

DESCRIPTION

A PHARMACEUTICAL COMPOSITION COMPRISING PLANT WORMS AND MUIRAPUAMA

FIELD OF ART

The present invention relates to a composition directed to relieving physical and mental fatigue, and more particularly to a composition directed to relieving
5 physical and mental fatigue, stress, etc. and also to amelioration of or restoring from weakened constitution, etc. which comprises muirapuama and plant worms.

BACKGROUND ART

Muirapuama is a natural drug used on the
10 Amazon river basin as an invigorating or restoring tonic from the old time. Plant worms are also a natural drug used in China as a sedative or an antitussive from the old time.

Orally administering compositions containing a
15 muirapuama extract or an extract of plant worms alone as an effective ingredient are known, but a composition containing both muirapuama and plant worms together is not yet disclosed.

An object of the present invention is to
20 provide a composition having an intensified restoring effect of muirapuama on depressed physical strength or stamina due to stresses, etc. by plant worms and also



having effects on relieving of stresses and physical fatigue and on amelioration of or restoring from weakened constitution, etc. without any side effect, even if administered for a long time.

5 DISCLOSURE OF THE INVENTION

As a result of extensive studies, the present inventors found a novel combination of muirapuama with plant worms, which has a synergistic effect on relieving physical and mental fatigue due to stress, and
10 ameliorating weakened constitution, etc., where muirapuama can effectively normalize stresses, that is, disturbances in bodies due to various external and internal factors and plant worms can effectively promote metabolism and relieve physical and mental fatigue such
15 as general feeling of weariness, drowsiness, a feeling of expansion, etc. and established the present invention.

According to the present invention, there is provided a composition for relieving physical and mental fatigue and ameliorating weakened constitution, which
20 comprises muirapuama and plant worms as effective ingredients.

Original plants for muirapuama for use in the present invention are shrubs of family Olacaceae growing on the Amazon river basin in Brazil, including such
25 species as Ptychopetalum olacoides, Ptychopetlum uncinatum, and Liriosma ovata, among which the species Ptychopetalum olacoides is preferable. Needless to say,





the species Ptychopetlum uncinatum and Liriosma ovata can be used. In the present invention, roots of these original plants are used.

Plant worms are stomas of preferably the genus
5 Cordyceps of family Clavicipitaceae and larvas of insects on which the genus Cordyceps are parasitic. Those of genres Simizuomyces, Podonectrioides, and Torrubiella of the same family Clavicipitaceae can be also used.

The muirapuama of the present invention can be
10 used as an extract and the extract can be obtained in the following manner:

Finely shredded muirapuama roots are mixed with dilute ethanol and subjected to infusion for 2 days with occasional stirring, and the resulting infusion is
15 filtered. The residues are further mixed with dilute ethanol and subjected to infusion for 2 days with occasional stirring and the resulting infusion is also filtered. The resulting two filtrates are combined together and concentrated under reduced pressure to
20 obtain a muirapuama extract.

The plant worms of the present invention can be used as an extract or a fruid extract and the extracts can be obtained in the following manner:

Rough-shredded plant worms are mixed with
25 dilute ethanol and left for standing at room temperature for about 2 hours, and then the resulting solution is further mixed with dilute ethanol and subjected to infusion by leaving the solution for standing at room



temperature for 3 days to obtain an extract as an infusion. The thus obtained extract is left for standing at room temperature for 2 days and filtered through a filter paper to obtain a fluid extract.

5 According to the present invention, the effective dosage of muirapuama extract, for an adult is 10 to 5,000 mg/day, preferably 50 to 1,500 mg/day in terms of bulk natural drug, and the effective dosage of fluid extract of plant worms for an adult is 10 to 5,000
10 mg/day, preferably 50 to 1,000 mg/day in terms of bulk natural drug. That is, 0.002 to 500 parts by weight, preferably 0.03 to 30 parts by weight, more preferably 0.5 to 8 parts by weight, of a muirapuama extract is used
15 per part by weight of a fluid extract of plant worms in terms of bulk natural drugs.

The present composition can contain caffeine, water-soluble vitamins such as vitamin B₁, vitamin B₂, vitamin B₆, vitamin B₁₂, vitamin C, biotin, carnitine, pantotenic acid and nicotinic acid and their derivatives,
20 fat soluble vitamins such as vitamin A, vitamin E and their derivatives, taurine, amino acids such as arginine and other natural drugs, such as extracts or tinctures of agkistrodon, ginseng, astragalus root, polygonati root, licorice, poria sclerotium, rehmannia root, Japanese
25 angelica root, lycii fruit, cinnamon bark, velvet horn, barren-worts, cistanchis caulis, chinese gutta percha, schisandra fruit, eleutherococc, ophiopogon tuber, polygoni multiflori root, bovine bile, etc.



The present composition can be administered or taken directly as it is, or in such forms as medical preparations, for example, preparations for oral administration (e.g. granules, powder, capsules, tablets, 5 dry syrup, liquid preparations, etc.) or injection, or foods, for example, soft drinks or solid foods (e.g. biscuits), prepared by mixing with other known additives, for example, a vehicle, a disintegrator, a binder, a lubricant, an antioxidant, a coating agent, a coloring 10 agent, a corrigent, a surfactant, a plasticizer, a pH regulating agent, a refreshing agent, a suspending agent, a defoaming agent, a thickening agent, a dissolving aid, etc. according to the ordinary method or can be added to soft drinks or food as a functional ingredient or an 15 additive.

According to the present invention, a single composition of a muirapuama extract and a single composition of an extract of plant worms can be sealed in separate ampules, respectively and used upon mixing of 20 the single composition or used without the mixing simultaneously when administered.

The vehicle includes, for example, a sugar alcohol such as D-mannitol, xylitol and D-sorbitol, saccharides such as glucose, sucrose, lactose and fruit 25 sugar, crystalline cellulose, sodium carmellose, calcium hydrogen phosphate, wheat starch, rice starch, corn starch, potato starch, dextrin, β -cyclodextrin, light anhydrous silicic acid, titanium oxide, magnesium

metasilicate aluminate, etc.

The disintegrator includes, for example, low-substituted hydroxypropyl cellulose, calcium carboxymethyl cellulose, sodium croscarmellose

5 hydroxypropyl starch, partially gelatinized starch, etc.

The binder includes, for example, methyl cellulose, hydroxypropyl cellulose, hydroxypropylmethyl cellulose, polyvinylpyrrolidone, gelatin, gum arabic, ethyl cellulose, polyvinyl alcohol, pullulan, gelatinized
10 starch, agar, tragacanth, sodium alginate, propylene glycol alginate, etc.

The lubricant includes, for example, stearic acid, magnesium stearate, calcium stearate, polyoxyl stearate, cetanol, talc, hydrogenated oil, sucrose fatty
15 acid ester, dimethylpolysiloxane, yellow beeswax, white beeswax, etc.

The antioxidant includes, for example, dibutylhydroxytoluene (BHT), propyl gallate, butylhydroxyanisole (BHA), tocopherol, citric acid, etc.

20 The coating agent includes, for example, hydroxypropylmethyl cellulose, hydroxypropyl cellulose, methyl cellulose, ethyl cellulose, hydroxypropylmethyl cellulose phthalate, hydroxypropylmethyl cellulose acetate succinate, carboxymethylethyl cellulose,
25 cellulose acetate phthalate, polyvinyl acetal diethylaminoacetate, aminoalkyl methacrylate copolymer, hydroxypropylmethyl cellulose acetate succinate, methacrylic acid copolymer, polyvinyl acetate



diethylaminoacetate, shellac, etc.

The coloring agent includes, for example, a turmeric extract, riboflavin, carotin solution, titanium oxide, etc.

- 5 The surfactant includes, for example, polyoxyethylene hydrogenated castor oil, glycerin monostearate, sorbitan monostearate, sorbitan monolaurate, polyoxyethylene polyoxypropylene, polysolvates, sodium laurylsulfate, macrogols, sucrose
- 10 fatty acid ester, etc.

The plasticizer includes, for example, triethyl citrate, polyethylene glycol, triacetin, cetanol, etc.

- The pH regulating agent includes, for example,
- 15 citric acid, malic acid, sodium hydrogen phosphate, dipotassium hydrogen phosphate, etc.

The refreshing agent includes, for example, 1-menthol, mentha water, etc.

- The suspending agent includes, for example,
- 20 kaolin, sodium carmellose, xanthane gum, tragacanth, etc.

The defoaming agent includes, for example, dimethyl polysiloxane, silicone deforming agent, etc.

The thickening agent includes, for example, xanthane gum, tragacanth, methyl cellulose, dextrin, etc.

- 25 The dissolving aid includes, for example, ethanol, sucrose fatty acid ester, macrogol, etc.

In case of soft drinks, a particularly desired taste or flavor can be given by adding other



physiologically active substances, minerals, vitamins, hormones, nutrients, flavorings, etc. to the present composition, besides the above-mentioned additives.

POTENTIALITY OF INDUSTRIAL UTILIZATION

- 5 The present composition has a preventive or ameliorating effect on physical or mental fatigue, stresses and weakened constitution or promotion to recover therefrom, without any side effect, even if administered for a long time.

10 BRIEF DESCRIPTION OF DRAWINGS

- Fig. 1 shows durable swimming time of rats in forced swimming by administration of the present liquid preparation (plant worms and muirapuama), single liquid preparations of plant worms, and muirapuama, respectively
15 and control (purified water).

- Fig. 2 shows total intakes of the present liquid preparation (plant worms and muirapuama), single liquid preparations of plant worms, and muirapuama, respectively and control (purified water) by exercise
20 groups and non-exercise group.

BEST MODE FOR CARRING OUT THE INVENTION

The present invention will be described in detail below, referring to Examples and Test Examples, and drawings.



Example 1

Formulation

	Plant worms	100 mg (in terms of bulk natural drug)
5	Muirapuama	300 mg (in terms of bulk natural drug)
	Agkistrodon	250 mg (in terms of bulk natural drug)
	Taurine	500 mg
10	Ginseng	600 mg (in terms of bulk natural drug)
	Astragalus	300 mg (in terms of bulk natural drug)
	Polygonati root	300 mg (in terms of bulk natural drug)
15	Licorice root	150 mg (in terms of bulk natural drug)
	Poria sclerotium	300 mg (in terms of bulk natural drug)
20	Rehmannia root	200 mg (in terms of bulk natural drug)
	Japanese angelica root	200 mg (in terms of bulk natural drug)
	Lycii fruit	200 mg (in terms of bulk natural drug)
25	Cinnamon bark	150 mg (in terms of bulk natural drug)
	Velvet horn	300 mg (in terms of

	bulk natural drug)
Barren-worts	1000 mg (in terms of
	bulk natural drug)
Vitamin B ₂	5 mg
5 Vitamin B ₆	5 mg
Anhydrous caffeine	50 mg

The foregoing components were further mixed with appropriate amounts of sodium citrate, malic acid, sucrose, D-sorbitol solution, benzoic acid, 10 polyoxyethylene hydrogenated castor oil and distilled water to make 50 ml of liquid preparation.

Example 2

Formulation

	Plant worms	150 mg (in terms of
15		bulk natural drug)
	Muirapuama	350 mg (in terms of
		bulk natural drug)
	Agkistrodon	300 mg (in terms of
		bulk natural drug)
20	Taurine	500 mg
	Ginseng	600 mg (in terms of
		bulk natural drug)
	Astragalus root	300 mg (in terms of
		bulk natural drug)
25	Polygonati root	300 mg (in terms of
		bulk natural drug)

	Licorice	150 mg (in terms of bulk natural drug)
	Poria sclerotium	300 mg (in terms of bulk natural drug)
5	Rehmannia root	200 mg (in terms of bulk natural drug)
	Japanese angelica root	200 mg (in terms of bulk natural drug)
	Lycii fruit	200 mg (in terms of bulk natural drug)
10	Cinnamon bark	150 mg (in terms of bulk natural drug)
	Velvet horn	300 mg (in terms of bulk natural drug)
15	Barren-worts	1000 mg (in terms of bulk natural drug)
	Vitamin B ₂	5 mg
	Vitamin B ₆	5 mg
	Anhydrous caffeine	50 mg

20 The foregoing components were further mixed with appropriate amounts of citric acid, sodium citrate, sucrose, D-sorbitol solution, benzoic acid, polyoxyethylene hydrogenated castor oil and distilled water to make 50 ml of liquid preparation.

25 Example 3

Formulation

	Plant worms	300 mg (in terms of bulk natural drug)
	Muirapuama	300 mg (in terms of bulk natural drug)
5	Agkistrodon	250 mg (in terms of bulk natural drug)
	Taurine	500 mg
	Ginseng	600 mg (in terms of bulk natural drug)
10	Astragalus root	300 mg (in terms of bulk natural drug)
	Licorice root	100 mg (in terms of bulk natural drug)
	Poria sclerotium	250 mg (in terms of bulk natural drug)
15	Rehmannia root	300 mg (in terms of bulk natural drug)
	Japanese angelica root	300 mg (in terms of bulk natural drug)
20	Cistanchis caulis	300 mg (in terms of bulk natural drug)
	Chinese gutta percha	300 mg (in terms of bulk natural drug)
	Schisandra fruit	200 mg (in terms of bulk natural drug)
25	Cinnamon bark	200 mg (in terms of bulk natural drug)
	Velvet horn	300 mg (in terms of

	bulk natural drug)
Barren-worts	1000 mg (in terms of
	bulk natural drug)
Vitamin B ₂	5 mg
5 Vitamin B ₆	5 mg
Anhydrous caffeine	50 mg

The foregoing components were further mixed with appropriate amounts of citric acid, sodium citrate, sucrose, D-sorbitol solution, benzoic acid, 10 polyoxyethylene hydrogenated oil and distilled water to make 50 ml of liquid preparation.

Example 4

Formulation

	Plant worms	330 mg (in terms of
15		bulk natural drug)
	Muirapuama	450 mg (in terms of
		bulk natural drug)
	Agkistrodon	400 mg (in terms of
		bulk natural drug)
20	Taurine	500 mg
	Ginseng	600 mg (in terms of
		bulk natural drug)
	Astragalus root	300 mg (in terms of
		bulk natural drug)
25	Licorice root	100 mg (in terms of
		bulk natural drug)

	Poria sclerotium	250 mg (in terms of bulk natural drug)
	Rehmannia root	300 mg (in terms of bulk natural drug)
5	Japanese angelica root	300 mg (in terms of bulk natural drug)
	Cistanchis caulis	300 mg (in terms of bulk natural drug)
	Chinese gutta percha	300 mg (in terms of bulk natural drug)
10	Schisandra fruit	200 mg (in terms of bulk natural drug)
	Cinnamon bark	200 mg (in terms of bulk natural drug)
15	Velvet horn	300 mg (in terms of bulk natural drug)
	Barren-worts	1000 mg (in terms of bulk natural drug)
	Vitamin B ₂	5 mg
20	Vitamin B ₆	5 mg
	Anhydrous caffeine	50 mg

The foregoing components were further mixed with appropriate amounts of sodium citrate, malic acid, sucrose, D-sorbitol solution, benzoic acid,

25 polyoxyethylene hydrogenated oil and distilled water to make 50 ml of liquid preparation.

Example 5

Formulation

	Plant worms	100 mg (in terms of bulk natural drug)
5	Muirapuama	300 mg (in terms of bulk natural drug)
	Rehmannia root	1500 mg (in terms of bulk natural drug)
	Barren-worts	500 mg (in terms of bulk natural drug)
10	Eleutherococc	750 mg (in terms of bulk natural drug)
	Polygonati root	750 mg (in terms of bulk natural drug)
15	Velvet horn	250 mg (in terms of bulk natural drug)
	Ginseng	3000 mg (in terms of bulk natural drug)
	Ophiopogon tuber	1200 mg (in terms of bulk natural drug)
20	Schisandra fruit	500 mg (in terms of bulk natural drug)
	Polygoni multiflori root	750 mg (in terms of bulk natural drug)
25	Cinnamon bark	500 mg (in terms of bulk natural drug)

The foregoing components were uniformly mixed

with appropriate amounts of mannitol, hydroxypropyl cellulose, magnesium metasilicate aluminate, aspartame and flavoring and made into three packages of granules.

Example 6

5 Formulation

	Plant worms	300 mg (in terms of bulk natural drug)
	Muirapuama	300 mg (in terms of bulk natural drug)
10	Rehmannia root	1000 mg (in terms of bulk natural drug)
	Polygonati root	500 mg (in terms of bulk natural drug)
	Velvet horn	250 mg (in terms of bulk natural drug)
15	Ginseng	2000 mg (in terms of bulk natural drug)
	Vitamin B ₂	10 mg
	Vitamin B ₆	5 mg

20. The foregoing components were uniformly mixed with appropriate amounts of magnesium metasilicate aluminate, polysolvate 60 and propylene glycol, and the resulting mixture was uniformly filled into soft capsules to obtain 9 capsules of preparate.

25 Example 7

Formulation

	Plant worms	100 mg (in terms of bulk natural drug)
	Muirapuama	200 mg (in terms of bulk natural drug)
5	Barren-worts	500 mg (in terms of bulk natural drug)
	Velvet horn	200 mg (in terms of bulk natural drug)
10	Ginseng	600 mg (in terms of bulk natural drug)
	Polygoni multiflori root	300 mg (in terms of bulk natural drug)
	Bovine bile	650 mg (in terms of bulk natural drug)
15	L-arginine hydrochloride	100 mg
	dl-carnitine chloride	50 mg
	Vitamin A	2000 I. U.
	Vitamin B ₁	20 mg
20	Vitamin B ₂	15 mg
	Vitamin B ₆	5 mg
	Vitamin B ₁₂	10 µg
	Nicotinic acid amide	20 mg
	Calcium pantothenate	30 mg
25	Vitamin C	50 mg
	Vitamin E	5 mg

The foregoing components were uniformly mixed

with appropriate amounts of sodium hydrogen carbonate, polyvinyl pyrrolidone, light anhydrous silicic acid, magnesium stearate, polyethylene glycol, polysolvate 80 and flavoring to obtain 9 tablets of prepareate.

5 Test Example 1

The following groups, each consisting of 7 male SD rats having an average body weight of 200 g, were tested by orally administering predetermined equal volumes of the following liquid preparations and
10 subjecting the rats to forced swimming to determine durable swimming time.

Group A: administered with the present liquid preparation (plant worms : 0.2 w/v% + muirapuama : 0.6 w/v% in terms of bulk natural drugs)

Group B: administered with a single liquid preparation of plant worms (0.8 w/v% in terms of bulk natural drug)

Group C: administered with a single liquid preparation of muirapuuama (0.8 w/v% in terms of bulk natural drug)

Group D: control (only purified water)

Results of durable swimming time of groups A, B, C and D are shown in Fig. 1.

25 As is evident from Fig. 1, the durable
swimming time is much more extended in case of Group A

with the present liquid preparation than those in case of Groups B and C with the single liquid preparations.

Test Example 2

Male SD rats having an average body weight of 200 g were divided into the following exercise groups each consisting of 5 rats and non-exercise groups each consisting of 7 rats, and the exercise groups were subjected to forced swimming tests by conducting forced swimming for 30 minutes per day for total 10 days while applying about 5- about 10% weight load per body weight to the respective rats, and by carrying out a two-bottle selective test with the following liquid preparations from the first day till the 10th day from the application of forced swimming load to determine their total intakes. The non-exercise groups were also tested in the same manner as above without any application of forced swimming under the weight load.

Group A: intake of the present liquid preparation (plant worms : 0.2 w/v% + muirapuama : 0.6 w/v% in terms of bulk natural drugs)

Group B: intake of a single liquid preparation of plant worms (0.8 w/v% in terms of original natural drugs)

Group C: intake of a single liquid preparation of muirapuama (0.8 w/v% in terms of bulk natural drug)

Group D: control (intake of purified water)

The total intakes of the exercise groups and the non-exercise groups were compared, and the results are shown in Fig. 2.

- 5 As is evident from Fig. 2, the total intake of the present liquid preparation A by the exercise group is drastically increased, as compared with the total intakes of the single liquid preparations B and C by the exercise groups.

21

CLAIM



1. A composition comprising plant worms and muirapuama.

FIG.1

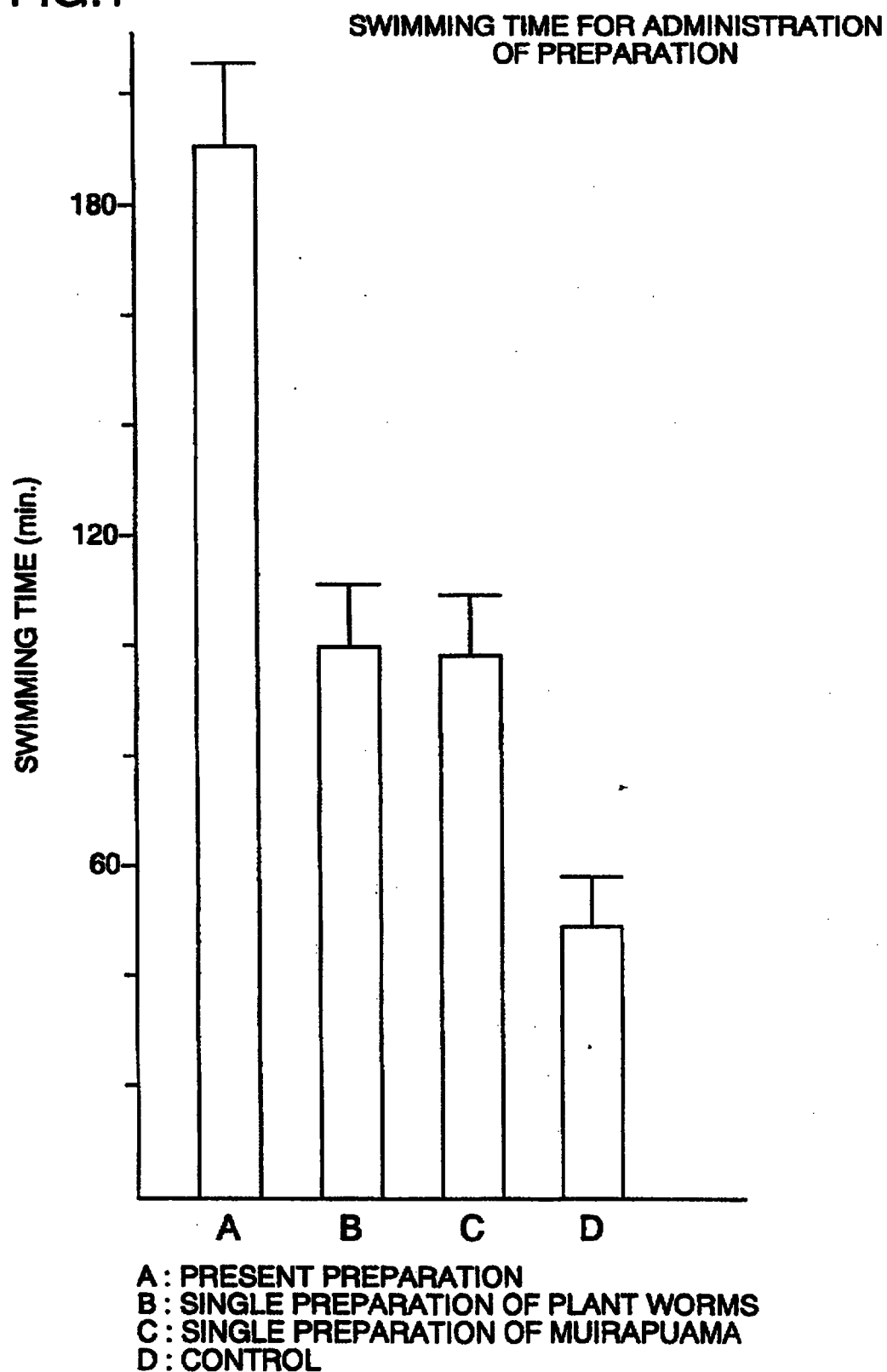
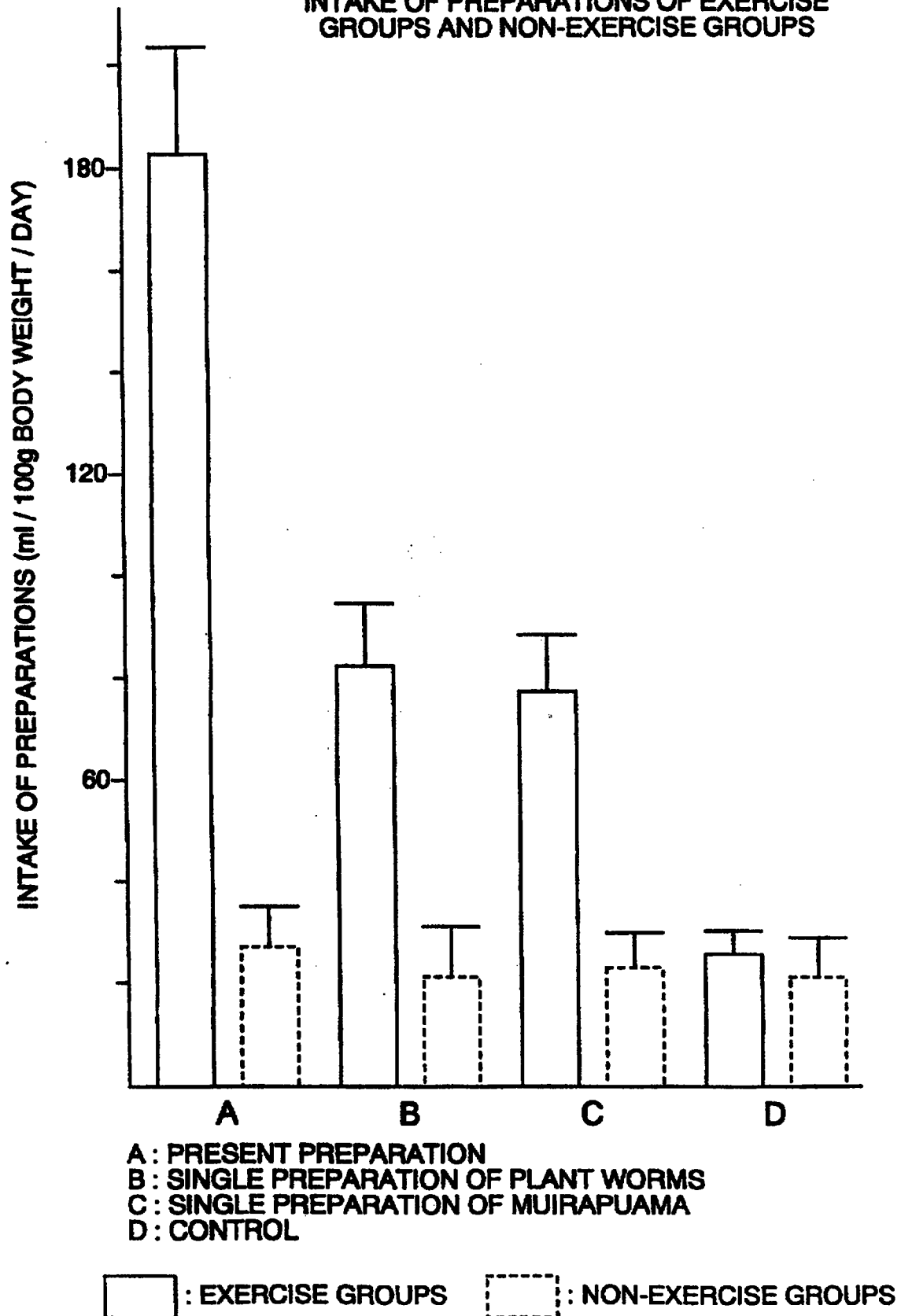


FIG.2

INTAKE OF PREPARATIONS OF EXERCISE
GROUPS AND NON-EXERCISE GROUPS

the species Ptychopetlum uncinatum and Liriosma ovata can be used. In the present invention, roots of these original plants are used.

Plant worms are stomas of preferably the genus
5 Cordyceps of family Clavicipitaceae and larvas of insects on which the genus Cordyceps are parasitic. Those of genres Simizuomyces, Podonectrioides, and Torrbiella of the same family Clavicipitaceae can be also used.

The muirapuama of the present invention can be
10 used as an extract and the extract can be obtained in the following manner:

Finely shredded muirapuama roots are mixed with dilute ethanol and subjected to infusion for 2 days with occasional stirring, and the resulting infusion is
15 filtered. The residues are further mixed with dilute ethanol and subjected to infusion for 2 days with occasional stirring and the resulting infusion is also filtered. The resulting two filtrates are combined together and concentrated under reduced pressure to
20 obtain a muirapuama extract.

The plant worms of the present invention can be used as an extract or a fruid extract and the extracts can be obtained in the following manner:

Rough-shredded plant worms are mixed with
25 dilute ethanol and left for standing at room temperature for about 2 hours, and then the resulting solution is further mixed with dilute ethanol and subjected to infusion by leaving the solution for standing at room

temperature for 3 days to obtain an extract as an infusion. The thus obtained extract is left for standing at room temperature for 2 days and filtered through a filter paper to obtain a fluid extract.

5 According to the present invention, the effective dosage of muirapuama extract, for an adult is 10 to 5,000 mg/day, preferably 50 to 1,500 mg/day in terms of bulk natural drug, and the effective dosage of fluid extract of plant worms for an adult is 10 to 5,000
10 mg/day, preferably 50 to 1,000 mg/day in terms of bulk natural drug. That is, 0.002 to 500 parts by weight, preferably 0.03 to 30 parts by weight, more preferably 0.5 to 8 parts by weight, of a muirapuama extract is used per part by weight of a fluid extract of plant worms in
15 terms of bulk natural drugs.

 The present composition can contain caffeine, water-soluble vitamins such as vitamin B₁, vitamin B₂, vitamin B₆, vitamin B₁₂, vitamin C, biotin, carnitine, pantotenic acid and nicotinic acid and their derivatives,
20 fat soluble vitamins such as vitamin A, vitamin E and their derivatives, taurine, amino acids such as arginine and other natural drugs, such as extracts or tinctures of agkistrodon, ginseng, astragalus root, polygonati root, licorice, poria sclerotium, rehmannia root, Japanese
25 angelica root, lycii fruit, cinnamon bark, velvet horn, barren-worts, cistanchis caulis, chinese gutta percha, schisandra fruit, eleutherococc, ophiopogon tuber, polygoni multiflori root, bovine bile.

The present composition can be administered or taken directly as it is, or in such forms as medical preparations, for example, preparations for oral administration (e.g. granules, powder, capsules, tablets, 5 dry syrup, liquid preparations) or injection, or foods, for example, soft drinks or solid foods (e.g. biscuits), prepared by mixing with other known additives, for example, a vehicle, a disintegrator, a binder, a lubricant, an antioxidant, a coating agent, a coloring 10 agent, a corrigent, a surfactant, a plasticizer, a pH regulating agent, a refreshing agent, a suspending agent, a defoaming agent, a thickening agent, a dissolving aid, etc. according to the ordinary method or can be added to soft drinks or food as a functional ingredient or an 15 additive.

According to the present invention, a single composition of a muirapuama extract and a single composition of an extract of plant worms can be sealed in separate ampules, respectively and used upon mixing of 20 the single composition or used without the mixing simultaneously when administered.

The vehicle includes, for example, a sugar alcohol such as D-mannitol, xylitol and D-sorbitol, saccharides such as glucose, sucrose, lactose and fruit 25 sugar, crystalline cellulose, sodium carmellose, calcium hydrogen phosphate, wheat starch, rice starch, corn starch, potato starch, dextrin, β -cyclodextrin, light anhydrous silicic acid, titanium oxide, magnesium

metasilicate aluminate, etc.

The disintegrator includes, for example, low-substituted hydroxypropyl cellulose, calcium carboxymethyl cellulose, sodium croscarmellose
 5 hydroxypropyl starch, partially gelatinized starch.

The binder includes, for example, methyl cellulose, hydroxypropyl cellulose, hydroxypropylmethyl cellulose, polyvinylpyrrolidone, gelatin, gum arabic, ethyl cellulose, polyvinyl alcohol, pullulan, gelatinized
 10 starch, agar, tragacanth, sodium alginate, propylene glycol alginate.

The lubricant includes, for example, stearic acid, magnesium stearate, calcium stearate, polyoxyl stearate, cetanol, talc, hydrogenated oil, sucrose fatty
 15 acid ester, dimethylpolysiloxane, yellow beeswax, white beeswax.

The antioxidant includes, for example, dibutylhydroxytoluene (BHT), propyl gallate, butylhydroxyanisole (BHA), tocopherol, citric acid.

20 The coating agent includes, for example, hydroxypropylmethyl cellulose, hydroxypropyl cellulose, methyl cellulose, ethyl cellulose, hydroxypropylmethyl cellulose phthalate, hydroxypropylmethyl cellulose acetate succinate, carboxymethylethyl cellulose,
 25 cellulose acetate phthalate, polyvinyl acetal diethylaminoacetate, aminoalkyl methacrylate copolymer, hydroxypropylmethyl cellulose acetate succinate, methacrylic acid copolymer, polyvinyl acetate

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diethylaminoacetate, shellac.

The coloring agent includes, for example, a turmeric extract, riboflavin, carotin solution, titanium oxide.

5 The surfactant includes, for example, polyoxyethylene hydrogenated castor oil, glycerin monostearate, sorbitan monostearate, sorbitan monolaurate, polyoxyethylene polyoxypropylene, polysolvates, sodium laurylsulfate, macrogols, sucrose
10 fatty acid ester.

The plasticizer includes, for example, triethyl citrate, polyethylene glycol, triacetin, cetanol.

The pH regulating agent includes, for example,
15 citric acid, malic acid, sodium hydrogen phosphate, dipotassium hydrogen phosphate.

The refreshing agent includes, for example, l-menthol, mentha water.

The suspending agent includes, for example,
20 kaolin, sodium carmellose, xanthane gum, tragacanth.

The defoaming agent includes, for example, dimethyl polysiloxane, silicone deforming agent.

The thickening agent includes, for example, xanthane gum, tragacanth, methyl cellulose, dextrin.

25 The dissolving aid includes, for example, ethanol, sucrose fatty acid ester, macrogol.

In case of soft drinks, a particularly desired taste or flavor can be given by adding other

physiologically active substances, minerals, vitamins, hormones, nutrients, flavorings, to the present composition, besides the above-mentioned additives.

5 The present composition has a preventive or ameliorating effect on physical or mental fatigue, stresses and weakened constitution or promotion to recover therefrom, without any side effect, even if administered for a long time.

10

Fig. 1 shows durable swimming time of rats in forced swimming by administration of the present liquid preparation (plant worms and muirapuama), single liquid preparations of plant worms, and muirapuama, respectively
15 and control (purified water).

Fig. 2 shows total intakes of the present liquid preparation (plant worms and muirapuama), single liquid preparations of plant worms, and muirapuama, respectively and control (purified water) by exercise
20 groups and non-exercise group.

The present invention will be described in detail below, referring to Examples and Test Examples, and drawings.

COMPOSITION FOR RELIEVING PHYSICAL AND MENTAL FATIGUE
AND AMELIORATING WEAKENED CONSTITUTION

The present invention relates to a composition directed to relieving physical and mental fatigue and also to amelioration of or restoring from weakened constitution, etc. which comprises muirapuama and plant worms.

Muirapuama is a natural drug used on the Amazon river basin as an invigorating or restoring tonic from the old time. Plant worms are also a natural drug used in China as a sedative or an antitussive from the old time.

Orally administering compositions containing a muirapuama extract or an extract of plant worms alone as an effective ingredient are known, but a composition containing both muirapuama and plant worms together is not yet disclosed.

Dialog Information Service, File 377, Derwent Drug File, Dialog Accession No. 00510368, Derwent Accession No. 92-51335 describes the use of a composition comprising muirapuama for the treatment of physical and mental fatigue.

An object of the present invention is to provide a composition having an intensified restoring effect of muirapuama on depressed physical strength or stamina due to stresses by plant worms and also

having effects on relieving of stresses and physical fatigue and on amelioration of or restoring from weakened constitution without any side effect, even if administered for a long time.

5

As a result of extensive studies, the present inventors found a novel combination of muirapuama with plant worms, which has a synergistic effect, on relieving physical and mental fatigue due to stress, and
10 ameliorating weakened constitution, where muirapuama can effectively normalize stresses, that is, disturbances in bodies due to various external and internal factors and plant worms can effectively promote metabolism and relieve physical and mental fatigue such
15 as general feeling of weariness, drowsiness, a feeling of expansion, and established the present invention.

According to the present invention, there is provided a composition for relieving physical and mental fatigue and ameliorating weakened constitution, which
20 comprises muirapuama and plant worms as effective ingredients.

Original plants for muirapuama for use in the present invention are shrubs of family Olacaceae growing on the Amazon river basin in Brazil, including such
25 species as Ptychopetalum olacoides, Ptychopetlum uncinatum, and Liriosma ovata, among which the species Ptychopetalum olacoides is preferable. Needless to say,

the species Ptychopetlum uncinatum and Liriosma ovata can be used. In the present invention, roots of these original plants are used.

Plant worms are stomas of preferably the genus
5 Cordyceps of family Clavicipitaceae and larvas of insects on which the genus Cordyceps are parasitic. Those of genuses Simizuomyces, Podonectrioides, and Torrbiella of the same family Clavicipitaceae can be also used.

The muirapuama of the present invention can be
10 used as an extract and the extract can be obtained in the following manner:

Finely shredded muirapuama roots are mixed with dilute ethanol and subjected to infusion for 2 days with occasional stirring, and the resulting infusion is
15 filtered. The residues are further mixed with dilute ethanol and subjected to infusion for 2 days with occasional stirring and the resulting infusion is also filtered. The resulting two filtrates are combined together and concentrated under reduced pressure to
20 obtain a muirapuama extract.

The plant worms of the present invention can be used as an extract or a fruid extract and the extracts can be obtained in the following manner:

Rough-shredded plant worms are mixed with
25 dilute ethanol and left for standing at room temperature for about 2 hours, and then the resulting solution is further mixed with dilute ethanol and subjected to infusion by leaving the solution for standing at room

temperature for 3 days to obtain an extract as an infusion. The thus obtained extract is left for standing at room temperature for 2 days and filtered through a filter paper to obtain a fluid extract.

5 According to the present invention, the effective dosage of muirapuama extract, for an adult is 10 to 5,000 mg/day, preferably 50 to 1,500 mg/day in terms of bulk natural drug, and the effective dosage of fluid extract of plant worms for an adult is 10 to 5,000
10 mg/day, preferably 50 to 1,000 mg/day in terms of bulk natural drug. That is, 0.002 to 500 parts by weight, preferably 0.03 to 30 parts by weight, more preferably 0.5 to 8 parts by weight, of a muirapuama extract is used per part by weight of a fluid extract of plant worms in
15 terms of bulk natural drugs.

 The present composition can contain caffeine, water-soluble vitamins such as vitamin B₁, vitamin B₂, vitamin B₆, vitamin B₁₂, vitamin C, biotin, carnitine, pantotenic acid and nicotinic acid and their derivatives,
20 fat soluble vitamins such as vitamin A, vitamin E and their derivatives, taurine, amino acids such as arginine and other natural drugs, such as extracts or tinctures of agkistrodon, ginseng, astragalus root, polygonati root, licorice, poria sclerotium, rehmannia root, Japanese
25 angelica root, lycii fruit, cinnamon bark, velvet horn, barren-worts, cistanchis caulis, chinese gutta percha, schisandra fruit, eleutherococc, ophiopogon tuber, polygoni multiflori root, bovine bile.

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The present composition can be administered or taken directly as it is, or in such forms as medical preparations, for example, preparations for oral administration (e.g. granules, powder, capsules, tablets, 5 dry syrup, liquid preparations) or injection, or foods, for example, soft drinks or solid foods (e.g. biscuits), prepared by mixing with other known additives, for example, a vehicle, a disintegrator, a binder, a lubricant, an antioxidant, a coating agent, a coloring 10 agent, a corrigent, a surfactant, a plasticizer, a pH regulating agent, a refreshing agent, a suspending agent, a defoaming agent, a thickening agent, a dissolving aid, etc. according to the ordinary method or can be added to soft drinks or food as a functional ingredient or an 15 additive.

According to the present invention, a single composition of a muirapuama extract and a single composition of an extract of plant worms can be sealed in separate ampules, respectively and used upon mixing of 20 the single composition or used without the mixing simultaneously when administered.

The vehicle includes, for example, a sugar alcohol such as D-mannitol, xylitol and D-sorbitol, saccharides such as glucose, sucrose, lactose and fruit 25 sugar, crystalline cellulose, sodium carmellose, calcium hydrogen phosphate, wheat starch, rice starch, corn starch, potato starch, dextrin, β -cyclodextrin, light anhydrous silicic acid, titanium oxide, magnesium

metasilicate aluminate, etc.

The disintegrator includes, for example, low-substituted hydroxypropyl cellulose, calcium carboxymethyl cellulose, sodium croscarmellose
5 hydroxypropyl starch, partially gelatinized starch.

The binder includes, for example, methyl cellulose, hydroxypropyl cellulose, hydroxypropylmethyl cellulose, polyvinylpyrrolidone, gelatin, gum arabic, ethyl cellulose, polyvinyl alcohol, pullulan, gelatinized
10 starch, agar, tragacanth, sodium alginate, propylene glycol alginate.

The lubricant includes, for example, stearic acid, magnesium stearate, calcium stearate, polyoxyl stearate, cetanol, talc, hydrogenated oil, sucrose fatty
15 acid ester, dimethylpolysiloxane, yellow beeswax, white beeswax.

The antioxidant includes, for example, dibutylhydroxytoluene (BHT), propyl gallate, butylhydroxyanisole (BHA), tocopherol, citric acid.

20 The coating agent includes, for example, hydroxypropylmethyl cellulose, hydroxypropyl cellulose, methyl cellulose, ethyl cellulose, hydroxypropylmethyl cellulose phthalate, hydroxypropylmethyl cellulose acetate succinate, carboxymethylethyl cellulose,
25 cellulose acetate phthalate, polyvinyl acetal diethylaminoacetate, aminoalkyl methacrylate copolymer, hydroxypropylmethyl cellulose acetate succinate, methacrylic acid copolymer, polyvinyl acetate

diethylaminoacetate, shellac.

The coloring agent includes, for example, a turmeric extract, riboflavin, carotin solution, titanium oxide.

5 The surfactant includes, for example, polyoxyethylene hydrogenated castor oil, glycerin monostearate, sorbitan monostearate, sorbitan monolaurate, polyoxyethylene polyoxypropylene, polysolvates, sodium laurylsulfate, macrogols, sucrose
10 fatty acid ester.

The plasticizer includes, for example, triethyl citrate, polyethylene glycol, triacetin, cetanol.

The pH regulating agent includes, for example,
15 citric acid, malic acid, sodium hydrogen phosphate, dipotassium hydrogen phosphate.

The refreshing agent includes, for example, 1-menthol, mentha water.

The suspending agent includes, for example,
20 kaolin, sodium carmellose, xanthane gum, tragacanth.

The defoaming agent includes, for example, dimethyl polysiloxane, silicone deforming agent.

The thickening agent includes, for example, xanthane gum, tragacanth, methyl cellulose, dextrin.

25 The dissolving aid includes, for example, ethanol, sucrose fatty acid ester, macrogol.

In case of soft drinks, a particularly desired taste or flavor can be given by adding other

physiologically active substances, minerals, vitamins, hormones, nutrients, flavorings, to the present composition, besides the above-mentioned additives.

5 The present composition has a preventive or ameliorating effect on physical or mental fatigue, stresses and weakened constitution or promotion to recover therefrom, without any side effect, even if administered for a long time.

10

Fig. 1 shows durable swimming time of rats in forced swimming by administration of the present liquid preparation (plant worms and muirapuama), single liquid preparations of plant worms, and muirapuama, respectively
15 and control (purified water).

Fig. 2 shows total intakes of the present liquid preparation (plant worms and muirapuama), single liquid preparations of plant worms, and muirapuama, respectively and control (purified water) by exercise
20 groups and non-exercise group.

The present invention will be described in detail below, referring to Examples and Test Examples, and drawings.

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(54) Title: A PHARMACEUTICAL COMPOSITION COMPRISING PLANT WORMS AND MUIRAPUAMA (57) Abstract A composition comprising plant worms and muirapuama is very effective for relieving physical and mental fatigue and ameliorating weakened constitution without any side effect, even administered for a long time.		