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| (54) Title: TOPICAL MOISTURIZING COMPOSITION AND METHOD (57) Abstract The present invention comprises methods and compositions for topically treating keratinous structures of humans and animals including skin, hair, fingernails, toenails, hooves, and horns. | | |

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TOPICAL MOISTURIZING COMPOSITION AND METHOD

15 **Technical Field**

20 The present invention is related to a process and composition for moisturizing and rejuvenating keratinous tissues including skin, hair, fingernails, and toenails of humans and animals, and also hooves and horns of animals. More particularly, the present invention relates to topically applying the composition disclosed herein in order to treat the affected keratinous tissue.

Background of the Invention

25 The skin is the largest organ in the body and serves several important functions that are essential to life. The skin retards dehydration and also acts as a barrier to the invasion of various pathogens and noxious substances. Skin is composed of the epidermis, or upper layer, and the subjacent dermis. The epidermis is the superficial layer and gives rise to the nails, hair, 30 sebaceous glands, sweat glands, and the parenchyma of mammary glands. The epidermis is composed of several layers. As cells from the deeper layer, the stratum germinativum, move toward the surface, they begin to synthesize the intracellular protein keratin. During subsequent movement, these cells lose their 35 distinct nuclei and form the outermost layer of the epidermis known as the stratum corneum which is comprised of several

layers of cornified epidermal cells that are embedded in an intercellular matrix of semi-polar and polar lipids. This layer acts as a transport route for various drugs, such as hydrocortisone, and also acts as a barrier to the transport of other drugs and cosmetics (Elias et al., *Journal of Investigative Dermatology* 73: 339-348, 1979). In addition, this lipid layer of the stratum corneum assists in the retention of water. The water content of the stratum corneum has a profound influence on the appearance, flexibility, texture, and dryness of the skin, and also on the absorption of drugs and other molecules into and through the skin.

With increasing age, the skin gradually loses ceramides and water and becomes drier, less flexible and supple, more wrinkled, and scaly in appearance. One of the major objectives of the cosmetic industry is to retard the drying and wrinkling of the skin that occurs with normal aging or as the result of exposure to wind, sun, cold and chemicals. As the mean age of the population increases, more people are seeking products that will retard the effects of aging on the skin and will essentially rejuvenate the skin. Increasing the moisture content of the skin is one mechanism for achieving this objective. Furthermore, enhanced skin hydration facilitates the transport of pharmaceuticals across the epidermis to reach the underlying dermis and subjacent capillaries of the lymphatic and circulatory systems.

Another objective of the cosmetic industry is to retard the drying of the hair, fingernails and toenails, which all arise from the epidermis. In addition to enhancing the youthful appearance of an individual, increased hydration of these structures prevents the painful effects of cracked nails and itchy, scaly scalp. In animals, similar problems can occur with fingernails and toenails and also with horns and hooves which are all epidermal derivatives. For example, cracked hooves can result in lameness or in injury to the coronary band, the primary growth and nutritional source for the hoof wall. Injuries to the coronary band can cause serious permanent defects in the growth of the hoof wall.

5 The formation of organogels containing lecithin dissolved with isopropyl palmitate or other solvents, and water, has been described by Luisi et al., *Colloid and Polymer Science* 268: 356-374 (1990) and Scartazzini et al., *The Journal of Physical Chemistry* 92: 829-833 (1988). Williman et al., *Journal of Pharmaceutical Sciences* 81:871-874 (1992), examined the efficacy of lecithin organogels for use in the transdermal delivery of drugs such as scopolamine and broxaterol. Williman et al., also observed that lecithin organogels had no detrimental effect on skin when compared to control samples treated with physiological saline (see page 872, column. 2, paragraph 3, *Journal of Pharmaceutical Sciences* 81:871-874 (1992)).

10 Catz et al., in U.S. Patent No. 5,238,933, discloses skin permeation enhancer systems which increase the permeability of the skin to transdermally administered, pharmacologically active agents.

15 Smith, in U.S. Patent No. 3,952,099, discloses dermatological compositions for enhancing the penetration of pharmacologically active agents, such compositions comprising a sugar ester in combination with a sulfoxide or phosphine oxide.

20 Loucks, in U.S. Patent No. 4,701,471, discloses a cosmetic and pharmaceutical composition comprising bovine bone marrow acids mixed with lecithin for prevention of the fatty acid oxidation and odor putrefaction.

25 In U.S. Patent No. 3,957,971, Oleniacz discloses moisturizing units for treating keratinous tissue comprising liposomes having a ternary lipid mixture of lecithin, dicetyl phosphate, and a sterol.

30 Sakai et al., in U.S. Patent No. 4,760,096, discloses a skin moisturizing method and preparation containing a combination of a phosphatide such as soy lecithin, and one or more C₁₀-C₃₀ carboxylic acid sterol esters.

35 U.S. Patent No. 4,783,450 to Fawzi et al. discloses the use of lecithin as a skin penetration enhancer for transdermal delivery of the drug procaterol through skin.

5 A method and composition for increasing the moisture of epidermal structures are needed. The composition should be easy to apply topically, enhance moisture retention, and also have the capacity to deliver compounds that will assist in moisturizing and rejuvenating keratinous structures such as the skin hair, fingernails, toenails, hooves and horns.

Summary of the Invention

10 In one embodiment, the present invention provides an easy to use therapeutic and cosmetic process for treating dry skin and for alleviating the associated irritation and cracking of the skin by topically applying the composition disclosed herein. Use of this process and composition increases the moisture content of the skin, reduces wrinkling, and provides a rejuvenated appearance to
15 the skin. In addition, this invention has great utility for the treatment of dry and brittle fingernails and toenails, and the adjacent skin that often is dry and cracked. In another embodiment, this invention is a therapeutic and cosmetic process for application to animals with cracked and damaged horns and/or
20 hooves. A horn or hoof dressing in show horses and cattle would produce a more vibrant and healthy appearance. In addition, rapid closure of cracks in hooves would prevent invasion by foreign material and reduce the incidence of infection.

25 An additional embodiment of the invention is a therapeutic and cosmetic process for the treatment of dry and thinning hair to provide increased hair growth and thickness. It is understood that the present invention also encompasses a method and composition for delivery of molecules including, but not limited, to elastin, collagen and collagen fragments, glucosamine, glucosamine
30 sulfate, glycerol, urea, ceramides, dimethicone, N-decylmethyl sulfoxide, salicylic acid, lanolin, chondroitin sulfate, hyaluronic acid, squalene, and various alpha hydroxy compounds such as lactic acid, citric acid, and glycolic acid, into the epidermis, dermis and other keratinous tissue.

35 The present invention can include other pharmaceutically acceptable components such as gelling agents, compounding

agents, scents and the like. The composition of the present invention can also include other pharmaceutically active agents such as antibacterial, antifungal, antiprotozoal or antiviral agents.

5 This invention addresses the need for an easy-to-use topical treatment for cosmetic and therapeutic purposes of keratinous structures including the skin, nails, and hair of humans and animals, and also for the treatment of the nails, hair, hooves, and horns of animals.

10 Accordingly, it is an object of the invention to provide a composition and method for treating skin of humans and animals, especially dry and cracked skin, to increase the moisture of the skin.

15 It is another object of the invention to provide a composition and method for treating skin of humans and animals to decrease the wrinkled appearance of the skin.

Still another object of the invention is to provide a composition and method for treating skin to rejuvenate the skin and decrease the aged appearance of the skin.

20 It is another object of the invention to provide a method for topically applying an improved composition to animal or human keratinous tissue for enhancing the penetration of pharmacologically active substances into keratinous tissue, especially the epidermis and dermis of the skin, without damaging the tissue or causing adverse systemic effects.

25 Another object of the invention is to provide a composition and method for treating psoriasis.

Yet object of the invention is to provide a composition and method for treating eczema.

30 Still another object of the invention is to provide a composition and method for treating windburn, chapped lips, sunburn, and skin dehydrated due to exposure to chemicals.

Another object of the invention is to provide a composition and method for treating cracked fingernails and toenails of humans and animals.

Still another object of the invention is to provide a composition and method for treating cracked hooves and horns of animals.

5 Yet another object of the invention is to provide a composition and method for treating the cracked teats of animals and humans to prevent mastitis.

Another object of the invention is to provide a composition and method for treating dry and thinning hair of humans and animals.

10 Still another object of the invention is to provide a composition and method for treating calluses, corns, and any other skin conditions involving drying of the skin.

These and other objects, features and advantages of the present invention will become apparent after a review of the following detailed description of the disclosed embodiments and the appended claims.

Detailed Description of the Invention

20 The term "lecithin" is used to mean a phosphatide called phosphatidylcholine and can be isolated from soybean, eggs and other sources including, but not limited to, heart, brain, and liver. Lecithin is a mixture of the diglycerides of steric, palmitic, and oleic acids, linked to the choline ester of phosphoric acid. Soybean lecithin is a preferred lecithin and may contain the following acids; palmitic, stearic, palmitoleic, oleic, linoleic, linolenic and arachidonic as described in the *Merck Index* (Ninth edition, 1976, page 711).

25 The term PLURONIC refers to poloxamer compounds and are sold collectively under the trademark PLURONIC (BASF, Parsippany, NJ). PLURONIC F-127 corresponds to poloxamer 407, a polyoxypropylene-polyoxyethylene block copolymer described by Schmolka in the *Journal of Biomedical Materials Research* 6: 571-582, (1972).

35 The term "moisturize" or derivatives thereof, relates to the conservation or enhancement of the water content of the

keratinous tissue of animals and humans, with particular reference to the skin, hair, nails, hooves and horns.

5 "Topical" application is used to mean local administration of the composition and its various embodiments, for example, in the treatment of dry skin.

The term "pharmacologically active agent" relates to any chemical material or compound suitable for topical administration which includes any desired local effect on animal or human tissue contacted therewith and is sometimes referred to as a "penetrant".

10 The term "pharmaceutically effective carrier" is used herein to mean any liquid, gel, salve, solvent, liquid, diluent, fluid ointment base, and the like, which is suitable for use in contact with living animal or human tissue without causing adverse physiological responses, and which does not interact with the other components of the composition in a deleterious manner.

15 By the term "therapeutically effective amount" of a molecule, drug or pharmacologically active agent is meant a nontoxic but sufficient amount to provide the desired therapeutic effect.

20 The "enhanced penetration" caused by the method and compositions of this invention, such as lecithin organogel, PLURONIC (BASF, Parsippany, NJ), and N-decylmethyl sulfoxide can be observed in many ways known to those skilled in the art.

25 The term "keratinous tissue" as used herein, means skin, fingernails, toenails, hooves, horns and hair, and any other cells containing keratin. The present invention provides a method and composition for topically treating damaged or diseased keratinous tissue resulting from any number of causes including, but not limited to: aging; chemical drying; radiation; burns from wind, sun, fire, cold, frostbite, radiation or chemicals; and dehydration

30 resulting from skin disease, abrasion, sun, chemicals, wind, cold, fire, renal disease, colonic disease, hemorrhage, vasopressin imbalances, hypothalamic dysfunction, neurohypophyseal dysfunction, or other endocrine abnormalities.

35 The present invention includes a composition for topical treatment of keratinous tissue comprising the following

components; lecithin, isopropyl palmitate and water. The combination of lecithin, isopropyl palmitate, and water is called lecithin organogel. The present invention optionally includes lecithin organogel in combination with an approximately 20% solution of PLURONIC F-127 (BASF, Parsippany, NJ), otherwise known as poloxamer 407, in a ratio of approximately 1 : 4. Other PLURONICS may be used in the present invention. It is to be understood that the soy lecithin of the present invention is a preferred lecithin source and may be dissolved in isopropyl palmitate to achieve a final concentration in the composition of from approximately 20% - 90%, with a more preferred final concentration of from approximately 20% - 40%. Lecithins may optionally be derived from eggs, and organs such as heart, brain and liver, and used at concentrations of approximately 20% - 99%, with more preferred final concentrations of from approximately 20% - 40%. The composition according to the present invention can be in the form of lotions, salves, creams, ointments, liposomes, sprays, or gels. The desired form is lotions, ointments and salves. Liposomes are described in detail by Oleniacz in U.S. Patent No. 3,957,971, the entirety of which is hereby incorporated by reference.

Although not wanting to be bound by the following hypothesis, it is believed that the method and composition of the present invention cause an increase the water content of the skin, perhaps by increasing the fluid content of the epidermis and dermis. It is believed that the composition of the invention enhances diffusion of moisturizers, surfactants, and emollients into and possibly through the epidermal and dermal layers of the skin. It is understood that the present invention also encompasses a method and composition for delivery of molecules into the skin. These molecules optionally include, but are not limited to, elastin, collagen and collagen fragments, glucosamine, glucosamine sulfate, glycerol, urea, ceramides, dimethicone, N-decylmethyl sulfoxide, salicylic acid, lanolin, chondroitin sulfate, hyaluronic acid, squalene, and various alpha hydroxy compounds such as lactic acid, citric acid, and glycolic acid. N-decylmethyl sulfoxide

is included in the composition in a final concentration range of from 0.01% to 1% with a preferred range of 0.1% to 0.5%.

By allowing the passage of collagen fragments and elastin, for example, into the skin, the present invention increases the water content of the skin and decreases the wrinkled appearance. Glucosamine, or glucosamine derivatives such as glucosamine sulfate, that stimulate components of the extracellular matrix, can also be added to the present invention to plump up the appearance of the granular and basal cell layers.

A gelling agent optionally may be added to the formulation. Gelling agents that are suitable for use in the present invention include, but are not limited to, cellulose ethers, alginates, polyacrylates, bentonite, gelatin, tragacanth, polyvinylpyrrolidone, polyvinyl alcohol, and polyoxyethylene/polyoxypropylene block copolymers, some of which are known as poloxamers. The poloxamer compounds are sold collectively under the trademark PLURONIC (BASF, Parsippany, NJ). PLURONIC F-127 corresponds to poloxamer 407. Other PLURONICS may be used in the present invention.

Optionally, a preservative, such as sorbic acid, can be added to the composition. Other preservatives well known to those of ordinary skill in the art can be used in the composition.

Agents for improving the aroma of the formulation can optionally be added to the composition. A desired aroma improving agent is honey almond oil (PCAA, Kinghurst, Houston, TX). Other aroma improving agents include, but are not limited to, avocado oil, sesame oil, castor oil, olive oil, grapeseed oil, clove oil, groundnut oil, corn oil, lemon oil, coconut oil, lime oil, hazelnut oil, jojoba oil, carthamus oil and wheatgerm oil. The oils can be added individually or in combination. It is to be understood that various fragrances and assorted floral scents may be optionally added to the composition and are commercially available (PCAA, Houston, TX). Stabilizers, antioxidants, preservatives, humectants, regreasing agents, solvents or auxiliaries can be added to improve stability and/or adhesiveness of the formulations.

In addition, antimicrobial agents can be optionally added to the composition of the present invention if required. Addition of an antimicrobial agent is desirable when treating inflammatory conditions associated with acne, psoriasis or eczema.

5 The composition of the present invention can be administered topically either once daily or several times per day depending upon the nature and severity of the condition being treated.

10 It will be appreciated that other embodiments and uses will be apparent to those skilled in the art and that the invention is not limited to these specific illustrative examples.

Example 1

Lecithin Organogel Composition Prepared With Pluronic

15 A preferred composition was prepared as described below. The lecithin organogel was prepared by dissolving 20 g of soy lecithin granules (PCAA, Houston, TX) in 20 ml of isopropyl palmitate (PCAA, Houston, TX). The mixture was stirred periodically for 24 hours until the soy lecithin granules were dissolved. The PLURONIC gel 20% stock solution was prepared by dissolving 16 g of PLURONIC F127 powder (BASF, Parsippany, NJ), also called poloxamer 407, in 80 ml of purified water. Potassium sorbate (160 mg; PCAA, Houston, TX) was added to the PLURONIC gel 20% stock solution as a preservative. This was placed in the refrigerator at about 4°C for about 24 hours and stirred periodically.

25 The composition was prepared by mixing 20 ml of the lecithin organogel with 2 ml of the honey almond oil (PCAA, Houston, TX) until a smooth mixture was prepared. Honey almond oil was added for fragrance. Next, 80 ml of the PLURONIC gel 20% stock solution was mixed in until a gel formed. A blender was used for this mixing step at room temperature with disinfected equipment. The gel was stored at room temperature.

Example 2

Lecithin Organogel Composition Prepared Without Pluronic

5 In another embodiment of the present invention, the composition described in Example 1 was prepared using lecithin organogel without the addition of the PLURONIC gel 20% stock solution. The final concentration of lecithin organogel was in the range of 20 - 40 % by modifying the ratio of lecithin organogel to water.

Example 3

Hand Treatment of Human Subjects

10 The lecithin organogel composition (not including PLURONIC) was topically applied in cream form to the skin of one hand of each of 10 human volunteers (9 - 65 years of age) with a history of dry skin (xerosis) consisting of chapped hands while the other hand received treatment with control creams. These
15 control creams labeled "A", consisted of three commercial hand creams. Another portion of each "A" cream was removed and mixed with lecithin organogel in a 1:1 ratio to create the experimental cream labeled "B". The study was done in a "blind" manner, volunteers chose either the "A" or "B" cream and were
20 unaware whether they used control or experimental cream. Treatment continued for 7 days. Repeated application of the cream after washing and before bedtime was stressed to the participants. After 3 additional days, the volunteers applied the other cream for 7 days. The skin was subjectively evaluated for
25 softness and feel. All 10 subjects reported superior results in promoting healing and moisturizing the skin. The treated skin appeared smoother, softer and younger and many cracks disappeared. In addition, 2 of the volunteers were afflicted with eczema which was asymptomatic after treatment with the
30 experimental cream.

Example 4

Application of Composition to the Human Face

35 A 46 year old woman exhibited wrinkling of the periorbital skin at the lateral margin of the orbit. The composition was

5 applied topically to this region 2 to 3 times per day. Within 10 days the wrinkled appearance of the skin was dramatically diminished. This skin appeared fuller and smoother. The wrinkling of the skin was greatly reduced with fine lines generally less evident

Example 5

Application of the Composition to the Skin Adjacent to Fingernails and Toenails

10 Several human volunteer subjects exhibited dry and cracked skin at the bases of the fingernails and in the skin at the distal tips of the fingernails. They applied the cream for 3 to 4 times daily for 3 to 7 days and within 72 hours observed a reduction in the cracked appearance of the skin. Cracks that had developed into
15 deep grooves began to gradually close. Within 7 days, most of these cracks had completely disappeared and pain was greatly abated.

Example 6

Treatment of Hair

20 The fur of rats was shaved and various treatments applied, including lecithin organogel with PLURONIC, lecithin organogel with N-decylmethyl sulfoxide and alpha hydroxyacids (glycolic or lactic acids partially neutralized with sodium hydroxide), urea
25 and salicylic acid. The results showed a qualitative increase in the hair shaft diameter. In addition, regrowth of the hair was faster after treatment with lecithin organogel containing PLURONIC.

In vitro treatment of hair with alpha hydroxyacids, N-decylmethyl sulfoxide, salicylic acid and urea increased hair shaft
30 diameter by about 20% when examined with a micrometer under a microscope.

One embodiment of this application to hair is to use alpha hydroxy compounds which have a low pH (about 1.2), adjust the pH to a value of about 5-5.5 with a base such as sodium
35 hydroxide, and apply a 20-25% concentration to the hair overnight. The hair would be washed the next morning, thereby

enhancing absorption of water into the hair. The result would be thicker and more luxurious hair.

Claims:

- 5 1. A method of treating keratinous tissue of a human or animal comprising the step of topically applying to the keratinous tissue a composition comprising lecithin, isopropyl palmitate, and water.
- 10 2. The method of Claim 1, further comprising poloxamer 407.
3. The method of Claim 1, further comprising N-decylmethyl sulfoxide.
- 15 4. The method of Claim 1, further comprising compositions selected from the group consisting of antimicrobial, antibacterial, antifungal, antiprotozoal, and antiviral agents.
- 20 5. The method of Claim 1, further comprising glucosamine or glucosamine sulfate.
- 25 6. The method of Claim 1, further comprising molecules selected from the group consisting of alpha hydroxy compounds, glycolic acid, citric acid, and lactic acid.
- 30 7. The method of Claim 1, further comprising molecules selected from the group consisting of glycerol, urea, ceramides, squalene, elastin, salicylic acid, dimethicone, lanolin, chondroitin sulfate, hyaluronic acid, collagen, and collagen fragments.
- 35 8. The method of Claim 1, in the form selected from the group consisting of lotions, salves, creams, liposomes, sprays, and gels.

9. A method of treating psoriasis comprising the step of topically applying to the skin of the human or animal a composition comprising lecithin, isopropyl palmitate, and water.

5 10. A method of treating eczema comprising the step of topically applying to the skin of the human or animal a composition comprising lecithin, isopropyl palmitate, and water.

INTERNATIONAL SEARCH REPORT

International application No.

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A. CLASSIFICATION OF SUBJECT MATTER

IPC(6) :A61K 31/685

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

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 514/78

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

NONE

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

NONE

C. DOCUMENTS CONSIDERED TO BE RELEVANT

| Category* | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
|-----------|--|-----------------------|
| Y | US 3,957,971 A (OLENIACZ) 18 May 1976, see entire document. | 1-10 |
| Y | US 4,760,096 A (SAKAI et al.) 26 July 1988, see entire document. | 1-10 |

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Further documents are listed in the continuation of Box C.

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See patent family annex.

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