

DESCRIPTION

TITLE OF INVENTION: COMPOSITION FOR SUPPRESSING DECLINE IN
CURIOSITY OR IMPROVING CURIOSITY

5

TECHNICAL FIELD

[0001]

The present invention relates to a composition for suppressing a decline in
curiosity or improving curiosity, for example.

10

BACKGROUND ART

[0002]

Human abilities can be broadly classified into cognitive abilities and non-
cognitive abilities. Cognitive abilities are intellectual abilities necessary for acquiring
15 information, reasoning, and the like, and typical examples thereof include memory,
executive function, and attention. Non-cognitive abilities are abilities that cannot be
measured by cognitive abilities, and examples thereof include curiosity, perseverance to
carry things through (resilience), and the like.

[0003]

Curiosity has been regarded as a driving force (intrinsic motivation) for free
activities such as “want to know” or “want to experience”, that is, so-called exploratory
behavior. Motivation for exploratory behavior, which is the basis of curiosity, includes
target information or stimuli. According to the type and directionality of such
information, curiosity can be classified into, for example, intellectual curiosity
25 motivated by intellectual information, interpersonal curiosity motivated by interpersonal
information, and the like. A high level of curiosity is considered to be associated with
various beneficial effects such as promotion of mental and physical health, and thus
curiosity has attracted attention in various situations. Scales for measuring curiosity
have also been studied (Non-Patent Literature 1 to 3).

30 [0004]

L-ergothioneine is a type of sulfur-containing amino acid and is known to have
a variety of useful effects. For example, Non-Patent Literature 4 describes that, as a
result of administering ergothioneine to mice and performing a novel object exploration
test to evaluate its effects on learning function, an exploration time for the novel object
35 increased.

CITATION LIST

- Non-Patent Literature

[0005]

- 5 Non-Patent Literature 1: Nishikawa et al., “Individual Differences in Trait Curiosities and Their Relations to Mental Health and Psychological Well-being”, Journal of Japan Health Medicine Association, Vol. 24(1): pp. 40-48, 2015

- Non-Patent Literature 2: Nishikawa et al., “Development of an Epistemic Curiosity Scale: Diverse Curiosity and Specific Curiosity”, The Japanese Journal of Educational Psychology, 2015, Vol. 63, Issue 4, pp. 412-425
- 10

Non-Patent Literature 3: Nishikawa et al., “Development of an Interpersonal Curiosity Scale: Exploration of curiosity about personal emotions, privacy, and attributes”, The Japanese journal of psychology, 2022, Vol. 93, Issue 5, pp. 436-446

- Non-Patent Literature 4: Mitamura et al., “Tamogitake Ganyu Seibun Erugochionein ni yoru Gakushu Kino Kojo Koka” (Effects of Ergothioneine Contained in Tamogi-take on Improvement of Learning Function), Abstracts of the 63rd Annual Meeting of Japanese Society for Food Science and Technology, p. 95 (2Ep1), 2016
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SUMMARY OF INVENTION

- 20 - Technical Problem

[0006]

- The evaluation system of Non-Patent Literature 4 is an experiment that utilizes a habit of mice to show interest in a novel object, in which an object remembered in the past and a newly presented object are displayed side by side and a relative exploration
- 25 time for the novel object is evaluated. This evaluation system is used as a test of memory and learning for evaluating the extent to which mice remember the past object, and is not a test for evaluating curiosity. In fact, Non-Patent Literature 4 concludes that ergothioneine improved the learning function of mice. In Non-Patent Literature 4, the effect of ergothioneine on curiosity is not investigated.

- 30 [0007]

The present invention aims to provide a composition for suppressing a decline in curiosity or improving curiosity.

- Solution to Problem

- 35 [0008]

As a result of intensive studies to solve the above issue, the present inventors have found that L-ergothioneine or a salt thereof has an effect of suppressing a decline in curiosity or improving curiosity.

[0009]

5 In other words, the present invention relates to, for example, but is not limited to, the following composition for suppressing a decline in curiosity or improving curiosity.

(1) A composition for suppressing a decline in curiosity or improving curiosity containing L-ergothioneine or a salt thereof.

10 (2) The composition according to the clause (1), wherein the curiosity is at least one selected from the group consisting of daily curiosity, intellectual curiosity, and interpersonal curiosity.

(3) The composition according to the clause (1) or (2), which is a composition for suppressing a decline in curiosity or improving curiosity in a human.

15 (4) The composition according to any one of the clauses (1) to (3), which is an oral composition.

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

20 (6) Use of L-ergothioneine or a salt thereof for suppressing a decline in curiosity or improving curiosity.

(7) A method for suppressing a decline in curiosity or improving curiosity, the method including administering L-ergothioneine or a salt thereof.

- Advantageous Effects of Invention

25 [0010]

The present invention can provide a composition for suppressing a decline in curiosity or improving curiosity.

DESCRIPTION OF EMBODIMENTS

30 [0011]

The composition for suppressing a decline in curiosity or improving curiosity of the present invention contains L-ergothioneine or a salt thereof. The composition for suppressing a decline in curiosity or improving curiosity of the present invention contains L-ergothioneine or a salt thereof as an active ingredient. Hereinafter, the
35 composition for suppressing a decline in curiosity or improving curiosity of the present

invention may also be referred to as the composition of the present invention.

[0012]

L-ergothioneine is a type of sulfur-containing amino acid. The salt of L-ergothioneine may be any pharmacologically acceptable salt or a dietary acceptable salt, and may be either an acidic salt or a basic salt. Examples of the acidic salt include inorganic acidic salts such as hydrochloride, sulfate, nitrate, and phosphate; and organic acidic 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.

[0013]

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

[0014]

L-ergothioneine or a salt thereof is a compound that is present in naturally occurring products as well as food and beverages and that has a history of safe use. Thus, for example, in terms of safety, long-term ingestion of L-ergothioneine or a salt thereof is less likely to cause problems. The present invention can provide a highly safe composition for suppressing a decline in curiosity or improving curiosity.

[0015]

The composition of the present invention is used for suppressing a decline in curiosity or improving curiosity.

Curiosity refers to a driving force (intrinsic motivation) for exploratory behavior. Exploratory behavior refers to free activities such as “want to know” and “want to experience”. In the present invention, the curiosity also encompasses showing interest in something and an ability to engage in something with interest. In the present invention, suppressing a decline in curiosity or improving curiosity usually refers to suppressing a decline in the level of curiosity or improving the level of curiosity.

[0016]

Suppressing a decline in curiosity includes suppressing a decline in curiosity, preventing a decline in curiosity, maintaining curiosity, delaying progression of a decline in curiosity, stopping a decline in curiosity, and the like. Improving curiosity includes increasing curiosity, reducing a degree of a decline in curiosity, recovering declined curiosity, and the like. Recovery includes at least partial recovery.

[0017]

Intrinsic motivation for exploratory behavior, which is the basis of curiosity, includes target information or stimuli. According to the type of such information, for example, curiosity can be classified into daily curiosity, intellectual curiosity, interpersonal curiosity, and the like. The composition of the present invention may be used for suppressing a decline in one type of curiosity or improving one type of curiosity, or may be used for suppressing a decline in two or more types of curiosity or improving two or more types of curiosity. In an embodiment of the present invention, the curiosity is preferably at least one selected from the group consisting of daily curiosity, intellectual curiosity, and interpersonal curiosity, more preferably intellectual curiosity. The composition of the present invention can be favorably used for suppressing a decline in at least one type of curiosity selected from the group consisting of daily curiosity, intellectual curiosity, and interpersonal curiosity or improving the at least one type of curiosity. The level of curiosity can be evaluated using a curiosity scale.

[0018]

Daily curiosity is curiosity associated with motivation that affects medium- or long-term responses to opportunities and events that may occur in daily life, such as ways of thinking and attitudes in life. Daily curiosity includes medium- or long-term engagement with various opportunities in daily life and positive acceptance of various events. It has been reported that a high level of daily curiosity brings favorable effects

on health and well-being (Non-Patent Literature 1).

[0019]

The level of daily curiosity can be evaluated using the Japanese version of the Curiosity and Exploration Inventory-II (CEI-II) (Non-Patent Literature 1 above). The Japanese version of the Curiosity and Exploration Inventory-II (CEI-II) (hereinafter referred to as the Japanese version CEI-II) is a Japanese translation of The Curiosity and Exploration Inventory-II (CEI-II) developed by Kashdan et al. (Reference 1 below).

Reference 1: Kashdan TB et al., “The Curiosity and Exploration Inventory-II: Development, Factor Structure, and Psychometrics”, Journal of research in personality 43: 987-998, 2009.

[0020]

The Japanese version CEI-II consists of a total of 9 items (9 statements). Subtypes of daily curiosity include stretching curiosity (Stretching) and embracing curiosity (Embracing). Stretching curiosity is curiosity to seek new opportunities in order to promote personal growth. Embracing curiosity is curiosity to positively accept even unexpected events. Stretching curiosity represents a willingness to expand into new domains, and embracing curiosity represents an ability to tolerate and enjoy novelty and uncertainty. It is pointed out that these types of curiosity broaden the range of knowledge and skills, contribute to efforts toward goals and self-acceptance, and lead to health and well-being (“Shogen (Introduction)” of Non-Patent Literature 1 above).

[0021]

The 9 items of the Japanese version CEI-II are Items 1 to 9 below (Non-Patent Literature 1 above).

1. I am the type of person who really enjoys the uncertainty of everyday life.
2. I am at my best when doing a task that is complex or challenging.
3. Everywhere I go, I am out looking for new things or experiences.
4. I view challenging situations as an opportunity to grow and learn.
5. I like to do things that are a little frightening.
6. I am always looking for experiences that challenge how I think about myself and the world.
7. I prefer jobs that are excitingly unpredictable.
8. I frequently seek out opportunities to challenge myself and grow as a person.
9. I am the kind of person who embraces unfamiliar people, events, and places.

[0022]

Subjects rate the degree to which each of the above 9 statements applies to

themselves, and the results are used to evaluate the level of curiosity, such as stretching curiosity and embracing curiosity.

The stretching curiosity is evaluated based on Items 2, 4, 6, and 8 above. The embracing curiosity is evaluated based on Items 1, 3, 5, 7, and 9 above. Further, the daily curiosity is evaluated based on an item average (referred to as CEI-II scale score) of Items 1 to 9 (all items) above. In evaluation of the daily curiosity using the Japanese version CEI-II, a higher degree of applicability to an individual item indicates a higher level of curiosity related to the corresponding item. The evaluation can be performed by the method described in EXAMPLES below.

10 [0023]

In an embodiment, the daily curiosity is preferably the curiosity evaluated by the Japanese version CEI-II, more preferably at least one selected from the group consisting of the stretching curiosity evaluated by the Japanese version CEI-II, the embracing curiosity evaluated by the Japanese version CEI-II, and the curiosity (daily curiosity) evaluated using the above CEI-II scale score, still more preferably the embracing curiosity and/or the daily curiosity. In an embodiment, the composition of the present invention is preferably used for suppressing a decline in at least one type of curiosity selected from the group consisting of the stretching curiosity, the embracing curiosity, and the daily curiosity evaluated using the Japanese version CEI-II or improving the at least one type of curiosity, and is more preferably used for suppressing a decline in the embracing curiosity and/or the daily curiosity or improving the embracing curiosity and/or the daily curiosity.

[0024]

Daily curiosity provides favorable effects on health and well-being. The composition of the present invention can be used, for example, for maintaining health or for suppressing a decline in well-being or improving well-being through suppressing a decline in curiosity or improving curiosity.

[0025]

Intellectual curiosity refers to intrinsic motivation for exploratory behavior in an intellectual information domain such as problems and tasks, and includes an interest in intellectual information and an ability to engage in intellectual information with interest. Intellectual curiosity includes two types, diverse curiosity and specific curiosity. Diverse curiosity is motivation to explore new information widely. Specific curiosity is motivation to explore specific information in order to solve cognitive dissonance such as discrepancies or contradictions. Diverse curiosity can also be

understood as curiosity to broadly seek new information without setting a specific goal. Specific curiosity can also be understood as curiosity to set a specific goal and deeply investigate known information. In an embodiment of the present invention, suppressing a decline in intellectual curiosity or improving intellectual curiosity may be suppressing a decline in diverse curiosity and/or specific curiosity or improving diverse curiosity and/or specific curiosity, or may be suppressing a decline in diverse curiosity and specific curiosity or improving diverse curiosity and specific curiosity, or suppressing a decline in specific curiosity or improving specific curiosity.

[0026]

Intellectual curiosity can be evaluated using an intellectual curiosity scale. The intellectual curiosity scale may consist of, for example, the following 12 items (12 statements) (Non-Patent Literature 2 above). The level of intellectual curiosity can be evaluated by assessing the degree to which the following 12 items apply.

1. I explore new ideas.

2. I like to try new things.

3. I am not satisfied unless I learn all the knowledge necessary to understand a certain idea.

4. I feel unsettled unless I understand an answer, and I feel a need to somehow understand it.

5. I look for new things and experiences wherever I go.

6. I keep thinking until I obtain a clear and definite answer.

7. I have a strong interest in all matters.

8. When an unexpected event occurs, I investigate it until I understand the cause.

9. I have a strong interest in things that no one has done before.

10. I am willing to engage even in tasks that I have never attempted before.

11. I carefully think for a long time in order to solve a problem.

12. When learning things, I want to investigate them thoroughly.

[0027]

The diverse curiosity is evaluated based on Items 1, 2, 5, 7, 9, and 10 above. The specific curiosity is evaluated based on Items 3, 4, 6, 8, 11, and 12 above. A higher degree of applicability to an individual item indicates a higher level of curiosity related to the corresponding item. The evaluation can be performed by the method described in EXAMPLES below.

[0028]

In the present invention, the intellectual curiosity is preferably one evaluated by an intellectual curiosity scale, more preferably the diverse curiosity evaluated using Items 1, 2, 5, 7, 9, and 10 above and/or the specific curiosity evaluated using Items 3, 4, 6, 8, 11, and 12 above, still more preferably the specific curiosity.

5 [0029]

The role of diverse curiosity has been pointed out with respect to adaptation to complex and changing environments, such as a transition from student life to working life and job changes. Suppressing a decline in diverse curiosity or improving diverse curiosity can result in effects such as enhancement of adaptability to changing
10 environments. In addition, specific curiosity is associated with sensitivity to inconsistencies and contradictions as well as persistence in pursuing problem solving. Suppressing a decline in specific curiosity or improving specific curiosity can result in effects such as increased interest in learning.

[0030]

15 Interpersonal curiosity is motivation to acquire interpersonal information. More specifically, interpersonal curiosity is intrinsic motivation for exploratory behavior in an interpersonal information domain, such as human psychology and privacy. Interpersonal curiosity includes an interest in interpersonal information. Interpersonal curiosity includes three types: emotions, privacy, and attributes. The level
20 of interpersonal curiosity can be evaluated using an interpersonal curiosity scale.

[0031]

The interpersonal curiosity scale may consist of, for example, the following 11 items (11 statements) (Non-Patent Literature 3 above; Reference 2: Kazuji Nishikawa (2017), "Types of interpersonal curiosity: A progress report on the development of
25 interpersonal curiosity scale (3)", Proceedings of the 26th Annual Meeting of the Japan Society of Personality Psychology, p. 72). The level of interpersonal curiosity can be evaluated by assessing the degree to which the following 11 items apply.

1. I am curious about the contents of other people's diaries.
2. I try to read people's emotions from their voices.
- 30 3. I try to read people's feelings from their gestures.
4. I pry into what people are thinking by observing their facial expressions.
5. I want to know other people's secrets.
6. I want to ask where people currently live.
7. I enjoy gossiping.
- 35 8. I try to understand people's feelings by observing their behavior.

9. I want to ask where people are originally from.

10. I want to know what kind of special skills other people have.

11. I want to know about people's romantic history.

[0032]

5 The curiosity about personal emotions is evaluated based on Items 2, 3, 4, and 8 above. The curiosity about privacy is evaluated based on Items 1, 5, 7, and 11 above. The curiosity about personal attributes is evaluated based on Items 6, 9, and 10 above. A higher degree of applicability to an individual item indicates a higher level of curiosity related to the corresponding item. The evaluation can be performed by the
10 method described in EXAMPLES below.

[0033]

 In the present invention, the interpersonal curiosity may be at least one selected from the group consisting of curiosity about personal emotions, curiosity about privacy, and curiosity about personal attributes. Preferred among these is curiosity about
15 privacy. The interpersonal curiosity is preferably one evaluated by an interpersonal curiosity scale, and preferably at least one type of curiosity selected from the group consisting of the curiosity about personal emotions evaluated based on Items 2, 3, 4, and 8 above; the curiosity about privacy evaluated based on Items 1, 5, 7, and 11 above; and the curiosity about personal attributes evaluated based on Items 6, 9, and 10 above,
20 more preferably the curiosity about privacy evaluated based on Items 1, 5, 7, and 11 above.

[0034]

 Interpersonal curiosity is said to affect empathy, sociability, social competence, psychological well-being, and the like (Non-Patent Literature 3 above). Interpersonal
25 curiosity is also considered to affect social roles, such as building friendly relationships and establishing social status. Suppressing a decline in interpersonal curiosity or improving interpersonal curiosity can result in effects such as suppressing a decline in empathy or improving empathy and suppressing a decline in sociability or improving sociability. In an embodiment, the composition of the present invention can be used, for
30 example, for suppressing a decline in empathy or improving empathy or for suppressing a decline in sociability or improving sociability through suppressing a decline in interpersonal curiosity or improving interpersonal curiosity.

[0035]

 In an embodiment of the present invention, the curiosity is more preferably at
35 least one type of curiosity selected from the group consisting of embracing curiosity,

specific curiosity, and curiosity about privacy, still more preferably embracing curiosity. These types of curiosity are preferably types of curiosity evaluated by the above curiosity scales. The composition of the present invention is favorably used for suppressing a decline in the above curiosity or improving the above curiosity.

5 [0036]

As shown in EXAMPLES described below, L-ergothioneine has an effect of suppressing a decline in curiosity or improving curiosity. L-ergothioneine or a salt thereof can be used as an active ingredient for suppressing a decline in curiosity or improving curiosity.

10 As described above, Non-Patent Literature 4 describes that ergothioneine improved memory and learning functions in mice. However, curiosity, particularly in humans, for example, is considered to be complex. Non-Patent Literature 4 merely describes examination of exploratory behavior of mice toward a novel object, and does not confirm effects on human curiosity. In addition, no report exists that shows
15 effectiveness of a compound that improves memory and learning functions in suppressing a decline in curiosity or improving curiosity. The effect of suppressing a decline in curiosity or improving curiosity confirmed in EXAMPLES described below is an effect of L-ergothioneine or a salt thereof that has not been known to date.

[0037]

20 Since the composition of the present invention has an effect of suppressing a decline in curiosity or improving curiosity, the composition can be used for preventing or ameliorating conditions or diseases that can be prevented or ameliorated through suppressing a decline in curiosity or improving curiosity. Examples of conditions or diseases that are expected to be prevented through suppressing a decline in curiosity or
25 improving curiosity include dementia, depression, and schizophrenia. Preventing conditions or diseases includes preventing the onset of conditions or diseases, delaying the onset, reducing the incidence rate, reducing the risk of onset, and the like. Ameliorating conditions or diseases includes helping a subject recover from the conditions or diseases, alleviating symptoms, improving symptoms, delaying
30 progression of symptoms, preventing progression, and the like. Recovery includes partial recovery.

[0038]

The composition of the present invention may be either an oral composition or a parenteral composition, and is preferably an oral composition. The oral composition
35 may specifically be a food or beverage, an oral pharmaceutical product, an oral quasi-

pharmaceutical product, or the like, preferably a food or beverage or an oral pharmaceutical product, more preferably a food or beverage. The parenteral composition may be a parenteral pharmaceutical product, a parenteral quasi-pharmaceutical product, a cosmetic product, or the like. The composition of the present invention may be a material or preparation to be added to a food or beverage, a pharmaceutical product, a quasi-pharmaceutical product, a cosmetic product, or the like. [0039]

The composition of the present invention is applicable to either therapeutic use (medical use) or non-therapeutic use (non-medical use). The term non-therapeutic is a concept that does not include medical activities, i.e., surgery, therapy, or diagnosis of humans. [0040]

The composition of the present invention may be in any form such as solid (e.g., powder, granule, or tablet), liquid, or paste. The composition of the present invention may contain any additive or any component in addition to L-ergothioneine or a salt thereof as long as the effect of the present invention is not impaired. Such an additive and component can be selected according to, for example, the form of the composition. For example, when the composition of the present invention is provided as an oral composition, the composition may contain any additive that can be commonly used for oral compositions such as foods and beverages, pharmaceutical products, quasi-pharmaceutical products, and the like. [0041]

For example, in the case where the composition of the present invention is provided as a food or beverage, L-ergothioneine or a salt thereof may be combined with a component usable in foods and beverages (e.g., a food material or an optional food additive) to provide various types of foods and beverages. Examples of the foods and beverages include, but are not limited to, general foods and 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, foods for the sick, 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. [0042]

In the case where the composition of the present invention is provided as a

pharmaceutical product or a quasi-pharmaceutical product, for example, L-ergothioneine or a salt thereof can be combined with a pharmacologically acceptable carrier or an optional additive to provide pharmaceutical products or quasi-pharmaceutical products in various dosage forms. Such a carrier or additive 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 two or more of these may be used. The form of administration (ingestion) of a pharmaceutical product or a quasi-pharmaceutical product may be oral or parenteral (e.g., transdermal, transmucosal, enteral, or injection) administration. In the case where the composition of the present invention is provided as a pharmaceutical product or a quasi-pharmaceutical product, the composition is preferably provided as 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 dosage forms for parenteral administration include injections, intravenous agents, ointments, lotions, adhesive skin patches, suppositories, nasal agents, and transpulmonary agents (inhalants).

[0043]

In the case where the composition of the present invention is provided as a cosmetic product, L-ergothioneine or a salt thereof can be combined with a cosmetically acceptable carrier, additive, and the like. The cosmetic product may be in any product form.

[0044]

In the case where the composition of the present invention is provided as a food or beverage, pharmaceutical product, quasi-pharmaceutical product, cosmetic product, or the like, the composition may be produced by any method, and can be produced by a common method using L-ergothioneine or a salt thereof.

[0045]

The amount of L-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, for example. The amount of L-ergothioneine or a salt thereof in the composition of the present invention in terms of L-ergothioneine is, for example, preferably 0.0001% by weight or more, more preferably 0.001% by weight or more, and preferably 90% by weight or less, more preferably 50% by weight or less. In an embodiment, the amount

of L-ergothioneine or a salt thereof in the composition of the present invention in terms of L-ergothioneine is preferably 0.0001 to 90% by weight, more preferably 0.001 to 50% by weight. The amount of L-ergothioneine or a salt thereof can be determined by liquid chromatography-mass spectrometry (LC-MS).

5 [0046]

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

10 [0047]

The composition of the present invention can be ingested or administered by a method appropriate to the form thereof. In an embodiment, preferably, the composition of the present invention is orally ingested (orally administered). The administration amount (also referred to as intake) of the composition of the present invention is not limited. The administration amount may be any amount sufficient to achieve the effect of suppressing a decline in curiosity or improving curiosity and may appropriately be set according to the form of administration, the method of administration, the weight of a subject, and the like.

15 [0048]

The composition of the present invention may be ingested by or administered to any subject (also referred to as administration subject). Examples of the administration subject include humans and non-human mammals, with humans being preferred. The composition of the present invention is preferably a composition for suppressing a decline in curiosity or improving curiosity in a human. In an embodiment, the administration subject may be a subject who needs or wants to suppress a decline in curiosity or improve curiosity. Examples of the subject include middle-aged and older persons. In an embodiment, the composition of the present invention is favorably used as a composition for suppressing a decline in curiosity or improving curiosity in middle-aged and older persons. The middle-aged and older persons include elderly persons. The elderly persons may be humans aged 60 years or older, for example. The middle-aged and older persons may be humans aged 40 years or older, for example. In an embodiment, among the middle-aged and older persons, subjects aged 40 years or older and younger than 65 years are preferred. The administration subject may be a healthy person. For example, the composition of the

present invention can be used in healthy persons for the purpose of suppressing a decline in curiosity or improving curiosity. In an embodiment of the present invention, particularly preferred subjects are healthy humans aged 40 years or older and younger than 65 years.

5 [0049]

In an embodiment, in the case where the composition of the present invention is orally ingested by or administered to a human (adult) as a subject, the administration amount of L-ergothioneine or a salt thereof in terms of L-ergothioneine per day is preferably 2 mg or more, more preferably 5 mg or more, still more preferably 7 mg or
10 more, and preferably 50 mg or less, more preferably 25 mg or less, still more preferably 20 mg or less. In an embodiment, the administration amount of the composition of the present invention as the administration amount of L-ergothioneine or a salt thereof (in terms of L-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, even more preferably 7 to 20
15 mg. Preferably, the above amount of the compound is ingested or administered in one or more portions per day, for example, one or several portions (e.g., two or three portions) per day. In an embodiment, preferably, the above amount of L-ergothioneine or a salt thereof is orally ingested by or administered to a human. The above administration amount may be an administration amount per 60 kg body weight. In an
20 embodiment, the composition of the present invention can be used for ingestion by a human or administration to a human of the above amount of L-ergothioneine or a salt thereof per 60 kg body weight per day.

[0050]

The amount of L-ergothioneine or a salt thereof in the composition of the
25 present invention in terms of L-ergothioneine 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.

[0051]

The composition of the present invention may be labeled with, for example, a
30 function of suppressing a decline in curiosity or improving curiosity, or a function resulting from the above function. Examples of the label include labels of functions such as “enhancing curiosity”, “maintaining curiosity”, and “suppressing a decline in curiosity”. In an embodiment, preferably, the composition of the present invention is a food or beverage labeled with any of the above functions. The label may be one
35 indicating use for obtaining any of the functions. The label may be attached to the

composition itself, or may be attached to a container or package of the composition.

[0052]

The present invention also encompasses the following method.

A method for suppressing a decline in curiosity or improving curiosity, the
5 method including administering L-ergothioneine or a salt thereof.

This method may be a therapeutic method or may be a non-therapeutic method.

[0053]

The present invention also encompasses the following use.

Use of L-ergothioneine or a salt thereof for suppressing a decline in curiosity or
10 improving curiosity.

This use may be therapeutic use or may be non-therapeutic use.

Administering L-ergothioneine or a salt thereof to a subject enables
suppressing a decline in curiosity or improving curiosity. Curiosity and preferred
embodiments thereof are the same as described above for the composition of the present
15 invention.

[0054]

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

[0055]

In the above method and use, L-ergothioneine or a salt thereof is used in an
amount sufficient to achieve a desired effect (also referred to as effective amount). A
preferred administration amount of L-ergothioneine or a salt thereof, a preferred
30 administration subject, and the like are the same as described above for the composition
of the present invention. L-ergothioneine or a salt thereof may be administered directly
or may be administered in the form of a composition containing L-ergothioneine or a
salt thereof. For example, the composition of the present invention described above
may be used.

35 [0056]

The present invention also encompasses use of L-ergothioneine or a salt thereof in the production of a composition for suppressing a decline in curiosity or improving curiosity. The present invention also encompasses L-ergothioneine or a salt thereof for use in suppressing a decline in curiosity or improving curiosity.

5 [0057]

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. The upper limits and the lower limits herein may be used in any
10 combination to form a range.

The academic literature and patent literature mentioned herein are all incorporated herein by reference.

EXAMPLES

15 [0058]

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

[0059]

<Example 1>

20 In order to examine the effect of L-ergothioneine (hereinafter referred to as ergothioneine) on curiosity, a randomized, double-blind, placebo-controlled clinical trial was conducted in healthy men and women aged 40 years or older and younger than 65 years (test food group: 50 subjects; control group: 50 subjects).

[0060]

25 Methods

The following test food and control food were used as evaluation foods.

Test food: hard capsules (HPMC (hydroxypropyl methyl cellulose), white No. 2) filled with 8 mg of ergothioneine (GMP-certified >99.5% L-EGT, Tetrahedron, France) per capsule.

30 Control food: hard capsules (HPMC, white No. 2) filled with 8 mg of food-grade dextrin (Matsutani Chemical Industry Co., Ltd., Japan) per capsule.

The control food was identical with the test food except that it contained 8 mg of dextrin instead of 8 mg of ergothioneine. The test food and the control food were prepared so as not to be distinguishable from each other in appearance, flavor, and the
35 like.

[0061]

Before the start of ingestion of the test food or the control food (Week 0), curiosity of each subject was evaluated using curiosity scales (pre-ingestion test). Subjects in the test food group ingested one capsule of the test food once daily, and
 5 subjects in the control group ingested one capsule of the control food once daily, for 16 weeks. After ingestion of the test food or the control food for 16 weeks, curiosity of each subject was evaluated again (16-week post-ingestion test).

[0062]

Curiosity was evaluated by questionnaire. “Daily curiosity”, “intellectual
 10 curiosity”, and “interpersonal curiosity” were evaluated.

[0063]

Daily curiosity

The daily curiosity was evaluated using the Japanese version of the Curiosity and Exploration Inventory-II (CEI-II) (the Japanese version CEI-II) developed by
 15 Nishikawa et al. (Non-Patent Literature 1 above).

[0064]

The Japanese version CEI-II consists of a total of 9 items (9 statements), and subtypes of curiosity include stretching curiosity and embracing curiosity. The questionnaire included the following 9 items.

- 20 1. I am the type of person who really enjoys the uncertainty of everyday life.
2. I am at my best when doing a task that is complex or challenging.
3. Everywhere I go, I am out looking for new things or experiences.
4. I view challenging situations as an opportunity to grow and learn.
5. I like to do things that are a little frightening.
- 25 6. I am always looking for experiences that challenge how I think about myself and the world.
7. I prefer jobs that are excitingly unpredictable.
8. I frequently seek out opportunities to challenge myself and grow as a person.
9. I am the kind of person who embraces unfamiliar people, events, and places.

30 [0065]

Each subject read the above 9 items and selected, from the following options 1 to 5, the option that described the degree to which each item applied to the subject’s usual feelings and behaviors.

- 1: does not apply at all; 2: slightly applies; 3: applies; 4: considerably applies;
- 35 5: applies very much

[0066]

The numerical values of the response options (1 to 5) were used as scores to evaluate the level of curiosity. For example, when a subject selected “1: does not apply at all”, the score was set to “1 point”, and when a subject selected “5: applies very much”, the score was set to “5 points”.

The stretching curiosity was evaluated based on Items 2, 4, 6, and 8 above. The embracing curiosity was evaluated based on Items 1, 3, 5, 7, and 9 above. For each subject, an average of Items 2, 4, 6, and 8 (an average of the scores of the respective items) was calculated and used as a stretching curiosity scale score. An average of Items 1, 3, 5, 7, and 9 was calculated and used as an embracing curiosity scale score. Further, for each subject, an average of all items (Items 1 to 9) was calculated and used as a CEI-II scale score. The CEI-II scale score can be used to evaluate the daily curiosity. Thereafter, for each group, an average of the stretching curiosity scale scores, an average of the embracing curiosity scale scores, and an average of the CEI-II scale scores were calculated. A higher curiosity scale score is evaluated as a higher level of the corresponding curiosity. The results are shown in Table 1.

[0067]

Intellectual curiosity

In the evaluation of intellectual curiosity, diverse curiosity and specific curiosity were evaluated. The questionnaire included the following 12 items (12 statements) (Non-Patent Literature 2 above).

1. I explore new ideas.
2. I like to try new things.
3. I am not satisfied unless I learn all the knowledge necessary to understand a certain idea.
4. I feel unsettled unless I understand an answer, and I feel a need to somehow understand it.
5. I look for new things and experiences wherever I go.
6. I keep thinking until I obtain a clear and definite answer.
7. I have a strong interest in all matters.
8. When an unexpected event occurs, I investigate it until I understand the cause.
9. I have a strong interest in things that no one has done before.
10. I am willing to engage even in tasks that I have never attempted before.
11. I carefully think for a long time in order to solve a problem.

12. When learning things, I want to investigate them thoroughly.

[0068]

Each subject selected, from the following options 1 to 5, the option that described the degree to which each of the statements of the above 12 items applied to themselves.

1: does not apply at all; 2: does not really apply; 3: neither applies nor does not apply; 4: somewhat applies; 5: applies very much

[0069]

Similarly to the above evaluation of daily curiosity, the numerical values of the response options (1 to 5) were used as scores to evaluate the level of curiosity. In the evaluation of intellectual curiosity, the diverse curiosity was evaluated based on Items 1, 2, 5, 7, 9, and 10 above. The specific curiosity was evaluated based on Items 3, 4, 6, 8, 11, and 12 above. For each subject, an average of Items 1, 2, 5, 7, 9, and 10 (an average of the scores of the respective items) was calculated and used as a diverse curiosity scale score. An average of Items 3, 4, 6, 8, 11, and 12 was calculated and used as a specific curiosity scale score. Thereafter, for each group, an average of the diverse curiosity scale scores and an average of the specific curiosity scale scores were calculated. The results are shown in Table 1.

[0070]

20 Interpersonal curiosity

In the evaluation of interpersonal curiosity, curiosity about personal emotions, curiosity about privacy, and curiosity about personal attributes were evaluated. The questionnaire included the following 11 items (11 statements) (Non-Patent Literature 3 and Reference 2 above).

- 25 1. I am curious about the contents of other people's diaries.
2. I try to read people's emotions from their voices.
3. I try to read people's feelings from their gestures.
4. I pry into what people are thinking by observing their facial expressions.
5. I want to know other people's secrets.
- 30 6. I want to ask where people currently live.
7. I enjoy gossiping.
8. I try to understand people's feelings by observing their behavior.
9. I want to ask where people are originally from.
10. I want to know what kind of special skills other people have.
- 35 11. I want to know about people's romantic history.

[0071]

Each subject selected, from the following options 1 to 5, the option that described the degree to which each of the statements of the above 11 items applied to themselves.

- 5 1: does not apply; 2: does not really apply; 3: neither applies nor does not apply; 4: somewhat applies; 5: applies

[0072]

Similarly to the above evaluation of daily curiosity, the numerical values of the response options (1 to 5) were used as scores to evaluate the level of curiosity. In the
10 evaluation of interpersonal curiosity, the curiosity about personal emotions was evaluated based on Items 2, 3, 4, and 8 above. The curiosity about privacy was evaluated based on Items 1, 5, 7, and 11 above. The curiosity about personal attributes was evaluated based on Items 6, 9, and 10 above.

For each subject, an average of Items 2, 3, 4, and 8 (an average of the scores of
15 the respective items) was calculated and used as a scale score of curiosity about personal emotions. An average of Items 1, 5, 7, and 11 was calculated and used as a scale score of curiosity about privacy. An average of Items 6, 9, and 10 was calculated and used as a scale score of curiosity about personal attributes. Thereafter, for each
20 group, an average of the scale scores of curiosity about personal emotions, an average of the scale scores of curiosity about privacy, and an average of the scale scores of curiosity about personal attributes were calculated. The results are shown in Table 1.

[0073]

Statistical analysis

For evaluation of efficacy, 99 subjects excluding 1 subject who dropped out
25 were analyzed. An unpaired t-test was used for between-group comparisons of changes. A paired t-test was used for within-group comparisons. The level of significance was set at $p < 0.05$.

[0074]

Results

30 A total of 100 subjects (test food group: 50 subjects; control group: 50 subjects) participated in this clinical trial. The final numbers were 50 subjects in the test food group and 49 subjects in the control group. Among all subjects, 51 were female (26 in the test food group and 25 in the control group) and 49 were male (24 in the test food group and 25 in the control group); the mean age was 53.4 ± 6.0 years in
35 the test food group and 53.6 ± 6.2 years in the control group, and no statistically

significant difference was observed between the groups ($p > 0.05$).

[0075]

Table 1 shows the results of evaluation of curiosity for each group. The results are presented as mean $\pm$ standard deviation of curiosity scale scores.

5 Within-group comparison: paired t-test ($\dagger$: $p < 0.1$; #: $p < 0.05$)

Between-group comparison: unpaired t-test ($\dagger$: $p < 0.1$; *: $p < 0.05$)

10 In Table 1, Week 0 indicates the results of pre-ingestion test, and Week 16 indicates the results of 16-week post-ingestion test. Change shown in Table 1 is the difference between the curiosity scale score at the 16-week post-ingestion test and the curiosity scale score at the pre-ingestion test; p-value (1) indicates a within-group comparison of the scores of the pre-ingestion test and the 16-week post-ingestion test, and p-value (2) indicates a between-group comparison of the changes.

[0076]

[Table 1]

Type of curiosity		Group	Week 0	Week 16	p-value (1)	Change	p-value (2)
Daily curiosity	Stretching	Control	2.23 ± 0.77	2.27 ± 0.83	0.710	0.04 ± 0.67	0.685
		Test food	2.17 ± 0.87	2.25 ± 0.80	0.261	0.09 ± 0.53	
	Embracing	Control	2.27 ± 0.68	2.38 ± 0.82	0.260	0.11 ± 0.68	0.587
		Test food	2.30 ± 0.88	2.47 ± 0.88	#0.019	0.18 ± 0.51	
	CEI-II	Control	2.25 ± 0.69	2.33 ± 0.78	0.396	0.08 ± 0.63	0.603
		Test food	2.24 ± 0.81	2.37 ± 0.78	#0.048	0.14 ± 0.47	
Intellectual curiosity	Diverse	Control	3.40 ± 0.70	3.32 ± 0.88	0.310	-0.09 ± 0.60	0.471
		Test food	3.57 ± 0.69	3.57 ± 0.79	0.928	-0.01 ± 0.52	
	Specific	Control	3.30 ± 0.61	3.29 ± 0.72	0.890	-0.01 ± 0.51	†0.083
		Test food	3.21 ± 0.61	3.39 ± 0.64	#0.026	0.18 ± 0.55	
Interpersonal curiosity	Personal emotions	Control	3.58 ± 0.78	3.59 ± 0.84	0.898	0.01 ± 0.55	0.596
		Test food	3.71 ± 0.79	3.78 ± 1.00	0.422	0.08 ± 0.66	
	Privacy	Control	2.48 ± 0.94	2.54 ± 0.98	0.516	0.06 ± 0.60	0.330
		Test food	2.13 ± 0.78	2.30 ± 0.86	#0.036	0.17 ± 0.56	
	Personal attributes	Control	2.73 ± 1.08	2.88 ± 1.14	0.154	0.15 ± 0.72	0.951
		Test food	2.72 ± 1.06	2.88 ± 1.17	0.230	0.16 ± 0.93	

[0077]

For daily curiosity, intellectual curiosity, and interpersonal curiosity, the test food group showed a smaller decrease in curiosity scale scores or a greater increase in curiosity scale scores compared with the control group. This indicates that, in the test food group, a decline in curiosity was suppressed or curiosity was improved compared with the control group. In particular, significant differences before and after ingestion of ergothioneine were confirmed for specific curiosity, embracing curiosity, CEI-II, and curiosity about privacy. No significant differences before and after ingestion were observed in the control group. In the between-group comparison, specific curiosity showed a tendency toward improvement upon ingestion of ergothioneine ($p < 0.1$).

CLAIMS

[Claim 1] A composition for suppressing a decline in curiosity or improving curiosity, comprising L-ergothioneine or a salt thereof.

5

[Claim 2] The composition according to claim 1, wherein the curiosity is at least one selected from the group consisting of daily curiosity, intellectual curiosity, and interpersonal curiosity.

10

[Claim 3] The composition according to claim 1 or 2, which is a composition for suppressing a decline in curiosity or improving curiosity in a human.

[Claim 4] The composition according to claim 1 or 2, which is an oral composition.

15

[Claim 5] The composition according to claim 1 or 2, which is a food or beverage.

[Claim 6] Use of L-ergothioneine or a salt thereof for suppressing a decline in curiosity or improving curiosity.

20

[Claim 7] A method for suppressing a decline in curiosity or improving curiosity, the method comprising administering L-ergothioneine or a salt thereof.