

**FLAVONOID POLYPHENOL DRUG SELF-EMULSIFYING COMPOSITION,
PREPARATION METHOD THEREFOR, PHARMACEUTICAL COMPOSITION
THEREOF AND APPLICATION THEREOF**

5 TECHNICAL FIELD

The present disclosure relates to a flavonoid polyphenol drug self-emulsifying composition, a method for preparing the same, a pharmaceutical composition and a use thereof, which belong to the field of medicines.

BACKGROUND

- 10 At present, flavonoid polyphenol compounds are generally divided into three categories: (1) small molecular phenolic acids such as salicylic acid, cinnamic acid, p-hydroxycinnamic acid, caffeic acid, ferulic acid and chlorogenic acid; (2) tannins which are polyphenol polymers and divided into condensed tannins and hydrolytic tannins, where the condensed tannins are polyphenols formed by linking flavanols through C4-C6 or C4-C8 bonds and having different
15 degrees of polymerization and also referred to as proanthocyanidin, and the hydrolytic tannins are formed by ester formation of gallic acid or ellagic acid with hydroxyl groups on sugars such as glucose; (3) polyhydroxyflavonoids, where one type of polyhydroxyflavonoid is anthocyanins (glycosides of anthocyanidins) which are one of plant pigments, and the other type of polyhydroxyflavonoid is flavonoids in narrow sense and glycosides thereof, where aglycones
20 include flavones, flavonols, dihydroflavones, dihydroflavonols, isoflavones, dihydroisoflavones, chalcone, orange ketone, flavan, anthocyanidins, bisflavones and flavonoids (reference document 1: Advances in intestinal biotransformation of polyphenol constituents [C]. Eighth Academic Annual Meeting of Chinese Medicine Chemistry Branch of Chinese Traditional Medicine Society, 2013).
- 25 Studies show that flavonoid polyphenol drugs have many pharmacological effects in various aspects, such as good effects in aspects of anti-tumor, anti-coagulation, anti-bacteria, hormone regulation, anti-oxidation, anti-aging, anti-atherosclerosis, anti-infection, anti-osteoporosis, anti-virus, anti-microorganism, blood fat regulation and lowering blood sugar.

Limited by physical and chemical properties, oral preparations of the flavonoid polyphenol

drugs has low bioavailability, resulting in a poor effect of oral treatment. Therefore, it is clinically important to increase the maximum plasma concentrations (C_{max}) and blood exposure (area-under-the-curve, AUC) of oral administration through pharmaceutical techniques.

- 5 A self-emulsifying drug delivery system (SEDDS) is a homogeneous mixture of oil phases, an emulsifier and a co-emulsifier and can be used as a drug loading and delivery tool. After oral administration, the SEDDS can be rapidly and spontaneously emulsified to form oil-in-water emulsion droplets in the environment of gastrointestinal peristalsis and an aqueous medium of gastrointestinal fluid.
- 10 Zhiqin WANG et al. have reported that a self-microemulsion encapsulating proanthocyanidins has been prepared with caprylic capric triglyceride as an oil phase, polyoxyethylene 40 castor oil as an emulsifier and 1,2-propanediol as a co-emulsifier. Rapid emulsification is achieved when the three components have a mass ratio of 1:3:1 with a drug loading of 10%. Polyoxyethylene 40 castor oil, 1,2-propanediol and caprylic capric triglyceride were weighed at
15 the mass ratio and stirred uniformly in a water bath of 37 °C, then a formulation amount of proanthocyanidins was mixed and dissolved therein, and the mixture was balanced at 37 °C for 1 h so that the self-microemulsion encapsulating proanthocyanidins was obtained, which has an average particle size of 63.6±0.7 nm after diluted 100 times with water (reference document 2: Chinese Patent Drug, 2013, 35 (12): 2749-2752).
- 20 Weiling ZHANG et al. have reported that excessive quercetin ingredient was subjected to magnetic stirring with polyethylene glycol glyceryl oleate as an oil phase, polyoxyethylene 35 castor oil as an emulsifier and diethylene glycol monoethyl ether as a co-emulsifier which have a ratio of 27.0:55.6:17.4 (w:w:w) in a water bath with a constant temperature of 60 °C, so as to prepare a supersaturated solution of quercetin. The mixture was oscillated for 24 h at room
25 temperature, balanced, and centrifuged at 4000 r/min for 10 min, and the supernatant was taken so that a self-microemulsion encapsulating quercetin ingredient was prepared. The self-microemulsion has a maximum drug loading of 67.87 mg/g and an average particle size of 25.26 nm after diluted 50 times with water (reference document 3: Journal of Shandong University, 2016, 54 (3): 41-49).
- 30 Zemin LI et al. have reported that excessive curcumin ingredient was mixed uniformly with a medium chain fatty acid (medium-chain triglyceride (MCT)) as an oil phase, polyoxyethylene hydrogenated castor oil (Cremophor RH40) as an emulsifier and polyethylene glycol-400

(PEG-400) as a co-emulsifier which have a ratio of 2:6:2 (w/w), vortexed for 5 min, and shaken for 48 h at 37 °C with exclusion of light. The sample was taken out and centrifuged for 10 min at 12000 r/min, and the supernatant was precisely taken so that a self-microemulsion encapsulating curcumin ingredient was prepared, which has significantly improved solubility.

- 5 The self-microemulsion has a maximum drug loading of 55.30 mg/g and an average particle size of 11.8 nm after diluted 100 times with water (reference document 4: Journal of Chengdu Medical College, 2017, 12 (2): 155-59).

Lu CAO et al. have reported that glycerol triacetate was used as an oil phase, Cremophor EL and Cremophor RH40 were used as emulsifiers, and isopropanol was used as a co-emulsifier,
10 where a ratio of glycerol triacetate:Cremophor EL:Cremophor RH40:isopropanol was 22:27:13.5:37.8 (w/w). They were mixed uniformly through magnetic stirring in a water bath of 37 °C so that a blank self-microemulsion was obtained. A proper amount of resveratrol was added to the blank self-microemulsion and dissolved through ultrasonic waves so that a self-microemulsion of resveratrol was obtained. The self-microemulsion of resveratrol has a
15 drug loading of 45 mg/g and an average particle size of 15 nm after diluted 100 times with water (reference document 5: Lu CAO, Formulation and Studies of Resveratrol-SMEDDS [D]. Hebei: Hebei Medical University, 2014).

Self-microemulsions of proanthocyanidins, quercetin, curcumin and resveratrol were prepared according to the methods in reference documents 2 to 5, respectively. These
20 self-microemulsions were stored at 4 °C and at room temperature for 5 days, one month and two months, separately. Changes in appearance and physical stability of the self-microemulsions were observed. The results show that self-microemulsions of flavonoid polyphenol drug prepared according to the formulations in reference documents 2 to 5 have obvious stability defects: semi-solids or precipitates easily form after placement at 4 °C, and drugs are
25 precipitated after placement at room temperature for a period of time.

In addition, Xue KE et al. have reported that a blank self-macroemulsifying drug delivery system (SMEDDS) was prepared according to a formulation with Migly-col812/Maisine35-1(1:1) as oil phases, Cremphor EL35/labrasol (2:1) as emulsifiers and Transcutol P as a co-emulsifier, excessive baicalein was added, stirred and dissolved in a water
30 bath of 37 °C, taken out after 24 h, and centrifuged at a high speed of 12000 r·min⁻¹ for 15 min, and the supernatant was taken, that is, a self-microemulsion encapsulating baicalein ingredient was prepared, which has a maximum drug loading of 18.1±1.11 mg/g and forms a stable and uniform microemulsion within 3 minutes after diluted 100 times with purified water. The

formed microemulsion has a particle size of 27.2 ± 0.56 nm. Compared with baicalein ingredient (oral gavage), the self-microemulsion of baicalein, when orally administered to rats, increases the $C_{\max}$ by 3.1 times and relative bioavailability (AUC) by 3.77 times (reference document 6: Chinese Journal of New Drugs, 2010, 19 (5): 371-395).

5 Wenli LIU et al. have reported that with caprylic capric triglyceride (ODO, 25%) as an oil phase, Cremophor RH40 (53.57%) as an emulsifier and Transcutol P (21.43%) as a co-emulsifier, excessive baicalein ingredient and the oil phase, emulsifier and co-emulsifier were stirred at 37 °C for 48 h, the mixture was centrifuged at 12000 rpm for 20 min, and the supernatant was taken so that a self-microemulsion encapsulating baicalein ingredient was prepared, which has a
10 maximum drug loading of 32.02 mg/g and a particle size of 27.54 nm after emulsified with water. Compared with a baicalein ingredient suspension (dispersed in a solution of 0.5% sodium carboxymethylcellulose), the self-microemulsion of baicalein, when orally administered to rats, increases the $C_{\max}$ by 1.6 times and relative bioavailability (AUC) by 2.01 times (reference document 7: Fitoterapia, 2012, 83: 1532-1539).

15 The self-microemulsions prepared in reference documents 6 and 7 significantly improve the oral bioavailability of baicalein. However, confirmatory experiments show that the self-microemulsions still have the defects below.

(1) The prepared self-microemulsions of baicalein are easy to form semi-solids or precipitates after placement at 4 °C, and drugs are precipitated after placement at room temperature for one
20 month.

(2) Under the given conditions of the oil phase, emulsifier and co-emulsifier, the drug loading of baicalein is difficult to be further increased, which cannot meet the requirement for the drug loading in a clinical treatment dosage.

(3) Compared with baicalein ingredient, the self-microemulsions increase the $C_{\max}$ and the
25 AUC to limited degrees.

In addition, Changshun LIU et al. have compared the pharmacokinetics of baicalin (BG), a baicalin-phospholipid complex (BGPC), a baicalin-loaded SMEDDS (BG-SMEDDS) and an SMEDDS with the baicalin-phospholipid complex as an intermediate (BGPC-SMEDDS) in rats. The results show that compared with BG, the BGPC, BG-SMEDDS and BGPC-SMEDDS have
30 increased plasma concentrations and the $C_{\max}$ are 3.89, 11.01 and 6.70 times of that in BG and

the $AUC_{0\rightarrow 24h}$ are 2.46, 2.86 and 2.38 times of that in BG. That is, for the C_{max} , a self-microemulsion of baicalin > a self-microemulsion of the baicalin-phospholipid complex > the baicalin-phospholipid complex; and for $AUC_{0\rightarrow 24h}$, the self-microemulsion of baicalin > the baicalin-phospholipid complex > the self-microemulsion of the baicalin-phospholipid complex.

5 SUMMARY

An ideal drug-loading self-emulsifying composition should satisfy the following conditions: (1) when stored for a long time under refrigeration or at room temperature, the self-emulsifying composition should be a clear and transparent liquid with uniform appearance and is not layered; (2) when stored for a long time under refrigeration or at room temperature, the self-emulsifying composition should be a clear and transparent liquid with uniform appearance and should not be solidified or precipitated, so as to avoid the process of "heating and melting a drug mixture" before use and reduce drug degradation; (3) there should be a high self-emulsification efficiency and nano-sized emulsion droplets should be formed through quickly and spontaneously emulsifying after dilution with a certain amount of water in a simulated gastrointestinal environment; (4) emulsion droplets formed through spontaneous emulsification of the self-emulsifying mixture in the gastrointestinal tract after directly taken orally should be nano-sized (1–1000 nm) rather than micron-sized ($>1\ \mu m$).

For a drug-loading SEDDS, different drugs have different drug loads and stability due to different physical and chemical properties. In addition, changes in an oil phase, emulsifier, co-emulsifier and ratio will affect the drug loading and self-emulsification efficiency, thereby affecting the mucosal permeability and bioavailability of the SEDDS, which generally has no laws to follow.

Inventors have found through intensive researches on pharmaceutical preparations of flavonoid polyphenol drug that a self-emulsifying system prepared by using a flavonoid polyphenol drug-phospholipid complex as an intermediate, which is formulated by phospholipids and flavonoid polyphenol drug selected from baicalein, proanthocyanidin, quercetin, curcumin and resveratrol, has the beneficial effects of good stability, a high drug loading, high bioavailability and the like.

In view of this, in one aspect, the present disclosure provides a flavonoid polyphenol drug self-emulsifying composition. The flavonoid polyphenol drug self-emulsifying composition includes a flavonoid polyphenol drug-phospholipid complex, an oil phase, an emulsifier and a

co-emulsifier, where the flavonoid polyphenol drug includes one or more selected from the group consisting of baicalein, proanthocyanidin, quercetin, curcumin and resveratrol.

Optionally, the flavonoid polyphenol drug may further include other flavonoid polyphenol drugs in addition to baicalein, proanthocyanidin, quercetin, curcumin and resveratrol, where the other
5 flavonoid polyphenol drugs are one or more selected from the group consisting of wogonin, ferulic acid, catechin, magnolol, honokiol, apigenin, hesperetin, rotenone, isobavachalcone, aureusidin, delphinidin and ginkgetin.

Preferably, the flavonoid polyphenol drug is baicalein, proanthocyanidin, quercetin, curcumin or resveratrol. Optionally, the flavonoid polyphenol drug self-emulsifying composition has a drug
10 loading of 10–110 mg/g, preferably 10–100 mg/g. Optionally, the flavonoid polyphenol drug self-emulsifying composition has a particle size of 10–1000 nm.

Optionally, in the flavonoid polyphenol drug-phospholipid complex, a mass ratio of the flavonoid polyphenol drug to phospholipid is 1:1–1:15, optionally, 1:1–1:8.

The flavonoid polyphenol drug-phospholipid complex is compounded of the flavonoid
15 polyphenol drug and the phospholipid material. Optionally, the flavonoid polyphenol drug-phospholipid complex has a drug compounding rate of greater than or equal to 80%.

Optionally, the flavonoid polyphenol drug is flavonoid polyphenol drug extracts extracted from traditional Chinese medicine and/or chemically synthesized flavonoid polyphenol drug.

Optionally, the baicalein may be artificially synthesized baicalein, an effective component
20 extracted from a plant and having a baicalein content of greater than 50%, or a product prepared by a plant extract through transformation or recrystallization.

Optionally, the phospholipid is one or more selected from the group consisting of natural phospholipids and synthetic phospholipids.

Optionally, the natural phospholipids include one or more selected from the group consisting of
25 soybean phospholipid and egg-yolk phospholipid.

Optionally, the synthetic phospholipids include one or more selected from the group consisting of phosphoglyceride, sphingomyelin, phosphatidylcholine, phosphatidylethanolamine, phosphatidyl serine, phosphatidylinositol, phosphatidyl glycerol, glycerophosphatidic acid,

distearyl phosphatidylcholine, dipalmitoyl phosphatidylcholine, dipalmitoyl phosphatidylethanolamine and dimyristoyl phosphatidylcholine. Preferably, the synthetic phospholipids are one or more selected from the group consisting of phosphatidylcholine, phosphatidylethanolamine, phosphatidylglycerol and glycerophosphatidic acid.

- 5 Optionally, the oil phase is one or more selected from the group consisting of vegetable oils and vegetable oil derivatives.

Optionally, the vegetable oils include one or more selected from the group consisting of soybean oil, corn oil, olive oil, coconut oil, peanut oil, camellia oil and castor oil;

- 10 Optionally, the vegetable oil derivatives include one or more selected from the group consisting of sorbitan oleate, glyceryl oleate, glyceryl linoleate, polyethylene glycol glyceryl oleate (labrafil®1944cs), glycerol monolinoleate (Maisine35-1), ethyl oleate, ethyl linoleate, C8/C10 monoglyceride, coconut oil C8/C10 diglyceride, coconut oil C8/C10 triglyceride, caprylic acid triglyceride, caprylic acid diglyceride, caprylic acid monoglyceride, capric acid monoglyceride, capric acid diglyceride, capric acid triglyceride, caprylic capric monoglyceride, caprylic capric
15 glyceride, caprylic capric triglyceride, isopropyl myristate, polyethylene glycol glyceryl linoleate (Labrafil®M2125CS), polyethylene glycol glyceryl laurate (Gelucire), and propylene glycol monocaprylate (Capryol 90).

Preferably, the oil phase is one or more selected from the group consisting of soybean oil, castor oil, ethyl oleate, isopropyl myristate and caprylic capric glyceride.

- 20 Optionally, the emulsifier is one or more selected from the group consisting of caprylic capric polyethylene glycol glyceride (labrasol or labraosol), polyethylene glycol (including PEG-200, PEG-400, PEG-600, PEG-800 (the number after PEG represents an average molecular weight)), Tween (including Tween 20, Tween 21, Tween 40, Tween 60, Tween 61, Tween 80, Tween 81 and Tween 85, preferably Tween 80, Tween 60, Tween 20), Span 80, polyethylene glycol
25 glyceryl oleate (labrafil®1944cs), polyethylene glycol glyceryl linoleate (Labrafil®M2125CS), phospholipids and octyl phenyl polyoxyethylene ether (X-100). Preferably, the emulsifier is one or more of caprylic capric polyethylene glycol glyceride (labrasol or labraosol), Tween 80, Tween 85, Triton X-100 and labrafil®1944cs.

- 30 Optionally, the co-emulsifier is one or more selected from the group consisting of ethanol, propylene glycol, propylene carbonate, ethylene glycol monoethyl ether, glycerol furfural,

dimethyl isosorbide, propylene glycol monocaprylate (Capryol 90), diethylene glycol monoethyl ether (transcutol HP or transcutol P), polyethylene glycol (including PEG-200, PEG-400, PEG-600 and PEG-800 (the number after PEG represent an average molecular weight)), glycerol, caprylic capric polyethylene glycol glyceride (labraosol) and benzyl alcohol.

- 5 Preferably, the co-emulsifier is one or more of diethylene glycol monoethyl ether (transcutol HP or transcutol P), polyethylene glycol 400 (PEG-400), ethanol and propylene glycol monocaprylate (Capryol 90).

- 10 Optionally, based on a total mass ratio of the oil phase, the emulsifier and the co-emulsifier being 100%, the oil phase accounts for 10–50% (preferably 20–40%), the emulsifier accounts for 30–60% (preferably 40–60%), and the co-emulsifier accounts for 20–60% (preferably 30–50%).

In another aspect, the present disclosure provides a method for preparing the preceding flavonoid polyphenol drug self-emulsifying composition. The method includes the following preparation steps.

- 15 (1) A flavonoid polyphenol drug-phospholipid complex is prepared: flavonoid polyphenol drug and phospholipids are dissolved in an organic solvent, subjected to a compound reaction, and dried with the organic solvent removed so that the flavonoid polyphenol drug-phospholipid complex is obtained.

- 20 Optionally, the organic solvent is one or more selected from the group consisting of ethyl acetate, tetrahydrofuran, methanol, acetone, ethanol, absolute ethanol, n-propanol, isopropanol, n-butanol, isobutanol, tert-butanol, diethyl ether, methyl ethyl ether, dioxane, butanone, petroleum ether, hexane, cyclohexane, dichloromethane, chloroform, carbon tetrachloride, DMSO and DMF, preferably one or more of ethyl acetate, tetrahydrofuran, methanol, ethanol, cyclohexane, DMSO and DMF.

- 25 (2) The flavonoid polyphenol drug self-emulsifying composition is prepared: the flavonoid polyphenol drug-phospholipid complex obtained in step (1) is fully mixed with an oil phase, an emulsifier and a co-emulsifier in any sequence.

For example, the flavonoid polyphenol drug-phospholipid complex obtained in step (1) may be fully mixed with the oil phase, the emulsifier and the co-emulsifier directly.

Alternatively, the oil phase, the emulsifier and the co-emulsifier are mixed uniformly so that a blank self-emulsifying concentrate is prepared, and then the flavonoid polyphenol drug-phospholipid complex obtained in step (1) is added to the prepared blank self-emulsifying concentrate and fully mixed therewith.

- 5 Alternatively, the flavonoid polyphenol drug-phospholipid complex obtained in step (1) is dissolved in any one of the oil phase, the emulsifier or the co-emulsifier, and then the other two of the oil phase, the emulsifier or the co-emulsifier are added and fully mixed.

10 In another aspect, the present disclosure provides a pharmaceutical composition. The pharmaceutical composition includes the preceding flavonoid polyphenol drug self-emulsifying composition and an optional pharmaceutically acceptable excipient.

Optionally, a dosage form of the pharmaceutical composition includes an oral preparation, an injection preparation, a transdermal administration preparation, a mucosal administration preparation, a pulmonary inhalation administration preparation or an enteral administration preparation. Optionally, the dosage form of the pharmaceutical composition includes drops, oral
15 liquids, tablets, capsules (including soft capsules and hard capsules), granules, infusion granules, films, gel, powders, emulsions, dripping pills, suppositories, aerosols, sprays, powder aerosols, patches, adhesive plasters, solutions, ointments or cream.

The pharmaceutically acceptable excipient may be any conventional excipient in the field of pharmaceutical preparations. A particular excipient is selected depending on a mode of
20 administration for treating a particular patient or a type and state of disease of the particular patient. For example, the pharmaceutically acceptable excipient includes conventional diluents, carriers, fillers, binders, wetting agents, disintegrants, absorption promoters, surfactants, adsorption carriers and lubricants in the pharmaceutical field. If necessary, flavors, preservatives and sweeteners may also be added to the pharmaceutical composition.

25 In another aspect, the present disclosure provides a use of the preceding flavonoid polyphenol drug self-emulsifying composition or the preceding pharmaceutical composition for preparing drugs for anti-bacteria, antiviral, anti-inflammation, inhibiting allergy, regulating immunity, anti-tumor, anti-oxidation, anti-aging, anti-ultraviolet radiation, treatment of hormone deficiency, anti-hypertension, lowering blood fat, anti-atherosclerosis, anti-senile dementia, treatment of
30 hand-foot-mouth diseases, anti-osteoporosis or liver protection.

Beneficial effects:

The flavonoid polyphenol drug self-emulsifying composition of the present disclosure has the beneficial effects of good stability, a high drug loading and high bioavailability.

5 The flavonoid polyphenol drug self-emulsifying composition of the present disclosure is a uniform liquid in appearance and has a drug loading which can reach more than 100 mg/g (W flavonoid polyphenol drug/W composition).

10 The flavonoid polyphenol drug self-emulsifying composition of the present disclosure has a good self-emulsifying ability. After diluted 10–1000 times with water, the flavonoid polyphenol drug self-emulsifying composition can be quickly emulsified to form droplets with a particle size of 10–1000 nm.

BRIEF DESCRIPTION OF DRAWINGS

FIG. 1 is a graph showing a concentration-time curve of baicalin in the plasma of rats in test groups A, B and C in Test Example 2.

15 FIG. 2 is a graph showing a concentration-time curve of baicalein in the plasma of rats in test groups A, B and C in Test Example 2.

DETAILED DESCRIPTION

Specific embodiments of the present disclosure are described below in detail. It is to be understood that the embodiments described herein are intended to illustrate and not to limit the present disclosure.

20 In the following Examples 1 to 5, a compounding rate of flavonoid polyphenol drug and phospholipids in a flavonoid polyphenol drug-phospholipid complex is measured through high-performance liquid chromatography (HPLC).

HPLC conditions:

Chromatography column: Agilent ZORBAX SB C18 column (250 mm×4.6 mm, 5 μm);

25 Mobile phase: 0.05% phosphoric acid-methanol (35:65, v/v);

Flowrate: 1.0 mL/min;

Column temperature: 25 °C (normal temperature);

Injection volume: 10 µL detection wavelength: 275 nm.

Determination method: 24 mg of flavonoid polyphenol drug is accurately weighed for reference,
5 put in a 10 mL volumetric flask, added with absolute ethanol to be dissolved, and diluted to
volume. 1 mL was accurately transferred into a 100 mL volumetric flask and added with
absolute ethanol to be diluted to a solution with a concentration of 24 µg/ml as a reference
solution. 135 mg of flavonoid polyphenol drug-phospholipid complex is accurately weighed,
put in a 50 mL volumetric flask, dissolved with absolute ethanol, diluted to a mark, and shaken
10 uniformly. 1 mL is accurately transferred into a 25 mL volumetric flask, added with absolute
ethanol to be dissolved, diluted to the mark, and shaken uniformly as test solution A. 135 mg of
flavonoid polyphenol drug-phospholipid complex is accurately weighed, put in a 50 mL
volumetric flask, added with n-hexane to be dissolved, diluted to volume, shaken uniformly, and
filtered through a 0.45 µm organic membrane. 1 mL of the filtrate is accurately transferred into
15 a 25 mL volumetric flask, blown with nitrogen for removing the solvent, added with absolute
ethanol to be dissolved, diluted to the mark, and shaken uniformly as test solution B. The
reference solution, test solution A and test solution B are accurately measured for 10 µL each
and determined according to the preceding HPLC method. The chromatogram is recorded and
the content of the flavonoid polyphenol drug-phospholipid complex is calculated by an external
20 standard method according to a peak area, which are recorded as Wsum and Wcom, separately.

The compounding rate is calculated by the following formula:

Compounding rate% = (Wcom/Wsum)*100%.

Example 1 Baicalein-phospholipid complexes prepared at different drug-lipid ratios (a mass ratio of baicalein ingredient to soybean phospholipids)

25 Baicalein ingredient and soybean phospholipids were accurately weighed according to the
drug-lipid ratio in Table 1, put in a 1000 mL rotary evaporation flask, added with an appropriate
amount of tetrahydrofuran, mixed therewith, and shaken uniformly. After baicalein ingredient
and phospholipids were dissolved completely and a compound solution was clear, the rotary
evaporation flask stood still for 15–30 min and put on a rotary evaporator so that the solvent

was evaporated at 40 °C. After the substance in the rotary evaporation flask foamed and was in a honeycomb shape, continual rotary evaporation was performed for 1–2 hours. After the baicalein-phospholipid complex was prepared, the rotary evaporation flask was put in a drying box to be dried for 3 days, and then the solids, the baicalein-phospholipid complexes, were gently scraped off and put in the drying box to be stored for later use.

Table 1 Formulations of baicalein-phospholipid complexes with different drug-lipid ratios and compounding rates thereof

Complex No.	BAPC-1	BAPC-2	BAPC-3	BAPC-4	BAPC-5
Drug-lipid ratio (w:w)	1:3	1:4	1:5	1:6	1:7
Compounding rate (%)	99.5	100.5	99.3	100.2	99.1

Example 2 Baicalein-phospholipid complexes prepared using different organic solvents

The same method was used as in Example 1 except that the baicalein ingredient and soybean phospholipids were fed at a mass ratio of 1:3.5 (w/w) and ethyl acetate, methanol, acetone, ethanol, absolute ethanol, n-propanol, isopropanol, n-butanol, isobutanol, tert-butanol, diethyl ether, methyl ethyl ether, dioxane, butanone, petroleum ether, hexane, cyclohexane, dichloromethane, chloroform, carbon tetrachloride, DMSO and DMF were used as solvents for preparing the baicalein-phospholipid complexes. The compounding rates were determined.

The results show that when the preceding organic solvents were used, all the resulting baicalein-phospholipid complexes have a compounding rate of greater than 80%.

Example 3 Baicalein-phospholipid complexes prepared using different phospholipids

The same method was used as in Example 1 except that baicalein and phospholipids were fed at a mass ratio of 1:3.5 (w/w) and natural phospholipids such as egg-yolk phospholipid or soybean phospholipid or synthetic phospholipids such as phosphoglyceride, sphingomyelin, phosphatidylcholine, phosphatidylethanolamine, phosphatidyl serine, phosphatidylinositol, phosphatidyl glycerol, glycerophosphatidic acid, distearyl phosphatidylcholine, dipalmitoyl phosphatidylcholine, dipalmitoyl phosphatidylethanolamine or dimyristoyl phosphatidylcholine were used as lipids material for preparing the baicalein-phospholipid complexes. The

compounding rates were determined.

The results show that all the baicalein-phospholipid complexes prepared using the preceding phospholipids have a compounding rate of greater than 80%.

Example 4 Baicalein-phospholipid complexes prepared using baicalein ingredient from different sources

The same method was used as in Example 1 except that baicalein ingredient and soybean phospholipids were fed at a mass ratio of 1:3.5 (w/w) and chemically synthesized baicalein or baicalein extracts (with a baicalein content of greater than or equal to 50%) extracted from traditional Chinese medicine were used for preparing a series of baicalein-phospholipid complexes. The compounding rates were determined.

The synthesized baicalein used in this example was purchased from Nanjing Zelang Biotechnology Co., Ltd.

The baicalein extract used in this example was prepared by the following method: scutellaria baicalensis powder was sieved through a 20-mesh sieve, added with water five times the scutellaria baicalensis powder, enzymatically hydrolyzed at 38 °C for 24 h, dried to a constant weight so that the enzymatically hydrolyzed scutellaria baicalensis powder was obtained; then, ethanol with different concentrations (10%, 30%, 50%, 70%, 100%) was added 10 times the powder separately, extracted three times under an ultrasonic power of 70%, 20 minutes each time, and filtered. The filtrate was distilled under reduced pressure and dried to a constant weight so that baicalein extracts with different contents were obtained.

As a result, all the baicalein-phospholipid complexes have a compounding rate of greater than 80%.

Example 5 Preparation of different flavonoid polyphenol drug-phospholipid complexes

The same method was used as in Example 1 except that proanthocyanidin, quercetin, curcumin or resveratrol and soybean phospholipids were fed at a mass ratio of 1:3.5 (w/w) for preparing a series of flavonoid polyphenol drug-phospholipid complexes. The results show that the drug compounding rate is greater than 90%, see Table 2.

Table 2 Drug compounding rates of different flavonoid polyphenol drug-phospholipid complexes

Complex No.	BAPC-6	BAPC-7	BAPC-8	BAPC-9
Drug	Proanthocyanidin	Quercetin	Curcumin	Resveratrol
Compounding rate (%)	98.2	99.1	97.8	99.5

In the following examples, comparative examples and test examples:

1. The particle size of the flavonoid polyphenol drug self-emulsifying composition after being emulsified is determined by the following method:

200 μ L of the flavonoid polyphenol drug self-emulsifying composition is transferred using a pipette and slowly added to 20 mL of distilled water (a water bath of 37 °C, slowly stirring). The emulsification time of the flavonoid polyphenol drug self-emulsifying composition is recorded, and the emulsified solution is directly measured with a laser particle size analyzer for its particle size.

2. The drug loading of the flavonoid polyphenol drug self-emulsifying composition is determined by the following method:

0.5 g of the flavonoid polyphenol drug self-emulsifying composition is accurately weighed, put in a 10 mL volumetric flask, dissolved with absolute ethanol, diluted to the mark, and shaken uniformly. 1 mL was accurately transferred into a 50 mL volumetric flask, added with 95% ethanol (containing 0.02% VC) to be dissolved, diluted to the mark, and shaken uniformly as a test solution. 30 mg of flavonoid polyphenol drug ingredient is accurately weighed, put in a 25 mL volumetric flask, added with absolute ethanol to be dissolved, and diluted to volume. 1 mL was accurately transferred into a 50 mL volumetric flask and added with 95% ethanol (containing 0.02% VC) to be diluted to a solution with a concentration of 24 μ g/mL as a reference solution. The test solution and the reference solution are accurately measured for 10 μ L each and injected into a liquid chromatograph for separation and analysis. The chromatography column is Agilent ZORBAX SB C18 column (250 mm $\times$ 4.6 mm, 5 μ m), the mobile phase is 0.05% phosphoric acid-methanol (35:65, v/v), the flowrate is 1.0 mL/min, the column temperature is 25 °C, and the detection wavelength is 275 nm. The chromatogram is

recorded and the drug loading of the flavonoid polyphenol drug self-emulsifying composition is calculated by the external standard method according to the peak area.

Example 6 Screening of an oil phase, emulsifier, co-emulsifier used in the flavonoid polyphenol drug self-emulsifying composition and a ratio thereof

5 (a) Preliminary preparation of a self-emulsifying composition of baicalein

(1) Baicalein and soybean phospholipids were fed at a mass ratio of 1:3.5 (w/w), subjected to a compound reaction with tetrahydrofuran as a solvent, then removed the organic solvent and dried so that the baicalein-phospholipid complex was obtained.

10 (2) With ethyl oleate as the oil phase, caprylic capric polyethylene glycol glyceride (labraosol) as the emulsifier and transcitol HP as the co-emulsifier, the oil phase, emulsifier and co-emulsifier were accurately weighed at a ratio of 2:5:3, put in an appropriate container, and mixed uniformly so that a blank self-emulsifying concentrate was obtained.

15 (3) An appropriate amount (30% of the weight of the blank self-emulsifying concentrate) of the baicalein-phospholipid complex in step (1) was weighed, put in the blank self-emulsifying concentrate in step (2), and placed in an air bath oscillator at a temperature of 25 °C and a rotation speed of 210 rpm. After the baicalein-phospholipid complex was completely dissolved, the self-emulsifying composition of baicalein was obtained.

The results show that the prepared self-emulsifying composition of baicalein is a uniform solution, can be emulsified completely within 2 min, and has a particle size of 10–1000 nm.

20 (b) Self-emulsifying compositions of baicalein prepared using different emulsifiers

25 The self-emulsifying composition of baicalein was prepared by the same method as in (a) except that labrasol was replaced with one of PEG-400, Tween 80, Tween 60, Tween 20, Tween 85, Span 80, polyethylene glycol glyceryl oleate (labrafil®1944cs), polyethylene glycol glyceryl linoleate (Labrafil®M2125CS), phospholipids and octyl phenyl polyoxyethylene ether (Triton X-100), a combination of caprylic capric polyethylene glycol glyceride and Tween 80, a combination of caprylic capric polyethylene glycol glyceride and PEG-400, a combination of caprylic capric polyethylene glycol glyceride and octyl phenyl polyoxyethylene ether, a combination of caprylic capric polyethylene glycol glyceride and phospholipids, a combination of Tween 80 and PEG-400, a combination of Tween 80 and octyl phenyl polyoxyethylene ether

or a combination of Tween 80 and phospholipids as the emulsifier for preparing the self-emulsifying composition of baicalein.

The results show that the prepared self-emulsifying composition of baicalein is a uniform solution, can be emulsified completely within 2 min, and has a particle size of 10–1000 nm.

5 (c) Self-emulsifying compositions of baicalein prepared using different co-emulsifiers

The self-emulsifying composition of baicalein was prepared by the same method as in (a) except that transcitol HP was replaced with one of ethanol, propylene glycol, polyethylene glycol, propylene carbonate, ethylene glycol monoethyl ether, glycerol furfural, dimethyl isosorbide, transcitol P, PEG 400, glycerol, labraosol and benzyl alcohol, a combination of transcitol HP and ethanol, a combination of transcitol HP and propylene glycol, a combination of transcitol HP and PEG 400, a combination of transcitol HP and glycerol, a combination of transcitol HP and ethylene glycol monoethyl ether, a combination of labraosol and ethanol, a combination of labraosol and propylene glycol, a combination of labraosol and PEG 400 or a combination of labraosol and glycerol as the co-emulsifier and Tween 80 was used as the emulsifier for preparing the self-emulsifying composition of baicalein.

The results show that the prepared self-emulsifying composition of baicalein is a uniform solution, can be emulsified completely within 2 min, and has a particle size of 10–1000 nm.

(d) Self-emulsifying compositions of baicalein prepared using different oil phases

The self-emulsifying composition of baicalein was prepared by the same method as in (a) except that ethyl oleate was replaced with one of soybean oil, corn oil, olive oil, coconut oil, peanut oil, camellia oil, castor oil, sorbitan oleate, glyceryl oleate, glyceryl linoleate, polyethylene glycol glyceryl oleate (labrafil®1944cs), Maisine35-1, ethyl linoleate, C8/C10 monoglyceride, coconut oil C8/C10 diglyceride, coconut oil C8/C10 triglyceride, caprylic acid triglyceride, caprylic acid diglyceride, caprylic acid monoglyceride, capric acid monoglyceride, capric acid diglyceride, capric acid triglyceride, caprylic capric monoglyceride, caprylic capric glyceride, caprylic capric triglyceride, isopropyl myristate, polyethylene glycol glyceryl linoleate (Labrafil®M2125CS), Gelucire and Capryol 90, a combination of ethyl oleate and caprylic capric glyceride, a combination of ethyl oleate and isopropyl myristate, a combination of ethyl oleate and soybean oil, a combination of polyethylene glycol glyceryl linoleate and ethyl linoleate, a combination of polyethylene glycol glyceryl linoleate and olive oil, a

combination of polyethylene glycol glyceryl linoleate and caprylic acid monoglyceride as the oil phase, and Tween 80 was used as the emulsifier for preparing the self-emulsifying composition of baicalein.

The results show that the prepared self-emulsifying composition of baicalein is a uniform solution, can be emulsified completely within 2 min, and has a particle size of 10–1000 nm.

(e) Self-emulsifying compositions of baicalein prepared using different ratios of the oil phase, the emulsifier and the co-emulsifier

(1) Baicalein and soybean phospholipids were fed at a mass ratio of 1:3.5 (w/w), subjected to a compound reaction with tetrahydrofuran as a solvent, then removed the organic solvent and dried so that the baicalein-phospholipid complex was obtained.

(2) With ethyl oleate as the oil phase, Tween 80 as the emulsifier and transcitol HP as the co-emulsifier, the oil phase, emulsifier and co-emulsifier were accurately weighed at a ratio of 10%:60%:30%, 20%:50%:30% or 20%:40%:40% based on a total mass ratio of the three components being 100%, put in an appropriate container, and mixed uniformly so that a blank self-emulsifying concentrate was obtained.

(3) An appropriate amount (30% of the weight of the blank self-emulsifying concentrate) of the baicalein-phospholipid complex in step (1) was weighed, put in the blank self-emulsifying concentrate in step (2), and placed in an air bath oscillator at a temperature of 25 °C and a rotation speed of 210 rpm. After the baicalein-phospholipid complex was completely dissolved, the self-emulsifying composition of baicalein was obtained.

The results show that the prepared self-emulsifying composition of baicalein is a uniform solution, can be emulsified completely within 2 min, and has a particle size of 10–1000 nm.

Example 7 Investigation of the drug loading of the flavonoid polyphenol drug self-emulsifying composition

(1) Flavonoid polyphenol drug (baicalein, proanthocyanidin, quercetin, curcumin and resveratrol) and soybean phospholipids were fed at a mass ratio of 1:3.5 (w/w), subjected to a compound reaction with tetrahydrofuran as a solvent, then removed the organic solvent and dried so that the baicalein-phospholipid complex, the proanthocyanidin-phospholipid complex, the quercetin-phospholipid complex, the curcumin-phospholipid complex and the

resveratrol-phospholipid complex were obtained, respectively.

(2) With ethyl oleate as the oil phase, labraosol as the emulsifier and transcuto HP as the co-emulsifier, the oil phase, emulsifier and co-emulsifier were accurately weighed at a ratio of 2:5:3, put in an appropriate container, and mixed uniformly so that a blank self-emulsifying concentrate was obtained.

(3) An appropriate amount of the baicalein-phospholipid complex, the proanthocyanidin-phospholipid complex, the quercetin-phospholipid complex, the curcumin-phospholipid complex or the resveratrol-phospholipid complex in step (1) was weighed, put in 5 g of oil phase (ethyl oleate) or the blank self-emulsifying concentrate in step (2), heated to 37 °C, and stirred or sheared so that each phospholipid complex was fully mixed and dissolved. They were placed at room temperature for 24 hours to observe whether the drug was precipitated. If no drug was precipitated, an appropriate amount of each phospholipid complex was added and operated in the same manner until the drug was precipitated. The supernatant was taken and centrifuged at 12000 r/min for 20 min. Then, the supernatant was taken and the saturated solubility of each flavonoid polyphenol drug-phospholipid complex in the oil phase and the blank self-emulsifying concentrate was determined by the preceding HPLC method.

The test results show that the baicalein-phospholipid complex can increase the saturated solubility of baicalein in oil from 0.3 mg/g to more than 60 mg/g and increase the saturated solubility of baicalein in the blank self-emulsifying concentrate (the drug load of the self-emulsifying composition of baicalein) from 20 mg/g to more than 100 mg/g.

The phospholipid complexes of proanthocyanidin, quercetin, curcumin and resveratrol can increase the saturated solubility of their respective active pharmaceutical ingredient in oil to more than 60 mg/g and increase the saturated solubility in the blank self-emulsifying concentrate to more than 100 mg/g.

The above tests show that the flavonoid polyphenol drug self-emulsifying composition of the present disclosure has a high drug loading.

Example 8 Self-emulsifying compositions of baicalein prepared using different oil phases with the baicalein-phospholipid complex as an intermediate

(1) Baicalein and soybean phospholipids were fed at a mass ratio of 1:3.5 (w/w), subjected to a compound reaction with tetrahydrofuran as a solvent, then removed the organic solvent and dried so that the baicalein-phospholipid complex was obtained.

(2) With labrosol as the emulsifier and transcitol HP as the co-emulsifier and using different oil phases shown in Table 3, the oil phase, emulsifier and co-emulsifier were accurately weighed at a ratio of 2:5:3, put in an appropriate container, and mixed uniformly so that a blank self-emulsifying concentrate was obtained.

(3) An appropriate amount of the baicalein-phospholipid complex in step (1) (fed according to a drug loading of 50 mg/g) was weighed, put in the blank self-emulsifying concentrate in step (2), and placed in an air bath oscillator at a temperature of 25 °C and a rotation speed of 210 rpm. After the baicalein-phospholipid complex was completely dissolved, the self-emulsifying composition of baicalein was obtained. The drug loading and the particle size after emulsification were determined. The results are shown in Table 3.

Table 3 Self-emulsifying compositions of baicalein prepared using different oil phases

Composition No.	Oil Phase	Drug Loading (mg/g)	Emulsification Time (min)	Particle Size (nm)
SEDDS-1	Soybean oil	50.23	1	320
SEDDS-2	Castor oil	50.76	1	150
SEDDS-3	Ethyl oleate	50.15	1	280
SEDDS-4	Isopropyl myristate	50.34	1	403
SEDDS-5	Ethyl oleate:caprylic capric glyceride (1:1)	50.54	1	230

Example 9 Self-emulsifying compositions of baicalein prepared using different emulsifiers with the baicalein-phospholipid complex as an intermediate

(1) Baicalein and soybean phospholipids were fed at a mass ratio of 1:3.5 (w/w), subjected to a compound reaction with tetrahydrofuran as a solvent, then removed the organic solvent and

dried so that the baicalein-phospholipid complex was obtained.

(2) With ethyl oleate as the oil phase and transcitol HP as the co-emulsifier and using different emulsifiers shown in Table 4, the oil phase, emulsifier and co-emulsifier were accurately weighed at a ratio of 2:5:3, put in an appropriate container, and mixed uniformly so that a blank self-emulsifying concentrate was obtained.

(3) An appropriate amount of the baicalein-phospholipid complex in step (1) (fed according to a drug loading of 50 mg/g) was weighed, put in the blank self-emulsifying concentrate in step (2), and placed in an air bath oscillator at a temperature of 25 °C and a rotation speed of 210 rpm. After the baicalein-phospholipid complex was completely dissolved, the self-emulsifying composition of baicalein was obtained. The drug loading and the particle size after emulsification were determined. The results are shown in Table 4.

Table 4 Self-emulsifying compositions of baicalein prepared using different emulsifiers

Composition No.	Emulsifier	Drug Loading (mg/g)	Emulsification Time (min)	Particle Size (nm)
SEDDS-6	Labrasol	50.28	1	280
SEDDS-7	Tween 80	50.34	1	335
SEDDS-8	Triton X-100	50.68	1	280
SEDDS-9	Labrafil®1944cs	50.10	1	200
SEDDS-10	Span 80	50.27	1	450

Example 10 Self-emulsifying compositions of baicalein prepared using different co-emulsifiers with the baicalein-phospholipid complex as an intermediate

(1) Baicalein and soybean phospholipids were fed at a mass ratio of 1:3.5 (w/w), subjected to a compound reaction with tetrahydrofuran as a solvent, then removed the organic solvent and dried so that the baicalein-phospholipid complex was obtained.

(2) With ethyl oleate as the oil phase and labrosol as the emulsifier and using different co-emulsifiers shown in Table 5, the oil phase, emulsifier and co-emulsifier were accurately weighed at a ratio of 2:5:3, put in an appropriate container, and mixed uniformly so that a blank

self-emulsifying concentrate was obtained.

(3) An appropriate amount of the baicalein-phospholipid complex in step (1) (fed according to a drug load of 50 mg/g) was weighed, put in the blank self-emulsifying concentrate in step (2), and placed in an air bath oscillator at a temperature of 25 °C and a rotation speed of 210 rpm.

- 5 After the baicalein-phospholipid complex was completely dissolved, the self-emulsifying composition of baicalein was obtained. The drug loading and the particle size after emulsification were determined. The results are shown in Table 5.

Table 5 Self-emulsifying compositions of baicalein prepared using different co-emulsifiers

Composition No.	Co-emulsifier	Drug Loading (mg/g)	Emulsification Time (min)	Particle Size (nm)
SEDDS-11	Transcutol HP	50.54	1	280
SEDDS-12	Capryol 90	50.42	1	450
SEDDS-13	Ethanol	50.41	1	170
SEDDS-14	Propylene glycol	50.23	1	300
SEDDS-15	Glycerol	50.19	1	610

10 **Example 11 Self-emulsifying compositions of baicalein prepared at different ratios of the oil phase, emulsifier and co-emulsifier with the baicalein-phospholipid complex as an intermediate**

- 15 (1) Baicalein and soybean phospholipids were fed at a mass ratio of 1:3.5 (w/w), subjected to a compound reaction with tetrahydrofuran as a solvent, then removed the organic solvent and dried so that the baicalein-phospholipid complex was obtained.

(2) With ethyl oleate as the oil phase, labrosol as the emulsifier and transcutol HP as the co-emulsifier, the oil phase, emulsifier and co-emulsifier were accurately weighed at different ratios of the oil phase, emulsifier and co-emulsifier in Table 6, put in an appropriate container, and mixed uniformly so that a blank self-emulsifying concentrate was obtained.

- 20 (3) An appropriate amount of the baicalein-phospholipid complex in step (1) (fed according to a

drug loading of 50 mg/g) was weighed, put in the blank self-emulsifying concentrate in step (2), and placed in an air bath oscillator at a temperature of 25 °C and a rotation speed of 210 rpm. After the baicalein-phospholipid complex was completely dissolved, the self-emulsifying composition of baicalein was obtained. The drug loading and the particle size after emulsification were determined. The results are shown in Table 6.

Table 6 Self-emulsifying compositions of baicalein prepared at different ratios of the oil phase, emulsifier and co-emulsifier

Composition No.	Oil phase:Emulsifier:Co-emulsifier (w/w)	Drug Loading (mg/g)	Emulsification Time (min)	Particle Size (nm)
SEDDS-16	2:4:4	50.31	1	730
SEDDS-17	2:5:3	50.29	1	280
SEDDS-18	2:6:2	50.51	1	260
SEDDS-19	3:4:3	50.30	1	440
SEDDS-20	3:5:2	50.11	1	370

Example 12 Self-emulsifying compositions of baicalein with different drug loads prepared with the baicalein-phospholipid complex as an intermediate

(1) Baicalein and soybean phospholipids were fed at a mass ratio of 1:3.5 (w/w), subjected to a compound reaction with tetrahydrofuran as a solvent, then removed the organic solvent and dried with so that the baicalein-phospholipid complex was obtained.

(2) With ethyl oleate as the oil phase, labrosol as the emulsifier and transcitol HP as the co-emulsifier, the oil phase, emulsifier and co-emulsifier were accurately weighed at a ratio of 2:5:3, put in an appropriate container, and mixed uniformly so that a blank self-emulsifying concentrate was obtained.

(3) Different amounts of the baicalein-phospholipid complex in step (1) were weighed, put in the blank self-emulsifying concentrate in step (2), and placed in an air bath oscillator at a temperature of 25 °C and a rotation speed of 210 rpm. After the baicalein-phospholipid complex was completely dissolved, the self-emulsifying compositions of baicalein with different drug loads were obtained. The drug load and the particle size after emulsification were determined.

The results are shown in Table 7.

Table 7 Self-emulsifying compositions of baicalein with different drug loading

Composition No.	Drug Loading (mg/g)	Emulsification Time (min)	Particle Size (nm)
SEDDS-21	20.18	1	98
SEDDS-22	50.14	1	280
SEDDS-23	70.44	1	400
SEDDS-24	80.65	1	480
SEDDS-25	100.27	1	500

Example 13 Self-emulsifying compositions of baicalein prepared with
5 baicalein-phospholipid complexes with different drug-lipid ratios as intermediates

(1) With ethyl oleate as the oil phase, labrosol as the emulsifier and transcitol HP as the co-emulsifier, the oil phase, emulsifier and co-emulsifier were accurately weighed at a ratio of 2:5:3, put in an appropriate container, and mixed uniformly so that a blank self-emulsifying concentrate was obtained.

10 (2) A series of baicalein-phospholipid complexes in Example 1 (fed according to a drug loading of 100 mg/g) were weighed, put in the blank self-emulsifying concentrate in step (1), and placed in an air bath oscillator at a temperature of 25 °C and a rotation speed of 210 rpm. After the baicalein-phospholipid complex was completely dissolved, the self-emulsifying composition of
 15 baicalein was obtained. The drug loading and the particle size after emulsification were determined. The results are shown in Table 8.

Table 8 Self-emulsifying compositions of baicalein prepared using baicalein-phospholipid complexes with different drug-lipid ratios

Composition No.	Baicalein-Phospholipid Complex No.	Drug Load (mg/g)	Emulsification Time (min)	Particle Size (nm)
SEDDS-26	BAPC-1	100.12	1	472
SEDDS-27	BAPC-2	100.23	1	513

SEDDS-28	BAPC-3	100.33	1	535
SEDDS-29	BAPC-4	100.41	1	564
SEDDS-30	BAPC-5	100.27	1	593

Example 14 preparation of different self-emulsifying compositions of flavonoid polyphenol drug

(1) With ethyl oleate as the oil phase, labrosol as the emulsifier and transcitol HP as the co-emulsifier, the oil phase, emulsifier and co-emulsifier were accurately weighed at a ratio of 2:5:3, put in an appropriate container, and mixed uniformly so that a blank self-emulsifying concentrate was obtained.

(2) A series of flavonoid polyphenol drug-phospholipid complexes (fed according to a drug loading of 20 mg/g for preparing compositions SEDDS-31, SEDDS-32, SEDDS-33 and SEDDS-34 and fed according to a drug loading of 100 mg/g for preparing compositions SEDDS-35, SEDDS-36, SEDDS-37 and SEDDS-38) were weighed, put in the blank self-emulsifying concentrate in step (1), and placed in an air bath oscillator at a temperature of 25 °C and a rotation speed of 210 rpm. After the flavonoid polyphenol drug-phospholipid complex was completely dissolved, the flavonoid polyphenol drug self-emulsifying composition was obtained. The drug loading and the particle size after emulsification were determined. The self-emulsifying compositions of flavonoid polyphenol drug with different drug loading and different particle sizes were obtained. The results are shown in Table 9.

Table 9 Self-emulsifying compositions of flavonoid polyphenol drug prepared using different flavonoid polyphenol drug-phospholipid complexes

Composition No.	Phospholipid Complex No.	Drug Loading (mg/g)	Emulsification Time (min)	Particle Size (nm)
SEDDS-31	BAPC-6	20.05	1	85
SEDDS-32	BAPC-7	20.71	1	92
SEDDS-33	BAPC-8	20.32	1	76
SEDDS-34	BAPC-9	20.18	1	105
SEDDS-35	BAPC-6	100.22	1	476

SEDDS-36	BAPC-7	100.47	1	535
SEDDS-37	BAPC-8	100.32	1	512
SEDDS-38	BAPC-9	100.13	1	581

As can be seen from the results of Examples 6 to 14, all the self-emulsifying compositions of flavonoid polyphenol drug of the present disclosure can be quickly emulsified to form nano-sized droplets. Self-emulsifying compositions of flavonoid polyphenol drug with different drug loading are prepared in Examples 7 to 12. The flavonoid polyphenol drug self-emulsifying composition of the present disclosure has a drug loading of more than 100 mg/g as required.

Test Example 1 Investigation of the physical stability of the self-emulsifying composition of baicalein of the present disclosure, flavonoid polyphenol self-microemulsions in documents 2-7 and the self-emulsifying composition in Comparative Example 1

(1) Comparative Example 1 Preparation of a self-emulsifying composition of baicalein encapsulating baicalein ingredient

With ethyl oleate as an oil phase, Tween 80 as an emulsifier and transcitol HP as a co-emulsifier, the oil phase, emulsifier and co-emulsifier were accurately weighed at a ratio of 2:5:3, put in an appropriate container, and mixed uniformly so that a blank self-emulsifying concentrate was obtained. Baicalein ingredient was weighed, put in the blank self-emulsifying concentrate, and placed in an air bath oscillator at a temperature of 25 °C and a rotation speed of 210 rpm, oscillated for 24 h, and centrifuged at 12000 rpm for 15 min. The supernatant was taken so that the self-emulsifying composition of baicalein encapsulating baicalein ingredient was prepared.

(2) Comparative Example 2 Preparation of a self-emulsifying composition for a silymarin-phospholipid complex

According to the method in *Studies on Self-Microemulsifying Drug Delivery Systems (SMEDDS) of Silymarin and Silymarin-Phospholipid Complex* [D] (Linjie LIU, Shenyang, Shenyang Pharmaceutical University, 2007), with acetone as a solvent, silymarin and soybean phospholipids with a mass ratio of 1:1 were heated to reflux at 55 °C, concentrated under reduced pressure to a liquid volume, quickly added to n-hexane so that a yellow precipitate was obtained. The upper liquid, which was a yellow-white emulsion, was filtered under reduced pressure, and the precipitate was washed with n-hexane and dried in a vacuum drying oven at

room temperature so that yellow-white solids were obtained, that is, the silymarin-phospholipid complex. 70 g of the silymarin-phospholipid complex was weighed, added with 250 g of a mixture of ethyl oleate and MCT (1:1), vortexed to be dissolved, added with 200 g of Cremophor EL and 50 g of Transcutol, and mixed gently in a water bath of 37 °C so that the self-emulsifying composition was obtained.

(3) According to the formulations and preparation methods described in documents 2 to 7 (as described in the background of the present application), a proanthocyanidin self-microemulsion YZ-1, a quercetin self-microemulsion YZ-2, a curcumin self-microemulsion YZ-3, a resveratrol self-microemulsion YZ-4, a baicalein self-microemulsion YZ-5 and a baicalein self-microemulsion YZ-6 were prepared respectively.

(4) YZ-1, YZ-2, YZ-3, YZ-4, YZ-5, YZ-6, the self-emulsifying composition in Comparative Example 1 and the self-emulsifying composition of silymarin in Comparative Example 2, and the self-emulsifying composition of baicalein, self-emulsifying composition of proanthocyanidin, self-emulsifying composition of quercetin, self-emulsifying composition of curcumin and self-emulsifying composition of resveratrol prepared in the above examples of the present disclosure were placed at 4 °C and room temperature for 5 days, one month and two months, separately. The changes in appearance were observed and the physical stability was investigated. The relevant results are shown in Table 10.

Table 10

Name		Initial	5 days		1 month		2 months	
			4 °C	Room temperature	4 °C	Room temperature	4 °C	Room temperature
YZ-1		Clear and transparent	Semi-solid	Clear and transparent	Semi-solid	Clear and transparent	Semi-solid	Drug precipitate
YZ-2		Clear and transparent	Precipitate	Clear and transparent	Precipitate	Drug precipitate	Precipitate	Drug precipitate
YZ-3		Clear and transparent	Semi-solid	Clear and transparent	Semi-solid	Drug precipitate	Semi-solid	Drug precipitate

YZ-4		Clear and transparent	Semi-solid	Clear and transparent	Semi-solid	Clear and transparent	Semi-solid	Drug precipitate
YZ-5		Clear and transparent	Drug precipitate	Clear and transparent	Drug precipitate	Drug precipitate	Drug precipitate	Drug precipitate
YZ-6		Clear and transparent	Semi-solid	Clear and transparent	Semi-solid	Drug precipitate	Semi-solid	Drug precipitate
Comparative Example 1		Clear and transparent	Clear and transparent	Clear and transparent	Clear and transparent	Clear and transparent	Drug precipitate	Clear and transparent
Comparative Example 2		Clear and transparent	Drug precipitate	Clear and transparent	Drug precipitate	Clear and transparent	Drug precipitate	Clear and transparent
SEDDS-4		Clear and transparent	Clear and transparent	Clear and transparent	Clear and transparent	Clear and transparent	Clear and transparent	Clear and transparent
SEDDS-8		Clear and transparent	Clear and transparent	Clear and transparent	Clear and transparent	Clear and transparent	Clear and transparent	Clear and transparent
SEDDS-12		Clear and transparent	Clear and transparent	Clear and transparent	Clear and transparent	Clear and transparent	Clear and transparent	Clear and transparent
SEDDS-16		Clear and transparent	Clear and transparent	Clear and transparent	Clear and transparent	Clear and transparent	Clear and transparent	Clear and transparent
SEDDS-25		Clear and transparent	Clear and transparent	Clear and transparent	Clear and transparent	Clear and transparent	Clear and transparent	Clear and transparent
SEDDS-29		Clear and transparent	Clear and transparent	Clear and transparent	Clear and transparent	Clear and transparent	Clear and transparent	Clear and transparent
SEDDS-31		Clear and transparent	Clear and transparent	Clear and transparent	Clear and transparent	Clear and transparent	Clear and transparent	Clear and transparent

SEDDS-32		Clear and transparent	Clear and transparent	Clear and transparent	Clear and transparent	Clear and transparent	Clear and transparent	Clear and transparent
SEDDS-33		Clear and transparent	Clear and transparent	Clear and transparent	Clear and transparent	Clear and transparent	Clear and transparent	Clear and transparent
SEDDS-34		Clear and transparent	Clear and transparent	Clear and transparent	Clear and transparent	Clear and transparent	Clear and transparent	Clear and transparent
SEDDS-35		Clear and transparent	Clear and transparent	Clear and transparent	Clear and transparent	Clear and transparent	Clear and transparent	Clear and transparent
SEDDS-36		Clear and transparent	Clear and transparent	Clear and transparent	Clear and transparent	Clear and transparent	Clear and transparent	Clear and transparent
SEDDS-37		Clear and transparent	Clear and transparent	Clear and transparent	Clear and transparent	Clear and transparent	Clear and transparent	Clear and transparent
SEDDS-38		Clear and transparent	Clear and transparent	Clear and transparent	Clear and transparent	Clear and transparent	Clear and transparent	Clear and transparent

5 The results show that a series of self-emulsifying compositions of flavonoid polyphenol drug prepared according to documents 2 to 7 and Comparative Examples 1 and 2 are easy to form semi-solids or precipitates after placement at 4 °C, and the drug precipitates appear after placement at room temperature for 1 to 2 months, exhibiting poor stability.

The self-emulsifying compositions of flavonoid polyphenol drug with flavonoid polyphenol drug-phospholipid complexes as carriers in the present disclosure are still clear and transparent in appearance and have high stability after placed at 4 °C and room temperature for 2 months.

Test Example 2 Study on Plasma Pharmacokinetics

- 10 (1) Preparation of a self-emulsifying composition of baicalein with a baicalein-phospholipid complex as an intermediate

(a) Baicalein and soybean phospholipids were fed at a mass ratio of 1:3.5 (w/w), subjected to a compound reaction with tetrahydrofuran as a solvent, then removed the organic solvent and dried so that the baicalein-phospholipid complex was obtained. (b) With ethyl oleate as an oil phase, Tween 80 as an emulsifier and transcitol HP as a co-emulsifier, the oil phase, emulsifier and co-emulsifier were accurately weighed at a ratio of 2:5:3, put in an appropriate container, and mixed uniformly so that a blank self-emulsifying concentrate was obtained. (c) An appropriate amount of the baicalein-phospholipid complex in step (a) was weighed, put in the blank self-emulsifying concentrate in step (b), and placed in an air bath oscillator at a temperature of 25 °C and a rotation speed of 210 rpm. After the baicalein-phospholipid complex was completely dissolved, the self-emulsifying composition of baicalein was obtained. The self-emulsifying composition was emulsified completely within 1 min after diluted with water 100 times and it was determined that the particle size was 10 nm and the drug loading was 20 mg/g.

(2) Test groups

Test group A: The self-emulsifying composition of baicalein prepared with the baicalein-phospholipid complex as the intermediate in the preceding step (1) of the present disclosure (hereinafter labeled BAPC-SMEDDS) was administered.

Test group B: The self-emulsifying composition of baicalein encapsulating baicalein ingredient in Comparative Example 1 (hereinafter labeled OBA-SMEDDS) was administered.

Test group C: Baicalein ingredient (hereinafter labeled BA) was administered.

(3) Test animals

Sprague-Dawley rats (male, 200 g) were fed for one week before tests, forbidden to eat rather than drink the night before the tests, and supplied with water freely during the tests.

(4) Mode of administration and dosage

15 rats were randomly divided into three groups (test group A, test group B and test group C, separately), with 5 rats in each group. Gavage (2–3 mL) was provided at a dose of 40 mg/kg. 0.3 mL of blood was taken from the retro-orbital venous plexus at 5, 15, 30, 45, 60 and 75 min and 3, 6, 8, 10, 12 and 24 h after administration, placed in a pre-heparinized 1.5 mL conical centrifuge tube, and centrifuged at 4000 r/min for 15 min. The upper plasma was aspirated,

stored in the refrigerator at -80 °C, and thawed at normal temperature before determination.

(5) Determination of a plasma concentration

5 Treatment of plasma samples: 100 µL of plasma was taken, placed in a 1.5 mL conical centrifuge tube, added with 10 µL of ascorbic acid (200 mg/mL), 20 µL of an internal standard solution (500 ng/ml) and 300 µL of methanol, vortexed for 60s, and centrifuged at 12000 r/min for 10 min. Then, the supernatant was aspirated, placed in a centrifuge tube, concentrated through centrifugation to remove the solvent (40 °C), added with 200 µL of methanol:water (80:20) to be dissolved, vortexed for 30s, and centrifuged at 12000 r/min for 5min. 20 µL of the supernatant was injected and the plasma concentration was determined under the following
10 chromatography conditions (liquid chromatography-mass spectrometry).

HPLC conditions:

Chromatography column: Agilent ZORBAX SB C18 column (250 mm×4.6 mm, 5 µm);

Flowrate: 1.0 mL/min;

Injection volume: 20 µL;

15 Column temperature: 25 °C;

Mobile phase (gradient elution, see Table 11): acetonitrile-0.1% formic acid as an eluent.

Table 11 Gradient elution of LC mobile phase

Time (min)	Flowrate (mL/min)	Ratio of eluents (%) (v/v)	
		acetonitrile	0.1% formic acid
0	1.0	20	80
5	1.0	30	70
20	1.0	50	50
25	1.0	20	80
30	1.0	20	80

Mass spectrometry conditions:

Electrospray ion source (ESI), positive ion mode, multiple reaction monitoring (MRM);

Other parameters: an atomizer pressure of 40 psi, a drying gas flowrate of 9 L/min, a drying gas temperature of 350 °C, a capillary voltage of 4000V and a split ratio of 1:2.

5 MRM detection ion pair for quantification: baicalin [M+H]⁺+447.0→271.1;

Baicalein [M+H]⁺+271.1→122.8;

6-hydroxyflavone [M+H]⁺+239.0→137.0.

(6) Test results

10 6.1 After taken orally into the body, baicalein is rapidly metabolized into baicalin in intestinal epithelial cells and liver tissues. The concentration-time curve of baicalin in plasma and related pharmacokinetic parameters are shown in FIG. 1 and Table 12.

15 The results show that the C_{max} and AUC_(0-t) of the self-emulsifying composition of baicalein with the baicalein-phospholipid complex as an intermediate of the present disclosure is 7.7 times and 4.5 times higher than those of baicalein ingredient, respectively and 1.9 times and 1.3 times higher than those of the self-emulsifying composition of baicalein encapsulating baicalein, respectively. The relative bioavailability of BAPC-SMEDDS and the relative bioavailability of OBA-SMEDDS (relative to baicalein ingredient) calculated based on the concentration of baicalin in plasma are 448.7% and 342.5%, respectively.

Table 12 Plasma pharmacokinetic parameters of baicalin

Name	Unit	BAPC-SMEDDS	OBA-SMEDDS	BA
AUC (0-t)	mg/L*min	3802.1±1194.3	2901.7±210.9	847.3±302.003
AUC (0-∞)	mg/L*min	3823.3±1198.7	2939.2±220.8	848.9±301.8
MRT (0-t)	min	320.0±44.5	420.2±69.2	354.9±34.4
MRT (0-∞)	min	327.6±47.0	436.2±88.8	357.7±36.5
Tmax	min	42.0±26.8	45.0±18.4	57.0±16.4
Cmax	mg/L	15.3±2.2	8.2±1.9	2.0±0.6

Relative bioavailability	%	448.7	342.5	100.0
--------------------------	---	-------	-------	-------

6.2 The concentration-time curve of baicalein in plasma and related pharmacokinetic parameters are shown in FIG. 2 and Table 13. The $C_{\max}$ and $AUC_{(0-t)}$ of the self-emulsifying composition of baicalein with the baicalein-phospholipid complex as an intermediate of the present disclosure is 4.6 times and 3.7 times higher than those of baicalein ingredient, respectively and 1.9 times and 1.2 times higher than those of the self-emulsifying composition of baicalein encapsulating baicalein, respectively. The relative bioavailability of BAPC-SMEDDS and the relative bioavailability of OBA-SMEDDS (relative to baicalein ingredient) calculated based on the concentration of baicalein in plasma are 374.4% and 302.3%, respectively.

10

Table 13 Plasma pharmacokinetic parameters of baicalein

Name	Unit	BAPC-SMEDDS	OBA-SMEDDS	BA
AUC (0-t)	$\mu\text{g/L} \cdot \text{min}$	59404.7 $\pm$ 18640.9	47961.5 $\pm$ 10615.8	15864.8 $\pm$ 8964.4
AUC (0- ∞)	$\mu\text{g/L} \cdot \text{min}$	59612.0 $\pm$ 18614.0	51506.9 $\pm$ 10466.6	15880.4 $\pm$ 8996.5
MRT (0-t)	min	254.2 $\pm$ 41.1	355.1 $\pm$ 71.4	239.8 $\pm$ 51.6
MRT (0- ∞)	min	259.6 $\pm$ 48.9	476.3 $\pm$ 234.6	240.5 $\pm$ 52.8
Tmax	min	48.0 $\pm$ 16.4	39.0 $\pm$ 27.2	75.0 $\pm$ 64.5
Cmax	$\mu\text{g/L}$	451.0 $\pm$ 365.6	238.0 $\pm$ 72.5	99.1 $\pm$ 42.0
Relative bioavailability	%	374.4	302.3	100.0

What is claimed is:

1. A flavonoid polyphenol drug self-emulsifying composition, comprising a flavonoid polyphenol drug-phospholipid complex, an oil phase, an emulsifier and a co-emulsifier, wherein the flavonoid polyphenol drug comprises one or more selected from the group consisting of
5 baicalein, proanthocyanidin, quercetin, curcumin and resveratrol;
- optionally, the flavonoid polyphenol drug further comprise other flavonoid polyphenol drugs in addition to baicalein, proanthocyanidin, quercetin, curcumin and resveratrol, wherein the other flavonoid polyphenol drugs are one or more selected from the group consisting of wogonin,
10 ferulic acid, catechin, magnolol, honokiol, apigenin, hesperetin, rotenone, isobavachalcone, aureusidin, delphinidin and ginkgetin;
- optionally, the flavonoid polyphenol drugs are baicalein, proanthocyanidin, quercetin, curcumin or resveratrol;
- optionally, the flavonoid polyphenol drug self-emulsifying composition has a drug loading of 10–110 mg/g, preferably 10–100 mg/g;
- 15 optionally, the flavonoid polyphenol drug self-emulsifying composition has a particle size of 10–1000 nm.
2. The flavonoid polyphenol drug self-emulsifying composition according to claim 1, wherein in the flavonoid polyphenol drug-phospholipid complex, a mass ratio of the flavonoid polyphenol drug to phospholipid is 1:1–1:15, optionally, 1:1–1:8.
- 20 3. The flavonoid polyphenol drug self-emulsifying composition according to claim 1 or 2, wherein the phospholipids are one or more selected from the group consisting of natural phospholipids and synthetic phospholipids;
- optionally, the natural phospholipids comprise one or more selected from the group consisting of soybean phospholipid and egg-yolk phospholipid;
- 25 optionally, the synthetic phospholipids comprise one or more selected from the group consisting of phosphoglyceride, sphingomyelin, phosphatidylcholine, phosphatidylethanolamine, phosphatidyl serine, phosphatidylinositol, phosphatidyl glycerol, glycerophosphatidic acid, distearyl phosphatidylcholine, dipalmitoyl phosphatidylcholine, dipalmitoyl phosphatidylethanolamine and dimyristoyl phosphatidylcholine; preferably, the synthetic
30 phospholipids are one or more selected from the group consisting of phosphatidylcholine, phosphatidylethanolamine, phosphatidylglycerol and glycerophosphatidic acid.

4. The flavonoid polyphenol drug self-emulsifying composition according to any one of claims 1 to 3, wherein the oil phase is one or more selected from the group consisting of vegetable oils and vegetable oil derivatives;

optionally, the vegetable oils comprise one or more selected from the group consisting of soybean oil, corn oil, olive oil, coconut oil, peanut oil, camellia oil and castor oil;

optionally, the vegetable oil derivatives comprise one or more selected from the group consisting of sorbitan oleate, glyceryl oleate, glyceryl linoleate, polyethylene glycol glyceryl oleate, glycerol monolinoleate, ethyl oleate, ethyl linoleate, C8/C10 monoglyceride, coconut oil C8/C10 diglyceride, coconut oil C8/C10 triglyceride, caprylic acid triglyceride, caprylic acid diglyceride, caprylic acid monoglyceride, capric acid monoglyceride, capric acid diglyceride, capric acid triglyceride, caprylic capric monoglyceride, caprylic capric glyceride, caprylic capric triglyceride, isopropyl myristate, polyethylene glycol glyceryl linoleate, polyethylene glycol glyceryl laurate and propylene glycol monocaprylate;

preferably, the oil phase is one or more selected from the group consisting of soybean oil, castor oil, ethyl oleate, isopropyl myristate and caprylic capric glyceride.

5. The flavonoid polyphenol drug self-emulsifying composition according to any one of claims 1 to 4, wherein the emulsifier is one or more selected from the group consisting of caprylic capric polyethylene glycol glyceride, polyethylene glycol, Tween, Span 80, polyethylene glycol glyceryl oleate, polyethylene glycol glyceryl linoleate, phospholipids, octyl phenyl polyoxyethylene ether;

preferably, the emulsifier is one or more of caprylic capric polyethylene glycol glyceride, Tween 80, Tween 85, octyl phenyl polyoxyethylene ether, polyethylene glycol glyceryl oleate.

6. The flavonoid polyphenol drug self-emulsifying composition according to any one of claims 1 to 5, wherein the co-emulsifier is one or more selected from the group consisting of ethanol, propylene glycol, propylene carbonate, ethylene glycol monoethyl ether, glycerol furfural, dimethyl isosorbide, propylene glycol monocaprylate, diethylene glycol monoethyl ether, polyethylene glycol, glycerol, caprylic capric polyethylene glycol glyceride and benzyl alcohol;

preferably, the co-emulsifier is one or more of diethylene glycol monoethyl ether, polyethylene glycol 400, ethanol and propylene glycol monocaprylate.

7. The flavonoid polyphenol drug self-emulsifying composition according to any one of claims 1 to 6, wherein based on a total mass ratio of the oil phase being 100%, the emulsifier and the co-emulsifier, the oil phase accounts for 10–50% (preferably 20–40%), the emulsifier accounts for 30–60% (preferably 40–60%), and the co-emulsifier accounts for 20–60% (preferably 30–

50%).

8. A method for preparing the flavonoid polyphenol drug self-emulsifying composition according to any one of claims 1 to 7, comprising the following preparation steps:

5 (1) a flavonoid polyphenol drug-phospholipid complex is prepared: flavonoid polyphenol drug and phospholipid are dissolved in an organic solvent, subjected to a compound reaction, and dried with the organic solvent removed so that the flavonoid polyphenol drug-phospholipid complex is obtained;

10 optionally, the organic solvent is one or more selected from the group consisting of ethyl acetate, tetrahydrofuran, methanol, acetone, ethanol, absolute ethanol, n-propanol, isopropanol, n-butanol, isobutanol, tert-butanol, diethyl ether, methyl ethyl ether, dioxane, butanone, petroleum ether, hexane, cyclohexane, dichloromethane, chloroform, carbon tetrachloride, DMSO and DMF, preferably one or more of ethyl acetate, tetrahydrofuran, methanol, ethanol, cyclohexane, DMSO and DMF;

15 (2) the flavonoid polyphenol drug self-emulsifying composition is prepared: the flavonoid polyphenol drug-phospholipid complex obtained in step (1) is fully mixed with an oil phase, an emulsifier and a co-emulsifier in any sequence;

optionally, the flavonoid polyphenol drug-phospholipid complex obtained in step (1) is fully mixed with the oil phase, the emulsifier and the co-emulsifier directly; or

20 the oil phase, the emulsifier and the co-emulsifier are mixed uniformly so that a blank self-emulsifying concentrate is prepared, and then the flavonoid polyphenol drug-phospholipid complex obtained in step (1) is added to the prepared blank self-emulsifying concentrate and fully mixed therewith; or

25 the flavonoid polyphenol drug-phospholipid complex obtained in step (1) is dissolved in any one of the oil phase, the emulsifier or the co-emulsifier, and then the other two of the oil phase, the emulsifier or the co-emulsifier are added and fully mixed.

9. A pharmaceutical composition, comprising the flavonoid polyphenol drug self-emulsifying composition according to any one of claims 1 to 7 and an optional pharmaceutically acceptable excipient;

30 optionally, a dosage form of the pharmaceutical composition comprises an oral preparation, an injection preparation, a transdermal administration preparation, a mucosal administration preparation, a pulmonary inhalation administration preparation or an enteral administration preparation;

optionally, the dosage form of the pharmaceutical composition comprises drops, oral liquids, tablets, capsules, granules, infusion granules, films, gel, powders, emulsions, dripping pills, suppositories, aerosols, sprays, powder aerosols, patches, adhesive plasters, solutions, ointments or cream.

- 5 10. A use of the flavonoid polyphenol drug self-emulsifying composition according to any one
of claims 1 to 7 or the pharmaceutical composition according to claim 9 for preparing drugs for
anti-bacteria, antiviral, anti-inflammation, inhibiting allergy, regulating immunity, anti-tumor,
anti-oxidation, anti-aging, anti-ultraviolet radiation, treatment of hormone deficiency,
anti-hypertension, lowering blood fat, anti-atherosclerosis, anti-senile dementia, treatment of
10 hand-foot-mouth diseases, anti-osteoporosis or liver protection.