【DESCRIPTION】

【Invention Title】

COSMETIC COMPOSITION FOR IMPROVING SKIN WHITENING

【Technical Field】

[1] The present invention relates to a cosmetic composition for improving skin whitening.

【Background Art】

[2] Human skin color is determined by various factors such as activity of melanocytes which produces melanin pigment, distribution of blood vessels, thickness of skin and presence or absence of pigment such as carotenoid or bilirubin inside and outside of human body and the like. Among these, black pigment called melanin produced in melanocytes has the most important influence on the color of human skin. Formation of melanin pigment is influenced by a genetic factor, a physiological factor related to hormone secretion, stress and the like, and an environmental factor such as UV irradiation. Melanin being present in the skin has an important function to protect the body from UV, however, a study of the functional cosmetic product intended to improve whitening, for treating or relieving skin pigmentation abnormality such as spots, freckles or pigmentation due to melanin

overproduction, and excessive melanin pigmentation produced by UV exposure and the like has been actively conducted.

[3] As a representative raw material having a whitening effect, Kojic acid was used in combination with cosmetics or medicines, however, since the use of Kojic acid was discontinued due to its insufficient whitening effect, safety concerns for skin, and problems of formulation, stability and the like when formulated, demand for new raw materials which may be used as an alternative component to Kojic acid is increasing.

[4] Meanwhile, a cosmetic product having a whitening effect of preventing pigmentation has been developed by studies on activity or production inhibition of tyrosinase, inhibition of a mediator promoting melanin production, reduction and photooxidation inhibition of produced melanin, excretion promotion of melanin, UV cut and the like.

[5] As the production of a mediator promoting melanin production is increased, the length of dendrite of melanocytes is increased, thereby facilitating transfer of melanin to surrounding cells to increase pigmentation (Biol. Pharm. Bull. 34(5) 748-754(2011)). Thus, the present inventors conducted a study on the material having a whitening effect by inhibiting production of PGE_2 as a mediator promoting melanin production.

[6] As a result, the present inventors provided a cosmetic composition for improving skin whitening, having a whitening effect by inhibiting increase of prostaglandin E_2 (PGE_2) which is a mediator promoting melanin production to inhibit melanin production, thereby completing the present invention.

【Disclosure】

【Technical Problem】

[7] An object of the present invention is to provide a cosmetic composition for improving skin whitening.

[8] Another object of the present invention is to provide a cosmetic composition for improving skin whitening by inhibition of a mediator promoting melanin production.

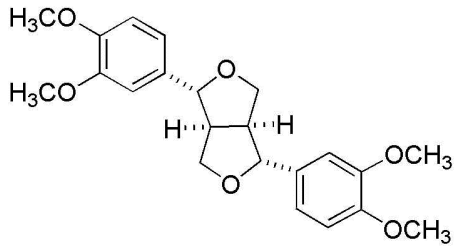
[9] Another object of the present invention is to provide health functional food for improving skin whitening.

[10] Another object of the present invention is to provide health functional food for improving skin whitening having a skin whitening improvement effect by consuming the food as inner beauty food.

【Technical Solution】

[11] In one general aspect, a cosmetic composition for improving skin whitening includes a compound represented by the following Chemical Formula 1 as an effective component:

[12] [Chemical Formula 1]



[13]

[14] As an exemplary embodiment of the present invention, the compound of the present invention may provide a cosmetic composition for improving skin whitening which is characterized by inhibiting the activity of PGE_2 (prostaglandin E_2) to inhibit melanin production, but not limited thereto.

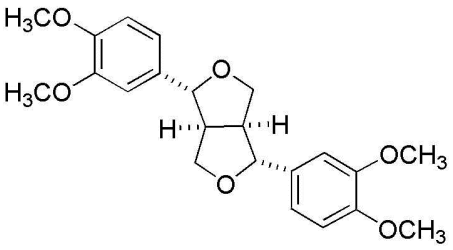
[15] As an exemplary embodiment of the present invention, the compound of the present invention may provide a cosmetic composition for improving skin whitening which is characterized by inhibiting melanocyte dendritic cell (DC) formation by proteinase-activated receptor-2 (PAR-2), but not limited thereto.

[16] As an exemplary embodiment of the present invention, a cosmetic composition for improving skin whitening which is characterized in that the compound is included at 0.001 to 10 wt% based on the total weight of the composition may be illustrated, but not limited thereto.

[17] In another general aspect, a method of inhibiting melanin pigmentation by treating keratinocytes and melanocytes with a compound represented by the following

Chemical Formula 1 to inhibit increase of PGE_2 (prostaglandin E_2) is provided:

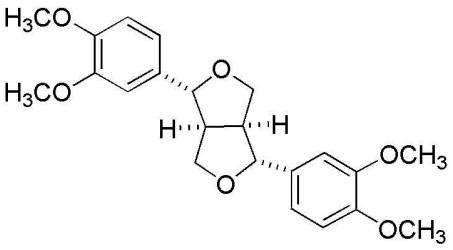
[18] [Chemical Formula 1]



[19]

[20] In another general aspect, a method of inhibiting melanocyte dendritic cell (DC) formation by proteinase-activated receptor-2 (PAR-2), by treating keratinocytes and melanocytes with a compound represented by the following Chemical Formula 1:

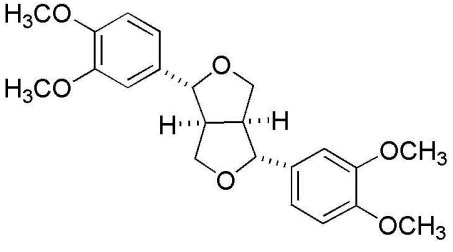
[21] [Chemical Formula 1]



[22]

[23] In another general aspect, health functional food for improving skin whitening includes a compound represented by the following Chemical Formula 1 as an effective component:

[24] [Chemical Formula 1]



[25]

[26] As an exemplary embodiment of the present invention, the health functional food is characterized in that it is inner beauty food, but not limited thereto.

【Advantageous Effects】

[27] The present invention may provide a cosmetic composition for improving skin whitening having a skin whitening effect, by a method of inhibiting melanin production by inhibiting the production of PGE_2 (prostaglandin E_2) as a mediator promoting melanin production.

[28] Further, a cosmetic product for improving skin whitening having excellent skin whitening improvement efficacy and low cytotoxicity, as well as health functional food for improving skin whitening may be provided, using the cosmetic composition for improving skin whitening by the present invention. The health functional food for improving skin whitening is consumed in the form of inner beauty food, thereby having a better skin whitening improvement effect.

【Description of Drawings】

The above and other objects, features and advantages of the present invention will become apparent from the following description of preferred embodiments given in

conjunction with the accompanying drawings, in which:

[29] FIG. 1 is a result of evaluating prostaglandin E_2 (PGE_2) inhibitory efficacy.

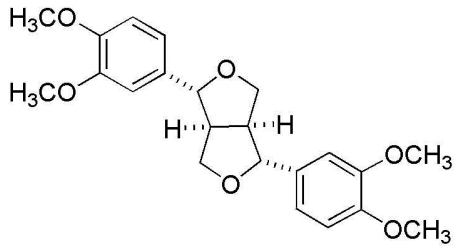
[30] FIG. 2 is a result of an experiment of inhibiting melanocyte dendritic cell formation.

【Best Mode】

[31] Hereinafter, the embodiments of the present invention will be described in detail with reference to accompanying drawings.

[32] In order to achieve the object of the present invention, the present invention provides a cosmetic composition for improving skin whitening, including a compound represented by the following Chemical Formula 1 as an effective component:

[33] [Chemical Formula 1]

[34] 

[35] The above compound is known to be effective in anti-inflammatory, antibacterial and bactericidal actions and the like, and thus, has been used to lower blood pressure, and as an anti-inflammatory agent in sinusitis, headache, toothache, rhinitis and the like. However, the present

inventors first discovered that the compound having such anti-inflammatory effect has efficacy of improving skin whitening, and completed the present invention for providing a cosmetic composition for improving skin whitening including the compound as an effective component.

[36] As an exemplary embodiment of the present invention, the compound may provide a cosmetic composition for improving skin whitening which is characterized by inhibiting the activity of PGE_2 (prostaglandin E_2) to inhibit melanin production, thereby preventing pigmentation, but not limited thereto.

[37] When PGE_2 which is an inflammatory substance is increased in cells by protease-activated receptor-2 (PAR-2), the length of dendrites of surrounding melanocytes is increased to facilitate the transfer of melanin to surrounding cells, thereby increasing pigmentation by melanin formation.

[38] Thus, the present invention provides a cosmetic composition for improving skin whitening by using the compound represented by the above Chemical Formula 1 of the present invention to inhibit the production of PGE_2 caused by the activity of protease-activated receptor-2 (PAR-2) to inhibit melanin formation, for inhibiting the production of a mediator promoting melanin production like PGE_2 which is an inflammatory substance, thereby inhibiting pigmentation.

[39] More specifically, the inhibition of melanin formation may be performed by using the compound of the present invention to prevent the production of PGE_2 which is the mediator promoting melanin production, thereby inhibiting melanocyte dendritic cell (DC) formation caused by PGE_2 to inhibit the transfer of melanin to surrounding cells to inhibit pigmentation.

[40] Accordingly, the cosmetic composition for improving skin whitening of the present invention may prevent the increase of the mediator promoting melanin production to inhibit melanin production, which may prevent the transfer of melanin to surrounding cells to inhibit pigmentation by melanin production, as a method of inhibiting melanocyte dendritic cell (DC) formation caused by the mediator promoting melanin production.

[41] As an exemplary embodiment of the present invention, a co-culturing system of keratinocytes and melanocytes may be treated with the compound to perform a skin whitening effect test. That is, it may be confirmed that the cells are treated with the compound to inhibit the production of PGE_2 which is a mediator promoting melanin production, thereby verifying skin whitening efficacy.

[42] As an exemplary embodiment of the present invention, protease-activated receptor-2 (PAR-2) may be activated in the cells to cause the production of PGE_2 which is an

inflammatory substance, and then when the cells are treated with the compound, an experiment for confirming whether the production of PGE_2 which is a mediator promoting melanin production is inhibited in a compound concentration-dependent manner may be performed, thereby confirming that the compound inhibits melanin production caused by PGE_2 to have a skin whitening effect.

[43] As another exemplary embodiment of the present invention, a co-culturing system of keratinocytes and melanocytes is treated with the compound to evaluate the efficacy of inhibiting melanocyte dendritic cell formation.

[44] As described above, as PGE_2 which is an inflammatory substance is increased by PAR-2 activation, the length of surrounding melanocyte dendrites is increased to facilitate transfer of melanin to surrounding cells, thereby causing pigmentation. Accordingly, the skin whitening effect by melanin production inhibition was proved by an experiment for confirming whether melanocyte dendritic cell (DC) formation is inhibited by the compound represented by the above Chemical Formula 1 of the present invention, when melanocytes are treated with the compound.

[45] In addition, the cosmetic composition for improving skin whitening of the present invention may further include vegetable estrogen as necessary, but not limited thereto. The vegetable estrogen is called phytoestrogen which is

natural estrogen derived from vegetables, and has similar function and structure to those of estrogen, and has the same function as estrogen in vivo.

[46] More specifically, a *Larrea cuneifolia Cav.* extract having a significance of an estrogen activity like the compound of the present invention may be included. The extract is a plant of an evergreen shrub in the family Zygophyllaceae, and known to be used to treat indigestion as a folk remedy in South America, however, the efficacy thereof has never been scientifically revealed, and pharmacological actions such as anti-inflammatory, anti-bacterial and antiviral actions of *L.tridentata* or *L. divaricata* shrub as the plant of *Larrea* genus have been reported.

[47] Surprisingly, a larger effect on skin whitening improvement may be exhibited by adding this *Larrea cuneifolia Cav.* extract to the composition of the present invention. The extract is a phytoestrogen component which may replace the function of estrogen which declines with age, and is assumed to have an influence on melanocyte formation and tyrosinase activity inhibition, and to inhibit production of keratinocytes producing melanosomes to help skin whitening.

[48] In addition, the present invention includes Steroidic Saponoside which is a steroid analogue, and further

includes a Kigelia Africana extract having an anti-inflammatory effect on skin, thereby imparting an effect of maintaining skin tissue elasticity, and above all, when used with the *Larrea cuneifolia Cav.* extract which is phytoestrogen in combination, helps activation of phytoestrogen to have a synergistic effect on skin whitening.

[49] In the cosmetic composition for improving skin whitening of the present invention, the cosmetic composition for improving skin whitening which is characterized in that the compound represented by the following Chemical Formula 1 is included at 0.001 to 10 wt% based on the total weight of the composition may be provided, but not limited thereto. More specifically, it is preferred to include the compound at 0.1 to 10 wt% for having the best efficacy of the whitening effect.

[50] When the compound is included within the above range, raw material efficacy is the highest, and the skin whitening effect is the best without causing skin irritation, but not limited thereto.

[51] The formation of the cosmetic composition for improving skin whitening is not particularly limited, and may be properly selected as desired. For example, the composition may be manufactured into a formulation such as toner, beauty wash, lotion, massage cream, nutritional

cream, moisturizer cream, hand cream, foundation, essence, pack, soap, cleansing foam, cleansing lotion, cleansing cream, body lotion or body cleanser, but not limited thereto.

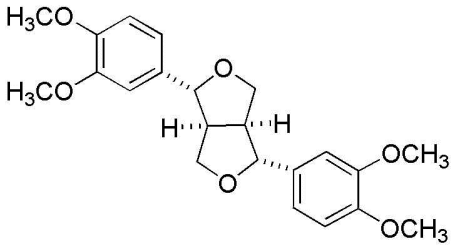
[52] Depending on the formulation, a carrier component may be further included, and properly added thereto depending on the formulation. For example, a solvent, a solvation agent or an emulsifier may be used, which may be for example, water, ethanol, isopropanol, ethyl carbonate, ethyl acetate, benzyl alcohol, benzyl benzoate, propylene glycol, glycerol aliphatic ester, polyethylene glycol, fatty acid ester of sorbitan, aliphatic alcohol sulfate, aliphatic alcohol ether sulfate, sulfosuccinic acid monoester, isethionate, imidazolinium derivatives, methyl taurate, sarcosinate, fatty acid amide ether sulfate, alkylamidobetaine, aliphatic alcohol, fatty acid glyceride, fatty acid diethanolamide, vegetable oil, lanolin derivatives or ethoxylated glycerol fatty acid ester, but not limited thereto.

[53] In addition to the above additives, components included in a general cosmetic composition may be formulated as necessary. As a formulating component included additionally, oil and fat components, moisturizers, emollient agents, surfactants, organic and inorganic pigments, organic powder, UV absorbers,

antiseptics, bactericides, antioxidants, plant extracts, pH adjusting agents, alcohols, colorants, perfumes, blood circulation accelerators, coolants, antiperspirants, purified water and the like may be listed, but not limited thereto.

[54] In another general aspect, health functional food for improving skin whitening including a compound represented by the following Chemical Formula 1 as an effective component is provided:

[55] [Chemical Formula 1]

[56] 

[57] The health functional food for improving skin whitening may be provided as various forms of food additives or functional food. As the health functional food for improving skin whitening, for example, leached tea, liquid tea, beverage, fermented milk, cheese, yogurt, juice, probiotic agent, health supplement food and the like may be processed, and also it may be used in various forms of food additives as desired. In addition, the formulation of health functional food may be in various forms of solutions, emulsions, viscous mixtures, tablets, powder, pills and the like, and administered by various methods of

simply drinking, injection, spraying or squeezing.

[58] Preferably, the health functional food for improving skin whitening is consumed in the form of inner beauty food, thereby having a better skin whitening improvement effect. The inner beauty is inner beauty food called 'eating cosmetic product or beauty food', and referred to the food absorbing various good components for skin into the body to render skin constitution to be healthy. The inner beauty food may be selected and consumed according to each individual considering the skin condition and lifestyle as the cosmetic products are selected depending on the skin type. More preferably, when using the cosmetic product including the cosmetic composition and the inner beauty food including the compound in combination, the skin whitening improvement effect is remarkably high as compared with using only the cosmetic product, thereby having a greater skin whitening improvement effect.

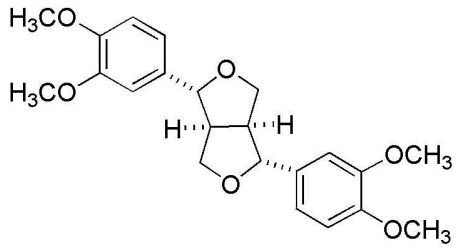
[59] Hereinafter, the present invention will be described in more detail by the following Examples. These Examples are provided only to illustrate the present invention, and it will be evident to a person skilled in the art that the scope of the present invention is not construed to be limited to those Examples.

[60]

[61] Material information of the compound of Chemical

Formula 1

[62] [Chemical Formula 1]



[63]

[64] CAS No.:526-06-7

[65] Molecular Weight: 396.44

[66] Supplier: Sigma-Aldrich

[67] Origin plant: Rutaceae family

[68]

[69] (Example 1) Experiment of prostaglandin E_2(PGE_2) production inhibition

[70] HaCat cells (human immortal keratinocytes) which are human-derived keratinocytes and melanocytes were cultured using a co-culturing system, and then the cells were treated with 10 uM of SLIGLV (Ser-Leu-Ile-Gly-Lys-Val-amide) as an inducer for activating proteinase-activated receptor-2 (PAR-2). After treating with SLIGLV to activate PAR-2 to promote PGE_2 production, the cells were treated with the compound of Chemical Formula 1 at concentrations of 0 uM, 12.5 uM, 25 uM and 50 uM. After a certain period of time, the amount of PGE_2 protein secreted in the culture medium of cells was measured by ELISA. As a result, it was confirmed that the PGE_2 production inhibition rate in the

group treated with the compound at high concentrations of 25 uM and 50 uM was about 40%, based on the PGE_2 production rate (100%) of a control group which was not treated with the compound when cultured for 6 days or more, thereby having the PGE_2 production inhibiting effect. The results are illustrated in FIG. 1.

[71]

[72] (Example 2) Experiment of inhibiting melanocyte dendritic cell (DC) formation

[73] HaCat cells (human immortal keratinocytes) which are human-derived keratinocytes and melanocytes were cultured using a co-culturing system, and then the cells were treated with 10 uM of SLIGLV (Ser-Leu-Ile-Gly-Lys-Val-amide) as an inducer for activating proteinase-activated receptor-2 (PAR-2) to produce an inflammatory substance PGE_2. After treating with SLIGLV to activate PAR-2 to promote PGE_2 production, the cells were treated with the compound of Chemical Formula 1 at concentrations of 0 uM, 25 uM and 50 uM. After a certain period of time, the melanocytes were immunostained with a tyrosinase antibody, thereby observing the length of melanocyte dendritic cells (DC). The results are illustrated in FIG. 2, and it was confirmed that the group treated with the compound of Chemical Formula 1 had significantly inhibited melanocyte dendritic cell (DC) formation, as compared with the group

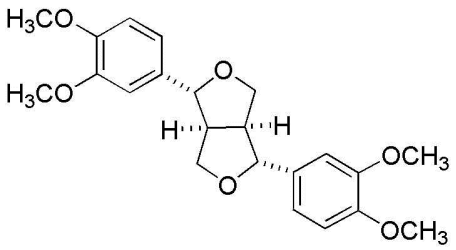
treated only SLIGLV as a positive control group. In addition, in the group treated with the compound and a *Larrea cuneifolia Cav.* extract in combination, melanocyte dendritic cell (DC) formation was significantly inhibited.

【CLAIMS】

【Claim 1】

A cosmetic composition for improving skin whitening, comprising a compound represented by the following Chemical Formula 1 as an effective component:

[Chemical Formula 1]



【Claim 2】

The composition of claim 1, wherein the compound inhibits prostaglandin E_2 (PGE_2) activity to inhibit melanin production in skin.

【Claim 3】

The composition of claim 2, wherein the compound inhibits melanocyte dendritic cell (DC) formation by proteinase-activated receptor-2 (PAR-2).

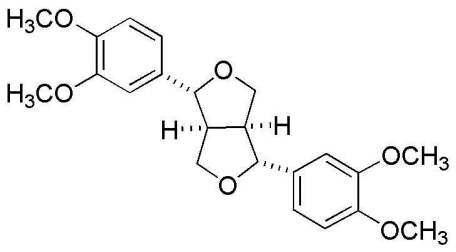
【Claim 4】

The composition of claim 1, wherein the compound is included at 0.001 to 10 wt%, based on the total weight of the composition.

【Claim 5】

A method of inhibiting melanin pigmentation, by treating keratinocytes and melanocytes with a compound represented by the following Chemical Formula 1 to inhibit increase of prostaglandin E_2 (PGE_2):

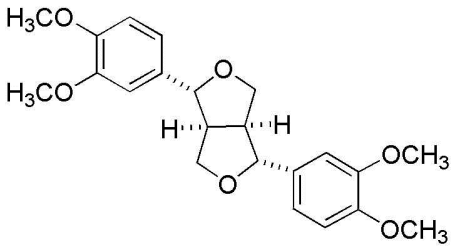
[Chemical Formula 1]



【Claim 6】

A method of inhibiting melanocyte dendritic cell (DC) formation by proteinase-activated receptor-2 (PAR-2), by treating keratinocytes and melanocytes with a compound represented by the following Chemical Formula 1:

[Chemical Formula 1]

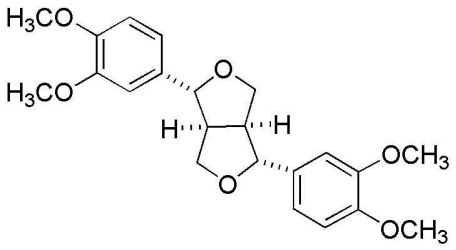


【Claim 7】

Health functional food for improving skin whitening,

comprising a compound represented by the following Chemical Formula 1 as an effective component:

[Chemical Formula 1]



【Claim 8】

The health functional food of claim 7, wherein the food is inner beauty food.