

DESCRIPTION

COSMETIC COMPOSITION CONTAINING AN OLEANOLIC ACID

Technical Field

5 The present invention relates to a solubilized cosmetic composition containing, as an active ingredient for reducing wrinkles, oleanolic acid encapsulated in nano-liposomes.

Background Art

 The skin is the primary barrier of the human body. It protects the organs from changes in
10 temperature and humidity and from damage from the external environment, such as UV radiation or pollutants. It also plays an important role in homeostasis, for example, in regulating body temperature. However, excessive chemical and physical stimulation, stress, malnutrition and the like are harmful to the normal functions of the skin and accelerate skin aging phenomena, such as elasticity loss, keratinization and wrinkle formation. Cosmetic products, which have been used to
15 prevent such phenomena and keep the skin healthy and elastic, have various problems in that they mostly have various problems insufficient effects or cause skin side effects (Korean Patent Laid-Open Publication No. 10-2010-0064451).

 Studies on raw materials having the effect of preventing skin aging without causing skin side effects have been actively conducted, and as a result, it was found that a skin cosmetic
20 composition containing oleanolic acid exhibits an excellent effect of preventing skin aging. Oleanolic acid, a kind of hydroxy pentacyclic terpene, is the active ingredient of many natural plants, such as *Eriobotrya japonica (loquata)*, *Perilla frutescens*, *Staphylea holocarpa* and the like, and is also found in fruits such as apples or pears. It has pharmacological effects, such as anti-inflammatory, anticancer, anti-allergic, anti-depressant, antibacterial and antifungal effects, and
25 particularly exhibits anti-inflammatory and skin irritation alleviating effects by stimulating the physiological activity of the skin. In addition, with respect to anti-aging functions, oleanolic acid

stimulates the synthesis of procollagen important in collagen production, stimulates the synthesis of ceramide and filaggrin, which are important in aging prevention. Moreover, it has a dual anti-aging system which stimulates the production of collagen and prevents the destruction of collagen by inhibiting the activity of MMP-1 that is an enzyme destroying polymer proteins such as produced collagen. Oleanolic acid having excellent effects on the reduction in skin wrinkles as described above has been used as a raw material in various emulsion-type cosmetic formulations to reduce skin wrinkles, but is substantially insoluble in water, and the content of oleanolic acid in cosmetic products is limited due to problems associated with stability and unstable activity. Particularly, because of this insoluble property, it is impossible to use oleanolic acid directly as a wrinkle reducing agent in solubilized formulations such as cosmetic lotion.

In recent years, it was reported that the stability of oleanolic acid can be increased by encapsulating oleanolic acid into nanoemulsions having a size of 100-150 nm using a skin lipid-like composition and nanotechnology and further encapsulating the oleanolic acid with a polymer emulsifier using the natural polysaccharide inulin and that the encapsulated oleanolic acid can be used in all types of cosmetic formulations. However, oleanolic acid encapsulated as described above should be introduced into emulsion-type formulations at a temperature of 50 °C or below and a low homomixing speed in order to prevent the capsules from being broken during the preparation process. Particularly, problems associated with the stability and unstable activity of oleanolic acid are still present in solubilized formulations. In addition, the use of encapsulated oleanolic acid is more expensive than the use of non-encapsulated oleanolic acid. Further, it can adversely affect the sensory feel of the product, because additional components other than oleanolic acid are used to encapsulate oleanolic acid.

Furthermore, the worldwide market size of certified organic cosmetic products is increasing, and only oleanolic acid is being recognized as a natural functional component for reducing wrinkles. However, when oleanolic acid is encapsulated using a skin lipid-like composition and nanotechnology as described above, it cannot be used as a certified organic

cosmetic raw material, because it contains a large number of components which are not acceptable in certified organic cosmetic products.

Disclosure

5 Technical Problem

The present invention has been made in order to solve the above-described problems occurring in the prior art, and an object of the present invention is to provide a solubilized cosmetic composition wherein oleanolic acid having an excellent effect of reducing wrinkles is stably encapsulated in nano-liposomes without using additional components other than oleanolic acid.

Technical Solution

In order to accomplish the above object, the present invention provides a cosmetic composition containing, as an active ingredient, oleanolic acid encapsulated in nano-liposomes.

Advantageous Effects

In the cosmetic composition according to the present invention, oleanolic acid effective in reducing skin wrinkles is stably encapsulated in nano-liposomes, and thus the transdermal absorption rate of oleanolic acid is increased by the nano-liposomes. Thus, the cosmetic composition of the present invention exhibits an excellent effect of reducing skin wrinkles by reducing stimulating collagen synthesis. Moreover, the production cost of the cosmetic composition can be reduced, because an additional raw material for stabilizing oleanolic acid is not used. In addition, the cosmetic composition of the present invention can provide a fresh and moist touch feel after absorption and can satisfy the consumer's demand for certified organic anti-wrinkle functional cosmetic products, which is increasing worldwide.

Best Mode

The present invention provides a cosmetic composition containing oleanolic acid as an active ingredient, and the cosmetic composition may be formulated in a solubilized form. In the cosmetic composition, oleanolic acid is encapsulated in nano-liposomes and is stabilized by the nano-liposomes. Thus, the stability and solubility of oleanolic acid in the solubilized formulation can be increased, and the transdermal absorption rate thereof can be increased.

Oleanolic acid that is used in the present invention is a unique component recognized as a natural anti-wrinkle functional component. The cosmetic composition of the present invention contains oleanolic acid in an amount of 0.0001-5.0 wt%, and preferably 0.0005-1.0 wt%, based on the total weight of the composition. If the content of oleanolic acid in the composition is less than 0.0001 wt%, a distinct effect cannot be obtained, and if the content of oleanolic acid is more than 5.0 wt%, an increase in the content will not lead to a distinct increase in the anti-wrinkle effect and will adversely affect the stability of the formulation.

Nano-liposomes which are formed during the preparation of the solubilized cosmetic composition of the present invention refer to liposomes having an average particle diameter of 10-500 nm. The nano-liposomes that are formed in the present invention preferably have a size of 50-300 nm. If the average particle diameter of the nano-liposomes is more than 300 nm, improvements in skin penetration and formulation stability, among the technical effects to be achieved by the present invention, will be very insignificant.

The nano-liposomes that are formed to stabilize oleanolic acid in the present invention are prepared by a mixture containing a polyol, an oily component, a surfactant, a phospholipid, and water. Also, the nano-liposomes encapsulating oleanolic acid in the solubilized cosmetic composition are naturally formed during the preparation of the solubilized cosmetic composition without having to carry out high-pressure emulsification or a separate preparation process.

The polyol that is used in the inventive solubilized cosmetic composition containing the nano-liposomes is not specifically limited, but is preferably one or more selected from the group

consisting of propylene glycol, dipropylene glycol, 1,3-butylene glycol, glycerin, methylpropanediol, isopropylene glycol, pentyleneglycol, erythritol, xylitol, sorbitol, and mixtures thereof. In addition, the polyol is used in an amount of 5-50 wt%, and preferably 15-30 wt%, based on the total weight of the solubilized cosmetic composition containing the nano-liposomes.

5 The oily component that is used in the inventive solubilized cosmetic composition containing the nano-liposomes may be selected from among various components known in the art. Preferred examples of the oily component include hydrocarbon-based oils such as hexadecane and paraffin oil, ester-based synthetic oils, silicone oils such as dimethicone and cyclodimethicone, animal and plant oils such as sunflower oil, corn oil, soybean oil, avocado oil, sesame oil and fish
10 oil, ethoxylated alkyl ether oil, propoxylated alkyl ether oil, sphingoid lipids such as phytosphingosine, sphingosine and sphinganine, cerebroside cholesterol, sitosterol cholesteryl sulfate, sitosterol sulfate, C₁₀₋₄₀ fatty alcohols, and mixtures thereof. The content of the oily component in the solubilized cosmetic composition is 0.01-10.0 wt%, and preferably 1.0-5.0 wt%, based on the total weight of the solubilized cosmetic composition comprising the nano-liposomes.

15 The surfactant that is used in the solubilized cosmetic composition of the present invention may be any surfactant known in the art. Examples of the surfactant that is used in the present invention include anionic surfactants, cationic surfactants, amphoteric surfactants and nonionic surfactants. Preferably, anionic surfactants and nonionic surfactants may be used in the present invention. Specific examples of the anionic surfactants include alkyl acyl glutamate, alkyl
20 phosphate, alkyl lactate, dialkyl phosphate and trialkyl phosphate. Specific examples of the non-ionic surfactants include polysorbate, alkoxylated alkyl ether, alkoxylated alkyl ester, alkyl polyglycoside, polyglyceryl ester and sugar ester. The content of the surfactant in the solubilized cosmetic composition is 0.001-5.0 wt%, and preferably 0.1-1.0 wt%, based on the total weight of the solubilized cosmetic composition comprising the nano-liposomes.

25 A phospholipid in the nano-liposomes that are formed in the present invention is an amphoteric lipid, and examples thereof includes natural phospholipids (e.g., egg lecithin, soybean

lecithin or sphingomyelin) and synthetic phospholipids (e.g., dipalmitoylphosphatidylcholine or hydrogenated lecithin), preferably lecithin. More preferably, the phospholipid is a naturally occurring saturated or unsaturated lecithin extracted from soybean or egg yolk. In general, the naturally occurring lecithin has a phosphatidylcholine content of 23-95% and a
5 phosphatidylethanolamine content of 20% or less. The content of the phospholipid in the preparation of the inventive solubilized cosmetic composition containing the nano-liposomes is 0.01-5.0 wt%, and preferably 0.5-2.0 wt%, based on the total weight of the solubilized cosmetic composition.

Water in the inventive solubilized cosmetic composition containing the nano-liposomes is
10 generally distilled water and is used in an amount of 25.0-90.0 wt% based on the total weight of the solubilized cosmetic composition.

The solubilized cosmetic composition of the present invention contains oleanolic acid, and thus can particularly be used as an anti-aging composition having an excellent effect of reducing skin wrinkles.

15 The formulation of the composition of the present invention is not specifically limited. In view of a transparent or suspended appearance and advantages in use, the composition of the present invention may be used as basic cosmetic compositions such as skin softener, nourishing lotion, spray, mist or gel, hair cosmetic compositions such as hair growth agents, including hair tonic, hair essence or hair treatment, and other medical drugs and quasi-drugs. In addition, it may
20 also be used as a skin wrinkle-reducing agent, which shows an excellent effect and is safe without side effects when being applied to the human skin.

The cosmetic composition according to the present invention may contain additives which are generally used in the cosmetic field or the skin science field, for example, fatty substance, organic solvent, solubilizing agent, thickener, gelling agent, softener, antioxidant, suspending
25 agent, stabilizer, foaming agent, fragrance, surfactant, water, ionic or non-ionic emulsifying agent, filler, metal ion sequestering agent, metal ion chelating agent, preservative, vitamins, blocker,

wetting agent, essential oil, dye, pigment, hydrophilic or hydrophobic activator, lipid vesicle, or other components which are generally used in cosmetic products. These additives are introduced in amounts which are generally used in the cosmetic field or the skin science field.

5 Mode for Invention

Hereinafter, the present invention will be described in further detail with reference to examples and test examples. It is to be understood, however, that the following examples, test examples and preparation examples are for illustrative purposes only and are not intended to limit the scope of the present invention.

10 Reference Example 1: Preparation of solubilized cosmetic lotion containing oleanolic acid stabilized with nano-liposomes

According to the compositions shown in Table 1 below, wrinkle-reducing solubilized cosmetic lotions of Examples 1 to 3 and Comparative Example 1 to 4 were prepared.

Lotions of Examples 1 to 3 are solubilized cosmetic lotions containing nano-liposomes
 15 formed according to the present invention, and lotions of Comparative Examples 1 and 2 contain general solubilizing agents different from those of Examples 1 to 3, and lotion of Comparative Example 3 contains an encapsulated oleanolic acid nanobase. Lotion of Comparative Example 4 is a lotion containing an oleanolic acid dissolved in a 4:1 mixture of ethanol and propylene glycol.

Table 1 (unit: wt%)

	Component	Examp le 1	Examp le 2	Examp le 3	Compa rative Examp le 1	Compa rative Examp le 2	Compa rative Examp le 3	Compa rative Examp le 4
1	Hydrogenated lecithin	0.05	0.2	1.0	-	-	0.2	-
2	PEG-60 hydrogenated castor oil	-	-	-	1.8	-	-	-
3	caprylic/capryl glucoside	-	-	-	-	3.6	-	-
4	Propylene glycol	25	25	25	25	25	25	20
5	Glycerin	4.00	4.00	4.00	4.00	4.00	4.00	-
6	Dicaprylyl carbonate	q.s.	q.s.	q.s.	q.s.	q.s.	q.s.	-
7	Oleanolic acid	0.05	0.05	0.05	0.05	0.05	-	0.05

8	Preservative	q.s.	q.s.	q.s.	q.s.	q.s.	q.s.	-
9	Fragrance	q.s.	q.s.	q.s.	q.s.	q.s.	q.s.	-
10	Ethanol	4.0	4.0	4.0	4.0	4.0	4.0	balance
11	Purified water	balance	balance	balance	balance	balance	balance	-
12	Dermofeel PA-3	0.02	0.02	0.02	0.02	0.02	0.02	-
13	Betaine	2.00	2.00	2.00	2.00	2.00	2.00	-
14	Xanthan gum	0.2	0.2	0.2	0.2	0.2	0.2	-
15	Encapsulated oleanolic nanobase (containing 0.05 wt% oleanolic acid)	-	-	-	-	-	2.5	-

The lotions were prepared in the following manner.

1) Components 1 to 3 and polyol components 4 to 5 were mixed and dissolved by heating to 80 °C, and then components 6 to 9 were added thereto and uniformly mixed.

5 2) The mixture of step 1) was cooled to 65 °C, and then ethanol (component 10) was added thereto and sufficiently mixed.

3) Aqueous part components 11 to 14 were mixed uniformly and heated to 65 °C, after which the mixture was uniformly mixed with the mixture of step 2).

4) The mixture of step 3) was cooled to room temperature and stored.

10 Meanwhile, in the preparation of the lotion of Comparative Example 3, an encapsulated oleanolic acid nanobase (component 15) was added after step 3).

Test Example 1: Evaluation of stability of composition

In order to evaluate the stability of the wrinkle-reducing cosmetic composition with time, the solubilized cosmetic lotions prepared in Examples 1 to 3 and Comparative Examples 1 to 4
15 were stored for 1 month in each of a room temperature incubator, a 45 °C incubator and an incubator that was circulated from -10 °C to 45 °C at 12-hr intervals, and then the changes in the appearances of the lotions were observed.

Table 2

Items	Kind of surfactant (solubilizing agent)	Average par ticl e	Stability

		size (nm)									
			Room temperature			45 °C			Circulated temperature		
			Next day	1 week	4 weeks	Next day	1 week	4 weeks	Next day	1 week	4 weeks
Example 1	0.05% hydrogenated lecithin	376	good	good	Separated	good	Separated	Separated	good	good	Separated
Example 2	0.20% hydrogenated lecithin	257	good	good	good	good	good	good	good	good	good
Example 3	1.00% hydrogenated lecithin	234	good	good	Precipitated	good	good	Precipitated	good	good	Precipitated
Comparative Example 1	1.80% PEG-60 hydrogenated castor oil	245	Separated	-	-	Separated	-	-	Separated	-	-
Comparative Example 2	3.60% caprylic/capryl glucoside	241	Separated	-	-	Separated	-	-	Separated	-	-
Comparative Example 3	0.20% hydrogenated lecithin	240	good	good	good	good	good	Separated	good	Separated	-

As can be seen from the results in Table 2 above, the lotions of Examples 1 to 3, which contain oleanolic acid encapsulated in nano-liposomes, were stable over a long period of time compared to the lotions of Comparative Examples 1 and 2, which contain other general solubilizing agents. Also, from the comparison between Example 2 and Comparative Examples 1 and 2, it can be seen that the amount of the surfactant used in Example 2 in which oleanolic acid was stabilized by encapsulation in nano-liposomes was significantly smaller than the amount of the surfactant used in Comparative Examples 1 and 2. This suggests that, when oleanolic acid is encapsulated in nano-liposomes formed, the amount of the surfactant to be used in the formulation

can be significantly reduced, and the risk of skin irritation, which is caused by the use of a large amount of a surfactant, can be avoided.

Test Example 2: Comparison of sensory feeling between a composition containing oleanolic acid stabilized with nano-liposomes and a composition containing encapsulated oleanolic

5 acid

In order to evaluate the sensory feelings of the compositions of Example 2 and Comparative Example 3, a sensory test was performed for the wrinkle-reducing cosmetic compositions prepared in Example 2 and Comparative Example 3. Twenty 25-35 years old women were selected as subjects. Each of the cosmetic compositions was applied to the back of the hand of each subject according to a general method, and then the satisfaction of the sensory feeling of each composition was evaluated. The sensory evaluation of each composition was performed with respect to a total of 4 items, including stickiness, absorption feeling, moist feeling and nourishing feeling, on the basis of the following criteria: very superior (10), superior (7.5), moderate (5), inferior (2.5) and very inferior (0). The values of the evaluation were averaged and shown in Table 3 below.

Table 3

Items of sensory feeling	Example 2	Comparative Example 3
Stickiness	8.4	3.1
Absorption feeling	9.8	5.2
Moist feeling	8.5	8.2
Nourishing feeling	6.9	6.3

From the comparison between the composition of Example 2, which contains oleanolic acid stabilized with nano-liposomes formed in the formulation, and the composition of Comparative Example 3, which contains encapsulated oleanolic acid, it can be seen that, because the amount of the stabilizing agent used to prepared the encapsulated oleanolic acid nanobase in Comparative Example 3 was larger by about 2.4 wt% than that in Example 2, the stabilizing agent

in Comparative Example 3 had an adverse effect on the sensory feeling. Also, as can be seen in Table 3 above, the sensory feeling of the formulation (Example 2) containing oleanolic acid stabilized with nano-liposomes formed therein is significantly excellent compared to the formulation of Comparative Example 3.

5 Test Example 3: Measurement of effect on stimulation of collagen biosynthesis

The effect of the composition of Example 2 on the stimulation of collagen biosynthesis was measured comparatively with those of tocopherol and EGCG, which are known to stimulate collagen biosynthesis. First, human fibroblasts (PromoCell, Germany) were seeded in a 24-well plate at a density of 10^5 cells and cultured to a confluence of about 90%. The cells were cultured in
10 serum-free DMEM medium for 24 hours, and then treated with 10^{-4} M of each of the composition of Example 2, tocopherol and EGCG in serum-free medium. Then, the cells were incubated in a CO_2 incubator for 24 hours. The supernatant of each of the cell cultures was collected, and the amount of procollagen in the supernatant was measured using a procollagen type (I) ELISA kit. The results of the measurement are shown in Table 4 below. In Table 4, the values of synthesis are
15 expressed as percentages relative to the untreated group taken as 100.

Table 4

Group	Synthesis (%)
Example 2	134
Untreated group	100
Tocopherol	113
EGCG	120

As can be seen in Table 4 above, the composition of Example 2 stimulates collagen biosynthesis and has a significantly better effect on the stimulation of collagen biosynthesis
20 compared to tocopherol and EGCG, which are known to stimulate collagen biosynthesis.

Test Example 4: Measurement of absorption into skin

Absorption into the skin was measured on the skin of guinea pigs using Frantz permeation cells. Immediately before the experiment, abdominal skin of guinea pigs was collected and cut to

a size of 1 cm². The cut skin was placed in a permeation cell having a permeation lens diameter of 0.9 cm and was fixed by a clamp. 0.2 g of each of the sample of Comparative Example 4, which contains a solution of oleanolic acid in ethanol and propylene glycol (4:1), and the sample of Example 2, which contains oleanolic acid stabilized with nano-liposomes, was applied to one side of the skin (donor container), and the other side (receptor container) was brought into contact with a solvent consisting of a 4:1 mixture of purified water and ethanol. The temperature during the experiment was maintained at 32 °C (actual skin temperature). After the start of the experiment, a portion of the solvent was collected at intervals of a given time, and then the amount of oleanolic acid absorbed into the skin was measured by HPLC. The results of the measurement were expressed as skin absorption per applied concentration ($\mu\text{g}/\text{cm}^2/\text{wt}\%$) and are shown in Table 5 below.

HPLC analysis conditions

- column: Waters Novapak C18 (3.9 mm * 250 mm, 4 μm)
- solvent flow rate: 1 mL/min
- detection UV: 210 nm
- sample measurement concentration: 10-100 $\mu\text{g}/\text{mL}$
- injected sample amount: 20 μL
- eluent: MeOH/0.1% H₃PO₄ = 82/18

Table 5

Time	Example 2	Comparative Example 4
0	0	0
4	16.22	3.52
8	36.13	8.59
16	55.60	10.25

As can be seen from the results in Table 5 above, the composition of Example 2, which contains oleanolic acid stabilized with nano-liposomes formed therein, showed a significantly large amount of transdermal absorption compared to that of Comparative Example 2.

CLAIMS

1. A cosmetic composition for stimulating collagen biosynthesis or anti-ageing containing an oleanolic acid encapsulated in nano-liposomes as the sole active ingredient for
5 stimulating collagen biosynthesis or anti-ageing,

wherein the oleanolic acid is in an amount of 0.0001 - 5.0 wt% based on the total weight of the composition,

wherein the nano-liposomes that are formed to stabilize oleanolic acid are prepared by a mixture containing a polyol, an oily component, a surfactant, a phospholipid, and water,

10 wherein the polyol is selected from the group consisting of propylene glycol, glycerin and mixtures thereof, and

wherein the phospholipid is selected from natural or synthetic lecithin.

2. The cosmetic composition of claim 1, wherein the nano-liposomes having the oleanolic acid encapsulated therein is contained in an amount of 0.001-50 wt% based on the
15 total weight of the composition.

3. The cosmetic composition of claim 1, wherein the nano-liposomes have an average particle diameter of 50-300 nm.

4. The cosmetic composition of claims 1 to 3, wherein the composition is a solubilized formulation.

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