

DESCRIPTION

TITLE OF INVENTION: COMPOSITION FOR SUPPRESSING DECREASE IN
OR IMPROVING SKIN BARRIER FUNCTION, COMPOSITION FOR
5 SUPPRESSING DECREASE IN OR IMPROVING EXPRESSION OF TYPE 4
COLLAGEN, AND METHOD FOR SCREENING SUBSTANCES HAVING ACTION
TO SUPPRESS DECREASE IN OR IMPROVE SKIN BARRIER FUNCTION

TECHNICAL FIELD

10 [0001]

The present invention relates to a composition for
suppressing a decrease in or improving skin barrier
function and a composition for suppressing a decrease in or
improving expression of type IV collagen. The present
15 invention also relates to a method of suppressing a
decrease in skin barrier function or improving the skin
barrier function and a method of suppressing a decrease in
expression of type IV collagen or improving the expression.
The present invention also relates to a method of screening
20 for a substance having an effect of suppressing a decrease
in or improving skin barrier function.

BACKGROUND ART

[0002]

25 Skin is primarily composed of two layers including
the epidermis and the dermis from the surface. The
epidermis is composed of four layers including a basal
layer, a spinous layer, a granular layer, and a cornified
layer in ascending order. The basal layer adheres to the
dermis via a basement membrane. The basement membrane is
30 composed of components such as type IV collagen and type
VII collagen and has functions such as a function of
connecting the basal layer in the epidermis with the dermis.
The functions unfortunately decrease with age.

35 [0003]

Skin has a barrier function that prevents entry of foreign substances into the living body from the outside and keeps water in the skin by preventing water in the body from excessively evaporating from the skin. A decrease in skin barrier function due to factors such as aging causes troubles such as dry skin. Patent Literature 1 discloses an agent for improving skin barrier function containing components such as an extract of *Aspalathus linearis*.

10

CITATION LIST

- Patent Literature
[0004]

Patent Literature 1: JP 2009-256244 A

15

SUMMARY OF INVENTION

- Technical Problem
[0005]

20

The present invention aims to provide a composition for suppressing a decrease in or improving skin barrier function capable of suppressing a decrease in skin barrier function or improving the function. The present invention also aims to provide a composition for suppressing a decrease in or improving expression of type IV collagen. The present invention also aims to provide a method of suppressing a decrease in skin barrier function or improving the function, and a method of suppressing a decrease in expression of type IV collagen or improving the expression. The present invention also aims to provide a method of screening for a substance having an effect of suppressing a decrease in or improving skin barrier function.

30

- Solution to problem
[0006]

35

The present inventor made studies to solve the above

problem, and found out that suppression of a decrease in expression of type IV collagen or improvement of the expression in skin cells suppresses a decrease in skin barrier function or improves the function. The present
5 inventor made further studies based on the above finding, and completed the present invention.

[0007]

The present invention encompasses but is not limited to the following composition for suppressing a decrease in
10 or improving skin barrier function, the composition for suppressing a decrease in or improving expression of type IV collagen, and the like.

(1) A composition for suppressing a decrease in or improving skin barrier function by suppressing a decrease
15 in or improving expression of type IV collagen, the composition containing, as an active ingredient, at least one extract selected from the group consisting of an extract of a plant belonging to the genus *Rosa* of the family Rosaceae, an extract of a grape seed and/or a grape
20 skin, an extract of a yeast belonging to the genus *Yarrowia*, an extract of a plant belonging to the genus *Camellia* of the family Theaceae, an extract of a plant belonging to the genus *Filipendula* of the family Rosaceae, and an extract of a plant belonging to the genus *Mentha* of the family
25 Lamiaceae.

(2) The composition for suppressing a decrease in or improving skin barrier function according to (1) above, wherein the plant belonging to the genus *Rosa* of the family Rosaceae is a rose, the yeast belonging to the genus
30 *Yarrowia* is *Yarrowia lipolytica*, the plant belonging to the genus *Camellia* of the family Theaceae is tea plant, the plant belonging to the genus *Filipendula* of the family Rosaceae is meadowsweet, and the plant belonging to the genus *Mentha* of the family Lamiaceae is peppermint.

35 (3) The composition for suppressing a decrease in or

improving skin barrier function according to (1) or (2) above, wherein the plant belonging to the genus *Rosa* of the family Rosaceae is a rose petal containing at least one compound selected from the group consisting of a
5 delphinidin-type anthocyanin, a rosacyanin compound, and a rosadelphin compound, the plant belonging to the genus *Camellia* of the family Theaceae is a tea plant leaf, the plant belonging to the genus *Filipendula* of the family Rosaceae is a meadowsweet flower, and the plant belonging
10 to the genus *Mentha* of the family Lamiaceae is a whole plant of peppermint.

(4) A composition for suppressing a decrease in or improving skin barrier function, the composition containing, as an active ingredient, an extract of a plant belonging to
15 the genus *Hamamelis* of the family Hamamelidaceae and/or an extract of a plant belonging to the genus *Plantago* of the family Plantaginaceae.

(5) The composition for suppressing a decrease in or improving skin barrier function according to (4) above,
20 wherein the plant belonging to the genus *Hamamelis* of the family Hamamelidaceae is American witch-hazel and the plant belonging to the genus *Plantago* of the family Plantaginaceae is greater plantain.

(6) The composition for suppressing a decrease in or
25 improving skin barrier function according to (4) or (5) above, wherein the plant belonging to the genus *Hamamelis* of the family Hamamelidaceae is an American witch-hazel leaf and the plant belonging to the genus *Plantago* of the family Plantaginaceae is a greater plantain seed.

30 (7) The composition for suppressing a decrease in or improving skin barrier function according to any one of (4) to (6) above, wherein the composition suppresses a decrease in or improves skin barrier function by suppressing a decrease in or improving basement membrane function.

35 (8) The composition for suppressing a decrease in or

improving skin barrier function according to (7) above, wherein the composition suppresses a decrease in or improving basement membrane function by suppressing a decrease in or improving expression of type IV collagen.

5 (9) A composition for suppressing a decrease in or improving skin barrier function, the composition containing, as an active ingredient, an agent for suppressing a decrease in or improving basement membrane function.

10 (10) The composition for suppressing a decrease in or improving skin barrier function according to (9) above, wherein the agent for suppressing a decrease in or improving basement membrane function suppresses a decrease in or improving basement membrane function by suppressing a decrease in or improving expression of type IV collagen.

15 (11) A composition for suppressing a decrease in or improving expression of type IV collagen, the composition containing, as an active ingredient, at least one extract selected from the group consisting of an extract of a plant belonging to the genus *Rosa* of the family Rosaceae, an
20 extract of a grape seed and/or a grape skin, an extract of a yeast belonging to the genus *Yarrowia*, an extract of a plant belonging to the genus *Camellia* of the family Theaceae, an extract of a plant belonging to the genus *Hamamelis* of the family Hamamelidaceae, an extract of a
25 plant belonging to the genus *Filipendula* of the family Rosaceae, an extract of a plant belonging to the genus *Plantago* of the family Plantaginaceae, and an extract of a plant belonging to the genus *Mentha* of the family Lamiaceae.

30 (12) The composition for suppressing a decrease in or improving expression of type IV collagen according to (11) above, wherein the plant belonging to the genus *Rosa* of the family Rosaceae is a rose, the yeast belonging to the genus *Yarrowia* is *Yarrowia lipolytica*, the plant belonging to the genus *Camellia* of the family Theaceae is tea plant, the
35 plant belonging to the genus *Hamamelis* of the family

Hamamelidaceae is American witch-hazel, the plant belonging to the genus *Filipendula* of the family Rosaceae is meadowsweet, the plant belonging to the genus *Plantago* of the family Plantaginaceae is greater plantain, and the
 5 plant belonging to the genus *Mentha* of the family Lamiaceae is peppermint.

(13) The composition for suppressing a decrease in or improving expression of type IV collagen according to (11) or (12) above, wherein the plant belonging to the genus
 10 *Rosa* of the family Rosaceae is a rose petal containing at least one compound selected from the group consisting of a delphinidin-type anthocyanin, a rosacyanin compound, and a rosadelphin compound, the plant belonging to the genus *Camellia* of the family Theaceae is a tea plant leaf, the
 15 plant belonging to the genus *Hamamelis* of the family Hamamelidaceae is an American witch-hazel leaf, the plant belonging to the genus *Filipendula* of the family Rosaceae is a meadowsweet flower, the plant belonging to the genus *Plantago* of the family Plantaginaceae is a greater plantain
 20 seed, and the plant belonging to the genus *Mentha* of the family Lamiaceae is a whole plant of peppermint.

(14) The composition according to any one of (1) to (13) above, wherein the composition is a topical agent for skin.

25 (15) The composition according to any one of (1) to (14) above, wherein the composition is a cosmetic.

(16) Use of an extract for suppressing a decrease in skin barrier function or improving the skin barrier function by suppressing a decrease in or improving
 30 expression of type IV collagen, the extract including at least one selected from the group consisting of an extract of a plant belonging to the genus *Rosa* of the family Rosaceae, an extract of a grape seed and/or a grape skin, an extract of a yeast belonging to the genus *Yarrowia*, an
 35 extract of a plant belonging to the genus *Camellia* of the

family Theaceae, an extract of a plant belonging to the genus *Filipendula* of the family Rosaceae, and an extract of a plant belonging to the genus *Mentha* of the family Lamiaceae.

5 (17) Use of an extract for suppressing a decrease in skin barrier function or improving the skin barrier function, the extract including an extract of a plant belonging to the genus *Hamamelis* of the family Hamamelidaceae and/or an extract of a plant belonging to
10 the genus *Plantago* of the family Plantaginaceae.

 (18) Use of an extract for suppressing a decrease in expression of type IV collagen or improving the expression, the extract including at least one selected from the group consisting of an extract of a plant belonging to the genus
15 *Rosa* of the family Rosaceae, an extract of a grape seed and/or a grape skin, an extract of a yeast belonging to the genus *Yarrowia*, an extract of a plant belonging to the genus *Camellia* of the family Theaceae, an extract of a plant belonging to the genus *Hamamelis* of the family
20 Hamamelidaceae, an extract of a plant belonging to the genus *Filipendula* of the family Rosaceae, an extract of a plant belonging to the genus *Plantago* of the family Plantaginaceae, and an extract of a plant belonging to the genus *Mentha* of the family Lamiaceae.

25 (19) A method of suppressing a decrease in skin barrier function or improving the skin barrier function by suppressing a decrease in or improving expression of type IV collagen, the method including administering at least one extract selected from the group consisting of an
30 extract of a plant belonging to the genus *Rosa* of the family Rosaceae, an extract of a grape seed and/or a grape skin, an extract of a yeast belonging to the genus *Yarrowia*, an extract of a plant belonging to the genus *Camellia* of the family Theaceae, an extract of a plant belonging to the
35 genus *Filipendula* of the family Rosaceae, and an extract of

a plant belonging to the genus *Mentha* of the family Lamiaceae.

(20) A method of suppressing a decrease in skin barrier function or improving the skin barrier function, the method including administering an extract of a plant belonging to the genus *Hamamelis* of the family Hamamelidaceae and/or an extract of a plant belonging to the genus *Plantago* of the family Plantaginaceae.

(21) A method of suppressing a decrease in expression of type IV collagen or improving the expression, the method including administering at least one extract selected from the group consisting of an extract of a plant belonging to the genus *Rosa* of the family Rosaceae, an extract of a grape seed and/or a grape skin, an extract of a yeast belonging to the genus *Yarrowia*, an extract of a plant belonging to the genus *Camellia* of the family Theaceae, an extract of a plant belonging to the genus *Hamamelis* of the family Hamamelidaceae, an extract of a plant belonging to the genus *Filipendula* of the family Rosaceae, an extract of a plant belonging to the genus *Plantago* of the family Plantaginaceae, and an extract of a plant belonging to the genus *Mentha* of the family Lamiaceae.

(22) A method of screening for a substance having an effect of suppressing a decrease in or improving skin barrier function, the method including: a step of culturing in vitro human epidermal keratinocytes in a medium containing a test substance and separately in a control medium not containing the test substance; and a step of comparing an expression level of type IV collagen between the keratinocytes cultured in the medium containing a test substance and the keratinocytes as a control cultured in the control medium, wherein the test substance is selected as a substance having an effect of suppressing a decrease in or improving skin barrier function when the expression level of type IV collagen in the keratinocytes cultured in

the medium containing the test substance is higher than the expression level of type IV collagen in the keratinocytes as a control.

5 - Advantageous Effects of Invention
[0008]

The present invention can provide a composition for suppressing a decrease in or improving skin barrier function capable of suppressing a decrease in skin barrier
10 function or improving the function. The present invention can also provide a composition for suppressing a decrease in or improving expression of type IV collagen. The present invention can also provide a method of suppressing a decrease in skin barrier function or improving the
15 function, and a method of suppressing a decrease in expression of type IV collagen or improving the expression. The present invention can also provide a method of screening for a substance having an effect of suppressing a decrease in or improving skin barrier function.

20

DESCRIPTION OF EMBODIMENTS

[0009]

A first aspect of the present invention is a composition for suppressing a decrease in expression of
25 type IV collagen, the composition containing, as an active ingredient, at least one extract selected from the group consisting of an extract of a plant belonging to the genus *Rosa* of the family Rosaceae, an extract of a grape seed and/or a grape skin, an extract of a yeast belonging to the
30 genus *Yarrowia*, an extract of a plant belonging to the genus *Camellia* of the family Theaceae, an extract of a plant belonging to the genus *Hamamelis* of the family Hamamelidaceae, an extract of a plant belonging to the genus *Filipendula* of the family Rosaceae, an extract of a
35 plant belonging to the genus *Plantago* of the family

Plantaginaceae, and an extract of a plant belonging to the genus *Mentha* of the family Lamiaceae. The composition for suppressing a decrease in or improving expression of type IV collagen of the first aspect of the present invention is also referred to as a composition of the first aspect of the present invention.

The at least one extract has an effect of suppressing a decrease in expression of type IV collagen or improving the expression. Suppressing a decrease in expression of type IV collagen includes suppression of progress of the decrease in expression of type IV collagen, maintenance of the expression of type IV collagen, reduction (ease) of the level of the decrease in expression of type IV collagen, and the like. Improving expression of type IV collagen includes recovery of expression of type IV collagen, and the like. Recovery includes at least partial recovery. The expression of type IV collagen includes expression of a gene encoding type IV collagen and expression of type IV collagen at the protein level, and herein may refer to one or both of them. Type IV collagen is preferably human type IV collagen, more preferably human collagen α -1(IV) chain. The human collagen α -1(IV) chain is a protein encoded by the COL4A1 gene. In one embodiment, the composition for suppressing a decrease in or improving expression of type IV collagen of the present invention can be used to suppress a decrease in expression of type IV collagen in a human or improving the expression by suppressing a decrease in expression of the human collagen α -1(IV) chain or improving the expression.

[0010]

The expression of type IV collagen is decreased (the expression level is lowered) by external factors such as UV and internal factors such as aging.

As described later in EXAMPLES, suppression of a decrease in expression of type IV collagen or improvement

of the expression in epidermal keratinocytes suppressed a decrease in transepithelial electrical resistance (TEER) of the skin or improved the resistance. This demonstrates that a decrease in skin barrier function was suppressed or
5 the skin barrier function was improved. A specific mechanism for suppression of a decrease in skin barrier function or improvement of the function by suppressing a decrease in or improving expression of type IV collagen is not clear but presumably as follows. Suppressing a
10 decrease in or improving expression of type IV collagen which is a component of a basement membrane suppressed a decrease in basement membrane function or improved the function, which enabled maintenance of skin homeostasis and finally led to suppression of a decrease in skin barrier
15 function or improvement of the function. Suppressing a decrease in basement membrane function or improving the function is therefore expected to be able to suppress a decrease in skin barrier function or improve the skin barrier function. The extract of any of the plants or the
20 yeast have an excellent effect of suppressing a decrease in or improving expression of type IV collagen to be usable for suppressing a decrease in basement membrane function or improving the function.

In terms of the effect of suppressing a decrease in
25 or improving expression of type IV collagen, the at least one extract in the composition of the first aspect of the present invention preferably includes at least one selected from the group consisting of an extract of a plant belonging to the genus *Rosa* of the family Rosaceae, an
30 extract of a grape seed and/or a grape skin, and an extract of a plant belonging to the genus *Filipendula* of the family Rosaceae.

[0011]

The skin barrier function refers to a barrier
35 function of the skin that prevents entry of foreign

substances into the living body from the outside and keeps water in the skin by preventing water in the body from excessively evaporating from the skin. Suppressing a decrease in skin barrier function includes suppression of progress of the decrease in skin barrier function, maintenance of the skin barrier function, and reduction (ease) of the level of the decrease in skin barrier function. Improving the skin barrier function includes recovery of the skin barrier function. The decrease in skin barrier function may include a decrease in skin barrier function due to aging, a decrease in skin barrier function due to exposure to UV, and the like.

[0012]

As described above, suppressing a decrease in or improving basement membrane function can suppress a decrease in skin barrier function or improve the function.

A second aspect of the present invention is a composition for suppressing a decrease in or improving skin barrier function containing, as an active ingredient, an agent for suppressing a decrease in or improving basement membrane function. Hereafter, the composition for suppressing a decrease in or improving skin barrier function of the second aspect of the present invention may be also referred to as a composition of the second aspect of the present invention.

[0013]

The basement membrane is known to function as a mechanical support connecting the epidermis and the dermis, a selective filter for substance exchange between the epidermis and the dermis, and the like. Suppressing a decrease in expression of a basement membrane component such as type IV collagen or improving the expression is effective for suppressing a decrease in or improving basement membrane function.

The agent for suppressing a decrease in or improving

basement membrane function may be any agent having an effect of suppressing a decrease in or improving basement membrane function, such as an agent having an effect of suppressing a decrease in or improving expression of a basement membrane component. The agent for suppressing a decrease in or improving basement membrane function preferably suppresses a decrease in basement membrane function or improves the basement membrane function by suppressing a decrease in or improving expression of type IV collagen. The agent for suppressing a decrease in or improving basement membrane function used may be, for example, the above-mentioned extract of any of the plants or the yeast having an effect of suppressing a decrease in or improving expression of type IV collagen. In one embodiment, the agent for suppressing a decrease in or improving basement membrane function used may include at least one extract selected from the group consisting of an extract of a plant belonging to the genus *Rosa* of the family Rosaceae, an extract of a grape seed and/or a grape skin, an extract of a yeast belonging to the genus *Yarrowia*, an extract of a plant belonging to the genus *Camellia* of the family Theaceae, an extract of a plant belonging to the genus *Hamamelis* of the family Hamamelidaceae, an extract of a plant belonging to the genus *Filipendula* of the family Rosaceae, an extract of a plant belonging to the genus *Plantago* of the family Plantaginaceae, and an extract of a plant belonging to the genus *Mentha* of the family Lamiaceae.

Among the above extracts, the agent for suppressing a decrease in or improving basement membrane function preferably includes at least one selected from the group consisting of an extract of a plant belonging to the genus *Rosa* of the family Rosaceae, an extract of a grape seed and/or a grape skin, and an extract of a plant belonging to the genus *Filipendula* of the family Rosaceae.

[0014]

A third aspect of the present invention is a composition for suppressing a decrease in or improving skin barrier function by suppressing a decrease in or improving expression of type IV collagen, the composition containing, as an active ingredient, at least one extract selected from the group consisting of an extract of a plant belonging to the genus *Rosa* of the family Rosaceae, an extract of a grape seed and/or a grape skin, an extract of a yeast belonging to the genus *Yarrowia*, an extract of a plant belonging to the genus *Camellia* of the family Theaceae, an extract of a plant belonging to the genus *Filipendula* of the family Rosaceae, and an extract of a plant belonging to the genus *Mentha* of the family Lamiaceae. Hereafter, the composition for suppressing a decrease in or improving skin barrier function of the third aspect of the present invention is also referred to as a composition of the third aspect of the present invention.

In the composition of the third aspect of the present invention, the extract preferably includes at least one selected from the group consisting of an extract of a grape seed and/or a grape skin, an extract of a yeast belonging to the genus *Yarrowia*, an extract of a plant belonging to the genus *Camellia* of the family Theaceae, and an extract of a plant belonging to the genus *Filipendula* of the family Rosaceae.

[0015]

A fourth aspect of the present invention is a composition for suppressing a decrease in or improving skin barrier function, the composition containing, as an active ingredient, an extract of a plant belonging to the genus *Hamamelis* of the family Hamamelidaceae and/or an extract of a plant belonging to the genus *Plantago* of the family Plantaginaceae. Hereafter, the composition for suppressing a decrease in or improving skin barrier function of the fourth aspect of the present invention is also referred to

as a composition of the fourth aspect of the present invention. The composition of the fourth aspect of the present invention preferably contains, as an active ingredient, an extract of a plant belonging to the genus
5 *Hamamelis* of the family Hamamelidaceae.
[0016]

The extracts used in the composition of the third aspect and the composition of the fourth aspect of the present invention have an effect of suppressing a decrease
10 in or improving expression of type IV collagen. Containing any of the extracts, the compositions can suppress a decrease in or improving basement membrane function. In one embodiment, the compositions for suppressing a decrease in or improving skin barrier function of the third and
15 fourth aspects of the present invention can be used for suppressing a decrease in skin barrier function or improving the skin barrier function by suppressing a decrease in or improving basement membrane function. The composition for suppressing a decrease in or improving skin
20 barrier function of the fourth aspect of the present invention can be used for suppressing a decrease in skin barrier function or improving the skin barrier function by suppressing a decrease in or improving basement membrane function which is achieved by suppressing a decrease in or
25 improving expression of type IV collagen. In one embodiment, the composition for suppressing a decrease in or improving skin barrier function of the fourth aspect of the present invention can be used for suppressing a decrease in or improving skin barrier function by
30 suppressing a decrease in or improving expression of type IV collagen.
[0017]

Hereinbelow, the composition for suppressing a decrease in or improving expression of type IV collagen of
35 the first aspect of the present invention and the

compositions for suppressing a decrease in or improving skin barrier function of the second, third, and fourth aspects of the present invention are collectively referred to as compositions of the present invention. In the
5 compositions of the present invention, two or more of the extracts may be used in combination as active ingredients.
[0018]

In the present invention, the plant belonging to the genus *Rosa* of the family Rosaceae is a rose belonging to
10 the genus *Rosa* of the family Rosaceae, typified by *Rosa hybrida* (scientific name).

The plant belonging to the genus *Rosa* of the family Rosaceae is preferably a rose containing at least one compound selected from the group consisting of a
15 delphinidin-type anthocyanin, a rosacyanin compound, and a rosadelphin compound, more preferably a rose containing, in its petals, at least one compound selected from the group consisting of a delphinidin-type anthocyanin, a rosacyanin compound, and a rosadelphin compound. In particular,
20 preferred is a rose containing a delphinidin-type anthocyanin in its petals.
[0019]

The delphinidin-type anthocyanin is a pigment mostly contained in violet or blue petals. Examples of the
25 delphinidin-type anthocyanin include delphinidin, malvidin, petunidin, and compounds obtained by modifying the foregoing pigments with a saccharide or an acyl group. Examples of a rose containing a delphinidin-type anthocyanin include roses showing blue to wisteria colors,
30 such as SUNTORY blue rose APPLAUSE®. Whether or not the rose contains a delphinidin-type anthocyanin can be determined by HPLC by the method disclosed in JP 5697040 B2.
[0020]

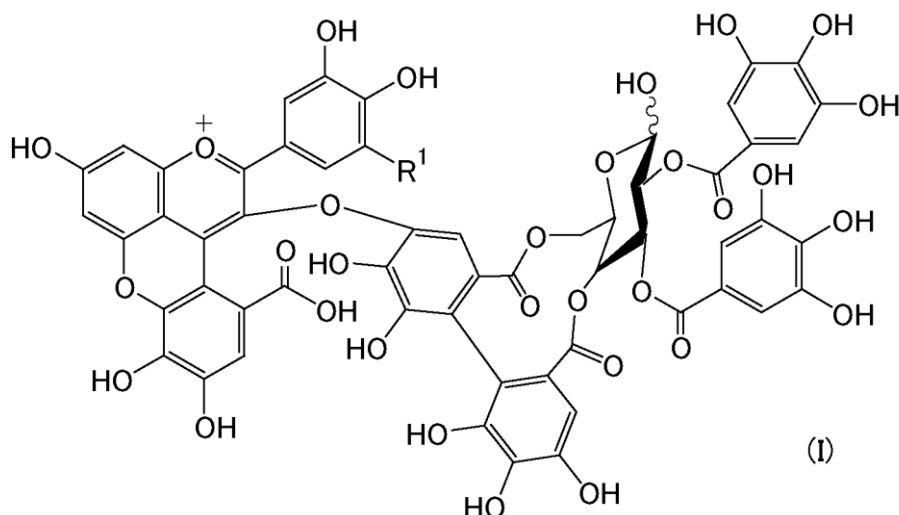
The rosacyanin compound includes at least one
35 compound selected from the group consisting of rosacyanin

A1, rosacyanin A2, and rosacyanin B. A rose containing a rosacyanin compound may be any rose containing at least one of the above-mentioned compounds. The rose preferably contains rosacyanin A1, rosacyanin A2, and rosacyanin B.

5 Rosacyanin A1 is a compound represented by the following formula (I) wherein R^1 is a hydrogen atom. Rosacyanin A2 is a compound represented by the following formula (II) wherein R^2 is a hydrogen atom. Rosacyanin B is a compound represented by the following formula (III) wherein R^3 is a
10 hydrogen atom.

[0021]

[Chem. 1]

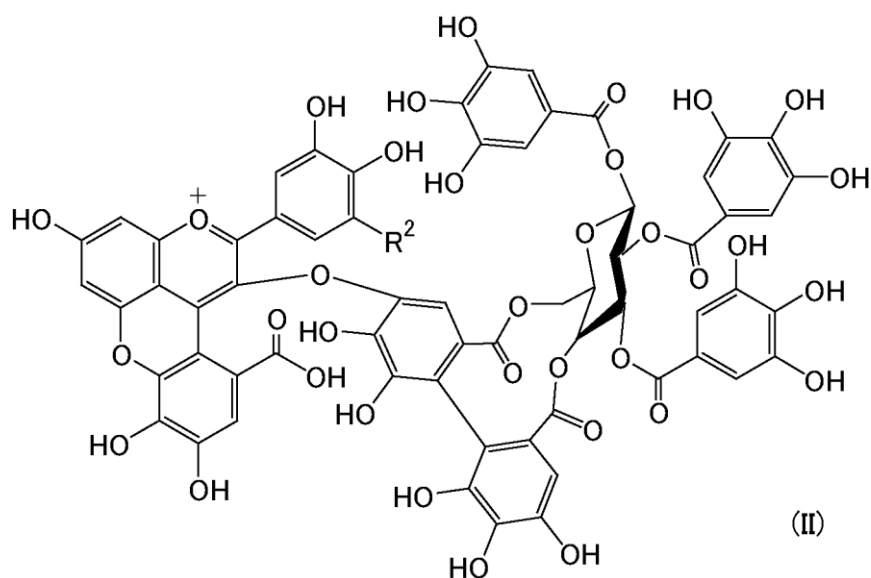


[0022]

15 In the formula, coordination (wave line) of a hydroxy group at position 1 of glucose indicates tautomerism between an α form and a β form, and R^1 is a hydrogen atom or a hydroxyl group.

[0023]

20 [Chem. 2]

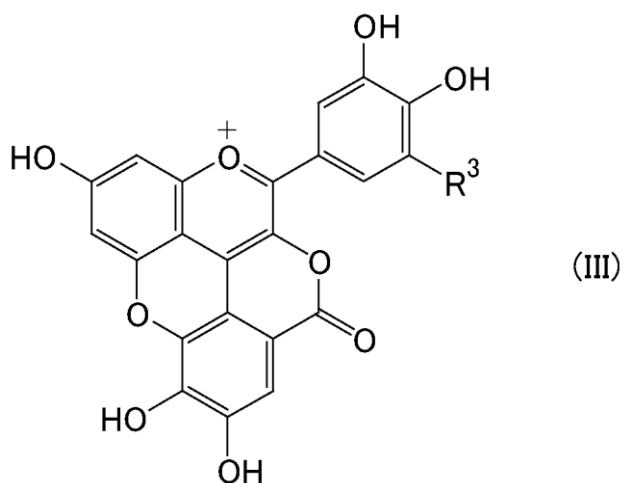


[0024]

In the formula, R^2 is a hydrogen atom or a hydroxy group.

5 [0025]

[Chem. 3]



[0026]

10 In the formula, R^3 is a hydrogen atom or a hydroxy group.

[0027]

Examples of the rose containing a rosacyanin compound include blue to wisteria-colored roses, such as Madame Violet, Purple Rain, Lavande, Manhattan Blue, Chantilly

Lace, Blue Moon, Tasogare, Charles de Gaulle, Violet Dolly, Blue Ribbon, Aozora, Lady X, Blue Bajou, and Sterling Silver. These roses are preferred as they contain a rosacyanin compound in their petals.

5 [0028]

The rosadelphin compound includes at least one compound selected from the group consisting of rosadelphin A1, rosadelphin A2, and rosadelphin B. The rose containing a rosadelphin compound is a rose containing at least one of
10 the above compounds. Preferably, the rose is a rose containing rosadelphin A1, rosadelphin A2, and rosadelphin B. Rosadelphin A1 is a compound represented by the formula (I) wherein R¹ is a hydroxy group. Rosadelphin A2 is a compound represented by the formula (II) wherein R² is a
15 hydroxy group. Rosadelphin B is a compound represented by the formula (III) wherein R³ is a hydroxy group.

[0029]

Wild roses do not contain the rosadelphin compound. In roses into which a gene encoding flavonoid 3',5'-hydroxylase (hereafter, also referred to as a flavonoid
20 3',5'-hydroxylase gene) is introduced by a technique such as gene recombination or in roses carrying the flavonoid 3',5'-hydroxylase gene which are obtained from genetically modified roses as a parent, delphinidin which is a blue
25 pigment is synthesized. To the synthesized delphinidin is bound a gallate or a tellimagrandin, thereby producing a rosadelphin compound.

[0030]

Roses containing the rosadelphin compound used may be
30 roses into which a flavonoid 3',5'-hydroxylase gene is introduced by a technique such as gene recombination or roses carrying a flavonoid 3',5'-hydroxylase gene which are obtained from genetically modified roses as a parent. Examples of the roses include roses such as SUNTORY blue
35 rose APPLAUSE®. SUNTORY blue rose APPLAUSE® is known to

have petals containing rosacyanin A1, rosacyanin A2, rosacyanin B, rosadelphin A1, rosadelphin A2, and rosadelphin B (e.g., WO 2010/110382). SUNTORY blue rose APPLAUSE® is available from Suntory Flowers Ltd. (Tokyo, Japan). Roses carrying a flavonoid 3',5'-hydroxylase gene can be produced by the method disclosed in WO 2010/110382 or the like. Examples of the flavonoid 3',5'-hydroxylase gene include a plant-derived gene disclosed in WO 2004/020637. Preferred is a flavonoid 3',5'-hydroxylase gene derived from pansy belonging to the genus *Viola* (e.g., *Viola* spp. Cv. black Pansy). Roses containing a flavonoid 3',5'-hydroxylase gene are preferred as they contain a rosadelphin compound in their petals. All of the academic and patent literatures described herein are incorporated herein by reference.

[0031]

The rosacyanin compound and/or the rosadelphin compound contained in roses can be confirmed, for example, by HPLC-TOF-MS by the method disclosed in WO 2010/110382, WO 2015/178385, or the like.

[0032]

The grape seed and the grape skin refer to a seed and a skin of a grape (scientific name: *Vitis* spp.) which is a plant belonging to the genus *Vitis* of the family Vitaceae. The variety of a grape is not limited, and examples thereof include black grapes such as Cabernet Sauvignon, Concord, Merlot, Muscat Bailey A; and white grapes such as Chardonnay and Koshu. Among these, Chardonnay and black grapes are preferred, black grapes are more preferred, and Cabernet Sauvignon, Merlot, and the like are still more preferred. The grape for the extract of a grape seed and/or a grape skin may include one or more varieties of grapes. The extract of a grape seed and/or a grape skin is preferably an extract of a grape seed and a grape skin.

[0033]

The yeast belonging to the genus *Yarrowia* is preferably *Yarrowia lipolytica*. The extract of a yeast belonging to the genus *Yarrowia* is preferably an extract of *Yarrowia lipolytica*.

5 [0034]

The plant belonging to the genus *Camellia* of the family Theaceae is preferably tea plant (scientific name: *Camellia sinensis*).

10 The plant belonging to the genus *Hamamelis* of the family Hamamelidaceae is preferably American witch-hazel (scientific name: *Hamamelis virginiana*).

The plant belonging to the genus *Filipendula* of the family Rosaceae is preferably meadowsweet (scientific name: *Filipendula ulmaria*).

15 [0035]

The plant belonging to the genus *Plantago* of the family Plantaginaceae is preferably greater plantain (scientific name: *Plantago major*).

20 The plant belonging to the genus *Mentha* of the family Lamiaceae is preferably peppermint (scientific name: *Mentha x piperita*).

[0036]

25 The extract of the plant can be prepared using any of the following parts of the plants described above: root, rhizome, stem, leaf, branch, bark, flower, seed (including seed coat, germ, albumen, hypocotyl, cotyledon, and the like), fruit (including pulp and pericarp), or a combination of two or more of these parts. The extract of the plant can be produced by extracting any of these parts
30 of the plants with a solvent.

The following parts can be mentioned as examples of preferred parts for producing the extract of the plant. Preferred examples of the extract of the plant in the present invention include extracts of the following parts
35 of the plant.

In the case of the plant belonging to the genus *Rosa* of the family Rosaceae, a flower, in particular, a petal is preferred. In the case of a grape, a seed and/or a skin is/are used, and a seed and a skin are preferably used. In
5 the cases of the plant belonging to the genus *Camellia* of the family Theaceae and the plant belonging to the genus *Hamamelis* of the family Hamamelidaceae, a leaf is preferred. In the case of the plant belonging to the genus *Filipendula* of the family Rosaceae, a flower is preferred. In the case
10 of the plant belonging to the genus *Plantago* of the family Plantaginaceae, a seed is preferred. In the case of the plant belonging to the genus *Mentha* of the family Lamiaceae, a whole plant is preferred.

Any of the above-mentioned parts of the plant may be
15 directly extracted, or may be crushed, cut, or dried before extraction. In the present invention, a plant extract may be directly extracted from any of the above plants, or may be extracted from a crushed, cut, or dried product of any of the above plants. An extract from a crushed, cut, or
20 dried product of any of the above plants is preferred.
[0037]

Any plant extraction method may be used to obtain a plant extract. An extraction method commonly used to extract plant components can be used. The extraction
25 method can be suitably selected, and extraction conditions are also not limited. For example, preferably, a plant extract is extracted from any of the above plants with a solvent (extraction solvent) at room temperature or under heating. In preparation of a plant extract, any of the
30 above plants as raw materials may be directly extracted, or may be crushed, cut, or dried before extraction.
[0038]

The extraction solvent used to prepare a plant extract may be suitably selected, and one commonly used to
35 extract plant components can be used. Examples of the

extraction solvent include water; C1-C5 monohydric alcohols such as methanol, ethanol, propanol, and butanol; C2-C5 polyhydric alcohols such as ethylene glycol, propylene glycol, 1,2-butylene glycol, 1,3-butylene glycol, 1,4-butylene glycol, and 2,3-butylene glycol; ketones such as acetone and methyl ethyl ketone; esters such as methyl acetate and ethyl acetate; open-chain or cyclic ethers such as tetrahydrofuran and diethyl ether; polyethers such as polyethylene glycol; and squalane. Any of these may be used alone, or a mixed solvent (mixture) of two or more thereof may be used. Among the C1-C5 monohydric alcohols, C1-C4 monohydric alcohols are preferred; C2-C4 monohydric alcohols are more preferred; and ethanol is still more preferred. Among the C2-C5 polyhydric alcohols, C2-C4 di- or trihydric alcohols are preferred; dihydric alcohols are more preferred; and 1,3-butylene glycol is still more preferred. Of these, the extraction solvent is preferably water, a C1-C5 monohydric alcohol, a C2-C5 polyhydric alcohol, or a mixed solvent of two or more thereof; more preferably water, a C2-C4 monohydric alcohol or an aqueous solution thereof, or a C2-C4 dihydric alcohol or an aqueous solution thereof; still more preferably water, ethanol, an aqueous solution of ethanol, 1,3-butylene glycol, or an aqueous solution of 1,3-butylene glycol; particularly preferably water, an aqueous solution of ethanol, or an aqueous solution of 1,3-butylene glycol. In one embodiment, the concentration of ethanol or 1,3-butylene glycol in an aqueous solution of ethanol or an aqueous solution of 1,3-butylene glycol, respectively, is preferably 10 to 98 vol%, more preferably 30 to 90 vol%, still more preferably 30 to 70 vol%. The solvent extracts can be suitably used as the plant extracts in the present invention.

[0039]

An acid or alkali may be added during extraction to adjust the pH of the extraction solvent. The extraction is

preferably followed by removal of plant residues (the plant or its parts after extraction) from the resulting liquid extract. The method of removing the plant residues from the liquid extract is not limited. For example, a known
5 separation means such as filtration or centrifugation can be used.

[0040]

For example, the following method can be used as an example of the plant extraction method. A plant is
10 directly finely crushed, or a dried product of a plant is finely crushed. Then, an extraction solvent in an amount 0.1 to 30 times that of the crushed product is added for extraction at normal pressure and room temperature preferably for 10 minutes to 15 days, more preferably 30
15 minutes to 10 days, still more preferably 1 hour to 7 days, or at a temperature near the boiling point of the extraction solvent preferably for about 10 minutes to 1 day (more preferably for 10 minutes to 2 hours), followed by filtration to obtain a filtrate. The extraction may be
20 performed under standing still or suitable stirring. The resulting liquid filtrate (liquid plant extract) may be directly used as a plant extract, or may be diluted, concentrated, dried, or the like, if necessary.

[0041]

25 In the present invention, a liquid plant extract obtained by extraction can be directly used as a plant extract. The liquid plant extract may be diluted, concentrated, or dried by a known method to provide a dilute solution, concentrate, or powder, or may be prepared
30 in the form of a paste, as long as the effects of the present invention are not impaired. Examples of the drying method include freeze drying and spray drying. In addition, the liquid plant extract or its concentrate, dried powder, or the like may be further purified by deodorizing,
35 decolorizing, or the like, if necessary, without impairing

the effects of the present invention. Such a purification method may be any usual means.

The plant extracts in the present invention encompass liquid extracts extracted with various solvents which were
5 obtained by the extraction method as described above, and diluted solutions, concentrates, and dried powders of such liquid extracts; and purified products thereof. The extracts may be diluted or dissolved in a solvent different from the extraction solvent.

10 The plant extracts are also commercially available, and commercial products can be used.

[0042]

The extract of a yeast belonging to the genus *Yarrowia* is preferably an extract of a cell or a cell
15 culture of a yeast belonging to the genus *Yarrowia*. Examples of the extract of a cell or a cell culture include those obtained by subjecting a cell or a cell culture (preferably a cell culture liquid) containing a cell to a fungal disruption treatment such as autolysis or enzymatic
20 decomposition to dissolve a yeast content into the culture medium or the like (cell disruption product), and those obtained by removing cell residues from the cell or the cell culture (cell disruption product) after the cell disruption treatment. Preferred is an extract obtained by
25 subjecting a cell or a cell culture (preferably a cell culture liquid) containing a cell to autolysis. The cell disruption product or a product obtained by removing cell residues from the cell disruption product may be subjected to sterilization such as heat treatment, if necessary. The
30 yeast extract may be one subjected to such sterilization. The extract of a yeast belonging to the genus *Yarrowia* may be in any form such as a paste, a suspension, a concentrate, a liquid, or a powder.

[0043]

35 In one embodiment, the extract of a plant belonging

to the genus *Rosa* of the family Rosaceae is preferably an extract of a rose (preferably its petals) in ethanol or in an aqueous solution of ethanol.

5 The extract of a grape seed and/or a grape skin is preferably an extract of a grape seed and/or a grape skin in ethanol or in an aqueous solution of ethanol.

10 The extract of a plant belonging to the genus *Camellia* of the family Theaceae is preferably an extract of tea plant (preferably its leaves) in ethanol or in an aqueous solution of ethanol.

15 The extract of a plant belonging to the genus *Hamamelis* of the family Hamamelidaceae is preferably an extract of American witch-hazel (preferably its leaves) in 1,3-butylene glycol or in an aqueous solution of 1,3-butylene glycol.

20 The extract of a plant belonging to the genus *Filipendula* of the family Rosaceae is preferably an extract of meadowsweet (preferably its flowers) in 1,3-butylene glycol or in an aqueous solution of 1,3-butylene glycol. The extract of a plant belonging to the genus *Plantago* of the family Plantaginaceae is preferably an extract of greater plantain (preferably its seeds) in ethanol or in an aqueous solution of ethanol.

25 The extract of a plant belonging to the genus *Mentha* of the family Lamiaceae is preferably an extract of peppermint (preferably a whole plant thereof) in ethanol, in an aqueous solution of ethanol, or in hot water.
[0044]

30 The compositions of the present invention may have any form. Examples include powders, granules, pastes, solids, and liquids, and any of which can be suitably selected. As long as the effects of the present invention are not impaired, other components may be added, in addition to the extract, to the compositions of the present
35 invention. The other components may be components that can

be used in products such as cosmetics, foods and beverages, and pharmaceutical and quasi-pharmaceutical products, which are described later.

5 The composition for suppressing a decrease in or
improving expression of type IV collagen and the
composition for suppressing a decrease in or improving skin
barrier function of the present invention may be provided
as an agent, for example, but it is not limited thereto.
The agent may be provided as a composition by itself or as
10 a composition containing the agent. In one embodiment, the
compositions of the present invention may be referred to as
agents for suppressing a decrease in or improving
expression of type IV collagen or agents for suppressing a
decrease in or improving skin barrier function.
15 [0045]

 The composition for suppressing a decrease in or
improving expression of type IV collagen of the first
aspect of the present invention is used to suppress a
decrease in expression of type IV collagen or improve the
20 expression in a subject, preferably to suppress a decrease
in expression of type IV collagen or improve the expression
in the skin of the subject. The compositions for
suppressing a decrease in or improving skin barrier
function of the second, third, and forth aspects of the
25 present invention are used to suppress a decrease in skin
barrier function or improve the function.

 The compositions of the present invention can be used
to prevent or ameliorate troubles caused by a decrease in
skin barrier function, a decrease in basement membrane
30 function, or a decrease in expression of type IV collagen,
for example. Examples of the troubles include dry skin,
itchy skin, rough skin, sensitive skin, and damaged skin.
In one embodiment, the compositions of the present
invention can be used to prevent or ameliorate dry skin,
35 itchy skin, rough skin, sensitive skin, damaged skin, or

the like by suppressing a decrease in or improving skin barrier function or by suppressing a decrease in or improving expression of type IV collagen. Prevention of troubles encompasses prevention of onset, delay of onset, and lower incidence. Amelioration of troubles encompasses alleviation of symptoms, good reversal of symptoms, and suppression of progression of symptoms.

[0046]

The compositions of the present invention can be used in various applications such as cosmetics, foods and beverages, and pharmaceutical and quasi-pharmaceutical products. The compositions of the present invention each may be a cosmetic, a food or beverage, or a pharmaceutical or quasi-pharmaceutical product by itself for suppressing a decrease in or improving expression of type IV collagen, or for suppressing a decrease in or improving skin barrier function; or may be a material, a preparation, or the like that is added to such a cosmetic, food or beverage, pharmaceutical or quasi-pharmaceutical product, or the like.

[0047]

The compositions of the present invention are each suitably used as a topical agent for skin. The topical agent for skin encompasses cosmetics and pharmaceutical and quasi-pharmaceutical products. Preferably, the topical agent for skin is a cosmetic.

The compositions of the present invention each can also be used as a pharmaceutical or quasi-pharmaceutical product, other than the topical agent for skin.

In another embodiment, the compositions of the present invention each can also be provided as a food or beverage. The following describes a case where the compositions of the present invention each are provided as a topical agent for skin such as a cosmetic or a pharmaceutical or quasi-pharmaceutical product, a food or beverage, or the like.

[0048]

When the compositions or the like of the present invention are each provided as a topical agent for skin, the dosage form and the like are not limited, and may be
5 provided in any form. Examples include solutions, emulsions, creams, gels, powders, aerosols, mists, capsules, and sheets. Preferably, the topical agent for skin is a cosmetic. The product form of the cosmetic is also not limited. Examples include skin care cosmetics such as face
10 wash, makeup remover, skin lotion, essence lotion, face pack, emulsion, cream, and sunscreen lotion; makeup cosmetics such as foundation, makeup base, lipstick, eyeshadow, eyeliner, mascara, eyebrow pencil, brush, and nail enamel; hair cosmetics such as shampoo, hair
15 conditioner, hair styling products, hair dyes, and hair growth products; cleansing agents such as soap and body wash; and bath salts.

[0049]

The above cosmetics may suitably contain one or more
20 cosmetically acceptable carriers, additives, and like other components, without impairing the effects of the present invention. Examples include water, alcohols, oils, surfactants, thickeners, metal soaps, gelling agents, powders, chelating agents, water-soluble polymers, film
25 forming agents, resins, inclusion compounds, antimicrobial agents, deodorants, salts, pH adjusting agents, ultraviolet light absorbers, extracts from microorganisms/plants/animals other than those mentioned above, keratolytic agents, enzymes, hormones, other
30 vitamins, humectants, antiseptics, anti-inflammatory agents, and perfumes. The cosmetics can be produced by a usual production method in which, for example, any of the extracts used as an active ingredient is mixed with one or more cosmetically acceptable components described above,
35 and the mixture is then processed into a desired form.

[0050]

When the topical agent for skin is provided as a pharmaceutical or quasi-pharmaceutical product, components such as pharmaceutically or quasi-pharmaceutically acceptable carriers and additives may be used, without impairing the effects of the present invention. Examples of such components include excipients, binders, disintegrants, lubricants, antioxidants, and colorants. One or more of these components can be used, if necessary.

10 [0051]

The compositions of the present invention each can also be provided as a pharmaceutical or quasi-pharmaceutical product, other than the topical agent for skin described above. Such a pharmaceutical or quasi-pharmaceutical product may be administered orally or parenterally. The pharmaceutical or quasi-pharmaceutical product can be provided in the form of a formulation for oral administration (agent for internal use) or a formulation for parenteral administration. Examples of the dosage form of the formulation for oral administration include liquids, tablets, powders, fine granules, granules, sugar-coated tablets, capsules, suspensions, emulsions, and chewable tablets. Examples of the dosage form of the formulation for parenteral administration include injections and infusions. In such a pharmaceutical or quasi-pharmaceutical product, components such as pharmaceutically or quasi-pharmaceutically acceptable carriers and additives may be used. Examples of such components include excipients, binders, disintegrants, lubricants, antioxidants, colorants, and taste masking agents. One or more of these components can be used, if necessary. The pharmaceutical or quasi-pharmaceutical product can be produced by a usual production method in which, for example, any of the extracts used as an active ingredient is mixed with one or more pharmaceutically or

15
20
25
30
35

quasi-pharmaceutically acceptable components, and the mixture is then processed into a desired form.

[0052]

When the compositions of the present invention each
5 are provided as a food or beverage, the food or beverage is not limited, and examples include general foods and beverages, health foods, foods with function claims, and foods for specified health uses. The form of the food or beverage is also not limited. The health foods, foods with
10 function claims, and foods for specified health uses can be provided in the form of various formulations such as liquids, tablets, powders, fine granules, granules, sugar-coated tablets, capsules, suspensions, emulsions, chewable tablets, and liquid foods.

15 [0053]

These foods and beverages may contain food- or beverage acceptable ingredients, such as other food or beverage materials and additives for foods and beverages, without impairing the effects of the present invention.
20 Such foods and beverages can be produced by a usual production method. For example, the method may only require adding any of the extracts used as an active ingredient in the present invention to food or beverage materials or the like in the production of foods and
25 beverages.

[0054]

When the compositions of the present invention each are a topical agent for skin, a pharmaceutical or quasi-pharmaceutical product other than the topical agent for
30 skin, or a food or beverage, the amount of the extract used as an active ingredient (in terms of dry matter) in the composition is preferably 0.0000001 to 100 wt%, more preferably 0.000001 to 100 wt%, still more preferably 0.00001 to 10 wt%. The amount is the total amount when the
35 composition contains two or more extracts.

[0055]

The amount of each of the compositions of the present invention to be used is not limited, as long as the amount achieves the effect of suppressing a decrease in or
5 improving skin barrier function or the effect of suppressing a decrease in or improving expression of type IV collagen (effective dose), and can be suitably set according to the subject's conditions, weight, sex, age, or other factors. Preferably, the amount of each of the
10 compositions of the present invention is determined such that the amount of the extract (in terms of dry matter) as an active ingredient in a topical agent for skin such as a cosmetic is, for example 0.01 to 500 mg per adult (60 kg) per day. Preferably, the dose of the extract (in terms of
15 dry matter) when orally administered as a pharmaceutical or quasi-pharmaceutical product is, for example, 0.01 to 500 mg per adult (60 kg) per day. Preferably, the intake of the extract (in terms of dry matter) as a food or beverage is, for example, 0.01 to 500 mg per adult (60 kg) per day.
20 The above amount of the extract can be applied, fed, or administered at once or in several portions. The amount is the total amount when the composition contains two or more extracts. The timing at which a topical agent for skin containing the extract is applied to the skin and the
25 timing at which a food, beverage, pharmaceutical product, or quasi-pharmaceutical product containing the plant extract is fed (administered) are not limited.

[0056]

Subjects to which the compositions of the present
30 invention are applicable (subject for administration) are not limited. For example, the compositions are applicable to a human or non-human mammal, preferably a human. Examples of subjects include those who want or need to suppress a decrease in or improve skin barrier function and
35 those who want or need to suppress a decrease in or improve

expression of type IV collagen. Examples of such subjects include those who realize their skin troubles such as dry skin, itchy skin, rough skin, sensitive skin, or damaged skin. The compositions of the present invention each can
5 be fed or administered by various methods known per se, in accordance with the form, dosage form, or the like thereof. In one embodiment, the compositions of the present invention each are preferably applied to the skin.

[0057]

10 Any of the extracts used as an active ingredient of the compositions of the present invention can be used for suppressing a decrease in expression of type IV collagen of a subject or improving the expression. Any of the extracts can be used for suppressing a decrease in skin barrier
15 function of a subject or improving the skin barrier function, preferably for suppressing a decrease in skin barrier function or improving the skin barrier function by suppressing a decrease in or improving expression of type IV collagen.

20 [0058]

The present invention also encompasses the following uses and methods.

Use of an extract for suppressing a decrease in skin barrier function or improving the skin barrier function by
25 suppressing a decrease in or improving expression of type IV collagen, the extract including at least one selected from the group consisting of an extract of a plant belonging to the genus *Rosa* of the family Rosaceae, an extract of a grape seed and/or a grape skin, an extract of
30 a yeast belonging to the genus *Yarrowia*, an extract of a plant belonging to the genus *Camellia* of the family Theaceae, an extract of a plant belonging to the genus *Filipendula* of the family Rosaceae, and an extract of a plant belonging to the genus *Mentha* of the family Lamiaceae.

35 A method of suppressing a decrease in skin barrier

function or improving skin barrier function by suppressing a decrease in or improving expression of type IV collagen, the method including administering at least one extract selected from the group consisting of an extract of a plant
5 belonging to the genus *Rosa* of the family Rosaceae, an extract of a grape seed and/or a grape skin, an extract of a yeast belonging to the genus *Yarrowia*, an extract of a plant belonging to the genus *Camellia* of the family Theaceae, an extract of a plant belonging to the genus
10 *Filipendula* of the family Rosaceae, and an extract of a plant belonging to the genus *Mentha* of the family Lamiaceae.
[0059]

Use of an extract for suppressing a decrease in skin barrier function or improving skin barrier function, the
15 extract including an extract of a plant belonging to the genus *Hamamelis* of the family Hamamelidaceae and/or an extract of a plant belonging to the genus *Plantago* of the family Plantaginaceae.

A method of suppressing a decrease in skin barrier
20 function or improving skin barrier function, the method including administering an extract of a plant belonging to the genus *Hamamelis* of the family Hamamelidaceae and/or an extract of a plant belonging to the genus *Plantago* of the family Plantaginaceae.
25 [0060]

Use of an extract for suppressing a decrease in expression of type IV collagen or improving the expression, the extract including at least one selected from the group consisting of an extract of a plant belonging to the genus
30 *Rosa* of the family Rosaceae, an extract of a grape seed and/or a grape skin, an extract of a yeast belonging to the genus *Yarrowia*, an extract of a plant belonging to the genus *Camellia* of the family Theaceae, an extract of a plant belonging to the genus *Hamamelis* of the family
35 Hamamelidaceae, an extract of a plant belonging to the

genus *Filipendula* of the family Rosaceae, an extract of a plant belonging to the genus *Plantago* of the family Plantaginaceae, and an extract of a plant belonging to the genus *Mentha* of the family Lamiaceae.

5 A method of suppressing expression of type IV collagen or improving the expression, the method including administering the at least one extract.
[0061]

10 The extract is administered (applied) preferably to the skin and can be used for suppressing a decrease in skin barrier function or improving the function, for suppressing a decrease in expression of type IV collagen in the skin or improving the expression, or for suppressing a decrease in basement membrane function or improving the function. In
15 one embodiment, the extract can be used to prevent or ameliorate troubles caused by a decrease in skin barrier function, a decrease in basement membrane function, or a decrease in expression of type IV collagen. The extract can be used for preventing or ameliorating troubles such as
20 dry skin, itchy skin, rough skin, sensitive skin, or damaged skin by suppressing a decrease in or improving skin barrier function, or by suppressing a decrease in or improving expression of type IV collagen in the skin.
[0062]

25 In the uses and methods, the extracts, subjects for administration, the amount of the extract, preferred embodiments thereof, and the like are the same as described above for the compositions of the present invention. Each extract may be directly used or may be used in combination
30 with other components. The compositions of the present invention may be used. Each extract can be used in the form of the topical agent for skin, food or beverage, or the like described above.

 Each use may be therapeutic or non-therapeutic. Each
35 method may be therapeutic or non-therapeutic. The "non-

therapeutic" is a concept that does not include medical activities, i.e., a concept that does not include methods of surgery, therapy, or diagnosis of humans.

[0063]

5 In other aspects, the present invention provides use of any of the extracts to produce a composition for suppressing a decrease in or improving skin barrier function; and use of any of the extracts to produce a composition for suppressing a decrease in or improving
10 expression of type IV collagen. The extracts, preferred embodiments thereof, and the like are the same as described above for the compositions of the present invention.

 In still other aspects, the present invention provides use of an agent for suppressing a decrease in or
15 improving basement membrane function for suppressing a decrease in skin barrier function or improving the skin barrier function; and a method of suppressing a decrease in skin barrier function or improving the skin barrier function, including administering an agent for suppressing
20 a decrease in or improving basement membrane function.

 The agent for suppressing a decrease in or improving basement membrane function, preferred embodiments thereof, and the like are the same as described above.

[0064]

25 The present invention also encompasses a method of screening for a substance having an effect of suppressing a decrease in or improving skin barrier function. Next, the screening method of the present invention is described.

 The method of screening for a substance having an
30 effect of suppressing a decrease in or improving skin barrier function of the present invention includes: a step of culturing in vitro human epidermal keratinocytes in a medium containing a test substance and separately in a control medium not containing the test substance; and a
35 step of comparing the expression level of type IV collagen

between the keratinocytes cultured in the medium containing a test substance and the keratinocytes as a control cultured in the control medium, wherein the test substance is selected as a substance having an effect of suppressing a decrease in or improving skin barrier function when the expression level of type IV collagen in the keratinocytes cultured in the medium containing the test substance is higher than the expression level of type IV collagen in the keratinocytes as a control.

10 [0065]

The screening method of the present invention includes culturing in vitro human epidermal keratinocytes in a medium containing a test substance and separately in a control medium not containing the test substance. The human epidermal keratinocytes are commercially available, and a commercial product can be used.

The test substance is not limited. Examples thereof include liquid plant extracts, cell extracts, supernatants of cell cultures, fermentation products, proteins, peptides, vitamins, and synthetic compounds. These may be known substances or novel substances.

[0066]

The step of culturing in vitro human epidermal keratinocytes in a medium containing a test substance and separately in a control medium not containing the test substance is also referred to as a culturing step. The step of comparing the expression level of type IV collagen between the keratinocytes (also referred to as test keratinocytes) cultured in the medium containing the test substance and the keratinocytes as a control cultured in the control medium is also referred to as a type IV collagen expression level comparing step.

[0067]

The conditions for culturing human epidermal keratinocytes in the culturing step are not limited, and

known conditions may be employed. The medium containing a test substance can be prepared by mixing a test substance in a medium. The medium used may be one used for culturing of human epidermal keratinocytes, and a commercial product
5 may be used. Examples of the medium include HuMedia-KB2 (available from Kurabo Industries ltd.) and DMEM. To the medium may be added additives such as insulin, human EGF, hydrocortisone, a blood serum, and an antibacterial agent. The culture time is not limited, and may be suitably set
10 according to culture conditions and the like. The control medium used may be the same as the medium containing a test substance except that the test substance is not contained. For example, human epidermal keratinocytes may be cultured in the medium containing a test substance and separately in
15 the control medium preferably for 1 to 72 hours, more preferably 3 to 48 hours.

In the culturing step, a stress may be imposed such as irradiation with UV or an oxidative stress. For example, culturing under stress such as irradiation with UV or an
20 oxidative stress enables screening for a substance which is more effective for suppressing a decrease in skin barrier function due to the stress or improving the skin barrier function under stress.

[0068]

25 The culturing step is followed by the type IV collagen expression level comparing step. After the culturing, the expression level of type IV collagen is compared between the keratinocytes cultured in the medium containing a test substance and the keratinocytes as a
30 control cultured in the control medium. When the expression level of type IV collagen in the keratinocytes cultured in the medium containing a test substance is higher than the expression level of type IV collagen in the keratinocytes as a control, the test substance is selected
35 as a substance having an effect of suppressing a decrease

in or improving skin barrier function.

[0069]

The expression level of type IV collagen can be determined by measuring the amount of mRNA encoding type IV collagen or the amount of type IV collagen protein. The
5 amount of mRNA or protein can be measured by a known method.

The amount of mRNA encoding type IV collagen can be measured by a technique such as quantitative PCR, Northern blotting, microarray analysis, or live imaging using a
10 fluorescent probe. The amount of type IV collagen protein can be measured by a technique such as immunochemical assay or mass analysis. Examples of the immunochemical assay include Enzyme Linked Immunosorbent Assay (ELISA) and Western blotting. The amount of protein can be also
15 measured using a commercial ELISA kit (available from MyBioSource, Inc.). The base sequence and amino acid sequence (ORF) of human type IV collagen are known. The base sequence (mRNA) is registered with Accession No. AH002741 in Genbank (public database). A person skilled in
20 the art can easily design and synthesize a primer for measuring the amount of mRNA encoding type IV collagen, as well as amplification of DNA.

[0070]

As described above, suppression of a decrease in
25 expression of type IV collagen or improvement of the expression can suppress a decrease in or improve skin barrier function. Therefore, when the expression level of type IV collagen in the test keratinocytes is higher than the expression level of type IV collagen in the
30 keratinocytes as a control, the test substance can be determined as a substance having an effect of suppressing a decrease in or improving skin barrier function. The screening method enables screening for a substance having an effect of suppressing a decrease in or improving skin
35 barrier function.

EXAMPLES

[0071]

5 The following describes the present invention with reference to examples, but the present invention is not limited to these examples.

[0072]

<Preparation Example 1>

10 Plant-derived extracts were prepared. The plants and their parts used in the extraction are listed below.

- (1) Rose (*Rosa hybrida*, "SUNTORY blue rose APPLAUSE®", Suntory Flowers Ltd.): petal
- (2) Grape (*Vitis* spp.) (Cabernet Sauvignon): seed and skin
- (3) Tea plant (*Camellia sinensis*): leaf
- 15 (4) American witch-hazel (*Hamamelis virginiana*): leaf
- (5) Meadowsweet (*Filipendula ulmaria*): flower
- (6) Greater plantain (*Plantago major*): seed
- (7) Peppermint (*Mentha x piperita*): whole plant

20 The rose ("SUNTORY blue rose APPLAUSE") is a blue-colored rose containing a delphinidin-type anthocyanin, rosacyanin A1, rosacyanin A2, and rosacyanin B, as well as rosadelphin A1, rosadelphin A2, and rosadelphin B, in its petals.

[0073]

25 Crushed products of the plants (1) to (7) were each immersed in a solvent for extraction. More specifically, crushed products of the plants (1), (2), (3), (6), and (7) were each immersed in a 30 to 90 vol% aqueous solution of ethanol in an amount of 10 times the amount of the crushed
30 product, and extracted over 10 minutes to 7 days with stirring once a day at room temperature. Thus, liquid extracts were obtained. The plants (4) and (5) were each extracted by the above method except that the aqueous solution of ethanol was changed to an aqueous solution of
35 1,3-butylene glycol.

[0074]

The obtained liquid extracts were subjected to filtering for removal of plant residues, and the resulting filtrates were obtained as liquid plant extracts.

5 The obtained liquid plant extracts were each concentrated in an evaporator, and then freeze-dried. Thus, the extract of each plant was obtained in the form of powder. The powdery plant extracts (rose petal extract, grape seed and skin extract, tea plant leaf extract, 10 American witch-hazel leaf extract, meadowsweet flower extract, greater plantain seed extract, and peppermint extract) were used as extract samples in the following evaluation.

[0075]

15 <Preparation Example 2>

Yarrowia lipolytica was cultured, followed by autolysis and subsequent heating for disinfection and sterilization. Thus, a powdery *Yarrowia lipolytica* extract was obtained.

20 In the following examples, the above powder was used as an extract sample of *Yarrowia lipolytica*.

[0076]

<Example 1> Influence of overexpression of type IV collagen on skin barrier under inflammatory stimulus

25 A plasmid incorporating COL4A1 (RefSeq ID: NM_001845.6) downstream of a CMV promoter was created (hereafter, referred to as COL4A1 plasmid). According to the recommended protocol, the COL4A1 plasmid and Lipofectamine 3000 Reagent (available from Thermo Fisher Scientific) were diluted with Opti-MEM® I Reduced Serum Media (available from Thermo Fisher Scientific) (hereafter, 30 referred to as Opti-MEM) to give two solutions (hereafter, referred to as Opti-MEM solutions) different in plasmid concentration (plasmid concentration: 5 µg/mL or 20 µg/mL). 35 As a control, a solution containing Opti-MEM instead of the

plasmid was also produced.

[0077]

Using HuMedia-KG2 (hereafter, referred to as a recommended medium) (available from Kurabo Industries ltd.),
5 normal adult human epidermal keratinocytes (available from Kurabo Industries ltd.) were seeded to Cell Culture Insert for 24-well plates (available from Millipore Corporation) at a concentration of 3×10^4 cells/200 μ L/well. Immediately after the seeding, 10 μ L of either of the Opti-
10 MEM solutions were added. To the 24-well plate (available from AGC Techno Glass Co., Ltd.) was added 900 μ L of the recommended medium. After 30 minutes, a hydrogen peroxide solution (Nacalai Tesque, Inc.) was added to some of the groups to a final concentration of 100 μ M (H_2O_2 treatment).
15 After four hours from seeding, the medium was changed with the recommended medium. After 24 hours from seeding, the medium was changed with the recommended medium having a Ca^{2+} concentration increased to 1.41 mM by addition of $CaCl_2$ (hereafter, referred to as an irregular recommended medium).
20 The medium was changed with the irregular recommended medium every several days.

[0078]

The transepithelial electrical resistance (TEER ($\Omega \cdot cm^2$)) was evaluated using Millicell ERS-2 (available
25 from Merck KGaA) after 96, 120, and 144 hours from seeding. The cells were lysed using isogen (available from Nippon Gene Co., Ltd.) after 144 hours from seeding, and then mRNA was extracted. Subsequently, cDNA was synthesized using High-Capacity cDNA Reverse Transcription Kit and RNase
30 Inhibitor (both available from Thermo Fisher Scientific), followed by quantitative PCR using TaqMan Fast Universal PCR Master Mix (available from Thermo Fisher Scientific) and a primer. Thus, the expression level of human type IV collagen A1 (COL4A1) was evaluated. As an endogenous
35 control, Eukaryotic 18S rRNA was used.

[0079]

The primer (COL4A1) for measuring the COL4A1 expression level and the primer (Eukaryotic 18S rRNA) for quantifying the endogenous control were #Hs00266237_m1 and #Hs99999901_s1 (both available from Thermo Fisher Scientific), respectively.

[0080]

Tables 1 and 2 show the results. Table 1 shows the COL4A1 gene expression level relative to the COL4A1 expression level of a plasmid-free and H₂O₂-untreated group (H₂O₂ (-), plasmid (-)) which is set to 1. In Tables 1 and 2, "H₂O₂ (+)" refers to a H₂O₂-treated group. "Plasmid (-)" means that the COL4A1 plasmid was not added and "Plasmid (+)" means that the COL4A1 plasmid was added. The symbol "*" indicates a significant difference (p < 0.05) (Dunnett's test (vs a plasmid-free and H₂O₂-treated group)). In response to H₂O₂ stimulation, the COL4A1 expression level was lowered. Introduction of the COL4A1 plasmid was confirmed to have a significant and dose-dependent effect of suppressing a decrease in or improving the expression on the H₂O₂-stimulated groups (*: p < 0.05).

[0081]

[Table 1]

	H ₂ O ₂ (-), Plasmid (-)	H ₂ O ₂ (+), Plasmid (-)	H ₂ O ₂ (+), Plasmid (+)	H ₂ O ₂ (+), Plasmid (+)
H ₂ O ₂	-	H ₂ O ₂ 100 µM	H ₂ O ₂ 100 µM	H ₂ O ₂ 100 µM
Plasmid	-	-	Plasmid 0.05 µg	Plasmid 0.20 µg
COL4A1 expression level	1.00	0.61	25.70 *	86.39 *

25 [0082]

Table 2 shows the TEER values after 144 hours from seeding. The symbol "*" indicates a significant difference (p < 0.05) (Dunnett's test (vs a plasmid-free and H₂O₂-treated group)). In response to H₂O₂ stimulation, the TEER was significantly lowered. Introduction of the COL4A1 plasmid was confirmed to have a dose-dependent and significant (in the high-dose group) effect of improving TEER on the H₂O₂-stimulated groups (*: p < 0.05).

[0083]

[Table 2]

	H ₂ O ₂ (-), Plasmid (-)	H ₂ O ₂ (+), Plasmid (-)	H ₂ O ₂ (+), Plasmid (+)	H ₂ O ₂ (+), Plasmid (+)
H ₂ O ₂	-	H ₂ O ₂ 100 μ M	H ₂ O ₂ 100 μ M	H ₂ O ₂ 100 μ M
Plasmid	-	-	Plasmid 0.05 μ g	Plasmid 0.20 μ g
TEER (Ω -cm ²)	51.00 *	38.33	44.19	50.06 *

[0084]

- 5 <Examples 2 to 9> Evaluation on effect of suppressing a decrease in or improving type IV collagen gene expression in extract sample

Using the recommended medium, a normal adult human epidermal keratinocyte (available from Kurabo Industries ltd.) was seeded to a 12-well plate (available from AGC Techno Glass Co., Ltd.) at a concentration of 5×10^4 cells/mL/well and cultured for 48 hours. The medium was changed with the recommended medium containing an extract sample to start sample treatment. After 30 minutes from the start of sample treatment, a hydrogen peroxide solution (available from Nacalai Tesque, Inc.) was added to a final concentration of 100 μ M. After three hours from the start of hydrogen peroxide solution treatment, the medium was changed with the recommended medium not containing the extract sample. After 48 hours from the start of sample treatment, the cells were lysed in Buffer RLT (containing 1% 2-mercapto ethanol, available from Qiagen N. V.) and collected, and mRNA was extracted using RNeasy Mini Kit and RNase-Free DNase Set (available from Qiagen N. V.). Then, synthesis of cDNA and quantitative PCR were performed and the COL4A1 expression level was evaluated by the same methods as in Example 1.

[0085]

As the control, cells were cultured in the same manner except that dimethyl sulfoxide (DMSO) was added, instead of the extract sample, to a final concentration of 0.1%. To the cultured cells was added a hydrogen peroxide solution, and the COL4A1 expression level was evaluated by

the same methods.

[0086]

The extract sample used in each of Examples 2 to 9 was the rose petal extract, the grape seed and skin extract, the tea plant leaf extract, the American witch-hazel leaf extract, the meadowsweet flower extract, the greater plantain seed extract, the *Yarrowia lipolytica* extract, or the peppermint extract prepared in Preparation Example 1 or 2. The extract sample was dissolved in ultra-pure water or DMSO before addition to the medium. The concentration of the extract sample in the medium was set to 5 to 20 µg/mL. In the case where the extract sample was dissolved in ultra-pure water, DMSO was separately added. Thus, the recommended medium containing any of the extract samples was set to have a final concentration of DMSO of 0.1%.

[0087]

Table 3 shows the results of Examples 2 to 9 (average of N = 3 to 4). The results in Table 3 are relative values (%) of the COL4A1 expression level in the cells treated with the extract sample to the COL4A1 expression level of the control which is set to 100%. The symbol "*" indicates a significant difference ($p < 0.05$) to the control (Student's t-test). Table 3 shows the results of the cases where the COL4A1 expression level was highest within the ranges of the extract sample (test substance) concentration of 5 to 20 µg/mL. The rose petal extract, the grape seed and skin extract, the tea plant leaf extract, the American witch-hazel leaf extract, the meadowsweet flower extract, the greater plantain seed extract, the *Yarrowia lipolytica* extract, and the peppermint extract were each confirmed to have a significant effect of suppressing a decrease in COL4A1 expression or improving the expression relative to the control (*: $p < 0.05$).

[0088]

[Table 3]

	Sample	COL4A1 expression level	Significant difference
Example 2	Rose petal extract	277%	*
Example 3	Grape seed and skin extract	248%	*
Example 4	Tea plant leaf extract	155%	*
Example 5	American witch-hazel leaf extract	151%	*
Example 6	Meadowsweet flower extract	271%	*
Example 7	Greater plantain seed extract	142%	*
Example 8	<i>Yarrowia lipolytica</i> extract	147%	*
Example 9	Peppermint extract	178%	*

[0089]

<Examples 10 to 15> Evaluation on effect of suppressing a decrease in or improving skin barrier function of extract sample

Using the recommended medium containing an extract sample, a normal adult human epidermal keratinocyte was seeded to Millicell Cell Culture Insert at a concentration of 3×10^4 cells/200 μ L/well. After 30 minutes from seeding, a hydrogen peroxide solution was added to a final concentration of 100 μ M. After four hours from seeding, the medium was changed with the recommended medium not containing the extract sample. After 24 hours from seeding, the medium was changed with the irregular recommended medium. Then, the transepithelial electrical resistance (TEER) was evaluated by the same method as in Example 1.

[0090]

As the control, cells were cultured by the same method except that the recommended medium to which DMSO was added to a final concentration of 0.1% was used instead of the recommended medium containing the extract sample. To the cells was added a hydrogen peroxide solution, and the transepithelial electrical resistance was evaluated by the same methods.

[0091]

The extract sample used in each of Examples 10 to 15 was the extract shown in Table 4 prepared in Preparation Example 1 or 2. The extract sample was dissolved in ultra-pure water or DMSO before addition to the medium. The

concentration of the extract sample in the medium was set to 5 to 20 µg/mL. In the case where the extract sample was dissolved in ultra-pure water, DMSO was separately added. Thus, the recommended medium containing any of the extract samples was set to have a final concentration of DMSO of 0.1%.

[0092]

Table 4 shows the results (average of N = 4 to 6). The results in Table 4 are relative values (%) of TEER of the cells treated with the extract sample to the TEER of the control which is set to 100%. Table 4 shows the results of the cases where the TEER value was highest within the ranges of the concentration of the extract sample (test substance) of 5 to 20 µg/mL and the measuring time of 96 to 144 hours after seeding. Six extracts were confirmed to have an effect of suppressing a decrease in or improving TEER. The grape seed and skin extract, the tea plant leaf extract, the American witch-hazel leaf extract, the meadowsweet flower extract, and the *Yarrowia lipolytica* extract were confirmed to have a significant difference relative to the control (*: $p < 0.05$) (Student's t-test).

[0093]

[Table 4]

	Sample	TEER	Significant difference
Example 10	Rose petal extract	117%	
Example 11	Grape seed and skin extract	119%	*
Example 12	Tea plant leaf extract	114%	*
Example 13	American witch-hazel leaf extract	123%	*
Example 14	Meadowsweet flower extract	135%	*
Example 15	<i>Yarrowia lipolytica</i> extract	117%	*

25 [0094]

The above plant extracts and the *Yarrowia lipolytica* extract were found to have an effect of suppressing a decrease in skin barrier function or improving the function.

CLAIMS

Claim 1. A composition for suppressing a decrease in or improving skin barrier function by suppressing a
5 decrease in or improving expression of type IV collagen,
the composition comprising, as an active ingredient:

at least one extract selected from the group
consisting of an extract of a plant belonging to the genus
Rosa of the family Rosaceae, an extract of a grape seed
10 and/or a grape skin, an extract of a yeast belonging to the
genus *Yarrowia*, an extract of a plant belonging to the
genus *Camellia* of the family Theaceae, an extract of a
plant belonging to the genus *Filipendula* of the family
Rosaceae, and an extract of a plant belonging to the genus
15 *Mentha* of the family Lamiaceae.

Claim 2. The composition for suppressing a decrease
in or improving skin barrier function according to claim 1,
wherein the plant belonging to the genus *Rosa* of the
20 family Rosaceae is a rose,
the yeast belonging to the genus *Yarrowia* is *Yarrowia*
lipolytica,
the plant belonging to the genus *Camellia* of the
family Theaceae is tea plant,
25 the plant belonging to the genus *Filipendula* of the
family Rosaceae is meadowsweet, and
the plant belonging to the genus *Mentha* of the family
Lamiaceae is peppermint.

30 Claim 3. The composition for suppressing a decrease
in or improving skin barrier function according to claim 1
or 2,
wherein the plant belonging to the genus *Rosa* of the
family Rosaceae is a rose petal containing at least one
35 compound selected from the group consisting of a

delphinidin-type anthocyanin, a rosacyanin compound, and a rosadelphin compound,

the plant belonging to the genus *Camellia* of the family Theaceae is a tea plant leaf,

5 the plant belonging to the genus *Filipendula* of the family Rosaceae is a meadowsweet flower, and

the plant belonging to the genus *Mentha* of the family Lamiaceae is a whole plant of peppermint.

10 Claim 4. A composition for suppressing a decrease in or improving skin barrier function, the composition comprising, as an active ingredient:

an extract of a plant belonging to the genus *Hamamelis* of the family Hamamelidaceae and/or an extract of
15 a plant belonging to the genus *Plantago* of the family Plantaginaceae.

Claim 5. The composition for suppressing a decrease in or improving skin barrier function according to claim 4,
20 wherein the plant belonging to the genus *Hamamelis* of the family Hamamelidaceae is American witch-hazel and the plant belonging to the genus *Plantago* of the family Plantaginaceae is greater plantain.

25 Claim 6. The composition for suppressing a decrease in or improving skin barrier function according to claim 4 or 5,

wherein the plant belonging to the genus *Hamamelis* of the family Hamamelidaceae is an American witch-hazel leaf
30 and

the plant belonging to the genus *Plantago* of the family Plantaginaceae is a greater plantain seed.

Claim 7. The composition for suppressing a decrease
35 in or improving skin barrier function according to any one

of claims 4 to 6,

wherein the composition suppresses a decrease in skin barrier function or improves skin barrier function by suppressing a decrease in or improving basement membrane function.

Claim 8. The composition for suppressing a decrease in or improving skin barrier function according to claim 7, wherein the composition suppresses a decrease in or improving basement membrane function by suppressing a decrease in or improving expression of type IV collagen.

Claim 9. A composition for suppressing a decrease in or improving skin barrier function, the composition comprising, as an active ingredient:

an agent for suppressing a decrease in or improving basement membrane function.

Claim 10. The composition for suppressing a decrease in or improving skin barrier function according to claim 9, wherein the agent for suppressing a decrease in or improving basement membrane function suppresses a decrease in or improving basement membrane function by suppressing a decrease in or improving expression of type IV collagen.

Claim 11. A composition for suppressing a decrease in or improving expression of type IV collagen, the composition comprising, as an active ingredient:

at least one extract selected from the group consisting of an extract of a plant belonging to the genus *Rosa* of the family Rosaceae, an extract of a grape seed and/or a grape skin, an extract of a yeast belonging to the genus *Yarrowia*, an extract of a plant belonging to the genus *Camellia* of the family Theaceae, an extract of a plant belonging to the genus *Hamamelis* of the family

Hamamelidaceae, an extract of a plant belonging to the
genus *Filipendula* of the family Rosaceae, an extract of a
plant belonging to the genus *Plantago* of the family
Plantaginaceae, and an extract of a plant belonging to the
5 genus *Mentha* of the family Lamiaceae.

Claim 12. The composition for suppressing a decrease
in or improving expression of type IV collagen according to
claim 11,

10 wherein the plant belonging to the genus *Rosa* of the
family Rosaceae is a rose,
 the yeast belonging to the genus *Yarrowia* is *Yarrowia*
lipolytica,
 the plant belonging to the genus *Camellia* of the
15 family Theaceae is tea plant,
 the plant belonging to the genus *Hamamelis* of the
family Hamamelidaceae is American witch-hazel,
 the plant belonging to the genus *Filipendula* of the
family Rosaceae is meadowsweet,
20 the plant belonging to the genus *Plantago* of the
family Plantaginaceae is greater plantain, and
 the plant belonging to the genus *Mentha* of the family
Lamiaceae is peppermint.

25 Claim 13. The composition for suppressing a decrease
in or improving expression of type IV collagen according to
claim 11 or 12,

 wherein the plant belonging to the genus *Rosa* of the
family Rosaceae is a rose petal containing at least one
30 compound selected from the group consisting of a
delphinidin-type anthocyanin, a rosacyanin compound, and a
rosadelphin compound,
 the plant belonging to the genus *Camellia* of the
family Theaceae is a tea plant leaf,
35 the plant belonging to the genus *Hamamelis* of the

family Hamamelidaceae is an American witch-hazel leaf,
the plant belonging to the genus *Filipendula* of the
family Rosaceae is a meadowsweet flower,
the plant belonging to the genus *Plantago* of the
5 family Plantaginaceae is a greater plantain seed, and
the plant belonging to the genus *Mentha* of the family
Lamiaceae is a whole plant of peppermint.

Claim 14. The composition according to any one of
10 claims 1 to 13,
wherein the composition is a topical agent for skin.

Claim 15. The composition according to any one of
claims 1 to 14,
15 wherein the composition is a cosmetic.

Claim 16. Use of an extract for suppressing a
decrease in skin barrier function or improving the skin
barrier function by suppressing a decrease in or improving
20 expression of type IV collagen,
the extract comprising at least one selected from the
group consisting of an extract of a plant belonging to the
genus *Rosa* of the family Rosaceae, an extract of a grape
seed and/or a grape skin, an extract of a yeast belonging
25 to the genus *Yarrowia*, an extract of a plant belonging to
the genus *Camellia* of the family Theaceae, an extract of a
plant belonging to the genus *Filipendula* of the family
Rosaceae, and an extract of a plant belonging to the genus
Mentha of the family Lamiaceae.

30
Claim 17. Use of an extract for suppressing a
decrease in skin barrier function or improving the skin
barrier function,
the extract comprising an extract of a plant
35 belonging to the genus *Hamamelis* of the family

Hamamelidaceae and/or an extract of a plant belonging to the genus *Plantago* of the family Plantaginaceae.

Claim 18. Use of an extract for suppressing a
5 decrease in expression of type IV collagen or improving the expression,

the extract comprising at least one selected from the group consisting of an extract of a plant belonging to the genus *Rosa* of the family Rosaceae, an extract of a grape
10 seed and/or a grape skin, an extract of a yeast belonging to the genus *Yarrowia*, an extract of a plant belonging to the genus *Camellia* of the family Theaceae, an extract of a plant belonging to the genus *Hamamelis* of the family Hamamelidaceae, an extract of a plant belonging to the
15 genus *Filipendula* of the family Rosaceae, an extract of a plant belonging to the genus *Plantago* of the family Plantaginaceae, and an extract of a plant belonging to the genus *Mentha* of the family Lamiaceae.

20 Claim 19. A method of suppressing a decrease in skin barrier function or improving skin barrier function by suppressing a decrease in or improving expression of type IV collagen, the method comprising

administering at least one extract selected from the
25 group consisting of an extract of a plant belonging to the genus *Rosa* of the family Rosaceae, an extract of a grape seed and/or a grape skin, an extract of a yeast belonging to the genus *Yarrowia*, an extract of a plant belonging to the genus *Camellia* of the family Theaceae, an extract of a
30 plant belonging to the genus *Filipendula* of the family Rosaceae, and an extract of a plant belonging to the genus *Mentha* of the family Lamiaceae.

Claim 20. A method of suppressing a decrease in skin
35 barrier function or improving skin barrier function, the

method comprising

administering an extract of a plant belonging to the genus *Hamamelis* of the family Hamamelidaceae and/or an extract of a plant belonging to the genus *Plantago* of the family Plantaginaceae.

Claim 21. A method of suppressing a decrease in expression of type IV collagen or improving the expression, the method comprising

administering at least one extract selected from the group consisting of an extract of a plant belonging to the genus *Rosa* of the family Rosaceae, an extract of a grape seed and/or a grape skin, an extract of a yeast belonging to the genus *Yarrowia*, an extract of a plant belonging to the genus *Camellia* of the family Theaceae, an extract of a plant belonging to the genus *Hamamelis* of the family Hamamelidaceae, an extract of a plant belonging to the genus *Filipendula* of the family Rosaceae, an extract of a plant belonging to the genus *Plantago* of the family Plantaginaceae, and an extract of a plant belonging to the genus *Mentha* of the family Lamiaceae.

Claim 22. A method of screening for a substance having an effect of suppressing a decrease in or improving skin barrier function, the method comprising:

a step of culturing in vitro human epidermal keratinocytes in a medium containing a test substance and separately in a control medium not containing the test substance ; and

a step of comparing an expression level of type IV collagen between the keratinocytes cultured in the medium containing a test substance and the keratinocytes as a control cultured in the control medium,

wherein the test substance is selected as a substance having an effect of suppressing a decrease in or improving

skin barrier function when the expression level of type IV collagen in the keratinocytes cultured in the medium containing the test substance is higher than the expression level of type IV collagen in the keratinocytes as a control.