

DESCRIPTION

TITLE OF INVENTION: AGENT FOR INHIBITING REDUCTION OF
DECOMPOSITION OF MODIFIED ELASTIN, AGENT FOR MAINTAINING
5 NORMAL ELASTIC FIBERS, AGENT FOR INHIBITING FORMATION OF
ELASTIN-ELAFIN COMPLEX, AND COMPOSITION CONTAINING SAID
AGENTS

TECHNICAL FIELD

10 [0001]

The present invention relates to an agent for
inhibiting a reduction in breakdown of denatured elastin,
an agent for maintaining normal elastin fibers, and an
agent for inhibiting formation of an elastin-elafin complex.
15 The present invention also relates to a composition for
inhibiting a reduction in breakdown of denatured elastin, a
composition for maintaining normal elastin fibers, and a
composition for inhibiting formation of an elastin-elafin
complex. Further, the present invention relates to a
20 method of inhibiting formation of an elastin-elafin complex,
a method of inhibiting a reduction in breakdown of
denatured elastin, a method of maintaining normal elastin
fibers, and the like. Still further, the present invention
relates to use of an active ingredient for inhibiting
25 formation of an elastin-elafin complex, use of an active
ingredient for inhibiting a reduction in breakdown of
denatured elastin, and use of an active ingredient for
maintaining normal elastin fibers.

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BACKGROUND ART

[0002]

Elastin is a major component of elastin fibers
(elastic fibers) and is widely expressed in tissues such as
skin, blood vessels, and lungs which require elasticity for
35 expression of their functions. For example, in the dermis

of the skin, elastin fibers function to impart elasticity to the skin and maintain resiliency, but the elastin fibers are degenerated by factors such as aging and ultraviolet light, resulting in loss of elasticity and the like. In particular, exposure of the skin to ultraviolet light over many years causes accumulation and deposition of denatured elastin on the dermis, which is considered to be a factor that causes scarce elasticity and many wrinkles, i.e., solar elastosis.

10 [0003]

One of possible factors that cause local accumulation of denatured elastin as observed in solar elastosis is reduced breakdown of denatured elastin. In the dermis exposed to ultraviolet light, colocalization of elastin fibers and elafin is observed, which suggests formation of a protein complex between elastin and elafin. Elafin is an inhibitor of elastase. Elastin, once bonded to elafin to form a complex (elastin-elafin complex), shows resistance to elastase-mediated breakdown.

20 [0004]

Rare sugars, which are defined as monosaccharides and their derivatives that are scarce in nature, have been reported to have various beneficial effects. For example, Patent Literature 1 discloses D-psicose as a skin function improving composition. Patent Literature 2 discloses a cosmetic product and the like containing one or more ketohexoses.

[0005]

Patent Literature 3 discloses that L-arginine, zinc chloride, magnesium chloride, fructose, and the like have an effect of promoting the recovery of skin barrier function. Patent Literature 4 discloses a topical agent for skin containing fructose and L-arginine-L-aspartate, wherein the agent is excellent in prevention and improvement of skin irritation and is less likely to cause

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stickiness, papules, pustules, dark blisters, erythema, and the like.

CITATION LIST

- 5 - Patent Literature
[0006]
Patent Literature 1: JP 2017-36276 A
Patent Literature 2: JP 2004-529958 T
Patent Literature 3: JP 3948588 B
10 Patent Literature 4: JP H05-112442 A

SUMMARY OF INVENTION

- Technical Problem
[0007]
- 15 As described above, an elastin-elafin complex formed by bonding between elastin and elafin shows resistance to elastase. Thus, formation of an elastin-elafin complex reduces breakdown of elastin and slows down elastin fiber turnover. Inhibiting formation of an elastin-elafin
20 complex can, for example, inhibit a reduction in breakdown of denatured elastin and promote elastin fiber turnover. Inhibiting formation of an elastin-elafin complex is also likely to inhibit or reduce accumulation of denatured elastin, thus allowing for maintenance of normal elastin
25 fibers. As described above, Patent Literature 1 relates to a skin function improving composition containing D-psicose and/or a derivative thereof as an active ingredient(s), and discloses that application of the composition to the skin increases collagen IV and also increases elastin in both
30 oxytalan and elaunin fibers, thus improving skin elasticity. Patent Literature 2 discloses psicose as a ketohexose, and discloses that a cosmetic product or a dermatological preparation containing psicose provides effects such as maintenance and recovery of skin barrier properties,
35 prevention or reduction of dryness, prevention or reduction

of pigmentation disorders, and prevention or reduction of aging. Patent Literature 3 discloses an effect of fructose on the recovery of skin barrier function. Patent Literature 4 discloses that a topical agent for skin
5 containing fructose has an effect of preventing skin irritation. However, Patent Literatures 1 to 4 are silent about studies on substances having an effect of inhibiting formation of an elastin-elafin complex.

[0008]

10 The present invention aims to provide an agent for inhibiting formation of an elastin-elafin complex and a composition for inhibiting formation of an elastin-elafin complex, which are capable of inhibiting formation of an elastin-elafin complex. The present invention still also
15 aims to provide a method of inhibiting formation of an elastin-elafin complex, a method of inhibiting a reduction in breakdown of denatured elastin, a method of maintaining normal elastin fibers, and the like. The present invention also aims to provide use of an active ingredient for
20 inhibiting formation of an elastin-elafin complex, for inhibiting a reduction in breakdown of denatured elastin, or for maintaining normal elastin fibers.

- Solution to Problem

25 [0009]

As a result of extensive studies to solve the above issue, the present inventor found that psicose, fructose, and derivatives thereof have an effect of inhibiting formation of an elastin-elafin complex, and the present
30 invention was thus completed.

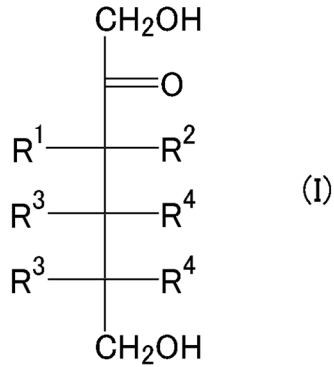
[0010]

The present invention encompasses the following agent for inhibiting formation of an elastin-elafin complex and the like, but the present invention is not limited thereto.

35 (1) An agent for inhibiting a reduction in breakdown

of denatured elastin, the agent containing, as an active ingredient, at least one of a compound represented by the following formula (I) or a derivative thereof:

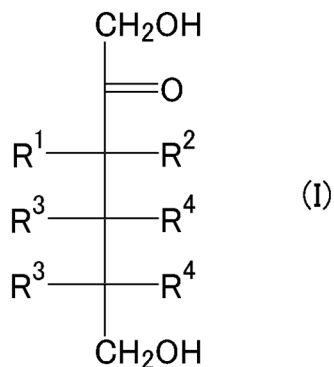
[Chem. 1]



wherein in the formula (I), R^1 to R^4 may be the same or different and each represent a hydrogen atom or a hydroxy group, R^2 is a hydroxy group when R^1 is a hydrogen atom, R^2 is a hydrogen atom when R^1 is a hydroxy group, R^4 is a hydroxy group when R^3 is a hydrogen atom, and R^4 is a hydrogen atom when R^3 is a hydroxy group.

(2) An agent for maintaining normal elastin fibers, the agent containing, as an active ingredient, at least one of a compound represented by the following formula (I) or a derivative thereof:

[Chem. 2]



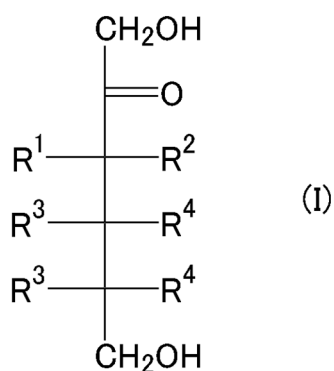
wherein in the formula (I), R^1 to R^4 may be the same or different and each represent a hydrogen atom or a hydroxy group, R^2 is a hydroxy group when R^1 is a hydrogen atom, R^2 is a hydrogen atom when R^1 is a hydroxy group, R^4 is a

hydroxy group when R^3 is a hydrogen atom, and R^4 is a hydrogen atom when R^3 is a hydroxy group.

(3) The agent according to (1) or (2) above, wherein the agent inhibits formation of an elastin-elafin complex.

5 (4) An agent for inhibiting formation of an elastin-elafin complex, the agent containing, as an active ingredient, at least one of a compound represented by the following formula (I) or a derivative thereof:

[Chem. 3]



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wherein in the formula (I), R^1 to R^4 may be the same or different and each represent a hydrogen atom or a hydroxy group, R^2 is a hydroxy group when R^1 is a hydrogen atom, R^2 is a hydrogen atom when R^1 is a hydroxy group, R^4 is a hydroxy group when R^3 is a hydrogen atom, and R^4 is a hydrogen atom when R^3 is a hydroxy group.

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(5) The agent for inhibiting formation of an elastin-elafin complex according to (4) above, wherein the agent is for use in promoting elastin fiber turnover by inhibiting formation of an elastin-elafin complex.

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(6) A composition for inhibiting a reduction in breakdown of denatured elastin, the composition containing the agent for inhibiting a reduction in breakdown of denatured elastin according to (1) or (3) above.

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(7) A composition for maintaining normal elastin fibers, the composition containing the agent for maintaining normal elastin fibers according to (2) or (3) above.

(8) A composition for inhibiting formation of an elastin-elafin complex, the composition containing the agent for inhibiting formation of an elastin-elafin complex according to (4) or (5) above.

5 (9) The agent according to any one of (1) to (5) above or the composition according to any one of (6) to (8) above, wherein the compound represented by the formula (I) or a derivative thereof is at least one of psicose or fructose.

10 (10) The agent according to any one of (1) to (5) above or the composition according to any one of (6) to (8) above, wherein in the formula (I), R^1 is a hydrogen atom, R^2 is a hydroxy group, R^3 is a hydrogen atom, and R^4 is a hydroxy group.

15 (11) The agent according to any one of (1) to (5) and (9) above or the composition according to any one of (6) to (9) above, wherein in the formula (I), R^1 is a hydroxy group, R^2 is a hydrogen atom, R^3 is a hydrogen atom, and R^4 is a hydroxy group.

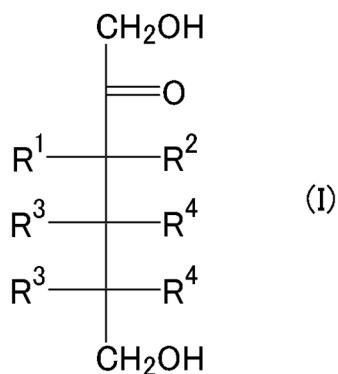
20 (12) The composition according to any one of (6) to (11) above, wherein the composition is a topical agent for skin.

(13) The composition according to any one of (6) to (11) above, wherein the composition is a cosmetic.

25 (14) The composition according to any one of (6) to (11) above, wherein the composition is a food or beverage.

(15) A method of inhibiting formation of an elastin-elafin complex or a reduction in breakdown of denatured elastin, the method including administering at least one of
30 a compound represented by the following formula (I) or a derivative thereof as an active ingredient:

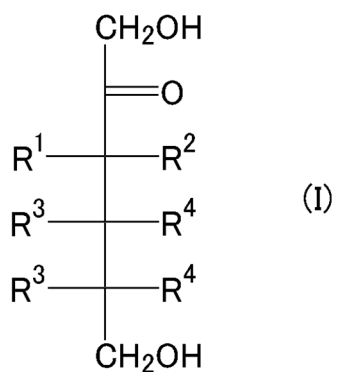
[Chem. 4]



wherein in the formula (I), R^1 to R^4 may be the same or different and each represent a hydrogen atom or a hydroxy group, R^2 is a hydroxy group when R^1 is a hydrogen atom, R^2 is a hydrogen atom when R^1 is a hydroxy group, R^4 is a hydroxy group when R^3 is a hydrogen atom, and R^4 is a hydrogen atom when R^3 is a hydroxy group.

(16) A method of maintaining normal elastin fibers, the method including administering at least one of a compound represented by the following formula (I) or a derivative thereof as an active ingredient:

[Chem. 5]

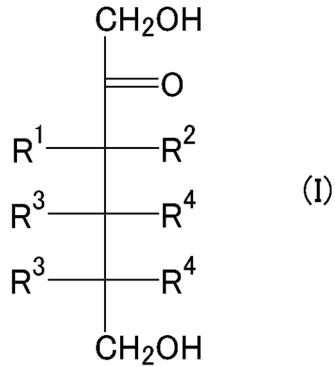


wherein in the formula (I), R^1 to R^4 may be the same or different and each represent a hydrogen atom or a hydroxy group, R^2 is a hydroxy group when R^1 is a hydrogen atom, R^2 is a hydrogen atom when R^1 is a hydroxy group, R^4 is a hydroxy group when R^3 is a hydrogen atom, and R^4 is a hydrogen atom when R^3 is a hydroxy group.

(17) Use of at least one of a compound represented by the following formula (I) or a derivative thereof for

inhibiting formation of an elastin-elafin complex, for inhibiting a reduction in breakdown of denatured elastin, or for maintaining normal elastin fibers:

[Chem. 6]



wherein in the formula (I), R^1 to R^4 may be the same or different and each represent a hydrogen atom or a hydroxy group, R^2 is a hydroxy group when R^1 is a hydrogen atom, R^2 is a hydrogen atom when R^1 is a hydroxy group, R^4 is a hydroxy group when R^3 is a hydrogen atom, and R^4 is a hydrogen atom when R^3 is a hydroxy group.

- Advantageous Effects of Invention

[0011]

The present invention can provide, for example, an agent for inhibiting formation of an elastin-elafin complex and a composition for inhibiting formation of an elastin-elafin complex, which are capable of inhibiting formation of an elastin-elafin complex. The present invention can also provide a method of inhibiting formation of an elastin-elafin complex, a method of inhibiting a reduction in breakdown of denatured elastin, a method of maintaining normal elastin fibers, and the like. The present invention can also provide use of an active ingredient for inhibiting formation of an elastin-elafin complex, for inhibiting a reduction in breakdown of denatured elastin, or for maintaining normal elastin fibers.

[0012]

Inhibiting formation of an elastin-elafin complex can inhibit a reduction in breakdown of denatured elastin. Inhibiting formation of an elastin-elafin complex can also contribute to maintaining normal elastin fibers. The present invention can provide a method of inhibiting formation of an elastin-elafin complex, a method of inhibiting a reduction in breakdown of denatured elastin, a method of maintaining normal elastin fibers, and the like.

DESCRIPTION OF EMBODIMENTS

[0013]

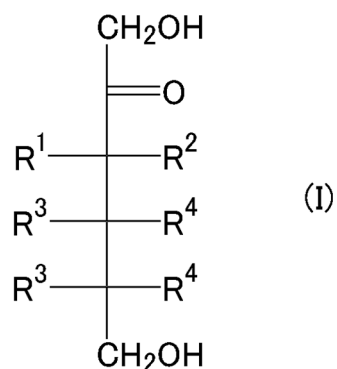
The present invention is described below. The present invention is not limited to the following embodiments, and modifications can be made without departing from the scope of the present invention.

[0014]

The agent for inhibiting formation of an elastin-elafin complex of the present invention contains, as an active ingredient(s), a compound represented by the following formula (I) and/or a derivative thereof:

[0015]

[Chem. 7]



[0016]

In the formula (I), R^1 to R^4 may be the same or different and each represent a hydrogen atom or a hydroxy group, R^2 is a hydroxy group when R^1 is a hydrogen atom, R^2 is a hydrogen atom when R^1 is a hydroxy group, R^4 is a

hydroxy group when R^3 is a hydrogen atom, and R^4 is a hydrogen atom when R^3 is a hydroxy group.

[0017]

The formula (I) is a formula representing a chain
5 structure of psicose or fructose. Psicose and fructose
each isomerize, for example, in an aqueous solution, into a
mixture with a ring structure. Examples of derivatives of
the compound represented by the formula (I) include ring
structures of the compound represented by the formula (I),
10 aldonic acid, uronic acid, sugar alcohols, and amino sugars.
The "compounds represented by the formula (I) and
derivatives thereof" are preferably psicose, fructose, and
derivatives thereof, more preferably psicose and/or
fructose. Herein, the expression "compounds represented by
15 the formula (I) and/or derivatives thereof" can be replaced
by another expression "psicose, fructose, and/or
derivatives thereof". Hereinafter, a description may be
given using the expression "psicose, fructose, and/or
derivatives thereof".

20 [0018]

As shown in Examples described later, the active
ingredient has an effect of inhibiting bonding between
elastin and elafin and formation of a complex (elastin-
elafin complex). The active ingredient is used for
25 inhibiting formation of an elastin-elafin complex.
Inhibiting formation of an elastin-elafin complex can be
rephrased as "inhibiting bonding between elastin and
elafin".

As described above, formation of an elastin-elafin
30 complex reduces breakdown of elastin. Inhibiting formation
of an elastin-elafin complex can inhibit a reduction in
breakdown of denatured elastin. Inhibiting a reduction in
breakdown of denatured elastin is likely to promote elastin
fiber turnover and inhibit or reduce accumulation of
35 denatured elastin in tissues such as skin. Inhibiting a

reduction in breakdown of denatured elastin is also likely to allow for maintenance of normal elastin fibers.

[0019]

In the present invention, the term "normal elastin
5 fibers" refers to elastin fibers with their inherent function and physical properties (e.g., strength and viscoelasticity). The term "denatured elastin" refers to elastin fibers and components thereof (e.g., tropoelastin and elastin breakdown products) whose function and physical
10 properties are impaired as compared to those inherent thereto.

In the present invention, the simple term "elastin" and the term "elastin" in an elastin-elafin complex encompass tropoelastin, which is a precursor of elastin
15 fibers, elastin in elastin fibers, and tropoelastin and/or elastin fibers in which partial structural change, breakdown, or fragmentation associated with aging or irritation are observed.

The expression "maintenance of normal elastin fibers"
20 refers to inhibiting a reduction in the amount of normal elastin fibers and inhibiting a reduction in inherent function and physical properties. The phrase "inhibiting a reduction in the amount of normal elastin fibers and inhibiting a reduction in inherent function and physical
25 properties" refers to inhibiting a reduction in the amount of normal elastin fibers and inhibiting a reduction in inherent function and physical properties by use of psicose, fructose, and/or derivatives thereof used as an active ingredient(s) in the present invention, as compared to no
30 use of these active ingredients.

[0020]

In one embodiment, the agent for inhibiting formation of an elastin-elafin complex of the present invention is suitably used for promoting elastin fiber turnover by
35 inhibiting formation of an elastin-elafin complex. The

active ingredient inhibits formation of an elastin-elafin complex, and can thus be used for inhibiting a reduction in breakdown of denatured elastin and for maintaining normal elastin fibers.

5 Thus, the present invention also encompasses an agent for inhibiting a reduction in breakdown of denatured elastin and an agent for maintaining normal elastin fibers, which contain psicose, fructose, and/or derivatives thereof as an active ingredient(s).

10 [0021]

 Hereinafter, the agent for inhibiting formation of an elastin-elafin complex, the agent for inhibiting a reduction in breakdown of denatured elastin, and the agent for maintaining normal elastin fibers of the present
15 invention are also collectively referred to as the "agent for inhibiting complex formation or the like".

[0022]

 The agent for inhibiting complex formation or the like of the present invention may contain two or more of
20 psicose, fructose, and/or derivatives thereof as active ingredients in combination. The presence of psicose is particularly preferred because of its high effect of inhibiting formation of an elastin-elafin complex.

[0023]

25 Psicose is a monosaccharide classified as a ketose having a ketone group in its structure. Psicose is obtainable by any means. For example, it may be extracted from nature or synthesized by a chemical or biological method. For example, psicose can be obtained by reaction
30 of fructose with isomerase.

[0024]

 The origin of psicose for use in the present invention is not limited. A commercially available purified product of psicose can be used for adjusting the
35 content to a predetermined amount. Psicose for use in the

present invention is preferably D-psicose (a compound represented by the formula (I) in which R¹ is a hydrogen atom, R² is a hydroxy group, R³ is a hydrogen atom, and R⁴ is a hydroxy group).

5 [0025]

Similarly to psicose, fructose is a monosaccharide classified as a ketose having a ketone group in its structure. Fructose is obtainable by any means. For example, it may be extracted from nature or synthesized by a chemical or biological method. For example, fructose can be obtained by reaction of glucose with isomerase.

[0026]

The origin of fructose for use in the present invention is not limited. A commercially available purified product of fructose can be used for adjusting the content to a predetermined amount. Fructose for use in the present invention is preferably D-fructose (a compound represented by the formula (I) in which R¹ is a hydroxy group, R² is a hydrogen atom, R³ is a hydrogen atom, and R⁴ is a hydroxy group).

[0027]

When psicose is obtained by reaction of fructose with isomerase, the reaction is a reversible equilibrium reaction, and a mixture of psicose and fructose is obtained. When the agent or composition of the present invention contains psicose and fructose as active ingredients, the mole ratio of psicose to fructose (psicose:fructose) therein is preferably 1:10 to 10:1.

[0028]

30 The present invention may use a derivative of psicose and/or a derivative of fructose.

The term "derivative" refers to a compound derived from a starting compound by converting the molecular structure through a chemical reaction. For example, derivatives of hexasaccharides include sugar alcohols and

amino sugars. In the case of psicose and fructose, their derivatives include sugar alcohols in which the ketone group is converted into an alcohol group, uronic acid in which the alcohol group is oxidized, and amino sugars in which the alcohol group is replaced by a NH_2 group. The derivative of psicose for use in the present invention is preferably a derivative of D-psicose. The derivative of fructose for use in the present invention is preferably a derivative of D-fructose. When the derivative of D-psicose and the derivative of D-fructose are contained as active ingredients for use in the present invention, the mole ratio thereof is preferably 1:1.

[0029]

As described above, psicose for use in the present invention is preferably D-psicose (a compound represented by the formula (I) in which R^1 is a hydrogen atom, R^2 is a hydroxy group, R^3 is a hydrogen atom, and R^4 is a hydroxy group). Fructose for use in the present invention is preferably D-fructose (a compound represented by the formula (I) in which R^1 is a hydroxy group, R^2 is a hydrogen atom, R^3 is a hydrogen atom, and R^4 is a hydroxy group). Herein, the expression "psicose, fructose, and/or derivatives thereof" used throughout the descriptions includes "D-psicose, D-fructose, and/or derivative thereof".

[0030]

The agent for inhibiting complex formation or the like of the present invention may consist of at least one active ingredient selected from psicose, fructose, and derivatives thereof, or may also contain other components, additives, and the like.

The agent for inhibiting formation of an elastin-elafin complex, the agent for inhibiting a reduction in breakdown of denatured elastin, and the agent for maintaining normal elastin fibers of the present invention can be directly used as an agent for inhibiting formation

of an elastin-elafin complex, an agent for inhibiting a reduction in breakdown of denatured elastin, and an agent for maintaining normal elastin fibers, respectively. Each of these agents can also be added to a composition for inhibiting formation of an elastin-elafin complex or the like (described later). The agent for inhibiting complex formation or the like of the present invention is suitably used as an active ingredient of the composition for inhibiting formation of an elastin-elafin complex or the like.

[0031]

A composition for inhibiting formation of an elastin-elafin complex, which contains the agent for inhibiting formation of an elastin-elafin complex of the present invention, is also encompassed by the present invention. A composition for inhibiting a reduction in breakdown of denatured elastin, which contains the agent for inhibiting a reduction in breakdown of denatured elastin of the present invention, is also encompassed by the present invention. A composition for maintaining normal elastin fibers, which contains the agent for maintaining normal elastin fibers of the present invention, is also encompassed by the present invention.

The composition for inhibiting formation of an elastin-elafin complex, the composition for inhibiting a reduction in breakdown of denatured elastin, and the composition for maintaining normal elastin fibers of the present invention are also collectively referred to as a "composition for inhibiting complex formation or the like". The composition for inhibiting complex formation or the like of the present invention contains the active ingredient.

The agent for inhibiting complex formation or the like and the composition for inhibiting complex formation or the like of the present invention can be suitably used

for inhibiting formation of an elastin-elafin complex in the skin, for inhibiting a reduction in breakdown of denatured elastin in the skin, or for maintaining normal elastin fibers in the skin, for example.

5 [0032]

The agent for inhibiting complex formation or the like and the composition for inhibiting complex formation or the like of the present invention are applicable for either therapeutic use (medical use) or non-therapeutic use
10 (non-medical use).

The agent for inhibiting complex formation or the like and the composition for inhibiting complex formation or the like of the present invention, which contain the active ingredient, can be used for, for example, preventing
15 or ameliorating conditions or symptoms for which inhibition of formation of an elastin-elafin complex is desired. In one embodiment, the agent for inhibiting complex formation or the like and the composition for inhibiting complex formation or the like of the present invention can be used
20 for, for example, preventing or ameliorating solar elastosis or the like by inhibiting formation of an elastin-elafin complex. The agent for inhibiting complex formation or the like and the composition for inhibiting complex formation or the like of the present invention are
25 also useful for cosmetic purposes such as maintenance of skin elasticity and prevention or amelioration of wrinkles and/or sagging by inhibiting formation of an elastin-elafin complex. The term "preventing" or "prevention" encompasses prevention of onset, delay of onset, and decrease in
30 incidence. The term "ameliorating" or "amelioration" encompasses alleviation of symptoms, good reversal of symptoms, suppression of progression of symptoms, and cure of symptoms.

[0033]

35 The composition for inhibiting complex formation or

the like of the present invention can be used in various applications such as cosmetics, foods and beverages, and pharmaceutical and quasi-pharmaceutical products. The composition for inhibiting complex formation or the like of the present invention may be a cosmetic, a food or beverage, or a pharmaceutical or quasi-pharmaceutical product by itself for inhibiting formation of an elastin-elafin complex, for inhibiting a reduction in breakdown of denatured elastin, or for maintaining normal elastin fibers; 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. [0034]

The composition for inhibiting complex formation or the like of the present invention is suitably used as a topical agent for skin, for example. The topical agent for skin encompasses cosmetics and pharmaceutical and quasi-pharmaceutical products. Preferably, the topical agent for skin is a cosmetic. In one embodiment, in the case of using the composition for inhibiting complex formation or the like for inhibiting formation of an elastin-elafin complex in the skin, for inhibiting a reduction in breakdown of denatured elastin in the skin, or for maintaining normal elastin fibers in the skin, the composition for inhibiting complex formation or the like is preferably provided as a topical agent for skin, and is more preferably provided as a cosmetic.

The composition for inhibiting complex formation or the like of the present invention can also be used as a pharmaceutical or quasi-pharmaceutical product, other than the topical agent for skin.

In another embodiment, the composition for inhibiting complex formation or the like can also be provided as a food or beverage. The following describes a case where the composition for inhibiting complex formation or the like of

the present invention is 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.
[0035]

5 When the composition for inhibiting complex formation or the like of the present invention is provided as a topical agent for skin, the dosage form and the like are not limited, and may be provided in any form. Examples include solutions, emulsions, creams, gels, powders,
10 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 wash, makeup remover, skin lotion, essence lotion, face pack, emulsion, cream, and
15 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 conditioner, hair styling products, hair dyes, and hair growth products; cleansing agents such as
20 soap and body wash; and bath salts.
[0036]

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

ingredient is mixed with one or more cosmetically acceptable components described above, and the mixture is then processed into a desired form.

[0037]

5 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
10 of such components include excipients, binders, disintegrants, lubricants, antioxidants, and colorants. One or more of these components can be used, if necessary.

[0038]

 The composition for inhibiting complex formation or
15 the like of the present invention 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
20 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
25 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
30 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
35 necessary. The pharmaceutical or quasi-pharmaceutical

product can be produced by a usual production method in which, for example, the active ingredient is mixed with one or more pharmaceutically or quasi-pharmaceutically acceptable components, and the mixture is then processed
5 into a desired form.

[0039]

When the composition for inhibiting complex formation or the like of the present invention is provided as a food or beverage, the food or beverage is not limited, and
10 examples include general foods and beverages, health foods, foods with function claims, foods for specified health uses, dietary supplements, and foods for the sick. The form of the food or beverage is also not limited. The health foods, foods with function claims, foods for specified health uses,
15 dietary supplements, and the like 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.

20 [0040]

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.
25 Such food and beverages can be produced by a usual production method. For example, the method may only require adding the active ingredient to food or beverage materials or the like in the production of foods and beverages.

30 [0041]

When the composition for inhibiting complex formation or the like of the present invention is a topical agent for skin, a pharmaceutical or quasi-pharmaceutical product other than the topical agent for skin, or a food or
35 beverage, the amount of the active ingredient, for example,

in terms of the weight of the active ingredient, in the composition is preferably 0.0000001 to 100 wt%, more preferably 0.000001 to 100 wt%, still more preferably 0.000001 to 10 wt%, yet still more preferably 0.000001 to 5 wt%, particularly preferably 0.000001 to 4.5 wt%. The amount is the total amount when the composition contains two or more active ingredients.

[0042]

The amount of the composition for inhibiting complex formation or the like of the present invention to be used is not limited, as long as the amount achieves the effect of inhibiting formation of an elastin-elafin complex, and can be suitably set according to the subject's conditions, weight, sex, age, or other factors. In the case of a topical agent for skin such as a cosmetic, the amount of the active ingredient is, for example, preferably 0.00001 to 10 g, more preferably 0.0001 to 1 g per adult (60 kg) per day. The amount may also be 0.00001 to 500 mg. In the case of oral administration of a pharmaceutical or quasi-pharmaceutical product, the dose of the active ingredient is, for example, preferably 0.00001 to 10 g, more preferably 0.0001 to 1 g per adult (60 kg) per day. The dose may also be 0.00001 to 500 mg. In the case of a food or beverage, the intake of the active ingredient is, for example, preferably 0.00001 to 100 g, more preferably 0.0001 to 10 g, particularly preferably 0.001 to 1 g per adult (60 kg) per day. The intake may also be 0.00001 to 500 mg. The above amount of the active ingredient can be ingested or administered at once or in several portions. The timing at which a topical agent for skin containing the active ingredient is applied (administered) to the skin and the timing at which a food or beverage or a pharmaceutical or quasi-pharmaceutical product containing the active ingredient is ingested or administered are not limited.

[0043]

The composition for inhibiting complex formation or the like of the present invention is applicable to any Subject (administration subject). For example, the composition is applicable to a human or non-human mammal, preferably a human. Examples of suitable subjects include those who want or need to inhibit formation of an elastin-elafin complex, those who want or need to inhibit a reduction in breakdown of denatured elastin, and those who want or need to maintain normal elastin fibers. Examples of such subjects include men and women who are concerned about undesirable changes in the skin, particularly wrinkles and/or sagging, due to ultraviolet light exposure (particularly, overexposure to ultraviolet light) and/or aging.

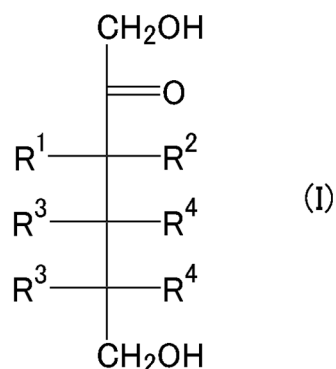
[0044]

The present invention also encompasses the following use and methods.

Use of a compound represented by the following formula (I) and/or a derivative thereof for inhibiting formation of an elastin-elafin complex, for inhibiting a reduction in breakdown of denatured elastin, or for maintaining normal elastin fibers:

[0045]

[Chem. 8]



25

[0046]

In the formula (I), R^1 to R^4 may be the same or different and each represent a hydrogen atom or a hydroxy

group, R^2 is a hydroxy group when R^1 is a hydrogen atom, R^2 is a hydrogen atom when R^1 is a hydroxy group, R^4 is a hydroxy group when R^3 is a hydrogen atom, and R^4 is a hydrogen atom when R^3 is a hydroxy group.

5 [0047]

A method of inhibiting formation of an elastin-elafin complex, the method including administering an active ingredient selected from a compound represented by the following formula (I) and a derivative thereof; a method of inhibiting a reduction in breakdown of denatured elastin, the method including administering the active ingredient; and a method of maintaining normal elastin fibers, the method including administering the active ingredient

15 The active ingredient is preferably applied to the skin, and is suitably used for inhibiting formation of an elastin-elafin complex in the skin, for inhibiting a reduction in breakdown of denatured elastin in the skin, or for maintaining normal elastin fibers in the skin.

20 [0048]

In the use and methods, the active ingredient, administration subjects, preferred embodiments thereof, and the like are the same as described above for the agent for inhibiting complex formation or the like and the composition for inhibiting complex formation or the like of the present invention. The active ingredient may be directly used or may be used in combination with other components. The agent for inhibiting complex formation or the like or the composition for inhibiting complex formation or the like of the present invention may be used. The active ingredient can be used in the form of the topical agent for skin, food or beverage, or the like described above.

35 The use may be therapeutic or non-therapeutic. The methods may be therapeutic or non-therapeutic. The "non-

performed by the following method. A dilution buffer was a 0.5% serum albumin-containing phosphate buffered saline (PBS). The active ingredient (D-psicose powder or D-fructose powder) was dissolved in dimethyl sulfoxide (DMSO).

5 A solution obtained by diluting tropoelastin and serum albumin to a concentration of 20 µg/mL in a bicarbonate buffer (14 mM sodium hydrogen carbonate, 6 mM sodium carbonate) was added in an amount of 100 µL to each well of a 96-well plate.

10 The 96-well plate was sealed with a parafilm, followed by reaction at 4°C for 24 hours. The reaction solution was removed, and a wash buffer (0.5% Tween 20 in PBS) was added in an amount of 150 µL to each well, followed by removal of the wash buffer. This procedure was
15 repeated three times. Hereinafter, this step is referred to as "washing out". Then, a blocking buffer (5% skim milk in PBS) was added in an amount of 100 µL to each well, followed by reaction at room temperature for one hour. After washing out the blocking buffer, a complex formation
20 reaction was performed. For the complex formation reaction of each sample, a complex reaction solution (containing elafin (final concentration: 1 µg/mL), the active ingredient (D-psicose or D-fructose) (final concentration: 0.1 to 100 µg/mL), and DMSO (final concentration: 0.1%)) in
25 a dilution buffer was added in an amount of 50 µL to each well for reaction at 37°C for one hour.

[0053]

After washing out the complex reaction solution, an elafin-recognizing primary antibody reaction solution was
30 added for reaction at 37°C for one hour. After washing out the primary antibody reaction solution, a horseradish peroxidase label-specific secondary antibody reaction solution was added for reaction at room temperature for one hour. After washing out the secondary antibody reaction
35 solution, a TMB (3,3',5,5'-tetramethylbenzidine) solution

was added in an amount of 100 μ L to each well for reaction at room temperature for 30 minutes. 1 M phosphoric acid was added in an amount of 100 μ L to each well to terminate the reaction. Then, the absorbance was measured using a microplate reader (wavelength: 450 nm).
[0054]

As a negative control, a dilution buffer containing elafin (final concentration: 1 μ g/mL) and DMSO (final concentration: 0.1%) was added in an amount of 50 μ L to each well, instead of the complex reaction solution containing elafin and D-psicose or D-fructose, in the complex formation reaction. As a background, a dilution buffer containing DMSO (final concentration: 0.1%) (not containing either elafin or the active ingredient) was added in an amount of 50 μ L to each well, instead of the complex reaction solution containing elafin and the active ingredient (D-psicose or D-fructose) in the complex formation reaction. Other than that, the reaction with the antibody reaction solution was performed by the same method as in the sample containing the active ingredient, and the absorbance was measured using a microplate reader (wavelength: 450 nm).
[0055]

Reagents and the like used in the assay were all commercial products. Tropoelastin was unmodified full-length human tropoelastin (#T0706 available from Sigma-Aldrich). Elafin was full-length human elafin to which a polyhistidine tag (His-tag) was added to the C-terminal (#12187-H08H available from Sino Biological Inc.).
[0056]

The elastin-elafin complex formation inhibition rate (%) was calculated from the absorbance at 450 nm of D-psicose or D-fructose (sample), the negative control, and the background, using the following calculation formula. The test was performed with $n = 4$ to 6 for D-psicose or D-

fructose (sample), the negative control, and the background, and the complex formation inhibition rate was determined from the average absorbance at 450 nm.

Complex formation inhibition rate (%) = $100 - 100 \times (\text{Ab}(\text{S}) - \text{Ab}(\text{NC})) / (\text{Ab}(\text{PC}) - \text{Ab}(\text{NC}))$
[0057]

In the formula, Ab(S) is the absorbance at a wavelength of 450 nm of D-psicose or D-fructose (sample). Ab(NC) is the absorbance at a wavelength of 450 nm of the background. Ab(PC) is the absorbance at a wavelength of 450 nm of the negative control. Dunnett's test was used for the significant test (vs. negative control) (significance level: $p < 0.05$).
[0058]

Table 1 shows the elastin-elafin complex formation inhibition rate of D-psicose or D-fructose. Table 1 below shows higher inhibition rates determined by performing the same test twice.
[0059]

[Table 1]

Sample	Complex formation inhibition rate (%)
D-psicose (0.01 µg/mL)	14.9
D-fructose (100 µg/mL)	10.3

[0060]

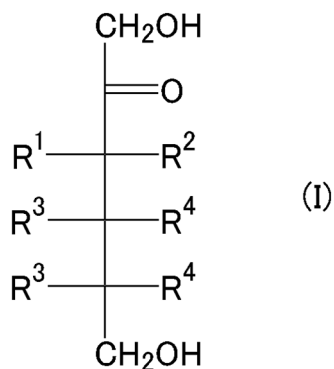
Example 1 confirmed that the test substances (D-psicose and D-fructose) can be used as active ingredients for inhibiting a reduction in breakdown of denatured elastin, for maintaining normal elastin fibers, or for inhibiting formation of an elastin-elafin complex.

CLAIMS

Claim 1. An agent for inhibiting a reduction in
breakdown of denatured elastin, the agent comprising, as an
5 active ingredient:

at least one of a compound represented by the
following formula (I) or a derivative thereof:

[Chem. 1]

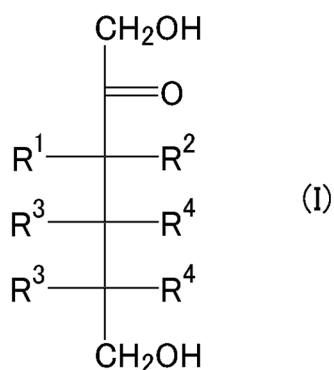


10 wherein in the formula (I), R^1 to R^4 may be the same or
different and each represent a hydrogen atom or a hydroxy
group, R^2 is a hydroxy group when R^1 is a hydrogen atom, R^2
is a hydrogen atom when R^1 is a hydroxy group, R^4 is a
hydroxy group when R^3 is a hydrogen atom, and R^4 is a
15 hydrogen atom when R^3 is a hydroxy group.

Claim 2. An agent for maintaining normal elastin
fibers, the agent comprising, as an active ingredient:

at least one of a compound represented by the
20 following formula (I) or a derivative thereof:

[Chem. 2]



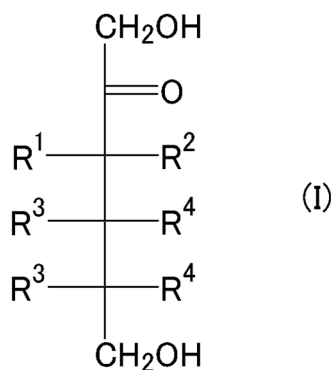
wherein in the formula (I), R¹ to R⁴ may be the same or different and each represent a hydrogen atom or a hydroxy group, R² is a hydroxy group when R¹ is a hydrogen atom, R² is a hydrogen atom when R¹ is a hydroxy group, R⁴ is a hydroxy group when R³ is a hydrogen atom, and R⁴ is a hydrogen atom when R³ is a hydroxy group.

Claim 3. The agent according to claim 1 or 2,
wherein the agent inhibits formation of an elastin-elafin complex.

Claim 4. An agent for inhibiting formation of an elastin-elafin complex, the agent comprising, as an active ingredient:

at least one of a compound represented by the following formula (I) or a derivative thereof:

[Chem. 3]



wherein in the formula (I), R¹ to R⁴ may be the same or different and each represent a hydrogen atom or a hydroxy

group, R^2 is a hydroxy group when R^1 is a hydrogen atom, R^2 is a hydrogen atom when R^1 is a hydroxy group, R^4 is a hydroxy group when R^3 is a hydrogen atom, and R^4 is a hydrogen atom when R^3 is a hydroxy group.

5

Claim 5. The agent for inhibiting formation of an elastin-elafin complex according to claim 4,

wherein the agent is for use in promoting elastin fiber turnover by inhibiting formation of an elastin-elafin
10 complex.

Claim 6. A composition for inhibiting a reduction in breakdown of denatured elastin, the composition comprising:
the agent for inhibiting a reduction in breakdown of
15 denatured elastin according to claim 1 or 3.

Claim 7. A composition for maintaining normal elastin fibers, the composition comprising:
the agent for maintaining normal elastin fibers
20 according to claim 2 or 3.

Claim 8. A composition for inhibiting formation of an elastin-elafin complex, the composition comprising:
the agent for inhibiting formation of an elastin-
25 elafin complex according to claim 4 or 5.

Claim 9. The agent according to any one of claims 1 to 5 or the composition according to any one of claims 6 to 8,
30 wherein the compound represented by the formula (I) or a derivative thereof is at least one of psicose or fructose.

Claim 10. The agent according to any one of claims 1 to 5 or the composition according to any one of claims 6 to
35

8,

wherein in the formula (I), R^1 is a hydrogen atom, R^2 is a hydroxy group, R^3 is a hydrogen atom, and R^4 is a hydroxy group.

5

Claim 11. The agent according to any one of claims 1 to 5 and 9 or the composition according to any one of claims 6 to 9,

10 wherein in the formula (I), R^1 is a hydroxy group, R^2 is a hydrogen atom, R^3 is a hydrogen atom, and R^4 is a hydroxy group.

Claim 12. The composition according to any one of claims 6 to 11,

15 wherein the composition is a topical agent for skin.

Claim 13. The composition according to any one of claims 6 to 11,

20 wherein the composition is a cosmetic.

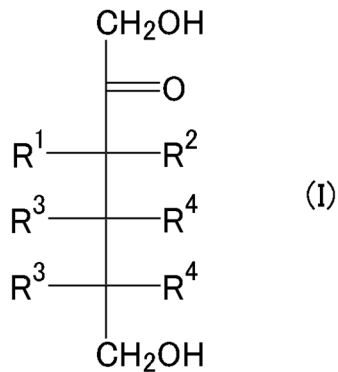
Claim 14. The composition according to any one of claims 6 to 11,

wherein the composition is a food or beverage.

25 Claim 15. A method of inhibiting formation of an elastin-elafin complex or a reduction in breakdown of denatured elastin, the method comprising:

administering at least one of a compound represented by the following formula (I) or a derivative thereof as an
30 active ingredient:

[Chem. 4]

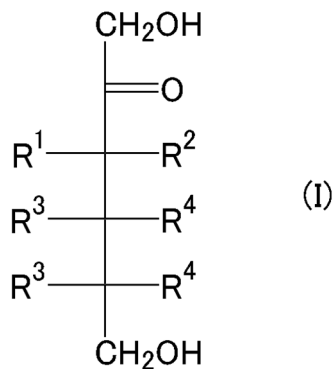


wherein in the formula (I), R¹ to R⁴ may be the same or different and each represent a hydrogen atom or a hydroxy group, R² is a hydroxy group when R¹ is a hydrogen atom, R² is a hydrogen atom when R¹ is a hydroxy group, R⁴ is a hydroxy group when R³ is a hydrogen atom, and R⁴ is a hydrogen atom when R³ is a hydroxy group.

Claim 16. A method of maintaining normal elastin fibers, the method comprising:

administering at least one of a compound represented by the following formula (I) or a derivative thereof as an active ingredient:

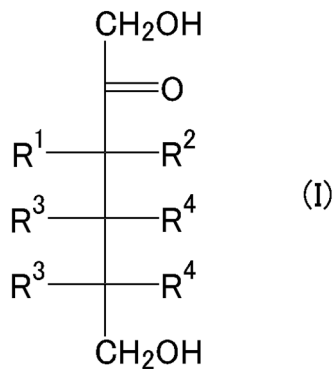
[Chem. 5]



wherein in the formula (I), R¹ to R⁴ may be the same or different and each represent a hydrogen atom or a hydroxy group, R² is a hydroxy group when R¹ is a hydrogen atom, R² is a hydrogen atom when R¹ is a hydroxy group, R⁴ is a hydroxy group when R³ is a hydrogen atom, and R⁴ is a hydrogen atom when R³ is a hydroxy group.

Claim 17. Use of at least one of a compound represented by the following formula (I) or a derivative thereof for inhibiting formation of an elastin-elafin complex, for inhibiting a reduction in breakdown of denatured elastin, or for maintaining normal elastin fibers:

[Chem. 6]



wherein in the formula (I), R^1 to R^4 may be the same or different and each represent a hydrogen atom or a hydroxy group, R^2 is a hydroxy group when R^1 is a hydrogen atom, R^2 is a hydrogen atom when R^1 is a hydroxy group, R^4 is a hydroxy group when R^3 is a hydrogen atom, and R^4 is a hydrogen atom when R^3 is a hydroxy group.