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RATION METHOD

(57) Abstract: Disclosed is a rapidly disintegrating oral formulation comprising a herbal extract. The oral formulation of the present invention can be rapidly dissolved or disintegrated in the mouth and, therefore, easily applied to patients via oral administration. In particular, the formulation is effectively administered to patients with weak swallowing functions such as pediatric and/or elderly patients, patients with mental illnesses and so on. In addition, unlike other general formulations for oral administration, the formulation of the present invention which is simply taken or swallowed without water is useful for patients who are on a trip or do not have immediate access to water. Accordingly, it is expected that the rapidly disintegrating oral formulation of the present invention will improve patient compliance if applied to manufacture of herbal extract or oriental medicine based formulations.

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COMPOSITION FOR FAST DISINTEGRATING TABLET CONTAINING HERBAL EXTRACT AND ITS PREPARATION METHOD

Technical Field

The present invention relates to a composition for a formulation rapidly disintegrating in the mouth and a preparation method thereof and, more particularly, to a composition for an oral formulation comprising an herbal extract with improved fast disintegration properties and a method for preparation thereof.

An oral formulation rapidly disintegrating in the mouth, that is, a rapidly disintegrating oral formulation according to the present invention means a formulation that spontaneously dissolves or disintegrates in the mouth, and, thus, is capable of being administered without water.

Background Art

It is known that some patients suffer from difficulty in swallowing tablets or capsules and even about 20% of patients reject formulations administered in tablet form. However, a rapidly disintegrating oral formulation, which is rapidly dissolving or disintegrating (often referred to as a “rapidly disintegrating formulation”) in the mouth, can be easily taken by a patient. Especially, such formulations can be efficiently applied to patients who experience difficulty swallowing, for example, pediatric and/or elderly patients, patients with mental illnesses (psychiatric patients) and so on. Unlike other general formulations for oral administration, the rapidly disintegrating formulation capable of being swallowed without water is preferably employed under different circumstances, in particular, that a patient is on a trip, does not have immediate access to water, or has difficulty in swallowing a tablet form of drug. Accordingly, it is expected that the rapidly disintegrating oral formulation will improve patient compliance if applied to manufacture of herbal extract or oriental medicine based formulations.

A number of conventional techniques or methods for manufacturing formulations for oral administration capable of being rapidly dissolved and/or disintegrated in the mouth have been disclosed. For example, Japanese Patent Laid-Open Publication No. H9-48726 proposed a rapidly disintegrating oral formulation including a shape retention material, fabricated by wetting a drug

containing granular materials through humidification and compression molding and drying the wetted material to form a shaped product, wherein the shape retention material was exemplified by sugars, sugar alcohols and aqueous polymers. Japanese Patent Laid-Open Publication No. H5-271054 disclosed a tablet manufacturing method comprising tablet-pressing a mixture of drugs and sugars with desired water content sufficient to moisturize a surface of sugar particles and drying the treated mixture to produce a tablet. Japanese Patent Laid-Open Publication No. H8-291051 described a tablet manufacturing method comprising moisturizing a mixture including a drug, an aqueous binder and an aqueous excipient after tablet-pressing the same at low pressure and drying the wetted mixture to produce a tablet. However, all of the inventions described in the above publications have problems in that the mixture is wetted or moisturized state difficult to treat using any conventional tablet presses and, in addition, moisturizing and drying steps are necessarily conducted after the tableting process thereby causing increase of processing steps.

Other techniques have also been proposed, including, for example, a method for production of a drug formulation that comprises dissolving or suspending medical ingredients in an aqueous solvent, filling a preformed mold such as a blister pack with the solution or suspension, and lyophilizing the solution or suspension (as disclosed in US Patent Nos. 4371516 and 4946684) or vacuum drying the solution (as disclosed in US Patent No. 5466464) so as to remove water from the solution. Most compositions used in these methods typically comprise pharmacologically active medical ingredients in an amount of 0.001 to 50% by weight ("wt.-%") relative to total weight of the compositions and the balance of other additives such as an excipient, a disintegrating agent and/or a sweetening agent. However, the above methods also have a problem of decreased disintegration speed if applied to manufacture of rapidly disintegrating formulations containing more than 40% active ingredient. In addition, if a single dose of the active ingredient is more than 0.5mg, an amount of the formulation increases to more than 1g which is inconvenient to orally receive or swallow.

Furthermore, Korean Patent Laid-Open Publication No. 0098009 describes a method for manufacturing a rapidly disintegrating oral tablet which comprises granulating a mixture containing pharmacologically active water-soluble ingredients and an adsorption agent to form a granular substance,

preparing a composition containing the granular substance as well as D-mannitol and a disintegrating agent, and compression molding the composition to produce the tablet. For the tablet manufactured using the above composition and applied to manufacture a rapidly disintegrating formulation, a ratio of D-mannitol and the disintegrating agent to the formulation ranged from 50 to 99%. Accordingly, when a single dose of the pharmacologically active ingredients is about 0.5g dry weight, the rapidly disintegrating formulation substantially becomes 1 to 50g in a single dose which is too much for a patient to swallow, thereby decreasing patient compliance. In particular, the above publication suggested that the rapidly disintegrating tablet manufactured using any of the conventional techniques described above preferably had a small size, for example, a table diameter ranging from 6 to 9mm corresponding to a tablet weight ranging from 80 to 250mg.

Disclosure of Invention

Technical Problem

As a result of extensive studies in regard to reduction of content of an excipient other than active ingredients and simplification of a process for preparation of a tablet formulation thereby improving patient compliance, the inventors found a solution to minimize weight of the formulation, which has never been proposed among conventional methods in the related art. The present invention is designed to alleviate bitterness of traditional herbal extracts and, in turn, enhance medical compliance in patients, particularly, pediatric patients.

Accordingly, the present invention is devised to solve the conventional problems described above and an object of the present invention is to provide a rapidly disintegrating oral formulation easily acceptable even by pediatric or elderly patients, which is fabricated by greatly reducing amount of an excipient to decrease weight of the formulation and, if the active ingredients comprise bitter herbal extracts, improving the taste of the formulation to eliminate patient discomfort during disintegration in the mouth.

Technical Solution

Active ingredients used in the present invention include herbal extracts in liquid or powder form. The present invention provides a formulation with improved taste and rapid disintegration in the mouth, which is fabricated by adding a small amount of a disintegrating agent, a binder, a sweetening agent and/or flavors to an active ingredient substantially comprising an herbal extract in a liquid or powder form and lyophilizing the mixture.

The herbal extract used in the present invention may include water-soluble extracts soluble in water and/or extracts obtained using an organic solvent.

Best Mode

Hereinafter, the present invention will be described in more detail.

The present invention uses an herbal extract or dried herbal extract powder. When using the herbal extract, the extract is preferably concentrated to a desired concentration before use in order to maximize reduction in volume of a final formulation. More preferably, the herbal extract is dried via spray drying or lyophilization then re-dissolved to achieve a desired concentration effective to more correctly regulate a dose of the extract. In this regard, content of the herbal extract in a dried formulation preferably ranges from 20 to 99.9wt.% and, more preferably, 40 to 99wt.%. If the content is less than 20wt.%, a volume of the entire formulation increases, causing discomfort to patients during oral administration thereof, thereby possibly causing a decrease in patient medical compliance (hereinafter referred to as "patient compliance"). On the other hand, with the content of more than 99.9wt.%, it is difficult to expect desirable effects of other additives.

A solid content in a water-soluble solution before lyophilization preferably ranges 5 to 60wt.% and, more preferably, 10 to 45wt.%. If the content is less than 5wt.%, a volume of the formulation increases while cohesiveness of the same decreases, resulting in fragile formulation, although the formulation has a short disintegration time. In addition, when the content is more than 60wt.%, a viscosity of the formulation increases, possibly causing trouble during processing and increasing disintegration time.

During the lyophilization, a chamber containing a mixture may be maintained at a low temperature for a constant period of time and, at the

beginning of drying, the temperature is preferably maintained at -10°C or less. A time period required for the lyophilization depends on an amount of the mixture to be lyophilized and/or a concentration of the herbal extract. In particular, raising the temperature after maintaining the low temperature for at least 1 hour, the combined mixture is dried. One reason for maintaining the low temperature during lyophilization is because the herbal extract is concentrated to induce a sample lyophilized to have a very low melting point due to freezing point depression. However, even an aqueous solution with high concentration exhibits melting point elevation according to the Clapeyron Equation when a pressure of the solution decreases under vacuum, thereby maintaining the lyophilized condition. Consequently, although a surface of the lyophilized sample does not melt during lyophilization, the vacuum pressure effect is not transferred to the internal portion of the sample at the beginning of lyophilization so that the inside of the sample becomes liquefied before completing lyophilization, thus causing a surface blooming defect. As a result, the formulation cannot maintain an original form as lyophilized in a mold.

The mold used in the present invention is not particularly limited but preferably includes a mold with a small height but wider surface areas of top and bottom sides of the mold. This is because a penetration depth of saliva must be shortened in order to decrease disintegration time, and this is achieved when an oral formulation has a greater surface area contacting a tongue portion on which a relatively large amount of saliva is gathered.

In order to improve formulation taste, the formulation may further include a variety of additives such as a bitterness masking agent, a sweetening agent, flavors, etc. Such additives may include any commercially available additive approved for human use, for example, at least one selected from a group consisting of polyvinyl pyrrolidone derivatives such as crospovidone, sodium carboxymethylcellulose, sodium starch glycolate, croscarmellose sodium, low-substituted hydroxypropyl cellulose, aspartame, ascorbic acid, citric acid, thaumatin, maltitol, sorbitol, mannitol, erythritol, lactitol, xylitol, reduced (hydrogenated) starch hydrolysates, saccharine, Licorice extract, stevia sweetener, mogrososide, sucrose, isomerized sugar, palatinose, isomalto-oligosaccharide, malto-oligosaccharide, fructo-oligosaccharide, soybean oligosaccharide, fructose, lactose, maltose, glucose, xylose, isomerized lactose, galacto-oligosaccharide, xylo-oligosaccharide, dextrose syrup and fruit flavors. The additives more

preferably include at least one selected from a group consisting of crospovidone, sodium carboxymethylcellulose, croscarmellose sodium, sodium starch glycolate, low-substituted hydroxypropyl cellulose, aspartame, ascorbic acid and fruit flavors. An amount of the additive contained in a composition for a rapidly disintegrating formulation according to the present invention ranges from 0.001 to 40% by weight ("wt.%") and, more preferably, 0.001 to 20wt.% relative to total weight of the composition. With a content of less than 0.001wt.%, the additive cannot sufficiently improve bitterness of the herbal extract. On the other hand, additional improvement is not expected even when the content exceeds 40wt.%.

For a rapidly disintegrating formulation formed using a lyophilization method, the formulation exhibits excellent rapid disintegration but contains a high concentration of herbal extract. Adding an additive to this formulation, surface blooming and/or surface unevenness may occur in the prepared rapidly disintegrating formulation. In order to remove this defect, a particular additive for improving the surface of the formulation can be contained in the formulation, in addition to use of the lyophilization method. Such additive is not particularly limited but preferably includes at least one selected from a group consisting of: polyvinyl pyrrolidone derivatives such as crospovidone, povidone, etc.; starches such as sodium starch glycolate, starch, pregelatinized starch, gelatin, corn starch, tapioca starch, etc.; cellulose and derivatives thereof such as sodium carboxymethylcellulose, calcium carboxymethylcellulose, croscarmellose sodium, low-substituted hydroxypropylcellulose, hydroxylpropylcellulose, low-substituted cellulose, microcrystalline cellulose, methylcellulose, etc.; and saccharides such as mannose, sucrose, xylitol, mannitol, trehalose, glucose, maltitol, lactose, fructose, etc. More preferably, the composition of the present invention includes at least one additive selected from a group consisting of crospovidone, carboxymethylcellulose sodium, croscarmellose sodium, sodium starch glycolate and low-substituted hydroxypropylcellulose. An amount of the additive ranges from 0.5 to 60wt.% and, more preferably, 1 to 30wt.% relative to total weight of the composition. Minimal improvement in surface blooming is obtained when the additive amount is less than 0.5wt.%. When the amount exceeds 60wt.%, the entire dose of the formulation is too large to orally administer to a patient thereby possibly reducing patient compliance.

Mode for invention

Hereinafter, the present invention will become apparent from the following detailed description of preferred embodiments and examples, which are proposed for illustrative purposes only and are not intended to restrict the spirit and scope of the invention.

Examples

[Preparation of herbal extracts]

Preparation Example 1: Preparation of Hyeonggaeyeongyotang (an herbal tea containing Nepetae Herba aqua and Forsythia Fructus, referred to as "herbal tea") extract powder

Main ingredients contained in a wrapper (dose) of the herbal tea:

- Saposhnikoviae Radix and Lonicerae Flos; 8g per each,

- Angelicae Gigantis Radix, Cnidii Rhizoma and Paeoniae Radix; 5g per each,

- Nepetae Herba aqua, Forsythia Fructus, Bupleuri Radix, Aurantii Fructus, Scutellariae Radix, Gardeniae Fructus, Dahuricae Radix, Platycodi Radix, Ulmi cortex, Akebiae caulis and Retinervus luffae Fructus; 4g per each, and

- Glycyrrhizae Radix; 2g.

Extraction procedure:

1 pack (comprising 20 wrappers, 1 wrapper=77g), that is, 1540g of the herbal tea was placed in a clay pot for preparing medicine and 6L of water was added thereto. After boiling the mixture for 3 hours, the resulting concentrate was lyophilized by a conventional method. Yield: 20.048% (lyophilized weight as a percentage of the total weight of the original herbal tea).

Preparation Example 2: Preparation of Sopungyangjetang (a medicinal herbal tea) extract powder

Main ingredients contained in a wrapper of the herbal tea:

- Angelicae gigantis Radix, Moutan Cortex Radicis and Rehmanniae Radix; 12g per each,

- Glycyrrhizae Radix, Lonicerae Flos, Saposhnikoviae Radix, Spirodela polyrhiza schneider, Forsythia Fructus, Paeonia Radix, Cnidii Rhizoma, Nepetae Herba aqua and Bombycis Corpus; 4g per each, and

- Menthae Herba, Rhinoceri Cornu and Scutellariae Radix; 2g per each.

Extraction procedure:

1 pack (comprising 20 wrappers, 1 wrapper=72g), that is, 1560g of the herbal tea was placed in a clay pot for preparing medicine and 6L of water was added thereto. After boiling the mixture for 3 hours, the resulting concentrate was lyophilized by a conventional method. Yield: 14.91% (lyophilized weight as a percentage of the total weight of the original herbal tea).

Preparation Example 3: Preparation of Sopungsan (a medicinal herbal tea) extract powder

Main ingredients contained in a wrapper of the herbal tea:

- Spirodela polyrhiza schleider; 12g per each, and

- Glycyrrhizae Radix, Sophorae Radix, Angelicae gigantis Radix, Cannabis Fructus, Akebiae Caulis, Saposhnikoviae Radix, Rehmanniae Radix, Gypsum Fibrosum, Cryptotympana atrata, Forsythia Fructus, Arctium lappa linne, Atractylodes Rhizoma, Nepetae Herba aqua and Sesamum indicum linne; 4g per each.

Extraction procedure:

1 pack (comprising 20 wrappers, 1 wrapper=68g), that is, 1360g of the herbal tea was placed in a clay pot for preparing medicine and 6L of water was added thereto. After boiling the mixture for 3 hours, the resulting concentrate was lyophilized by a conventional method. Yield: 12.58% (lyophilized weight as a percentage of the total weight of the original herbal tea).

Examples 1 to 36

The formulations according to Examples 1 to 36 were produced by the following procedure:

Admixing particular herbal extract powders and additives listed in Tables 1 to 3 together in a certain ratio, a composition was prepared. After dissolving or dispersing the prepared composition in water, the solution was poured into a mold and frozen in a lyophilization chamber at -40°C. After maintaining the chamber at -40°C for 3 hours, the temperature of the chamber was moderately elevated to 40°C by 5°C per hour to dry the composition in the chamber. The resulting formulation had a thickness of 4mm.

Table 1

Composition	Example (wt. g)											
	1	2	3	4	5	6	7	8	9	10	11	12
Hyeonggae-yeongyotang extract powder	6	6	6	6	6	6	6	6	6	6	6	6
Crospovidone	1.2	-	-	-	1.2	1.2	1.2	1.2	-	-	1.2	1.2
Sodium carboxymethyl-cellulose	-	-	-	-	-	-	-	-	0.3	0.3	0.05	0.1
Sodium starch glycolate	-	0.15	-	-	-	-	-	-	-	-	-	-
Low-substituted hydroxypropyl-cellulose	-	-	0.75	-	-	-	-	-	-	-	-	-
Croscarmellose sodium	-	-	-	0.15	-	-	-	-	-	-	-	-
Ascorbic acid	-	-	-	-	-	0.2	-	0.2	-	0.2	0.2	0.2
Aspartame	-	-	-	-	0.06	0.06	0.06	0.06	0.06	0.06	0.06	0.06
Fruit flavors	-	-	-	-	-	-	0.01	0.01	0.01	0.01	0.01	0.01
Water	15	15	15	15	15	15	15	15	15	15	15	15

Table 2

Composition	Example (wt. g)											
	13	14	15	16	17	18	19	20	21	22	23	24
Sopungyangje-tang extract powder	6	6	6	6	6	6	6	6	6	6	6	6
Crospovidone	1.2	-	-	-	1.2	1.2	1.2	1.2	-	-	1.2	1.2
Sodium carboxymethyl-cellulose	-	-	-	-	-	-	-	-	0.3	0.3	0.05	0.1
Sodium starch glycolate	-	0.15	-	-	-	-	-	-	-	-	-	-
Low-substituted hydroxypropyl-cellulose	-	-	0.75	-	-	-	-	-	-	-	-	-
Croscarmellose sodium	-	-	-	0.15	-	-	-	-	-	-	-	-
Ascorbic acid	-	-	-	-	-	0.2	-	0.2	-	0.2	0.2	0.2
Aspartame	-	-	-	-	0.06	0.06	0.06	0.06	0.06	0.06	0.06	0.06
Fruit flavors	-	-	-	-	-	-	0.01	0.01	0.01	0.01	0.01	0.01
Water	15	15	15	15	15	15	15	15	15	15	15	15

Table 3

Composition	Example (wt. g)											
	25	26	27	28	29	30	31	32	33	34	35	36
Sopungsan extract powder	6	6	6	6	6	6	6	6	6	6	6	6
Crospovidone	1.2	-	-	-	1.2	1.2	1.2	1.2	-	-	1.2	1.2
Sodium carboxymethyl-cellulose	-	-	-	-	-	-	-	-	0.3	0.3	0.05	0.1

Sodium starch glycolate	-	0.15	-	-	-	-	-	-	-	-	-	-
Low-substituted hydroxypropyl-cellulose	-	-	0.75	-	-	-	-	-	-	-	-	-
Croscarmellose sodium	-	-	-	0.15	-	-	-	-	-	-	-	-
Ascorbic acid	-	-	-	-	-	0.2	-	0.2	-	0.2	0.2	0.2
Aspartame	-	-	-	-	0.06	0.06	0.06	0.06	0.06	0.06	0.06	0.06
Fruit flavors	-	-	-	-	-	-	0.01	0.01	0.01	0.01	0.01	0.01
Water	15	15	15	15	15	15	15	15	15	15	15	15

Comparative Example 1

A formulation was produced by compressing the composition for a rapidly disintegrating formulation according to Example 8 by means of a conventional process.

Comparative Example 2

A formulation was produced by compressing the composition for a rapidly disintegrating formulation according to Example 10 by means of a conventional process.

Comparative Example 3

A formulation was produced by compressing the composition for a rapidly disintegrating formulation according to Example 12 by means of a conventional process.

Comparative Example 4

After dissolving 6g of the herbal tea extract powder prepared by Preparation Example 1 in 15g of water, the solution was poured into a mold and frozen in a lyophilization chamber at -70°C, followed by lyophilization at room temperature according to a conventional method.

Comparative Example 5

After dissolving 6g of the herbal tea extract powder prepared by Preparation Example 1 in 15g of water, the solution was poured into a mold and frozen in a lyophilization chamber at -40°C. After maintaining the chamber at -40°C for 3 hours, the temperature of the chamber was moderately elevated to 40°C by 5°C per hour to dry the composition in the chamber. The resulting

formulation had a thickness of 4mm.

Experimental Example 1: Measurement of disintegration time of the rapidly disintegrating formulation according to the present invention

5 The rapidly disintegrating formulation of the present invention was subjected to disintegration time measurement.

After preparing test samples of the formulations produced according to Examples 1 to 36 and Comparative Examples 1 to 3, each of the specimens was orally administered to five (5) volunteers. More particularly, the sample was placed on the tongue of each person and time taken for the sample to completely disintegrate was measured.

Table 4

Disintegration time (sec) (mean±sd)		Disintegration time (sec) (mean±sd)	
Example 1	29±10	Example 21	34±13
Example 2	31±1	Example 22	22±8
Example 3	29±4	Example 23	26±8
Example 4	22±7	Example 24	31±9
Example 5	23±7	Example 25	28±11
Example 6	23±13	Example 26	31±5
Example 7	33±28	Example 27	28±6
Example 8	31±18	Example 28	21±7
Example 9	35±12	Example 29	22±9
Example 10	21±9	Example 30	21±13
Example 11	27±7	Example 31	31±11
Example 12	33±10	Example 32	30±13
Example 13	31±9	Example 33	36±12
Example 14	30±3	Example 34	20±8
Example 15	28±6	Example 35	26±7
Example 16	23±7	Example 36	32±10
Example 17	22±9	Comparative Example 1	289±43
Example 18	24±8	Comparative Example 2	451±120
Example 19	30±15	Comparative Example 3	251±82
Example 20	29±17		

15 As shown in Table 4, it was found that, if a rapidly disintegrating formulation of the present invention is produced by the preparation method of the

present invention, all compositions used for production of the formulation exhibit reduced disintegration time (see Examples 1 to 36). Whereas, when the formulations were produced by other methods (see Comparative Examples 1 to 3), the disintegration time was considerably extended even with the same composition.

Experimental Example 2: Appearance comparison of rapidly disintegrating formulations

Appearance of the rapidly disintegrating formulation produced in Example 8 was observed and compared to that of the formulation produced in Comparative Example 4. The formulation according to the present invention (Example 8) showed favorable surface quality without surface blooming, while the formulation produced using common lyophilization (Comparative Example 4) exhibited surface blooming.

Experimental Example 3: Determination of bitterness masking effect of the rapidly disintegrating formulation according to the present invention

In order to determine bitterness masking effects of rapidly disintegrating formulations produced as described above, the following experiments were performed:

After preparing test samples of the formulations produced according to Examples 1 to 36 and Comparative Example 5, each of the samples was orally administered to some volunteers. More particularly, the sample was placed on the tongue of each person and a masking effect of bitterness of the sample was measured. The results are shown in Table 5.

Table 5

Degree of bitterness in mouth ¹⁾		Degree of bitterness in mouth ¹⁾	
Example 1	2	Example 20	1
Example 2	2	Example 21	2
Example 3	2	Example 22	1
Example 4	2	Example 23	1
Example 5	1	Example 24	1
Example 6	1	Example 25	2
Example 7	1	Example 26	2

Example 8	1	Example 27	2
Example 9	2	Example 28	2
Example 10	1	Example 29	1
Example 11	1	Example 30	1
Example 12	1	Example 31	1
Example 13	2	Example 32	1
Example 14	2	Example 33	2
Example 15	2	Example 34	1
Example 16	2	Example 35	1
Example 17	1	Example 36	1
Example 18	1	Comparative Example 5	4
Example 19	1		

¹⁾ The degree of bitterness for the formulation applied in the mouth was determined on the following criteria.

- 1: no bitterness
- 2: slight bitterness
- 3: strong bitter taste
- 4: unpleasant taste caused by very strong bitterness

As shown in Table 5, the formulation produced using the composition according to Comparative Example 5 had an unpleasant taste caused by very strong bitterness. Conversely, it was found that the formulations produced using the compositions according to Examples 1 to 36 exhibited excellent bitterness masking effects such that the volunteers were substantially unaware of bitterness of the formulations.

Industrial Applicability

The present invention provides a rapidly disintegrating formulation for oral administration comprising an herbal extract. This formulation can be conveniently and correctly applied to patients who experience difficulty swallowing, such as pediatric and/or elderly patients, via oral administration. Alternatively, the formulation of the present invention has additional advantages

including, for example, increased carrying convenience and easy dosage, so as to preferably improve patient compliance in drug administration.

CLAIMS

1. A rapidly disintegrating oral formulation comprising 40 to 99wt.% of at least one herbal extract as an active ingredient, prepared by lyophilization.

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2. The formulation according to claim 1, further comprising at least one additive selected from a group consisting of crospovidone, sodium carboxymethylcellulose, sodium starch glycolate, croscarmellose sodium, low-substituted hydroxypropylcellulose, aspartame, ascorbic acid, citric acid, thaumatin, maltitol, sorbitol, mannitol, erythritol, lactitol, xylitol, reduced (hydrogenated) starch hydrolysates, saccharine, Licorice extract, stevia sweetener, mogrososide, sucrose, isomerized sugar, palatinose, isomalto-oligosaccharide, fructo-oligosaccharide, soybean oligosaccharide, fructose, lactose, maltose, glucose, galacto-oligosaccharide, malto-oligosaccharide, xylo-oligosaccharide, dextrose syrup, xylose, isomerized lactose, and fruit flavors, in an amount ranging from 0.001 to 20wt.% relative to total weight of the formulation, for masking bitterness.

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3. The formulation according to claim 1 or 2, further comprising at least one additive selected from a group consisting of crospovidone, povidone, sodium starch glycolate, starch, pregelatinized starch, gelatin, corn starch, tapioca starch, sodium carboxymethylcellulose, calcium carboxymethylcellulose, carboxymethylcellulose, croscarmellose sodium, methylcellulose, low-substituted hydroxypropylcellulose, hydroxypropylcellulose, low-substituted cellulose, microcrystalline cellulose, methylcellulose, cellulose, mannose, sucrose, xylitol, mannitol, trehalose, glucose, maltitol, lactose and fructose, in an amount ranging from 1 to 30wt.% relative to total weight of the formulation, for improving surface quality of the formulation.

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4. The formulation according to any one of claims 1 to 3, wherein the herbal extract is an extract obtained by using water or an organic solvent, or a typical herbal formulation for an oriental medicine.

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5. A method for preparation of a rapidly disintegrating oral formulation comprising an herbal extract, which includes:

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mixing an additive with herbal extract powder;
dispersing or dissolving the mixture in an aqueous solution;
pouring the mixture into a mold and lyophilizing the mixture in a
lyophilization chamber at a temperature ranging from -80 to -10 °C;
5 maintaining the chamber at a temperature ranging from -50 to -10 °C for
10 hours; and
moderately elevating the temperature to dry the lyophilized product.

6. The method according to claim 5, wherein a solid content of the
10 formulation in the aqueous solution ranges from 10 to 45wt.% before
lyophilization.

A. CLASSIFICATION OF SUBJECT MATTER*A61K 9/26(2006.01)i, A61K 9/20(2006.01)i, A61K 47/26(2006.01)i, A61K 47/32(2006.01)i, A61K 9/20(2006.01)i*

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 8 : as above

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

EKIPASS(KIPO internal), CAS(ON LINE), PUBMED

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US 5288501 A (MERZ + CO. GMBH & CO.) 22 February 1994 (22.02.1994) See abstract; column 1, lines 16-43; column 4, lines 55-68; column 5, lines 11-21; examples 1 and 2; claims.	1-3
A	-----	5, 6
Y	SHEN, L. et al. "Research progress on the oral solid rapidly disintegrating dosage form." ZHONGGUO ZHONG YAO ZA ZHI. 2005, vol.30, no.2, pp.89-92. See abstract.	1-3
A	-----	5, 6
Y	FU, Y. et al. "Orally fast disintegrating tablets: developments, technologies, taste-masking and clinical studies." CRIT. REV. THER. DRUG CARRIER SYST. 2004, vol.21, no.6, pp.433-476. See abstract.	1-3
A	-----	5, 6
A	WO 00/57857 A1 (YUHAN CORPORATION) 5 October 2000 (05.10.2000) See the whole document.	1-3, 5, 6



Further documents are listed in the continuation of Box C.



See patent family annex.

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search

06 OCTOBER 2008 (06.10.2008)

Date of mailing of the international search report

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INTERNATIONAL SEARCH REPORT

International application No.

PCT/KR2008/002555**Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)**

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☐ Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
3. ☒ Claims Nos.: 4
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.
- ☐ The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.
- ☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

International application No.

PCT/KR2008/002555

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO 01/03672 A1 (LABORATOIRES PROGRAPHARM) 18 January 2001 (18.01.2001) See the whole document.	1-3, 5, 6
A	WO 99/09958 A1 (SMITHKLINE BEECHAM CORPORATION) 4 March 1999 (04.03.1999) See the whole document.	1-3, 5, 6

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No.

PCT/KR2008/002555

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