DESCRIPTION

TITLE OF INVENTION: ANTIFATIGUE COMPOSITION AND COMPOSITION FOR IMPROVING, SUPPRESSING REDUCTION OF, AND MAINTAINING ENERGY PRODUCTION PERFORMANCE

TECHNICAL FIELD

[0001]

The present invention relates to an anti-fatigue composition. The present invention also relates to a composition for improving or maintaining energy production capacity or reducing a decline in energy production capacity. The present invention also relates to use of at least one sesamin-class compound and lutein and/or a fatty acid ester thereof for suppressing, alleviating, or reducing fatigue. The present invention also relates to use of at least one sesamin-class compound and lutein and/or a fatty acid ester thereof for improving or maintaining energy production capacity or reducing a decline in energy production capacity.

BACKGROUND ART

[0002]

Energy production means production of energy required by humans and non-human animals to maintain life activities.

Most of the energy is produced in mitochondria that are a type of organelles. Sugar, lipids, amino acids, and other nutrition sources taken from food are metabolized by glycolysis, pentose phosphate pathway, and citric acid pathway and converted into nicotinamide adenine dinucleotide (NADH). Then, NADH electrons are transferred to protein in mitochondrial respiratory chains (electron transport chains), and energy is produced in the form of adenosine triphosphate (ATP).

A decline in the amount of ATP production is known to cause various problems. For example, in the case of humans, such problems include an increase in risk of developing obesity and diabetes due to reduced metabolic capacity, muscle strength decline, increase in fatigue, lethargy/decline in concentration, and depression.

[0003]

Maintaining the amount of ATP production is important in fatigue alleviation, maintenance of concentration, muscle-based exercise, and maintenance of vitality of mind and body.

[0004]

Various agents for increasing energy production have been known which contain substrates required for ATP production such as carbohydrates, amino acids, and lipids. Patent Literature 1 discloses a composition for improving metabolism for energy production from fatty acids in cells, the composition containing a xanthophyll as an active ingredient.

[0005]

As described above, the substrates required for ATP production are converted into ATP via mitochondrial electron transport chains. However, mitochondrial function decline prevents production of ATP, even if there are more substrates.

It is known that mitochondrial function decline is caused by aging and oxidative stress and results in a decline in the amount of ATP production (Non-Patent Literatures 1 and 3).

[0006]

In the case of ingestion of an ingredient as a supplement that reduces a decline in mitochondrial function, a form that allows easy intake by consumers for continuous ingestion is desirable. For example, small tablets and small capsules are desirable particularly for

the elderly because swallowing function declines with aging. A supplement tends to be bulky particularly when it contains multiple ingredients, so that it is desirable to use an ingredient that is highly effective even when used in a small amount or a combination of such ingredients in order to reduce the volume of a tablet or capsule.

[0007]

Sesamin is a lignan compound found in sesame and has been reported as having an antioxidant effect. According to a report using a diabetic mouse model, sesamin has an action that reduces a decline in mitochondrial function by an antioxidant effect (Non-Patent Literature 4). Sesamin is also known to exert, based on its antioxidant effect, an action that reduces mitochondrial active oxygen production and an action that reduces mitochondrial membrane potential drop (Non-Patent Literature 2). According to another report, sesamin activates PGC1α involved in mitochondrial biogenesis (Patent Literature 2).

[0008]

According to another report, lutein has an action that activates mitochondrial function in a neuronal cell line (Non-Patent Literature 5). It has been reported that ingestion of a mixture containing lutein alleviates mental stress (Non-Patent Literature 6) and eye strain (Non-Patent Literatures 7 and 8).

CITATION LIST

- Patent Literature

[0009]

Patent Literature 1: JP 2009-215170 A
Patent Literature 2: WO 2018/079719

- Non-Patent Literature

[0010]

Non-Patent Literature 1: Conley, Kevin E., et al.

"Oxidative capacity and ageing in human muscle", The Journal of physiology 526.1 (2000): 203-210.
Non-Patent Literature 2: Maharjan, Sunita, et al. "Mitochondrial impairment triggers cytosolic oxidative stress and cell death following proteasome inhibition", Scientific reports 4 (2014): 5896.
Non-Patent Literature 3: Kudryavtseva, Anna V., et al. "Mitochondrial dysfunction and oxidative stress in aging and cancer", Oncotarget 7.29 (2016): 44879.
Non-Patent Literature 4: Takada, Shingo, et al. "Sesamin prevents decline in exercise capacity and impairment of skeletal muscle mitochondrial function in mice with high-fat diet-induced diabetes", Experimental Physiology 100.11 (2015): 1319-1330.
Non-Patent Literature 5: Xie K, et al. "Modulation of mitochondrial respiration underpins neuronal differentiation enhanced by lutein", Neural Regen Res. 2019 Jan; 14(1): 87-99.
Non-Patent Literature 6: Stringham NT, et al. "Supplementation with macular carotenoids reduces psychological stress, serum cortisol, and sub-optimal symptoms of physical and emotional health in young adults", Nutr Neurosci. 2018 May; 21(4): 286-296.
Non-Patent Literature 7: Stringham JM, et al. "Macular Carotenoid Supplementation Improves Visual Performance, Sleep Quality, and Adverse Physical Symptoms in Those with High Screen Time Exposure", Foods. 2017 Jun 29;6(7). pii: E47.
Non-Patent Literature 8: Kawabata F, et al. "Effects of dietary supplementation with a combination of fish oil, bilberry extract, and lutein on subjective symptoms of asthenopia in humans", Biomed Res. 2011 Dec; 32(6): 387-93.

SUMMARY OF INVENTION

- Technical Problem

[0011]

Humans and the like constantly require energy to maintain life activities, so that there is a desire for a highly safe method of promoting production of energy, using an ingredient which can be continuously ingested without concern for side effects. There has been suggested a method of increasing the amount of energy production by ingestion of substrates of energy production, however, its effect is limited in a state of mitochondrial function decline. While some food ingredients are known to have an action that improves energy production, it is desirable to use an ingredient that exerts its effect even when used in a small amount or to use a combination of such ingredients in terms of easy ingestion and safety for continuous ingestion.

[0012]

The present invention aims to provide a composition which can improve or maintain mitochondrial function or reduce a decline in mitochondrial function, which is effective in improving or maintaining energy production capacity or reducing a decline in energy production capacity and effective in anti-fatigue, and which is highly safe and suitable for continuous ingestion.

- Solution to Problem

[0013]

The present inventors conducted extensive studies to solve the problems described above. They studied ingredients which can be used to improve or maintain mitochondrial function or reduce a decline in mitochondrial function. As a result, the present inventors found that when a sesamin-class compound as a component that maintains and activates mitochondrial function is combined with lutein and/or a fatty acid ester thereof as a component that activates mitochondrial function, the resulting

combination can improve or maintain mitochondrial function and/or energy production capacity or can reduce a decline in mitochondrial function and/or energy production capacity in a more effective (synergistic) manner than when the sesamin-class compound is used alone or when lutein and/or a fatty acid ester thereof is used alone.

[0014]

Specifically, the present invention relates to, but is not limited to, an anti-fatigue composition, a composition for improving or maintaining energy production capacity or reducing a decline in energy production capacity, use, and the like described below.

(1) An anti-fatigue composition containing at least one sesamin-class compound and at least one of lutein or a fatty acid ester thereof.

(2) The composition according to (1) above, wherein the composition suppresses, alleviates, or reduces fatigue by improving or maintaining energy production capacity or reducing a decline in energy production capacity.

(3) The composition according to (2) above, wherein the improving or maintaining energy production capacity or reducing a decline in energy production capacity is mediated by improving or maintaining mitochondrial function or reducing a decline in mitochondrial function.

(4) A composition for improving or maintaining energy production capacity or reducing a decline in energy production capacity, the composition containing: at least one sesamin-class compound and at least one of lutein or a fatty acid ester thereof.

(5) The composition according to (4) above, wherein the improving or maintaining energy production capacity or reducing a decline in energy production capacity is mediated by improving or maintaining mitochondrial function or reducing a decline in mitochondrial function.

(6) The composition according to any one of (1) to

(5) above, wherein the at least one sesamin-class compound is at least one of sesamin or episesamin.

(7) The composition according to any one of (1) to (6) above, wherein a mole ratio of the at least one of lutein or a fatty acid ester thereof to the sesamin-class compound is 0.003 to 125.

(8) The composition according to any one of (1) to (7) above, wherein the composition is an oral composition.

(9) The composition according to any one of (1) to (8) above, wherein the composition is a food or beverage.

(10) The composition according to any one of (1) to (9) above, wherein the composition is labeled with at least one function claim selected from the group consisting of "alleviating fatigue", "alleviating feelings of fatigue", "alleviating discomfort", "reducing a decline in motivation", "facilitating energy production", and "maintaining and improving vitality".

(11) Use of at least one sesamin-class compound and at least one of lutein or a fatty acid ester thereof for suppressing, alleviating, or reducing fatigue.

(12) Use of at least one sesamin-class compound and at least one of lutein or a fatty acid ester thereof for improving or maintaining energy production capacity or reducing a decline in energy production capacity.

(13) A method of suppressing, alleviating, or reducing fatigue, the method including administering at least one sesamin-class compound and at least one of lutein or a fatty acid ester thereof.

(14) A method of improving or maintaining energy production capacity or reducing a decline in energy production capacity, the method including administering at least one sesamin-class compound and at least one of lutein or a fatty acid ester thereof.

- Advantageous Effects of Invention

[0015]

The present invention can provide a composition which can improve or maintain mitochondrial function or reduce a decline in mitochondrial function, which is effective in improving or maintaining energy production capacity or reducing a decline in energy production capacity and effective in anti-fatigue, and which is highly safe and suitable for continuous ingestion.

BRIEF DESCRIPTION OF DRAWINGS

[0016]

FIG. 1 is a graph showing effects of a sesamin-episesamin mixture (SE) and lutein on the amount of ATP production by.

DESCRIPTION OF EMBODIMENTS

[0017]

The anti-fatigue composition of the present invention contains at least one sesamin-class compound and lutein and/or a fatty acid ester thereof. The anti-fatigue composition of the present invention contains at least one sesamin-class compound and lutein and/or a fatty acid ester thereof as active ingredients.

The composition for improving or maintaining energy production capacity or reducing a decline in energy production capacity of the present invention contains at least one sesamin-class compound and lutein and/or a fatty acid ester thereof. The composition for improving or maintaining energy production capacity or reducing a decline in energy production capacity of the present invention contains at least one sesamin-class compound and lutein and/or a fatty acid ester thereof as active ingredients.

Energy production means production of energy required by humans and non-human animals to maintain life

activities.

The anti-fatigue composition and the composition for improving or maintaining energy production capacity or reducing a decline in energy production capacity of the present invention are also collectively referred to as "the composition of the present invention" below.

[0018]

(Sesamin-class compound)

In the present invention, the term "the sesamin-class compound" is a collective term for compounds including sesamin and its analogs. Sesamin is one of main lignan compounds found in sesame. Examples of the sesamin analogs include episesamin and dioxabicyclo[3.3.0]octane derivatives described in JP H04-9331 A. One of these compounds or two or more thereof may be used as the at least one sesamin-class compound. Specific examples of the sesamin-class compound include sesamin, episesamin, sesaminol, episesaminol, sesamol, and sesamolin. Stereoisomers or racemates of these compounds may be used alone or in mixture. In addition, metabolites of the sesamin-class compound (e.g., those described in JP 2001-139579 A) are also sesamin analogs included in the sesamin-class compound of the present invention, and can also be used in the present invention, as long as they exhibit the effect(s) of the present invention. In the present invention, sesamin and/or episesamin can be suitably used as the at least one sesamin-class compound. Sesamin and episesamin can be more suitably used. When sesamin and episesamin are used, the ratio of these components is not limited. For example, the ratio of sesamin to episesamin by weight is preferably 1:0.1 to 1:9, more preferably 1:0.3 to 1:3, still more preferably 1:0.5 to 1:2.

[0019]

The sesamin-class compound for use in the present invention is not limited in any way by its form, production

method, or the like. The sesamin-class compound is one of main lignan-class compounds of sesame and is contained in an amount of about 0.5 to 1.0 wt% in sesame. For example, when the sesamin-class compound is sesamin, sesamin extracted from sesame oil by a known method (e.g., the method described in JP H04-9331 A) can be used (hereinafter, such sesamin is called a sesamin extract or purified sesamin). Commercially available sesame oil (in liquid form) can also be used as is. However, when sesame oil is used, the characteristic flavor of sesame oil is sometimes evaluated as being organoleptically undesirable. Thus, a tasteless and odorless sesamin extract (or purified sesamin) from sesame oil is preferably used. In addition, since sesame oil has a low sesamin content, use of sesame oil to incorporate a desirable amount of sesamin results in excess volume per unit dose of a composition to be prescribed. This sometimes causes inconvenience in ingestion. In particular, in the case where the composition is formulated for oral administration, the preparation (e.g., tablet or capsule) becomes so bulky that it causes trouble in ingestion. Thus, use of sesamin extract (or purified sesamin) from sesame oil is preferred because it does not require a large amount of ingestion. The sesamin-class compound can also be obtained by synthesis. For example, sesamin and episesamin can be synthesized by the method of Beroza et al. (J. Am. Chem. Soc., 78, 1242 (1956)). Metabolites of sesamin and episesamin can be synthesized by the method of Urata et al. (Chem. Pharm. Bull. (Tokyo), 56(11), 1611-2 (2008)).

[0020]

(Lutein and/or a fatty acid ester thereof)

The composition of the present invention contains lutein and/or a fatty acid ester thereof.

Lutein is one of carotenoids. Lutein and fatty acid esters thereof are found in plants and the like, and can be

prepared, for example, by extraction from plants. Fatty acid esters of lutein are found, for example, in green and yellow vegetables such as spinach, kale, broccoli, squash, carrots, and paprika; fruits such as oranges, peaches, papaya, prunes, mangoes, avocados, raspberries, and rose hips; and marigold petals. In the present invention, the composition of the present invention may contain, for example, a raw material derived from plants rich in lutein and/or fatty acid esters thereof, as long as the effect(s) of the present invention is achieved.

Commercially available lutein and fatty acid esters thereof can also be used.

[0021]

Fatty acid esters of lutein are fatty acid esters each in which a fatty acid is bonded to one or two hydroxy groups of lutein. Examples of the fatty acid in a fatty acid ester of lutein include C4-C20 fatty acids, preferably C8-C18 fatty acids. The composition of the present invention may contain one fatty acid ester of lutein or two or more fatty acid esters thereof. Hydrolysis of fatty acid esters of lutein generates lutein.

[0022]

The sesamin-class compound and the lutein and fatty acid esters thereof are found in natural products and food and beverages. They are compounds with a long history of consumption and recognized high safety. Thus, the sesamin-class compound and the lutein and fatty acid esters thereof are suitable for continuous ingestion and long-term ingestion.

[0023]

The composition of the present invention contains the at least one sesamin-class compound and the lutein and/or a fatty acid ester thereof as active ingredients.

A combination of the sesamin-class compound and the lutein and/or a fatty acid ester thereof produces a

significantly excellent effect of improving or maintaining mitochondrial function or reducing a decline in mitochondrial function. Improving or maintaining mitochondrial function or reducing a decline in mitochondrial function can produce an effect of improving or maintaining energy production capacity or reducing a decline in energy production capacity. The effect of improving or maintaining mitochondrial function or reducing a decline in mitochondrial function and the effect of improving or maintaining energy production capacity or reducing a decline in energy production capacity, which are produced by a combination of the sesamin-class compound and the lutein and/or a fatty acid ester thereof, is a synergistic effect superior to an additive effect predictable from an effect produced by use of the sesamin-class compound alone or by use of lutein and/or a fatty acid ester thereof alone.

[0024]

In the composition of the present invention, the weight ratio of the total amount of lutein and/or a fatty acid ester thereof in terms of lutein to the total amount of the sesamin-class compound ((total amount of lutein and/or a fatty acid ester thereof in terms of lutein)/total amount of sesamin-class compound) is preferably 0.005 to 200, more preferably 0.01 to 40, still more preferably 0.4 to 16, in order to synergistically enhancing the action that improves or maintains mitochondrial function or that reduces a decline in mitochondrial function or the action that improves or maintains energy production capacity or that reduces a decline in energy production capacity.

In the present invention, the mole ratio of lutein and/or a fatty acid ester thereof to the sesamin-class compound is preferably 0.003 to 125, more preferably 0.006 to 25, still more preferably 0.25 to 10, particularly preferably 0.3 to 10. The mole ratio is the ratio of the

total number of moles of lutein and/or a fatty acid ester thereof to the total number of moles of the sesamin-class compound ((total number of moles of lutein and/or a fatty acid ester thereof)/total number of moles of sesamin-class compound).

The action that improves or maintains energy production capacity or that reduces a decline in energy production capacity can be enhanced by enhancing the action that improves or maintains mitochondrial function or that reduces a decline in mitochondrial function. Improving or maintaining mitochondrial function and/or energy production capacity or reducing a decline in mitochondrial function and/or energy production capacity is effective in suppressing, alleviating, or reducing fatigue. In the composition of the present invention, adjusting the ratio of the sesamin-class compound and the lutein and/or a fatty acid ester thereof to the total number of moles of the sesamin-class compound within the above range is also preferred in terms of anti-fatigue action.

[0025]

The composition for improving or maintaining energy production capacity or reducing a decline in energy production capacity of the present invention can be used to, for example, improve or maintain energy production capacity or reduce a decline in energy production capacity, which is mediated by improving or maintaining mitochondrial function or reducing a decline in mitochondrial function. The composition of the present invention can be used as a composition for improving or maintaining energy production capacity or reducing a decline in energy production capacity, which is mediated by improving or maintaining mitochondrial function or reducing a decline in mitochondrial function.

The anti-fatigue composition of the present invention can suppress, alleviate, or reduce fatigue by improving or

maintaining energy production capacity or reducing a decline in energy production capacity, and the anti-fatigue composition can be used for such purposes. The anti-fatigue composition of the present invention can be used to suppress, alleviate, or reduce fatigue by improving or maintaining energy production capacity or reduce a decline in energy production capacity, which is mediated by improving or maintaining mitochondrial function or reducing a decline in mitochondrial function.

[0026]

Use of at least one sesamin-class compound and lutein and/or a fatty acid ester thereof can synergistically enhance their actions that improve or maintain mitochondrial function or reduce a decline in mitochondrial function or that improve or maintain energy production capacity or reduce a decline in energy production capacity. Thus, the above actions can be exerted with the use of the sesamin-class compound as well as the lutein and/or a fatty acid ester thereof as active ingredients for improving or maintaining energy production capacity or reducing a decline in energy production capacity or for anti-fatigue even when the amounts of these active ingredients are small. This enables a reduction in intake of the active ingredients. A reduced intake leads to easy intake, resulting in an anti-fatigue composition more suitable for continuous ingestion and a composition for improving or maintaining energy production capacity or reducing a decline in energy production capacity, for example.

[0027]

Herein, the term "fatigue" means a decline in physical and/or mental vitality due to physical or mental causes. Fatigue is usually associated with feelings of fatigue (e.g., discomfort and reduced motivation for activities) and the like. The term "anti-fatigue" refers to suppress, alleviate, or reduce fatigue. The term

"suppressing fatigue" encompasses increasing resistance to fatigue, preventing fatigue (including reducing risks in a subject at risk of fatigue), and the like. The term "alleviating fatigue" encompasses alleviating fatigue symptoms (e.g., feelings of fatigue) and the like. The term "reducing fatigue" encompasses helping recovery from fatigue, reducing fatigue symptoms, and the like.

The anti-fatigue composition of the present invention can be used, for example, to suppress, alleviate, or reduce physical and/or mental fatigue, and to suppress, alleviate, or reduce feelings of physical and/or mental fatigue. In particular, the anti-fatigue composition can be preferably used to suppress, alleviate, or reduce physical fatigue, and to suppress, alleviate, or reduce feelings of physical fatigue. The anti-fatigue composition of the present invention can be used to, for example, prevent or ameliorate a condition or disease accompanied by fatigue. The condition or disease accompanied by fatigue may be a chronic fatigue syndrome, for example. Prevention of a condition or disease encompasses prevention of disease onset, delay of disease onset, reduction in disease incidence, reduction of risk of disease onset, and the like. Amelioration of a condition or disease encompasses recovery of the subject from a condition or disease, alleviation of a condition or disease symptom, favorable change in a condition or disease symptom, delay or prevention of progress of a condition or disease, and the like.

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

[0028]

Herein, it suffices as long as the mitochondrial

function is evaluated based on common knowledge in the technical field to which the present invention belongs to. Any method may be used for evaluation. For example, the mitochondrial function can be evaluated by continuously evaluating the oxygen consumption rate (OCR) of mitochondria during ATP synthesis in cells as the measurement target, using an extracellular flux analyzer, while adding ATP synthase inhibitors (e.g., oligomycin and rotenone) and an uncoupler (e.g., carbonyl cyanide-p-trifluoromethoxy phenylhydrazone (FCCP)) thereto. Evaluation items may be, for example, basal respiration, ATP production capacity, and maximal respiration, which are major indices for evaluation of mitochondrial function. The mitochondrial function can be evaluated by analyzing these evaluation items.

[0029]

The 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 composition of the present invention may be a food or beverage, a pharmaceutical product, a quasi-pharmaceutical product, feed, or the like by itself for anti-fatigue or for improving or maintaining energy production capacity or reducing a decline in energy production capacity, or the composition of the present invention may be a material, a preparation, or the like that is added thereto.

For example, the composition of the present invention may be provided as an agent or the like, but it is not limited thereto. The agent can be directly provided as a composition or can be provided as a composition containing the agent. In one embodiment of the present invention, the anti-fatigue composition of the present invention can be regarded as an anti-fatigue agent.

The composition of the present invention may be an

oral composition or a parenteral composition, preferably an oral composition. The oral composition may be a food or beverage, an oral pharmaceutical product, an oral quasi-pharmaceutical product, or feed, preferably a food or beverage or an oral pharmaceutical product, more preferably a food or beverage.

[0030]

The composition of the present invention may contain optional additives and optional components, in addition to at least one sesamin-class compound and lutein and/or a fatty acid ester thereof, as long as the effect(s) of the present invention is not impaired. Such additives and components can be selected according to the composition form or the like. Those that can be used generally in foods, beverages, pharmaceutical products, quasi-pharmaceutical products, feed, and the like can be used. 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.

[0031]

For example, when the composition of the present invention is provided as a food or beverage, a component usable in food and beverages (e.g., a food material or an optional food additive) can be added to at least one sesamin-class compound and lutein and/or a fatty acid ester thereof to provide various types of foods or beverages. Non-limiting examples of the foods or beverages include general foods and beverages, health foods, health beverages, foods with function claims, foods for specified health uses, dietary supplements, and foods and beverages for the sick. The health foods, the foods with function claims, the foods for specified health uses, dietary supplements, and the like can be used, for example, in various forms of preparations such as fine granules,

tablets, granules, powders, capsules, chewable tablets, dry syrups, syrups, liquids, beverages, and liquid foods.
[0032]

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 at least one sesamin-class compound and lutein and/or a fatty acid ester thereof to provide various dosage forms of pharmaceutical products or quasi-pharmaceutical products. Such a carrier, an 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 quasi-pharmaceutical product may be an oral or parenteral (transdermal, transmucosal, or enteral administration, injection, or the like). 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 the dosage forms of preparations for oral administration include liquids, tablets, powders, fine granules, granules, sugar-coated tablets, capsules, suspensions, emulsions, and chewable tablets. The pharmaceutical product may be for non-human animals.
[0033]

When the composition of the present invention is provided as feed, at least one sesamin-class compound and lutein and/or a fatty acid ester thereof are 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 dogs, cats, and birds.

[0034]

The amount of sesamin-class compound in the composition of the present invention is not limited and can be set according to the form of the composition of the like.

The total amount of sesamin-class compound in the composition of the present invention is, for example, preferably 0.001 wt% or more, more preferably 0.01 wt% or more, still more preferably 0.05 wt% or more and is preferably 10 wt% or less, more preferably 5 wt% or less.

In one embodiment, the total amount of sesamin-class compound in the composition is preferably 0.001 to 10 wt%, more preferably 0.01 to 10 wt%, still more preferably 0.05 to 5 wt%.

[0035]

The total amount of lutein and/or a fatty acid ester thereof in the composition of the present invention is not limited and can be set according to its form or the like.

The total amount of lutein and/or a fatty acid ester thereof in the composition of the present invention in terms of lutein, for example, is preferably 0.001 wt% or more, more preferably 0.01 wt% or more, still more preferably 0.05 wt% or more, and is preferably 10 wt% or less, more preferably 5 wt% or less.

In one embodiment, the total amount of lutein and/or a fatty acid ester thereof in the composition in terms of lutein is preferably 0.001 to 10 wt%, more preferably 0.01 to 10 wt%, still more preferably 0.05 to 5 wt%.

[0036]

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 dose of the

composition of the present invention may be any amount that produces an effect of improving or maintaining mitochondrial function or reducing a decline in mitochondrial function, an effect of improving or maintaining energy production capacity or reducing a decline in energy production capacity, and/or an anti-fatigue effect. The dose may be appropriately set according to the administration form, administration method, body weight of a subject, and the like.

[0037]

In one embodiment, when a human (adult) is subjected to oral ingestion or administration of the composition of the present invention, the total administration amount of the sesamin-class compound is preferably 0.5 mg or more, more preferably 1 mg or more, still more preferably 3 mg or more, and is preferably 200 mg or less, more preferably 100 mg or less, still more preferably 80 mg or less per 60 kg body weight per day. The total administration amount of the lutein and/or a fatty acid ester thereof in terms of lutein is preferably 0.5 mg or more, more preferably 1 mg or more, still more preferably 3 mg or more, and is preferably 200 mg or less, more preferably 100 mg or less, still more preferably 80 mg or less per 60 kg body weight per day.

In one embodiment, in the case of a human (adult), the total administration amount of the sesamin-class compound is preferably 0.5 to 200 mg, more preferably 1 to 100 mg, still more preferably 3 to 80 mg per 60 kg body weight per day. In the case of a human (adult), the total administration amount of the lutein and/or a fatty acid ester thereof in terms of lutein is preferably 0.5 to 200 mg, more preferably 1 to 100 mg, still more preferably 3 to 80 mg per 60 kg body weight per day.

The sesamin-class compound and the lutein and/or a fatty acid ester thereof in the above amounts are 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, the sesamin-class compound and the lutein and/or a fatty acid ester thereof in the above amounts are orally ingested by or orally administered to a human.

In one embodiment, the composition of the present invention can be used to subject a human to ingestion or administration of the sesamin-class compound and the lutein and/or a fatty acid ester thereof in the above amounts per 60 kg body weight per day.

When the composition contains two or more sesamin-class compounds, the total administration amount of the sesamin-class compounds is the sum of these compounds. The total administration amount of lutein and/or a fatty acid ester thereof is the sum of lutein and its fatty acid ester.

In one embodiment, preferably, sesamin and/or episesamin is orally ingested by or administered to a human (adult) in an amount of preferably 0.5 to 200 mg, more preferably 1 to 100 mg, still more preferably 3 to 80 mg per 60 kg body weight per day as the total administration amount of sesamin and/or episesamin.

[0038]

Preferably, the composition of the present invention is continuously ingested or administered. The above effect(s) is likely to be enhanced when the sesamin-class compound and the lutein and/or a fatty acid ester thereof are continuously ingested or administered. In one embodiment, the composition of the present invention is continuously ingested or administered for preferably one week or more, more preferably four weeks or more, still more preferably eight weeks or more, particularly preferably 12 weeks or more.

[0039]

The subject (administration subject) subjected to ingestion or administration of the composition of the present invention is not limited. Examples include humans and non-human animals. Examples of the non-human animals include industrial animals, pets, and laboratory animals. Specifically, the term "industrial animals" refers to animals that are bred for industrial purposes. Examples include farm animals such as cows, horses, pigs, goats, and sheep; poultry such as chickens, ducks, quals, turkeys, and ostriches; and fish such as yellowtail, young yellowtail, red seabream, Japanese horse mackerel, carp, rainbow trout, and eel. The term "pets" refers to pet animals or companion animals such as dogs, cats, common marmosets, birds, and hamsters. The term "laboratory animals" refers to mice, rats, guinea pigs, beagles, miniature pigs, rhesus monkeys, crab-eating monkeys, and other animals that are used in research in fields of medicine, biology, agronomy, pharmacy, and the like.

[0040]

The administration subject of the composition of the present invention is preferably a human or non-human mammal, more preferably a human.

In one embodiment, the administration subject may be one needing or wanting to improve or maintain mitochondrial function or reduce a decline in mitochondrial function, one needing or wanting to improve or maintain energy production capacity or reduce a decline in energy production capacity, or one needing or wanting to suppress, alleviate, or reduce fatigue. As described above, aging is known to cause a decline in mitochondrial function and a decline in energy production capacity. In one embodiment, preferably, subjects of the composition of the present invention are middle-aged people. The composition of the present invention may be an anti-fatigue composition for middle-

aged people (preferably for the elderly) or a composition for improving or maintaining energy production capacity or reducing a decline in energy production capacity. The middle-aged people may be people who are 40 years old and older, for example. The term "middle-aged people" encompasses the elderly. The composition of the present invention can also be used on healthy people, for example, in order to produce the effect of improving or maintaining mitochondrial function or reducing a decline in mitochondrial function, the effect of improving or maintaining energy production capacity or reducing a decline in energy production capacity, and/or the anti-fatigue effect.

[0041]

To the composition of the present invention may be attached one or more labels indicating "alleviating fatigue", "alleviating feelings of fatigue", "alleviating discomfort", "reducing a decline in motivation", "facilitating energy production", "maintaining and improving vitality", "becoming less susceptible to fatigue", "maintaining vitality", "becoming full of energy", or the like. In one embodiment, to the composition of the present invention may be attached one or more labels selected from the group consisting of "alleviating fatigue", "alleviating feelings of fatigue", "alleviating discomfort", "reducing a decline in motivation", "facilitating energy production", and "maintaining and improving vitality". For example, the feelings of fatigue may be those to which one becomes more sensitive with aging. The energy production may be one that occurs in cells or mitochondria. In one embodiment of the present invention, preferably, the composition of the present invention is a food or beverage labeled with one or more function claims described above. These labels may be labels indicating use for obtaining these functions.

[0042]

The present invention also encompasses use of at least one sesamin-class compound and lutein and/or a fatty acid ester thereof in production of an anti-fatigue composition. The present invention also encompasses use of at least one sesamin-class compound and lutein and/or a fatty acid ester thereof in production of a composition for improving or maintaining energy production capacity or reducing a decline in energy production capacity.

[0043]

The present invention also encompasses the following methods:

a method of suppressing, alleviating, or reducing fatigue, the method including administering at least one sesamin-class compound and lutein and/or a fatty acid ester thereof; and

a method of improving or maintaining energy production capacity or reducing a decline in energy production capacity, the method including administering at least one sesamin-class compound and lutein and/or a fatty acid ester thereof.

[0044]

The present invention also encompasses the following uses:

use of at least one sesamin-class compound and lutein and/or a fatty acid ester thereof for suppressing, alleviating, or reducing fatigue; and

use of at least one sesamin-class compound and lutein and/or a fatty acid ester thereof for improving or maintaining energy production capacity or reducing a decline in energy production capacity.

The above uses and methods may be therapeutic or non-therapeutic.

Administering at least one sesamin-class compound and lutein and/or a fatty acid ester thereof to the subject can

improve or maintain mitochondrial function or reduce a decline in mitochondrial function, which results in the effect of improving or maintaining energy production capacity or reducing a decline in energy production capacity and the anti-fatigue effect. The fatigue is preferably physical fatigue.

At least one sesamin-class compound and lutein and/or a fatty acid ester thereof may be administered simultaneously or separately. Preferably, they are administered simultaneously.

[0045]

In the above uses and methods, preferred embodiments of the sesamin-class compound, lutein and/or a fatty acid ester thereof, ratio thereof, and the like are the same as those of the composition of the present invention described above. In one embodiment, the weight ratio of the total administration amount of the lutein and/or a fatty acid ester thereof in terms of lutein to the total administration amount of the sesamin-class compound ((total administration amount of lutein and/or a fatty acid ester thereof in terms of lutein)/total administration amount of sesamin-class compound) is preferably 0.005 to 200, more preferably 0.01 to 40, still more preferably 0.4 to 16.

The composition of the present invention may contain one sesamin-class compound or two or more sesamin-class compounds as the at least one sesamin-class compound. The composition of the present invention may contain lutein and a fatty acid ester thereof. In the above uses, preferably, at least one sesamin-class compound and lutein and/or a fatty acid ester thereof are administered to (ingested by) the subject at least once a day, for example, one to several times (e.g., two to three times) a day. In the above uses, preferably, at least one sesamin-class compound and lutein and/or a fatty acid ester thereof are orally administered (ingested). The above uses are preferably for

humans or non-human mammals, more preferably for humans.

[0046]

The above uses only require use of at least one sesamin-class compound and lutein and/or a fatty acid ester thereof in amounts (effective amounts) that produce a desirable effect(s). Preferred administration amounts, administration subjects, and the like of the sesamin-class compound as well as the lutein and/or a fatty acid ester thereof are the same as those of the composition of the present invention described above. The sesamin-class compound as well as the lutein and/or a fatty acid ester thereof may be directly administered or may be administered in the form of a composition containing the sesamin-class compound and the lutein and/or a fatty acid ester thereof. For example, the composition of the present invention described above may be used.

[0047]

In the above uses and methods, at least one sesamin-class compound (or a composition containing the same) and lutein and/or a fatty acid ester thereof (or a composition containing the same) are separately prepared. Then, they are substantially simultaneously ingested or administered; or one of them is ingested or administered first, and the other is ingested or administered later while the effect of the first one is still lasting. This results in an action that enhances the effect(s) intended by the present invention, which is(are) produced by the composition containing at least one sesamin-class compound and lutein and/or a fatty acid ester thereof (the effect of improving or maintaining mitochondrial function or reducing a decline in mitochondrial function, the effect of improving or maintaining energy production capacity or reducing a decline in energy production capacity, and/or the anti-fatigue effect). Thus, the present invention also encompasses, for example, a kit containing at least one

sesamin-class compound (or a composition containing the same) and lutein and/or a fatty acid ester thereof (or a composition containing the same).

EXAMPLES

[0048]

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

[0049]

In the examples and comparative examples, a mixture of sesamin and episesamin at a weight ratio of 1:1 was used as a sesamin-episesamin mixture. Hereinafter, the sesamin-episesamin mixture is sometimes described as SE.

[0050]

<Examples 1 to 3: Evaluation test of mitochondrial function of cells treated with sesamin-episesamin mixture (SE) and lutein>

To examine mitochondrial function, TIG-3 cells (cells derived from fetal lung) at 5.5×10^3 cells/well were seeded onto cell culture plates and cultured at 37°C with CO_2 (5%) for 24 hours. After 24 hours of culturing, a sesamin-episesamin mixture and lutein were added to each medium in the wells at the respective concentrations shown in Table 1 below and cultured for 24 hours. The mole ratio (lutein/sesamin-class compound) of the lutein to the sesamin-class compound in the medium was 0.3 in Example 1, 3 in Example 2, and 10 in Example 3. Subsequently, the media containing the sesamin-episesamin mixture and the lutein were removed, and the cells in the wells were treated for two hours in media containing H_2O_2 (800 μM). Subsequently, each medium was replaced with an analysis medium, and the oxygen consumption rate was analyzed using an analyzer (XF analyzer, Agilent Technologies Japan, Ltd.). After completion of analysis, the nuclei were

stained with Hoechst, and the cells were photographed by a fluorescence microscope "BZ-x" (Keyence Corporation). The number of cells was counted by image analysis. The amount of ATP production, which indicates mitochondrial function, can be evaluated by measuring the amount of decrease in oxygen consumption rate of the living cells by the XF analyzer. Specifically, an ATP synthase inhibitor (oligomycin) was added to the wells after the oxygen consumption rate of basal respiration of the living cells in the wells was measured. Then, the amount of decrease in oxygen consumption rate (pmol/min/10^3 cells) due to addition of oligomycin was measured. The result was regarded as the amount of ATP production. The basal respiration indicates cellular energy demand at baseline. A part of the basal respiration is used for ATP production. The amount of decrease in oxygen consumption rate by addition of oligomycin indicates the amount of ATP production. Table 1 shows the results obtained.

[0051]

<Reference Example 1: Evaluation test of mitochondrial function of untreated group>

To examine mitochondrial function, TIG-3 cells at 5.5 × 10^3 cells/well were seeded onto cell culture plates and cultured at 37°C with CO_2 (5%) for 24 hours. The oxygen consumption rate in Reference Example 1 was analyzed and the number of cells was counted as in Example 1, except that the cells were further cultured for 24 hours without adding a sesamin-episesamin mixture and lutein to the medium 24 hours after the first culturing and without treating the cells in the wells with a medium containing H_2O_2 (800 μM) for two hours. The amount of ATP production was also measured. Table 1 shows the results obtained.

[0052]

<Comparative Example 1: Evaluation test of mitochondrial function of H_2O_2-treated group>

To examine mitochondrial function, TIG-3 cells at 5.5 × 10^3 cells/well were seeded onto cell culture plates and cultured at 37°C with CO_2 (5%) for 24 hours. The oxygen consumption rate in Comparative Example 1 was analyzed and the number of cells was counted as in Example 1, except that the cells were further cultured for 26 hours without adding a sesamin-episesamin mixture and lutein to the medium 24 hours after the first culturing. The amount of ATP production was also measured. Table 1 shows the results obtained.

[0053]

<Comparative Examples 2 to 5: Evaluation test of mitochondrial function of cells treated with sesamin-episesamin mixture or lutein>

To examine mitochondrial function, TIG-3 cells at 5.5 × 10^3 cells/well were seeded onto cell culture plates and incubated at 37°C with CO_2 (5%) for 24 hours. A sesamin-episesamin mixture (Comparative Example 2) or lutein (Comparative Examples 3 to 5) was added 24 hours after the first culturing to each medium in the wells at the respective concentrations shown in Table 1 below and cultured for 24 hours. Other than that, the oxygen consumption rate in each of Comparative Examples 2 to 5 was analyzed and the number of cells was counted as in Example 1. The amount of ATP production was also measured. Table 1 shows the results obtained.

[0054]

[Table 1]

	H_2O_2 (μM)	SE (nM)	Lutein (nM)	Number of n	Measured value (pmol/min/10^3cells)	Standard error of measured values	Relative value (%)	Standard error of relative values
Reference Example 1	-	-	-	3	10.7	0.5	-	-
Comparative Example 1	800	-	-	2	5.6	-(1)	100.0	-(1)
Comparative Example 2	800	100	-	2	5.8	-(1)	102.8	-(1)
Comparative Example 3	800	-	30	3	5.3	0.4	94.5	7.0
Comparative Example 4	800	-	300	3	5.9	0.5	105.4	8.9
Comparative Example 5	800	-	1000	3	5.7	0.4	101.3	7.8
Example 1	800	100	30	3	6.6	0.7	117.7	12.4
Example 2	800	100	300	3	6.4	0.6	114.3	10.9
Example 3	800	100	1000	3	6.4	0.2	113.4	3.6

(1): No standard error calculation because n = 2

[0055]

In Table 1, values in "Measured value" (pmol/min/10^3 cells) show the amount of ATP production (the amount of decrease in oxygen consumption rate by the ATP synthase inhibitor) determined above. The "measured values" of Examples 1 to 3 and Comparative Examples 1 to 5 shown in Table 1 were divided by the "measured values" of Comparative Example 1, and the resulting values were each multiplied by 100 (100 × (measured value of one of examples and comparative examples)/(measured value of Comparative Example 1)). The thus-obtained values are shown as "Relative value (%)" (value relative to Comparative Example 1) in Table 1.

Values obtained by subtracting 100 (%) (Comparative Example 1) from the relative values (%) of Examples 1 to 3 and Comparative Examples 2 to 5 in Table 1 are each regarded as “Recovery rate (%)” relative to Comparative Example 1. A higher recovery rate means a larger amount of ATP production. FIG. 1 shows the recovery rate (%) determined for each of the examples and comparative examples (recovery rate relative to Comparative Example 1). In FIG. 1, SE indicates a sesamin-episesamin mixture.

In FIG. 1, "Comparative Example 4 + Comparative Example 2" is the sum of the recovery rate in Comparative Example 2 and the recovery rate in Comparative Example 4. "Comparative Example 5 + Comparative Example 2" is the sum of the recovery rate in Comparative Example 2 and the recovery rate in Comparative Example 5. "Comparative Example 4 + Comparative Example 2" and "Comparative Example 5 + Comparative Example 2" show the recovery rate of a combination of the sesamin-class compound and the recovery rate of the lutein (Examples 2 and 3), which can be predicted from the recovery rate of the sesamin-class compound alone (Comparative Example 2) and the recovery rate of the lutein alone (Comparative Example 4 or 5).

[0056]

As shown in Table 1, the amount of ATP production was decreased by 47.5% relative to the control group (Reference Example 1) by the treatment with 800 μM H_2O_2 according to Comparative Example 1. The treatment with the lutein at a concentration of 300 nM according to Comparative Example 4 or 1000 nM according to Comparative Example 5 increased the amount of ATP production by 5.4% (Comparative Example 4) or 1.3% (Comparative Example 5) as compared to the H_2O_2-treated group according to Comparative Example 1.

The treatment with the sesamin-episesamin mixture (100 nM) according to Comparative Example 2 increased the amount of ATP production by 2.8% as compared to the H_2O_2-treated group according to Comparative Example 1. This confirms that the treatment with the sesamin-episesamin mixture increases or maintains the amount of ATP production or reduces a decrease in the amount of ATP production. The group treated with the sesamin-episesamin mixture at a concentration of 100 nM and the lutein at a concentration of 30 nM according to Example 1, the group treated with the sesamin-episesamin mixture at a concentration of 100 nM and the lutein at a concentration of 300 nM according to Example 2, or the group treated with the sesamin-episesamin mixture at a concentration of 100 nM and the lutein at a concentration of 1000 nM according to Example 3 showed an increase in the amount of ATP production by 17.7% in Example 1, 14.3% in Example 2, and 13.4% in Example 3 as compared to the H_2O_2-treated group according to Comparative Example 1. As also shown in FIG. 1, these values are greater than the sum of the recovery rate of the amount of ATP production from the treatment with the sesamin-episesamin mixture alone and the recovery rate of the amount of ATP production from the treatment with the lutein alone. This confirms that the treatment with the lutein and the sesamin-episesamin mixture did not simply

additively increase the amount of ATP production, but the combination of the sesamin-episesamin mixture and the lutein synergistically increased the amount of ATP production. In other words, the compositions containing the sesamin-episesamin mixture and the lutein show a synergistic effect of increasing or maintaining the amount of ATP production or reducing a decrease in the amount of ATP production, owing to the presence of both the sesamin-episesamin mixture and the lutein. Thus, these compositions were confirmed to exert the effect(s) even when used in a small amount.

[0057]

The above clearly shows that the combination of the sesamin-episesamin mixture and the lutein produces a synergistic effect of increasing or maintaining the amount of ATP production or reducing a decline in the amount of ATP production. Thus, the compositions containing at least one sesamin-class compound and lutein and/or a fatty acid ester thereof were found to be capable of effectively improving or maintaining mitochondrial function or reducing a decline in mitochondrial function. Use of at least one sesamin-class compound and lutein and/or a fatty acid ester thereof in combination can improve or maintain energy production capacity or reduce a decline in energy production capacity. This can produce the anti-fatigue effect.

[0058]

<Example 4: Human test>

(Evaluation sample)

Food in which the contents were encapsulated with a coating containing gelatin and glycerol was produced as test food. The contents were obtained by dispersing the sesamin-episesamin mixture and the lutein with a glycerol fatty acid ester in an edible vegetable oil such that three capsules contain 10 mg sesamin-episesamin mixture and 10 mg

lutein. Another food was produced using the same material as the test food but without using the sesamin-episesamin mixture and the lutein and regarded as control food. The test food and the control food were the same in terms of calories, protein content, lipid content, and carbohydrate content per three capsules, and these foods were indistinguishable from the appearance and the like.

[0059]

(Evaluation method)

The control food (three capsules per day) or the test food (three capsules per day) were ingested by male and female subjects of 40 years or older and younger than 65 years old (30 people per group) who were more susceptible to fatigue with aging. The test day was scheduled at the beginning of the ingestion and on week 8 of the ingestion. On the test day, the feelings of fatigue after the visit (feelings of fatigue (1)) were measured. Subsequently, Kraepelin test as mental fatigue stress (mental stress) was performed (two times, 15 minutes per time with a five-minute break). After the test, the feelings of fatigue (feelings of fatigue (2)) were measured. Subsequently, the subjects were subjected to exercise as physical fatigue stress (physical stress) for 30 minutes using an ergometer (Aerobike® EZ101, Konami Sports & Life). After the exercise, the feelings of fatigue (feelings of fatigue (3)) were measured. The exercise intensity was set to a range of 3.5 to 6.8 METs which is a range of activities in daily life. The exercise intensity was adjusted to eliminate individual differences. After the exercise, a 60-minute break was taken. Then, the feelings of fatigue (feelings of fatigue (4)) were measured. Further, the feelings of fatigue on the following morning (feelings of fatigue (5)) were measured.

[0060]

The feelings of fatigue were evaluated using Visual

Analogue Scale (VAS). Specifically, each subject indicated the level of feelings of fatigue by marking on a 10-cm straight line with "Feeling the best without any feelings of fatigue" at the left end (0 cm) and "Feeling the worst and too fatigued to do anything" at the right end (10 cm). The distance (cm) of the mark from the left end on the 10-cm straight line was measured to obtain measured values of the feelings of fatigue. The amount of change in feelings of fatigue at each point on week 8 was calculated from the following formulas (i) to (iv), using the measured values of the feelings of fatigue (1) to (5).

[0061]

Amount of change in feelings of fatigue at visit = (Feelings of fatigue at visit on week 8 (1)) - (Feelings of fatigue at visit on week 0 (1)) Formula (i)

[0062]

Amount of change in feelings of fatigue by physical stress = {(Feelings of fatigue immediately after exercise stress on week 8 (3)) - (Feelings of fatigue after the Kraepelin test on week 8 (2))} - {(Feelings of fatigue immediately after exercise stress on week 0 (3)) - (Feelings of fatigue after Kraepelin test on week 0 (2))} Formula (ii)

[0063]

Amount of change in feelings of fatigue after a break = (Feelings of fatigue 60 minutes after exercise stress 60 minutes on week 8 (4)) - (Feelings of fatigue 60 minutes after exercise stress on week 0 (4)) Formula (iii)

[0064]

Amount of change in feelings of fatigue on the following morning = (Feelings of fatigue on the following morning on week 8 (5)) - (Feelings of fatigue on the following morning on week 0 (5)) Formula (iv)

[0065]

(Analysis 1: Analysis on subject of effectiveness analysis)

An analysis was performed excluding the subjects who met exclusion criteria (six people in the test food group, four people in the control food group). Table 2 shows the results of the amount of change in feelings of fatigue at the visit. Significance was tested by paired t-test (before and after difference (relative to the feelings of fatigue on week 0) #: $p < 0.10$).

Only the test food group showed a tendency to reduce the feelings of fatigue at the visit. This confirms that the compositions containing the sesamin-class compound and the lutein reduce the feelings of fatigue in daily life.

[0066]

[Table 2]

	Test food (n = 24)	Control food (n = 26)
At visit	$-0.8 \pm 0.4^{\#}$	-0.5 ± 0.4

[0067]

(Analysis 2: Subgroup analysis)

An analysis was performed on the subjects who were determined as being systemically exposed to the stress in a proper manner (8 people per group), using the formulas (ii) to (iv). Table 3 shows the results (amount of change in feelings of fatigue). Significance was tested by paired t-test for comparison before and after the test and by unpaired t-test for comparison between the groups (before and after difference (relative to the feelings of fatigue on week 0) #: $p < 0.10$; †: $p < 0.05$; difference between groups §: $p < 0.10$).

[0068]

[Table 3]

	Test food (n = 8)	Control food (n = 8)
Feelings of fatigue by physical stress	-1.2 ± 0.6$^{\#}$	-0.7 ± 0.4$^{\#}$
After break	-1.0 ± 0.6†	-0.5 ± 0.7
On the following morning	-2.4 ± 0.5†,§	-0.8 ± 0.7

[0069]

The test food group showed a greater range of reduction in feelings of fatigue from the physical stress than the control food group. This shows that the compositions containing a combination of the sesamin-class compound and the lutein can reduce the feelings of fatigue from the physical fatigue stress.

The ingestion of the test food significantly reduced the feelings of fatigue after the break and on the following morning. This shows that the compositions containing the sesamin-class compound and the lutein act on recovery from fatigue after the physical fatigue stress and/or mental fatigue stress.

CLAIMS

Claim 1. Non-therapeutic use of at least one sesamin-class compound and at least one of lutein or a fatty acid ester thereof for suppressing, alleviating, or reducing fatigue,

wherein the at least one sesamin-class compound is at least one of sesamin or episesamin, and

a mole ratio of the at least one of lutein or a fatty acid ester thereof to the sesamin-class compound is 0.3 to 10.

Claim 2. Non-therapeutic use of at least one sesamin-class compound and at least one of lutein or a fatty acid ester thereof for improving or maintaining energy production capacity or reducing a decline in energy production capacity,

wherein the at least one sesamin-class compound is at least one of sesamin or episesamin, and

a mole ratio of the at least one of lutein or a fatty acid ester thereof to the sesamin-class compound is 0.3 to 10.