

A Traditional Chinese Medicine Composition To Treat Rheumatoid Arthritis and Preparation Method Thereof

Field of the Invention

The present invention relates to a traditional Chinese medicine composition and preparation method thereof. In particular, it relates to a traditional Chinese medicine composition to treat rheumatoid arthritis and preparation method thereof, and belongs to the field of medical art.

Background of the Invention

Rheumatism is a common and frequently encountered disease, and has a long onset period and various clinic appearances. It is refractory disease which needs a long period of therapy. It is difficult to diagnose, cure and research this kind of pathological change due to various reasons, such as the complicated cause and pathogenesis of the disease, the borderline and multidisciplinary appearance in clinic, and additionally the limitation of the science of Traditional Chinese Medicine and the divided cognition of this disease etc. In the science of Traditional Chinese Medicine, rheumatism is collectively called "Paralysis Syndrome". It is recorded in Article 43 of Paralysis Syndrome Section of "Huangdi Neijing Suwen" that the three evils, wind, cold and wet, combine and cause appearance of paralysis syndrome. Domination of wind causes peripatetic paralysis, domination of cold causes pain paralysis, and domination of wet cause sticky paralysis. The therapeutic principal of this symptom is to eliminate wind, remove wet, warm meridian, and expel cold to expel these three kinds of pathogens to cure the disease.

Summary of the Invention

One of the purposes of the present invention is to provide a traditional Chinese medicine composition to treat rheumatoid arthritis; another purpose is to provide a method of preparing this composition.

The present invention can be implemented through the following three technical schemes:

Scheme 1: The constitutes and formula of crude drugs for the traditional Chinese medicine composition are as follows(according to weight ratio):

Ant	280-500 parts
Radix Salviae Miltiorrhizae	100-200 parts
Radix Aconiti Preparata	35-100 parts
Radix Ginseng	20-80 parts
Caulis Spatholobi	30-75 parts
Ramulus Cinnamomi	25-80 parts ;

Wherein scheme 1, the constitutes and formula of crude drugs for traditional Chinese medicine composition are preferably as follows:

Ant	300-400 parts
Radix Salviae Miltiorrhizae	120-150 parts
Radix Aconiti Preparata	40-70 parts
Radix Ginseng	30-50 parts
Caulis Spatholobi	40-60 parts
Ramulus Cinnamomi	35-50 parts .

Scheme 2: The constitutes and formula of crude drugs for the traditional Chinese medicine composition are as follows(according to weight ratio):

Ant	280-500 parts
Radix Salviae Miltiorrhizae	100-200 parts
Radix Aconiti Preparata	35-100 parts
Radix Ginseng	20-80 parts
Caulis Spatholobi	30-75 parts
Ramulus Cinnamomi	25-80 parts
Cortex Kalopanax	25-70 parts
Herba speranskiae tuberculatae	25-70 parts
Cortex Phellodendri	25-70 parts
Rhizoma Atractylodis	25-70 parts

Rhizoma Alismatis	25-70 parts
Herba Lycopodii	25-70 parts
Semen Coicis	35-70 parts ;

Wherein scheme 2, the constitutes and formula of crude drugs for traditional Chinese medicine composition are preferably as follows:

Ant	300-400 parts
Radix Salviae Miltiorrhizae	120-150 parts
Radix Aconiti Preparata	40-70 parts
Radix Ginseng	30-50 parts
Caulis Spatholobi	40-60 parts
Ramulus Cinnamomi	35-50 parts
Cortex Kalopanax	35-50parts
Herba speranskiae tuberculatae	35-50 parts
Cortex Phellodendri	35-50 parts
Rhizoma Atractylodis	35-50 parts
Rhizoma Alismatis	35-50 parts
Herba Lycopodii	35-50 parts
Semen Coicis	45-70 parts .

Scheme 3: The constitutes and formula of crude drugs for the traditional Chinese medicine composition as follows(according to weight ratio):

Ant	280-500 parts
Radix Salviae Miltiorrhizae	100-150 parts
Radix Aconiti Preparata	35-70 parts
Radix Ginseng	20-50 parts
Caulis Spatholobi	30-75 parts
Semen Coicis	35-70 parts
Cortex Kalopanax	25-70 parts
Herba speranskiae tuberculatae	25-70 parts
Cortex Phellodendri	25-50parts

Rhizoma Atractylodis	25-50 parts
Rhizoma Alismatis	25-50 parts
Herba Lycopodii	25-50 parts
Ramulus Cinnamomi	25-50 parts
Scolopendra	4-10 parts
Zaocys	4-10 parts ;

Wherein scheme 3, the composition constitutes and formula of crude drugs for traditional Chinese medicine are preferably as follows:

Ant	300-400 parts
Radix Salviae Miltiorrhizae	120-140 parts
Radix Aconiti Preparata	45-60 parts
Radix Ginseng	20-50 parts
Caulis Spatholobi	45-60 parts
Semen Coicis	45-60 parts
Cortex Kalopanax	35-60 parts
Herba speranskiae tuberculatae	35-60 parts
Cortex Phellodendri	25-40 parts
Rhizoma Atractylodis	25-40 parts
Rhizoma Alismatis	25-40 parts
Herba Lycopodii	25-40 parts
Ramulus Cinnamomi	25-40 parts
Scolopendra	4-10 parts
Zaocys	4-10 parts .

According to pharmaceutical methods, various clinical acceptable dosage forms can be prepared by the medical composition of the present invention, including but not limited to one of the following forms: tablets, capsules, pills, granules, suspension, dripping pills, and oral liquid preparation, etc.

In each technical scheme of the present invention, the manufacturing process of capsule of each traditional Chinese medicine composition is as follows:

Pulverize crude drugs: ant, Radix Ginseng, Radix Aconiti Preparata, and/or Scolopendra, Zaocys to fine powder, sieve and mix well; pulverize Radix Salviae Miltiorrhizae, Ramulus Cinnamomi and/or Rhizoma Atractylodis to coarse powder respectively, percolate with 70-90% alcohol as solvent, pressure reduction concentrate the percolate by recovering alcohol to obtain the extract with relative density of 1.30-1.32(55°C). Combine the residues with Caulis Spatholobi, and/or Semen Coicis, Cortex Kalopanax, Herba speranskiae tuberculatae, Cortex Phellodendri, Rhizoma Alismatis, Herba Lycopodii and decoct with water for two times, 1.5 hours each time, combine all the decoction, filter, pressure reduction concentrate the filtrates to obtain the extract with relative density of 1.35-1.38(60°C), add the above fine powder and the extracts of Radix Salviae Miltiorrhizae and the others, mix well, make granules, dry, crush, sieve, and fill into the capsules for use.

In each technical scheme of the present invention, the manufacturing process of dripping pills of each traditional Chinese medicine composition is as follows:

Pulverize the crude drugs : ant, Radix Ginseng, Radix Aconiti Preparata, and/or Scolopendra, Zaocys to fine powder, sieve and mix well; pulverize Radix Salviae Miltiorrhizae, Ramulus Cinnamomi and/or Rhizoma Atractylodis to coarse powder respectively, percolate with 70-90% alcohol as solvent, pressure reduction concentrate the percolate by recovering alcohol to obtain the extract with relative density of 1.30-1.32(55°C). Combine the residues with Caulis Spatholobi, and/or Semen Coicis, Cortex Kalopanax, Herba speranskiae tuberculatae, Cortex Phellodendri, Rhizoma Alismatis, Herba Lycopodii and decoct with water for two times, 1.5 hours each time, combine all the decoction, filter, pressure reduction concentrate the filtrates to obtain the extract with relative density of 1.35-1.38(60°C) , add the above fine powder and the extracts of Radix Salviae Miltiorrhizae and the others, mix well, make granules, add the above granules in PEG molten by hexane, stir well, transfer the mixture to the feeding container of dropping machine, keep the temperature at 90°C and drop into methyl silicone oil cooled until 5~10°C at the speed of 30 r/min, take out the dripping pills and remove the coolant by absorption, and dry for use.

In each technical scheme of the present invention, all the traditional Chinese medicine compositions have the function of invigorating the kidney and spleen, promoting blood flow and clearing out the vein, expelling wind-evil and removing wetness, eliminating cold to stop pain. It can be effectively used in the treatment of lingering arthralgia with weak, arthralgia, intumescence and morning stiffness, numbness and

stickiness, difficult to flex and extend, rigor and deforming, the rheumatism and rheumatoid arthritis with above symptoms.

The prescription composition of the present invention is reasonable and the manufacturing process is advanced, which meets the needs of thinking and method in developing modern traditional Chinese medicine and establish a new way to the scientific research of traditional Chinese medicine.

Compared with pills, the capsule of the present invention has the following superiorities: smaller dosage, quick dissolubility in intestine and stomach, complete absorption, operate quickly, convenient to take and so on.

Various animal models of inflammation and pain were established, and rats and mice were orally administrated with the capsule of the present invention with dose of 0.75-3g/kg (correspond to 7.5-30 times as human's daily dosage), and demonstrated that the said capsule has the anti-inflammatory and analgesic effects. The said capsule can obviously relieve the primary and the secondary affection of voix pedis swelling and adjuvant-induced arthritis of rats induced by egg albumen and methanal. It can inhibit the capillary permeability of mouse's abdominal cavity in the early stage, and can inhibit the transmigration of leukocyte under the rat's skin, and also can inhibit the forming of granuloma induced by cotton ball in the later stage of inflammation. It can relieve the mouse's pain induced by hot plate stimulus and acetic acid's writhing response. It can inhibit LPS induced AA rat's PM and can release IL-1; indirect luminescence immunoassay indicates that this drug can increase the quantity of Ts cells, and the ratio of $L^3T^+_4/Lyt-2^+$ cells was obviously lower than control group.

The etiopathogenesis, diseased region and peculiarity of rat's adjuvant-induced arthritis are similar to human's rheumatoid arthritis. The primarily pathological changes of the voix pedis injected with adjuvant belongs to a non-specific inflammation, and the secondary pathological changes of the voix pedis injected no adjuvant belongs to immunoreactive inflammation. The said capsule can inhibit rat AIA, which indicate that it has effect of inhibiting rheumatoid arthritis. It has effect of inhibiting swelling induced by egg albumen and methanal, it can inhibit increasing capillary permeability of mouse's abdominal cavity induced by acetic acid and can inhibit the transmigration of leukocyte under the rat's skin induced by CMC. All above indicate that the said capsule has releasing effect in the early stage of inflammation. It can inhibit the forming of granulomatous induced by cotton ball indicates it has anti-inflammatory effect in the

multiplication period of inflammation. In the experiments of the mouse's pain induced by hot plate stimulus and acetic acid's writhing response, the capsule can prolong eclipse period and decrease the number of times, which indicate that it can elevate the tolerance to the pain and more or less has some analgesic effect.

The present invention is described further through the following experiments and examples.

Experiment 1: Anti-Inflammatory Action of the present Invention

1. Effect on Voix Pedis Swelling of Rat Induced by Egg Albumen

50 rats with body weight of 180-200g were randomly divided into 5 groups: high, middle, low dosage of the capsule, Tripterygii Wilfordii group and control, 10 rats each group, gaster-poured once a day for 7 days continuously. One hour after the last intragastric infusion, subcutaneous inject 0.1ml of 10% fresh egg albumen with NS in the middle of each rat's right post voix pedis, then measure the thickness of voix pedis using vernier caliper at 15min, 30min and 4 hours before and after injection. The position and closeness in each measurement were the same. The difference of thickness before injection and after injection was the swelling degree in different time. The results were showed in Table 1, compared with control, except for no obvious change in 15min for low dosage, all the other groups had the obvious effect of releasing swelling within 4 hours. Moreover, the effect was correlated to the dosage.

Table 1: Effect on Voix Pedis Swelling of Rats induced by Egg Albumen

Groups	Dosage(g/kg)	Number of rat	Degree of swelling (mm, $\bar{X} \pm S$)		
			15min	30min	4h
Control		10	1.7 $\pm$ 0.2	2.1 $\pm$ 0.4	1.6 $\pm$ 0.2
The said capsule group	3	10	1.0 $\pm$ 0.2***	1.5 $\pm$ 0.3***	1.0 $\pm$ 0.2***
The said capsule group	1.5	10	1.3 $\pm$ 0.2***	1.7 $\pm$ 0.2**	1.2 $\pm$ 0.2***
The said capsule group	0.75	10	1.4 $\pm$ 0.4*	1.7 $\pm$ 0.3**	1.3 $\pm$ 0.2***
Tripterygii Wilfordii group	triptolide 66 μ g	10	1.0 $\pm$ 0.2***	1.2 $\pm$ 0.4***	1.0 $\pm$ 0.2***

Compared with control: ***P<0.01 **P<0.05 *P>0.05

2. Effect on Voix Pedis Swelling of Rat Induced by Methanal

50 rats, with same body weight and the groups as Experiment 1 were gaster-poured 1 time each day for 10 days. The thickness of voix pedis on the 7th day was measured by vernier caliper. Then subcutaneous inject 0.1ml of 2.5% methanal in the middle of each rat's right post voix pedis, measure the thickness of voix pedis at 12h, 24, and 72h after injection. The difference of thickness between before injection and after injection was the swelling degree in different time. The results were shown in Table 2: compared with control, all the residue groups had the obvious effect of releasing swelling from 12 to 72 hours. The difference is significance in statistics. Moreover, the effect was correlated to the dosage.

Table 2: Effect on Voix Pedis Swelling of Rats Induced by Methanal

Groups	Dosage(g/kg)	Number of rat	Degree of swelling (mm, $\bar{X} \pm S$)		
			12h	24h	72h
Control		10	2.1±0.4	2.1±0.4	2.3±0.4
The said capsule group	3	10	1.3±0.3***	1.6±0.2***	1.4±0.3***
The said capsule group	1.5	10	1.6±0.3***	1.8±0.2***	1.7±0.3***
The said capsule group	0.75	10	1.7±0.3**	2.0±0.3***	1.8±0.3***
Tripterygii Wilfordii group	triptolide 66μg	10	1.3±0.3***	1.6±0.2***	1.4±0.3***

Compared with control: ***P<0.01 **P<0.05

3. Effect on Rat's AIA

40 male rats with body weight of 170-190g were randomly divided into 5 groups: high, middle, low dosage of the capsule, Tripterygii Wilfordii group and control, 8 rats each group. Subcutaneous inject 0.05ml Freund's complete adjuvant (FCA) in the middle of each rat's left behind voix pedis to cause inflammation, (the preparation methods of FCA: liquid paraffin with Lanolin (2:1), heat them to 70°C and mix well, autoclaving; then and 7.5mg Bacillus Calmette-Guerin Vaccine per 1ml). 6days after the forming of the inflammation, gaster-poured 1 time each day for 20 days. Measure the volume of both posterior part voix pedis. The difference between posterior part and anterior part in the same side was the swelling degree. Meanwhile measure the body weight, and observe the change. The results were shown in Table 3, 4, and 5.

Table 3: Effect on the Primary Affection of Rat's AIA

Group	Dosage (g/kg)	Number of rat	Swelling degree of left pedes after inject adjuvant (mL)			
			8 日	13 日	18 日	23 日
Control group		8	0.34±0.06	0.41±0.05	0.42±0.05	0.34±0.05
The said capsule group	1.5	8	0.30±0.06*	0.33±0.06**	0.33±0.04***	0.29±0.04**
The said capsule group	0.75	8	0.32±0.05*	0.37±0.05*	0.37±0.04**	0.32±0.03*
Tripterygii Wilfordii group	triptolide 66μg	8	0.28±0.04**	0.31±0.05***	0.31±0.05***	0.27±0.05**

Compared with control: *P>0.05 **P<0.05 ***P<0.01

Table 4: Effect on the secondary affection of rat's AIA

Group	Dosage (g/kg)	Number of rat	Swelling degree of left pedes after inject adjuvant (mL)		
			15d	20d	25d
Control group		8	0.24±0.06	0.26±0.07	0.21±0.05
The said capsule group	3	8	0.15±0.04***	0.14±0.04***	0.12±0.03***
The said capsule group		8	0.17±0.04**	0.18±0.06**	0.15±0.03***
The said capsule group	0.75	8	0.20±0.03*	0.20±0.03**	0.17±0.04*
Tripterygii Wilfordii group	triptolide 66μg	8	0.15±0.03***	0.15±0.03***	0.12±0.02***

Compared with control: *P>0.05 **P<0.05 ***P<0.01

Table 5: Effect on the body weight of rat's AIA

Group	Dosage(g/kg)	Number of rat	The body weight after inject adjuvant(mL) (g, $\bar{X} \pm S$)		
			0d	15d	25d
Control group		8	184±7	190±8	194±9
The said capsule group	3	8	183±7	199±9	209±9***
The said capsule group	1.5	8	186±6	198±9	207±9**
The said capsule group	0.75	8	185±7	195±7	202±7
Tripterygii Wilfordii group	triptolide 66µg	8	185±7	200±7**	208±7***

Compared with control: **P<0.05 ***P<0.01

The above results indicated that the primary affection of swelling was the most obvious at half a month after inject adjuvant, and it of the capsule group was relieved obviously. The opposite side of pedes and the joint of forward pedes were swelling with no injection, namely the secondary affection of immunoreactive inflammation. This kind of inflammation was also obviously relieved in capsule group with high, middle and low dosage. The rats in control group ate less, and their body weigh was decreased. Compared with capsule group, the significance difference between the control and the capsule was obvious at the 25th day.

4. Effect on Capillary Permeability of Mouse's Abdominal Cavity

50 white mice, with body weight of 20-24g, half female and half male, were randomly divided into four groups: high, center, and the low dosage (lavage) of the said capsule, Hydrocortisone (i.m) group and control group. The mouse were administered once a day for 5 days, inject intravenously 0.1ml/10g of 0.5% azovan blue isotonic Na chloride into each mouse tail after 1 hour of the last administration, then intraperitoneal inject with 0.2ml of 0.6% glacial acetic acid physiological saline to each. Then execute them on cervical vertebra after 20 minutes, cut the belly open, flush the abdominal cavity with 6ml of the physiological saline for several times, collect the eluates , add isotonic Na chloride to 10ml, centrifuge at 3000 rpm for 15

minutes, measure the absorbability of supernatant at wave length of 590nm. The results were shown in Table 6. When the abdominal cavity inflammation was induced by acetic acid and capillary permeability was increased, the effusion of influxed staining solution and the capillary permeability were reduced by the use of the said capsule, which demonstrated the said capsule had the anti-inflammation function. The difference between high dose group and control group was obvious statistically.

Table 6 Effect on the Increase of Capillary Permeability of Rat Abdominal Cavity

Group	Dosage (g/kg)	Route of administration	Number of rat	Absorbability of colorant from abdominal cavity $\bar{X} \pm S$	Inhibition ratio (%)	P
Control group			10	0.172 $\pm$ 0.091		
The said capsule group	3	ig	8	0.101 $\pm$ 0.021	41.3	<0.05
The said capsule group	1.5	ig	7	0.116 $\pm$ 0.064	32.6	>0.05
The said capsule group	0.75	ig	9	0.110 $\pm$ 0.023	36.0	>0.05
Hydrocortisone group	0.02	im	7	0.153 $\pm$ 0.054	11.0	>0.05

5 Effect on Leukoplania in Carboxymethyl Cellulose of Rat

24 rats with body weight of 300 $\pm$ 60g, half female and half male, were randomly divided into 4 groups of high, low dosage of the said capsule, Radix Tripterygii Wilfordii Tablets group and control group, 6 rats each group. Gaster-poured once a day for 3 days continuously. On second day of administration, cut and sterilize every rat's capill on the nape, hypodermoclysis infuse with 5ml of air. On the next day, infuse 5ml of 1.5% carboxymethyl cellulose(CMC) physiological saline into air sac for inflammation, draw-off 0.1ml of CMC liquid from air sac after 3 and 7.5 hours respectively, influx it into 3ml of brilliant cresyl blue staining solution, mix well and stain, count the number of leucocytes under microscope. The results were shown in Table 7. As a bland pro-inflammatory agent, CMC was injected into rat subcutaneously, inducing aggregation of leucocyte partly, increasing lencocyte count of displacing liquid. The count of control group was higher than normal general one, whereas each administration group was decreased, which indicates that the acute inflammatory was inhibited. As a result of the larger error method, only a low dose of three hours

of lower value compared with control group had statistically significant differences.

Table 7 Effect on Euko (cyto) Plania in Subcutaneous CMC of Rat

Group	Dosage (g/kg)	Number of rat	Number of leucocyte in CMC ($10^9/L$)	
			3 hours	7.5 hours
Control group		6	11.4±5.6	18.8±9.0
The said capsule group	4	6	8.7±1.9	12.8±7.5
The said capsule group	2	6	5.6±2.1**	12.2±3.3
Tripterygium Wilfordii group	triptolide 66µg	6	7.8±2.0	13.3±2.8

6. Effect on the formation of granuloma of rat's tampon

50 rats with body weight of $168 \pm 11g$ were randomly divided into six groups: high, middle, and the low dosage of the said capsule, Tripterygium Wilfordii group and control group, 10 rats each group. Incise on median line of the lower abdomen, embed 20mg of autoclaved cotton ball into left and right subcutaneous groin respectively using tweezers for eyes. Gaster-poured on that day, once a day for 7 days. Execute the rats and strip the tampon wrapped with granulation tissue, and place it in baking oven at temperature of $50^\circ C$, weigh after 12 hours, the resultant weight minus the weight of cotton ball was thus net weight of granuloma. The results were shown in Table 8. The subjects of high, medium dose can significantly reduce the weight of granuloma that inhibit desmoplasia of chronic inflammation.

Table 8 Effect on the formation of granuloma of rat's tampon

Group	Dosage (g/kg)	Number of rat	Granuloma (mg)	P
Control group		10	99.8±16.5	
The said capsule group	3	10	81.0±5.4	<0.01
The said capsule group	1.5	10	84.5±5.3	<0.05
The said capsule group	0.75	10	98.3±16.1	>0.05
Tripterygium Wilfordii group	triptolide 66µg	10	82.2±11.0	<0.05

Example 2: the said capsule's analgesic effect

1. Hot Plate method

Provide female mouse (unpregnancy) with body weight of 18 to 22 grams, and put them on the metal plate of thermostatic waterbath at a temperature of $55\pm 0.5^{\circ}\text{C}$ respectively. Record the reaction time between the time the mouse was put on the hot plate to the time they lick their metalegs using electric 1/100 stop watch. Choose 50 mouse whose reaction time range from 10-30 seconds, and randomized them into 5 groups: the high, middle and low dosage of the said capsule group respectively, the *Tripterygium Wilfordii* group and control group, with 10 mouse in each group. Gaster-poured once a day for 7 days continuously. After one hour after the last administration, record the hot plate reaction time as the method mentioned above, and count the extended rate of reaction time and significance of difference of each administration group compared with control group. The result had been shown at Table 9. Each dosages of the said capsule can significantly prolong the reaction time of heat stimulation, and increase threshold of pain.

Table 9 Effect on reaction times by hot plate method to mouse

Group	Dosage (g/kg)	Numbers of mouse	RT (s)	Change rate (%)	P
Control group		10	22.1 ± 5.8	100	<0.01
The said capsule group	3	10	64.1 ± 7.9	290	<0.01
The said capsule group	1.5	10	46.5 ± 8.2	210	<0.01
The said capsule group	0.75	10	38.6 ± 6.8	175	<0.01
<i>Tripterygium Wilfordii</i> group	triptolide $66\mu\text{g}$	10	65.8 ± 7.5	298	<0.01

2. Writhing method to mouse

50 mouse were randomly divided into 5 groups, 10 mouse each group, and half male and half female. Gaster-poured once a day for 7 days continuously. After one hour after the last administration, inject each mouse (i.p.) 0.1ml/10g of 0.6% acetic solution, and observe each one's reactive writhing times immediately in 20 minutes. Count reactive inhibition ratio and significance of difference of each administration group compared with control group. As can be seen from Table 10, the said capsule can reduce over 50% of the pain induced by injecting acetic solution, and the difference was of highly significance.

Table 10 Effect on writhing response to mouse injected with acetic acid

Group	Dosage (g/kg)	Numbers of mouse	Writhing times ($\bar{X} \pm SD$)	Inhibition ratio (%)	P
Control group		10	48.4 $\pm$ 8.8		
The said capsule group	3	10	11.3 $\pm$ 4.5	76.6	<0.01
The said capsule group	1.5	10	18.1 $\pm$ 6.7	62.6	<0.01
The said capsule group	0.75	10	22.7 $\pm$ 7.6	53.1	<0.01
Tripterygium wilfordii group	triptolide 66 μ g	10	10.6 $\pm$ 4.5	78.1	<0.01

Example 3: The said capsule's function of immunological regulation

1. Effect on interleukin-1 (IL-1) activity of the rat with adjuvant-induced arthritis

Fizzer complete adjuvant (from Sigma Co.) was emulsified and injected subcutaneously and sterilely 0.1ml into the right meta voix pedis of each rat (σ^3 , 160 $\pm$ 20g) to establish a model of adjuvant-induced arthritis.

Preparation of peritoneal macrophage: Execute rats at 25th days after injecting complete adjuvant, then rapidly inject proper amount of Hank's solution into the belly of them, and rub their abdominal wall several times before collecting peritoneal fluid. Wash it with Hank's solution containing 5% calf serum twice, then prepare 1 $\times$ 10⁶/mL cell suspension with wholly swelling RPMI1640. Transfer into a culture plate with 24 wells, 1ml each well. Incubate them in a 5% CO₂ incubator overnight at a temperature of 37°C, abandon the supernatant fluid, wash with pre-warmed Hank's solution containing 5% calf serum at 37°C twice, and remove un-adherent cell. The residue was peritoneal macrophage.

2. IL-1 induction: Add 10 μ g/mL lipopolysaccharide (LPS) to the above culture plate with 24 wells, then incubate for 24 hours, centrifuge (2000rpm, 5min), collect the peritoneal fluid, and filter with micropore filter. This solution was the IL-1 sample to be detected.

3. Measurement of IL-1 bioactivity: Take 2-3 months Balb/c mouse's thymus at sterile condition, put it into flat plate containing Hank's solution, levigate through 100 mesh grit, filter with nylon net till it becomes

unicell suspension, wash twice with Hank's solution, and centrifugal method (1500rpm. 5min). Prepare mixed solution with ConA (2μg/mL) and thymocyte (1.5×10^7 /mL) with wholly swelling RPMI solution. Add 100μl of the above mixed solution and 100μl of the IL-1 sample to each well of culture plate with 96 wells, then incubate them for 72 hours in incubator containing 5% CO₂, add 10μl of 5mg/mL NTT to each well at 4 hours before termination, dissolve formazan granules with 150μL of acidic isopropanol (contain 0.04mol/L HCl) after 4 hours. Determine OD value by ELIASA on the wavelength of 570nm within 30 minutes. The results were shown in Table 11.

Table 11 Effect on IL-1 activity of AA rats

Group	Dosage (g/kg)	Number of rats	OD Value
Control group		6	0.24±0.01***
Model group		6	0.87±0.03
The said capsule group	5	6	0.48±0.03***
The said capsule group	2.5	6	0.54±0.01***
Prednisone group	5mg	6	0.34±0.02***

Compared with model group: ***P<0.01

The result indicates that LPS induce AA rat's PM_φ and releases IL-1 obviously above the normal level. The said capsule's function of inhibiting LPS and inducing rats release IL-1 indicates that it can inhibit or adjust AA rat's PM_φ releasing IL-1 exorbitantly.

2. Effect on mouse's DTH T cell subsets

36 Balb/c mice were randomly divided into 6 groups: control group, model group, said capsule high dosage group, said capsule middle dosage group, said capsule low dosage group and prednisone group, 6 mice each group. Smear barium sulfide suspension on the belly of 5 groups of mice to depilate, except the control group. Smear 25μl of 1% DNFB on each mouse's belly to cause sensitization the next day. On the second day smear again to strengthen the function. On the fifth day, smear 10μl of identical concentration of DNFB on each mouse's right ear, and execute the mouse 24 hours later, then take the splenic lymphocyte and carry out the detection of T cell subsets.

Methods: Dilute rat anti-mouse L_3T_4 and Lyt-2 monoclonal antibody with 0.1 NPBS by the ratio of 1:10 and FITC-rabbit anti-rat IgG monoclonal antibody with 0.1 MPBS by the ratio of 1:10. Imbibe 50 μ l of cultured splenic lymphocyte (2×10^6 Unit/mL) induced by ConA (2 μ g/mL) and transfer to V-type plate with 96 wells, centrifuge (1700rpm, 5min), abandon supernatant fluid, add 40 μ l of anti- L_3T_4 or Lyt-2 monoclonal antibody and mix with 40 μ l of RPMI1640 solution for non-specific stain as control. React in refrigerator at 4°C for 30 minutes. Add 100 μ l of Hank's solution to each well and centrifuge (1700rpm, 5min) for 3 times, abandon supernatant fluid, then add 40 μ l of FITC-rabbit anti-rat IgG and mix them up, react for 30 minutes in 4°C refrigerator. Add 100 μ L of Hank's solution in each well, and centrifuge (1700rpm, 5min), repeat for 3 times, abandon supernatant fluid. Add 10 μ L of Hank's solution in each well and mix well. Take 10 μ l of the above solution on a blood counting chamber and count the number under fluorescence microscope (excitation light at 490nm, barrier filter plate's transmission range from 520 to 530nm). Count 200 cells of each sample and observe the number of masc-fluorescyte cells in the above 200 cells. The number of masc-fluorescyte cells subtracting the number of non-specific stain masc-fluorescyte cells equals to the number of L_3T_4 or Lyt-2 masc-fluorescyte cells. As is shown in Table 12, the said capsule group of high dosage had the trend of increasing yt-2⁺ and decreasing the ratio of L_3T_4 (P<0.05).

Table 12 Effect on DTH T cell subsets of mouse

Group	Dosage (g/kg)	Numbers of mouse	Cells number (%)		$L_3T_4^+ / \text{Lyt-2}^+$
			$L_3T_4^+$	Lyt-2 ⁺	
Control group		6	54.1 $\pm$ 1.9	45.6 $\pm$ 2.7	1.19 $\pm$ 0.07***
Model group		6	64.9 $\pm$ 4.6	40.3 $\pm$ 2.1	1.56 $\pm$ 0.10
The said capsule group	5	6	62.7 $\pm$ 3.7	47.7 $\pm$ 5.4	1.34 $\pm$ 0.28**
The said capsule group	2.5	6	67.5 $\pm$ 4.2	45.4 $\pm$ 3.0	1.49 $\pm$ 0.14
The said capsule group	1.25	6	69.7 $\pm$ 3.7	40.0 $\pm$ 2.5	1.53 $\pm$ 0.10
Prednisone group	5mg	6	59.6 $\pm$ 7.5	56.2 $\pm$ 3.8***	1.21 $\pm$ 0.14***

Compared with control: **P<0.05, ***P<0.01

The dosage of the said capsule for human use was 2g each time, 3 times per day, and the total amount was

6g a day; the average dosage a day for adult (calculated by 60kg) was 0.1g/kg. Tripterygium Wilfordii Tablet was used as control drug, its dosage was 2 tablets each time, 3 times per day, and the total amount was 6 tablets per day which corresponds to 198µg of triptolide, and the average dosage a day was 3.3µg/kg by weight. The multiple of animal dosage to human dosage was converted by the above cardinal number.

The following examples have the same effect as the above experiments.

Example 1: Capsule

Ant	330g
Radix Salviae Miltiorrhizae	120g
Radix Aconiti Preparata	60g
Radix Ginseng	40g
Caulis Spatholobi	60g
Ramulus Cinnamomi	40g
Semen Coicis	60g
Cortex Kalopanax	60g
Herba speranskiae tuberculatae	60g
Cortex Phellodendri	40g
Rhizoma Atractylodis	40g
Rhizoma Alismatis	40g
Herba Lycopodii	40g
Scolopendra	5g
Zaocys	5g

1000 capsules were prepared according to normal manufacturing process. 0.5g each capsule, 3 times per day, 4 capsules each time.

Example 2: Capsule

Ant	400g
Radix Salviae Miltiorrhizae	130g
Radix Aconiti Preparata	65g
Radix Ginseng	50g

Caulis Spatholobi	50g
Ramulus Cinnamomi	30g
Semen Coicis	50g
Cortex Kalopanax	50g
Herba speranskiae tuberculatae	50g
Cortex Phellodendri	30g
Rhizoma Atractylodis	45g
Rhizoma Alismatis	30g
Herba Lycopodii	30g
Scolopendra	8g
Zaocys	8g

Pulverize ant, Radix Ginseng, Radix Aconiti Preparata, Scolopendra, Zaocys into fine powder, sieve and mix it; pulverize Radix Salviae Miltiorrhizae, Ramulus Cinnamomi, Rhizoma Atractylodis into coarse power respectively, percolate with 90% alcohol as solvent, evaporate alcohol from percolate, pressure reduction concentrate the percolate by recovering alcohol to obtain the extract with relative density of 1.30-1.32(55°C). Combine the residues with Caulis Spatholobi, Semen Coicis, Cortex Kalopanax, herba speranskiae tuberculatae, Cortex Phellodendri chinensis, Rhizoma Alismatis and Herba Lycopodii with water to decoct twice, 1.5 hours each time. Combine all the decoctions, filter, pressure reduction concentrate the filtrates to obtain the extract with relative density of 1.35-1.38(60°C). Mix the above fine power and each of extracts, mix well and make granules, dry, crush, sieve and fill in capsule for use. Fill in capsule, and each capsule contains 0.5g. Usage: take orally, with 4 capsules per time, 3 times per day.

Example 3: Oral Liquid

Ant	330g
Radix Salviae Miltiorrhizae	120g
Radix Aconiti Preparata	60g
Radix Ginseng	40g
Caulis Spatholobi	60g
Ramulus Cinnamomi	40g

In above six crude drugs, pulverize ant, Radix Ginseng, Radix Aconiti Preparata into fine powder, sieve and mix well; pulverize Radix Salviae Miltiorrhizae, Ramulus Cinnamomi into coarse power respectively, percolate with 90% alcohol as solvent, pressure reduction concentrate the percolate by recovering alcohol to obtain the extract with relative density of 1.30-1.32(55°C). Combine the residues with Caulis Spatholobi and decoct with water, filter, pressure reduction concentrate the filtrates to obtain the extract with relative density of 1.35-1.38(60°C). Mix the above fine power and the extracts of Radix Salviae Miltiorrhizae and the others, mix well and make granules. Extract the granules for 3 times with 60% alcohol, 2 hours for the first time, 1 hour for the second and third time each. Filter, then combine the filtrates, recover to non-alcohol. Add water to established amount, mix well, stand, filter, add sodium benzoate to the filtrate, heat to boil, cold, subpackage, sterilize and make oral liquid for use. Usage: take orally, 10ml each time, 3 times each day.

Example 4: Granule

Ant	400g
Radix Salviae Miltiorrhizae	130g
Radix Aconiti Preparata	65g
Radix Ginseng	50g
Caulis Spatholobi	50g
Ramulus Cinnamomi	30g

In above six crude drugs, pulverize ant, Radix Ginseng and Radix Aconiti Preparata to fine powder, sieve, and mix well; pulverize Radix Salviae Miltiorrhizae and Ramulus Cinnamomi to coarse powder respectively, percolate with 90% alcohol as solvent, pressure reduction concentrate the percolate by recovering alcohol to obtain the extract with relative density of 1.30-1.32(55°C). Combine the residues with Caulis Spatholobi and decoct with water, filter, pressure reduction concentrate the filtrates to obtain the extract with relative density of 1.35-1.38(60°C), combine the above fine powder and extracts of Radix Salviae Miltiorrhizae and the other crude drugs, mix well, then add proper amount of cane-sugar and dextrin, mix well, make granules with alcohol, dry and fill in bags for use. Usage: take orally, 3g each time, 3 times each day.

Example 5: Dropping Pill

Ant	400g
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Radix Salviae Miltiorrhizae	130g
Radix Aconiti Preparata	65g
Radix Ginseng	50g
Caulis Spatholobi	50g
Ramulus Cinnamomi	30g
Cortex Kalopanax	50g
Herba speranskiae tuberculatae	50g
Cortex Phellodendri	30g
Rhizoma Atractylodis	45g
Rhizoma Alismatis	30g
Herba Lycopodii	30g
Semen Coicis	50g

Pulverize ant, Radix Ginseng and Radix Aconiti Preparata to fine powder, sieve, and mix well; pulverize Radix Salviae Miltiorrhizae, Ramulus Cinnamomi and Rhizoma Atractylodis to coarse powder respectively, percolate with 90% alcohol as solvent, and pressure reduction concentrate the percolate by recovering alcohol to obtain the extract with relative density of 1.30-1.32(55°C). Combine the residues with Caulis Spatholobi, Semen Coicis, Cortex Kalopanax, Herba speranskiae tuberculatae, Cortex Phellodendri, Rhizoma Alismatis, and Herba Lycopodii, decoct with water, filter, pressure reduction concentrate the filtrates to obtain the extract with relative density of 1.35-1.38(60°C), combine the above fine powder and extracts of Radix Salviae Miltiorrhizae and the other crude drugs, mix well, make granules. Add the above granules in PEG molten by hexane, stir well, transfer the mixture to the feeding container of a dropping machine, keep the temperature (90°C) and drop into methyl silicone oil cooled until 5~10°C at the speed of 30 r/min. After shaping, take out of the dripping pills, and remove the coolant by absorption, and dry for use. Usage: take orally, 10 pills each time, 3 times each day.

Example 6: Soft Capsule

Ant	330g
Radix Salviae Miltiorrhizae	120g
Radix Aconiti Preparata	60g
Radix Ginseng	40g

Caulis Spatholobi	60g
Ramulus Cinnamomi	40g
Semen Coicis	60g
Cortex Kalopanax	60g
Herba speranskiae tuberculatae	60g
Cortex Phellodendri	40g
Rhizoma Atractylodis	40g
Rhizoma Alismatis	40g
Herba Lycopodii	40g

Pulverize ant, Radix Ginseng and Radix Aconiti Preparata to fine powder, sieve, and mix well; pulverize Radix Salviae Miltiorrhizae, Ramulus Cinnamomi and Rhizoma Atractylodis to coarse powder respectively, percolate with 90% alcohol as solvent, and pressure reduction concentrate the percolate by recovering alcohol to obtain the extract with relative density of 1.30-1.32(55°C). Combine the residues with Caulis Spatholobi, Semen Coicis, Cortex Kalopanax, Herba speranskiae tuberculatae, Cortex Phellodendri, Rhizoma Alismatis, and Herba Lycopodii, then decoct with water, combine all the decoction, filter, pressure reduction concentrate the filtrates to obtain the extract with relative density of 1.35-1.38(60°C), combine the above fine powder and extracts of Radix Salviae Miltiorrhizae and the other crude drugs, mix well, make granules. Take two thirds of the above granules and add 55% alcohol, stir well, stand for 30 hours to obtain the supernatant, recover alcohol from supernatant, concentrate and dry, mix with residue third of the granules, crush to impalpable powder, add proper amount of beeswax and vegetable oil, stir well, make suspension, then compress into soft capsules for use. Usage: take orally, 4 capsules each time, 3 times each day.

Example 7: Dropping Pill

Ant	330g
Radix Salviae Miltiorrhizae	120g
Radix Aconiti Preparata	60g
Radix Ginseng	40g
Caulis Spatholobi	60g
Ramulus Cinnamomi	40g

Semen Coicis	60g
Cortex Kalopanax	60g
Herba speranskiae tuberculatae	60g
Cortex Phellodendri	40g
Rhizoma Atractylodis	40g
Rhizoma Alismatis	40g
Herba Lycopodii	40g
Scolopendra	5g
Zaocys	5g

Pulverize ant, Radix Ginseng, Radix Aconiti Preparata, Scolopendra, and Zaocys to fine powder, sieve, and mix well; pulverize Radix Salviae Miltiorrhizae, Ramulus Cinnamomi and Rhizoma Atractylodis to coarse powder respectively, percolate with 90% alcohol as solvent , and pressure reduction concentrate the percolate by recovering alcohol to obtain the extract with relative density of 1.30-1.32(55°C). Combine the residues with Caulis Spatholobi, Semen Coicis, Cortex Kalopanax, Herba speranskiae tuberculatae, Cortex Phellodendri, Rhizoma Alismatis, and Herba Lycopodii, then decoct with water for two times, 1.5 hours each time, combine all the decoction, filter, pressure reduction concentrate the filtrates to obtain the extract with relative density of 1.35-1.38(60°C), combine the above fine powder and each of extracts, mix well, make granules. Add the above granules in PEG molten by hexane, stir well, transfer the mixture to the feeding container of a dropping machine, keep the temperature (90°C) and drop into methyl silicone oil cooled until 5~10°C at the speed of 30 r/min. After shaping, take out of the dripping pills, and remove the coolant by absorption, and dry for use.

Claims

1. A traditional Chinese medicine composition to treat Rheumatoid Arthritis, wherein the crude drugs for preparing the said composition include the crude drugs with the following weight ratio:

Ant	280-500 parts
Radix Salviae Miltiorrhizae	100-200 parts
Radix Aconiti Preparata	35-100parts
Radix Ginseng	20-80 parts
Caulis Spatholobi	30-75 parts
Ramulus Cinnamomi	25-80 parts.

2. A Chinese traditional medicine composition according to Claim 1, wherein the crude drugs for preparing the said composition include the crude drugs with the following weight ratio:

Ant	300-400 parts
Radix Salviae Miltiorrhizae	120-150 parts
Radix Aconiti Preparata	40-70parts
Radix Ginseng	30-50 parts
Caulis Spatholobi	40-60 parts
Ramulus Cinnamomi	35-50 parts.

3. A Chinese traditional medicine composition according to Claim 1, wherein the crude drugs for preparing the said composition include the crude drugs with the following weight ratio:

Ant	280-500 parts
Radix Salviae Miltiorrhizae	100-200 parts
Radix Aconiti Preparata	35-100 parts
Radix Ginseng	20-80 parts
Caulis Spatholobi	30-75 parts
Ramulus Cinnamomi	25-80 parts
Cortex Kalopanax	25-70 parts
Herba speranskiae tuberculatae	25-70 parts
Cortex Phellodendri	25-70 parts

Rhizoma Atractylodis	25-70 parts
Rhizoma Alismatis	25-70 parts
Herba Lycopodii	25-70 parts
Semen Coicis	35-70 parts.

4. A Chinese traditional medicine composition according to Claim 3, wherein the crude drugs for preparing the said composition include the crude drugs with the following weight ratio:

Ant	300-400 parts
Radix Salviae Miltiorrhizae	120-150 parts
Radix Aconiti Preparata	40-70 parts
Radix Ginseng	30-50 parts
Caulis Spatholobi	40-60 parts
Ramulus Cinnamomi	35-50 parts
Cortex Kalopanax	35-50 parts
Herba speranskiae tuberculatae	35-50 parts
Cortex Phellodendri	35-50 parts
Rhizoma Atractylodis	35-50 parts
Rhizoma Alismatis	35-50 parts
Herba Lycopodii	35-50 parts
Semen Coicis	45-70 parts.

5. A Chinese traditional medicine composition according to Claim 1, wherein the composition is prepared by the crude drugs with the following weight ratio:

Ant	280-500 parts
Radix Salviae Miltiorrhizae	100-150 parts
Radix Aconiti Preparata	35-70 parts
Radix Ginseng	20-50 parts
Caulis Spatholobi	30-75 parts
Semen Coicis	35-70 parts
Cortex Kalopanax	25-70 parts
Herba speranskiae tuberculatae	25-70 parts

Cortex Phellodendri	25-50 parts
Rhizoma Atractylodis	25-50 parts
Rhizoma Alismatis	25-50 parts
Herba Lycopodii	25-50 parts
Ramulus Cinnamomi	25-50 parts
Scolopendra	4-10 parts
Zaocys	4-10 parts.

6. A Chinese traditional medicine composition according to Claim 5, wherein the composition is prepared by the crude drugs with the following weight ratio:

Ant	300-400 parts
Radix Salviae Miltiorrhizae	120-140 parts
Radix Aconiti Preparata	45-60 parts
Radix Ginseng	20-50 parts
Caulis Spatholobi	45-60 parts
Semen Coicis	45-60 parts
Cortex Kalopanax	35-60 parts
Herba speranskiae tuberculatae	35-60 parts
Cortex Phellodendri	25-40 parts
Rhizoma Atractylodis	25-40 parts
Rhizoma Alismatis	25-40 parts
Herba Lycopodii	25-40 parts
Ramulus Cinnamomi	25-40 parts
Scolopendra	4-10 parts
Zaocys	4-10 parts.

7. A Chinese traditional medicine composition according to Claim 6, wherein the composition is prepared by the crude drugs with the following weight ratio:

Ant	330 parts
Radix Salviae Miltiorrhizae	120 parts
Radix Aconiti Preparata	60 parts

Radix Ginseng	40 parts
Caulis Spatholobi	60 parts
Semen Coicis	60 parts
Cortex Kalopanax	60 parts
Herba speranskiae tuberculatae	60 parts
Cortex Phellodendri	40 parts
Rhizoma Atractylodis	40 parts
Rhizoma Alismatis	40 parts
Herba Lycopodii	40 parts
Ramulus Cinnamomi	40 parts
Scolopendra	5 parts
Zaocys	5 parts.

8. A traditional Chinese medicine composition according to Claim 1-7, characterized in that it can be made into various Clinical acceptable dosage forms including: tablets, capsules, pills, granules, suspension, dripping pills, oral liquid preparation.

9. A traditional Chinese medicine composition according to Claim 5-7, characterized in that preparing the capsules by the following method: pulverize ant, Radix Ginseng, Radix Aconiti Preparata, Scolopendra and Zaocys into fine powder, sieve, and mix well; pulverize Radix Salviae Miltiorrhizae, Ramulus Cinnamomi and Rhizoma Atractylodis to coarse powder respectively, percolate with 70-90% alcohol as solvent, pressure reduction concentrate the percolate by recovering alcohol to obtain the extract with relative density of 1.30-1.32 at 55°C. Combine the residues with Caulis Spatholobi, Semen Coicis, Cortex Kalopanax, Herba speranskiae tuberculatae, Cortex Phellodendri, Rhizoma Alismatis, and Herba Lycopodii, then decoct with water for two times, 1.5 hours each time, combine all the decoction, filter, pressure reduction concentrate the filtrates to obtain the extract with relative density of 1.35-1.38 at 60°C, combine the above fine powder and extracts of Radix Salviae Miltiorrhizae and the other crude drugs, mix well, make granules, dry, crush, sieve, and fill into capsules for use.

10. A traditional Chinese medicine composition according to Claim 5-7, characterized in that preparing the dropping pills by the following method: pulverize ant, Radix Ginseng, Radix Aconiti Preparata,

Scolopendra, and Zaocys into fine powder, sieve, and mix well; pulverize Radix Salviae Miltiorrhizae, Ramulus Cinnamomi and Rhizoma Atractylodis into coarse powder respectively, percolate with 70-90% alcohol as solvent, and pressure reduction concentrate the percolate by recovering alcohol to obtain the extract with relative density of 1.30-1.32 at 55°C. Combine the residues with Caulis Spatholobi, Semen Coicis, Cortex Kalopanax, Herba speranskiae tuberculatae, Cortex Phellodendri, Rhizoma Alismatis, and Herba Lycopodii, then decoct with water for two times, 1.5 hours each time, combine all the decoction, filter, pressure reduction concentrate the filtrates to obtain the extract with relative density of 1.35-1.38 at 60°C, combine the above fine powder and extracts of Radix Salviae Miltiorrhizae and the other crude drugs, mix well, make granules, add the above granules in PEG molten by hexane, stir well, transfer the mixture to the feeding container of dropping machine, keep the temperature at 90°C and drop into methyl silicone oil cooled until 5~10°C at the speed of 30 r/min, take out the dripping pills and remove the coolant by absorption, and dry for use.