

A Chinese medicine composition and the extract of worms thereof and their preparation

Field of the invention

The present invention relates to a Chinese medicine composition for treating cardiovascular and cerebrovascular diseases, to extracts of Insect medicinal materials contained therein and to preparation thereof.

Background of the invention

Coronary atherosclerotic heart disease refers to accumulation of atheromatous plaques on the wall of coronary arteries, which results in narrowing or blocking blood vessel and causes myocardial ischemic and hypoxia. Coronary atherosclerotic heart disease and coronary spasm are within the scope of ischemic heart diseases.

Professor Yiling Wu first created and used the Collateral Theory of Chinese medical science to investigate the pathogenesis of coronary heart disease, and successfully developed “Tongxinluo” capsule comprising five kinds of insect medicinal materials including scorpion (*Buthus martensii* Karsch), centipede (*Scolopendra subspinipes mutilans* L. Koch), eupolyphaga seu steleophaga (*Eupolyphaga sinensis* Walker), hirudo (*Whitmania pigra* Whitman), and periostracum cicadae (*Cryptotympana pustulata* Fabricius) for treating coronary heart disease and angina pectoris. The “Tongxinluo” capsule has special curative effects on coronary heart disease, angina pectoris and cerebral thrombosis and the like, and is under patent protection of the Chinese Patent No. ZL01131203.3. The “Tongxinluo” capsule is made from scorpion, hirudo, centipede, eupolyphaga seu steleophaga, periostracum cicadae, radix ginseng (*Panax ginseng* C. A. Mey.), prepared frankincense (*Boswellia carterii* Birdw., *B. bhaw-dijiana* Birdw.), radix paeoniae rubra (*Paeonia lactiflora* Pall.), lignum dalbergiae odoriferae (*Dalbergia odorifera* T. Chen), lignum santali albi (*Santalum album* L.), borneol and semen ziziphi spinosae (*Ziziphus jujuba* Mill. var. *spinosa* (Bunge) Hu ex H. F. Chou),

which is characterized in that five kinds of insect medicinal materials, i.e. scorpion, centipede, eupolyphaga seu steleophaga, hirudo and periostracum cicadae, are used together to activate blood circulation and remove obstruction in the channels, arrest the wind and relieve convulsion. The “Tongxinluo” capsule exhibits advantageous curative effects on the treatment of coronary heart disease and angina pectoris, especially on variant angina pectoris.

There are many difficulties in the development and application of insect medicinal materials, such as most active components are not completely identified, the extraction and refinement process is not sophisticated, and standard reference substances are lacked, etc., therefore, in prior art, insect medicinal materials are usually crushed into powder by a conventional crushing method and then integrated to a medicine. However, there are several disadvantages in the conventional crushing process: 1) the cell structure of insect medicinal materials cannot be destroyed and thereby it's difficult for active components of the insect medicinal materials being released substantially from or dissolved out through cell membranes; 2) due to affecting by the mechanical performance during the crushing process, the temperature of the crushed materials may reach above 80°C, which brings negative influence on the stability of the active protein components of the insect medicinal materials; 3) different parts of the insect medicinal materials have various levels of crushing difficulty, and consequently the differential of particle sizes results in an uneven distribution of insect medicinal materials and affects the uniformity of product quality. These disadvantages directly affect the stability of the active components in a medicine composition and the absorption thereof by human body, and thereby the curative effects of the medicine composition may not be sufficiently performed.

CN 1593623A (Chinese Patent Application No. 200410049615.X) discloses an orally disintegrating tablet of “Tongxinluo” and preparation thereof, said orally disintegrating tablet comprises by weight 15-70 parts of water extracts of scorpion, centipede, eupolyphaga seu steleophaga, hirudo, and periostracum cicadae, 1-12 parts of ethanol extracts of radix ginseng and radix paeoniae rubra, 10-100 parts of inclusion compound of borneol and pharmaceutical

excipients respectively. The features of its preparation are: for herbal medicinal materials, macro-porous resin absorption technique is employed to remove impurities; while the five kinds of insect medicinal materials are extracted by ultrasonic oscillation, concentrated and separated by a rotating scraped film method.

In the above-mentioned ultrasonic extraction of the five insect medicinal materials which was conducted at room temperature, some active components cannot be extracted out, because they need to be extracted out at a relatively higher temperature. Therefore, this prior art preparation process not only affects the curative effects of the medicine composition, but also causes waste of precious insect medicinal materials.

In conventional preparations of Chinese medicines known from prior art, insect medicinal materials are usually treated by direct crushing, water decoction (95-100°C) , 60% ethanol warm extraction (60°C), and saline warm extraction (60°C), etc. Among these treatment methods, extraction at a lower temperature cannot extract the active components sufficiently, and water decoction (95-100°C) may destroy some of the active components.

Now, there is a demand to improve the prior art extraction technique for insect medicinal materials, especially to develop a new extraction technique for insect medicinal materials with combined extractions at a lower temperature and a higher temperature, depending on the medicinal components to be extracted.

Summary of the invention

After many years' investigation, the inventor found that the lower temperature extraction of active components of insect medicinal materials, such as scorpion (*Buthus martensii* Karsch), centipede (*Scolopendra subspinipes mutilans* L. Koch), eupolyphaga seu steleophaga (*Eupolyphaga sinensis* Walker), hirudo (*Whitmania pigra* Whitman), and periostracum cicadae (*Cryptotympana pustulata* Fabricius), is quite limited, far from the level of a

sufficient or complete extraction; after lower temperature dynamic reflux-extraction (i.e. it is under a reduced pressure by using a vacuum system to lower the boiling point and also make the solvent boil at a relatively low temperature, which avoids decomposition of active components of medicinal materials at a higher temperature, extracts quickly thermal-sensitive components of medicinal materials, lowers the cost and pollutions to the environment, and shortens the production period), the dregs of decoction is extracted then at a higher temperature. The curative effect of obtained extracts is significantly improved, as compared with that obtained simply by using lower temperature extraction or direct crushing, and the dose and the stimulation to stomach could be reduced.

Therefore, one object of the invention is to provide a Chinese medicine composition for treating cardiovascular and cerebrovascular diseases, to provide extracts of insect medicinal materials contained therein and to provide preparation thereof, which is advantageous over the prior art.

The preparation process of the inventive Chinese medicine composition for treating cardiovascular and cerebrovascular diseases comprises: taking scorpion, centipede, eupolyphaga seu steleophaga, hirudo, periostracum cicadae, radix ginseng (*Panax ginseng* C. A. Mey.), prepared frankincense (*Boswellia carterii* Birdw., *B. bhaw-dijiana* Birdw.), radix paeoniae rubra (*Paeonia lactiflora* Pall.), lignum dalbergiae odoriferae (*Dalbergia odorifera* T. Chen), lignum santali albi (*Santalum album* L.), borneol, and semen ziziphi spinosae (*Ziziphus jujuba* Mill. var. *spinosa* (Bunge) Hu ex H. F. Chou) according to prescribed amounts/ratios thereof, extracting above mentioned raw medicinal materials and mixing the obtained extracts to form medicines; wherein the extraction of scorpion, centipede, eupolyphaga seu steleophaga, hirudo and periostracum cicadae comprises the following steps: (1) crushing insect medicinal materials into coarse particles; (2) adding 8-12 times amount of water into the coarse particles, and the mixture is heated up to 25-65°C and extracted 1-3 times, each time for 1-5 hours, separating extracts from dregs of the decoction; (3) adding 8-12 times amount of water by volume to weight of the dregs into the dregs, and the mixture

is heated up to 70-100°C and then extracted 1-3 times, each time for 1-3 hours, separating extracts from dregs of the decoction; (4) combining extracts obtained in the process described above, concentrating and drying the obtained extracts to obtain end extracts of insect medicinal materials.

Another object of the present invention is to provide a formulation of the Chinese medicine composition prepared as described above in a form selected from any of tablets, oral disintegrating tablets, dispersible tablets, effervescent tablets, capsules, pills, granules, oral liquids, micro-pills, micro-capsules, and spray.

Further, another object of the present invention is to provide an extraction method of insect medicinal materials. Said insect medicinal materials comprises scorpion, centipede, eupolyphaga seu steleophaga, hirudo, and periostracum cicadae, and the method comprises following steps: (1) crushing the insect medicinal materials into coarse particles; (2) adding 8-12 times amount of water by volume to weight of the insect medicinal materials into the coarse particles, the mixture is heated up to 25-65°C and extracted 1-3 times, each time for 1-5 hours, separating extracts from dregs of the decoction; (3) adding 8-12 times amount of water by volume to weight of the dregs into the dregs, the mixture is heated up to 70-100°C and extracted 1-3 times, each time for 1-3 hours, separating extracts from dregs of the decoction; (4) combining, concentrating and drying the obtained extracts to obtain end extracts of the insect medicinal materials.

Accordingly, another object of the present invention is to provide extracts of said insect medicinal materials obtained by above described method, and extracts of said insect medicinal materials have a color ranging from brown yellow to dark yellow, a pungent flavor and a salty taste.

The present invention will be illustrated in detail below.

The inventive Chinese medicine composition comprises: radix ginseng 3-10 g, hirudo 3-11 g, eupolyphaga seu steleophaga 5-10 g, prepared frankincense 1-5 g, radix paeoniae rubra 3-9 g, lignum dalbergiae odoriferae 1-5 g, lignum santali albi 1-5 g, scorpion 3-9 g, periostracum cicadae 3-12 g, centipede 1-3 g, borneol 1-7 g, and semen ziziphi spinosae 3-10 g. More details are disclosed in ZL 01131203.3.

In extraction steps of the invention, the five medicinal materials of scorpion, centipede, eupolyphaga seu steleophaga, hirudo, and periostracum cicadae can be extracted separately or together. The extraction steps of said insect medicinal materials are described in detail below:

Step (1):

Said insect medicinal materials are crushed into coarse particles of 18-40 mesh, preferably 24 mesh.

Step (2):

8-12 times amount, preferably 10 times amount, of water by volume to weight of the insect medicinal materials is added into the coarse particles; the mixture is heated up to 25-65°C; and extracted 1-3 times, preferably 2 times; each time for 1-5 hours, preferably 3 hours; extract and dregs of the decoction are separated. In certain procedures of preparation, in this step a lower temperature water extraction, a lower temperature dynamic extraction, or an ultrasonic extraction, etc., could be used. When a lower temperature water extraction is used, the extraction temperature at about 50°C is preferred. When a lower temperature dynamic extraction is used, the extraction is conducted with stirring under a reduced pressure, such as a vacuum of 0.05 to 0.1 MPa, to make water boiling at a relatively low temperature, so as to make the extraction faster and more sufficient. When an ultrasonic extraction is used, it needs to control properly the output power and oscillation frequency of an ultrasonic extraction device; the output power of an ultrasonic extraction device in a range of 200-10000 W, preferably 250-8000 W, more preferable 1000-6000 W, most preferable 2000-6000 W is feasible, and the oscillation frequency of an ultrasonic extraction device in a range of 20-80 KHz, preferable 20-60 KHz, more preferable 30-50 KHz is feasible; and in laboratories,

200-2000 W and 20-80 KHz can be used; while for industry use, ultrasonic extraction could be conducted using 2000-10000 W and 20-80 KHz, preferably 3000-8000 W and 30-60 KHz, at a temperature controlled in a desired range. The extraction temperature of the ultrasonic extraction is preferred to be at 30-50°C, and more preferred to be at about 40°C.

Step (3):

8-12 times amount, preferably 10 times amount of water by volume to weight of the dregs is added into the dregs of step (2); the mixture is heated up to 70-100°C, preferably 95°C; and extracted 1-3 times, preferably 2 times; each time for 1-3 hours, preferably 2 hours; extracts and dregs of the decoction are separated.

Step (4):

The obtained extracts are combined, concentrated and dried to obtain end extracts of said insect medicinal materials. The concentration process of this step is favorably performed at 50-60°C to concentrate the extracts into a clear plaster of a density of 1.05-1.10 g/cm³; and the drying process is favorably performed at 50-60°C to dry the clear plaster under a reduced pressure.

In the preparation of the inventive Chinese medicine composition, the extraction of radix ginseng includes but not limited to any of following methods:

1. Radix ginseng is reflux-extracted by 4-12 times amount of a 40-95% ethanol by volume to weight of radix ginseng for 1-3 times, each time for 1-2 hours, and extracts are combined and filtered. The ethanol is recovered from the extracts and the residue after the ethanol recycle is concentration-dried or spray-dried to obtain end extracts of radix ginseng.
2. Radix ginseng is reflux-extracted by 4-12 times amount of a 40-95% ethanol by volume to weight of radix ginseng for 1-3 times, each time for 1-2 hours, and the extracts are combined and filtered. The ethanol is recovered from the extracts until there is no smell of ethanol. 6-8 times amount of water by volume to weight of the radix ginseng is added to dissolve the extracts. The solution is passed through a

pre-treated macro-porous resin column. The column is washed by 3-8 times of water by volume to that of the column till to colorless and the water eluent is discarded. Then the column is washed by 40-95% ethanol, and the eluent is concentrated to recover ethanol, and dried under a reduced pressure or spray-dried to obtain end extracts of radix ginseng.

3. Radix ginseng is reflux-extracted by 4-12 times amount of a 40-95% ethanol by volume to weight of the radix ginseng for 1-3 times, each time for 1-2 hours, and extracts are combined and filtered. The ethanol is recovered from the extracts until there is no smell of ethanol. 6-8 times amount of water by volume to weight of the radix ginseng is added to dissolve the extracts. The solution is passed through a pre-treated macro-porous resin column. The column is washed by 3-8 times of water by volume of the column to colorless and the water eluent is discarded. Then the column is washed by a 40-95% ethanol, and the eluent is passed through an alumina column then. The column is washed by a 40-80% ethanol, and the eluent is concentrated to recover ethanol, and dried or spray-dried to obtain end extracts of radix ginseng.
4. Radix ginseng is reflux-extracted by 4-12 times amount of water by volume to weight of the radix ginseng for 1-3 times, each time for 1-3 hours, and the extracts are combined, filtered and concentrated into 2-4 time of amount by volume to weight of radix ginseng. When it is still hot (40-80°C), the concentrated liquor is diluted by ethanol to an ethanol concentration of 40-90%, and let the solution stand for above 12 hours. Then the supernatant is taken and ethanol is recovered from the extracts until there is no smell of ethanol. 6-8 times amount of water by volume to weight of radix ginseng is added to dissolve the extracts. The solution is passed through a macro-porous resin column. The column is washed first by water to colorless and the water eluent is discarded. Then the column is washed by 3-8 times amount of a 40-95% ethanol by volume to that of the column, and the eluent is passed through an alumina column then. The column is washed by 3-6 times amount of a 40-80% ethanol by volume to that of the column, and the eluent is concentrated to

recover ethanol, and dried under a reduced pressure or spray-dried to obtain end extracts of radix ginseng.

According to the process for preparation of the inventive Chinese medicine composition, the extraction of radix paeoniae rubra includes, but not limited to, any of following methods:

1. Radix paeoniae rubra is reflux-extracted by 4-12 times amount of a 40-90% ethanol by volume to weight of radix paeoniae rubra for 1-4 times, each time for 1-3 hours, and the extracts are combined and filtered. The ethanol is recovered from the extracts and the residue after ethanol recovering is concentrated and dried or spray-dried to obtain end extracts of radix paeoniae rubra.
2. Radix paeoniae rubra is reflux-extracted by 4-12 times amount of a 40-90% ethanol by volume to weight of radix paeoniae rubra for 1-3 times, each time for 1-2 hours, and the extracts are combined and filtered. The ethanol is recovered from the extracts until there is no smell of ethanol. 6-8 times amount of water by volume to weight of radix paeoniae rubra is added to dissolve the extracts. The solution is passed through a pre-treated macro-porous resin column. The column is washed by 3-8 times of water by volume to that of the column till to colorless and the water eluent is discarded. Then the column is washed by 3-8 times amount of a 30-90% ethanol by volume to that of the column, and the eluent is concentrated after recovering ethanol, and dried under a reduced pressure or spray-dried to obtain end extracts of radix paeoniae rubra.
3. Radix paeoniae rubra is reflux-extracted by 4-12 times amount of a 40-90% ethanol by volume to weight of radix paeoniae rubra for 1-3 times, each time for 1-2 hours, and the extracts are combined and filtered. The ethanol is recovered from the extracts until there is no smell of ethanol. 6-8 times amount of water by volume to weight of radix paeoniae rubra is added to dissolve the extracts. The solution is passed through a pre-treated macro-porous resin column. The column is washed by 3-8 times amount of water by volume to that of the column till to colorless and the water eluent is discarded. Then the column is washed by 3-8 times amount of a

30-90% ethanol by volume to that of the column, and the ethanol eluent is passed through an alumina column then. The column is washed by a 30-80% ethanol, and the eluent is concentrated by recovering ethanol, and dried under a reduced pressure or spray-dried to obtain end extracts of radix paeoniae rubra.

4. Radix paeoniae rubra is reflux-extracted by 4-12 times amount of water by volume to weight of radix paeoniae rubra for 1-3 times, each time for 1-2 hours, and the extracts are combined and concentrated into 2-4 time amount by volume to weight of radix paeoniae rubra. When it is still hot (40-80°C), the concentrated liquor is diluted by ethanol to an ethanol concentration of 60-85%, and let it stand for above 12 hours. Then the supernatant is taken and the ethanol is recovered from the extracts until there is no smell of ethanol. 6-8 times amount of water by volume to weight of radix paeoniae rubra is added to dissolve the extracts. The solution is passed through a pre-treated macro-porous resin column. The column is washed by 3-8 times amount of water by volume to that of the column till to colorless, and the water eluent is discarded. Then the column is washed by 3-8 times amount of a 30-90% ethanol by volume to that of the column, and the eluent is passed through an alumina column then. The column is washed by 3-6 times amount of a 30-80% ethanol by volume to that of the column, and the eluent is concentrated by recovering ethanol, and dried under a reduced pressure or spray-dried to obtain end extracts of radix paeoniae rubra.
5. Radix paeoniae rubra is reflux-extracted by 4-12 times amount of a 30-90% ethanol by volume to weight of radix paeoniae rubra for 1-3 times, each time for 1-2 hours, and the ethanol extracts are combined and filtered. The ethanol is recovered from the extracts until there is no smell of ethanol. The extracts are dissolved with 6-8 times amount of water by volume to weight of radix paeoniae rubra and let it stand for above 12 hours. The supernatant is taken and passed through a pre-treated macro-porous resin column. The column is washed by 3-8 times amount by volume of water to that of the column till to colorless and the water eluent is discarded. Then the column is washed by 3-8 times amount of a 30-90% ethanol by volume to

that of the column, and the eluent is passed through an alumina column then. The column is washed by a 40-80% ethanol, and the eluent is concentrated after recovering ethanol, and dried under a reduced pressure or spray-dried to obtain end extracts of *radix paeoniae rubra*.

In the preparation of the inventive Chinese medicine composition, the extraction of *semen ziziphi spinosae* includes, but not limited to any of following methods:

1. *Semen ziziphi spinosae* is reflux-extracted by 4-12 times amount of a 40-90% ethanol by volume to weight of *semen ziziphi spinosae* for 1-3 times, each time for 1-3 hours, and the extracts are combined and filtered. The ethanol is recovered from the extracts and the residue after the ethanol recovering is concentrated under a reduced pressure and dried or spray-dried to obtain end extracts of *semen ziziphi spinosae*.
2. *Semen ziziphi spinosae* is reflux-extracted by 4-12 times amount of a 40-90% ethanol by volume to weight of *semen ziziphi spinosae* for 1-3 times, each time for 1-3 hours, and the extracts are combined and filtered. The ethanol is recovered from the extracts until there is no smell of ethanol. 6-8 times amount of water by volume to weight of *semen ziziphi spinosae* is added to dissolve the extracts. The solution is passed through a pre-treated macro-porous resin column. The column is washed by 3-8 times amount of water by volume to that of the column to colorless and the water eluent is discarded. Then the column is washed by 3-8 times amount of a 30-90% ethanol by volume to that of the column, and the eluent is concentrated after recovering ethanol, and dried or spray-dried to obtain end extracts of *semen ziziphi spinosae*.
3. *Semen ziziphi spinosae* is reflux-extracted by 4-12 times amount of a 40-95% ethanol by volume to weight of *semen ziziphi spinosae* for 1-3 times, each time for 1-3 hours, and the extracts are combined and filtered. The ethanol is recovered from the extracts until there is no smell of ethanol. The extracts are dissolved with 6-8 times amount of water by volume to weight of *semen ziziphi spinosae* and let the

solution stand for above 12 hours. The supernatant is taken and passed through a pre-treated macro-porous resin column. The column is washed by 3-8 times amount of water by volume to that of the column till to colorless and the water eluent is discarded. Then the column is washed by 3-8 times amount of a 30-90% ethanol by volume to that of the column, and the eluent is passed through an alumina column then. The column is washed by a 40-80% ethanol, and the eluent is concentrated after recovering ethanol, and dried under a reduced pressure or spray-dried to obtain end extracts of *semen ziziphi spinosae*.

4. *Semen ziziphi spinosae* is reflux-extracted by 4-12 times amount of water by volume to weight of *semen ziziphi spinosae* for 1-3 times, each time for 1-3 hours, and the water extracts are combined and concentrated into 2-4 times amount by volume to weight of *semen ziziphi spinosae*. When it is still hot (40-80°C), the concentrated liquor is diluted by ethanol to reach an ethanol concentration of 60-85%, and let the resulted solution stand for above 12 hours. Then the supernatant is taken and the ethanol is recovered from the extracts until there is no smell of ethanol. 6-8 times amount of water by volume to weight of *semen ziziphi spinosae* is added to dissolve the extracts. The solution is passed through a pre-treated macro-porous resin column. The column is washed by 6-8 times amount of water by volume to that of the column till to colorless and the water eluent is discarded. Then the column is washed by 3-8 times amount of a 30-90% ethanol by volume to that of the column, and the eluent is passed through an alumina column then. The column is washed by 3-6 times amount of a 30-80% ethanol by volume to that of the column, and the eluent is concentrated after recovering ethanol, and dried under a reduced pressure or spray-dried to obtain end extracts of *semen ziziphi spinosae*.

In the preparation of the inventive Chinese medicine composition, the extraction of the *lignum dalbergiae odoriferae* includes but not limited to any of following methods:

1. *Lignum dalbergiae odoriferae* is distilled with 4-15 times amount of water by volume to weight of *lignum dalbergiae odoriferae* to extract volatile oil for above 4

hours. The volatile essential oil is collected to obtain end extracts of *lignum dalbergiae odoriferae*.

2. *Lignum dalbergiae odoriferae* is extracted by supercritical CO₂ extraction, and a 70%-100% ethanol with an amount of 10-50% of *lignum dalbergiae odoriferae* by weight is added as a modifier. The extract is collected and dried to obtain end extracts of *lignum dalbergiae odoriferae*.
3. Volatile essential oil is extracted from *lignum dalbergiae odoriferae* by 4-15 times amount of petroleum ether by volume to weight of *lignum dalbergiae odoriferae* for above 4 hours and the volatile essential oil is collected to obtain end extracts of *lignum dalbergiae odoriferae*.

In the preparation of the inventive Chinese medicine composition, the extraction of *lignum santali albi* includes but not limited to any of following methods:

1. *Lignum santali albi* is distilled with 4-15 times amount of water by volume to weight of *lignum santali albi* to extract volatile essential oil for above 4 hours. The volatile essential oil is collected to obtain end extracts of *lignum santali albi*.
2. *Lignum santali albi* is extracted by supercritical CO₂ extraction, and 70%-100% ethanol with an amount by weight relative to 10-50% of *lignum santali albi* is added as a modifier. The extract is collected and dried to obtain end extracts of *lignum santali albi*.
3. Volatile essential oil is extracted from *lignum dalbergiae odoriferae* by 4-15 times amount of petroleum ether by volume to weight of *lignum santali albi* for above 4 hours and the volatile essential oil is collected to obtain end extracts of *lignum santali albi*.

In the preparation of the inventive Chinese medicine composition, the extraction of the prepared frankincense but not limited to any of following methods:

1. Prepared frankincense is distilled with 4-15 times amount of water by volume to weight of prepared frankincense to extract volatile essential oil for above 4 hours.

- The volatile essential oil is collected to obtain end extracts of prepared frankincense.
2. Prepared frankincense is distilled with 4-15 times amount of water by volume to weight of prepared frankincense to extract volatile essential oil for above 4 hours. The volatile essential oil is collected; the dregs are freeze dried; and the volatile essential oil and freeze dried dregs are extracts of prepared frankincense.
 3. Prepared frankincense is extracted by supercritical CO₂ extraction, and 70%-100% ethanol with an amount by volume to weight as 10-50% of prepared frankincense is added as a modifier. The extract is collected and dried to obtain end extracts of prepared frankincense.
 4. Volatile essential oil is extracted from prepared frankincense by 4-15 times amount of petroleum ether by volume to weight of prepared frankincense for above 4 hours and the volatile essential oil is collected to obtain end extracts of prepared frankincense.
 5. Prepared frankincense is distilled with 4-15 times amount of water by volume to weight of prepared frankincense to extract volatile essential oil for above 4 hours; the dregs are extracted by 4-15 times amount of ethanol by volume to weight of dregs or 1-3 times, and each time for 1-2 hours, the ethanol solution is combined and concentrated, dried under a reduced pressure or freeze dried; and the volatile essential oil and dried products are end extracts of prepared frankincense.

In the preparation of the inventive Chinese medicine composition, the inclusion compound of borneol is prepared by the following method: the prescribed amount of borneol is crushed into coarse particles of 60 mesh; 1-3 times amount of PEG-6000 by weight to that of borneol is heated to melt at 60-80°C and then the borneol powder is added with fast stirring. The mixture is crushed into fine powder such as 60 mesh after cooling at a lower temperature to obtain the inclusion compound of borneol.

In the preparation of the inventive Chinese medicine composition, except the insect medicinal materials, the rest seven Chinese medicinal materials are preferred to be extracted or prepared

by following steps respectively:

- a prescribed amount of *radix ginseng* is crushed into coarse particles and reflux-extracted by 10 times amount by volume of 70% ethanol to weight of *radix ginseng* for 2 times, each time for 2 hours, the extraction temperature is 95°C and the extracts are combined. The ethanol is recovered from the extracts until there is no smell of ethanol. Water is added to 10 times amount by volume of to weight of *radix ginseng*. Let the solution stand for 12 hours and then be filtered; the filtrate is passed through a pre-treated AB-8 macro-porous resin column. The column is washed by 4 times of water by volume to that of the column till to colorless and the water eluent is discarded. Then the column is washed by 5 times amount of a 70% ethanol by volume to that of the column, and the eluent is concentrated and then spray-dried to obtain end extracts of *radix ginseng*;
- a prescribed amount of *radix paeoniae rubra* is crushed into coarse particles and reflux-extracted by 10 times amount of a 50% ethanol by volume to weight of *radix paeoniae rubra* for 2 times, each time for 2 hours, the extraction temperature is 95°C and the extracts are combined. The ethanol is recovered from the extracts until there is no smell of ethanol. Water is added to 8 times amount by volume to weight of *radix paeoniae rubra*. Let the solution stand for 12 hours and then be filtered; the filtrate is passed through a pre-treated AB-8 macro-porous resin column. The column is washed by 5 times amount of water by volume to that of the column till to colorless and the water eluent is discarded. Then the column is washed by 5 time amount of a 70% ethanol by volume to that of the column, and the eluent is concentrated and spray-dried to obtain end extracts of *radix paeoniae rubra*;
- a prescribed amount of *semen ziziphi spinosae* is crushed into coarse particles and reflux-extracted by 10 times amount of a 80% ethanol by volume to weight of *semen ziziphi spinosae* for 2 times, each time for 2 hours, the extraction temperature is 95°C and the extracts are combined. The ethanol is recovered from the extracts until there is no smell of ethanol. Water is added to 8 times amount by volume to weight of *semen ziziphi spinosae*. Let the solution stand for 12 hours and then be

filtered; the filtrate is passed through pre-treated AB-8 macro-porous resin column. The column is washed by 4 times amount of water by volume to that of the column to colorless and the water eluent is discarded. Then the column is washed by 5 time amount of 80% ethanol by volume to that of the column, and the eluent is concentrated and spray-dried to obtain end extracts of *semen ziziphi spinosae*;

- a prescribed amount of *lignum dalbergiae odoriferae* is distilled with 8 times amount of water to by volume to weight of *lignum dalbergiae odoriferae* for 6 hours to extract the volatile essential oil;
- a prescribed amount of *lignum santali albi* is distilled with 8 times amount of water by volume to weight of *lignum santali albi* for 4 hours to extract the volatile essential oil;
- a prescribed amount of prepared frankincense is distilled with 8 times amount of water by volume to weight of prepared frankincense for 6 hours and the volatile essential oil is collected; the dregs are extracted by 6 times amount of ethanol by volume to weight of prepared frankincense for 2 times, and each time for 1 hour, the ethanol extracts are combined, then concentrated and dried under a reduced pressure;
- a prescribed amount of borneol is crushed into coarse particles and added into 2 times amount of a melt substrate PEG-6000 by volume to weight of borneol with fast stirring. The mixture is cooled at a lower temperature such as 0-20°C and crushed into fine powder.

In the extraction process of the above mentioned raw Chinese medicinal materials, said macro-porous resin column uses such macro-porous resin being selected from any of D101, NKA-9, DA201, DM130, WLD-3, HPD-400, HPD-450, HPD-500 and AB-8; said alumina column can be an acidic alumina column, a neutral alumina column or an alkaline alumina column.

In the extraction process of the above mentioned raw Chinese medicinal materials, said

extracts of *radix ginseng* contain not less than 10-60% total *momordica* saponins of *radix ginseng*; said extracts of *radix paeoniae rubra* contain not less than 15-70% total saponins of *radix paeoniae rubra*; said extracts of *semen ziziphi spinosae* contain not less than 10-60% total *momordica* saponins of *semen ziziphi spinosae*.

In the extraction process of the invention, said *lignum dalbergiae odoriferae*, *lignum santali albi* and prepared frankincense can be extracted separately, or two or three of them are extracted together.

The product of the inventive Chinese medicine composition prepared according to the above described method can be in any form of tablets, oral disintegrating tablets, dispersible tablets, effervescent tablets, capsules, pills, granules, oral liquids, micro-pills, micro-capsules, or spray. The excipient used in the formulation of the invention can be selected from any of disintegrants, fillers, lubricants, adhesives, absorbents, dispersants, surfactants, suspensions, preservatives, coloring agents, antioxidants, suspending agents, wetting agents, solubilizers, projectile agents, or coating agent, or a mixture thereof.

The insect medicinal materials of the invention comprise scorpion, centipede, *eupolyphaga seu steleophaga*, *hirudo*, and *periostracum cicadae*. These five insect medicinal materials can be extracted separately or together. The extraction steps of these insect medicinal materials have been set forth herebefore, thus it would not be repeated herein.

Compared with the prior art, the present invention combines a lower temperature extraction and a higher temperature extraction to extract insect medicinal materials efficiently. The curative effect of the obtained extracts has been well improved compared with that of the extracts obtained only by a lower temperature extraction, and thereby the amount of insect medicinal materials needed is significantly reduced. The Chinese medicine composition of the invention has advantages of representing an effective preparation process, having specific and significant curative effect and smaller dose is required, etc. From comparative

experiments of pharmacodynamics, it has been found that the formulations of the inventive composition have better curative effect on anti-myocardial ischemia, anti-platelet aggregation, and on treatments of coronary heart diseases, angina pectoris, myocardial infarction and the like.

Detailed description of preferred embodiments

While in the following detailed description the process and formulations of the invention will be described in relation to certain preferred embodiments thereof, it should be understood that present invention should not be limited to these embodiments.

Example 1

This example shows specific preparation of extracts of insect medicinal materials according to the invention and the Chinese medicine composition in the form of capsules containing the same.

Prescribed amounts of hirudo 2075 g, eupolyphaga seu steleophaga 1375 g, centipede 275 g, scorpion 1375 g, and periostracum cicadae 1375 g are crushed into coarse particles of 24 mesh. 10 times amount of water by volume to weight of these insect medicinal materials is added, and the mixture is heated up to 60°C and dynamic extracted for 3 hours. The extracts and dregs are separated. 8 times amount of water by volume to weight of dregs is added into the dregs and the mixture is heated up to 60°C and dynamic extracted for 2 hours. The extracts and dregs are separated again. 10 times amount of water by volume to weight of dregs is added into the dregs and the mixture is heated up to 95°C and dynamic extracted for 2 hours. Then the resulted extracts and dregs are separated. Another 8 times amount of water by volume to weight of dregs is added into the dregs and the mixture is heated up to 95°C and dynamic extracted for 1 hour. The extracts and dregs are separated once again. The four water extracts are combined and concentrated into a clear plaster of a density of 1.20 g/cm³ (measured at 40°C) at 55°C by a spherical vacuum concentration tank (Mode: QN-500,

manufactured by Wenzhou Lihong Light Industry Machinery Co., Ltd). The clear plaster is dried at 60°C in a vacuum drying oven (Mode: DGT2006, manufactured by Chongqing Hengda Instruments Manufacture Co. Ltd). End extracts of the insect medicinal materials 1180 g are obtained.

A prescribed amount of radix ginseng 1100 g is reflux-extracted by 10 times, 8 times and 6 times amount of a 70% ethanol by volume to weight of radix ginseng respectively, the extraction time is 2 hours, 2 hours, and 1 hour respectively, the extraction temperature is 95°C; the extracts are combined. The ethanol is recovered from the extracts until there is no smell of ethanol. Water is added to 10 times amount by volume to weight of radix ginseng (ml/g). Let the solution stand for 12 hours and be filtered; the filtrate is passed through a pre-treated AB-8 macro-porous resin column (manufactured by Wuxi Xuelang Chemical Equipments Co. Ltd.), the ratio of radix ginseng to resin is 1:2 (g/ml), and the aspect ratio of the column is 1:9. The column is washed by 4 times amount of water by volume to that of the column to colorless and the water eluent is discarded. Then the column is washed by 5 times amount of a 70% ethanol by volume to that of the column, and the eluent is concentrated and spray-dried to obtain column refined extracts of radix ginseng 40.5 g.

A prescribed amount of radix paeoniae rubra 950 g is crushed into coarse particles and reflux-extracted by 10 times, 8 times, and 6 times amount of a 50% ethanol by volume to weight of radix paeoniae rubra respectively, the extraction time is 2 hours, 2 hours, and 1 hour respectively, the extraction temperature is 95°C and the extracts are combined. The ethanol is recovered from the extracts and the rest solution is concentrated into a clear plaster of a density of 1.18 g/cm³ (measured at 55°C) and spray-dried to obtain end extracts of radix paeoniae rubra 250 g.

A prescribed amount of semen ziziphi spinosae 925 g is crushed into coarse particles and reflux-extracted by 8 times, 8 times, and 6 times amount of a 80% ethanol by volume to weight of semen ziziphi spinosae respectively, the extraction time is 2 hours, 2 hours, and 1

hour respectively, the extraction temperature is 95°C and the extracts are combined. The ethanol is recovered from the extracts and the rest solution is concentrated into a clear plaster at a density of 1.18 g/cm³ (measured at 50°C) and spray-dried to obtain end extracts of semen ziziphi spinosae 130 g.

Prescribed amounts of lignum dalbergiae odoriferae 475 g and lignum santali albi 450 g are distilled with water vapor for 6 hours to extract volatile essential oil. The volatile essential oil of lignum dalbergiae odoriferae and lignum santali albi 11 ml is obtained, and water extracts are concentrated into a clear plaster of a density of 1.18 g/cm³ (measured at 50°C) and spray-dried to obtain extracts of lignum dalbergiae odoriferae and lignum santali albi 18 g.

A prescribed amount of prepared frankincense 450 g is crushed into fine powder of 60 mesh.

A prescribed amount of borneol 275 g is crushed into fine particles and added into 280g melt substrate PEG-6000 (Polyethylene Glycol-6000, available from Tianjin Guangfu Fine Chemical Institution). The above mentioned volatile essential oil is added and the mixture is stirred well, poured out, cooled in a freezer and crushed into a powder of 60 mesh. 556 g inclusion compound of borneol and volatile essential oil is obtained.

Above mentioned extracts of insect medicinal materials, radix ginseng, radix paeoniae rubra, semen ziziphi spinosae, lignum dalbergiae odoriferae and lignum santali albi are combined and granulated with 70% ethanol, and then prepared frankincense powder and inclusion compounds of borneol and volatile essential oil are added, mixed well and filled into 20000 of capsules. The Chinese medicine composition prepared according to the method of the invention is obtained and referred to as “S1”.

Example 2

This example shows specific preparation of extracts of insect medicinal materials according to the invention and the Chinese medicine composition in the form of tablets containing the

same.

Prescribed amounts of *hirudo* 2075 g, *eupolyphaga seu steleophaga* 1375 g, centipede 275 g, scorpion 1375 g, and *periostracum cicadae* 1375 g are crushed into coarse particles of 24 mesh. 10 times, 8 times, and 8 times amounts of water by volume to weight of these insect medicinal materials are added respectively. The mixture is ultrasonic extracted for 3 times (250 W, 40 KHz and 35°C) and the extraction time is 2 hours, 2 hours, and 1 hour respectively. The water extracts are combined. 10 times and 8 times amounts of water by volume to weight of dregs are added into the dregs respectively and the mixture is heated up to 95°C and extracted for 2 hours and 1 hour respectively. The five extracts are combined and concentrated into a clear plaster of a density of 1.18 g/cm³ (measured at 40°C) under the same conditions of concentration, drying equipments and conditions as the ones in Example 1. The clear plaster is dried at a lower temperature under a reduced pressure. End extracts of *hirudo*, *eupolyphaga seu steleophaga*, centipede, scorpion, and *periostracum cicadae* 1175 g are obtained.

A prescribed amount of *radix ginseng* 1100 g is reflux-extracted by 10 times, 8 times and 6 times amounts of a 70% ethanol by volume to weight of *radix ginseng* respectively, the extraction time is 2 hours, 2 hours, and 1 hour respectively, the extraction temperature is 95°C; the extracts are combined. The ethanol is recovered from the extracts and the rest solution is concentrated into a clear plaster of a density of 1.10 g/cm³ (measured at 50°C) and spray-dried to obtain ethanol extracts of *radix ginseng* 220 g.

A prescribed amount of *radix paeoniae rubra* 950 g is crushed into coarse particles and reflux-extracted by 10 times, 8 times, and 6 times amounts of water by volume to weight of *radix paeoniae rubra* respectively, the extraction time is 2 hours, 2 hours, and 1 hour respectively, the extraction temperature is 99°C and the extracts are combined and concentrated into 1900 ml. Ethanol is added to an ethanol concentration of 70% by volume and let the solution stand for 12 hours. The supernatant is taken and the ethanol is recovered

from the supernatant and the rest solution is concentrated into a clear plaster of a density of 1.10 g/cm^3 (measured at 50°C) and spray-dried to obtain end extracts of *radix paeoniae rubra* 230 g.

A prescribed amount of *semen ziziphi spinosae* 925 g is crushed into coarse particles and reflux-extracted by 10 times, 8 times, and 6 times amount of water by volume to weight of *semen ziziphi spinosae* respectively, the extraction time is 2 hours, 2 hours, and 1 hour respectively, the extraction temperature is 99°C . Water extracts are combined and concentrated into 2 times amount by volume to weight of *semen ziziphi spinosae* (ml/g). When it is still hot (60°C), the concentrated liquor is diluted by ethanol to an ethanol concentration of 80% by volume, and let the solution stand for 12 hours. Then the supernatant is taken and the ethanol is recovered from the extracts until there is no smell of ethanol. The rest solution is concentrated into a clear plaster of a density of 1.10 g/cm^3 (measured at 50°C) and spray-dried to obtain end extracts of *semen ziziphi spinosae* 105 g.

Prescribed amounts of *lignum dalbergiae odoriferae* 475 g and *lignum santali albi* 450 g are distilled with water to extract volatile essential oil for 6 hours. The volatile essential oil of *lignum dalbergiae odoriferae* and *lignum santali albi* 11 ml is obtained, and water extracts are concentrated into a clear plaster of a density of 1.10 g/cm^3 (measured at 50°C) and spray-dried to obtain water extracts of *lignum dalbergiae odoriferae* and *lignum santali albi* 18 g.

A prescribed amount of prepared frankincense 450 g is crushed into fine powder.

275 g borneol is crushed into fine powder.

Above mentioned extracts of insect medicinal materials, *radix ginseng*, *radix paeoniae rubra*, *semen ziziphi spinosae*, *lignum dalbergiae odoriferae* and *lignum santali albi* are crushed into fine powder of 80 mesh, then mixed with prepared frankincense powder and granulated with

a 70% ethanol. After drying, a mixture borneol and volatile essential oil dissolved by a certain amount of ethanol is sprayed to the granulated mixture, and the space is sealed for half hour. The mixture is pressed into 20000 tablets. The formulation of the Chinese medicine composition prepared according to the process of the invention is obtained.

Example 3

This example shows specific preparation of extracts of insect medicinal materials according to the invention and the Chinese medicine composition in the form of soft capsules containing the same.

Prescribed amounts of *hirudo* 2075 g, *eupolyphaga seu steleophaga* 1375 g, centipede 275 g, scorpion 1375 g, and *periostracum cicadae* 1375 g are crushed into coarse particles of 24 mesh. 10 times, 8 times, and 8 times amounts of water by volume to weight of these insect medicinal materials are added respectively. The mixture is ultrasonic extracted for 3 times (1500 W, 40 KHz and 40°C) and the extraction time is 3 hours, 2 hours, and 2 hours respectively. The extracts are combined. 10 times and 8 times amounts of water by volume to weight of dregs are added into the dregs and hot extracted at 98°C respectively and the extraction time is 2 hours and 1 hour respectively. The five extracts are combined and concentrated into a clear plaster of a density of 1.10 g/cm³ (measured at 40°C) under the same conditions of concentration, drying equipments and conditions as the ones in Example 1. The clear plaster is dried at 55°C under a reduced pressure. 1170 g total water extracts of *hirudo*, *eupolyphaga seu steleophaga*, centipede, scorpion, and *periostracum cicadae* are obtained.

A prescribed amount of *radix ginseng* 1100 g is reflux-extracted by 10 times, 8 times and 6 times amounts of a 70% ethanol by volume to weight of *radix ginseng* respectively, the extraction time is 2 hours, 2 hours, and 1 hour respectively, the extraction temperature is 95°C; the extracts are combined. The ethanol is recovered from the extracts until there is no smell of ethanol. Water is added to 10 times amount by volume to weight of *radix ginseng*.

The solution stands for 12 hours and is filtered; the filtrate is passed through a pre-treated AB-8 macro-porous resin column (manufactured by Wuxi Xuelang Chemical Instrument), the ratio of radix ginseng to resin is 1:2 (g/ml), and the aspect ratio of the column is 1:9. The column is washed by 4 times of water by volume to that of the column to colorless and the water eluent is discarded. Then the column is washed by 5 times of a 70% ethanol by volume to that of the column, and the eluent is concentrated and spray-dried to obtain column refined extracts of radix ginseng 40.5 g.

A prescribed amount of radix paeoniae rubra 950 g is crushed into coarse particles and reflux-extracted by 10 times, 8 times, and 6 times amounts of a 50% ethanol by volume to weight of radix paeoniae rubra respectively, the extraction time is 2 hours, 1.5 hours, and 1 hour respectively, the extraction temperature is 95°C and the extracts are combined. The ethanol is recovered from the extracts until there is no smell of ethanol. Water is added to 10 times amount by volume to weight of radix paeoniae rubra. The solution stands for 12 hours and is filtered; the filtrate is passed through a pre-treated AB-8 macro-porous resin column (manufactured by Wuxi Xuelang Chemical Instrument), the ratio of radix paeoniae rubra to resin is 1:2.2 (g/ml), and the aspect ratio of the column is 1:8. The column is washed by 4 times of water by volume to that of the column to colorless and the water eluent is discarded. Then the column is washed by 6 times amount of a 70% ethanol by volume to that of the column, and the eluent is concentrated and spray-dried to obtain column refined extracts of radix paeoniae rubra 92.5 g.

A prescribed amount of semen ziziphi spinosae 925 g is crushed into coarse particles and reflux-extracted by 8 times, 8 times, and 6 times amounts of a 80% ethanol by volume to weight of semen ziziphi spinosae respectively, the extraction time is 2 hours, 2 hours, and 1 hour respectively, the extraction temperature is 95°C and the extracts are combined. Water is added to 10 times amount by volume to weight of semen ziziphi spinosae. The solution stands for 12 hours and is filtered; the filtrate is passed through pre-treated D-101 macro-porous resin column (manufactured by Wuxi Xuelang Chemical Instrument), the ratio of semen

ziziphi spinosae to resin is 1:2 (g/ml), and the aspect ratio of the column is 1:8. The column is washed by 4 times amount of water by volume to that of the column to colorless and the water eluent is discarded. Then the column is washed by 6 times amount of an 80% ethanol by volume to that of the column, and the eluent is concentrated and spray dried to obtain the column refined extracts of semen ziziphi spinosae 32 g.

Prescribed amounts of lignum dalbergiae odoriferae 475 g, lignum santali albi 450 g and prepared frankincense 450 g are distilled with water to extract volatile essential oil for 6 hours. The volatile essential oil of lignum dalbergiae odoriferae, lignum santali albi and prepared frankincense 24 ml is obtained.

A prescribed amount of borneol 275 g is crushed into fine powder.

Above mentioned extracts, volatile essential oil and borneol are mixed well and 1.9 times amount of vegetable oil by weight relative to obtained extracts is added. The mixture is grinded well by a colloid mill and forms 20000 of soft capsules. Oral dose: 3 times a day and 2-4 capsules each time.

Example 4

This example shows specific preparation of extracts of insect medicinal materials according to the invention and the Chinese medicine composition in the form of pills containing the same.

Prescribed amounts of hirudo 2075 g, eupolyphaga seu steleophaga 1375 g, centipede 275 g, scorpion 1375 g, and periostracum cicadae 1375 g are crushed into coarse particles of 24 mesh and extracted separately. The extraction steps for each of the insect medicinal materials are as follows: 10 times, 8 times amounts of water are added by volume to weight of the corresponding insect medicinal material respectively, the extraction temperature is 60°C, and the extraction time is 3 hours and 2 hours respectively. The extract and dregs are separated.

The dregs are extracted twice: 10 times and 8 times amounts of water by volume to weight of the dregs are added into the dregs respectively, the extraction temperature is 98°C, and the extraction time is 2 hours and 1 hour respectively. The four water extracts are combined and concentrated into a clear plaster of a density of 1.08 g/cm³ (measured at 40°C) under the same conditions of concentration, drying equipments and conditions as the ones in Example 1. The clear plaster is dried at 50°C under a reduced pressure to obtain water extracts of said insect medicinal materials. Water extracts of *hirudo*, *eupolyphaga seu steleophaga*, centipede, scorpion, and *periostracum cicadae* are 481 g, 262 g, 50 g, 255 g and 152g respectively and the total amount of water extracts of these insect medicinal materials is 1200 g.

A prescribed amount of *radix ginseng* 1100 g is reflux-extracted by 10 times, 8 times and 6 times amounts of a 70% ethanol by volume to weight of *radix ginseng* respectively, the extraction time is 2 hours, 2 hours, and 1 hour respectively, the extraction temperature is 95°C; the extracts are combined. The ethanol is recovered from the extracts until there is no smell of ethanol. Water is added to 10 times amount by volume to weight of *radix ginseng*. The solution stands for 12 hours and is filtered; the filtrate is passed through a pre-treated AB-8 macro-porous resin column (manufactured by Wuxi Xuelang Chemical Instrument), the ratio of *radix ginseng* to resin is 1:2 (g/ml), and the aspect ratio of the column is 1:9. The column is washed by 4 times amount of water by volume to that of the column to colorless and the water eluent is discarded. Then the column is washed by 5 times amount of a 70% ethanol by volume to that of the column, and the eluent is passed through a alumina column (weight ratio of *radix ginseng* and alumina is 1:1), and then the column is washed by a 50% ethanol, the eluent is concentrated to no ethanol smell and spray-dried to obtain column refined extracts of *radix ginseng* 34.5 g.

A prescribed amount of *radix paeoniae rubra* 950 g is crushed into coarse particles and reflux-extracted by 10 times, 8 times, and 6 times amount of a 50% ethanol by volume to weight of *radix paeoniae rubra* respectively, the extraction time is 2 hours, 1.5 hours, and 1 hour respectively, the extraction temperature is 95°C and the extracts are combined. The

ethanol is recovered from the extracts. The supernatant is passed through a pre-treated AB-8 macroporous resin column, the ratio of radix paeoniae rubra to resin is 1:2.3 (g/ml), and the aspect ratio of the column is 1:10. The column is washed by 5 times amount of water by volume to that of the column to colorless and the water eluent is discarded. Then the column is washed by 8 times amount of a 50% ethanol by volume to that of the column, and the eluent is concentrated and spray-dried to obtain the column refined extracts of radix paeoniae rubra 94.5 g.

A prescribed amount of semen ziziphi spinosae 925 g is crushed into coarse particles and reflux-extracted by 8 times, 8 times, and 6 times amount of an 80% ethanol by volume to weight of semen ziziphi spinosae respectively, the extraction time is 2 hours, 2 hours, and 1 hour respectively, the extraction temperature is 95°C and the extracts are combined. The supernatant is passed through a pre-treated HPD-400 macroporous resin column (manufactured by Cangzhou Enbao Chemical Co. Ltd), the ratio of the material to resin is 1:2 (g/ml), and the aspect ratio of the column is 1:8. The column is washed by 5 times amount of water by volume to that of the column to colorless and the water eluent is discarded. Then the column is washed by 7 times amount of an 80% ethanol by volume to that of the column, and the eluent is concentrated and spray-dried to obtain column refined extracts of semen ziziphi spinosae 34 g.

Prescribed amounts of lignum dalbergiae odoriferae 475 g, lignum santali albi 450 g and prepared frankincense 450 g are extracted by supercritical CO₂ extraction, and 95% ethanol with an amount by volume to weight as 30% of above mentioned medicinal materials is added as a modifier. The extract is collected and total extracts 205 g are obtained.

A prescribed amount of borneol 275 g is crushed into fine powder.

Above mentioned extracts, volatile essential oil and borneol are mixed well; the substrate PEG6000 after melt is mixed with the mixture at a ratio of mixture: substrate = 1:2; the

obtained mixture is kept at 70°C; and borneol and volatile essential oil are added and mixed well. The final mixture is dropped into liquid paraffin as a cooling agent at a rate of 40 drops/min and the drops are collected with removal of liquid paraffin by filter paper. 200000 pills are obtained and each of them is 27 mg. Oral dose: 2-3 times a day and 20-40 pills each time.

Comparative Example 1

This comparative example shows preparation of capsules of the Chinese medicine composition by using insect medicinal materials powder directly.

Prescribed amounts of *hirudo* 103.75 g, *eupolyphaga seu steleophaga* 68.75 g, centipede 13.75 g, scorpion 68.75 g, and *periostracum cicadae* 68.75 g are crushed mechanically into 318 g powder of 80 mesh.

A prescribed amount of *radix ginseng* 55 g is crushed and extracted by 10, 8 and 6 times amounts of a 70% ethanol by volume to weight of *radix ginseng* respectively, the extraction time is 2 hours, 2 hours, and 1 hour respectively; the extracts are combined. The ethanol is recovered from the extracts and the residue is concentrated and spray dried to obtain end extracts of *radix ginseng* 11 g.

A prescribed amount of *radix paeoniae rubra* 47.5 g is crushed and extracted by 10, 8 and 6 times amount of a 50% ethanol by volume to weight of *radix paeoniae rubra* respectively, the extraction time is 2 hours, 2 hours, and 1 hour respectively; the extracts are combined. The ethanol is recovered from the extracts and the residue is concentrated and spray-dried to obtain end extracts of *radix paeoniae rubra* 12.8 g.

A prescribed amount of *semen ziziphi spinosae* 46.25 g is crushed and extracted by 10, 8 and 6 times amount of an 80% ethanol by volume to weight of *semen ziziphi spinosae* respectively, the extraction time is 2 hours, 2 hours, and 1 hour respectively; the extracts are

combined. The ethanol is recovered from the extracts and the residue is concentrated and spray-dried to obtain end extracts of *semen ziziphi spinosae* 6.5 g.

Prescribed amounts of *lignum dalbergiae odoriferae* 23.75 g and *lignum santali albi* 22.50 g are distilled with water for 6 hours. The volatile essential oil of *lignum dalbergiae odoriferae* and *lignum santali albi* 0.5 ml is obtained.

A prescribed amount of prepared frankincense 22.50 g is crushed into fine powder of 60 mesh.

A prescribed amount of borneol 275 g is crushed into fine particles and 14 g melt substrate PEG-6000 (Polyethylene Glycol-6000, from Tianjin guangfu fine chemical institution) is added. The above mentioned volatile essential oil is added and the mixture is stirred well, poured out, cooled in a freezer and crushed into powder of 60 mesh. 27.5 g inclusion compound of borneol and volatile essential oil is obtained.

Above mentioned extracts of insect medicinal materials, *radix ginseng*, *radix paeoniae rubra*, *semen ziziphi spinosae*, *lignum dalbergiae odoriferae* and *lignum santali albi* are combined and granulated with a 70% ethanol, and then prepared frankincense powder and inclusion compounds of borneol and volatile essential oil are added, mixed well and filled into 1000 of capsules. The product D1 of the Chinese medicine composition is obtained.

Comparative Example 2

This comparative example shows preparation of extracts of insect medicinal materials by lower temperature ultrasonic and the Chinese medicine composition containing the same.

Prescribed amounts of *hirudo* 103.75 g, *eupolyphaga seu steleophaga* 68.75 g, centipede 13.75 g, scorpion 68.75 g, and *periostracum cicadae* 68.75 g are crushed into fine particles of 24 mesh. The fine particles are introduced into an ultrasonic tank and 6 times amount of

water by volume to weight of these insect medicinal materials is added. The mixture is ultrasonic extracted for 50 minutes, the output power and oscillation frequency are 250 W, 40 KHz respectively. The extraction temperature is controlled at 20°C and the extraction is run for 3 times. The extracts are combined and filtered. The filtrate is concentrated by a rotating scraped film method with a temperature controlled at 65°C, and dried to obtain ultrasonic water extracts 32 g.

The amount and preparation of radix ginseng, radix paeoniae rubra, semen ziziphi spinosae, lignum dalbergiae odoriferae, lignum santali albi, and borneol are the same as the ones in Example 1.

Above mentioned extracts of insect medicinal materials, radix ginseng, radix paeoniae rubra, semen ziziphi spinosae, lignum dalbergiae odoriferae and lignum santali albi are combined and granulated with 70% ethanol, and then prepared frankincense powder and inclusion compounds of borneol and volatile essential oil are added, mixed well and filled into 1000 of capsules. The product D2 of the Chinese medicine composition is obtained.

Comparative example 3

This comparative example shows preparation of capsules of the Chinese medicine composition by using insect medicinal materials powder directly.

Prescribed amounts of hirudo 103.75 g, eupolyphaga seu steleophaga 68.75 g, centipede 13.75 g, scorpion 68.75 g, and periostracum cicadae 68.75 g are crushed mechanically into 318 g fine particles of 80 mesh.

The amount and preparation of radix ginseng, radix paeoniae rubra, semen ziziphi spinosae, lignum dalbergiae odoriferae, lignum santali albi, and borneol are the same as the ones in Example 1.

Above mentioned extracts of insect medicinal materials, radix ginseng, radix paeoniae rubra, semen ziziphi spinosae, lignum dalbergiae odoriferae and lignum santali albi are combined and granulated with 70% ethanol, and then prepared frankincense powder and inclusion compounds of borneol and volatile essential oil are added, mixed well and filled into 1000 of capsules. The product D3 of the Chinese medicine composition is obtained.

Pharmacology experiment part:

Comparative experiment 1

This comparative experiment is to show the influences of Chinese medicine compositions prepared by different methods on acute myocardial ischemia of rats.

Grouping and administration: for capsules S1 prepared in Example 1, the doses are 1.2 g crude drug/Kg, 0.6 g crude drug/Kg and 0.3 g crude drug/Kg respectively; for capsules D1, D2 and D3 prepared in comparative examples 1-3, the dose is 0.6 g crude drug/Kg; sham-operated group and model control group are established in addition.

Experiment animals: SD rats, clean, 112 animals in total and half males/half females, weighting 220-240 g each, purchased from Beijing Vital River, license No. SCXK(Beijing) 2002-0003.

Modeling and index detecting method: after 30 minutes since last administration, the animals were brought to urethane anesthesia, measured the II-lead ECG before the surgery operation, skin is cut longitudinally about 2 cm along the left midclavicular line, muscle layer between the third and forth ribs is blunt dissected, chest and pericardium are opened, the right side of chest is pressed gently to expose the heart and the left anterior descending coronary artery is ligatured by line 0 (no ligation in the sham-operated group) at the left edge of the pulmonary arterial cone and the lower edge of the left atrial appendage by 1 mm through shallow myocardium, the heart is put back into the chest with rapid chest closure.

The fresh heart is taken out with residue blood expelled from cardiac chambers, washed with saline. The water is absorbed by filter paper. The heart is weighted after the removal of noncardiac tissues such as fat and blood vessels, and frozen at -4°C for about 1 hour. Along the atrioventricular groove from apex to base, the ventricular muscle is cut parallel into 0.1 cm thick slices. After being washed with saline, the slices are put in a 1% TTC solution (prepared with pH 7.4 phosphate buffer solution), stained in a 37°C water bath for 15 minutes, and immediately washed with distilled water after staining to remove excess dye. Infarct and non-infarct areas are separated and weighted to calculate the scope of myocardial infarction. Meanwhile, photos are taken for stained myocardial slices and an image analysis system is used to analyze total area of myocardium and myocardial infarction area. Typical pictures of ischemic myocardium are kept to calculate the area percentage of myocardial infarction.

Statistical method: the experiment data is presented by mean value $\pm$ standard deviation ($\bar{X} \pm SD$), Software SPSS 11.5 is used to run t test. t is an approximate pattern of standard normal distribution, as a basic concept of statistics.

Experiment results: detailed results are listed in Table 1.

Analysis: compared with model group and D1-D3, median and high dose groups of S1 have obviously reduced weight percentage of myocardial ischemia part to the heart ($P < 0.05$ or $P < 0.01$); compared with model group and D1-D3, low, median and high dose groups of S1 have obviously reduced weight percentage of myocardial ischemia part to the heart ($P < 0.05$). P is probability, a basic concept of statistics used to describe the possibility of random events to happen.

Table 1

Group	Number of animals	Dose g crude drug/kg	Area percentage of myocardial ischemia	weight percentage of myocardial ischemia
Sham-operated Group	14	—	0.0±0.0	0.0±0.0
Model Group	14	—	8.8±4.9 ^{△△}	13.2±3.7 ^{△△}
S1 Group	14	1.20	2.7±2.2*abc	8.2±3.2**
S1 Group	14	0.60	3.3±1.2*	8.6±3.1*
S1 Group	14	0.30	3.8±1.3*	8.7±5.1
D1 Group	14	0.60	4.5±1.3	10.7±2.7
D2 Group	14	0.60	5.2±2.0	11.2±3.3
D3 Group	14	0.60	4.9±2.1	9.8±2.3

Note: Compared with model group *P<0.05; ** P<0.01

Compared with sham-operated group ^{△△}P<0.01

Compared with D1 group a P<0.05

Compared with D2 group b P<0.05

Compared with D3 group c P<0.05

Comparative experiment 2

This experiment is to show the influence of Chinese medicine compositions prepared by different methods on focal cerebral ischemia of rats.

Grouping and administration: for capsules S1 prepared in Example 1, the doses are set to be 2.4 g crude drug/Kg/day, 1.2 g crude drug/Kg/day and 0.6 g crude drug/Kg/day referring to dose for human 4.557g crude drug/day, i.e. 0.076 g crude drug/kg body weight (standard body weight 60 kg); for capsules D1, D2 and D3 prepared in comparative examples 1-3, the dose is 1.2 g crude drug /Kg/day respectively; sham-operated group and model comparative group are established in addition.

Experiment animals: healthy Wistar rats, clean, half males and half females of 140, weighting 160-180 g each, purchased from Beijing Vital River, license No. SCXK(Beijing) 2003-0003, certificate of quality: no. 0048343.

Modeling and index detecting method: after anesthesia with chloral hydrate, the rats are fixed to lie on side. Except the sham-operated group, other groups are treated with the following operation: At the middle of eye canthus and external auditory canal cuts a small opening, temporalis muscle is exposed, the temporalis muscle is clamped by temporalis muscle clamps to separate to two sides, careful not to damage the facial nerve. Most part of the squamous bone is exposed, and then a hole is drilled in front and below about 2 mm of the joint part of zygomatic arch and squamous bone. Under an operating microscope, about 2 mm in diameter cranial window is opened by using a small straight strip clamp to expose the cerebral artery. 50% ferric trichloride solution (acid by adding diluted hydrochloric acid) 10 μ l is dropped on a small piece of filter paper, and the paper is put on the cerebral artery. After about 30 minutes, the artery becomes dark, the filter paper is removed, and local tissues are washed with saline. The rats are kept back to the cage after sutured layer by layer. Sham-operated group is treated in the same way except the treatment of ferric trichloride. After 24 hours since the surgery, blood of carotid artery is drained, and brains of animals decapitated are taken out with sense of smell, cerebellum and lower brain stem removed. The coronal is cut into 5 pieces by 4 cuts. The first cut is at the midpoint between the front pole of brain and optic chiasm, the second cut is at the optic chiasm and the third cut at the funnel handle, the fourth cut is between the funnel handle and posterior lobe tail end Brain slices are stained with red Tetrazolium (TTC). After stained, normal tissues turn red, and infarct organizations turn white. Each brain plane is projected to an aluminum foil of uniform density, and the infarct area is carefully taken out. The weight percentages of the infarct tissues to total brain and surgical side of half brain represent the scope of infarction (%).

Experiment results: brains of rats decapitated are taken out after 24 hours since the surgery, strained with TTC. The infract area is weighted and compared. Detailed results are listed in Table 2.

Table 2

Group	dose	Number of rats	percentages of the infarct area to half brain %	percentages of the infarct area to total brain %
Sham-operated Group	—	10	0±0	0±0
Model Group	—	10	9.02±2.01 ^{△△}	4.44±1.03 ^{△△}
S1 Group	2.4g/kg	10	3.63±1.87**abc	2.23±1.10**
S1 Group	1.2g/kg	10	5.81±2.60*	2.98±1.21*
S1 Group	0.6g/kg	10	7.15±1.85*	3.55±0.98*
D1 Group	1.2g/kg	10	6.44±1.23	3.42±0.83
D2 Group	1.2g/kg	10	5.33±1.10	2.89±0.94
D3 Group	1.2g/kg	10	6.52±2.12	3.22±1.02

Note: Compared with model group *P<0.05; ** P<0.01

Compared with sham-operated group ^{△△}P<0.01

Compared with D1 group a P<0.05

Compared with D2 group b P<0.05

Compared with D3 group c P<0.05

Claims

1. A process for preparation of a Chinese medicine composition, comprising taking scorpion, centipede, eupolyphaga seu steleophaga, hirudo, periostracum cicadae, radix ginseng, prepared frankincense, radix paeoniae rubra, lignum dalbergiae odoriferae, lignum santali albi, borneol, and semen ziziphi spinosae according to prescribed amounts thereof, extracting said raw medicinal materials and mixing the obtained extracts to form the composition; wherein the extraction of scorpion, centipede, eupolyphaga seu steleophaga, hirudo and periostracum cicadae comprises the following steps: (1) crushing insect medicinal materials into coarse particles; (2) adding 8-12 times amount by weight of water to that of the insect medicinal materials into the coarse particles, and the mixture is heated up to 25-65°C and extracted 1-3 times, each time for 1-5 hours, separating extracts from dregs of the decoction; (3) adding 8-12 times amount by weight of water to that of the dregs into the dregs, and the mixture is heated up to 70-100°C and extracted 1-3 times, each time for 1-3 hours, separating extracts from dregs of the decoction; (4) the obtained extracts are combined, concentrated and dried to obtain end extracts of insect medicinal materials.
2. Process as set forth in claim 1, wherein scorpion, centipede, eupolyphaga seu steleophaga, hirudo, and periostracum cicadae are extracted separately or together, and the extraction steps of said insect medicinal materials comprise:
Step (1): said insect medicinal materials are crushed into coarse particles of 18-40 mesh;
Step (2): 8-10 times amount by weight of water to that of the insect medicinal materials is added into the coarse particles; the mixture is heated up to 30-50°C and extracted 2-3 times, each time for 1-3 hours; the extract and dregs of the decoction are separated; this step uses water extraction under a reduced pressure or ultrasonic extraction;
Step (3): 8-12 times amount by weight of water to that of dregs is added into the dregs of step (2); the mixture is heated up to 75-100°C and extracted 2-3 times; each time for

1-3 hours; the extracts and dregs of the decoction are separated;

Step (4): the obtained extracts are combined and concentrated into clear plaster of a density of 1.05-1.20 g/cm³ at 50-60°C; the clear plaster is dried at 50-60°C under a reduced pressure.

3. Process as set forth in claim 2, wherein said extraction process in step (2) is conducted under a reduced pressure with a vacuum from 0.05 to 0.1 MPa and the extracts is stirred at the same time; or conducted using ultrasonic extraction, the output power and oscillation frequency are 200-10000 W, 20-80 KHz respectively.
4. Process as set forth in claim 3, wherein said extraction process in step (2) uses ultrasonic extraction and the output power and oscillation frequency are 1500-8000 W, 30-60 KHz respectively.
5. Process as set forth in any of claims 1-4, wherein radix ginseng, prepared frankincense, radix paeoniae rubra, lignum dalbergiae odoriferae, lignum santali albi, borneol, and semen ziziphi spinosae are treated by following steps:
 - a prescribed amount of radix ginseng is crushed and reflux-extracted by 10 times amount of a 70% ethanol by volume to weight of radix ginseng for 2 times, each time for 2 hours, the extraction temperature is 95°C and the extracts are combined; the ethanol is recovered from the extracts until there is no smell of ethanol; 8 times amount of water by volume to weight of radix ginseng is added to radix ginseng; Let the resulted solution stand for above 12 hours and be filtered; the filtrate is passed through a pre-treated AB-8 macro-porous resin column; the column is washed by 4 times amount of water by volume to that of the column to colorless and the water eluent is discarded; then the column is washed by 6 times amount of a 70% ethanol by volume to that of the column, and the eluent is concentrated and spray-dried to obtain end extracts of radix ginseng;

- a prescribed amount of *radix paeoniae rubra* is crushed and reflux-extracted by 10 times amount of 50% ethanol by volume to weight *radix paeoniae rubra* for 2 times, each time for 2 hours, the extraction temperature is 95°C and the extracts are combined; the ethanol is recovered from the extracts until there is no smell of ethanol; 10 times amount of water by volume to weight of *radix paeoniae rubra* is added to the extracts; Let the solution stand for above 12 hours and be filtered; the filtrate is passed through a pre-treated AB-8 macro-porous resin column; the column is washed by 4 times amount of water by volume to that of the column to colorless and the water eluent is discarded; then the column is washed by 6 times amount of a 60% ethanol by volume to that of the column, and the ethanol eluent is concentrated and spray-dried to obtain end extracts of *radix paeoniae rubra*;
- a prescribed amount of *semen ziziphi spinosae* is crushed and reflux-extracted by 10 times amount of an 80% ethanol by volume to weight of the extracts for 2 times, each time for 2 hours, the extraction temperature is 95°C and the extracts are combined; the ethanol is recovered from the extracts until there is no smell of ethanol; 8 times amount of water by volume to weight of *semen ziziphi spinosae* is added to the extracts; Let the solution stand for above 12 hours and be filtered; the filtrate is passed through a pre-treated AB-8 macro-porous resin column; the column is washed by 4 times amount of water by volume to that of the column to colorless and the water eluent is discarded; then the column is washed by 6 times amount of an 80% ethanol by volume to that of the column, and the ethanol eluent is concentrated and spray-dried to obtain end extracts of *semen ziziphi spinosae*;
- a prescribed amount of *lignum dalbergiae odoriferae* is distilled with 8 times amount of water by volume to weight of *lignum dalbergiae odoriferae* for 6 hours to extract its volatile essential oil;
- a prescribed amount of *lignum santali albi* is distilled with 8 times amount of water by volume to weight of *lignum santali albi* for 4 hours to extract its volatile essential oil;

- a prescribed amount of prepared frankincense is distilled with 8 times amount of water by volume to weight of prepared frankincense for 6 hours and the volatile essential oil is collected; the dregs are extracted by 6 times amount of ethanol by volume to weight of the dregs for 2 times, and each time for 1 hour, the ethanol extracts is combined and dried;
 - a prescribed amount of borneol is crushed into a fine particles and added into 2 times amount of melt substrate PEG-6000 by volume to weight of borneol with fast stirring; the mixture is cooled and crushed.
6. A product of the Chinese medicine composition prepared according to the method of any of claims 1-5, wherein the form of said product is selected from any of tablets, oral disintegrating tablets, dispersible tablets, effervescent tablets, capsules, pills, granules, oral liquids, micro-pills, micro-capsules, and spray.
7. A method of preparation of extracts of insect medicinal materials, wherein said insect medicinal materials comprises scorpion, centipede, eupolyphaga seu steleophaga, hirudo, and periostracum cicadae, and the method comprises following steps: (1) crushing the insect medicinal materials into coarse particles; (2) adding 8-12 times amount of water by volume to weight of insect medicinal materials into the coarse particles, the mixture is heated up to 25-65°C and extracted 1-3 times, each time for 1-5 hours, separating extracts from dregs of the decoction; (3) adding 8-12 times amount of water by volume to weight of the dregs into the dregs, the mixture is heated up to 70-100°C and extracted 1-3 times, each time for 1-3 hours, separating extracts from dregs of the decoction; (4) obtained extracts are combined, concentrated and dried to obtain end extracts of the insect medicinal materials.

8. The method as set forth in claim 7, wherein the extraction steps of said insect medicinal materials comprise:
Step (1): said insect medicinal materials are crushed into coarse particles of 18-40 mesh;
Step (2): 8-12 times amount of water by volume to weight of insect medicinal materials is added into the coarse particles; the mixture is heated up to 25-50°C and extracted 2-3 times, each time for 1-3 hours; extract and dregs of the decoction are separated; this step can use water extraction under a reduced pressure or ultrasonic extraction;
Step (3): 8-12 times amount of water by volume to weight of the dregs is added into the dregs of step (2); the mixture is heated up to 75-100°C and extracted 2-3 times; each time for 1-3 hours; the extracts and dregs of the decoction are separated;
Step (4): obtained extracts are combined and concentrated into clear plaster of a density of 1.05-1.10 g/cm³ at 50-60°C; the clear plaster is dried at 50-60°C under a reduced pressure.
9. The method as set forth in claim 7, wherein said extraction process in step (2) is conducted under a reduced pressure with a vacuum from 0.05 to 0.1 MPa and the extracts is stirred at the same time; or ultrasonic extraction is used, the output power and oscillation frequency are 200-10000 W, 20-80 KHz respectively.
10. The method as set forth in claim 9, wherein said extraction process in step (2) uses ultrasonic extraction and the output power and oscillation frequency are 1500-8000 W, 30-60 KHz respectively.
11. Extracts of insect medicinal materials prepared by the method of any of claims 7-10, wherein said extracts of insect medicinal materials have brown yellow to dark yellow color, pungent flavor and salty taste.