

DESCRIPTION

TITLE OF INVENTION: VASODILATION COMPOSITION CONTAINING
ERGOTHIONEINE

5

TECHNICAL FIELD

[0001]

The present invention relates to a vasodilator composition containing
ergothioneine and the like.

10

BACKGROUND ART

[0002]

In recent years, food components with homeostatic effects have been
vigorously researched and developed to prevent lifestyle diseases. One of the essential
15 functions for maintaining a healthy body is the circulatory function. Daily
consumption of foods that maintain or improve circulatory function may not only
improve the circulatory function but also alleviating conditions associated with
circulatory function, such as irregularities in blood pressure, stiff shoulders, headaches,
sensitivity to cold, and reduced cerebral circulation.

20

[0003]

ATP-sensitive potassium (K_{ATP}) channels close in response to an increase in
ATP concentration in cells and open in response to a decrease in ATP concentration or
an increase in ADP concentration in cells. K_{ATP} channels have been found in various
tissues including islet β cells, cardiac muscle, skeletal muscle, smooth muscle, and
25 central and peripheral neurons. Potassium channel openers (KCOs), developed as
antihypertensive drugs, have the action of activating K_{ATP} channels, and are now
attracting attention as targets of novel therapeutic agents for cardiovascular diseases
(Non-Patent Literature 1).

[0004]

30

Ergothioneine is an amino acid found in mushrooms and the like. L-
ergothioneine is present in nature. Patent Literature 1 discloses a vascular wall
strengthening agent containing soy protein and/or ergothioneine as active ingredients,
and reports that the participant experienced improved blood circulation and a reduction
in the appearance of dark circles under the eyes upon application of the vascular wall
35 strengthening agent under the eyes.

CITATION LIST

- Patent Literature

[0005]

5 Patent Literature 1: JP 2022-006753 A

- Non-Patent Literature

[0006]

Non-Patent Literature 1: Folia Pharmacol. Jpn. 126, 311 to 316 (2005)

10

SUMMARY OF INVENTION

- Technical Problem

[0007]

15 However, Patent Literature 1 does not disclose the vasodilatory effect of ergothioneine or its influence on K_{ATP} channels.

[0008]

The present invention aims to provide a vasodilator composition.

- Solution to Problem

20 [0009]

As a result of extensive studies to solve the above problem, the present inventors found that L-ergothioneine or a salt thereof has a vasodilatory effect.

[0010]

25 In other words, the present invention relates to, but is not limited to, the following vasodilator compositions.

(1) A vasodilator composition containing ergothioneine or a salt thereof as an active ingredient.

(2) The composition according to (1) above, wherein the composition is used for preventing or alleviating hypertension.

30 (3) The composition according to (1) or (2) above, wherein the composition induces vasodilation via an ATP-sensitive potassium channel.

(4) The composition according to any one of (1) to (3) above, wherein the composition is an oral composition.

35 (5) The composition according to any one of (1) to (4) above, wherein the composition is a food or beverage.

(6) The composition according to any one of (1) to (5) above, wherein the composition is labeled with at least one function selected from the group consisting of “inducing vasodilation for maintenance of blood flow”, “promoting blood circulation”, “preventing or alleviating hypertension”, “preventing or alleviating stiff shoulders”, “preventing or alleviating headaches”, “preventing or alleviating sensitivity to cold”, “preventing reduction in cerebral circulation”, and “improving cerebral circulation”.

(7) A method for inducing vasodilation, including administering ergothioneine or a salt thereof to a subject.

(8) Use of ergothioneine or a salt thereof for inducing vasodilation.

- Advantageous Effects of Invention

[0011]

The present invention can provide a vasodilator composition.

BRIEF DESCRIPTION OF DRAWINGS

[0012]

FIG. 1 is a graph showing the evaluation results of the inhibitory activity of L-ergothioneine against substrate binding to ATP-sensitive potassium channels.

FIG. 2 is a graph showing changes in diastolic blood pressure in a test food group and a control food group.

FIG. 3 is a graph showing changes in systolic blood pressure in the test food group and the control food group.

DESCRIPTION OF EMBODIMENTS

[0013]

A vasodilator composition of the present invention contains ergothioneine or a salt thereof as an active ingredient. Hereinbelow, the vasodilator composition of the present invention is also referred to as the composition of the present invention.

Ergothioneine is a type of sulfur-containing amino acid. In the present invention, ergothioneine is preferably L-ergothioneine.

The salt of ergothioneine is not limited as long as it is a pharmacologically acceptable salt or a dietarily acceptable salt, and it may be either an acid salt or a basic salt. Examples of the acid salt include inorganic acid salts such as hydrochloride, sulfate, nitrate, and phosphate; and organic acid salts such as acetate, citrate, maleate, malate, oxalate, lactate, succinate, fumarate, and propionate. Examples of the basic

salt include alkali metal salts such as sodium salt and potassium salt, and alkaline earth metal salts such as calcium salt and magnesium salt.

[0014]

Ergothioneine or a salt thereof is not limited in any way by its form, production method, or the like. Ergothioneine or a salt thereof that can be used may be a chemically synthesized product or a purified extract of a natural product. L-ergothioneine is abundantly present in golden/yellow oyster mushrooms (scientific name: *Pleurotus cornucopiae* var. *citrinopileatus*) belonging to the genus *Pleurotus* of the family *Pleurotaceae*. L-ergothioneine is also present in mushrooms such as common mushrooms (scientific name: *Agaricus bisporus*) including white button mushrooms, cremini mushrooms, and portabella mushrooms; grey oyster mushrooms (scientific name: *Pleurotus ostreatus*), shiitake (scientific name: *Lentinula edodes*), hen-of-the-woods (scientific name: *Grifola Frondosa*), reishi mushrooms (scientific name: *Ganoderma lucidum*), lion's mane mushrooms (scientific name: *Hericium erinaceus*), Yanagi-matsutake (scientific name: *Agrocybe aegerita*), girolles (scientific name: *Cantharellus cibarius*), porcini mushrooms (scientific name: *Boletus edulis*), and common morel mushrooms (scientific name: *Morchella esculenta*). When L-ergothioneine is obtained from a natural product, preferably, it is extracted from a golden/yellow oyster mushroom, for example. Ergothioneine or a salt thereof can also be produced by microbial fermentation. Ergothioneine or a salt thereof may be in an isolated form.

[0015]

L-ergothioneine or a salt thereof is present in natural products as well as food and beverages. These are compounds that have been consumed. Thus, for example, long-term ingestion of ergothioneine or a salt thereof is less likely to cause problems in terms of safety. The present invention can provide a highly safe vasodilator composition.

[0016]

As described in EXAMPLES below, L-ergothioneine inhibited substrate binding to ATP-sensitive potassium (K_{ATP}) channels. In addition, ingestion of L-ergothioneine resulted in a reduction in both diastolic blood pressure and systolic blood pressure compared to when it was not ingested.

Inhibition of substrate binding to K_{ATP} channels is known to open the K_{ATP} channels, leading to vasodilation. Thus, ergothioneine induces vasodilation via K_{ATP} channels. Ergothioneine or a salt thereof is capable of inducing vasodilation via K_{ATP}

channels. Ergothioneine or a salt thereof induces vasodilation to exert the effects including reduction in blood pressure.

[0017]

5 The composition of the present invention exhibits a vasodilatory effect and is used for preventing or alleviating conditions or diseases in which vasodilation is effective. The phrase "preventing conditions or diseases" as used herein encompasses suppressing the onset, delaying the onset, reducing the incidence rate, reducing the risk of onset, and the like. The phrase "alleviating conditions or diseases" encompasses helping a subject recover from conditions or diseases, alleviating conditions or disease
10 symptoms, making positive changes in conditions or disease symptoms, delaying or suppressing progression of conditions or diseases, and the like. The recovery encompasses partial recovery.

[0018]

15 The conditions or diseases in which vasodilation is effective include, for example, hypertension, stiff shoulders, headaches, sensitivity to cold, and reduced cerebral circulation. The vasodilatory effect is expected to prevent or alleviate hypertension, stiff shoulders, headaches, sensitivity to cold, and reduced cerebral circulation.

20 In particular, the composition of the present invention is preferably used for preventing or alleviating hypertension.

[0019]

The composition of the present invention may be an oral composition or a parenteral composition, preferably an oral composition.

25 The oral composition may specifically be a food or beverage, an oral pharmaceutical product, an oral quasi-pharmaceutical product, feed, or the like, preferably a food or beverage or an oral pharmaceutical product, more preferably a food or beverage. The composition of the present invention may be a material, preparation, or the like to be added to a food or beverage, a pharmaceutical product, a quasi-pharmaceutical product, feed, or the like.

30 [0020]

The composition of the present invention is applicable for therapeutic use (medical use) and non-therapeutic use (non-medical use). The "non-therapeutic" is a concept that does not include medical activities, i.e., a concept that does not include methods of surgery, therapy, or diagnosis of humans.

35 [0021]

The composition of the present invention can contain optional additives and optional components in addition to ergothioneine or a salt thereof, as long as the effects of the present invention are not impaired. Such additives and components can be selected according to the composition form or the like. When the composition of the present invention is provided as an oral composition, the composition may contain any additives and the like that can be commonly used for oral compositions such as food and beverages, pharmaceutical products, quasi-pharmaceutical products, feed, and the like.

[0022]

When the composition of the present invention is provided as a food or beverage, a pharmaceutical product, a quasi-pharmaceutical product, feed, or the like, any common method can be used for production.

The oral composition of the present invention may be in any form such as a solid (e.g., powder, granule, tablet), a liquid, or a paste.

[0023]

For example, when the composition of the present invention is provided as a food or beverage, components usable in food or beverages (e.g., food materials and optional food additives) can be added to ergothioneine or a salt thereof to provide various food or beverages. The food or beverage is not limited. Examples thereof include general food or beverages, health foods, health supplements, health drinks, foods with function claims, foods for specified health uses, and foods for the sick. The health foods, health supplements, foods with function claims, foods for specified health uses, and the like can be used in various forms of preparations such as fine granules, tablets, granules, powders, capsules, chewable tablets, dry syrups, syrups, liquid agents, beverages, energy drinks, and liquid foods.

[0024]

When the composition of the present invention is provided as a pharmaceutical product or a quasi-pharmaceutical product, for example, a pharmacologically acceptable carrier, an optional additive, or the like can be added to ergothioneine or a salt thereof to provide various dosage forms of pharmaceutical products or quasi-pharmaceutical products. Such a carrier, additive, or the like may be any pharmacologically acceptable one that can be used in pharmaceutical products or quasi-pharmaceutical products. Examples thereof include excipients, binders, disintegrants, lubricants, antioxidants, and colorants. One or more of these can be used. The form of administration (ingestion) of the pharmaceutical product or the quasi-pharmaceutical

product may be oral or parenteral (e.g., transdermal, transmucosal, enteral, or injection) administration. When the composition of the present invention is provided as a pharmaceutical product or a quasi-pharmaceutical product, it is preferably an oral pharmaceutical product or an oral quasi-pharmaceutical product. Examples of dosage forms for oral administration of a pharmaceutical product or a quasi-pharmaceutical product include liquids, tablets, powders, fine granules, granules, sugar-coated tablets, capsules, suspensions, emulsions, and chewable tablets. Examples of the dosage forms for parenteral administration include injections, intravenous agents, ointments, lotions, adhesive skin patches, suppositories, nasal agents, and transpulmonary agents (inhalants). The pharmaceutical product may be for non-human animals.

[0025]

When the composition of the present invention is provided as feed, ergothioneine or a salt thereof is simply added to feed. The feed includes feed additives. Examples of the feed include feed for farm animals such as cows, pigs, chickens, sheep, and horses; feed for small animals such as rabbits, rats, and mice; and pet food for animals such as dogs, cats, and birds.

[0026]

The subject (administration subject) who ingests the composition of the present invention or to whom the composition is administered is not limited. The administration subject is preferably a human or non-human mammal, more preferably a human.

In one embodiment, the administration subject may be, for example, a subject needing or wanting vasodilation or a subject needing or wanting to prevent or alleviate conditions or diseases in which vasodilation is effective. Examples of such a subject include middle-aged and older people. In one embodiment, the composition of the present invention is suitable as a vasodilator composition for middle-aged and older people; or a composition for middle-aged and older people, for preventing or alleviating conditions or diseases in which vasodilation is effective. The term "middle-aged and older people" includes the elderly. The middle-aged and older people may be those who are 40 years old and older, for example. In one embodiment, the elderly are preferred subjects among the middle-aged and older people. The elderly may be people who are 60 years old and older or 65 years old and older, for example. The administration subject may be a healthy person. For example, the composition of the present invention can be used in healthy people for purposes such as vasodilation; or preventing or alleviating conditions or diseases in which vasodilation is effective. In

the present invention, particularly preferred subjects are healthy people who are 60 years old and older but under 75 years old, and most preferred subjects are healthy people who are 60 years old or older but under 65 years old.

[0027]

5 The amount of ergothioneine or a salt thereof in the composition of the present invention is not limited and can be set according to the form of the composition or the like.

 The amount of ergothioneine or a salt thereof in the composition of the present invention in terms of ergothioneine is, for example, preferably 0.0001% by weight or
10 more, more preferably 0.001% by weight or more, while preferably 90% by weight or less, more preferably 50% by weight or less.

 In one embodiment, the amount of ergothioneine or a salt thereof in the composition of the present invention in terms of ergothioneine is preferably 0.0001 to 90% by weight, more preferably 0.001 to 50% by weight. The amount of
15 ergothioneine or a salt thereof can be measured by high-performance liquid chromatography (HPLC).

[0028]

 Herein, in the case of ergothioneine, the expression regarding the amount of ergothioneine or a salt thereof in terms of ergothioneine or an expression similar thereto
20 refers to the amount of ergothioneine; whereas in the case of a salt of ergothioneine, the expression or an expression similar thereto refers to a value obtained by multiplying the number of moles of the salt by the molecular weight of ergothioneine.

[0029]

 The composition of the present invention can be ingested or administered using
25 an appropriate method depending on the form thereof. In one embodiment, preferably, the composition of the present invention is orally ingested (orally administered). The administration amount (intake) of the composition of the present invention is not limited. The administration amount may be any amount sufficient to achieve the vasodilatory effect and may appropriately be set according to the form of administration,
30 administration method, the weight of the subject, and the like.

[0030]

 In one embodiment, when the composition of the present invention is ingested by or administered to a human (adjust) as a subject, the administration amount of ergothioneine or a salt thereof (in terms of ergothioneine) per day is preferably 2 mg or
35 more, more preferably 5 mg or more, still more preferably 7 mg or more, while

preferably 50 mg or less, more preferably 25 mg or less, still more preferably 20 mg or less. In one embodiment, the daily administration amount of the composition of the present invention as the amount of ergothioneine or a salt thereof (in terms of ergothioneine) to a human (adult) per day is preferably 2 to 50 mg, more preferably 5 to 25 mg, still more preferably 5 to 20 mg, further more preferably 7 to 20 mg.

Preferably, the compound in the above amount is ingested or administered in one or more portions per day, for example, in one to several portions (e.g., two or three portions) per day. In one embodiment, preferably, ergothioneine or a salt thereof in the above amount is orally ingested by or administered to a human. The above administration amount may be an administration amount per 60 kg body weight. In one embodiment, the composition of the present invention can be used to enable daily ingestion or administration of ergothioneine or a salt thereof in the above amount to a human per 60 kg body weight, for example.

[0031]

The amount of ergothioneine or a salt thereof in the composition of the present invention per adult daily intake is preferably 2 to 50 mg, more preferably 5 to 25 mg, still more preferably 5 to 20 mg, particularly preferably 7 to 20 mg, in terms of ergothioneine.

[0032]

The composition of the present invention may, for example, be labeled with a vasodilatory function; or a function resulting from vasodilation.

The composition of the present invention may, for example, be labeled with at least one function selected from the group consisting of “inducing vasodilation for maintenance of blood flow”, “promoting blood circulation”, “preventing or alleviating hypertension”, “preventing or alleviating stiff shoulders”, “preventing or alleviating headaches”, “preventing or alleviating sensitivity to cold”, “preventing reduction in cerebral circulation” and “improving cerebral circulation”.

In one embodiment, preferably, the composition of the present invention is a food or beverage labeled with one or more functions described above. The label may be one indicating use of the composition for obtaining the function. The label may be attached to the composition itself, or may be attached to a container or package of the composition.

[0033]

As described above, L-ergothioneine inhibits substrate binding to K_{ATP} channels. Thus, ergothioneine or a salt thereof can also be used as an active ingredient

for inhibiting substrate binding to K_{ATP} channels. In addition, the composition of the present invention may be used as an inhibitor of substrate binding to K_{ATP} channels. An inhibitor of substrate binding to K_{ATP} channels that contains ergothioneine or a salt thereof as an active ingredient is also an embodiment of the present invention.

5 [0034]

The present invention also encompasses the following method:

a method for inducing vasodilation, including administering ergothioneine or a salt thereof to a subject.

The method may be therapeutic or non-therapeutic.

10 [0035]

The present invention also encompasses the following use:

use of ergothioneine or a salt thereof for inducing vasodilation.

The use may be therapeutic or non-therapeutic.

Administering ergothioneine or a salt thereof to a subject enables vasodilation.

15 [0036]

In the above method and use, the preferred embodiments of ergothioneine or a salt thereof are the same as described above for the composition of the present invention. Ergothioneine or a salt thereof may include one type of ergothioneine or a salt thereof or two types of ergothioneine or a salt thereof. In the above method and use, preferably, ergothioneine or a salt thereof is administered to (ingested by) a subject at least once a day, for example, one to several times (e.g., two or three times) a day. In the above method and use, ergothioneine or a salt thereof is preferably orally administered (ingested). The above use is preferably for humans or non-human mammals, more preferably for humans.

20 [0037]

In the above method and use, ergothioneine or a salt thereof is simply used in an amount (effective amount) sufficient to achieve a desired effect. The preferred administration amount of ergothioneine or a salt thereof, preferred administration subjects, and the like are as described above for the composition of the present invention. Ergothioneine or a salt thereof may be administered directly or may be administered in the form of a composition containing the ergothioneine or a salt thereof. For example, the composition of the present invention described above may be used.

[0038]

35 The present invention encompasses use of ergothioneine or a salt thereof for producing a vasodilator composition.

The present invention encompasses use of ergothioneine or a salt thereof for producing a composition for preventing or alleviating hypertension.

The present invention also relates to ergothioneine or a salt thereof for use in preventing or alleviating hypertension.

5 [0039]

The numerical range defined by the lower limit and the upper limit herein, i.e., "the lower limit to the upper limit", includes the lower limit and the upper limit. For example, the range defined by "1 to 2" means 1 or more and 2 or less, with 1 and 2 being included. Herein, the range may be any combination of any upper limit and any
10 lower limit.

EXAMPLES

[0040]

The present invention is described in further detail below with reference to
15 examples. The present invention is not limited to these examples.

[0041]

<Example 1>

(Evaluation of inhibitory activity against substrate binding to ATP-sensitive potassium channels)

20 To evaluate the molecular targets of L-ergothioneine, an in vitro assay was conducted on ATP-sensitive potassium (K_{ATP}) channels. The in vitro assay was outsourced to Eurofins Panlabs and performed according to the following procedure.

[0042]

A membrane fraction (containing K_{ATP} channels, available from Eurofins
25 Cerep) in an amount of 400 μ g from rat cerebral cortex was incubated at 22°C for 60 minutes in a 50 mM Tris-HCl buffer (pH 7.4) with 0.1 nM [3 H]glibenclamide and L-ergothioneine (L-ergothioneine concentration: 100 μ M or 1000 μ M). Glibenclamide is a K_{ATP} channel inhibitor. Nonspecific binding was determined in the presence of 1 μ M glibenclamide (without L-ergothioneine). Since excess glibenclamide prevents
30 [3 H]glibenclamide from binding to K_{ATP} channels, the radioactivity detected therein represents nonspecific binding. The membrane fraction was filtered and washed, and the substrate-binding inhibitory activity of L-ergothioneine was evaluated based on the measured radioactivity. A larger amount of [3 H]glibenclamide binding to K_{ATP} channels results in higher radioactivity in the membrane fraction.

35 [0043]

FIG. 1 is a graph showing the evaluation results of the inhibitory activity of L-ergothioneine against substrate binding to ATP-sensitive potassium channels. The concentration (μM) along the horizontal axis indicates the concentration of L-ergothioneine.

5 The inhibitory activity (%) against substrate binding to K_{ATP} channels was determined by the following procedure. From the radioactivity of the membrane fraction in the reaction solution without L-ergothioneine (control) taken as 100% and the radioactivity of the membrane fraction in the reaction solution with L-ergothioneine, the relative activity (%) of the membrane fraction in the reaction solution with L-
10 ergothioneine (100 μM or 1000 μM) relative to the control was determined. When the binding of glibenclamide to K_{ATP} channels is inhibited by L-ergothioneine, the radioactivity of the membrane fraction decreases. The inhibitory activity (%) against substrate binding to K_{ATP} channels was determined by subtracting the relative activity (%) of the membrane fraction with L-ergothioneine from the radioactivity (100%) of the
15 membrane fraction in the control.

[0044]

L-ergothioneine inhibited the binding of glibenclamide as a substrate to K_{ATP} channels. It is known that opening of K_{ATP} channels induces vasodilation. Thus, L-ergothioneine presumably exerts a vasodilatory effect through K_{ATP} channels.

20 [0045]

<Example 2>

(Evaluation of blood pressure in human as subject)

To evaluate the effect of a supplement containing ergothioneine on human blood pressure, a placebo-controlled, randomized, double-blind, parallel-group
25 comparative study was conducted. In the study, the subjects were healthy adults who were 60 years old or older but under 65 years old (test food group: 9 people, control food group: 10 people, total: 19 people). They ingested a capsule with 8 mg of ergothioneine (test food) or a capsule without ergothioneine (control food) once a day for 12 weeks.

30 [0046]

First, the participants' blood pressure was assessed before the start of the study (i.e., prior to ingestion of the test food or control food). After 12 weeks of ingesting either the test food or the control food, the participants' blood pressure was measured again (Week 12 assessment). According to the study protocol, blood pressure was
35 measured on the non-dominant upper arm. Measurements were taken three times

consecutively in a seated position, after at least 10 minutes of rest following the participant's arrival. The median of the three measurements was used as the measurement for the assessment day. Blood pressure was measured under the supervision of a physician by a nurse or medical technician using a medical electronic sphygmomanometer AVE-1500 PASESA (Shisei Datum Co., Ltd.).

[0047]

(Evaluation food)

Two types of test foods were prepared, designed to be indistinguishable in appearance, flavor, and the like.

- Test food: capsule with the test substance (L-ergothioneine, 8 mg)
- Control food: capsule without the test substance

In addition to the test substance, the ingredients used in both types of capsules included dextrin, calcium stearate, and hydroxypropyl methylcellulose. The control food was produced using the same ingredients as the test food, except that it did not contain the test substance (L-ergothioneine).

[0048]

The average blood pressure (mmHg) of the 9 participants in the test food group was used as the blood pressure of the test food group. The average blood pressure (mmHg) of the 10 participants in the control food group was used as the blood pressure of the control food group. For each group, the change in blood pressure (Δ blood pressure (mmHg)) was calculated by subtracting the pre-study assessment blood pressure from the Week 12 assessment blood pressure. The change in blood pressure (Δ blood pressure (mmHg)) before the study was set to 0. Two blood pressures, diastolic blood pressure and systolic blood pressure, were measured. The change in diastolic blood pressure and the change in systolic blood pressure, Δ diastolic blood pressure (mmHg) and Δ systolic blood pressure (mmHg), were calculated.

[0049]

FIG. 2 is a graph showing changes in diastolic blood pressure in the test food group and the control food group. Between-group significance was tested using a two-sample t-test (**: $p < 0.01$, vs. control food group). As a result, a significant decrease in diastolic blood pressure was observed in the test food group.

In FIG. 2, black squares (■) represent the test food group, and white squares (□) represent the control group. On the horizontal axis, "0W" indicates the pre-study assessment, and "12W" indicates the Week 12 assessment.

[0050]

FIG. 3 is a graph showing changes in systolic blood pressure in the test food group and the control food group. Between-group significance was tested using a two-sample t-test (**: $p < 0.01$, vs. control food group). As a result, the increase in systolic blood pressure was more reduced in the test food group than in the control food group.

5 In FIG. 3, black squares (■) represent the test food group, and white squares (□) represent the control group. On the horizontal axis, “0W” indicates the pre-study assessment, and “12W” indicates the Week 12 assessment.

[0051]

10 The results of Examples 1 and 2 suggest that L-ergothioneine induces vasodilation via K_{ATP} channels, thus exhibiting the effect of improving the blood pressure (the effect of preventing or alleviating hypertension).

CLAIMS

Claim 1. A vasodilator composition comprising ergothioneine or a salt thereof as an active ingredient.

5

Claim 2. The composition according to claim 1,
wherein the composition is used for preventing or alleviating hypertension.

Claim 3. The composition according to claim 1 or 2,
10 wherein the composition induces vasodilation via an ATP-sensitive potassium
channel.

Claim 4. The composition according to claim 1 or 2,
wherein the composition is an oral composition.

15

Claim 5. The composition according to claim 4,
wherein the composition is a food or beverage.

Claim 6. The composition according to claim 1 or 2,
20 wherein the composition is labeled with at least one function selected from the
group consisting of “inducing vasodilation for maintenance of blood flow”, “promoting
blood circulation”, “preventing or alleviating hypertension”, “preventing or alleviating
stiff shoulders”, “preventing or alleviating headaches”, “preventing or alleviating
sensitivity to cold”, “preventing reduction in cerebral circulation”, and “improving
25 cerebral circulation”.

Claim 7. A method for inducing vasodilation, comprising
administering ergothioneine or a salt thereof to a subject.

30 Claim 8. Use of ergothioneine or a salt thereof for inducing vasodilation.