

【DESCRIPTION】

【Invention Title】

COMPOSITION FOR ENHANCING DEFENSES OF SKIN

5 **【Technical Field】**

The present disclosure relates to a composition for improving skin defensive power.

【Background Art】

10 For prevention or improvement of acne or skin trouble, tea tree oil, salicylic acid, triclosan, fruit acids, etc. that have antibacterial activity themselves have been used. However, since these substances may cause skin irritation due to their antibacterial activity, and relevant laws restrict allowable concentrations, they cannot be used at the concentrations that exhibit efficacy and it is difficult to achieve a
15 substantial effect. Accordingly, development of a substance that exhibits superior antibacterial and antiinflammatory effect without irritating the skin is necessary.

【References of Related Art】

【Patent Documents】

20 (Patent document 1) Korean Patent No. 10-0884616 (Feb. 12, 2009)
 (Patent document 2) Korean Patent Publication No. 10-2006-0043067 (May
15, 2006)

【Disclosure】

25 **【Technical Problem】**

The present disclosure is directed to providing a composition capable of enhancing skin defensive power.

【Technical Solution】

30 In a general aspect, there is provided a composition for improving skin defensive power, containing at least one of a protopanaxadiol compound and a

Japanese nutmeg (*Torreya nucifera*) extract as an active ingredient.

In another general aspect, there is provided a composition for improving skin defensive power, containing at least one of a protopanaxadiol compound and a Japanese nutmeg extract; and epigallocatechin gallate as an active ingredient.

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【Advantageous Effects】

A composition according to the present disclosure, which contains at least one of a protopanaxadiol compound and a Japanese nutmeg extract; and, optionally, epigallocatechin gallate can exhibit superior antibacterial and antiinflammatory activity of the skin by promoting the activity of antibacterial peptides and improving self-dense of the skin without irritation to the skin.

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【Description of Drawings】

Fig. 1 compares the effect of compound K, Japanese nutmeg seed oil, epigallocatechin gallate, mixtures thereof and tea tree oil on the expression of antibacterial peptides in the skin.

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【Best Mode】

As used herein, the term "skin" refers to a tissue that covers the outer body of an animal and is used in the broadest sense, including not only face or body but also scalp and hair. As used herein, the term "extract" is used in a broad sense including any substance extracted from a natural product, regardless of extraction method, extraction solvent, extracted ingredients or extract type. For example, the extract may be an oil ingredient extracted from a natural product. As used herein, the term "skin defensive power" refers to the ability of protecting the skin from external stimulation or toxin. The stimulation is broad sense that includes any stimulation harmful to the skin, including bacteria, virus, UV, dryness, injury, etc.

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Hereinafter, the present disclosure is described in detail.

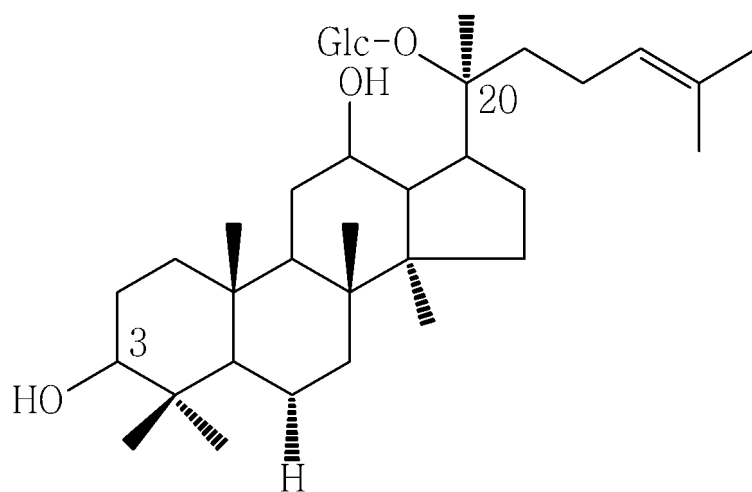
The skin opposes against bacterial invasion by secreting antibacterial peptides. Accordingly, a substance that promotes the activity of the antibacterial peptides in the skin may enhance the antibacterial and antiinflammatory activity of the skin by improving the skin's defensive power without irritating the skin.

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In an aspect, the present disclosure provides a composition for improving skin defensive power, containing at least one of a protopanaxadiol compound and a Japanese nutmeg extract as an active ingredient. The protopanaxadiol compound or Japanese nutmeg extract may enhance the skin defensive power by promoting the expression of antibacterial peptides in the skin. Accordingly, the composition containing at least one of the protopanaxadiol compound and the Japanese nutmeg extract may enhance the skin defensive power, specifically skin antibacterial and antiinflammatory activity, and may further improve acne and other skin troubles. In an exemplary embodiment of the present disclosure, the antibacterial peptide is a peptide that the expression of which is induced in response to external stimulation and controls invading pathogens. Representative examples include hBD1, hBD2, LL37 or RNase7, but are not limited thereto.

In an exemplary embodiment of the present disclosure, the protopanaxadiol compound is a kind of ginsenoside which is a ginseng saponin. In another exemplary embodiment of the present disclosure, the protopanaxadiol compound may be obtained by treating ginseng, specifically red ginseng, with an enzyme. In another exemplary embodiment of the present disclosure, the protopanaxadiol compound includes compound K. Compound K, also known as ginsenoside M1, is 20-O-(beta-D-glucopyranosyl)-20(S)-protopanaxadiol represented by Chemical Formula 1.

[Chemical Formula 1]



A composition according to an exemplary embodiment of the present

disclosure may contain 0.001-10 wt%, specifically 0.01-5 wt%, more specifically 0.1-3 wt%, of the protopanaxadiol compound based on the total weight of the composition. When the protopanaxadiol compound is contained in the above range, the desired effect of the present disclosure may be achieved adequately while satisfying both stability and safety of the composition. In addition, the above range may also be adequate in terms of cost effectiveness. Specifically, if the composition contains the protopanaxadiol compound in an amount less than 0.001 wt%, enhancing effect in the skin defensive power may be slight. And, if it contains the protopanaxadiol compound in an amount more than 10 wt%, the stability of the composition may decrease owing to decreased solubility of the protopanaxadiol compound toward a solvent.

In an exemplary embodiment of the present disclosure, the Japanese nutmeg extract includes an extract of the nut of Japanese nutmeg (*Torreya nucifera*), specifically an extract of Japanese nutmeg seed. In another exemplary embodiment of the present disclosure, the Japanese nutmeg extract includes oil and fat ingredient which is Japanese nutmeg oil, specifically Japanese nutmeg seed oil, obtained by squeezing Japanese nutmeg or extracting it using an organic solvent. The organic solvent includes one or more selected from a group consisting of alcohol, hexane, acetone, ethyl acetate, diethyl ether, ethyl methyl ketone and chloroform, but is not limited thereto.

In an exemplary embodiment of the present disclosure, the composition may contain 0.001-99 wt%, specifically 0.1-80 wt%, more specifically 10-50 wt%, of the Japanese nutmeg extract based on the total weight of the composition. When the Japanese nutmeg extract is contained in the above range, the desired effect of the present disclosure may be achieved adequately while satisfying both stability and safety of the composition. In addition, the above range may also be adequate in terms of cost effectiveness. Specifically, if the composition contains the Japanese nutmeg extract in an amount less than 0.001 wt%, enhancing effect in the skin defensive power may be slight.

The composition according to an exemplary embodiment of the present disclosure for improving skin defensive power may further contain epigallocatechin gallate. When the composition according to the present disclosure for improving

skin defensive power further contains epigallocatechin gallate, it may have better skin defensive power enhancing effect owing to having higher enhanced skin antibacterial and antiinflammatory activity.

In the present disclosure epigallocatechin gallate is a kind of polyphenol and catechin mainly found in green tea and is also represented by chemical formulation of (-)-epigallocatechin-3-gallate. In an exemplary embodiment of the present disclosure, the epigallocatechin gallate may be extracted from green tea.

The composition according to an exemplary embodiment of the present disclosure may contain 0.00001-10 wt%, specifically 0.0001-5 wt%, more specifically 0.001-1 wt%, of epigallocatechin gallate based on the total weight of the composition. When the epigallocatechin gallate is contained in the above range, the desired effect of the present disclosure may be achieved adequately while satisfying both stability and safety of the composition. In addition, the above range may also be adequate in terms of cost effectiveness. Specifically, if the composition contains the epigallocatechin gallate in an amount less than 0.00001 wt%, enhancing effect in the skin defensive power may be slight. And, if it contains the epigallocatechin gallate in an amount more than 10 wt%, it may difficult to ensure stability of a formulation since oxidation can occur easily.

In another aspect, the present disclosure provides a cosmetic composition containing at least one of a protopanaxadiol compound and a Japanese nutmeg extract; and, optionally, epigallocatechin gallate as an active ingredient. The cosmetic composition may exhibit skin defensive power enhancing effect, specifically superior antibacterial and antiinflammatory activity, and may further improve or prevent acne and other skin troubles.

The cosmetic composition according to the present disclosure may be provided as any formulation suitable for topical application. For example, it may be prepared in the form of solution, oil-in-water emulsion, water-in-oil emulsion, suspension, solid, gel, powder, paste, foam or aerosol. Such formulations may be prepared according to methods commonly employed in the art.

The cosmetic composition according to the present disclosure may further contain a humectant, an emollient, a surfactant, a UV absorbent, an antiseptic, a sterilizer, an antioxidant, a pH control agent, an organic or inorganic pigment, a

fragrance, a cooling agent or an antiperspirant. The amount of these ingredients included in the cosmetic composition may be easily determined by those skilled in the art within the range not negatively affecting the purpose and effect of the present disclosure. They may be contained in an amount of 0.01-5 wt%, specifically 0.01-3 wt%, based on the total weight of the composition.

In another aspect, the present disclosure provides a pharmaceutical composition containing at least one of a protopanaxadiol compound and a Japanese nutmeg extract and, optionally, epigallocatechin gallate as an active ingredient. The pharmaceutical composition may exhibit skin defensive power enhancing effect, specifically superior antibacterial and antiinflammatory activity, and may further improve or prevent acne and other skin troubles.

The pharmaceutical composition according to an aspect of the present disclosure may be administered orally or parenterally, for example, rectally, topically, transdermally, intravenously, intramuscularly, intraperitoneally or subcutaneously.

Formulations for oral administration include tablet, pill, hard or soft capsule, granule, powder, fine granule, liquid, emulsion or pellet, but are not limited thereto. These formulations may contain a diluent (e.g., lactose, dextrose, sucrose, mannitol, sorbitol, cellulose or glycine), a lubricant (e.g., silica, talc, stearic acid or polyethylene glycol) or a binder (e.g., magnesium aluminum silicate, starch paste, gelatin, tragacanth, methyl cellulose, sodium carboxymethyl cellulose or polyvinylpyrrolidone) in addition to the active ingredient. As occasion demands, it may also contain a pharmaceutical additive such as a disintegrant, an absorbent, a colorant, a flavor, a sweetener, etc. The tablet may be prepared by the common mixing, granulation or coating method.

Formulations for parenteral administration include injection, medicinal drop, lotion, ointment, gel, cream, suspension, emulsion, suppository, patch or spray, but are not limited thereto.

The administration dosage of the active ingredient of pharmaceutical composition according to an aspect of the present disclosure will vary depending on the age, gender, body weight, particular disease or pathological condition to be treated, or severity of the disease or pathological condition of the subject, administration route and discretion of a diagnoser. Determination of the

administration dosage considering these factors is in the level of those skilled in the art. A daily administration dosage may be, for example, 0.1-100 mg/kg/day, more specifically 5-50 mg/kg/day, but is not limited thereto.

5 **【Mode for Invention】**

Hereinafter, the present disclosure will be described in detail through an example and a test example. However, the following examples are for illustrative purposes only and it will be apparent to those of ordinary skill in the art that the scope of the present disclosure is not limited by the examples.

10 **[Example]**

Compound K was obtained by hydrolyzing red ginseng with an enzyme. Japanese nutmeg seed oil was obtained by squeezing the seed of Japanese nutmeg or extracting it using an organic solvent.

15 Epigallocatechin gallate (EGCG) was obtained as follows. First, green tea leaf (dry basis moisture content $\leq 3\%$) was hot-water reflux extracted at 30-70 °C for 1-24 hours using 10 times the volume of purified water. After filtration, the residue was removed and water-soluble ingredients were separated by filtering the remaining filtrate again. From the as-separated water-soluble ingredients, only epigallocatechin gallate was selectively precipitated and concentrated through
20 crystallization. After removing the filtrate remaining unprecipitated through filtration, the precipitate was purified by chromatography. Then, the solvent was evaporated to finally obtain high-purity epigallocatechin gallate.

25 **[Test Example] Effect evaluation of promoting expression of antibacterial peptides in skin**

After treating HaCaT keratinocytes (Dr. N.E. Fusenig, German Cancer Research Center, Heidelberg, Germany) with compound K, Japanese nutmeg seed oil, epigallocatechin gallate (EGCG), compound K + Japanese nutmeg seed oil, compound K + Japanese nutmeg seed oil + EGCG or tea tree oil, a change in gene
30 expression of representative skin antibacterial peptides hBD1, hBD2, LL37 and RNase7 was measured 24 hours later by real-time PCR. The change level of gene expression of each treated group relative to the untreated control is shown in Fig. 1

(mean) and Table 1 (mean $\pm$ standard deviation).

【Table 1】

	hBD1	hBD2	LL37	RNase7
Untreated control	1	1	1	1
Compound K	1.200431 $\pm$ 0.117122	1.2501451 $\pm$ 0.060240	1.4266929 $\pm$ 0.478567	1.2435783 $\pm$ 0.065722
Japanese nutmeg seed oil	1.136352 $\pm$ 0.067012	1.119184 $\pm$ 0.074302	1.209884 $\pm$ 0.175301	1.133979 $\pm$ 0.090271
EGCG	1.124634 $\pm$ 0.365302	1.120488 $\pm$ 0.032836	1.91 $\pm$ 1.000007883	1.158407 $\pm$ 0.164803
Compound K + Japanese nutmeg seed oil	1.209359 $\pm$ 0.0915457	1.320578 $\pm$ 0.165871	1.491648 $\pm$ 0.365904	1.310674 $\pm$ 0.164829
Compound K + Japanese nutmeg seed oil + EGCG	1.277801 $\pm$ 0.200185	1.351209 $\pm$ 0.095638	1.59781 $\pm$ 0.360825	1.899171 $\pm$ 0.095602
Tea tree oil	0.762495 $\pm$ 0.153398	0.993401 $\pm$ 0.022563	0.847556 $\pm$ 0.073745	0.919438 $\pm$ 0.127590

It can be seen that, whereas all of compound K, Japanese nutmeg seed oil, epigallocatechin gallate (EGCG), compound K + Japanese nutmeg seed oil, compound K + Japanese nutmeg seed oil + EGCG increase the expression of the skin antibacterial peptides hBD1, hBD2, LL37 and RNase7, tea tree oil, which is derived from a natural product and is frequently used in antibacterial cosmetics, inhibits the expression of the four genes. That is to say, although tea tree oil cannot enhance the skin's defensive power, compound K, Japanese nutmeg seed oil, epigallocatechin gallate (EGCG) and mixtures thereof can enhance the skin defensive power by activating antibacterial peptides in the skin.

Hereinafter, formulation examples of the composition according to an exemplary embodiment of the present disclosure will be described in detail however, it can be applied to variable types of formulation. And, the following formulation examples are not intended to limit the scope of the present disclosure and are for illustrative purposes only.

[Formulation Example 1] Lotion

A lotion is prepared according to a commonly employed method with the composition described in Table 2.

【Table 2】

Ingredients	Contents (wt)
Compound K	1.0
Japanese nutmeg seed oil	5.0
L-Ascorbic acid-2-magnesium phosphate	1.0
Water-soluble collagen (1% aqueous solution)	1.0
Sodium citrate	0.1
Citric acid	0.05
1,3-Butylene glycol	3.0
Purified water	balance

5 [Formulation Example 2] Cream

A cream is prepared according to a commonly employed method with the composition described in Table 3.

【Table 3】

Ingredients	Contents (wt)
Protopanaxadiol compound	2.0
Polyethylene glycol monostearate	2.0
Glycerin monostearate	5.0
Cetyl alcohol	4.0
Squalene	3.0
Tri-2-ethylhexanoate glyceryl	6.0
Sphingoglycolipid	1.0
1,3-Butylene glycol	7.0
Purified water	balance

[Formulation Example 3] Pack

10 A pack is prepared according to a commonly employed method with the composition described in Table 4.

【Table 4】

Ingredients	Contents (wt)
Japanese nutmeg extract	20.0
Polyvinyl alcohol	13.0
L-Ascorbic acid-2-magnesium phosphate	1.0
Lauroylhydroxyproline	1.0
Water-soluble collagen (1% aqueous solution)	2.0
1,3-Butylene glycol	3.0
Ethanol	5.0
Purified water	balance

[Formulation Example 4] Soft capsule

A protopanaxadiol compound (50 mg), a Japanese nutmeg extract (200 mg), epigallocatechin gallate (10 mg), a soybean extract (50 mg), soybean oil (180 mg), palm oil (2 mg), hydrogenated palm oil (8 mg), yellow beeswax (4 mg) and lecithin (6 mg) are mixed and prepared into a soft capsule according to a commonly employed method.

[Formulation Example 5] tablet

Compound K (10 mg), Japanese nutmeg seed oil (200 mg), epigallocatechin gallate (10 mg), a soybean extract (50 mg), glucose (100 mg), starch (96 mg) and magnesium stearate (4 mg) are mixed and 30% ethanol (40 mg) is added to form a granule. After drying, the granule is prepared into a tablet using a tablet making machine.

【CLAIMS】

【Claim 1】

A composition for improving skin defensive power, comprising at least one of a protopanaxadiol compound and a Japanese nutmeg (*Torreya nucifera*) extract as an active ingredient.

【Claim 2】

The composition according to claim 1, wherein the protopanaxadiol compound comprises compound K (20-O-(beta-D-glucopyranosyl)-20(S)-protopanaxadiol).

【Claim 3】

The composition according to claim 1, wherein the Japanese nutmeg extract comprises Japanese nutmeg seed oil.

【Claim 4】

The composition according to claim 1, wherein the composition comprises 0.001-10 wt% of the protopanaxadiol compound based on the total weight of the composition.

【Claim 5】

The composition according to claim 1, wherein the composition comprises 0.001-99 wt% of the Japanese nutmeg extract based on the total weight of the composition.

【Claim 6】

The composition according to claim 1, wherein the composition further comprises epigallocatechin gallate.

【Claim 7】

The composition according to claim 6, wherein the composition further

0.00001-10 wt% of epigallocatechin gallate based on the total weight of the composition.

【Claim 8】

5 The composition according to claim 1, wherein the composition enhances the antibacterial and antiinflammatory activity of the skin.

【Claim 9】

10 The composition according to claim 1, wherein the composition promotes the expression of antibacterial peptides in the skin.

【Claim 10】

 The composition according to any one of claims 1 to 9, wherein the composition is a cosmetic composition.

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