

DESCRIPTION

TITLE OF INVENTION: ORAL COMPOSITION AND SOFT CAPSULE AGENT

5 TECHNICAL FIELD

[0001]

The present invention relates to an oral composition containing ergothioneine or its salt, a fat or oil, and an emulsifier. The present invention also relates to a soft capsule containing the oral composition.

BACKGROUND ART

[0002]

Generally, a soft capsule containing a poorly oil-soluble active ingredient is produced by filling a gelatin-coated capsule with a dispersion prepared by dispersing the active ingredient in an edible fat or oil. According to Patent Literature 1, for example, a combination of multiple types of emulsifiers such as reacted monoglycerides and distilled monoglycerides is used to uniformly disperse an active ingredient in an edible fat or oil, whereby a liquid composition for filling soft capsules is provided in which a poorly oil-soluble component is dispersed in an edible fat or oil.

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CITATION LIST

- Patent Literature

[0003]

Patent Literature 1: JP 5405242 B

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SUMMARY OF INVENTION

- Technical Problem

[0004]

Ergothioneine is a poorly oil-soluble sulfur-containing amino acid and has various physiological

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activities including an antioxidant ability. Thus, foods such as supplements containing ergothioneine or its salt are useful for maintaining or promoting health. However, since ergothioneine is poorly oil-soluble, a composition
5 containing a fat or oil and ergothioneine is unfortunately prone to separation, thus leaving room for improvement. When a composition containing an active ingredient undergoes separation, the separation causes problems such as an undesirable appearance of a final product and a
10 difficulty in providing a final product containing a precisely desired amount of the active ingredient.
[0005]

The present invention aims to provide a separation-resistant and uniform oral composition containing
15 ergothioneine or its salt and a fat or oil.

- Solution to Problem

[0006]

The present invention encompasses the following oral
20 composition and the like.

(1) An oral composition containing: ergothioneine or its salt; a fat or oil; and an emulsifier having an HLB of 10 or less, wherein the emulsifier contains a polyhydric alcohol fatty acid ester having a C12-C22 saturated fatty
25 acid as a constituent fatty acid, and the fat or oil is contained at a content of 10 wt% or more.

(2) The oral composition according to (1) above, wherein the polyhydric alcohol fatty acid ester is at least one selected from the group consisting of a glycerol fatty
30 acid ester, a polyglycerol fatty acid ester, a sorbitan fatty acid ester, a propylene glycol fatty acid ester, and a sucrose fatty acid ester.

(3) The oral composition according to (1) or (2) above, wherein the saturated fatty acid has a carbon number
35 of 12 to 18.

(4) The oral composition according to any one of (1) to (3) above, wherein the emulsifier is contained at a content of 1 to 30 wt%.

(5) The oral composition according to any one of (1) to (4) above, wherein the oral composition is an oral composition for filling soft capsules.

(6) A soft capsule containing contents including the oral composition according to any one of (1) to (5) above; and a capsule coating.

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- Advantageous Effects of Invention
[0007]

The present invention can provide a separation-resistant and uniform oral composition containing ergothioneine or its salt and a fat or oil.

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DESCRIPTION OF EMBODIMENTS

[0008]

The oral composition of the present invention contains ergothioneine or its salt, a fat or oil, and an emulsifier having an HLB of 10 or less.

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[0009]

Ergothioneine is one of the sulfur-containing amino acids. In the present invention, ergothioneine is preferably L-ergothioneine.

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The salt of ergothioneine is not limited as long as it is a pharmacologically acceptable salt or a dietary 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

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magnesium salt.

[0010]

Ergothioneine or its salt is not limited in any way by its form, production method, or the like. Chemically synthesized ergothioneine or its salt may be used, or naturally extracted and purified ergothioneine or its salt may be used. L-ergothioneine is abundant 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 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 its salt can also be produced by microbial fermentation. Ergothioneine or its salt may be in an isolated form.

[0011]

The ergothioneine or its salt content of the oral composition of the present invention is not limited and may be set according to the form of the composition or the like.

In the oral composition of the present invention, the ergothioneine or its salt content in terms of ergothioneine is, for example, preferably 0.01 wt% or more, more preferably 0.1 wt% or more, and is preferably 10 wt% or

less, more preferably 5 wt% or less. In one embodiment, the ergothioneine or its salt content in terms of ergothioneine is preferably 0.01 to 10 wt%, more preferably 0.1 to 10 wt%, still more preferably 0.1 to 5 wt%. When
5 the ergothioneine or its salt content is in the above range, the separation of the oral composition of the present invention is prevented, and the oral composition of the present invention is allowed to efficiently exert physiological functions of ergothioneine or its salt.

10 Herein, regarding the expression for the amount in terms of ergothioneine or an expression similar thereto, in the case of ergothioneine, the expression refers to the ergothioneine content; whereas in the case of a salt of ergothioneine, the expression refers to a value obtained by
15 multiplying the molar number of the salt by the molecular weight of ergothioneine.

The ergothioneine content can be measured by high-performance liquid chromatography (HPLC).

[0012]

20 The oral composition of the present invention may contain any fat or oil that can be orally ingested by humans. Examples include edible fats and oils that are liquids at room temperature (25°C). Examples of such edible fats and oils include vegetable fats and oils such
25 as olive oil, sesame oil, rice germ oil, safflower oil, soybean oil, corn oil, rapeseed oil, palm oil, palm olein, palm kernel oil, sunflower oil, grape oil, cottonseed oil, coconut oil, and peanut oil; medium chain fatty acid triglyceride; squalene; and fish oil. Fish oil contains
30 many compounds such as triglycerides (fats and oils) containing, as constituent fatty acids, omega-3 fatty acids including fatty acids such as docosahexaenoic acid (DHA) and eicosapentaenoic acid (EPA). For example, the fish oil that may be used is a DHA-containing fat or oil in which
35 the content of a compound containing DHA as a constituent

fatty acid is concentrated to 40 wt% or more or 50 wt% or more in terms of DHA.

The expression for the content in terms of docosahexaenoic acid or an expression similar thereto
5 refers to the content in terms of free DHA obtained by isolating DHA by saponification or enzymatic treatment from a compound containing DHA as a constituent fatty acid.

In the oral composition of the present invention, one of these fats and oils may be used alone or two or more
10 thereof may be used in any combination.
[0013]

In the oral composition of the present invention, the fat or oil content is 10 wt% or more relative to the total amount of the composition. When the fat or oil content is
15 in the above range, the oral composition of the present invention is resistant to separation and uniform. The fat or oil content of the oral composition can be appropriately set according to applications and forms. For example, the fat or oil content may be 30 wt% or more, or 50 wt% or
20 more. The fat or oil content may also be, for example, 99 wt% or less, 98 wt% or less, or 90 wt% or less. In one embodiment, the fat or oil content may be 10 to 99 wt%, 30 to 98 wt%, or 50 to 90 wt% in the oral composition of the present invention. When the oral composition of the
25 present invention is liquid, the fat or oil content may be, for example, 40 wt% or more, or 50 wt% or more. The fat or oil content may also be, for example, 99 wt% or less, 98 wt% or less, or 90 wt% or less. When the oral composition of the present invention is liquid, in one embodiment, the
30 fat or oil content may be 40 to 99 wt% or 50 to 98 wt% in the oral composition of the present invention.

The compositional makeup and content of the fat or oil can be measured by gas chromatography (GC).
[0014]

35 The emulsifier contained in the oral composition of

the present invention has an HLB of 10 or less. When the emulsifier has an HLB of 10 or less, the oral composition of the present invention is resistant to separation and uniform. Here, the term "HLB" is an index indicating the
5 degrees of hydrophilicity and lipophilicity of an emulsifier, as calculated by the Griffin method. A lower HLB indicates a higher lipophilicity, and a higher HLB indicates a higher hydrophilicity. The HLB of the emulsifier is preferably 3 or more and 10 or less.

10 [0015]

The emulsifier contains a polyhydric alcohol fatty acid ester having a C12-C22 saturated fatty acid as a constituent fatty acid. When the emulsifier contains a polyhydric alcohol fatty acid ester having a C12-C22
15 saturated fatty acid as a constituent fatty acid, the oral composition is resistant to separation and uniform, increasing the solubility of ergothioneine or its salt of the oral composition in water. A high solubility of ergothioneine or its salt of the oral composition in water
20 is considered to indicate a good solubility of the ergothioneine or its salt in the body when the oral composition is ingested.

Preferably, the emulsifier for use in the oral composition of the present invention is not a polyhydric alcohol fatty acid ester whose main component contains an
25 unsaturated fatty acid as a constituent fatty acid.

[0016]

Preferably, the polyhydric alcohol fatty acid ester is at least one selected from the group consisting of a
30 glycerol fatty acid ester, a polyglycerol fatty acid ester, a sorbitan fatty acid ester, a propylene glycol fatty acid ester, and a sucrose fatty acid ester. The polyhydric alcohol fatty acid ester may be a compound with a monoester bond, a compound with a diester bond, or a compound with a
35 higher ester bond.

[0017]

Examples of the glycerol fatty acid ester include monoglycerides having one fatty acid bonded to glycerol and diglycerides having two fatty acids bonded to glycerol.

5 The glycerol fatty acid ester may be an organic acid monoglyceride further having an organic acid bonded to a hydroxy group of a monoglyceride. Examples of the organic acid include acetic acid, lactic acid, citric acid, succinic acid, and diacetyl tartaric acid. There is a case
10 where a glycerol fatty acid ester contains a trace amount of a triglyceride consisting of three fatty acids bonded to glycerol, but herein, such a triglyceride consisting of three fatty acids bonded to glycerol is treated as a fat or oil when calculating the content.

15 [0018]

The average degree of polymerization of glycerol constituting the polyglycerol fatty acid ester is not limited and is usually 2 or more and 10 or less.

The emulsifier is preferably a glycerol fatty acid
20 ester or a polyglycerol fatty acid ester because the oral composition of the present invention is resistant to separation when such an emulsifier is used.

[0019]

Examples of the C12-C22 saturated fatty acid include
25 lauric acid, myristic acid, pentadecyl acid, palmitic acid, margaric acid, stearic acid, arachidic acid, and behenic acid. Preferably, the emulsifier contains a polyhydric alcohol fatty acid ester having a C12-C18 saturated fatty acid as a constituent fatty acid. Preferred C12-C22
30 saturated fatty acids are lauric acid and stearic acid.

[0020]

Specific examples of the polyhydric alcohol fatty acid ester having a C12-C22 saturated fatty acid as a constituent fatty acid include glycerol fatty acid esters
35 such as lauric acid monoglyceride, palmitic acid

monoglyceride, stearic acid monoglyceride, behenic acid monoglyceride, monostearic acid diglyceride, behenic acid diglyceride, lactic acid ester of glycerol monostearate, and succinic acid ester of glycerol monostearate;

5 polyglycerol fatty acid esters such as pentaglyceryl hexastearate, decaglyceryl decastearate, and decaglyceryl pentastearate; propylene glycol fatty acid esters such as propylene glycol monolaurate, propylene glycol monopalmitate, propylene glycol monostearate, and propylene

10 glycol monobehenate; sorbitan fatty acid esters such as sorbitan monostearate; and sucrose fatty acid esters such as sucrose stearate. In particular, the polyhydric alcohol fatty acid ester is preferably stearic acid monoglyceride, behenic acid monoglyceride, diglyceride monostearate,

15 behenic acid diglyceride, lactic acid ester of glycerol monostearate, succinic acid ester of glycerol monostearate, decaglyceryl decastearate, decaglyceryl pentastearate, or sorbitan monostearate, because the oral composition of the present invention is resistant to separation and uniform

20 when such a polyhydric alcohol fatty acid ester is used.

[0021]

The emulsifier may contain one or more of the polyhydric alcohol fatty acid esters described above. When the emulsifier contains two or more of the polyhydric

25 alcohol fatty acid esters described above, the combination thereof is not limited. Yet, the oral composition of the present invention is more resistant to separation and more uniform when, for example, the emulsifier contains two or more polyhydric alcohol fatty acid esters having

30 constituent fatty acids with different carbon numbers.

[0022]

Preferably, the emulsifier mainly contains a polyhydric alcohol fatty acid ester having a C12-C22 saturated fatty acid as a constituent fatty acid, and the

35 emulsifier contains the polyhydric alcohol fatty acid ester

at a content of 60 wt% or more. The polyhydric alcohol fatty acid ester content of the emulsifier is more preferably 80 wt% or more, still more preferably 90 wt% or more.

5 The emulsifier may contain another component as long as the effect of the present invention is not impaired. Examples of the other component include polyhydric alcohol fatty acid esters containing a saturated fatty acid having 11 or less carbon atoms as a constituent fatty acid, and
10 polyhydric alcohol fatty acid esters containing a C12-C22 unsaturated fatty acid as a constituent fatty acid. In one embodiment, preferably, the emulsifier does not contain a polyhydric alcohol fatty acid ester having an unsaturated fatty acid as a constituent fatty acid.

15 The emulsifier may be a commercial product or a synthetic product. Polyhydric alcohol fatty acid esters having a C12-C22 saturated fatty acid as a constituent fatty acid can be synthesized by a known method.
[0023]

20 In the oral composition of the present invention, the emulsifier (HLB of 10 or less) content is preferably 1 wt% or more, more preferably 3 wt% or more, still more preferably 5 wt% or more relative to the total amount of the composition. The emulsifier content is also preferably
25 30 wt% or less, more preferably 25 wt% or less. In one embodiment, the emulsifier content is preferably 1 to 30 wt%, more preferably 3 to 25 wt%, still more preferably 5 to 25 wt% in the oral composition of the present invention.

 The emulsifier content can be measured by a method
30 such as GC or HPLC.
[0024]

 The oral composition of the present invention may be in any form such as a solid (e.g., powder, granule, or tablet), liquid, or paste. Preferably, the oral
35 composition of the present invention is liquid at 25°C.

Preferably, the oral composition of the present invention is a composition in which ergothioneine or its salt is uniformly dispersed in the fat or oil.

[0025]

5 Ergothioneine and its salts are compounds that are present in natural products and food and beverages and that have been consumed. Thus, for example, daily ingestion of ergothioneine or its salt is less likely to cause problems in terms of safety. The present invention can provide a
10 highly safe and easy-to-ingest oral composition.

[0026]

As described above, ergothioneine and its salts are known to provide various physiological activities and health functions. Known examples include antioxidant
15 action, brain function improving effect, anti-aging action, eye disease alleviating effect, whitening effect, UV absorbing effect, melanin production suppressing effect, active oxygen species scavenging effect, elastase activity inhibitory effect, wrinkle suppressing effect, anti-skin
20 sagging effect, and autophagy promoting effect.

Thus, the oral composition of the present invention can be suitably used for antioxidation, brain function improvement, anti-aging, eye disease alleviation, whitening, UV absorption, melanin production suppression,
25 active oxygen species scavenging, elastase activity inhibition, wrinkle suppression, anti-skin sagging, autophagy promotion, and the like.

[0027]

The oral composition of the present invention is
30 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 The oral composition of the present invention can be

provided in the form of a food or beverage, a pharmaceutical product, a quasi-pharmaceutical product, feed, or the like. The oral 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

[0028]

Specific examples of the oral composition include food or beverages, oral pharmaceutical products, oral quasi-pharmaceutical products, and feed, with food or beverages and oral pharmaceutical products being preferred, and food or beverages being more preferred.

[0029]

The composition of the present invention may contain optional additives and optional components in addition to ergothioneine or a salt thereof a fat or oil, and an emulsifier, as long as the effect of the present invention is not impaired. Such additives and components may be selected depending on the form of the oral composition, for example, and those generally usable in oral compositions such as food or beverages, pharmaceutical products, quasi-pharmaceutical products, and feed can be used. When the oral composition of the present invention is provided as a food or beverage, a pharmaceutical product, a quasi-pharmaceutical product, feed, or the like, any general method can be used for production.

[0030]

For example, when the oral 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 its salt, the fat or oil, and the emulsifier 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, soft capsules, chewable tablets, dry syrups, syrups, liquid agents, beverages, drink supplements, and liquid foods.

[0031]

10 When the oral 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 its salt, the fat or oil, and the emulsifier 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.

15 Examples thereof include excipients, binders, disintegrants, lubricants, antioxidants, and colorants. One or more of these can be used. Examples of the dosage form for oral administration of pharmaceutical products or quasi-pharmaceutical products include liquids, tablets, powders, fine granules, granules, sugar-coated tablets, capsules, soft capsules, suspensions, emulsions, and chewable tablets.

[0032]

 When the oral composition of the present invention is provided as feed, a mixture of ergothioneine or its salt, the fat or oil, and the emulsifier is simply added to feed. The feed includes feed additives. Examples of the feed include livestock feed for 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

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dogs, cats, and birds.

[0033]

The oral composition of the present invention may be ingested by or administered to any subject (administration
5 subject). The administration subject is preferably a human or non-human mammal, more preferably a human.

[0034]

In the oral composition of the present invention, the ergothioneine or its salt content in terms of ergothioneine
10 per adult daily intake is preferably 1 to 100 mg, more preferably 2 to 50 mg, still more preferably 5 to 25 mg, particularly preferably 5 to 20 mg.

The oral composition of the present invention is resistant to separation and uniform, which makes it easy to
15 provide a final product having a desirable appearance and containing a precisely desired amount of ergothioneine or its salt.

[0035]

<Method of preparing oral composition>

20 The oral composition of the present invention can be produced by mixing and stirring ergothioneine or its salt, the fat or oil, and the emulsifier. Preferably, the oral composition is produced by, for example, mixing and stirring the fat or oil and the emulsifier while heating to
25 about 60°C to 80°C, further adding ergothioneine or its salt thereto, and mixing and stirring them together. A preheated or melted emulsifier can be used. Any device may be used for mixing and stirring. For example, a high-speed agitator or high-speed grinding mill such as a biomixer, a
30 homojetter, or a colloid mill can be used.

[0036]

The oral composition of the present invention can be suitably used as the contents of soft capsules. For
example, the oral composition of the present invention is
35 suitable as a composition for filling soft capsules.

[0037]

<Soft capsule>

The present invention also relates to a soft capsule containing the contents including the oral composition and
5 a capsule coating.

In the soft capsule of the present invention, a soft capsule formed from a capsule coating is filled with the contents including the oral composition. The contents may consist of the oral composition. The capsule coating
10 (hereinafter sometimes also simply referred to as "the coating") can be formed from a base material commonly used in capsule coatings.

[0038]

<Method of producing soft capsule>

15 The oral composition prepared can be formed into a soft capsule, for example, by using a known soft capsule molding machine under heating. There are no limitations on the production of the soft capsule, and the soft capsule can be produced according to the production conditions of a
20 soft capsule encapsulation device.

[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
25 example, the range defined by "1 to 2" means 1 or more and 2 or less, with 1 and 2 being inclusive. Herein, the range may be any combination of any upper limit and any lower limit.

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EXAMPLES

[0040]

The present invention is more specifically described below with reference to Examples. The present invention is not limited to these Examples.

35 [0041]

Examples 1 to 10 and Comparative Examples 1 to 10
<Production and separability of composition>

Each of emulsifiers shown in Table 1 was mixed with a fat or oil described below, and each mixture was placed in a transparent polypropylene tube and heated at 70°C to dissolve the emulsifier. Subsequently, L-ergothioneine (125 mg) as ergothioneine was added to the mixture, followed by air cooling while mixing and stirring to form an entirely uniform mixture, whereby a composition was obtained. The fat or oil used was any one of safflower oil, DHA-containing fat or oil, and rice germ oil. Specifically, compositions prepared in Example 1 were: a composition 1-1 containing ergothioneine, safflower oil, and an emulsifier 1; a composition 1-2 containing ergothioneine, DHA-containing fat or oil, and the emulsifier 1; and a composition 1-3 containing ergothioneine, rice germ oil, and the emulsifier 1. Three compositions with different fat or oil types were prepared in each of Example 2 to 10 and Comparative Example 1 to 10 as in Example 1. The mixing ratio of the emulsifier and the fat or oil was as follows when the fat or oil was safflower oil: 1050 mg of emulsifier and 9325 mg of fat or oil (total of ergothioneine, emulsifier, and fat or oil: 10500 mg). The mixing ratio was as follows when the fat or oil was a DHA-containing fat or oil or rice germ oil: 1575 mg of emulsifier and 8800 mg of fat or oil (total of ergothioneine, emulsifier, and fat or oil: 10500 mg).
[0042]

Ergothioneine: L-ergothioneine (synthetic product)
DHA-containing fat or oil: fat or oil containing a compound containing docosahexaenoic acid as a constituent fatty acid at a content of 40 wt% or more in terms of docosahexaenoic acid
[0043]

After air cooling, each composition in the

polypropylene tube was visually checked for separation. The composition in which no separation was confirmed was rated as "o"; the composition in which separation was slightly confirmed was rated as " Δ ", and the composition
5 that underwent complete separation was rated as "x". Table 1 shows the results.

[0044]

[Table 1]

	Emulsifier					Fat or oil		
		HLB	Number of unsaturated bonds	Carbon number and content of main constituent fatty acid	Component	Safflower oil	DHA-containing fat or oil	Rice germ oil
Example 1	Emulsifier 1	3	0	18 (41.9 wt%) 22 (43.5 wt%)	Stearic acid monoglyceride or diglyceride Behenic acid monoglyceride or diglyceride	○	○	○
Example 2	Emulsifier 2	3	0	18	Decaglyceryl decaesterate	○	○	○
Example 3	Emulsifier 3	4	0	18	Propylene glycerol monostearate	△	△	△
Example 4	Emulsifier 4	5	0	18	Decaglyceryl pentastearate	○	○	○
Example 5	Emulsifier 5	5	0	18	Sorbitan monostearate	○	○	○
Example 6	Emulsifier 6	5	0	12	Lauric acid monoglyceride	○	△	○
Example 7	Emulsifier 7	5.4	0	12	Lauric acid monoglyceride	○	○	○
Example 8	Emulsifier 8	6	0	16 (33.2 wt%) 18 (65.8 wt%)	Monopalmitic acid diglyceride Monostearic acid diglyceride	○	△	○
Example 9	Emulsifier 9	8	0	18	Lactic acid ester of glycerol monostearate	○	○	○
Example 10	Emulsifier 10	10	0	18	Succinic acid ester of glycerol monostearate	○	○	○
Comparative Example 1	Emulsifier 11	3	0	8	Caprylic acid monoglyceride	×	×	×
Comparative Example 2	Emulsifier 12	3	1	18	Propylene glycol monooleate	×	×	×
Comparative Example 3	Emulsifier 13	4	1	18	Oleic acid monoglyceride	×	×	×
Comparative Example 4	Emulsifier 14	5	1	18	Sorbitan monooleate	×	×	×
Comparative Example 5	Emulsifier 15	7	0	10	Capric acid monoglyceride	×	×	×
Comparative Example 6	Emulsifier 16	7	1	18	Pentaglycerol trioleate	×	×	×
Comparative Example 7	Emulsifier 17	11	0	18	Decaglycerol distearate	△	△	×
Comparative Example 8	Emulsifier 18	12	0	18	Diglyceryl monostearate	×	×	△
Comparative Example 9	Emulsifier 19	13	0	14	Pentaglycerol monomyristate	×	×	×
Comparative Example 10	Emulsifier 20	13	1	18	Pentaglycerol monooleate	×	×	×

[0045]

The "Number of unsaturated bonds" in Table 1 indicates the number of double bonds in the main constituent fatty acid of the polyhydric alcohol fatty acid ester contained in the emulsifier.

The "Carbon number and content of main constituent fatty acid" indicate the carbon number of a fatty acid with the highest content among the constituent fatty acids of the polyhydric alcohol fatty acid ester contained in the emulsifier, and the content percentage of the fatty acid.

[0046]

The compositions of Examples 1 to 10 were prevented or substantially prevented from separation, regardless of the type of fat or oil, i.e., safflower oil, DHA-containing fat or oil, or rice germ oil. Emulsifiers 11 and 15 each having a constituent fatty acid with a carbon number of less than 12 were used in Comparative Examples 1 and 5, respectively. Emulsifiers 12 to 14, 16, and 20 each containing an unsaturated fatty acid as a constituent fatty acid were used in Comparative Examples 2 to 4, 6, and 10, respectively. Emulsifiers 17 to 20 each having an HLB value of more than 10 were used in Comparative Examples 7 to 10, respectively. In Comparative Examples 1 to 10, the compositions were completely separated when one or any of the following fats and oils was used: safflower oil, DHA-containing fat or oil, and rice germ oil.

[0047]

<Solubility of composition in water>

Next, among the compositions of Examples 1 to 10 and the compositions of Comparative Examples 7 and 8, those rated as "o" or "Δ" for the evaluation of the separability were dispersed in pure water, and the solubility of ergothioneine in water at the time of dispersion was checked by the following procedure. A good solubility in water is considered to indicate a good solubility of

ergothioneine in the body when the oral composition is ingested.

Each composition (168 mg) was weighed out into a 50 mL tube, and pure water (40 mL) was added to the tube. The composition was dispersed in pure water by ultrasonication for 60 minutes in a water bath at 30°C to 40°C. The supernatant (1 mL) of the dispersion was weighed out 60 minutes after the start of ultrasonication, followed by centrifugation at 15000 rpm for 3 minutes. The centrifuged supernatant was filtered through a 0.45 µm filter, and the resulting filtrate was used as a measurement sample. The measurement sample was analyzed by HPLC under the following conditions. The solubility rate of ergothioneine of the composition in water was calculated from the following formula based on the ergothioneine concentration determined by HPLC. Table 2 shows the results. A composition having a solubility rate of 60% or more 60 minutes after the start of ultrasonication was considered to have an excellent solubility in water.

[0048]

HPLC analysis conditions

HPLC device: LC-20AD (product name), available from Shimadzu Corporation

Analytical column: Capcell Pak C18 Type AQ (product Name), 4.6 mm I.D. × 150 mm, available from Osaka Soda., Ltd.

Mobile phase: 0.1% acetic acid aqueous solution

Analysis time: 10 min

Initial pressure: 5.8 MPa

Column temperature: 30°C

Flow rate: 1.0 mL/min

Injection volume: 10 µL

Detection: 254 nm

[0049]

[Math. 1]

$$\text{Solubility (\%)} = \frac{\text{Concentration determined by HPLC analysis } (\frac{\text{mg}}{\text{mL}})}{\text{Weighed value of composition (mg)} \times \frac{\text{Ergothioneine content of composition (g)}}{\text{Total weight of composition (g)}} / \text{Amount of pure water added (mL)}} \times 100$$

[0050]

[Table 2]

	Safflower oil	DHA-containing fat or oil	Rice germ oil
Example 1	97%	64%	92%
Example 2	67%	64%	72%
Example 3	67%	66%	78%
Example 4	81%	82%	88%
Example 5	66%	90%	94%
Example 6	88%	100%	98%
Example 7	101%	87%	90%
Example 8	118%	80%	72%
Example 9	64%	85%	100%
Example 10	67%	96%	94%
Comparative Example 7	57%	43%	-
Comparative Example 8	-	-	56%

5 [0051]

The solubility of ergothioneine in water was excellent in the compositions of Examples 1 to 10. In particular, the solubility of ergothioneine was significantly excellent in the compositions of Examples 6 and 7 in which the emulsifier was lauric acid monoglyceride, regardless of the type of fat or oil, i.e., safflower oil, DHA-containing fat or oil, or rice germ oil. When the fat or oil was safflower oil, the solubility of ergothioneine in water was significantly excellent in the compositions of Examples 1 and 8 in which the emulsifier containing two polyhydric alcohol fatty acid esters having

constituent fatty acids with different carbon numbers was used. When the fat or oil was a DHA-containing fat or oil or rice germ oil, the solubility of ergothioneine in water was significantly excellent in the compositions of Examples
5 6, 7, 9, and 10 in which the emulsifier whose polyhydric alcohol fatty acid ester was lauric acid monoglyceride or organic acid monoglyceride was used.

The solubility of ergothioneine in water was poor in the compositions of Comparative Examples 7 and 8, compared
10 to the compositions of Examples.

CLAIMS

Claim 1. An oral composition comprising:
ergothioneine or its salt;
5 a fat or oil; and
an emulsifier having an HLB of 10 or less,
wherein the emulsifier contains a polyhydric alcohol
fatty acid ester having a C12-C22 saturated fatty acid as a
constituent fatty acid, and the fat or oil is contained at
10 a content of 10 wt% or more.

Claim 2. The oral composition according to claim 1,
wherein the polyhydric alcohol fatty acid ester is at
least one selected from the group consisting of a glycerol
15 fatty acid ester, a polyglycerol fatty acid ester, a
sorbitan fatty acid ester, a propylene glycol fatty acid
ester, and a sucrose fatty acid ester.

Claim 3. The oral composition according to claim 1,
20 wherein the saturated fatty acid has a carbon number
of 12 to 18.

Claim 4. The oral composition according to claim 1,
wherein the emulsifier is contained at a content of 1
25 to 30 wt%.

Claim 5. The oral composition according to claim 1,
wherein the oral composition is an oral composition
for filling soft capsules.

30

Claim 6. A soft capsule comprising:
contents including the oral composition according to
any one of claims 1 to 5; and
a capsule coating.