 nm, greater than or equal to about 310 nm, greater than or equal to about 320 nm, greater than or equal to about

330 nm, greater than or equal to about 340 nm, greater than or equal to about 350 nm, greater than or equal to about 360 nm, greater than or equal to about 370 nm, greater than or equal to about 380 nm, greater than or equal to about 390 nm, greater than or equal to about 400 nm, greater than or equal to about 410 nm, greater than or equal to about 420 nm, greater than or equal to about 430 nm, greater than or equal to about 440 nm, greater than or equal to about 450 nm, greater than or equal to about 500 nm, greater than or equal to about 500 nm, or any range or value therein between.

[0101] In some embodiments, the liposomes encapsulating the enzymatic antioxidants (*e.g.*, ubiquinone) have an average diameter of about 50 nm to about 500 nm, about 50 nm to about 400 nm, about 50 nm to about 300 nm, about 50 nm to about 250 nm, about 100 nm to about 500 nm, about 100 nm to about 400 nm, about 100 nm to about 300 nm, 100 nm to about 250 nm, about 200 nm to about 500 nm, about 200 nm to about 400 nm, about 200 nm to about 300 nm, or any range or value therein. In some embodiments, the liposomes have an average diameter of about 250 nm. In some embodiments, the liposomes have an average diameter of 220 nm or less.

[0102] Humectants/Emollients

[0103] In some embodiments, a topical composition according to the present disclosure comprises one or more humectants and/or emollients. By way of non-limiting example, in some embodiments, the one or more humectants and/or emollients may comprise polyols, such as polyols having from 2 to 20 carbon atoms, including glycerol (glycerin); glycol derivatives (*e.g.*, propylene glycol, butylene glycol, pentylene glycol, hexylene glycol, dipropylene glycol, diethylene glycol, caprylyl glycol); and mixtures thereof. In some embodiments, the humectants and/or emollients may comprise glycerin sorbitol; sugars (*e.g.*, glucose, lactose, etc.); alkoxylated glucose derivatives; glucose ethers; panthenols (*e.g.*, D-panthenol, DL-panthenol); polyethylene glycols (PEGs); urea; sodium hyaluronate; caprylyl glycol; pantolactone; caprylic/capric triglyceride; coco-caprylate/caprate; pantolactone; squalane; soluble chitosan; hexanetriol; amino acids (*e.g.*, serine, citrulline, arginine, asparagine or alanine); alpha-hydroxy acids; salicylic acid; hyaluronic acid (HA); sodium lactate; sodium pyroglutamic acid (sodium PCA); aloe vera gel; or combinations thereof.

[0104] In some embodiments, the one or more humectants and/or emollients may be present at a concentration, individually or collectively, relative to the total weight of the composition, of at least about 0.1 wt.%, at least about 0.2 wt.%, at least about 0.3 wt.%, at least about 0.4 wt.%, at least about 0.5 wt.%, at least about 0.6 wt.%, at least about 0.7 wt.%, at least about 0.8 wt.%, at least about 0.9 wt.%, at least about 1.0 wt.%, at least about 1.2 wt.%, at least about 1.5 wt.%, at least about 1.8 wt.%, at least about 2.0 wt.%, at least about 2.5 wt.%, at least about 3.0 wt.%, at least about 3.5 wt.%, at least about 4.0 wt.%, at least about 4.5 wt.%, at least about 5.0 wt.%, at least about 5.5 wt.%, at least about 6.0 wt.%, at least about 6.5 wt.%, at least about 7.0 wt.%, at least about 7.5 wt.%, at least about 8.0 wt.%, at least about 8.5 wt.%, at least about 9.0 wt.%, at least about 9.5 wt.%, at least about 10 wt.%, or any range or value therein between.

[0105] In some embodiments, the one or more humectants and/or emollients may be present at a concentration, individually or collectively, relative to the total weight of the composition, of no greater than about 30 wt.%, no greater than about 25 wt.%, no greater than about 20 wt.%, no greater than about 15 wt.%, no greater than about 14 wt.%, no greater than about 13 wt.%, no greater than about 12 wt.%, no greater than about 11 wt.%, no greater than about 10.0 wt.%, no greater than about 9.5 wt.%, no greater than about 9.0 wt.%, no greater than about 8.5 wt.%, no greater than about 8.0 wt.%, no greater than about 7.5 wt.%, no greater than about 7.0 wt.%, no greater than about 6.5 wt.%, no greater than about 6.0 wt.%, no greater than about 5.5 wt.%, no greater than about 5.0 wt.%, no greater than about 4.5 wt.%, no greater than about 4.0 wt.%, no greater than about 3.5 wt.%, no greater than about 3.0 wt.%, or any range or value therein between.

[0106] In some embodiments, the one or more humectants and/or emollients may be present at a concentration, individually or collectively, relative to the total weight of the composition, of about 0.1 wt.%, about 0.2 wt.%, about 0.5 wt.%, about 0.8 wt.%, about 1.0 wt.%, about 1.2 wt.%, about 1.5 wt.%, about 1.8 wt.%, about 2.0 wt.%, about 2.2 wt.%, about 2.5 wt.%, about 2.8 wt.%, about 3.0 wt.%, about 3.2 wt.%, about 3.5 wt.%, about 3.8 wt.%, about 4.0 wt.%, about 4.2 wt.%, about 4.5 wt.%, about 4.8 wt.%, about 5.0 wt.%, about 5.5 wt.%, about 6.0 wt.%, about 6.5 wt.%, about 7.0 wt.%, about 7.5 wt.%, about 8.0 wt.%, about 8.5 wt.%, about

9.0 wt.%, about 9.5 wt.%, about 10.0 wt.%, about 15 wt.%, about 20 wt.%, about 25 wt.%, about 30 wt.%, or any range or value therein between.

[0107] In some embodiments, the one or more humectants and/or emollients may be present at a concentration, individually or collectively, relative to the total weight of the composition, of about 0.1 wt.% to about 30 wt.%, about 0.1 wt.% to about 25 wt.%, about 0.1 wt.% to about 20 wt.%, about 0.1 wt.% to about 15 wt.%, about 0.1 wt.% to about 14 wt.%, about 0.1 wt.% to about 13 wt.%, about 0.1 wt.% to about 12 wt.%, about 0.1 wt.% to about 11 wt.%, about 0.1 wt.% to about 10.0 wt.%, about 0.1 wt.% to about 8 wt.%, about 0.1 wt.% to about 5 wt.%, about 0.1 to about 4 wt.%, about 0.1 wt.% to about 3 wt.%, about 0.1 wt.% to about 2 wt.%, about 0.1 wt.% to about 1 wt.%, about 0.5 wt.% to about 30 wt.%, about 0.5 wt.% to about 25 wt.%, about 0.5 wt.% to about 20 wt.%, about 0.5 wt.% to about 15 wt.%, about 0.5 wt.% to about 10.0 wt.%, about 0.5 wt.% to about 8 wt.%, about 0.5 wt.% to about 5 wt.%, about 0.5 to about 4 wt.%, about 0.5 wt.% to about 3 wt.%, about 0.5 wt.% to about 2 wt.%, about 0.5 to about 1 wt.%, about 1 wt.% to about 30 wt.%, about 1 wt.% to about 25 wt.%, about 1 wt.% to about 20 wt.%, about 1 wt.% to about 15 wt.%, about 1 wt.% to about 10 wt.%, about 1 wt.% to about 8 wt.%, about 1 wt.% to about 5 wt.%, about 1 wt.% to about 4 wt.%, about 1 wt.% to about 3 wt.%, about 1 wt.% to about 2 wt.%, about 3 wt.% to about 30 wt.%, about 3 wt.% to about 25 wt.%, about 3 wt.% to about 20 wt.%, about 3 wt.% to about 15 wt.%, about 1 wt.% to about 10 wt.%, about 3 wt.% to about 8 wt.%, about 3 wt.% to about 5 wt.%, about 5 wt.% to about 30 wt.%, about 5 wt.% to about 25 wt.%, about 5 wt.% to about 20 wt.%, about 5 wt.% to about 15 wt.%, about 5 wt.% to about 10 wt.%, about 5 wt.% to about 8 wt.%, or any range or value therein.

Oils

[0108] In some embodiments, a topical composition according to the present disclosure comprises one or more oils. In some embodiments (*e.g.*, when the composition is in the form of an emulsion such as an oil-in-water or water-in-oil emulsion), the composition comprises an oily phase comprising one or more oils. By way of non-limiting example, the one or more oils may comprise vegetable oils, mineral oils, animal oils, or synthetic waxes, oils or butters, and mixtures thereof. In some embodiments, the oils may comprise: one or more mineral oils

(*e.g.*, PRIMOL 352®, MARCOL 82®, and MARCOL 152® sold by Esso); one or more vegetable oils (*e.g.*, almond oil, sweet almond oil, palm oil, soybean oil, sesame oil, sunflower oil, olive oil, etc.); hydrogenated vegetable oils; one or more animal oils or substitutes of vegetable origin (*e.g.*, lanolin, squalene or fish oil and derivatives thereof, such as perhydrosqualene, *e.g.*, sold as SOPHIDERM® by Sophim); one or more synthetic oils (*e.g.*, cetearyl isononanoate, such as CETIOL SN PH® by Cognis France, isononyl isononanoate, such as DUB ININ® sold by Stéarinerie Dubois, diisopropyl adipate, such as CRODAMOL DA® by Croda, isopropyl palmitate, such as CRODAMOL IPP® by Croda, caprylic/capric triglyceride, such as MIGLYOL 812® sold by Univar, hydrogenated polyisobutene, such as PARLEAM® products by Rossow); one or more silicone oils (*e.g.*, dimethicone, such as Q7-9120 Silicone Fluid®, with a viscosity of 20 cSt to 12 500 cSt, by Dow Corning, cyclomethicone, such as ST-Cyclomethicone 5NF®, by Dow Corning, or DC 9045 Elastomer Blend®, by Dow Corning); or any combination thereof.

[0109] In some embodiments, the one or more oils be present at a concentration, individually or collectively, relative to the total weight of the composition, of at least about 0.5 wt.%, at least about 0.6 wt.%, at least about 0.7 wt.%, at least about 0.8 wt.%, at least about 0.9 wt.%, at least about 1.0 wt.%, at least about 1.2 wt.%, at least about 1.5 wt.%, at least about 1.8 wt.%, at least about 2.0 wt.%, at last about 2.25 wt.%, at least about 2.5 wt.%, at least about 3.0 wt.%, at least about 3.5 wt.%, at least about 4.0 wt.%, at least about 4.5 wt.%, at least about 5.0 wt.%, at least about 5.5 wt.%, at least about 6.0 wt.%, at least about 6.5 wt.%, at least about 7.0 wt.%, at least about 7.5 wt.%, at least about 8.0 wt.%, at least about 8.5 wt.%, at least about 9.0 wt.%, at least about 9.5 wt.%, at least about 10 wt.%, at least about 15.0 wt.%, at least about 20.0 wt.%, or any range or value therein between.

[0110] In some embodiments, the one or more oils may be present at a concentration, individually or collectively, relative to the total weight of the composition, of no greater than about 35.0 wt.%, no greater than about 30 wt.%, no greater than about 25 wt.%, no greater than about 20 wt.%, no greater than about 19 wt.%, no greater than about 18 wt.%, no greater than about 17 wt.%, no greater than about 16 wt.%, no greater than about 15 wt.%, no greater than about 14 wt.%, no greater than about 13 wt.%, no greater than about 12 wt.%, no greater than about 11 wt.%, no greater than about 10.0 wt.%, no greater than about 9.5 wt.%, no

greater than about 9.0 wt.%, no greater than about 8.5 wt.%, no greater than about 8.0 wt.%, no greater than about 7.5 wt.%, no greater than about 7.0 wt.%, no greater than about 6.5 wt.%, no greater than about 6.0 wt.%, no greater than about 5.5 wt.%, no greater than about 5.0 wt.%, no greater than about 4.5 wt.%, no greater than about 4.0 wt.%, no greater than about 3.5 wt.%, no greater than about 3.0 wt.%, or any range or value therein between.

[0111] In some embodiments, the one or more oils may be present at a concentration, individually or collectively, relative to the total weight of the composition, of about 0.5 wt.%, about 0.8 wt.%, about 1.0 wt.%, about 1.2 wt.%, about 1.5 wt.%, about 1.8 wt.%, about 2.0 wt.%, about 2.2 wt.%, about 2.25 wt.%, about 2.5 wt.%, about 2.8 wt.%, about 3.0 wt.%, about 3.2 wt.%, about 3.5 wt.%, about 3.8 wt.%, about 4.0 wt.%, about 4.2 wt.%, about 4.5 wt.%, about 4.8 wt.%, about 5.0 wt.%, about 5.5 wt.%, about 6.0 wt.%, about 6.5 wt.%, about 7.0 wt.%, about 7.5 wt.%, about 8.0 wt.%, about 8.5 wt.%, about 9.0 wt.%, about 9.5 wt.%, about 10.0 wt.%, about 10.5 wt.%, about 11.0 wt.%, about 11.5 wt.%, about 12.0 wt.%, about 12.5 wt.%, about 13.0 wt.%, about 13.5 wt.%, about 14.0 wt.%, about 14.5 wt.%, about 15.0 wt.%, about 16 wt.%, about 17 wt.%, about 18 wt.%, about 19 wt.%, about 20 wt.%, about 21 wt.%, about 22 wt.%, about 23 wt.%, about 24 wt.%, about 25 wt.%, about 26 wt.%, about 27 wt.%, about 28 wt.%, about 29 wt.%, about 30 wt.%, about 35 wt.%, or any range or value therein between.

In some embodiments, the one or more oils may be present at a concentration, individually or collectively, relative to the total weight of the composition, of about 0.5 wt.% to about 35 wt.%, about 0.5 wt.% to about 30 wt.%, about 0.5 wt.% to about 25 wt.%, about 0.5 wt.% to about 20 wt.%, about 0.5 wt.% to about 15 wt.%, about 0.5 wt.% to about 10.0 wt.%, about 0.5 wt.% to about 5 wt.%, about 0.5 wt.% to about 4 wt.%, about 0.5 wt.% to about 3 wt.%, about 0.5 wt.% to about 2 wt.%, about 0.5 to about 1 wt.%, about 1 wt.% to about 30 wt.%, about 1 wt.% to about 25 wt.%, about 1 wt.% to about 20 wt.%, about 1 wt.% to about 15 wt.%, about 1 wt.% to about 10 wt.%, about 1 wt.% to about 8 wt.%, about 1 wt.% to about 5 wt.%, about 1 wt.% to about 4 wt.%, about 1 wt.% to about 3 wt.%, about 1 wt.% to about 2 wt.%, about 3 wt.% to about 30 wt.%, about 3 wt.% to about 20 wt.%, about 3 wt.% to about 15 wt.%, about 3 wt.% to about 10 wt.%, about 3 wt.% to about 8 wt.%, about 3 wt.% to

about 5 wt.%, about 5 wt.% to about 10 wt.%, about 5 wt.% to about 8 wt.%, or any range or value therein.

Water

[0112] A topical composition according to the present disclosure may comprise water at a concentration by weight, relative to the total weight of the composition, of about 0 wt.% to about 98 wt.%, about 5 wt.% to about 95 wt.%, about 10 wt.% to about 90 wt.%, about 15 wt.% to about 85 wt.%, about 20 wt.% to about 80 wt.%, about 25 wt.% to about 75 wt.%, about 30 wt.% to about 70 wt.%, about 35 wt.% to about 65 wt.%, or about 40 wt.% to about 60 wt.%, or any range or value therein. In some embodiments, the water is present at a concentration by weight, relative to the total weight of the composition, of about 5 wt.%, about 10 wt.%, about 15 wt.%, about 20 wt.%, about 25 wt.%, about 30 wt.%, about 35 wt.%, about 40 wt.%, about 45 wt.%, about 50 wt.%, about 55 wt.%, about 60 wt.%, about 65 wt.%, about 70 wt.%, about 75 wt.%, about 80 wt.%, about 85 wt.%, about 90 wt.%, about 95 wt.%, about 96 wt.%, about 97 wt.%, about 98 wt.%, about 99 wt.%, or any range or value therein between.

Composition pH

[0113] A topical composition according to the present disclosure may have any suitable pH for ensuring chemical and physical stability of the composition and any active ingredients contained therein, non-irritation to the skin, and prevention of dry skin, thereby enabling reduction in ROS, enhancement or preservation of elastogenesis, or enhancement of collagenesis.

[0114] In some embodiments, a topical composition according to the present disclosure has a pH of between about 3.0 and about 9.0, between about 3.0 and about 8.5, between about 3.0 and about 8.0, between about 3.0 and about 7.5, between about 3.0 and about 7.0, between about 3.0 and about 6.5, between about 3.0 and about 6.0, between about 3.0 and about 5.5, between about 3.0 and about 5.0, between about 3.0 and about 4.5, between about 3.5 and about 9.0, between about 3.5 and about 8.5, between about 3.5 and about 8.0, between about 3.5 and about 7.5, between about 3.5 and about 7.0, between about 3.5 and about 6.5,

between about 3.5 and about 6.0, between about 3.5 and about 5.5, between about 3.5 and about 5.0, between about 3.5 and about 4.5, between about 4.0 and about 9.0, between about 4.0 and about 8.5, between about 4.0 and about 8.0, between about 4.0 and about 7.5, between about 4.0 and about 7.0, between about 4.0 and about 6.5, between about 4.0 and about 6.0, between about 4.0 and about 5.5, between about 4.0 and about 5.0, between about 4.5 and about 9.0, between about 4.5 and about 8.5, between about 4.5 and about 8.0, between about 4.5 and about 7.5, between about 4.5 and about 7.0, between about 4.5 and about 6.5, between about 4.5 and about 6.0, between about 4.5 and about 5.5, between about 4.5 and about 5.0, or any range or value therein.

[0115] In some embodiments, a topical composition according to the present application may have a pH of about 3.0, about 3.1, about 3.2, about 3.3, about 3.4, about 3.5, about 3.6, about 3.7, about 3.8, about 3.9, about 4.0, about 4.1, about 4.2, about 4.3, about 4.4, about 4.5, about 4.6, about 4.7, about 4.8, about 4.9, about 5.0, about 5.1, about 5.2, about 5.3, about 5.4, about 5.5, about 5.6, about 5.7, about 5.8, about 5.9, about 6.0, about 6.1, about 6.2, about 6.3, about 6.4, about 6.5, about 6.6, about 6.7, about 6.8, about 6.9, about 7.0, about 7.1, about 7.2, about 7.3, about 7.4, about 7.5, about 7.6, about 7.7, about 7.8, about 7.9, about 8.0, about 8.1, about 8.2, about 8.3, about 8.4, about 8.5, about 8.6, about 8.7, about 8.8, about 8.9, about 9.0, or any range or value therein between.

[0116] In some embodiments, the topical composition has an acidic pH, such as less than about 7, less than about 6.5, less than about 6.0, less than about 5.5, less than about 5.0, less than about 4.5, or any range or value therein between. In some embodiments, the composition has a pH of 4.5 to 5.5, 4.5 to 6.0, 4.5 to 6.5, 4.5 to 7.0, 5.0 to 5.5, 5.0 to 6.0, 5.0 to 6.5, 5.0 to 7.0, 5.5 to 6.0, 5.5 to 6.5, or 5.5 to 7.0.

pH Adjusting Agents

[0117] In some embodiments, a topical composition may include one or more pH adjusting agents suitable for adjusting the pH of the composition to be in any of the ranges discussed above. In some embodiments, the pH adjusting agent may comprise one or more suitable mineral acids (*e.g.*, hydrochloric acid, nitric acid, phosphoric acid, phosphorous acid, sulfuric acid, etc.), carboxylic acids (*e.g.*, citric acid, glycolic acid, lactic acid, maleic acid, malic acid, succinic acid, glutaric acid, benzoic acid, malonic acid, salicylic acid, gluconic acid, etc.), polymeric acids (*e.g.*, straight-chain poly(acrylic) acid and its copolymers, such as maleic-acrylic, sulfonic-acrylic, and styrene-acrylic copolymers), cross-linked polyacrylic acids, poly(methacrylic) acids, carageenic acid, alginic acid, etc.), and any combination thereof.

[0118] The pH may be raised or made more alkaline by addition of any suitable alkaline pH adjusting agent (*e.g.*, sodium hydroxide, potassium hydroxide, sodium carbonate, sodium bicarbonate, etc.). In some embodiments, the one or more pH adjusting agents may comprise: ammonia; mono-, di-, and tri-alkyl amines (*e.g.*, trimethylamine); mono-, di-, and tri-alkanolamines (*e.g.*, monoethanolamine, diethanolamine, triethanolamine, isopropanolamine, diisopropanolamine, and triisopropanolamine); alkali metal and alkaline earth metal hydroxides (*e.g.*, sodium hydroxide, potassium hydroxide, lithium hydroxide, etc.); alkali metal and alkaline earth metal silicates; and other pH adjusters (*e.g.*, aminomethylpropanol (AMP-95), tetrahydroxypropylethylenediamine, ETHOMEEN® C-25 (PEG-15 cocoamine), etc.).

[0119] In some embodiments, the one or more pH adjusting agents comprises a buffering agent. A buffering agent is a chemical compound that is or compounds that are added to a solution to allow that solution to resist changes in pH as a result of either dilution or small additions of acids or bases. Effective buffer systems employ solutions which contain large and approximately equal concentrations of a conjugate acid-base pair (or buffering agents). A buffering agent employed herein may be any such chemical compound(s) which is pharmaceutically acceptable, including but not limited to salts (conjugates acids and/or bases)

of phosphates and citrates. In some aspects, the buffering agent comprises phosphate buffered saline (PBS) or an alternative phosphate buffer.

Preservatives

[0120] In some embodiments, the compositions disclosed herein comprises preservatives and/or preservative boosters. In some embodiments, preservatives may comprise of any one of phenoxyethanol, ethylhexylglycerin, sodium benzoate, or any combination thereof. In some embodiments, the preservative booster may further comprise of any one of caprylyl glycol, caprylhydroxamic acid, glycerin, sorbic acid, potassium sorbate, benzoic acid, disodium EDTA, or a combination thereof.

Other Ingredients

[0121] Topical compositions according to the present disclosure may comprise a broad range of optional ingredients or additives. The CTFA INTERNATIONAL COSMETIC INGREDIENT DICTIONARY (15th ed. 2014), which is incorporated by reference herein in its entirety, describes a wide variety of non-limiting cosmetic and pharmaceutical ingredients commonly used in the skin care industry, which are suitable for use in the topical compositions of the present disclosure. Non-limiting examples of genera of such ingredients include: abrasives, anti-acne agents, anticaking agents (*e.g.*, silica, distarch phosphate, etc.), binders, biological additives, bulking agents, chelating agents (*e.g.*, disodium EDTA), chemical additives; colorants; cosmetic astringents, cosmetic biocides, denaturants, drug astringents, external analgesics, film formers, fragrance components, opacifying agents, plasticizers, preservatives (*e.g.*, phenoxyethanol, ethylhexylglycerin, sodium benzoate, combinations of caprylhydroxamic acid, caprylyl glycol, and glycerin (*e.g.*, SPECTRASTAT™ 69038, etc.)), propellants, reducing agents, skin bleaching agents, skin-conditioning agents, skin protectants, solvents (*e.g.*, ethanol, 1,2-hexanediol, etc.), foam boosters, hydrotropes, solubilizing agents, suspending agents (nonsurfactant), sunscreen agents, ultraviolet light absorbers, and viscosity increasing agents (aqueous and nonaqueous), solubilizing agents, sequestrants, and keratolytics, plant extracts, dipeptides, tripeptides (*e.g.*, tripeptide-1) and derivatives thereof, tetrapeptides (*e.g.*, tetrapeptide-2 and derivatives thereof), hexapeptides (*e.g.*, hexapeptide-11, hexapeptide-12, hexapeptide-38, and derivatives

thereof), octapeptides (*e.g.*, octapeptide-45 and derivatives thereof), and any combination thereof. In some embodiments, the topical composition further comprises *Zingiber officinale* root extract, *Olea europaea* leaf extract, *Tremella fuciformis* extract, *Camellia sinensis* leaf extract, squalane, cetyl palmitate, lecithin, propanediol, phosphatidylcholine, lauryl glucoside, *Helianthus annuus* seed oil, sodium acrylates copolymer, or any combination thereof

[0122] When present, such additional ingredients are preferably present at relatively low concentrations, such as from about 0.001 wt.% to about 5 wt.%, about 0.001 wt.% to about 1 wt.%, about 0.001 wt.% to about 0.5 wt.%, about 0.001 wt.% to about 0.1 wt.%, about 0.001 wt.% to about 0.05 wt.%, about 0.001 wt.% to about 0.01 wt.%, or any range or value therein between.

Composition Forms

[0123] A topical composition according to the present disclosure may be in any galenical form that ensures the composition is stable, non-irritating to the skin, non-drying to the skin, and/or pleasant and easy to apply. In some embodiments, the topical composition is an emulsion (*e.g.*, oil-in water emulsion or water-in-oil emulsion), a gel, a cream, a cream-gel, a solution, suspension, lotion, milk, ointment, salve, foam (*e.g.*, aerosol or self-foaming composition), balm, paste, or sachet. In some embodiments, the topical composition is a serum. In some embodiments, the topical composition is an emulsion. In some embodiments, the topical composition is a gel. In some embodiments, the topical composition is a cream. In some embodiments, the topical composition is a galenical form suitable for a pump dispenser. In some embodiments, the topical composition is a cream/gel.

[0124] Methods of Use

[0125] Topical compositions according to the present disclosure may be used to treat skin (*e.g.*, by reducing the effects of UV exposure or aging on skin), to stimulate or preserve elastogenesis in skin, to stimulate or preserve collagenesis in skin, to stimulate or preserve production of elastin and collagen in skin, to reduce the amount of ROS in skin, to stimulate

or preserve the expression of CD44 in skin, to improve the appearance of skin, or to reduce the appearance of fine lines, wrinkles, or crepiness in skin.

[0126] In some embodiments, the methods of using a topical composition according to the present disclosure comprise administering the composition to the skin. In some embodiments, the methods of using a topical composition according to the present disclosure comprise instructing the administration of the composition to the skin. The instructing step may include, for example, instructions on product packaging, in a flier, in a pamphlet, on literature, at the shelf, in advertising (*e.g.*, on a website), oral or written instructions provided at the time of a sale of a product comprising the composition disclosed herein, oral or written instructions provided at the time of purchase of such product disclosed herein, or oral or written instructions provided at the time of delivery of such product disclosed herein, etc.

[0127] In one aspect, the present disclosure relates to a method for stimulating elastogenesis in skin, comprising instructing the administration of a topical composition according to any of the embodiments disclosed herein to the skin. In another aspect, the present disclosure relates to a method for stimulating elastogenesis in skin, comprising administering a topical composition according to any of the embodiments disclosed herein to the skin.

[0128] In one aspect, the present disclosure relates to a method for stimulating production of collagen fibers and elastin fibers in skin, the method comprising instructing the administration of the topical composition according to any of the embodiments disclosed herein to the skin. In another aspect, the present disclosure relates to a method for stimulating production of collagen fibers and elastin fibers in skin, the method comprising administering the topical composition according to any of the embodiments disclosed herein to the skin.

[0129] In one aspect, the present disclosure relates to a method for reducing the effects of aging in skin, the method comprising instructing the administration of the topical composition according to any of the embodiments disclosed herein to the skin. In another aspect, the present disclosure relates to a method for reducing the effects of aging in skin, the method comprising administering the topical composition according to any of the embodiments disclosed herein to the skin.

[0130] In one aspect, the present disclosure relates to a method for reducing the amount of ROS in skin, the method comprising instructing the administration of the topical composition according to any of the embodiments disclosed herein to the skin. In another aspect, the present disclosure relates to a method for reducing the amount of ROS in skin, the method comprising administering the topical composition according to any of the embodiments disclosed herein to the skin.

[0131] In one aspect, the present disclosure relates to a method for improving the appearance of skin, the method comprising instructing the administration of the topical composition according to any of the embodiments disclosed herein to the skin. In another aspect, the present disclosure relates to a method for improving the appearance of skin, the method comprising administering the topical composition according to any of the embodiments disclosed herein to the skin.

[0132] In one aspect, the present disclosure relates to a method for reducing the appearance of wrinkles or crepiness in skin, the method comprising instructing the administration of the topical composition according to any of the embodiments disclosed herein to the skin. In another aspect, the present disclosure relates to a method for reducing the appearance of wrinkles or crepiness in skin, the method comprising administering the topical composition according to any of the embodiments disclosed herein to the skin.

[0133] Topical compositions according to the present disclosure may be used with various treatment regimens. In some instances, the topical compositions described herein are administered once per day, twice per day, three times per day, or more. In some instances, the topical compositions described herein are administered once per day. The topical compositions described herein, in some embodiments, are administered daily, every day, every alternate day, five days per week, once per week, every other week, two weeks per month, three weeks per month, once per month, twice per month, three times per month, or more. In some embodiments, the topical compositions described herein are administered twice daily (*e.g.*, morning and evening).

[0134] In some embodiments, the topical compositions described herein are administered for at least 1 day, 2 days, 3 days, 4 days, 5 days, 6 days, 1 week, 2 weeks, 3 weeks, 1 month, 2

months, 3 months, 4 months, 5 months, 6 months, 7 months, 8 months, 9 months, 10 months, 11 months, 12 months, 18 months, 2 years, 3 years, 4 years, 5 years, 10 years, or more. In some embodiments, the topical compositions described herein are administered twice daily for at least or about 1 week, 2 weeks, 3 weeks, 1 month, 2 months, 3 months, 4 months, 5 months, 6 months, or more. In some embodiments, the topical compositions described herein are administered once daily, twice daily, three times daily, four times daily, or more than four times daily for at least or about 1 week, 2 weeks, 3 weeks, 1 month, 2 months, 3 months, 4 months, 5 months, 6 months, or more.

EXAMPLES

Example 1. Exemplary Antioxidant Formulation

[0135] An exemplary composition according to the present disclosure (referred to as “Formulation A” herein) is shown below in **Table 1**.

[0136] Formulation A includes: hydrophilic antioxidants, enzymatic antioxidants and lipophilic antioxidants. The hydrophilic antioxidants comprise sodium ascorbate (0.02-0.1%), encapsulated in a Vegan DDS liposome, ergothioneine, green tea extract, oleuropein, *Punica Granatum* (pomegranate) extract, ectoine, *Centella asiatica*, carnosine, and lactoferrin, encapsulated in a PRO-LIPO NEO™ liposome. The enzymatic antioxidants comprises ubiquinone, which may or may not be encapsulated in a liposome (*e.g.*, VITISPHERES™ Q10 liposome), betaine and *Tremella fuciformis*, which contains superoxide dismutase, glutathione peroxidase, and catalase enzymes. The lipophilic antioxidants include bisabolol, phytoene, phytofluene, and *Physalis angulata*.

[0137] The composition of Table 1 may be prepared by mixing the listed ingredients with water until the composition is homogenous. The lipophilic ingredients may be mixed with lipids such as triglycerides prior to adding it into the master mix. Lactoferrin may also be separately encapsulated in liposomes prior to adding it into the master mix. Mix all the ingredients thoroughly until the composition is homogenous and adjust pH of the composition to pH of 4-6.5.

[0138] Formulation A was compared to a leading commercial comparator (C E FERULIC®, SkinCeuticals®), comprising water, ethoxydiglycol, L-ascorbic acid (15%), glycerin, propylene glycol, laureth-23, phenoxyethanol, tocopherol, triethanolamine, ferulic acid, panthenol, and sodium hyaluronate.

Table 1. Formulation A

Ingredient	Concentration (wt.%)
Water	80-92
Caprylic/Capric Triglyceride	0.5-5
Glycerin	0.5-5
Sodium Acrylates Copolymer	0.5-2
Sodium Ascorbate	0.02-0.1
Ubiquinone	0.005 – 0.02
Lactoferrin	0.02-0.1
Ectoin	0.2-1.0
Carnosine	0.05-0.2
<i>Physalis Angulata</i> Extract	0.2-1
<i>Centella Asiatica</i> Extract	0.05-0.2
Ergothioneine	0.0005-0.005
<i>Dunaliella Salina</i> Extract	0.005-1.0
<i>Zingiber Officinale</i> (Ginger) Root Extract	0.0005-0.005
<i>Olea Europa</i> (Olive) Leaf Extract	0.05-0.2
<i>Tremella Fuciformis</i> Sporocarp Extract	0.01-0.1
<i>Camellia Sinensis</i> Leaf Extract	0.05-0.2
<i>Punica Granatum</i> Extract	0.05-0.2
Bisabolol	0.05-0.2
Squalane	0.5-3
Betaine	0.08-0.5
Cetyl Palmitate	0.2-2
Lecithin	0.2-1
Propanediol	0.2-1
C12-15 Alkyl Benzoate	0.2-1
Mannitol	0.05-0.2
Phosphatidylcholine	0.05-0.2
Lauryl Glucoside	0.01-0.15
Polyglyceryl-10 Laurate	0.005-0.03
Xanthan Gum	0.005-0.03
Cetyl Alcohol	0.005-0.03
Sodium Lauroyl Lactylate	0.005-0.03
Tocopheryl Acetate	0.001-0.01
Tocopherol	0.001-0.01
<i>Helianthus Annuus</i> (Sunflower) Seed Oil	0.0005-0.005
Phenoxyethanol	0.1-2
Potassium Sorbate	0.01-0.1
Ethylhexylglycerin	0.01-0.12
Caprylhydroxamic Acid	0.01-0.12
Sodium Benzoate	0.005-0.05

Caprylyl Glycol	0.1-1
Lactic Acid	0.005-0.05
Citric Acid	0.005-0.05

Example 2. Antioxidant Efficiency Studies

[0139] Antioxidant efficiency studies were conducted at Kosmoscience Technologies (Brazil). Two products were compared: Formulation A (present disclosure – see **Table 1**) and Formulation B (leading antioxidant on the market). The aim was to evaluate their protective effect against free radicals by semi-quantitatively measuring reactive oxygen (ROS) intermediates using the dichlorofluorescein diacetate (DCFH-DA) probe, which readily crosses the cell membrane through passive diffusion and undergoes deacetylation, producing an oxidant-sensitive 2',7'-dichlorofluorescein (DCHF). In the presence of ROS, DCHF is oxidized to the highly fluorescent dichlorofluorescein (DCF).

[0140] Skin fragments were obtained from healthy female subjects who underwent elective plastic surgery in the abdominal region. (The use of human skin fragments from elective surgeries for this study was submitted to the Research Ethics Committee of Universidade São Francisco – SP, CAAE 56005722.8.0000.5514, under the Opinion 5.503.565.) The skin fragments were fractionated into 1.5-cm² specimens, were packed in culture plates with specific culture media, and were incubated at 37 °C in the presence of 5% CO₂. Each skin sample was treated once with 25-30 mg/cm² of Formulation A or Formulation B.

[0141] After 48 hours of incubation, the skin specimens were subjected to a dose of 13 J/cm² of ultraviolet (UV) radiation, using a UVA Cube 400, SOL 500 H1 filter, and UV Meter (Honle UV America Inc., MA, USA). The skin fragments were then again exposed to Formulation A or Formulation B and maintained in culture conditions for another 24 hours.

[0142] Following the treatment period, the skin fragments were embedded in Tissue-Tek® O.C.T.[™], and serial histological sections of 12 µm were collected directly on slides silanized with a cryostat (Leica, GER – CRYOCUT 1800). Subsequently, the sections were washed with phosphate buffer (PB) and incubated for 1 minute with a solution (1:10,000 in PB) of DCFH-DA (Sigma, USA).

[0143] Immediately after this incubation, the slides were mounted using specific mounting media and analyzed under a microscope (OLYMPUS, JAP – BX53) using the CellSens software (©2010 OLYMPUS CORPORATION). The fluorescence intensity emitted by the oxidation of the DCFH-DA probe was determined from obtained images, which were quantified using the ImageJ software (version 1.48). A semi-quantification of free radical (FR) synthesis using DCFH-DA was performed using an ANOVA, which also allowed for measuring variation of the results and comparison between the groups treated with Formulation A (present disclosure) and Formulation B (commercial product). Then, Bonferroni's *post hoc* test was applied, using a significance level of 5% in both evaluations (GraphPad Prism v6).

[0144] **FIGs. 1A-1F** show the antioxidant effects of Formulation A (present disclosure; **FIGs. 1A-1C**) and Formulation B (commercial product; **FIGs. 1D-1F**) in human skin cultures subjected to ultraviolet (UV) radiation. As expected, UV exposure increased the green fluorescence signal by 141.85% ($P < 0.001$; **FIGs. 1B, 1E**) when compared to the unexposed control (**FIGs. 1A, 1D**), revealing the induction of oxidative stress and free radicals.

[0145] Referring to **FIG. 2**, treatment with the composition according to the present disclosure (Formulation A) decreased the green fluorescent signal by 74.06% ($P < 0.001$) compared with the UV-stressed group. Likewise, the commercial product (Formulation B) decreased the green fluorescent signal by 74.27% ($P < 0.001$) compared with the UV-stressed group. Both formulations A and B reduced oxidative stress in the skin by exerting a protective effect against the excessive increase in free radical synthesis induced by UV exposure. Formulations A and B exerted a substantial antioxidant and anti-aging effect, protecting the skin specimens from the deleterious effects of exposure to solar radiation. There was not a statistically significant difference between Formulation A and Formulation B. That is, the composition according to the present disclosure showed antioxidant activity at least on par with the commercial comparator.

Example 3. Elastin Conservation Assessment in an *Ex Vivo* Model

[0146] *Ex vivo* elastin conservation by Formulation A was evaluated *ex vivo* and compared to a leading commercial comparator containing L-ascorbic acid (Formulation B) by 3D Genomics (Carlsbad, CA). The following studies were conducted by 3D Genomics (Carlsbad CA) as an independent laboratory investigation. Initial skin culture and histology preparation involved photodamaged skin derived from patients undergoing facelift procedures (study approved under Veritas Institutional Review Board - Study ID # 3192). Discarded skin was received within 2 hours of removal from patients. All skin processing was conducted under BSL2 laboratory conditions. The skin was washed in PBS and defatted if necessary. Any visible hairs were shaved using a scalpel. The skin was then cut into ~5mm × 5mm to ~8mm × 8mm square pieces and placed into transwells suspended in 12-well plates.

[0147] A total of 1.0 mL of Skin Media (DMEM/Ham's F-12 (50:50), adenine hydrochloride hydrate, calcium chloride dihydrate, T3 tri-iodothyronine, insulin-transferrin-selenium-ethanolamine (ITS -X), penicillin/streptomycin fetal bovine serum (FBS), GlutaGRO, and gentamicin sulfate) was added to each well, and about 200 µL to 300 µL was added to each transwell to surround the skin sample while maintaining an air-exposed epidermal surface. Media was changed daily.

[0148] Three replicates were treated with Formulation A or Formulation B or were left untreated. Formulations were applied every 24 hours for 7 days, with media changes. The skin was then washed, fixed, and prepared for formalin fixation and paraffin embedding following standard procedures. Sections were cut and prepared for staining with tropoelastin and CD44 primary antibodies followed by fluorescent-conjugated secondary antibodies. DAPI was used to identify the nuclei. Multiple images were captured by immunofluorescence microscopy (Zeiss) (**FIGs. 3A-3C**) to obtain a stitched image of the entire section. The intensity of tropoelastin and CD44 was measured using ImageJ (**FIGs. 4A-4B**). The color channels were split, and the intensity of the red and yellow in the dermal-epidermal junction (DEJ) were measured across the entire section. The average values were assessed by a student's t-test, and $p < 0.05$ was considered significant.

[0149] As shown in **FIG. 3C** and **FIG. 4A**, the comparator (Formulation B) had a direct effect on elastin, evidenced by a significant reduction in tropoelastin in the dermal-epidermal junction (DEJ), accompanied by a weakened fiber appearance. Meanwhile, Formulation A showed an enhancement ($p < 0.05$) in tropoelastin (**FIG. 3B** and **FIG. 4A**) ($p < 0.05$). CD44 was also diminished to a greater extent by Formulation B (see **FIG. 3C** and **FIG. 4B**), compared to Formulation A (see **FIG. 3B** and **FIG. 4B**), but the difference was not significant ($p = 0.06$). Thus, Formulation A not only showed conservation of elastin, but produced an elastin matrix that was healthier in appearance than that produced by Formulation B, with increased plumped tropoelastin and conservation and stimulation of CD44.

Example 4. Elastin Staining After 12-Week Application of Antioxidant Composition

[0150] Five participants consented to having 2mm punch biopsies collected from the right pre-auricular area at baseline and after 12 weeks of applying a topical antioxidant composition according to the present application. The topical composition used in treating the participants was similar to Formulation A in Example 1 (see **Table 1**). However, the ubiquinone (Coenzyme Q-10) was not encapsulated by a liposome. The concentration of ubiquinone was the same as that shown in **Table 1**. The following ingredients associated with ubiquinone-encapsulating liposomes in Formulation A were also removed: cetyl palmitate, lauryl glucoside, sodium lauroyl lactylate, and lactic acid. The topical composition used for biopsy studies was otherwise identical to Formulation A.

[0151] Participants that elected to undergo biopsies were instructed to apply the topical composition on the face, including the pre-auricular area, twice per day for the duration of the study. All biopsies were evaluated for pre- and post-study topical use histological changes by an independent dermatopathologist. The following stains were performed on the obtained baseline and week 12 biopsies; Movat, Herovici and H&E (Hematoxylin and Eosin).

[0152] **FIGs. 5A-B, 6A-B, 7A-B, 8A-B, and 9A-B** show Movat-stained punch biopsies (10X) at baseline (**A**) and after 12 weeks (**B**) of applying the topical composition according to the present disclosure. The Movat-stained samples show elastin fibers in blue (see arrows). The results show stimulus of elastogenesis from applying the topical composition.

[0153] For example, **FIG. 5B** shows a greater number of elastin fibers when compared to baseline (**FIG. 5A**). The elastin fibers are more plump after applying the topical composition, and in the superficial reticular and papillary dermis, the images show fine fibers, where no such fibers are observed at baseline. The fine fibers indicate formation of new elastin fibers. Thus, not only are existing elastin fibers more dense and more widely distributed, but the topical composition of the present application also stimulated growth of new elastin fibers.

[0154] Similar results are shown in **FIG. 6A** (baseline) and **FIG. 6B** (12 weeks). In particular, **FIG. 6B** shows a greater number of elastin fibers after topical application, along with thicker fibers overall, when compared to baseline (**FIG. 6A**).

[0155] Likewise, **FIG. 7B** shows an increased number of dark blue elastin fibers, which are more widely distributed after 12 weeks of topical application, when compared to baseline (**FIG. 7A**).

[0156] **FIG. 8B** also shows a marked increase in elastin fiber distribution after 12 weeks of topical application when compared to baseline (**FIG. 8A**). Additionally, the epidermis and barrier region appear thicker (healthier) after 12 weeks of topical application, and the dermo-epidermal junction is better-demarcated with more robust undulations, indicating a healthier dermo-epidermal junction.

[0157] Finally, **FIG. 9B** shows a higher density, thicker, more widely distributed dark blue (Movat-stained) elastin fibers in the papillary and reticular dermis after 12 weeks of topical application, when compared to baseline (**FIG. 9A**).

[0158] The H&E-stained punch biopsies (**FIGs. 10A-B**) show generation of new collagen fibers (see arrows) in the papillary dermis after 12 weeks of topical application (**FIG. 10B**), which appear to have pushed down old solar elastosis, compared to baseline (**FIG. 10A**). The images show that topical application of the composition according to the present disclosure stimulates collagen production, as well as elastin production.

[0159] The Herovici-stained biopsies (**FIGs. 11A-B**) show collagen fibers in blue. After 12 weeks (**FIG. 11B**) of topical application, the biopsies show new early collagen formation in

the form of thin blue fibers (early mucopolysaccharide formation) (see arrows), when compared to baseline (FIG. 11A).

Example 5. Synergistic Activity of Sodium Ascorbate and Lactoferrin

[0160] To assess the relative activities of lactoferrin, sodium ascorbate, and combinations thereof in production of tropoelastin and CD44 expression, immunostaining experiments were conducted in *ex vivo* skin models, in which immunofluorescence imaging was carried out with antibodies to tropoelastin and CD44, with DAPI counterstaining. The following studies were conducted by 3D Genomics (Carlsbad CA) as an independent laboratory investigation.

[0161] Discarded skin was received within 2 hours of removal from patients. All skin processing was conducted under BSL2 laboratory conditions. The skin was washed in PBS and was defatted, if necessary. Any visible hairs were shaved using a scalpel. The skin was then cut into ~5mm × 5mm to ~8mm × 8mm square pieces and were placed into transwells suspended in 12-well plates. 1.0 mL of Skin Media was added to each well, and about 200 µL to 300 µL was added to each transwell to surround the skin sample while maintaining an air exposed epidermal surface. Media was changed daily.

[0162] Skin Media Recipe:

- DMEM/F12 Media – 500 mL
- Adenine – 50 µM
- CaCl₂ – 1.88 mM
- T3 Tri-iodothyronine – 0.02 nM
- Insulin-Transferrin-Selenium-Ethanolamine (ITS -X) – 5 mL
- Antibiotic-Antimycotic / Penicillin/Streptomycin – 5 mL
- 2% Heat Inactivated FBS – 10 mL
- Glutagro – 5 mL
- Gentamicin – 0.01 mg/mL

[0163] Skin samples in transwell cultures were maintained under standard conditions in the incubator for about 72 hours before initiating treatment.

[0164] Lactoferrin, sodium ascorbate and commercial anti-oxidant formulations were received from Alastin Skincare, Inc. About 100 μ L to 500 μ L of each compound formulation was placed on the surface of a sterile petri plate. Skin was retrieved from the transwell culture plate using sharp forceps to pick up the skin at the edge with minimal forcep compression of skin. The skin was gently swiped over the formulation to completely cover the epidermis and was then returned to the transwell culture plate. The treatment was repeated daily for seven days.

[0165] In this experiment, ten skin samples were processed, all from one individual. Five treatments were studied: untreated skin, lactoferrin, sodium ascorbate, lactoferrin + sodium ascorbate, and commercial formulation. The commercial formulation was C E Ferulic by SkinCeuticals® (L-ascorbic acid (Vitamin C) + Vitamin E + ferulic acid). Two skin samples were treated for each treatment.

[0166] After the course of treatment, the ten skin samples were washed twice in PBS and then fixed in 10% neutral buffered formalin ("NBF") for 24 hours at 4°C. The skin was then washed in PBS and then stored in 70% ethanol. The samples were then transferred to a histology service at the Moores Cancer Center, UC San Diego, for paraffin embedding.

[0167] FFPE blocks of the samples were received and sectioned for immunostaining. Slides were stained with 2 primary antibodies (anti-tropoelastin and anti-CD44). The primary antibodies were detected with fluor-conjugated secondary antibodies (anti-rabbit 647 and anti-mouse Cy3, respectively). Sections were counterstained with DAPI and imaged on a Zeiss Axio Observer running Zeiss Zen software.

[0168] **FIG. 12** shows immunostaining for untreated skin versus skin samples treated with either lactoferrin (**FIG. 12B**) or sodium ascorbate (**FIG. 12C**). Although lactoferrin and sodium ascorbate appear to preserve tropoelastin formation when compared to untreated samples, neither lactoferrin nor sodium ascorbate, alone, appears to cause a statistically significant increase tropoelastin formation over untreated skin (**FIG. 15**). This indicates that the monotherapies preserve, but do not enhance, elastogenesis. Meanwhile, both lactoferrin and sodium ascorbate appear to stimulate CD44 expression, with sodium ascorbate showing a greater stimulation of CD44 expression than lactoferrin (**FIG. 16**).

[0169] FIG. 13 shows immunostaining for skin samples treated with either lactoferrin (FIG. 13A), sodium ascorbate (FIG. 13B), and a combination of lactoferrin + sodium ascorbate (FIG. 13C). As shown in FIG. 13C and FIG. 15, the combination treatment causes a statistically significant increase in tropoelastin versus the monotherapies of lactoferrin or sodium ascorbate alone. Indeed, the signal intensity for tropoelastin for the combination treatment is over 5X the tropoelastin signal achieved for untreated skin, while the signal intensities achieved by the monotherapies do not show a statistically significant increase over untreated skin. Thus, lactoferrin and sodium ascorbate exhibit synergy in stimulation of elastogenesis.

[0170] Additionally, the combination of lactoferrin and sodium ascorbate produces tropoelastin in amounts that far exceed the tropoelastin production observed for the commercial comparator (C E Ferulic, SkinCeuticals®) (FIG.14B–C, FIG. 15).

[0171] For CD44, the lactoferrin monotherapy significantly increases CD44 expression over untreated skin, while the sodium ascorbate monotherapy even further enhances CD44 expression, at a level of nearly 6X that observed in untreated skin and 3X the level achieved by lactoferrin alone (FIGs. 12C, 13B, 16). The combination of lactoferrin and sodium ascorbate also stimulates CD44 expression, at nearly 5X the level observed in untreated skin, indicating that the combination preserves CD44 expression relative to sodium ascorbate alone. Again, the combination of lactoferrin and sodium ascorbate outperforms the commercial comparator in terms of CD44 expression (FIG. 16, FIG. 14C).

[0172] The compositions and methods illustratively described herein may suitably be practiced in the absence of any element or elements, limitation or limitations, not specifically disclosed herein. Thus, for example, the terms “comprising”, “including,” “containing”, etc. shall be read expansively and without limitation. Additionally, the terms and expressions employed herein have been used as terms of description and not of limitation, and there is no intention in the use of such terms and expressions of excluding any equivalents of the features shown and described or portions thereof. It is recognized that various modifications are possible within the scope of the disclosure claimed. Thus, it should be understood that although the present disclosure has been specifically disclosed by preferred embodiments and

optional features, modification and variation of the disclosure embodied therein herein disclosed may be resorted to by those skilled in the art, and that such modifications and variations are considered to be within the scope of this disclosure.

[0173] The disclosure has been described broadly and generically herein. Each of the narrower species and subgeneric groupings falling within the generic disclosure also form part of the methods. This includes the generic description of the methods with a proviso or negative limitation removing any subject matter from the genus, regardless of whether or not the excised material is specifically recited herein. The present technology is not to be limited in terms of the particular embodiments described in this application, which are intended as single illustrations of individual aspects of the present technology. Many modifications and variations of this present technology can be made without departing from its spirit and scope, as will be apparent to those skilled in the art. Functionally equivalent methods and apparatuses within the scope of the present technology, in addition to those enumerated herein, will be apparent to those skilled in the art from the foregoing descriptions. Such modifications and variations are intended to fall within the scope of the present technology. It is to be understood that this present technology is not limited to particular methods, reagents, compounds compositions or biological systems, which can, of course, vary. It is also to be understood that the terminology used herein is for the purpose of describing particular embodiments only, and is not intended to be limiting.

[0174] One skilled in the art readily appreciates that the present disclosure is well adapted to carry out the objects and obtain the ends and advantages mentioned, as well as those inherent therein. Modifications therein and other uses will occur to those skilled in the art. These modifications are encompassed within the spirit of the disclosure and are defined by the scope of the claims, which set forth non-limiting embodiments of the disclosure.

[0175] In addition, where features or aspects of the disclosure are described in terms of Markush groups, those skilled in the art will recognize that the disclosure is also thereby described in terms of any individual member or subgroup of members of the Markush group.

[0176] All references, articles, publications, patents, patent publications, and patent applications cited herein are incorporated by reference in their entireties for all purposes.

However, mention of any reference, article, publication, patent, patent publication, and patent application cited herein is not, and should not be taken as, an acknowledgment or any form of suggestion that they constitute valid prior art or form part of the common general knowledge in any country in the world.

ENUMERATED EMBODIMENTS

1. A topical composition comprising:
 - a hydrophilic antioxidant, wherein the hydrophilic antioxidant comprises sodium ascorbate;
 - an enzymatic antioxidant; and
 - a hydrophobic antioxidant.
2. The topical composition of embodiment 1, wherein the sodium ascorbate is present at a concentration of about 0.01 wt.% to about 1.0 wt.%, relative to the total weight of the composition.
3. The topical composition of embodiment 1 or embodiment 2, wherein the sodium ascorbate is present at a concentration of about 0.02 wt.% to about 0.10 wt.%, relative to the total weight of the composition.
4. The composition of any one of embodiments 1-3, wherein the hydrophilic antioxidant further comprises, lactoferrin, ergothioneine, oleuropein, *Punica granatum* extract, ectoine, *Centella asiatica* extract, carnosine, *Camellia sinensis* extract, or any combination thereof.
5. The composition of any one of embodiments 1-4, wherein the hydrophilic antioxidant comprises lactoferrin.
6. The topical composition of embodiment 4 or 5, wherein the lactoferrin is present at a concentration of 0.01 wt.% to 0.1 wt.%.

7. The topical composition of any one of embodiments 1-6, wherein the enzymatic antioxidant comprises ubiquinone, betaine, superoxide dismutase, catalase, glutathione peroxidase, or any combination thereof.
8. The topical composition of any one of embodiments 1-7, wherein the enzymatic antioxidant comprises ubiquinone.
9. The topical composition of embodiment 7 or embodiment 8, wherein the ubiquinone is present in the composition at a concentration of 0.001 wt.% to 0.1 wt.%, relative to the total weight of the composition.
10. The topical composition of any one of embodiments 7-9, wherein the ubiquinone is present in the composition at a concentration of 0.005 wt.% to 0.05 wt.%, relative to the total weight of the composition.
11. The topical composition of any one of embodiments 1-10, wherein the hydrophobic antioxidant comprises bisabolol, phytoene, phytofluene and physalis angulate, or any combination thereof.
12. The topical composition of any one of embodiments 1-11, wherein the hydrophobic antioxidant is present in the composition at a concentration of 0.1 wt.% to 1.2 wt.%, relative to the total weight of the composition.
13. The topical composition of any one of embodiments 1-12, wherein the sodium ascorbate is encapsulated in a first liposome.
14. The topical composition of embodiment 13, wherein the first liposome comprises phosphatidylcholine.

15. The topical composition any one of embodiments 1-14, further comprising a second hydrophilic antioxidant wherein the second antioxidant is lactoferrin encapsulated in a second liposome.
16. The topical composition of embodiment 15, wherein the second liposome comprises propanediol, lecithin, or any combination thereof.
17. The topical composition of embodiment 15 or embodiment 16, wherein the second liposome is different from the first liposome.
18. The topical composition of any one of embodiments 1-17, wherein the total concentration of antioxidants in the composition is less than 15 wt.%, relative to the total weight of the composition.
19. The topical composition of any one of embodiments 1-17, wherein the total concentration of antioxidants in the composition is less than 10 wt.%, relative to the total weight of the composition.
20. The topical composition of embodiment 1, wherein:
the hydrophilic antioxidant comprises sodium ascorbate and lactoferrin;
the enzymatic antioxidant comprises ubiquinone; and
the hydrophobic antioxidant comprises one or more of bisabolol, phytoene, phytofluene, *Physalis angulata* or a combination thereof.
21. The topical composition of embodiment 20, wherein:
the sodium ascorbate is present at a concentration of 0.02 wt.% to 0.1 wt.%;
the lactoferrin is present at a concentration of 0.02 wt.% to 0.08 wt.%; and
the ubiquinone is present at a concentration of 0.005 wt.% to 0.5 wt.%.

22. The topical composition of any one of the embodiments 1-21, wherein the sodium ascorbate, the enzymatic antioxidant, and the hydrophobic antioxidant are present at concentrations sufficient to reduce reactive oxygen species in skin.
23. The topical composition of any one of embodiments 1-21, wherein:
the sodium ascorbate and the lactoferrin are present at concentrations sufficient to synergistically promote elastogenesis or collagenesis in skin or to synergistically reduce ROS in skin; or
any combination of the sodium ascorbate, the lactoferrin, the enzymatic antioxidant, and the hydrophobic antioxidant are present at concentrations sufficient to synergistically promote at least one of elastogenesis or collagenesis in skin or to synergistically reduce ROS in skin.
24. A topical composition, comprising:
sodium ascorbate; and
lactoferrin,
wherein the sodium ascorbate and lactoferrin synergistically enhance elastogenesis.
25. The topical composition of embodiment 24, wherein the sodium ascorbate is present at a concentration of about 0.01 wt.% to about 1.0 wt.%, relative to the total weight of the composition.
26. The topical composition of embodiment 24 or embodiment 25, wherein the sodium ascorbate is present at a concentration of about 0.02 wt.% to about 0.10 wt.%, relative to the total weight of the composition.
27. The composition of any one of embodiments 24-26, wherein the lactoferrin is present at a concentration of 0.01 wt.% to 0.1 wt.%.
28. The topical composition of any one of embodiments 24-27, wherein the composition enhances tropoelastin production or CD44 expression in skin.

29. The topical composition of any one of embodiments 24-28, wherein the composition enhances tropoelastin production relative to a composition comprising only one of lactoferrin or sodium ascorbate.

30. The topical composition of any one of embodiments 24-30, wherein the composition preserves CD44 expression relative to a composition comprising sodium ascorbate but not comprising lactoferrin.

31. A method for stimulating production of collagen fibers and elastin fibers in skin, the method comprising:
administering the topical composition according to any one of embodiments 1-30 to the skin.

32. A method for reducing the effects of aging in skin, the method comprising:
instructing the administration of the topical composition according to any one of embodiments 1-30 to the skin.

33. A method for reducing the effects of aging in skin, the method comprising:
administering the topical composition according to any one of embodiments 1-30 to the skin.

34. A method for reducing the amount of ROS in skin, the method comprising:
instructing the administration of the topical composition according to any one of embodiments 1-30 to the skin.

35. A method for reducing the amount of ROS in skin, the method comprising:
administering the topical composition according to any one of embodiments 1-30 to the skin.

36. A method for improving the appearance of skin, the method comprising:
instructing the administration of the topical composition according to any one of embodiments 1-30 to the skin.

37. A method for improving the appearance of skin, the method comprising:
administering the topical composition according to any one of embodiments 1-30 to the skin.

38. A method for reducing the appearance of wrinkles or crepiness in skin, the method comprising: instructing the administration of the topical composition according to any one of embodiments 1-30 to the skin.

39. A method for reducing the appearance of wrinkles or crepiness in skin, the method comprising:
administering the topical composition according to any one of embodiments 1-30 to the skin.

40. A method for increasing tropoelastin production in skin, the method comprising:
instructing the administration of the topical composition according to any one of embodiments 1-30 to the skin.

41. A method for increasing tropoelastin production in skin, the method comprising:
administering the topical composition according to any one of embodiments 1-30 to the skin.

42. A method for increasing CD44 expression in skin, the method comprising: instructing the administration of the topical composition according to any one of embodiments 1-30 to the skin.

43. A method for increasing CD44 expression in skin, the method comprising:
administering the topical composition according to any one of embodiments 1-30 to the skin.

44. A composition according to any one of embodiments 1-30 for use in stimulating elastogenesis in skin, stimulating production of collagen fibers and elastin fibers in skin,

increasing tropoelastin production in skin, increasing CD44 expression in skin, reducing the effects of aging in skin, reducing the amount of ROS in skin, improving the appearance of skin, or reducing the appearance of wrinkles or crepiness in skin.

45. Use of a composition according to any one of embodiments 1-30 for stimulating elastogenesis in skin, stimulating production of collagen fibers and elastin fibers in skin, increasing tropoelastin production in skin, increasing CD44 expression in skin, reducing the effects of aging in skin, reducing the amount of ROS in skin, improving the appearance of skin, or reducing the appearance of wrinkles or crepiness in skin.

46. A composition according to any one of embodiments 1-30 for use in the manufacture of a medicament for stimulating elastogenesis in skin, stimulating production of collagen fibers and elastin fibers in skin, increasing tropoelastin production in skin, increasing CD44 expression in skin, reducing the effects of aging in skin, reducing the amount of ROS in skin, improving the appearance of skin, or reducing the appearance of wrinkles or crepiness in skin.

WHAT IS CLAIMED IS:

1. A topical composition comprising:
a hydrophilic antioxidant, wherein the hydrophilic antioxidant comprises sodium ascorbate;
an enzymatic antioxidant; and
a hydrophobic antioxidant.
2. The topical composition of claim 1, wherein the sodium ascorbate is present at a concentration of about 0.01 wt.% to about 1.0 wt.%, relative to the total weight of the composition.
3. The topical composition of claim 1 or claim 2, wherein the sodium ascorbate is present at a concentration of about 0.02 wt.% to about 0.10 wt.%, relative to the total weight of the composition.
4. The composition of any one of claims 1-3, wherein the hydrophilic antioxidant further comprises, lactoferrin, ergothioneine, oleuropein, *Punica granatum* extract, ectoine, *Centella asiatica* extract, carnosine, *Camellia sinensis* extract, or any combination thereof.
5. The composition of any one of claims 1-4, wherein the hydrophilic antioxidant comprises lactoferrin.
6. The topical composition of claim 4 or 5, wherein the lactoferrin is present at a concentration of 0.01 wt.% to 0.1 wt.%.
7. The topical composition of any one of claims 1-6, wherein the enzymatic antioxidant comprises ubiquinone, betaine, superoxide dismutase, catalase, glutathione peroxidase, or any combination thereof.

8. The topical composition of any one of claims 1-7, wherein the enzymatic antioxidant comprises ubiquinone.
9. The topical composition of claim 7 or claim 8, wherein the ubiquinone is present in the composition at a concentration of 0.001 wt.% to 0.1 wt.%, relative to the total weight of the composition.
10. The topical composition of any one of claims 1-9, wherein the hydrophobic antioxidant comprises bisabolol, phytoene, phytofluene and physalis angulate, or any combination thereof.
11. The topical composition of any one of claims 1-10, wherein the hydrophobic antioxidant is present in the composition at a concentration of 0.1 wt.% to 1.2 wt.%, relative to the total weight of the composition.
12. The topical composition of any one of claims 1-11, wherein the sodium ascorbate is encapsulated in a first liposome.
13. The topical composition of claim 12, wherein the first liposome comprises phosphatidylcholine.
14. The topical composition any one of claims 1-13, further comprising a second hydrophilic antioxidant wherein the second antioxidant is lactoferrin encapsulated in a second liposome.
15. The topical composition of claim 14, wherein the second liposome is different from the first liposome.

16. The topical composition of any one of claims 1-15, wherein the total concentration of antioxidants in the composition is less than 15 wt.%, relative to the total weight of the composition.
17. The topical composition of claim 1, wherein:
the hydrophilic antioxidant comprises sodium ascorbate and lactoferrin;
the enzymatic antioxidant comprises ubiquinone; and
the hydrophobic antioxidant comprises one or more of bisabolol, phytoene, phytofluene, *Physalis angulata* or a combination thereof.
18. The topical composition of claim 17, wherein:
the sodium ascorbate is present at a concentration of 0.02 wt.% to 0.1 wt.%;
the lactoferrin is present at a concentration of 0.02 wt.% to 0.08 wt.%; and
the ubiquinone is present at a concentration of 0.005 wt.% to 0.5 wt.%.
19. The topical composition of any one of claims 1-18, wherein the sodium ascorbate, the enzymatic antioxidant, and the hydrophobic antioxidant are present at concentrations sufficient to reduce reactive oxygen species in skin.
20. The topical composition of any one of claims 1-19, wherein:
the sodium ascorbate and the lactoferrin are present at concentrations sufficient to synergistically promote elastogenesis or collagenesis in skin or to synergistically reduce ROS in skin; or
any combination of the sodium ascorbate, the lactoferrin, the enzymatic antioxidant, and the hydrophobic antioxidant are present at concentrations sufficient to synergistically promote at least one of elastogenesis or collagenesis in skin or to synergistically reduce ROS in skin.
21. A topical composition, comprising:
sodium ascorbate; and

lactoferrin,

wherein the sodium ascorbate and lactoferrin synergistically enhance elastogenesis.

22. A method for stimulating production of collagen fibers and elastin fibers in skin, reducing the effects of aging in skin, reducing the amount of ROS in skin, improving the appearance of skin, reducing the appearance of wrinkles or crepiness in skin, increasing tropoelastin production in skin, or increasing CD44 expression in skin, the method comprising:

administering the topical composition according to any one of claims 1-21 to the skin;

and or

instructing the administration of the topical composition according to any one of claims 1-21 to the skin.

23. A composition according to any one of claims 1-21 for use in the manufacture of a medicament for stimulating elastogenesis in skin, stimulating production of collagen fibers and elastin fibers in skin, increasing tropoelastin production in skin, increasing CD44 expression in skin, reducing the effects of aging in skin, reducing the amount of ROS in skin, improving the appearance of skin, or reducing the appearance of wrinkles or crepiness in skin.