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(54) Title: PHARMACEUTICAL COMPOSITION FOR THE PREVENTION AND TREATMENT OF IRRITABLE BOWEL SYNDROME

(57) Abstract: Disclosed is a pharmaceutical composition for the prevention and treatment of irritable bowel syndrome including *Liriopis tuber* (tuber of *Liriope platyphylla* Wang et Tang, *Ophiopogon japonicus* Ker-Gawler or related plants of the same genuses) extract as an active ingredient. The *Liriopis tuber* extract has an excellent effect of suppressing visceral hypersensitivity and may be used for pharmaceutical compositions and health functional foods for the prevention and treatment of.

# Description

# Title of Invention: PHARMACEUTICAL COMPOSITION FOR THE PREVENTION AND TREATMENT OF IRRITABLE BOWEL SYNDROME

## Technical Field

[0001] The present invention relates to a pharmaceutical composition for the prevention and treatment of irritable bowel syndrome comprising *Liriopis tuber* extract as an active ingredient.

[0002]

## Background Art

[0003] Irritable bowel syndrome (IBS) is a chronic bowel disorder characterized by chronic abdominal pain, discomfort, bloating, and alteration of bowel habits including diarrhea and constipation in the absence of any detectable organic cause. Its symptoms are often aggravated by mental factors or social environments causing stresses. Of the patients who visit hospitals because of digestive diseases, 27.8% are IBS patients. Women patients outnumber men by 2 to 4 times. Of the patients who visit hospitals in Korea, those with diarrhea-predominant IBS are 30.8%, those with constipation-predominant IBS are 24.6%, and those with diarrhea-constipation alternating (or pain-predominant) IBS are 44.6%. Medication is used to relieve the symptoms. However, the medication therapy for IBS is not satisfactory and therapeutic gain is not large as compared to placebo. Medications for IBS may be classified into drugs that improve overall symptoms and those for individual symptoms. The drugs for abdominal pain include smooth muscle relaxant, antidepressant, opioid agonist, etc., the drugs for constipation-predominant IBS include fiber, laxative, 5-HT4 agonist, etc., and the drugs for diarrhea-predominant IBS include antidiarrheal, 5-$HT_3$ antagonist, etc. [Oh-Young Lee, *Korean Journal of Gastroenterology*, 47, p. 111-119, 2006; Poong-Lyul Lee, *Korean Journal of Gastroenterology*, 47, p. 94-100, 2006; Myung-Gyu Choi, *Korean Journal of Gastroenterology*, 47, p. 125-130; Hyo-Jin Park, *Korean Journal of Gastroenterology*, 47, p. 101-110, 2006; TT. Ashburn et al., *Nat. Rev. Drug Discov.*, 5(2), p 99-100, 2006; MJG Farthing, *BMJ*, 330, p. 429-430, 2005; MJG. Farthing, *Best Pract. Res. Clin. Gastroenterol.*, 18(4), p. 773-786, 2004].

[0004] Neurokinin receptors (NK), which are classified into NK1, NK2 and NK3 subtypes, are receptors to which tachykinins, including substance P (SP), neurokinin A and neurokinin B which are neuropeptides acting in the central and peripheral nervous systems, bind [S. Harrison et al., *Int. J. Biochem. Cell Biol.*, 33: p. 555-576, 2001]. The NK receptors are uniformly distributed in the central nervous system (e.g., amygdala,

hippocampus, hypothalamus and striatum of the brain, and spinal cord) and in the peripheral nervous system (e.g., skin, inflammatory cells, digestive system, respiratory system, cardiovascular system, etc.) and are closely related to important physiological functions as neuromodulator or neurotransmitter, in particular, bowel movement, visceral hypersensitivity, or the like [JH. La et al., *World J. Gastroenterol.*, 11(2), p. 237-241, 2005; MS Kramer, *Science*, 281(5383) p. 1624-1625. 1998; G. J. Sanger., *Br. J. Pharmacol.*, 141, p. 1303-1312, 2004]. Accordingly, researches are actively carried out on NK receptor antagonists as a new target for IBS treatment [R. A. Duffy, *Expert Opin. Emerg. Drugs*, 9(1), 2004; M. Camilleri, *Br. J. Pharmacol.*, 141, p. 1237-1248, 2004; G. J. Sanger., *Br. J. Pharmacol.*, 141, p. 1303-1312, 2004 ; A. Lecci et al., *Br. J. Pharmacol.*, 141, p1249-1263, 2004].

[0005] *Liriopis tuber* refers to the tuberous root (enlarged root) of *Liriope platyphylla* Wang et Tang or *Ophiopogon japonicus* Ker-Gawler. Related plants of the genus *Liriope* include *Liriopespicata* (*Liriopekoreana*) and *Liriope minor*, and those of the genus *Ophiopogon* include *Ophiopogon jaburan*. In China and Japan, *Ophiopogon japonicas* is used for medicinal purposes and *Liriopespicata* is used as a substitute. In Korea, *Liriope platyphylla* is used for medicinal purposes [J. S. Shin, *J. Crop. Sci.*, 47(3), p. 236-239, 2002; Korean Pharmacopeia; KFDA Good Agricultural and Collection Practices].

[0006] *Liriope platyphylla* is a grass-like perennial which grows 15 to 40 cm tall and has thin and long creeping stem underground. Roots are fibrous and thick and develop as tubers. The tuber resembles sweet potato, being round at the bottom and sharp at the top. The skin is thin and pale yellowish-brown, and the fleshy tuber is succulent, slightly translucent and glutinous [Encyclopedia of Oriental Herbal Medicine; Korean Pharmacopeia; KFDA Good Agricultural and Collection Practices]. Known pharmacological effects include antidiabetic, antibacterial, antiinflammatory and antithrombotic activities. The tuber contains several steroid saponins including ophiopogonin A, B, C and D and ophiopogon C. Besides, it is known to contain β-sitosterol, stigmasterol, etc. [Encyclopedia of Oriental Herbal Medicine; J. Kou et al., *Biol. Pharm. Bull.*, 29(6) p. 1267-1270, 2006; Watanabe et al., *Chem. Pharm. Bull.*, 25(11), p. 3049-3055, 1977; H. F. Dai et al., *Journal of Integrative Plant Biology*, 47(9), p. 1148-1152, 2005; H. F. Dai et al., *Arch. Pharm. Res.*, Vol. 28, No. 11, p. 1236-1238, 2005].

[0007] The inventors of the present invention found out that *Liriopis tuber* extract suppresses hypersensitivity to visceral pain and thus may be useful for a composition for the prevention and treatment of IBS, and completed the present invention.

[0008]

## Summary of Invention

## Technical Problem

[0009] An object of the present invention is to provide a pharmaceutical composition for the prevention and treatment of irritable bowel syndrome (IBS) including *Liriopis tuber* extract as an active ingredient.

[0010] Another object of the present invention is to provide a health functional food for preventing and improving IBS including *Liriopis tuber* extract as an active ingredient.

[0011]

## Solution to Problem

[0012] The present invention provides a pharmaceutical composition for the prevention and treatment of irritable bowel syndrome (IBS) including *Liriopis tuber* extract as an active ingredient.

[0013] The present invention also provides a health functional food for preventing and improving IBS including *Liriopis tuber* extract as an active ingredient.

[0014] As defined herein, the term "extract" refers to an extract of *Liriopis tuber* solubilized in water including purified water, $C_1$-$C_4$ low alcohol, a nonpolar solvent or a mixture solvent, preferably in ethanol.

[0015] The IBS includes one or more disease(s) selected from diarrhea-predominant IBS, constipation-predominant IBS and pain-predominant IBS.

[0016]

## Advantageous Effects of Invention

[0017] The *Liriopis tuber* extract of the present invention is excellent in suppressing visceral hypersensitivity and stress or in improving change in bowel habit caused by visceral hypersensitivity. Thus, it may be useful for a pharmaceutical composition and a health functional food for the prevention and treatment of irritable bowel syndrome (IBS).

[0018]

## Brief Description of Drawings

[0019] The above and other objects, features and advantages of the present invention will become apparent from the following description of preferred embodiments given in conjunction with the accompanying drawings, in which:

[0020] Fig. 1 compares the large intestine of the normal group with that of the colitis-induced group; and

[0021] Fig. 2 shows the effect of *Liriopis tuber* extract (LITT) in the colorectal distension (CRD) model. ( Normal: normal group (IBS-noninduced)

[0022] Vehicle: IBS-induced group

[0023] Alo: positive control group (oral administration of alosetron at 20 mg/kg)

[0024] LITT 100 mg: oral administration of *Liriopis tuber* extract at 100 mg/kg

[0025] LITT 300 mg: oral administration of *Liriopis tuber* extract at 300 mg/kg )

[0026]

## Best Mode for Carrying out the Invention

[0027] Hereinafter, the embodiments of the present invention will be described in detail.

[0028] The herbal extract of the present invention may be prepared as follows.

[0029] *Liriopis tuber* is dried in the shade and then triturated. The dried *Liriopis tuber* is extracted by agitation extraction, hot extraction, cold extraction, reflux cooling extraction, ultrasonic extraction or supercritical fluid extraction, preferably by hot extraction, at 80 ℃ for about 1 to 6 hours, preferably for 2 to 4 hours, using a solvent selected from water, $C_1$-$C_4$ low alcohol, nonpolar solvent and a mixture solvent thereof about 1 to 20 times, preferably about 3 to 10 times, the weight of the dried *Liriopis tuber*. Thus obtained extract is filtered, concentrated under reduced pressure or dried to obtain the herbal extract of the present invention.

[0030] The nonpolar solvent may be one or more of dichloromethane, chloroform, diethyl ether, ethyl acetate, hexane and a supercritical fluid.

[0031] When an aqueous alcohol solution is used as the mixture solvent, it may be an aqueous alcohol solution comprising water and the low alcohol at a proportion of 5% (v/v) to 95% (v/v), more preferably 30% (v/v) to 70% (v/v).

[0032] The present invention provides a pharmaceutical composition for the prevention and treatment of irritable bowel syndrome (IBS) comprising the herbal extract of *Liriopis tuber* obtained as above as an active ingredient.

[0033] The composition of the present invention comprises the herbal extract in an amount of 0.1 to 50 wt% based on the total weight of the composition.

[0034] However, the content may be changed depending on the physical condition of the patient and the kind and progress of the disease.

[0035] The composition comprising the *Liriopis tuber* extract of the present invention may further comprise an adequate vehicle, excipient or diluent commonly used for the preparation of pharmaceutical compositions.

[0036] The composition comprising the extract of the present invention may be formulated into formulations for oral administration, such as powder, granule, tablet, capsule, suspension, emulsion, syrup, aerosol, etc., or as formulation for external application, suppository and sterile injectable solution, according to common methods. Examples of the vehicle, excipient or diluent that may be included in the composition comprising the extract include lactose, dextrose, sucrose, sorbitol, mannitol, xylitol, erythritol, maltitol, starch, gum acacia, alginate, gelatin, calcium phosphate, calcium silicate, cellulose, methyl cellulose, microcrystalline cellulose, polyvinylpyrrolidone, water, methyl hydroxybenzoate, propyl hydroxybenzoate, talc, magnesium stearate and

mineral oil. During formulation, commonly used filler, extender, binder, wetting agent, disintegrant, surfactant, etc. are used as diluent or excipient. Solid formulations for oral administration include tablet, pill, powder, granule, capsule, or the like. The solid formulation is prepared by mixing the extract with at least one excipient, e.g., starch, calcium carbonate, sucrose, lactose, gelatin, etc. Also, a lubricant such as magnesium stearate may be used. Liquid formulations for oral administration include suspension, solution, emulsion, syrup, or the like. In addition to commonly used simple diluents such as water and liquid paraffin, various excipients, e.g., wetting agent, sweetener, aromatic, preservative, etc., may be included. Formulations for parenteral administration include sterilized aqueous solution, non-aqueous solution, suspension, emulsion, freeze-dried preparation and suppository. The non-aqueous solution or suspension may include propylene glycol, polyethylene glycol, vegetable oil such as olive oil, injectable ester such as ethyl oleate, or the like. A base for the suppository may be witepsol, macrogol, Tween 61, cocoa butter, laurin butter, glycerogelatin, etc.

[0037] A preferred administration dose of the extract of the present invention may be determined adequately by those skilled in the art, considering the physical condition and body weight of the patient, severity of the disease, drug type, administration route and administration period. Preferably, in order to attain a desired effect, the extract of the present invention may be administrated at a dose of 0.01 mg/kg to 10 g/kg per day, preferably 1 mg/kg to 1 g/kg per day. The administration may be made once a day or several times a day. The aforesaid administration dose does not limit the scope of the present invention by any means.

[0038] The composition of the present invention may be administered to mammals, including rat, mouse, cattle and human via various routes. All administration methods may be expected. For example, it may be administered orally, rectally, intravenously, intramuscularly, subcutaneously, intrauterinally or intracerebroventricularly.

[0039] The present invention also provides a health functional food for preventing or improving IBS comprising the *Liriopis tuber* extract having an effect of preventing or improving IBS and a sitologically allowed food supplement additive.

[0040] The composition comprising the extract of the present invention may be prepared into drugs, foods and drinks for preventing or improving IBS. The *Liriopis tuber* extract of the present invention may be added, for example, to various foods, drinks, gums, teas, vitamin supplements, dietary supplements, etc., and may be prepared in the forms of powders, granules, tablets, capsules or drinks.

[0041] Since the *Liriopis tuber* extract of the present invention has little toxicity and few side effects, it may be safely taken for a long time for preventive purposes.

[0042] The extract of the present invention may be added to food or drink for the purpose of preventing or improving IBS. In this case, the extract may be generally added in an

amount of 0.01 to 15 wt% based on the total weight of the food composition or in an amount of 0.02 to 10 g, preferably 0.3 to 1 g, based on 100 mL of the drink composition.

[0043] The health drink composition of the present invention may comprise liquid ingredients without limitations, in addition to the extract as an essential ingredient. Like other ordinary drinks, it may comprise various flavorings, natural carbohydrates, or the like. Examples of the natural carbohydrate include monosaccharides, e.g., glucose, fructose, etc., disaccharides, e.g., maltose, sucrose, etc., polysaccharides, e.g., dextrin, cyclodextrin, etc., common sugars, and sugar alcohols, e.g., xylitol, sorbitol, erythritol, etc. The flavoring may be either a naturally occurring flavoring (thaumatin, stevia extract (e.g., rebaudioside A, glycyrrhizin, etc.)) or a synthetic flavoring (saccharin, aspartame, etc.). In general, the natural carbohydrate may be used in an amount of about 1 to 20 g, preferably about 5 to 12 g, based on 100 mL of the composition of the present invention.

[0044] Besides, the composition of the present invention may comprise various nutrients, vitamins, minerals (electrolytes), synthetic and natural flavor agents, coloring agents, improving agents (cheese, chocolate, etc.), pectic acid and salts thereof, alginic acid and salts thereof, organic acids, protective colloidal thickening agents, pH controlling agents, stabilizers, preservatives, glycerin, alcohol, carbonizing agents used in carbonated drinks, or the like. Moreover, the composition of the present invention may include fruit pulp as used in preparing natural fruit juices, fruit juice drinks and vegetable drinks. These components may be used independently or in combination. Although the percentage of the additive is not of great importance, it is generally selected from a range of 0 to about 20 parts by weight per 100 parts by weight of the composition of the present invention.

[0045]

## Mode for the Invention

[0046] The examples and experiments will now be described. The following examples and experiments are for illustrative purposes only and not intended to limit the scope of this disclosure.

[0047]

[0048] Example 1: Preparation of *Liriopis tuber* extract (LITT)

[0049] 100 g of *Liriopis tuber* purchased from the Kyungdong Market (Seoul, Korea) was dried in the shade, cut finely, and then subjected to hot extraction while agitating well for 4 hours after adding 50% ethanol aqueous solution (0.7 L). After filtration, followed by concentration and drying, 61 g of *Liriopis tuber* extract (LITT) was obtained.

[0050]

[0051] Test Example 1: s effect of relieving visceral pain in colorectal distension (CRD) model

[0052] Animal test using colorectal distension (CRD) model [JH. La et al., *World J. Gastroenterol.*, Dec., 9(12): p. 2791-2795, 2003; Y.D. Choi et al., *Dig. Dis. Sci.*, Mar 21, Epub ahead of print, 2008] was carried out as follows in order to investigate the visceral pain relieving effect of the LITT obtained in Example 1.

[0053] Male Sprague-Dawley rats (Charles River) weighing 250-300 g were used. The rats were housed in an air-conditioned unit maintained at 25 ℃ and 50% humidity with 12 hour dark-light cycle, two in a cage. Food and water were available ad libitum. After accommodation for 5 days, colitis was induced. Supply of food was stopped 24 hours before inducing colitis and, after anesthetizing with isoflurane, a rubber catheter (PE 50) was inserted intrarectally to 8 cm from the anus.

[0054] After injecting 3.5% acetic acid (in 0.9% saline, 1 mL) into the lumen of the colon through the catheter and blocking the anus to prevent leakage, 0.9% saline (1 mL) was injected into the lumen of the colon through the same catheter 30 seconds later to rinse out the acetic acid solution. After inducement of inflammation, the rats were housed again in the cage and then observed. Inducement of inflammation was checked 2 days later. Occurrence of bloody excrement or diarrhea was regarded as induced inflammation. Upon opening of the abdominal cavity, soft stool was observed in the bowel, in contrast to the normal group. With the lapse of time after the inflammation inducement, bloody excrement and diarrhea stopped and the perianal areas were clean and not wet [Fig. 1].

[0055] On the 7th day after the colitis inducement, CRD was performed on the rats and visceral hypersensitivity was observed. s effect of relieving visceral hypersensitivity was assessed by screening out the animals that showed IBS-like symptoms [JH. La et al., *World J. Gastroenterol.*, Dec., 9(12): p. 2791-2795, 2003].

[0056] A 2 cm-long rubber balloon was inserted into the colon of the test animal. After inflating the balloon by filling water at 37 ℃ gradually from 0.1 mL to 1.0 mL, the response of the animal was assessed. In order to quantify the characteristic response of the test animals during CRD, i.e. abdominal withdrawal reflex (AWR), the AWR scores were used to assess the visceral pain. In addition to AWR score recording [E. D. Al-Chaer et al., *Gastroenterology*, Nov., 119(5), p. 1276-1285. 2000], pulse at the caudal artery was measured as an auxiliary index using a pulse measurement device.

[0057]

[Table 1]

[Table ]

| AWR score | Characteristic response |
|---|---|
| 0 | No behavioral response to distension |
| 1 | Brief head movements followed by immobility |
| 2 | Contraction of abdominal muscle without lifting of abdomen |
| 3 | Lifting of abdomen |
| 4 | Body arching and lifting of abdomen and pelvic structure |

[0058]

[0059] LITT prepared in Example 1 was dissolved in 0.5% CMC aqueous solution and orally administered at a dose of 100 mg/kg and 300 mg/kg. As positive control, alosetron (alosetron HCl; Jiangyin Yongda Chemical Co., Ltd.) was administered at a dose of 20 mg/kg. After stabilization for 50-60 minutes, CRD was performed and AWR score and pulse rate change were recorded. The areas under the curve (AUC) of AWR score and pulse rate change were calculated for the vehicle group, the positive control group and the LITT group. Statistical analysis was performed using Student's t-test. Significance was tested with $p < 0.05$.

[0060] In Fig. 2, "Normal" refers to the colitis-noninduced normal group, "Vehicle" refers to the colitis-induced group to which only the vehicle was orally administered, "Alo" refers to the colitis-induced group to which alosetron was orally administered at a dose of 20 mg/kg, "LITT 100 mg" refers to the colitis-induced group to which LITT was orally administered at a dose of 100 mg, and "LITT 300 mg" refers to the colitis-induced group to which LITT was orally administered at a dose of 300 mg. LITT (300 mg/kg) decreased both the AWR score and the pulse rate change in the IBS-induced group and resulted in superior visceral pain relieving effect as compared to alosetron (20 mg/kg), with an AWR score of about 65% and a pulse rate of 77% [Fig. 2].

[0061]

[0062] Test Example 2: Inhibition activity against neurokinin receptor

[0063] A cell line overexpressing neurokinin receptor, particularly NK type-1, (U-373MG glioma cell line) was purchased from the Korean Cell Line Bank and cultured (5% $CO_2$ ) using a culture medium (RPMI 1640 90%, fetal bovine serum 10%, penicillin 100 IU/mL, streptomycin 100 μg/mL, l-glutamine 2 mM, sodium pyruvate 1.0 mM) and subcultured every 6-8 days using 0.25% trypsin solution.

[0064] The U-373MG glioma cell line was seeded on a 24-well plate after dilution at various concentrations. After treating with probe-bound substance P (SP) at various concentrations 48 hours later and allowing to react, the binding of the fluorescent probe-

bound SP (Oregon Green®488 conjugate, Molecular Probes, Eugene, OR) to the receptor was measured using a fluorescence spectrometer and the optimized condition was established [VJ. Bennett et al., *BMC Chem. Biol.*, 1: 1, 2001]. L-733060 (estimated affinity = 0.8 nM), which is a non-peptide antagonist selectively binding to the receptor, was used as control substance [R. Bang et al., *J. Pharmacol. Exp. Ther.*, 305, p. 31-39, 2003].

[0065] LITT was dissolved in DMSO (final concentration ≤ 0.1%), diluted with distilled water, passed through a millipore membrane (0.22 μm, Millex-GV, U.S.A.) to create a sterile condition, and then administered at different concentrations (10 μg/mL and 50 μg/mL). The control cells were treated with vehicle (0.1% DMSO) and then treated with vehicle (DW) instead of SP. The SP-only group was pretreated with vehicle (0.1% DMSO) and then treated with SP (50 nM). The treatment group was pretreated for 1 hour, and treated with SP (50 nM) followed by L-733060 (50 nM) and SP (50 nM). After allowing to react in an incubator for 1 hour, the cells were washed with serum-free medium and dissolved in 5% Triton X-100. Then, fluorescence was measured (Ex 485/Em 528) on a black opaque 96-well plate. For each sample (n = 2), experiment was repeated 3 times independently. Statistical analysis was conducted by means of student's t-test compared to vehicle group ( ** $p < 0.01$).

[0066] As seen in Table 2, LITT showed superior inhibition activity of about 83% (L-733060: ~73%) at 50 μg/mL.

[0067] [Table 2]

[Table ]

| Sample | Concentration | Relative inhibitory activity (%) |
|---|---|---|
| Control | | 100 |
| Vehicle | | 0 |
| L-733060 | 50 nM | 72 ± 8** |
| LITT | 10 μg/mL | 11 ± 2 |
| | 50 μg/mL | 82 ± 7** |

[0068]

[0069] Exemplary, non-limiting formulation examples of the composition comprising the extract of the present invention are described below.

[0070]

[0071] Formulation Example 1: Preparation of powder

[0072] Extract prepared in Example 1 20 mg

[0073] Lactose 100 mg

[0074] Talc 10 mg

[0075] The above ingredients are mixed and filled in an airtight pouch.

[0076]

[0077] Formulation Example 2: Preparation of tablet

[0078] Extract prepared in Example 1 10 mg

[0079] Cornstarch 100 mg

[0080] Lactose 100 mg

[0081] Magnesium stearate 2 mg

[0082] The above ingredients are mixed and made into tablet according to a common tablet-making method.

[0083]

[0084] Formulation Example 3: Preparation of capsule

[0085] Extract prepared in Example 1 10 mg

[0086] Crystalline cellulose 3 mg

[0087] Lactose 14.8 mg

[0088] Magnesium stearate 0.2 mg

[0089] According to a common capsule-making method, the above ingredients are mixed and filled into a gelatin capsule.

[0090]

[0091] Formulation Example 4: Preparation of injection

[0092] Extract prepared in Example 1 10 mg

[0093] Mannitol 180 mg

[0094] Sterile distilled water for injection 2,974 mg

[0095] $Na_2HPO_4.12H_2O$ 26 mg

[0096] Injection is prepared with the above ingredients per ampule (2 mL) according to a common injection preparation method.

[0097]

[0098] Formulation Example 5: Preparation of solution

[0099] Extract prepared in Example 1 20 mg

[0100] Isomerized sugar 10 g

[0101] Mannitol 5 g

[0102] Purified water adequate

[0103] According to a common solution preparation method, the above ingredients are dissolved in purified water. After adding adequate amount of lemon flavor and mixing, purified water is added to make 100 mL. The solution is filled in a brown bottle.

[0104]

[0105] Formulation Example 6: Preparation of health food

[0106] Extract prepared in Example 1 1,000 mg

[0107] Vitamin mixture adequate

[0108] Vitamin A acetate 70 μg

[0109] Vitamin E 1.0 mg

[0110] Vitamin $B_1$ 0.13 mg

[0111] Vitamin $B_2$ 0.15 mg

[0112] Vitamin $B_6$ 0.5 mg

[0113] Vitamin $B_{12}$ 0.2 μg

[0114] Vitamin C 10 mg

[0115] Biotin 10 μg

[0116] Nicotinamide 1.7 mg

[0117] Folic acid 50 μg

[0118] Calcium pantothenate 0.5 mg

[0119] Mineral mixture adequate

[0120] Ferrous sulfate 1.75 mg

[0121] Zinc oxide 0.82 mg

[0122] Magnesium carbonate 25.3 mg

[0123] Potassium phosphate monobasic 15 mg

[0124] Calcium phosphate dibasic 55 mg

[0125] Potassium citrate 90 mg

[0126] Calcium carbonate 100 mg

[0127] Magnesium chloride 24.8 mg

[0128] The vitamin and mineral mixtures are added to improve health. Their contents may be varied. According to a common health food preparation method, the above ingredients are mixed and prepared into granule.

[0129]

[0130] Formulation Example 7: Preparation of health drink

[0131] Extract prepared in Example 1 1,000 mg

[0132] Citric acid 1,000 mg

[0133] Oligosaccharide 100 g

[0134] Plum concentrate 2 g

[0135] Taurine 1 g

[0136] Purified water to make 900 mL

[0137] According to a common health drink preparation method, the above ingredients are mixed and heated at 85 °C for about 1 hour under agitation. The resultant solution is filtered and collected in a 2 L container. It is sealed, sterilized and stored in a refrigerator until preparation of a health drink composition.

[0138] The above contents may be varied considering regional or ethnic preferences, such as age, country, purpose, or the like.

[0139]

[0140] The present application contains subject matter related to Korean Patent Application No. 2009-0008678, filed in the Korean Intellectual Property Office on February 4, 2009, the entire contents of which is incorporated herein by reference.

[0141] While the present invention has been described with respect to the specific embodiments, it will be apparent to those skilled in the art that various changes and modifications may be made without departing from the spirit and scope of the invention as defined in the following claims.

[0142]

# Claims

[Claim 1] A pharmaceutical composition for the prevention and treatment of irritable bowel syndrome comprising *Liriopis tuber* extract as an active ingredient.

[Claim 2] The pharmaceutical composition according to claim 1, wherein the *Liriopis tuber* is a tuber of at least one selected from *Ophiopogon japonicus* Ker-Gawler, *Liriope platyphylla* Wang et Tang and related plants of the same genuses.

[Claim 3] The pharmaceutical composition according to claim 1, wherein the extract is soluble in a solvent selected from water, $C_1$-$C_4$ low alcohol, a nonpolar solvent and a mixture solvent thereof.

[Claim 4] The pharmaceutical composition according to claim 3, wherein the mixture solvent comprises water and the $C_1$-$C_4$ low alcohol at a proportion of 5% (v/v) to 95% (v/v).

[Claim 5] The pharmaceutical composition according to claim 3, wherein the nonpolar solvent is dichloromethane, chloroform, diethyl ether, ethyl acetate, hexane or a supercritical fluid.

[Claim 6] The pharmaceutical composition according to any one of claims 1 to 5, wherein the extract is obtained by agitation extraction, hot extraction, cold extraction, reflux cooling extraction, ultrasonic extraction or supercritical fluid extraction using an extraction solvent about 1 to 20 times the weight of dried *Liriopis tuber*.

[Claim 7] The pharmaceutical composition according to any one of claims 1 to 5, which is prepared into a formulation for oral or parenteral administration.

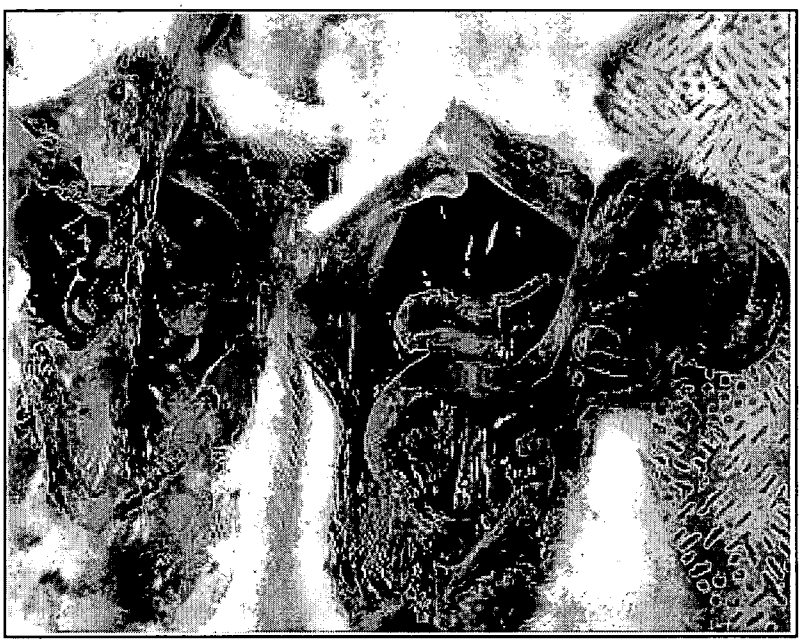
[Claim 8] The pharmaceutical composition according to any one of claims 1 to 5, wherein the irritable bowel syndrome is at least one selected from diarrhea-predominant irritable bowel syndrome, constipation-predominant irritable bowel syndrome and pain-predominant irritable bowel syndrome.

[Claim 9] The pharmaceutical composition according to any one of claims 1 to 5, wherein the extract inhibits NK receptor.

[Claim 10] A health functional food for preventing or improving irritable bowel syndrome comprising *Liriopis tuber* extract as an active ingredient.

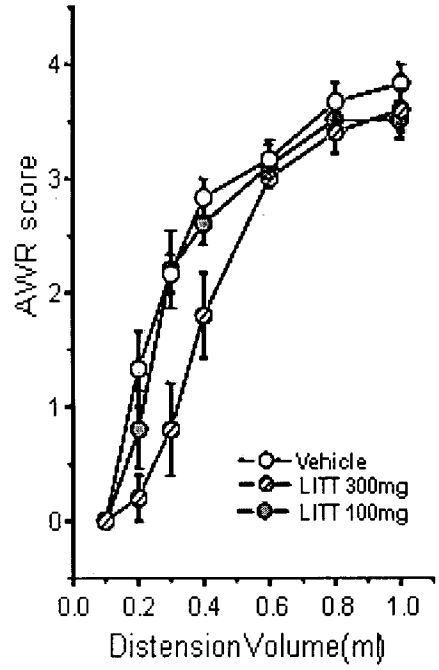
[Claim 11] The health functional food according to claim 10, which is in the form of powder, granule, tablet, capsule or drink.

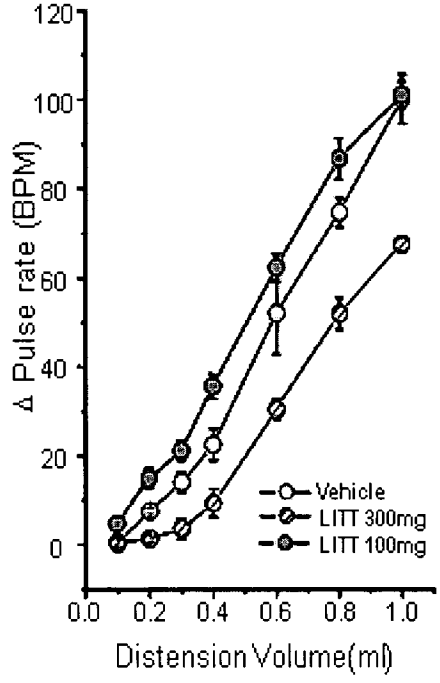
[Fig. 1]

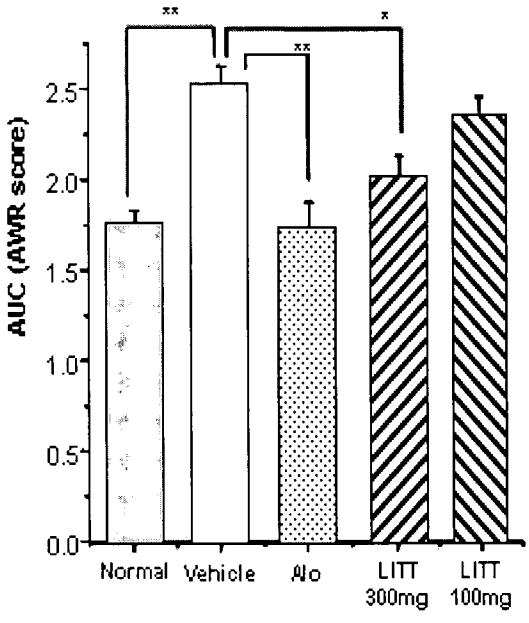


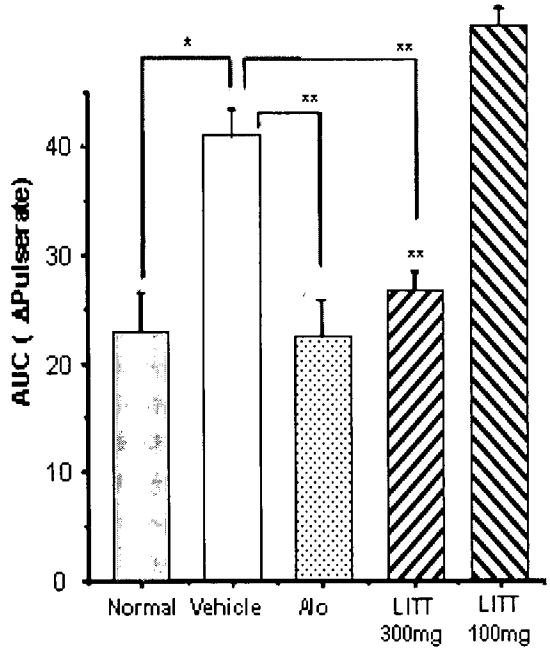
(Left): normal animal (Right): IBS-induced animal

[Fig. 2]


AWR score
Distension Volume(ml)
Vehicle
LITT 300mg
LITT 100mg


Δ Pulse rate (BPM)
Distension Volume(ml)
Vehicle
LITT 300mg
LITT 100mg


AUC (AWR score)
Normal
Vehicle
Alo
LITT 300mg
LITT 100mg


AUC ( ΔPulse rate)
Normal
Vehicle
Alo
LITT 300mg
LITT 100mg