

DESCRIPTION

Title of Invention: NUTRIENT TONIC CONTAINING BEE LARVAE

Technical Field

5 [0001] The present invention relates to a restorative tonic, a sexual function improver, a male climacteric symptom alleviator, and an anti-fatigue agent.

Background Art

10 [0002] One of the aging-related problems faced by men is the manifestation of male climacterium. It is estimated that about 40% of men in their forties to sixties experience some degree of male climacterium.

[0003] When male climacteric disorder occurs, various symptoms
15 (e.g., depression, despondency, annoyance, anxiety, nervousness, fatigue, loss of vigor, myositis, arthritis, muscle weakness, hot flashes, sweating, memory deterioration, sleep disorder, poor concentration, a sense of physical exhaustion, erectile dysfunction (ED), a decrease in sexual desire, and loss of
20 ejaculation sensation) are strongly manifested. Known is a method of determining the presence or absence of male climacteric disorder based on the measurement of blood testosterone concentration by a blood examination and a questionnaire. It has been pointed out that various stresses at work and home that men
25 in their most productive years have are significantly involved in the development of male climacteric disorder. In recent years, the number of middle-aged and older men suspected of climacteric disorder has tended to increase.

[0004] Male climacteric disorder exhibits the following pathology
30 on the basis of an age-related reduction in androgens: dysautonomia symptoms and neuropsychiatric symptoms similar to those of menopause in women appear, and are further complicated by a reduction in male function in most cases (Male Climacteric Disorder LOH, written by Akihiko Okuyama, I What is Male
35 Climacteric Disorder, D. From Viewpoint of Psychosomatic Medicine,

page 24 (Nanzando Co., Ltd.) 2007.). Meanwhile, with regard to the secretion of sex hormones typified by testosterone, the secretion of hormones including testosterone is regulated via negative feedback through a hypothalamic-pituitary-testicular axis (Male Climacteric Disorder LOH, written by Akihiko Okuyama, II Diagnosis of Male Climacteric Disorder, C. Measurement of Hormone and Evaluation Thereof, page 65 (Nanzando Co., Ltd.) 2007.). Therefore, it is difficult to determine the presence of male climacteric disorder with only a measurement value for testosterone.

[0005] In general, a test subject who is aware of a reduction in his vitality and exhibits a tendency of reduction in free testosterone in blood is diagnosed with late-onset hypogonadism (LOH), and androgen replacement therapy may be indicated therefor in order to maintain QOL. However, whereas hormone replacement therapy in women is in widespread use internationally, treatment for men does not fall within the scope of medicine except for the widespread use of, for example, a PDE5 inhibitor for ED.

[0006] For example, in Patent Literature 1 to 3, various ingredients that increase testosterone are reported.

[0007] In Patent Literature 1, it is reported that tangshenosides, lancemaside-A, and syringin contained in a plant of the genus *Codonopsis* each have an inhibitory action on the reduction in blood testosterone.

[0008] In Patent Literature 2, it is reported that geranylgeraniol has a testosterone-enhancing action.

[0009] In Patent Literature 3, it is reported that a black vinegar-related material, and a combination of the material and a specific material each remarkably promote the secretion of testosterone.

[0010] However, even androgen replacement therapy has a risk of side effects. In particular, prostate-specific antigen (PSA) serving as a prostate tumor marker requires caution. Accordingly, there is a demand for a climacteric symptom alleviator free of any androgen-like action.

[0011] In addition, "sildenafil" serving as a PDE5 inhibitor has been used as a drug for ED treatment. However, sildenafil has been reported to have side effects and a drug interaction, which, however, are temporary. For example, sildenafil serves to promote
5 the hypotensive action of a nitrovasodilator, for example, nitroglycerin, and hence combined use therewith is contraindicated. In addition, actions of sildenafil on the eyes have been found to cause cyanopsia, diplopia, erythropsia, and the like.

10 [0012] Incidentally, bee larvae have been eaten as nutrient sources for protein and the like in various countries and regions since ancient times. In recent years, there has been known a health food using, as a raw material, powder obtained by drying and pulverizing the bee larvae. The health food is rich in
15 protein, amino acids, vitamins, and minerals from the bee larvae. The bee larvae are known to have an antioxidant action as disclosed in Patent Literature 4, but much remains to be known about other actions thereof.

20 Citation List

Patent Literature

[0013] [PTL 1] JP 2006-306889 A

[PTL 2] JP 5382512 B2

[PTL 3] JP 2013-181031 A

25 [PTL 4] JP 5405067 B2

Summary of Invention

Technical Problem

[0014] It is an object of the present invention to provide a
30 restorative tonic, a sexual function improver, a male climacteric symptom alleviator, and an anti-fatigue agent each of which does not increase androgens and is highly safe.

Solution to Problem

35 [0015] The inventors of the present invention have made extensive

investigations in order to achieve the above-mentioned object,
and as a result, have found that a bee larva has a restorative
tonic action, a sexual function-improving action, a male
climacteric symptom-alleviating action, and an anti-fatigue
5 action, and moreover, the bee larva does not increase androgens
and is highly safe.

[0016] The present invention has been completed by making further
investigations on the basis of the above-mentioned findings, and
provides the following restorative tonic, sexual function
10 improver, male climacteric symptom alleviator, anti-fatigue agent,
etc.

[0017] Item 1. A restorative tonic, including a bee larva.

Item 2. A sexual function improver, including a bee larva.

Item 3. A male climacteric symptom alleviator, including a bee
15 larva.

Item 4. An anti-fatigue agent, including a bee larva.

Item 5. A vitality enhancer, including a bee larva.

Item 6. A restorative tonic according to Item 1, a sexual
function improver according to Item 2, a male climacteric symptom
20 alleviator according to Item 3, an anti-fatigue agent according
to Item 4, or a vitality enhancer according to Item 5, in which
the bee larva is a bee larva treated with a protease.

Item 7. A restorative tonic, sexual function-improving, male
climacteric symptom-alleviating, anti-fatigue, and/or vitality-
25 enhancing composition, including a bee larva.

Item 8. A restorative tonic, sexual function-improving, male
climacteric symptom-alleviating, anti-fatigue, and/or vitality-
enhancing food composition, including a bee larva.

Item 9. A composition according to Item 7 or 8, in which the bee
30 larva is a bee larva treated with a protease.

Item 10. A restorative tonic method, a sexual function-improving
method, a male climacteric symptom-alleviating method, a fatigue-
improving method, or a vitality-enhancing method, including a
step of administering an effective amount of a bee larva to a
35 mammal.

Item 11. A method according to Item 10, in which the bee larva is a bee larva treated with a protease.

Item 12. A use of a bee larva in production of a restorative tonic, a sexual function improver, a male climacteric symptom
5 alleviator, an anti-fatigue agent, or a vitality enhancer.

Item 13. A use according to Item 12, in which the bee larva is a bee larva treated with a protease.

Advantageous Effects of Invention

10 [0018] The bee larva has a restorative tonic action-improving action, a sexual function-improving action, a male climacteric symptom and anti-fatigue action, and hence is useful as an active ingredient of each of the restorative tonic, the sexual function improver, the male climacteric symptom alleviator, and the anti-
15 fatigue agent. Moreover, the bee larva does not increase androgens, and hence is highly safe.

Brief Description of Drawings

[0019] FIGS. 1 are graphs for showing (a) AMS scores (total), (b)
20 AMS scores (sexual factors), and (c) AMS scores (physical factors) before and after test food intake. Mean $\pm$ SE *p<0.05
**p<0.01

FIG. 2 is a graph for showing IIEF5 scores before and after test food intake. Mean $\pm$ SE *p<0.05 **p<0.01

25 FIG. 3 is a graph for showing the number of early morning erections before and after test food intake. Mean $\pm$ SE *p<0.05
**p<0.01

FIG. 4 is a graph for showing values for VAS for fatigue before and after test food intake. Mean $\pm$ SE *p<0.05 **p<0.01

30 FIG. 5 is a graph for showing SDS scores before and after test food intake. Mean $\pm$ SE *p<0.05 **p<0.01

FIGS. 6 are graphs for showing (a) TT levels and (b) FT levels before and after test food intake. Mean $\pm$ SE *p<0.05 **p<0.01

35 Description of Embodiments

[0020] Now, the present invention is described in detail.

[0021] A restorative tonic, a sexual function improver, a male climacteric symptom alleviator, and an anti-fatigue agent of the present invention each include a bee larva.

5 [0022] The restorative tonic, the sexual function improver, the male climacteric symptom alleviator, and the anti-fatigue agent of the present invention do not increase androgens, and hence are highly safe.

[0023] The term "androgens" is a collective term for steroid
10 hormones, which are also called male hormones, and encompasses, for example, dihydrotestosterone, dehydroepiandrosterone, androsterone, androstenedione, and epiandrosterone, in addition to testosterone, which is a typical example.

[0024] Herein, the bee larva means the larva and pupa of a bee.
15 The kind of bee is not particularly limited, and a wide range of known bees, such as honey bees, including a Japanese honey bee and a western honey bee, an Africanized honey bee, wasps (including *Vespula flaviceps*), a paper wasp, and a bumblebee, may be used. Of those, honey bees are preferred, and a western honey
20 bee is more preferred from the viewpoint of ease of availability. The bee may be male or female, and is preferably male.

[0025] The larva and pupa are not particularly limited as long as the larva and pupa have been hatched from an egg. In particular, the larva and pupa of a bee after a lapse of from 16 days to 23
25 days from hatching are preferably used, and the larva and pupa of a bee after a lapse of from 18 days to 21 days from hatching are more preferably used.

[0026] The bee larva has nutrients stored in its body. In particular, a male honey bee has long been used as a material in
30 traditional Chinese medicine, contains various amino acids including essential amino acids in a well-balanced manner, and is also rich in protein, lipids, saccharides, vitamins, such as B-vitamins, folic acid, nicotinic acid, and pantothenic acid, and minerals, such as zinc and selenium. As the physiological
35 activity and pharmacological action of the bee larva, there are

known an antibacterial action, an anti-inflammatory action, an antiviral action, an antiprotozoal action, an anti-tinnitus action, and the like.

[0027] In the present invention, the bee larva is used in the state of any of a raw bee larva and a product obtained by processing the raw bee larva. Specific examples of the product obtained by processing the bee larva include: a product obtained by pulverizing the bee larva (raw or dried); a product obtained by drying the bee larva (raw or pulverized); a product obtained by subjecting the bee larva (raw, dried, or pulverized) to heating treatment; and a product obtained by extracting the bee larva with water, hydrous ethanol, or the like. A preferred example thereof may be a dry powder of the bee larva prepared by drying the bee larva (raw), followed by pulverization.

[0028] Unless otherwise stated, the term "bee larva" as used in the present invention includes the following in addition to the raw bee larva: a processed product obtained by subjecting the bee larva to drying, pulverizing, or heating treatment; a product obtained by extracting the bee larva (including raw, dried, and pulverized ones) with water, hydrous ethanol, or the like; and products obtained by treating the bee larva and the processed products thereof with a protease (peptidase).

[0029] As a drying method, a known method to be adopted in general food processing, for example, natural drying, such as draft drying or sun drying, forced drying involving drying by heating with electricity or the like, or freeze-drying, may be used. Of those, freeze-drying is preferred. The drying time is not particularly limited, and for example, in the case of natural drying, such as draft or sun drying, the drying time may be about 3 days, and in the case of forced drying performed by heating with electricity or the like, the drying time may be from about 1 day to about 3 days at about 50°C. It is generally preferred that the drying be performed so as to achieve a water content of 10 mass% or less, preferably 5 mass% or less. When a water content of 10 mass% or less is difficult to achieve as in the case of

natural drying, such as draft or sun drying, treatment for further reducing the water content through the use of a freeze-dryer may be subsequently performed.

[0030] The pulverizing treatment (powderizing treatment) may be performed using a known method, for example, a method involving pulverization with a pulverizer (mill) or a method involving grinding with millstones.

[0031] The method of heating the bee larva is not particularly limited, and a preferred example thereof may be a method involving heat treatment at from 70°C to 120°C. The heating treatment may be simply performed by putting the bee larva (including raw, dried, and pulverized ones) into boiling water, and in order to prevent active ingredients, such as various vitamins and amino acids, from eluting as much as possible, a method involving steaming the bee larva with a vapor is suitably used for the heating treatment.

[0032] As an extraction method, a method involving adding water, hydrous ethanol, or the like to the bee larva (including raw, dried, and pulverized ones), stirring the mixture, and then centrifuging the resultant to obtain a supernatant, a method involving performing filtration with filter paper to obtain a filtrate, or the like is used.

[0033] When the bee larva and the processed products thereof are treated with a protease, it is expected that protein contained in the bee larva and the processed products thereof is turned to low-molecular-weight fragments to provide enzyme-treated products in which allergic reactions due to the protein are suppressed (enzyme-treated products having reduced allergenicity).

[0034] A suitable example of the protease to be used for subjecting the bee larva and the processed product thereof to the enzyme treatment may be a peptidase. The peptidase to be used only needs to have at least one of an endopeptidase action or an exopeptidase action.

[0035] Examples of the protease having at least endopeptidase activity include endopeptidases derived from animals (e.g.,

trypsin and chymotrypsin), endopeptidases derived from plants (e.g., papain), and endopeptidases derived from microorganisms (e.g., lactobacilli, yeast, fungi, *Bacillus subtilis*, and actinomycetes).

5 [0036] Examples of the protease having at least exopeptidase activity include carboxypeptidase, aminopeptidase, exopeptidases derived from microorganisms (e.g., lactobacilli, fungi of the genus *Aspergillus*, and fungi of the genus *Rhizopus*), and pancreatin and pepsin, each of which also has endopeptidase
10 activity.

[0037] Of such various enzymes, preferred examples of the enzyme having both exopeptidase activity and endopeptidase activity may include a peptidase produced by *Streptomyces griseus* (product name: Actinase AS), a peptidase produced by *Aspergillus orizae*
15 (product names: Protease A and Flavourzyme), and a peptidase produced by *Aspergillus melleus* (product name: Protease P).

[0038] In addition, preferred examples of the enzyme having an exoprotease action may include a peptidase produced by *Aspergillus orizae* (product name: Umamizyme G, Promod 192P,
20 Promod 194P, and Sumizyme FLAP), a peptidase produced by *Aspergillus sojae* (product name: Sternzyme B15024), a peptidase produced by the genus *Aspergillus* (product name: Kokulase P), and a peptidase produced by *Rhizopus oryzae* (product name: peptidase R).

25 [0039] Further, preferred examples of the enzyme having an endoprotease action may include a peptidase produced by *Bacillus subtilis* (product names: Orientase 22BF and Nucleicin), a peptidase produced by *Bacillus licheniformis* (product name: ALCALASE), a peptidase produced by *Bacillus stearothermophilus*
30 (product name: Protease S), a peptidase produced by *Bacillus amyloliquefaciens* (product name: Neutrase), and a peptidase produced by the genus *Bacillus* (product name: Prometax).

[0040] The enzyme treatment for reducing the allergenicity of the bee larva and the processed products thereof may be performed in
35 accordance with, for example, the description of JP 2009-159997 A.

[0041] The restorative tonic, the sexual function improver, the male climacteric symptom alleviator, and the anti-fatigue agent of the present invention may each include an additional ingredient as long as the effects of the present invention are not impaired. When such additional ingredient is included, the ratio of the bee larva in each of the restorative tonic, the sexual function improver, the male climacteric symptom alleviator, and the anti-fatigue agent may be, for example, from 0.01 mass% to 99 mass%, preferably from 1 mass% to 80 mass%, more preferably from 10 mass% to 70 mass%, and still more preferably from 20 mass% to 50 mass%.

[0042] Each of the restorative tonic, the sexual function improver, the male climacteric symptom alleviator, and the anti-fatigue agent of the present invention is not particularly limited in terms of its form, and may have the form of a preparation, for example, a powder, a granule, a tablet, a capsule, a solution, a suspension, or an emulsion.

[0043] The restorative tonic, the sexual function improver, the male climacteric symptom alleviator, and the anti-fatigue agent of the present invention may each be suitably used as an ingredient of each of a food composition, a quasi-drug, and a pharmaceutical (in particular, an oral pharmaceutical).

[0044] The restorative tonic, the sexual function improver, the male climacteric symptom alleviator, and the anti-fatigue agent of the present invention also encompass the meanings of a food and beverage intended for health, health maintenance and promotion, and the like (e.g., a health food, a functional food, a nutritional composition, a dietary supplement, a supplement, a food for health use, a food for specified health use, a food with nutrient function claims, or a food with function claims), a quasi-drug, and a pharmaceutical (in particular, an oral pharmaceutical). In addition, the restorative tonic, the sexual function improver, the male climacteric symptom alleviator, and the anti-fatigue agent of the present invention encompass the meanings of additives for imparting a restorative tonic action, a

sexual function-improving action, a male climacteric symptom-alleviating action, an anti-fatigue action, and a vitality-enhancing action.

[0045] In the food and beverage, an excipient, a glazing agent,
5 minerals, vitamins, flavonoids, quinones, polyphenols, an amino acid, a nucleic acid, an essential fatty acid, an algefacient, a binder, a sweetener, a disintegrating agent, a lubricant, a colorant, a flavoring, a stabilizer, an antiseptic agent, a slow-release adjuster, a surfactant, a solubilizer, a moisturizer, and
10 the like may be blended as required.

[0046] The kind of food and beverage is not particularly limited, and examples thereof include: beverages (e.g., soft beverages, such as coffee, juice, and tea beverages, milk beverages, lactobacillus beverages, yogurt beverages, carbonated beverages,
15 and alcoholic beverages, such as sake, western alcoholic beverages, and fruit liquors); spreads (e.g., pastry cream); pastes (e.g., fruit paste); western confectionery (e.g., chocolate, a doughnut, pie, a cream puff, gum, jelly, a candy, a cookie, cake, and pudding); Japanese confectionery (e.g., daifuku,
20 rice cake, a steamed bean-jam bun, sponge cake, anmitsu, and yokan); frozen desserts (e.g., ice cream, a popsicle, and sherbet); foods (e.g., curry, a beef bowl, mixed porridge, miso soup, soup, meat sauce, pasta, pickles, and a jam); and seasonings (e.g., a dressing, dried seasoning powder, a flavor
25 enhancer, and a soup mix).

[0047] A unit dosage form in the use as a supplement is not particularly limited and may be appropriately selected, and examples thereof include a tablet, a capsule, a granule, a solution, and a powder.

30 [0048] With regard to the ratio of the bee larva in the food and beverage, the concentration thereof may be, for example, from 0.01 mass% to 99 mass%, preferably from 1 mass% to 80 mass%, more preferably from 10 mass% to 70 mass%, and still more preferably from 20 mass% to 50 mass%.

35 [0049] The intake of the food and beverage may be appropriately

set depending on various conditions, such as the body weight, age, sex, and symptoms of the person who takes in the food and beverage.

[0050] The restorative tonic, the sexual function improver, the male climacteric symptom alleviator, and the anti-fatigue agent of the present invention may each be called a bee larva preparation when prepared as a quasi-drug or a pharmaceutical. In the quasi-drug or the pharmaceutical, the bee larva may be used alone, or may be used as a mixture with other pharmaceutical ingredients described in The Japanese Pharmacopoeia, such as vitamins and crude drugs.

[0051] When the restorative tonic, the sexual function improver, the male climacteric symptom alleviator, and the anti-fatigue agent of the present invention are each prepared as a quasi-drug or a pharmaceutical, the bee larva may be prepared, together with a pharmaceutically acceptable non-toxic carrier, diluent, or excipient, into the form of, for example, any of tablets (including an uncoated tablet, a sugar-coated tablet, an effervescent tablet, a film-coated tablet, a chewable tablet, a troche, and the like), a capsule, a pill, a powdery preparation (powder), a fine granule, a granule, a solution, a suspension, an emulsion, a syrup, and a paste to serve as an oral preparation.

[0052] The dose of the quasi-drug or the pharmaceutical may be appropriately determined depending on various conditions, such as the body weight, age, sex, and symptoms of a patient, and is desirably set to 0.5 g or more, preferably 0.7 g or more, more preferably 1 g or more per day in terms of the bee larva.

[0053] The ratio of the bee larva in the quasi-drug or the pharmaceutical is not particularly limited as long as the effects of the present invention are exhibited, and the concentration thereof may be, for example, from 0.01 mass% to 99 mass%, preferably from 1 mass% to 80 mass%, more preferably from 10 mass% to 70 mass%, and still more preferably from 20 mass% to 50 mass%.

[0054] The restorative tonic, the sexual function improver, the

male climacteric symptom alleviator, and the anti-fatigue agent of the present invention described above are applied to mammals including humans (preferably humans, in particular, men).

[0055] The food and beverage, the quasi-drug, and the
5 pharmaceutical of the present invention have a restorative tonic action, a sexual function-improving action, a male climacteric symptom-alleviating action, an anti-fatigue action, and a vitality-enhancing action. In addition, the food and beverage, the quasi-drug, and the pharmaceutical of the present invention
10 do not increase androgens, and hence are highly safe.

Examples

[0056] Now, the present invention is described in more detail by way of Examples. However, the present invention is by no means
15 limited to these Examples and the like.

[0057] [Test Example]

<Test Subject>

Through a questionnaire and examinations (a physical examination, a medical interview by a physician, a blood
20 examination, a questionnaire, and the like), eleven people each of whom: (1) was a man aged 35 years or more and 60 years or less; (2) had a score of 27 or more and 49 or less in the Aging Male Symptom (hereinafter referred to as AMS) scale; (3) had a free testosterone level of 8.5 pg/mL or more and less than 11.8
25 pg/mL; and (4) was married or had an opposite-sex partner were chosen as test subjects.

[0058] <Test Method>

The eleven test subjects each took in six capsules of a soft capsule-shaped bee larva-containing food containing 180 mg
30 of bee larvae per capsule daily for 12 weeks. Nutritional composition per capsule of the test food is shown in the following table.

[0059]

35 Table 1

Nutritional composition	Test food
Energy (kcal)	10.3
Protein (g)	0.8
Lipid (g)	0.6
Carbohydrate (g)	0.3
Sodium (mg)	7.8

[0060] The test subjects recorded daily subjective symptoms, living information, and the like, including the presence or absence of an early morning erection, in a journal during a
5 period from 1 week before the start of the test to the end of the intake.

[0061] At the start of the test and in the 12th week after the start of the intake, a medical examination by a physician, a questionnaire, a physical examination, a blood examination, and a
10 urine examination were performed to evaluate total testosterone (hereinafter referred to as TT), free testosterone (hereinafter referred to as FT), the Aging Male Symptom (hereinafter referred to as AMS) scale, the Self-rating depression scale (hereinafter referred to as SDS), a score for the simplified International
15 Index of Erectile Function (hereinafter referred to as IIEF5), and VAS for fatigue. In addition, the number of early morning erections during the test period was also adopted as an evaluation item.

[0062] The AMS score is a score based on a self-administered
20 questionnaire widely used in a medical interview for the symptoms of LOH, and includes five items of psychological factors (25 points), seven items of physical factors (35 points), and five items of sexual function factors (25 points), i.e., 17 items in total (85 points). For each item, an evaluation is made in the
25 five stages of "None," "Mild," "Moderate," "Severe," and "Extremely severe," and scores of from 1 to 5 are given, respectively. A higher score indicates that symptoms are more severe.

[0063] The SDS is an index indicating the degree of a depression
30 state, and includes twenty question items as to depressive

symptoms. A higher score indicates that symptoms are more severe.

[0064] The IIEF5 score is a score for a simplified five-item version of the International Index of Erectile Function (IIEF), and is an international index used in screening for ED and
5 assessment of a therapeutic effect thereon. A lower score indicates that symptoms are more severe.

[0065] The fatigue is determined in accordance with a VAS method as follows: the left end of a 10 cm straight line is defined as "the best feeling with no sense of tiredness, the likes of which
10 one has never experienced before" and the right end thereof is defined as "the worst feeling with such thorough tiredness as to make it impossible to do anything, the likes of which one has never experienced before," a position on the straight line corresponding to the fatigue is marked with the symbol "×," and
15 the distance from the left end to the marked position is expressed in a numerical value. A reduction in the numerical value indicates an improvement.

[0066] <Statistical Analysis>

In each set of data, a mean and a standard deviation were
20 determined for each group, and a Wilcoxon signed-rank sum test was performed for each of the AMS score, the IIEF5, the SDS, the number of early morning erections, and the VAS for fatigue.

[0067] A paired t-test was performed for each of the TT, the FT, the physical examination, a hematologic examination, and a blood
25 biochemical examination.

[0068] Each statistical analysis method was a two-tailed test, and significance levels were set to 5% and 1%.

[0069] <Results>

1. Efficacy Evaluation Items

30 1) AMS

In the AMS scores, significant reductions were observed in "total" (FIG. 1-a), "sexual factors" (FIG. 1-b), and "physical factors" (FIG. 1-c) at the end of the intake as compared to those at the start of the intake.

35 [0070] 2) IIEF5

In a comparison between the IIEF5 scores before and after test food intake, a significant increase was observed at the end of the intake (FIG. 2).

[0071] 3) Number of early morning erections

5 In a comparison of the number of early morning erections before and after test food intake, a significant increase was observed at the end of the intake (FIG. 3).

[0072] 4) VAS for Fatigue

10 In a comparison of the value for fatigue before and after test food intake, a significant reduction was observed at the end of the intake (FIG. 4).

[0073] 5) SDS

15 In a comparison of depressive symptoms before and after test food intake, a significant reduction was observed at the end of the intake (FIG. 5).

[0074] 2. Safety Evaluation Items

20 Each of the test subjects was checked for the TT and the FT (FIG. 6), the physical examination, the hematologic examination, the blood biochemical examination, and the urine examination, and as a result, no changes posing clinical problems were found.

[0075] During the test period, subjective symptoms were not found in the test subjects. In addition, also in the medical examination performed during the intake period, nothing considered to be an adverse event was found.

25 [0076] <Conclusion>

When the eleven men aged 35 years or more and 60 years or less who were dissatisfied with vitality in their daily lives were each allowed to take in six soft capsules of the bee larva-containing food per day for 12 weeks, significant reductions in AMS, significant increases in IIEF5 and number of early morning erections, and significant reductions in VAS serving as an evaluation of fatigue and SDS questionnaire were observed. Meanwhile, there were no changes in total and free testosterone levels. In other words, the bee larvae did not increase testosterone levels, and were observed to have a male climacteric

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symptom-alleviating effect, an anti-fatigue effect, and an anti-stress effect.

[0077] Formulation Examples

Now, Formulation Examples of the present invention are
5 described.

[0078] Formulation Example 1: Soft Capsule

To bee larvae in an amount corresponding to 1/6 of 1,080 mg, an edible oil and fat, beeswax, and vegetable lecithin derived from soybeans were added, and the mixture was filled into a soft
10 capsule containing gelatin and caramel color to provide a soft capsule preparation.

[0079] Formulation Example 2: Soft Capsule

180 mg of bee larvae were mixed with an edible oil and fat, γ -aminobutyric acid, glycerin, vegetable lecithin derived from
15 soybeans, beeswax, vitamin B2, and vitamin B12, and the mixture was filled into a soft capsule containing gelatin and caramel color to provide a soft capsule preparation.

[0080] Formulation Example 3: Soft Capsule

100 mg of bee larvae were mixed with an edible oil and fat,
20 maca extract powder, tongkat ali extract powder, *Cordyceps sinensis* mycelium powder, zinc-containing yeast, *Piper longum* extract powder, beeswax, and vegetable lecithin derived from soybeans, and the mixture was filled into a soft capsule containing gelatin and cacao color to provide a soft capsule
25 preparation.

Claims

[Claim 1]

A restorative tonic, comprising a bee larva.

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[Claim 2]

A sexual function improver, comprising a bee larva.

[Claim 3]

10 A male climacteric symptom alleviator, comprising a bee
larva.

[Claim 4]

An anti-fatigue agent, comprising a bee larva.