

DESCRIPTION

COMPOSITION FOR RAISING DEEP BODY TEMPERATURE

Technical Field

[0001]

The present invention relates to a composition for raising a deep body temperature.

Background Art

[0002]

Body temperature can be roughly classified into a shell temperature such as a body surface temperature and a deep body temperature. The shell temperature easily changes with the changes in ambient temperature, but the deep body temperature is kept within a certain range (Non Patent Literature 1). In this regard, a body temperature of a human decreases due to a life factor such as lack of exercise, or lack of sleep, or an external factor such as cooling, or excessive stress. Subsequently, due to the lowering in body temperature, symptoms such as sensitivity to cold, respiratory diseases, edema of lower limbs, and malaise of the body appear (Non Patent Literatures 2 to 5).

[0003]

It is effective to raise a body surface temperature as a temporary method for coping with the symptoms caused by a decrease in deep body temperature. In this regard, as a means of raising a body surface temperature, a method of taking heat into the body by using a heat retaining agent, ingesting warm food and drink, or the like, and a means of ingesting a Chinese herbal medicine or the like for the purpose of improving the blood flow are known (Patent Literatures 1 and 2).

[0004]

However, by such a means of raising a body temperature for the purpose of improving the blood flow, a deep body temperature cannot be raised, and a fundamental solution to the

lowering in the body temperature has not been provided (Patent Literatures 2 and 3).

[0005]

As a conventional technique regarding a material having an effect of normalizing the modulation of deep body temperature, a proanthocyanidin extracted from pine bark, an extract of a plant belonging to the genus *Cistanche* of the family *Orobanchaceae*, a quinoa extract, a black ginger extract, and the like are known (Patent Literatures 1 to 4).

[0006]

By the way, it has been found that among plant sterols, a compound having a cyclolanostane skeleton and a compound having a lophenol skeleton each have an effect of reducing a blood lipid peroxide level and an effect of suppressing the number of plaque formations in the thoracic aorta in an atherosclerotic model animal, and these compounds have been proposed for use as an antioxidant (Patent Literature 5).

Citation List

Patent Literature

[0007]

Patent Literature 1: JP 2006-143654 A

Patent Literature 2: JP 2011-157302 A

Patent Literature 3: JP 2010-260848 A

Patent Literature 4: JP 2014-15430 A

Patent Literature 5: WO 2010/058795

Non Patent Literature

[0008]

Non Patent Literature 1: Journal of the Society of Biomechanisms Japan, 16(1), 1992

Non Patent Literature 2: Journal of Japan Mibyou System Association, 13(1): 92-95, 2007

Non Patent Literature 3: Journal of the Showa University Society, 75(6): 652-656, 2015

Non Patent Literature 4: Research Bulletin of Miyazaki Prefectural Nursing University, 8(1): 13 to 27

Non Patent Literature 5: Nose Y. et al., Kawasaki Journal of Medical Welfare, 16(2), 58-63, 2011

Summary of Invention

Technical Problem

[0009]

As described above, the deep body temperature cannot be raised by means of the body temperature rise for the purpose of improving the blood flow, and therefore, the lowering in body temperature cannot be fundamentally solved.

Therefore, a problem of the present invention is to provide an agent for raising a deep body temperature and a food and drink composition for raising a deep body temperature, each of which is safe and exerts a non-transient effect for raising a deep body temperature.

Solution to Problem

[0010]

The present inventors have found that one or two or more compounds selected from the group consisting of a lophenol compound and a cyclolanostane compound have an action of raising a deep body temperature, and thus have completed the present invention.

[0011]

That is, the first aspect of the invention for solving the problem is an agent for raising a deep body temperature or a composition for raising a deep body temperature, including one or two or more compounds selected from the group consisting of a lophenol compound and a cyclolanostane compound as an active ingredient. In this regard, the terms of “composition” and

“agent” have the same meanings as each other in the present specification.

[0012]

The first aspect of the invention includes the following embodiments.

[0013]

In a preferred embodiment of the present invention, the one or two or more compounds selected from the group consisting of a lophenol compound and a cyclolanostane compound are one or two or more compounds selected from the group consisting of 4-methylcholest-7-en-3-ol, 4-methylergost-7-en-3-ol, 4-methylstigmast-7-en-3-ol, 9,19-cyclolanostane-3-ol, and 24-methylene-9,19-cyclolanostane-3-ol.

[0014]

Further, it is preferred that the present invention is in an embodiment in which the compounds are contained in the total amount of 0.00001% by mass or more.

[0015]

In addition, the present invention may also be an agent for raising a deep body temperature or a composition for raising a deep body temperature, including a composition containing 0.00001% by mass or more of one or two or more compounds selected from the group consisting of a lophenol compound and a cyclolanostane compound as an active ingredient.

[0016]

Further, it is preferred that the agent for raising a deep body temperature or the composition for raising a deep body temperature of the present invention is in an embodiment in which the agent for raising a deep body temperature or the composition for raising a deep body temperature is used for preventing and/or improving a disease caused by a decrease in deep body temperature.

[0017]

In particular, the agent for raising a deep body temperature or the composition for raising

a deep body temperature, of the present invention can be suitably used for sensitivity to cold caused by a decrease in deep body temperature and/or a disease of respiratory system caused by a decrease in deep body temperature.

[0018]

In addition, the present invention may also be a food and drink composition for raising a deep body temperature, including one or two or more compounds selected from the group consisting of a lophenol compound and a cyclolanostane compound as an active ingredient.

[0019]

In a preferred embodiment of the food and drink composition of the present invention, the one or two or more compounds selected from the group consisting of a lophenol compound and a cyclolanostane compound are one or two or more compounds selected from the group consisting of 4-methylcholest-7-en-3-ol, 4-methylergost-7-en-3-ol, 4-methylstigmast-7-en-3-ol, 9,19-cyclolanostane-3-ol, and 24-methylene-9,19-cyclolanostane-3-ol.

[0020]

Further, it is preferred that the food and drink composition of the present invention is in an embodiment in which the compounds are contained in the total amount of 0.00001% by mass or more.

[0021]

In addition, the present invention may also be a food and drink composition for raising a deep body temperature, including a composition containing 0.00001% by mass or more of the one or two or more compounds selected from the group consisting of a lophenol compound and a cyclolanostane compound as an active ingredient.

[0022]

Further, it is preferred that the food and drink composition for raising a deep body temperature of the present invention is in an embodiment in which the food and drink composition is

used for preventing and/or improving a disease caused by a decrease in deep body temperature.

[0023]

The food and drink composition for raising a deep body temperature of the present invention can be suitably used for sensitivity to cold caused by a lowering in deep body temperature and/or a disease of respiratory system caused by a decrease in deep body temperature.

[0024]

In addition, the second aspect of the invention for solving the problem is use of a compound selected from the group consisting of a lophenol compound and a cyclolanostane compound, in production of a composition for preventing or improving a disease caused by a decrease in deep body temperature, and the preferred embodiments of the compound are as described above.

[0025]

Further, in the second aspect of the invention, the following embodiments are included.

[0026]

Use of a composition containing a compound selected from the group consisting of a lophenol compound and a cyclolanostane compound in the total amount of 0.00001% by mass or more, in production of a composition for preventing or improving a disease caused by a lowering in deep body temperature.

[0027]

In a preferred embodiment of the present invention, the above-described composition for prevention or improvement is a composition for raising a deep body temperature.

[0028]

In a preferred embodiment of the present invention, the above-described composition for prevention or improvement is a composition for preventing or improving sensitivity to cold caused by a lowering in deep body temperature and/or a disease of respiratory system caused by a decrease

in deep body temperature.

[0029]

In addition, the third aspect of the invention for solving the problem is a compound selected from the group consisting of a lophenol compound and a cyclolanostane compound, which is used for preventing or improving a disease caused by a decrease in deep body temperature, and the preferred embodiments of the compound are as described above.

[0030]

In a preferred embodiment of the present invention, the above-described disease caused by a decrease in deep body temperature is sensitivity to cold caused by a decrease in deep body temperature and/or a disease of respiratory system caused by a lowering in deep body temperature.

[0031]

In a preferred embodiment of the present invention, the above-described compound is used for preventing or improving sensitivity to cold caused by a decrease in deep body temperature and/or a disease of respiratory system caused by a lowering in deep body temperature.

[0032]

Further, the fourth aspect of the invention for solving the problem is a method for preventing or improving a disease caused by a decrease in deep body temperature, including administering a compound selected from the group consisting of a lophenol compound and a cyclolanostane compound to a subject with a disease caused by a decrease in deep body temperature, and the preferred embodiments of the compound are as described above.

[0033]

In addition, the fourth aspect of the invention has the following embodiment as the preferred embodiment.

A composition containing the above-described compound selected from the group consisting of a lophenol compound and a cyclolanostane compound in the total of 0.00001% by

mass or more is administered to the subject.

[0034]

In a preferred embodiment of the present invention, the above-described disease caused by a decrease in deep body temperature is sensitivity to cold caused by a lowering in deep body temperature and/or a disease of respiratory system caused by a decrease in deep body temperature.

[0035]

In a preferred embodiment of the present invention, the above-described disease caused by a lowering in deep body temperature is a disease of respiratory system.

Brief Description of Drawings

[0036]

Fig. 1 is a graph showing changes in the deep body temperature in each group in Example 1.

Description of Embodiments

[0037]

Hereinafter, the preferred embodiment of the present invention will be described in detail. Note that the present invention is not limited to the following preferred embodiments, and can be changed freely within the scope of the present invention. In this regard, in the present specification, the percentages are expressed by mass unless otherwise specifically noted.

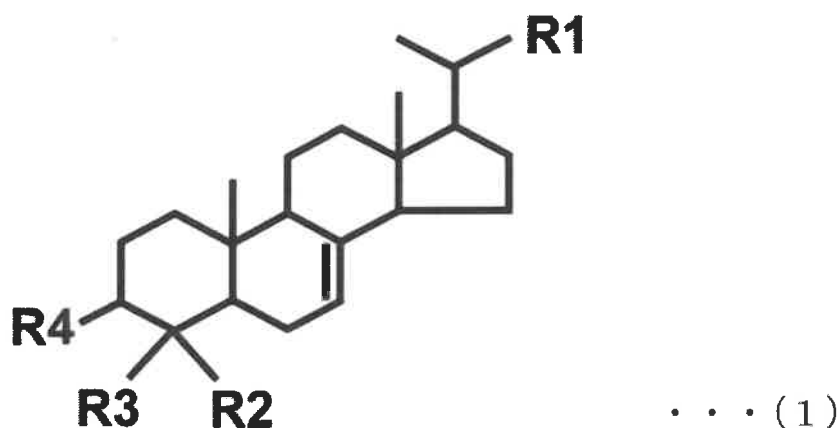
[0038]

An agent for raising a deep body temperature of the present invention contains a compound selected from the group consisting of a lophenol compound (compound 1), and a cyclolanostane compound (compound 2), as an active ingredient. The compound 1 and compound 2 are represented by the following general formula (1) and formula (2), respectively.

[0039]

[Chemical formula 1]

Compound 1



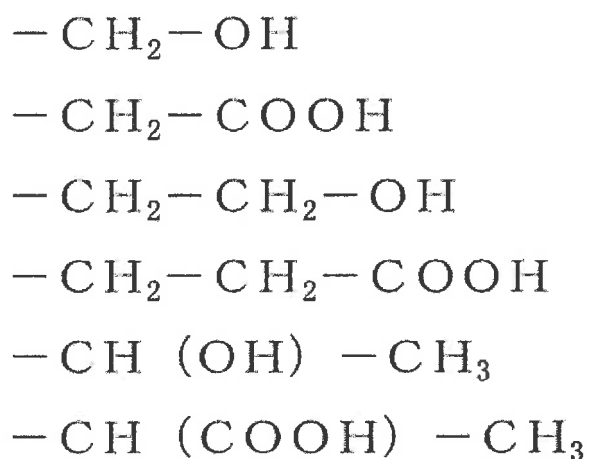
[0040]

In the general formula (1), R1 is an alkyl group or an alkenyl group including one or two double bonds, which is straight or branched chain having 5 to 16 carbon atoms. The alkyl or alkenyl group may be a substituted alkyl or alkenyl group, in which one or two hydrogen atoms are substituted with a hydroxyl group and/or a carbonyl group.

R2 and R3 each are independently a hydrogen atom or an alkyl group having 1 to 3 carbon atoms. Herein, as the alkyl group having 1 to 3 carbon atoms, a methyl group, an ethyl group and the like are preferable, and a methyl group is particularly preferable. The alkyl group may be a substituted alkyl group in which at least one hydrogen atom is substituted with a hydroxyl group and/or a carbonyl group.

[0041]

[Chemical formula 2]



[0042]

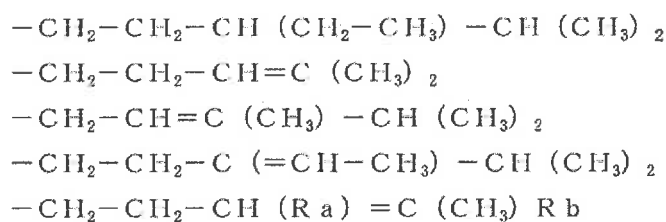
R4 forms C=O with a carbon atom constituting the ring, or is -OH or -OCOCH₃.

[0043]

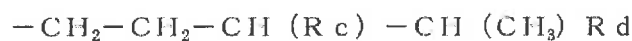
In the general formula (1), R1 is preferably any of groups represented by the following formulae.

[0044]

[Chemical formula 3]



(wherein R_a and R_b are any of a hydrogen atom, a hydroxyl group and a methyl group)



(wherein R_c and R_d are any of a hydrogen atom, a hydroxyl group and a methyl group)

[0045]

In the general formula (1), it is preferable that one of R2 and R3 is a hydrogen atom, and

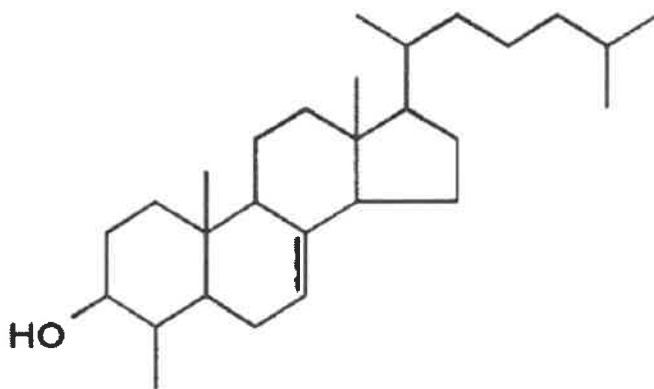
the other is a methyl group, and it is preferable that R4 is a hydroxy group.

[0046]

Compound 1 includes preferably 4-methylcholest-7-en-3-ol, 4-methylergost-7-en-3-ol and 4-methylstigmast-7-en-3-ol. Respective compounds have structures represented by the following formulae, respectively.

[0047]

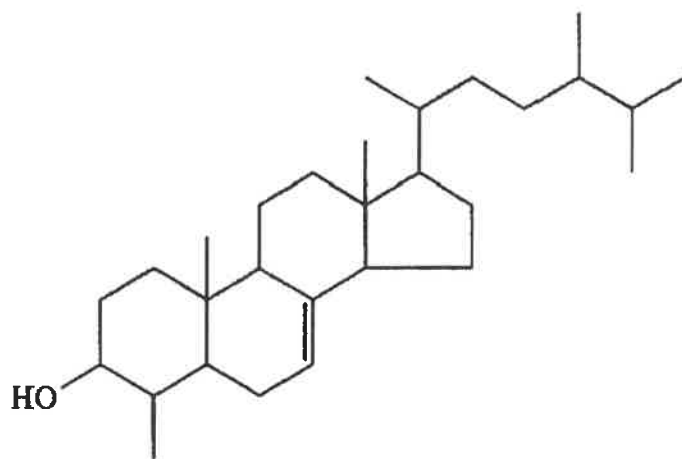
[Chemical formula 4]



4-Methylcholest-7-en-3-ol

[0048]

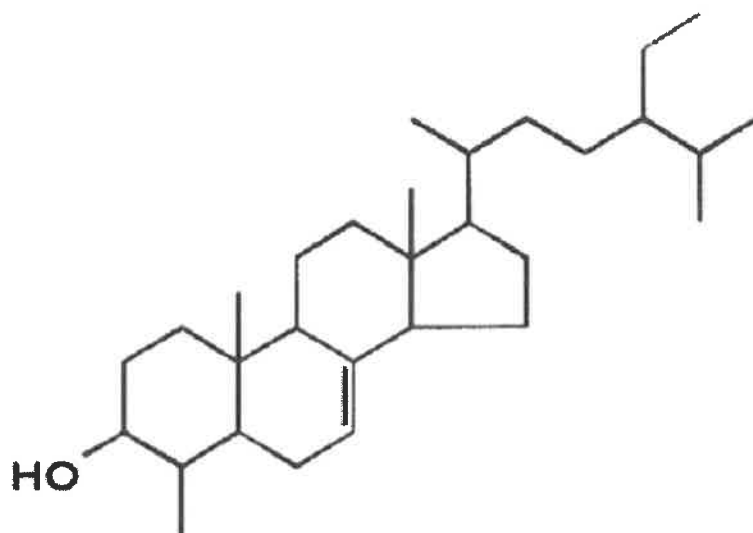
[Chemical formula 5]



4-Methylergost-7-en-3-ol

[0049]

[Chemical formula 6]



4-Methylstigmast-7-en-3-ol

[0050]

Compound 1 can be chemically manufactured in accordance with the known

manufacturing processes.

Compound 1 can be synthesized, for example, in accordance with supplement data described in Vitali Matyash et al., PLOS BIOLOGY, Volume 2, Issue 10, e280, 2004.

[0051]

Further, it is known that Compound 1 is contained in plants, and Compound 1 can be manufactured in accordance with the known process for manufacturing lophenol (Biochemistry Experimental Method 24, Fat Lipid Metabolism Experimental Method, authored by Akihiro YAMADA, Gakkai Shuppan Center, p. 174, 1989).

For example, Compound 1 can be extracted from plants which are known to contain Compound 1, using a method such as a hot water extraction method, an organic solvent extraction method, a supercritical extraction method and a subcritical extraction method (see, e.g., Japanese Patent No. 3905913). Compound 1 can be extracted, for example, from plants belonging to family *Liliaceae*, family *Leguminosae*, family *Gramineae*, family *Solanaceae* and family *Musaceae*.

The molecular weight and the structure of Compound 1 manufactured as described above can be determined or confirmed by a mass spectrometry (MS), a nuclear magnetic resonance spectral (NMR) method.

[0052]

Further, Compound 1 may be a pharmaceutically acceptable salt. The pharmaceutically acceptable salt includes both metal salts (inorganic salts) and organic salts, and as a list of them, that described in “Remington’s Pharmaceutical Sciences, 17th edition, 1985, p. 1418” is exemplified.

Specifically, inorganic salts such as a hydrochloride, a sulfate, a phosphate, a diphosphate, and a hydrobromide, and organic salts such as a malate, a maleate, a fumarate, a tartrate, a succinate, a citrate, an acetate, a lactate, a methanesulfonate, a p-toluenesulfonate, a pamoate, a salicylate, and a stearate are included without limitation.

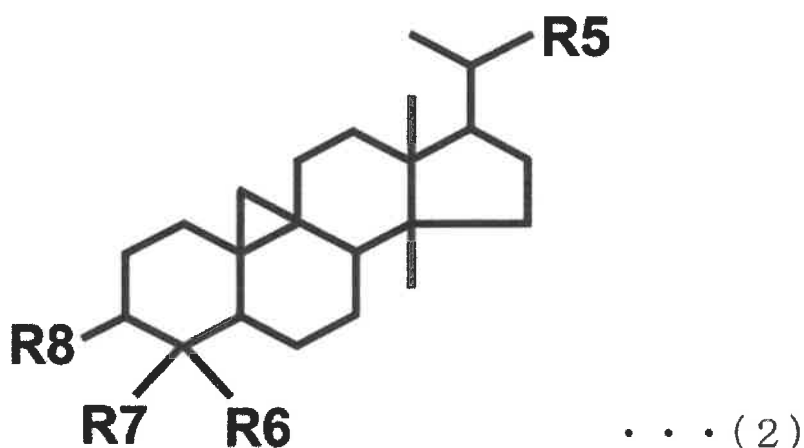
Meanwhile, Compound 1 may be a salt with a metal such as sodium, potassium, calcium,

magnesium and aluminum, or a salt with an amino acid such as lysine. Moreover, there may also be used a solvate such as a hydrate of the compounds or pharmaceutically acceptable salts thereof.

[0053]

[Chemical formula 7]

Compound 2



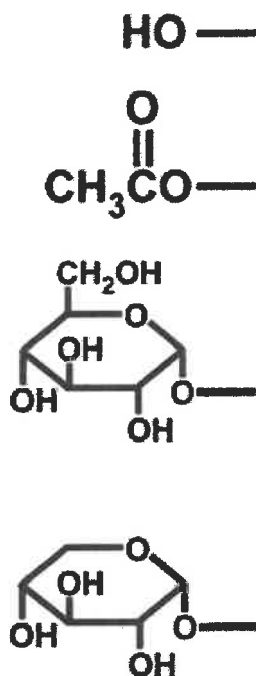
[0054]

In the general formula (2), R5 is an alkyl group or an alkenyl group including one or two double bonds, which is straight or branched chain having 6 to 8 carbon atoms. The alkyl or alkenyl group may be a substituted alkyl or alkenyl group in which one or two hydrogen atoms are substituted with a hydroxyl group and/or a carbonyl group.

R6 and R7 each are independently a hydrogen atom or a methyl group. R8 forms C=O with a carbon atom constituting the ring, or is any of the following formulae.

[0055]

[Chemical formula 8]

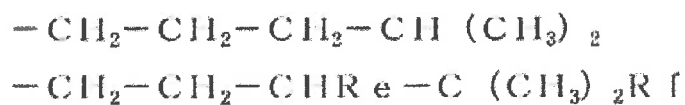


[0056]

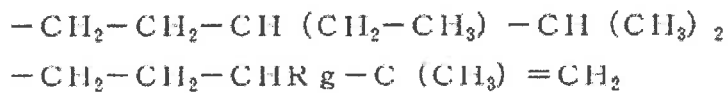
In the general formula (2), R5 is preferably any of groups represented by the following formulae.

[0057]

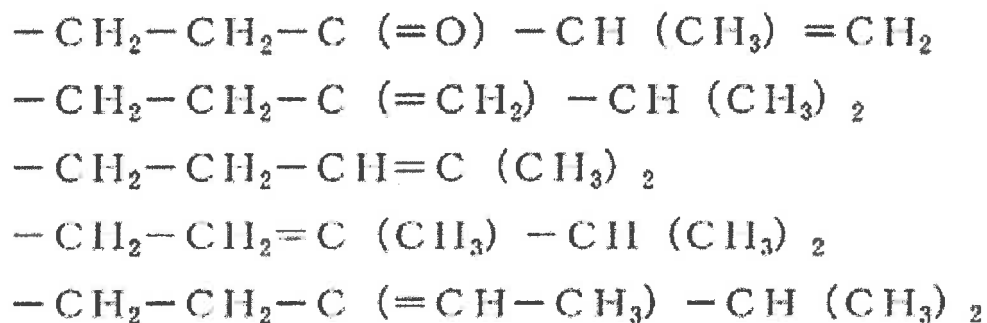
[Chemical formula 9]



(R_e is a hydrogen atom, a hydroxyl group or a methyl group, and R_f is a hydrogen atom or a hydroxyl group)



(R_g is a hydrogen atom, a hydroxyl group or a methyl group)



[0058]

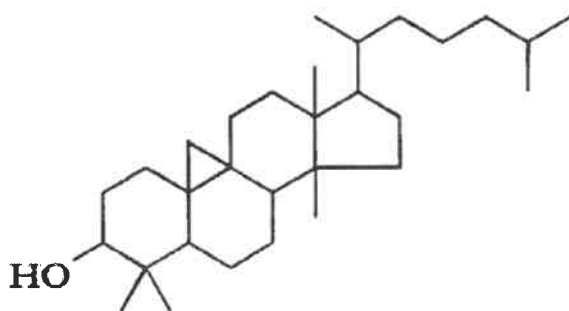
Further, in the general formula (2), it is preferable that one of R6 and R7 is a hydrogen atom, and the other is a methyl group, and it is preferable that R8 is a hydroxy group.

[0059]

Compound 2 includes preferably 9,19-cyclolanostan-3-ol and 24-methylene-9,19-cyclolanostan-3-ol. Respective compounds have structures represented by the following formulae, respectively.

[0060]

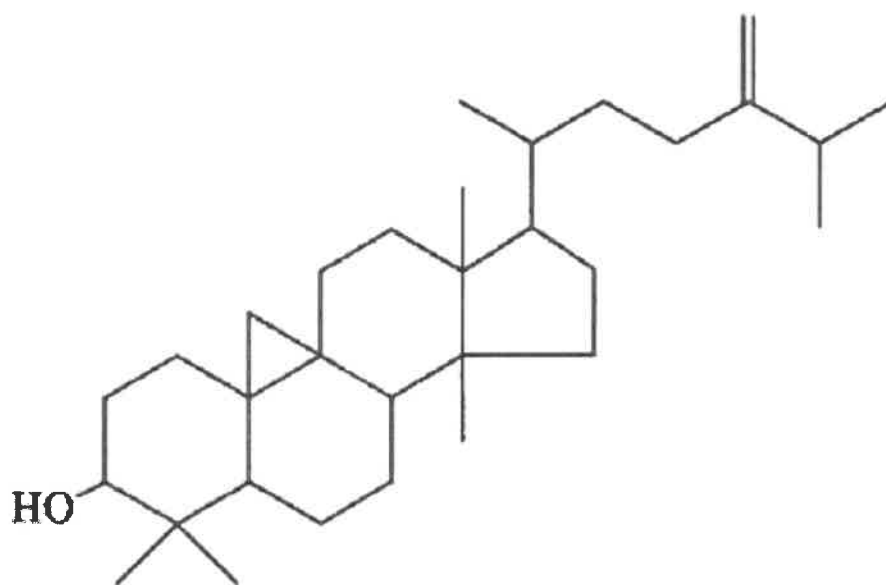
[Chemical formula 10]



9,19-Cyclolanostan-3-ol

[0061]

[Chemical formula 11]



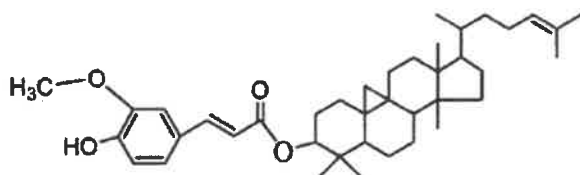
24-Methylene-9,19-cyclolanostan-3-ol

[0062]

Compound 2 can be chemically manufactured in accordance with the known manufacturing processes. For example, 24-methylene-9,19-cyclolanostan-3-ol (trivial name: 24-methylenecycloartanol) can be manufactured by the methods disclosed in JP-A No. 57-018617 and WO 2012/023599 (method of synthesis from γ -oryzanol). Alternatively, Compound 2 can be manufactured using a hydrolysate of cycloartenol ferulate as a starting substance, by the method disclosed in JP-A No. 2003-277269.

[0063]

[Chemical formula 12]



Cycloartenol ferulate

[0064]

Further, Compound 2 is also known to be contained in a plant belonging to family *Liliaceae*, family *Leguminosae*, family *Gramineae*, family *Solanaceae*, or family *Musaceae* (see [Phytochemistry, USA, 1977, vol. 16, pp. 140-141], [Handbook of phytochemical constituents of GRAS herbs and other economic plants, 1992, USA, CRC Press] or [Hager's Handbuch der Pharmazeutischen Praxis, vol. 2-6, 1969-1979, Deutschland, Springer Verlag, Berlin]). Hence, Compound 2 can be extracted from these plants using the known methods such as an organic solvent extraction method or a hot water extraction method (see, e.g., Japanese Patent No. 3924310). It is preferable that Compound 2 is extracted, for example, from plants of *Liliaceae Aloe*.

The molecular weight and the structure of the compound manufactured as described above can be determined or confirmed, for example, by mass spectrometry (MS) and nuclear magnetic resonance spectrometry (NMR).

[0065]

Further, Compound 2 may be a pharmaceutically acceptable salt. Such a salt is as exemplified concerning Compound 1.

[0066]

The agent of the present invention contains, as an active ingredient, a compound selected from the group consisting of Compound 1 and Compound 2. The compound may be one kind, that is, either of Compound 1 or Compound 2 alone, or may be a mixture of Compound 1 and Compound

2.

When Compound 1 or Compound 2 is used alone, either Compound 1 (mainly, 4-methylcholest-7-en-3-ol, 4-methylergost-7-en-3-ol, or 4-methylstigmast-7-en-3-ol) or Compound 2 (mainly, 9,19-cyclolanostan-3-ol or 24-methylene-9,19-cyclolanostan-3-ol) is preferable.

Among them, 4-methylcholest-7-en-3-ol is particularly preferable as Compound 1, and 9,19-cyclolanostan-3-ol is particularly preferable as Compound 2, from a view point of physical properties such as solubility which are considered when used as an active ingredient of the agent for raising a deep body temperature.

Further, when Compound 1 and Compound 2 are compared, Compound 1 (mainly, 4-methylcholest-7-en-3-ol, 4-methylergost-7-en-3-ol or 4-methylstigmast-7-en-3-ol) is more preferable.

Further, for each of Compound 1 or Compound 2, one kind of a compound may be used, or a plurality of compounds may be used by mixing them.

The agent of the present invention contains, as an active ingredient, preferably a compound selected from the group consisting of 4-methylcholest-7-en-3-ol, 4-methylergost-7-en-3-ol, 4-methylestigmast-7-en-3-ol, 9,19-cyclolanostan-3-ol and 24-methylene-9,19-cyclolanostan-3-ol.

[0067]

When both Compound 1 and Compound 2 are combined (mixture of Compound 1 and Compound 2), the range of the mass ratio of Compound 1 and Compound 2 includes, for example, the following:

Compound 1 : Compound 2 is preferably 5 : 1 to 1 : 5, further preferably 3 : 1 to 1 : 3, and particularly preferably 2 : 1 to 1 : 2.

[0068]

The content of the above-described compound in the composition for raising a deep body temperature of the present invention can be appropriately selected depending on the symptoms or the like, and the total amount of the compound is preferably at least 0.00001% by mass or more, more

preferably at least 0.0001% by mass or more, furthermore preferably at least 0.0005% by mass or more, and particularly preferably at least 0.001% by mass or more. Further, the upper limit of the amount in an agent for raising a deep body temperature of the present invention is not particularly limited, but the total amount is, for example, 90% by mass or less, preferably 70% by mass or less, and more preferably 50% by mass or less.

[0069]

In addition, the composition for raising a deep body temperature of the present invention can also be in an embodiment in which a composition containing 0.00001% by mass or more of a compound selected from the group consisting of a compound 1 and a compound 2 is included as an active ingredient.

As such a composition, for example, an extract obtained from a plant containing the above-described compound 1, an extract obtained from a plant containing the above-described compound 2, and an extract obtained from a plant containing both of the compound 1 and the compound 2, and a mixture thereof can be mentioned.

[0070]

In this regard, as the plant containing the compound 1 and the compound 2, for example, a plant of the family Liliaceae, the family Leguminosae, the family Poaceae, the family Solanaceae, the family Musaceae or the like can be mentioned.

[0071]

As an example of a natural plant containing the compounds, it is known that, in Aloe vera, compounds 1 (mainly, 4-methylcholest-7-en-3-ol, 4-methylergost-7-en-3-ol, and 4-methylstigmast-7-en-3-ol), and compounds 2 (mainly, 9,19-cyclolanostane-3-ol, and 24-methylene-9,19-cyclolanostane-3-ol) are contained.

[0072]

Therefore, by using Aloe vera as a raw material, any of 4-methylcholest-7-en-3-ol, 4-

methylergost-7-en-3-ol, or 4-methylstigmast-7-en-3-ol (compound 1), and any of 9,19-cyclolanostane-3-ol, or 24-methylene-9,19-cyclolanostane-3-ol (compound 2) are each purified, and a mixture containing a compound 1 and a compound 2 at a ratio that the compound 1 : the compound 2 is 5 : 1 to 1 : 5, preferably 3 : 1 to 1 : 3, and particularly preferably 2 : 1 to 1 : 2 can be obtained. The composition thus obtained is suitable as an active ingredient of the composition for raising a deep body temperature of the present invention.

[0073]

Further, an agent for raising a deep body temperature or a composition for raising a deep body temperature, of the present invention is preferably in an embodiment in which a composition containing one or two or more compounds selected from the group consisting of a lophenol compound and a cyclolanostane compound in the total amount of preferably at least 0.0001% by mass or more, more preferably at least 0.0005% by mass or more, and particularly preferably at least 0.001% by mass or more is included as an active ingredient.

[0074]

An agent for raising a deep body temperature or a composition for a deep body temperature, of the present invention can be used in an embodiment of a medicine or a pharmaceutical composition.

In a case of using the agent or composition in an embodiment of a medicine or a pharmaceutical composition, the agent for raising a deep body temperature of the present invention is preferably used in an embodiment in which the agent is orally or parenterally administered to a mammal including a human.

[0075]

An agent for raising a deep body temperature of the present invention is effective for preventing and/or improving the symptoms caused by a decrease in deep body temperature.

[0076]

In this regard, in the present specification, the concept of “prevention” includes reduction of a risk of developing a disease. Further, the concept of “improvement” includes both of the treatment of and the relief of symptoms.

[0077]

In the present invention, as the symptoms or disease caused by a decrease in deep body temperature, sensitivity to cold, a digestive system disease (vomiting, chronic diarrhea, loss of appetite, or loose stools), hypothermia, a respiratory disease (asthma, or phlegm-rheum), dizziness, orthostatic dizziness, orthostatic disorder (trouble waking up), edema of lower limbs, chronic malaise, feeling of enervation, or reduction in intellectual work capacity can be mentioned.

In this regard, the symptoms due to the sensitivity to cold defined in the present invention indicate symptoms particularly due to a lowering in deep body temperature among the symptoms caused by a decrease in deep body temperature, peripheral vasoconstriction, a decrease in blood flow, or the like.

Further, the digestive system disease defined in the present invention indicates a digestive system disease particularly due to a decrease in deep body temperature among the causes of a digestive system disease, for example, a lowering in deep body temperature, food poisoning, overdose of alcohol, sex hormone imbalance, and the like.

In addition, symptoms due to dizziness, orthostatic dizziness, orthostatic disorder (trouble waking up), edema of lower limbs, and chronic malaise, which are defined in the present invention, indicate symptoms particularly due to a lowering in deep body temperature among the symptoms due to a decrease in deep body temperature, heart failure, disturbance of the daily rhythm, and sex hormone imbalance.

The agent for raising a deep body temperature or composition for raising a deep body temperature of the present invention is effective for preventing and/or improving one or multiple symptoms among the above-described symptoms.

Among them, the food and drink composition of the present invention can be suitably used for sensitivity to cold caused by a lowering in deep body temperature, and a respiratory disease (asthma, or phlegm-rheum) caused by a lowering in deep body temperature.

[0078]

The form of the agent for raising a deep body temperature or composition for a deep body temperature of the present invention is not particularly limited, and can be appropriately selected depending on the usage. Specifically, as the form, a tablet, a pill, powder, a liquid, suspension, emulsion, granules, a capsule, syrup, a suppository, an injection, ointment, a patch preparation, eye drops, nose drops, or the like can be mentioned.

[0079]

The time of administration of the agent for raising a deep body temperature or composition for a deep body temperature of the present invention is not particularly limited, and can be appropriately selected depending on the target disease. Further, it is preferred that the dosage is determined depending on the dosage form, the usage, the patient age, the sex, other conditions, the severity of symptoms, and the like.

The dosage of the agent for raising a deep body temperature or composition for a deep body temperature of the present invention is appropriately selected depending on the usage, the patient age, the sex, the severity of symptoms, other conditions, and the like. In general, the dosage as a guide is in a range of preferably 0.0001 to 100 mg/day, more preferably 0.001 to 50 mg/day, and particularly preferably 0.01 to 10 mg/day, in terms of the amount of the active ingredient.

In addition, it is preferred that the agent for raising a deep body temperature or composition for a deep body temperature of the present invention is continuously used preferably for 3 weeks or more, more preferably for 6 weeks or more, and particularly preferably for 12 weeks or more.

[0080]

The agent for raising a deep body temperature or composition for a deep body temperature of the present invention may contain an additive agent that is generally used in a medicine. Examples of the additive agent include an excipient, a binding agent, a disintegrant, a lubricating agent, a stabilizer, a flavoring agent, a diluent, a surfactant, and a solvent for an injection.

[0081]

The agent for raising a deep body temperature or composition for a deep body temperature of the present invention can be produced by mixing the above-described compound as an active ingredient with a carrier for medicine. The agent for raising a deep body temperature of the present invention can be produced by formulating, for example, the above-described compound together with the above-described additive agents.

Further, the agent for raising a deep body temperature or composition for a deep body temperature of the present invention can also be produced by formulating an extract that has been obtained by performing an extraction using hot water or various solvents, supercritical extraction, or subcritical extraction, with the use of a known plant containing the above-described compound as a raw material together with the above-described additive agents.

In particular, the agent for raising a deep body temperature or composition for a deep body temperature of the present invention, which contains a compound 1 and a compound 2 at a mass ratio in a specific range, can be produced by mixing respective compounds at a mass ratio in the above-described range. In addition, such an agent for raising a deep body temperature or composition for a deep body temperature can also be produced by using a known plant or the like containing a compound 1 and a compound 2 as a raw material, and an extract prepared by a method such as an extraction using hot water or various solvents, supercritical extraction, or subcritical extraction.

[0082]

Further, the present invention may also be a food and drink composition for raising a

deep body temperature. In the present invention, the “food and drink composition” includes feed that is ingested by an animal other than a human, in addition to a food and drink that is ingested by a human.

[0083]

The food and drink composition for raising a deep body temperature of the present invention contains a compound selected from the group consisting of a compound 1 and a compound 2, as an active ingredient. The compound may be one kind, that is, either a compound 1 or a compound 2 singly alone, or may be a mixture of a compound 1 and a compound 2.

In a case where a compound 1 or a compound 2 is used alone, the compound is preferably either a compound 1 (mainly, 4-methylcholest-7-en-3-ol, 4-methylergost-7-en-3-ol, or 4-methylstigmast-7-en-3-ol), or a compound 2 (mainly, 9,19-cyclolanostane-3-ol, or 24-methylene-9,19-cyclolanostane-3-ol).

Among them, in view of physical properties such as solubility, which are considered in a case where a food and drink composition for raising a deep body temperature is used as an active ingredient, 4-methylcholest-7-en-3-ol is particularly preferred as the compound 1, and 9,19-cyclolanostane-3-ol is particularly preferred as the compound 2.

In addition, in a case where the compound 1 and the compound 2 are compared with each other, the compound is more preferably the compound 1 (mainly, 4-methylcholest-7-en-3-ol, 4-methylergost-7-en-3-ol, or 4-methylstigmast-7-en-3-ol).

Further, also in each of the compound 1 and the compound 2, one compound may be used singly alone, or multiple compounds may be used as a mixture thereof.

The food and drink composition for raising a deep body temperature of the present invention preferably contains as an active ingredient, a compound selected from the group consisting of 4-methylcholest-7-en-3-ol, 4-methylergost-7-en-3-ol, 4-methylstigmast-7-en-3-ol, 9,19-cyclolanostane-3-ol, and 24-methylene-9,19-cyclolanostane-3-ol.

[0084]

In a case where both of the compound 1 and the compound 2 are combined with each other (mixture of the compound 1 and the compound 2), as the range of the mass ratio of the compound 1 to the compound 2, for example, the following mass ratios can be mentioned.

The ratio of the compound 1 : the compound 2 is preferably 5 : 1 to 1 : 5, furthermore preferably 3 : 1 to 1 : 3, and particularly preferably 2 : 1 to 1 : 2.

[0085]

The content of the compound in the food and drink composition for raising a deep body temperature of the present invention can be appropriately selected depending on the symptoms or the like, and the total amount is preferably at least 0.00001% by mass or more, more preferably at least 0.0001% by mass or more, furthermore preferably at least 0.0005% by mass or more, and particularly preferably at least 0.001% by mass or more. In addition, the upper limit of the amount in the food and drink composition for raising a deep body temperature of the present invention is not particularly limited, and as the total amount, 90% by mass or less, preferably 70% by mass or less, or more preferably 50% by mass or less can be mentioned.

[0086]

Further, the food and drink composition for raising a deep body temperature of the present invention includes a composition containing a compound selected from the group consisting of a compound 1 and a compound 2, as an active ingredient. The compounds may be contained in one kind alone, or in multiple kinds thereof.

As such a composition, for example, an extract obtained from a plant containing the above-described compound 1, an extract obtained from a plant containing the above-described compound 2, and an extract obtained from a plant containing both of the compound 1 and the compound 2, and a mixture thereof can be mentioned.

[0087]

For example, as an example of the compound contained in a natural plant, it is known that, in Aloe vera, compounds 1 (mainly, 4-methylcholest-7-en-3-ol, 4-methylergost-7-en-3-ol, and 4-methylstigmast-7-en-3-ol), and compounds 2 (mainly, 9,19-cyclolanostane-3-ol, and 24-methylene-9,19-cyclolanostane-3-ol) are contained.

[0088]

Therefore, by using Aloe vera as a raw material, any of 4-methylcholest-7-en-3-ol, 4-methylergost-7-en-3-ol, or 4-methylstigmast-7-en-3-ol (compound 1), and any of 9,19-cyclolanostane-3-ol, or 24-methylene-9,19-cyclolanostane-3-ol (compound 2) are each purified, and a mixture containing a compound 1 and a compound 2 at a ratio that the compound 1 : the compound 2 is 5 : 1 to 1 : 5, preferably 3 : 1 to 1 : 3, and particularly preferably 2 : 1 to 1 : 2 can be obtained. The composition thus obtained is suitable as an active ingredient of the food and drink composition for raising a deep body temperature of the present invention.

[0089]

In addition, it is preferred that the food and drink composition for raising a deep body temperature of the present invention is in an embodiment in which a composition containing one or two or more compounds selected from the group consisting of a lophenol compound and a cyclolanostane compound in the total amount of preferably at least 0.00001% by mass or more, more preferably at least 0.0001% by mass or more, furthermore preferably at least 0.0005% by mass or more, and particularly preferably at least 0.001% by mass or more is included as an active ingredient.

[0089]

The food and drink composition for raising a deep body temperature of the present invention is effective for preventing and/or improving the symptoms and disease caused by a lowering in deep body temperature.

In the food and drink composition for raising a deep body temperature of the present

invention, the symptoms and disease caused by a lowering in deep body temperature are similar to those of a subject in need of prevention or improvement therefor in the described-above embodiment of a medicine.

[0091]

Further, the amount of the compound in the food and drink composition for raising a deep body temperature may also be an amount suitable for ingesting the compound in the total amount in a range of preferably 0.0001 to 100 mg/day, more preferably 0.001 to 50 mg/day, and particularly preferably 0.01 to 10 mg/day depending on the embodiment. Therefore, it is preferred that the food and drink composition for raising a deep body temperature of the present invention is used to ingest the above-described compound in the total amount of preferably 0.0001 to 100 mg/day, more preferably 0.001 to 50 mg/day, and particularly preferably 0.01 to 10 mg/day.

In addition, it is preferred that the food and drink composition for raising a deep body temperature of the present invention is continuously used preferably for 3 weeks or more, more preferably for 6 weeks or more, and particularly preferably for 12 weeks or more.

[0092]

The food and drink composition for raising a deep body temperature is preferably a food with health claims. The term "food with health claims" means a food that is directly or indirectly indicated with an effect of preventing a disease or an effect of reducing a risk of developing a disease, or a food that is filed with Consumer Affairs Agency as a food indicating the functionality on the product package on the basis of scientific evidence with the responsibility of the business operator. For example, at present, a food sold in the form of a food for specified health use, a food with function claims, a dietary supplement, or the like in Japan can be mentioned.

[0093]

As the form of the food and drink composition for raising a deep body temperature, it is not particularly limited, and a drink such as a soft drink, a carbonated drink, a nutritional drink, a

fruit juice drink, or a lactic acid bacteria drink (including a concentrated stock solution or powder for preparation of such a drink) are particularly preferred from the viewpoint of efficiently ingesting the above-described compound.

[0094]

Further, as to the form of a functional food and drink, a supplement in a granular state, in a tablet shape, or in a liquid state is also preferred in that it is easy for a person who ingests the functional food and drink to know the ingestion amount of the active ingredient.

[0095]

In addition, it is also preferred that such a functional food and drink is in the form that an indication of application of “for preventing or improving the symptoms caused by a decrease in deep body temperature”, or “for raising a deep body temperature” is attached. That is, it is preferred that the food and drink composition for raising a deep body temperature of the present invention is sold as a food and drink composition for preventing and/or improving the symptoms caused by a decrease in deep body temperature, which contains a compound selected from the group consisting of a compound 1 and a compound 2, as an active ingredient, and to which application of, for example, “for raising a deep body temperature” is attached.

[0096]

The above-described “indication” includes all indications having a function to inform a consumer the above-described application. That is, if the indication is an indication that can recall and analogize the above-described application, regardless of the purpose of indication, the content of indication, the object and medium to be indicated, and the like, all of such indications fall into the above-described “indication”.

Further, the above-described “indication ... is attached” means that there is an indication action that is allowed to recognize the indication by associating the indication with a food and drink composition (product) for raising a deep body temperature.

The indication action is preferably an indication action with which a consumer can directly recognize the above-described application. Specifically, description action of the above-described application to a product or product packaging thereof according to the food and drink composition for raising a deep body temperature of the present invention, and description action of the above-described application to an advertisement, a price list, or a transaction document (including a document provided by an electromagnetic means) regarding a product can be mentioned.

[0097]

On the other hand, as the content (indication content) to be indicated, an indication approved by the government or the like (for example, an indication that is approved on the basis of various systems established by the government, and performed in a manner based on such an approval) is preferred.

For example, an indication of a health food, a functional food and drink, an enteral nutritive food, a food for special dietary uses, a food with health claims, a food for specified health uses, a food with nutrient function claims, a food with function claims, a quasi drug, or the like can be mentioned. In particular, an indication approved by Consumer Affairs Agency, for example, an indication approved under the food system for specified health use or a system similar thereto can be mentioned. As an example of the latter one, an indication as a food for specified health uses, an indication as a qualified food for specified health uses, an indication of giving an influence on the structure and function of the body, an indication of reducing a risk of developing a disease, or the like can be mentioned. In detail, an indication as a food for specified health uses (particularly, indication of application of health) prescribed in the Ordinance for Enforcement of the Health Promotion Act (Japanese Ordinance of the Ministry of Health, Labour and Welfare No. 86 of April 30, 2003), and an indication similar thereto can be listed as typical examples.

[0098]

The wording indicating the above-described application is not limited to the wording of “for preventing and/or improving the symptoms caused by a decrease in deep body temperature”, or “for raising a deep body temperature”, and even if any wording other than the above wording, of course the wording is included in the scope of the present invention as long as it expresses an action or effect of preventing or improving the symptoms caused by a decrease in deep body temperature.

Further, it is preferred that the food and drink composition for raising a deep body temperature of the present invention includes in addition to the indication of the above-described application, an indication of the active ingredient, and further an indication indicating the relationship between the application and the active ingredient.

[0099]

The food and drink composition for raising a deep body temperature can be produced by mixing a compound selected from a compound 1 and a compound 2 as an active ingredient. The food and drink composition for raising a deep body temperature of the present invention can be produced, for example, by mixing the compound with a raw material for a food and drink composition, and processing the obtained mixture.

In addition, the food and drink composition for raising a deep body temperature can also be produced by processing an extract that has been obtained by performing an extraction using hot water or various solvents, supercritical extraction, or subcritical extraction, with the use of a known plant containing the above-described compound as a raw material together with a raw material for a food and drink composition.

[00100]

Further, in a case where the form of the food and drink composition for raising a deep body temperature is made to a supplement in a granular state, in a tablet shape, or in a liquid state, it is preferred that the compound that is an active ingredient is formulated together with, for example, saccharides such as lactulose, maltitol, and lactitol, and other saccharides including, for example,

dextrin, starch, and the like; proteins such as gelatin, soy protein, and maize protein; amino acids such as alanine, glutamine, and isoleucine; polysaccharides such as cellulose, and gum arabic; fats and oils such as soybean oil, and neutral fatty acid triglyceride; and the like.

Examples

[00101]

Next, the present invention will be described in more detail with reference to Examples, however, the present invention is not limited to the following Examples.

[00102]

[Production Example 1]

(Production of lophenol compound (compound 1))

By using a homogenizer, 100 kg of mesophyll of aloe vera gel (transparent gel part) was liquefied, and into the liquefied material, 100 L of a mixture of ethyl acetate and butanol (at a mixture ratio of ethyl acetate : butanol = 3 : 1) was added, and the obtained mixture was stirred. The stirred mixture was left to stand overnight, and then an ethyl acetate and butanol mixture and a water layer was separated to recover the ethyl acetate and butanol mixture. The ethyl acetate and butanol mixture was concentrated under reduced pressure. The mass of an extract of the recovered ethyl acetate and butanol mixture was 13.5 g.

A solution in which 13 g of the extract was dissolved in 1 ml of a chloroform and methanol (at a mixture ratio of chloroform : methanol = 1 : 1) mixture was passed through a column filled with 400 g of silica gel 60 (manufactured by Merck KGaA), and the extract was adsorbed on the column, and then the elution was performed by a stepwise gradient method in which the methanol concentration is raised stepwisely, with the use of a chloroform and methanol mixture (at each of the mixture ratios of chloroform : methanol = 100 : 1, 25 : 1, 10 : 1, 5 : 1, and 1 : 1), and the obtained elute was fractionated for every mixture at each of the mixture ratios. It was confirmed that among these obtained fractions, the lophenol compound of the present invention was present in

a fraction that had been eluted at the mixture ratio of chloroform : methanol = 25 : 1, by normal phase and reversed phase thin-layer chromatography (silica gel 60F254 and RP-18F2543 manufactured by Merck KGaA).

After removing the solvent of this fraction, the fraction was dissolved in 1 ml of a mixture of chloroform and methanol (at a mixture ratio of chloroform : methanol = 1 : 1), the obtained mixture was passed through a column filled with 100 g of silica gel 60, the fraction was adsorbed on the column, and then eluted with 1100 ml of a mixture of hexane and ethyl acetate (at a mixture ratio of hexane : ethyl acetate = 4 : 1). The eluted fraction was fractionated into portions of 300 ml (fraction A), 300 ml (fraction B), and 500 ml (fraction C) in this order.

It was confirmed that a lophenol compound being the compound 1 of the present invention was concentrated into the fraction A by normal phase and reversed phase thin-layer chromatography, and further, the fraction A was separated by using high-performance liquid chromatography (HPLC) equipped with COSMOSIL C18 (manufactured by NACALAI TESQUE, INC.) with a mixture of chloroform and hexane (at a mixture ratio of chloroform : hexane = 85 : 15) to obtain 4-methylcholest-7-en-3-ol, 4-methylergost-7-en-3-ol, and 4-methylstigmast-7-en-3-ol in amounts of 1.3 mg, 1.2 mg, and 1 mg, respectively. The structure of each of the compounds was confirmed by mass spectrometry (MS) analysis and nuclear magnetic resonance (NMR).

[00103]

[Production Example 2]

(Production of cyclolanostane compound (compound 2))

Into 8.0 g of γ -oryzanol (manufactured by Oryza Oil & Fat Chemical Co., Ltd.), 250 ml of distilled water, 50 g of sodium hydroxide, 150 ml of isopropanol, 150 ml of ethanol, and 150 ml of methanol were added, and the obtained mixture was heated under reflux for 2 hours by using a mantle heater. After the reaction, the reaction mixture was added into 1300 ml of water, and the generated white precipitate was suction filtered to obtain a solid matter. In order to wash the

remaining alkali, the obtained residue was suspended in 1000 ml of water, and then the suction filtration was performed again. This process was repeated twice, and the final residue was lyophilized under reduced pressure to obtain 5.91 g of oryzanol hydrolysate. The hydrolysate was purified by HPLC to obtain 2435 mg of cycloartenol, and 1543 mg of 24-methylene-9,19-cyclolanostane-3-ol (compound 2).

Next, by using the obtained cycloartenol, synthesis of 9,19-cyclolanostane-3-ol (compound 2) was performed.

Into an autoclave, 302 mg of cycloartenol, 150 ml of isopropanol, and 1.0 g of 5% palladium-supported carbon catalyst in a powder form were charged, these materials were sealed in the autoclave, the inside of the autoclave was replaced with nitrogen gas, and then hydrogen gas was introduced to the autoclave while applying a pressure of 3 kg/cm². The materials were heated while being stirred, and at the time point at which the temperature reached 50°C, the pressure of hydrogen was adjusted to 5 kg/cm², and the reaction was performed for 6 hours while maintaining the pressure by supplementing the absorbed hydrogen. The reaction mixture was filtered to remove the catalyst, the filtrate was concentrated, and then purified by silica gel column chromatography (eluent: chloroform 100%), to obtain 275 mg of 9,19-cyclolanostane-3-ol.

[00104]

[Production Example 3]

(Preparation of sample with the mixture of lophenol compound and cyclolanostane compound added)

By using the 4-methylcholest-7-en-3-ol, 4-methylergost-7-en-3-ol, and 4-methylstigmast-7-en-3-ol obtained in Production Example 1, and the 9,19-cyclolanostane-3-ol, and 24-methylene-9,19-cyclolanostane-3-ol obtained in Production Example 2, a mixture of a lophenol compound and a cyclolanostane compound, which had a mass ratio of the lophenol compound to the cyclolanostane compound of lophenol compound (compound 1) : cyclolanostane compound (compound 2) = 1 : 1,

was obtained.

By using propylene glycol (manufactured by Wako Pure Chemical Industries, Ltd.), the mixture of a lophenol compound and a cyclolanostane compound was dispersed to prepare a solution diluted 5000 times. The solution was diluted 100 times with distilled water to prepare a test sample 1.

That is, a test sample 1 containing a compound 1 (lophenol compound) and a compound 2 (cyclolanostane compound) in the total amount of 0.0002% by mass was produced.

[00105]

[Example 1]

In the present Example, an action of raising a deep body temperature of a composition containing a compound 1 and a compound 2 was examined.

[00106]

(1) Test sample

In the present Example, a test sample 1 obtained in the above Production Example 3 was used. In this regard, as a control sample, an aqueous 1% propylene glycol solution was used.

[00107]

(2) Test method

C57BL/6 mice each aged 6 weeks (manufactured by Japan SLC, Inc.) were preliminarily raised for one week on animal feed D12450B (manufactured by Research Diets, Inc.), and then the sample was switched to animal feed D12492 (manufactured by Research Diets, Inc.), and the mice was further raised for 2 weeks. The raised C57BL/6 mice were divided into a control group and a test sample group so that each group had 12 mice, and continuous administration of the test sample was started. In this regard, the continuous administration of the test sample was performed by administering a test sample 1 to each of the 12 mice so as to be 200 μ L/10 g body weight per day. On the other hand, in the control group, as a test sample, an aqueous 1% propylene glycol solution in

the same amount as that of the above test sample 1 was administered to each of the 12 mice.

After the lapse of 6 weeks and 12 weeks from the start of continuous administration of the test sample 1, a deep body temperature was checked by rectal temperature measurement (data logger “ONDOTORI” (TR-7wf) manufactured by T&D Corporation).

[00108]

(3) Test Results

The deep body temperatures after 6 weeks from the start of administration were shown in Table 1, the deep body temperatures after 12 weeks were shown in Table 2, and the changes in the deep body temperature of each group were shown in Fig. 1. In each of Tables, each of the values is expressed as an average value $\pm$ standard deviation of 12 mice, and the p value in each of Tables indicates a significance probability by a Student t test.

[00109]

[Table 1]

Table 1 Measurement results of deep body temperature (rectal temperature) (6-week ingestion)

Test group	Deep body temperature (°C)	p value (vs. control group)
Control group	36.15 $\pm$ 0.32	
Test sample group	36.28 $\pm$ 0.33	0.200

[0110]

[Table 2]

Table 2 Measurement results of deep body temperature (rectal temperature) (12-week ingestion)

Test group	Deep body temperature (°C)	p value (vs. control group)
Control group	35.85 $\pm$ 0.26	
Test sample group	36.09 $\pm$ 0.26	0.046

[0111]

Further, as a result of performing a similar test on a test sample containing 0.0002% by

mass of the above-described compound 1 alone, and also on a test sample containing 0.0002% by mass of the compound 2 alone, in all of the test samples, as with the case of the test sample 1, the deep body temperature showed a higher temperature as compared with that in the control group.

[0112]

(4) Consideration

From the results of Tables 1 and 2, as compared with those in the control group, the test sample group in which a test sample containing 0.0002% by mass of a cyclolanostane compound and a lophenol compound had been ingested had a deep body temperature higher than that in the control group.

In addition, when Tables 1 and 2 were compared with each other, the difference of the deep body temperature between the test sample group and the control group was larger in the 12-week ingestion than that in the 6-week ingestion.

[0113]

From the above, it was found that the cyclolanostane compound and the lophenol compound each have an action of raising a deep body temperature.

More specifically, it was found that 4-methylcholest-7-en-3-ol, 4-methylergost-7-en-3-ol, 4-methylstigmast-7-en-3-ol, 9,19-cyclolanostane-3-ol, and 24-methylene-9,19-cyclolanostane-3-ol each have an action of raising a deep body temperature.

[0114]

Further, it was found from the graph of Fig. 1 that in both of the 6-week ingestion and the 12-week ingestion, the deep body temperature in the test sample group is higher than that in the control group.

In addition, the change in the body temperature from the 6-week ingestion to the 12-week ingestion in the test sample group was -0.19°C , and on the other hand, the change in the body temperature from the 6-week ingestion to the 12-week ingestion in the control group was -0.30°C .

[0115]

In this regard, although a decrease in deep body temperature was observed from the 6-week ingestion to the 12-week ingestion in both of the test sample group and the control group, considering that the deep body temperature decreases due to an external factor such as cooling or stress, it can be said from the graph of Fig. 1 (comparison of changes in body temperature between the test sample group and the control group) that there was an effect of suppressing the lowering in deep body temperature in the test sample group.

[0116]

From the results of Tables 1 and 2, and Fig. 1, it was found that by ingesting a cyclolanostane compound and a lophenol compound in an amount of 0.00001% by mass or more, and desirably 0.0001% by mass or more, a more excellent action of raising a deep body temperature and a more excellent action of preventing a lowering in deep body temperature can be obtained.

Further, from the fact that an effect of raising a deep body temperature and an effect of preventing a lowering in deep body temperature were recognized in the test sample group in which a test sample containing a cyclolanostane compound and a lophenol compound had been ingested, it was found that there is an action of raising a deep body temperature and an action of preventing a lowering in deep body temperature also in a composition containing a cyclolanostane compound and a lophenol compound in an amount of 0.00001% by mass or more.

[0117]

[Example 2]

A medicine having an effect of raising a deep body temperature and made of the following composition was produced by the following method.

2% by mass of a composition containing 0.001% by mass of a mixture containing a lophenol compound produced in Production Example 1 and a cyclolanostane compound produced in Production Example 2 at a ratio of lophenol compound : cyclolanostane compound = 1 : 1, which

was prepared with the addition and dispersion of carboxymethyl cellulose (CMC: manufactured by Dai-ichi Kogyo Seiyaku Co., Ltd.), 2% by mass of medium chain fatty acid (MCT: manufactured by RIKEN VITAMIN Co., Ltd.), 4% by mass of glycerine fatty acid ester (manufactured by RIKEN VITAMIN Co., Ltd.), 0.5% by mass of saponin (manufactured by MARUZEN PHARMACEUTICALS CO., LTD.), 0.2% of ethanol (manufactured by Japan Alcohol Corporation), 1.3% by mass of maltitol (manufactured by HAYASHIBARA CO., LTD.), 78% of glycerin (manufactured by NOF CORPORATION), and further water were added and mixed so that the whole amount was 100% by mass, and a syrupy pharmaceutical preparation containing a mixture of a lophenol compound (compound 1) and a cyclolanostane compound (compound 2) in a final concentration of 0.00002% by mass was produced.

The medicament of the present Example is effective for improving the symptoms caused by a lowering in deep body temperature.

[0118]

[Example 3]

A food and drink composition made of the following composition and having an effect of preventing and/or improving the symptoms caused by a lowering in deep body temperature was produced by the following method.

By containing 4% of a mixture containing a lophenol compound produced in Production Example 1 and a cyclolanostane compound produced in Production Example 2 at a ratio of lophenol compound : cyclolanostane compound = 6.1 : 3.9, and additionally by mixing 2% of medium chain fatty acid (MCT: manufactured by RIKEN VITAMIN Co., Ltd.), 4% of glycerine fatty acid ester (manufactured by RIKEN VITAMIN Co., Ltd.), 0.5% of saponin (manufactured by MARUZEN PHARMACEUTICALS CO., LTD.), 0.2% of ethanol (manufactured by Japan Alcohol Corporation), 1.3% of maltitol (manufactured by HAYASHIBARA CO., LTD.), 78% of glycerin (manufactured by NOF CORPORATION), and 10% of water, a food additive agent containing a mixture of a

cyclolanostane compound and a lophenol compound was produced.

By adding the produced food additive agent into a drink and mixing uniformly, a food and drink composition containing a mixture of a lophenol compound (compound 1) and a cyclolanostane compound (compound 2) in a final concentration of 0.00002% by mass was produced.

[0119]

[Example 4]

By containing 0.2% of the test sample 1 produced in Production Example 3, and additionally by mixing 2% of medium chain fatty acid (MCT: manufactured by RIKEN VITAMIN Co., Ltd.), 4% of glycerine fatty acid ester (manufactured by RIKEN VITAMIN Co., Ltd.), 0.5% of saponin (manufactured by MARUZEN PHARMACEUTICALS CO., LTD.), 0.2% of ethanol (manufactured by Japan Alcohol Corporation), 1.3% of maltitol (manufactured by HAYASHIBARA CO., LTD.), 78% of glycerin (manufactured by NOF CORPORATION), and 10% of water, a food and drink composition containing a mixture of a cyclolanostane compound and a lophenol compound was produced.

[0120]

The food and drink composition of the present Example is effective for preventing and/or improving the symptoms caused by a lowering in deep body temperature.

Industrial Applicability

[0121]

The present invention can be used for preventing and/or improving the symptoms caused by a lowering in deep body temperature.

CLAIMS

1. A composition for raising a deep body temperature, comprising one or two or more compounds selected from the group consisting of a lophenol compound and a cyclolanostane compound as an active ingredient.
2. The composition for raising a deep body temperature according to claim 1, wherein a composition comprising one or two or more compounds selected from the group consisting of a lophenol compound and a cyclolanostane compound in an amount of 0.00001% by mass or more is used as an active ingredient.
3. The composition for raising a deep body temperature according to claim 1 or 2, wherein the composition for raising a deep body temperature is used for preventing and/or improving a disease caused by a lowering in deep body temperature.
4. The composition according to any one of claims 1 to 3, wherein the composition is a food and drink composition, or a pharmaceutical composition.
5. Use of one or two or more compounds selected from the group consisting of a lophenol compound and a cyclolanostane compound, in production of a composition for preventing or improving a disease caused by a lowering in deep body temperature.
6. One or two or more compounds selected from the group consisting of a lophenol compound and a cyclolanostane compound, used for preventing or improving a disease caused by a lowering in deep body temperature.
7. Use of one or two or more compounds selected from the group consisting of a lophenol compound and a cyclolanostane compound, wherein the one or two or more compounds are used for preventing or improving a disease caused by a lowering in deep body temperature.
8. A method for preventing or improving a disease caused by a lowering in deep body temperature, comprising administering one or two or more compounds selected from the group consisting of a lophenol compound and a cyclolanostane compound to a subject in need of

prevention or improvement of a disease caused by a lowering in deep body temperature.