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(73) Titulaire(s):
INNER MONGOLIA MINZU UNIVERSITY – Tongliao (China)

(72) Inventeur(s):
BAO Liming – China

(74) Mandataire(s):
BAUER-IP – 14800 Praha (Czech Republic)

(54) **MONGOLIAN MEDICINE COMPOSITION CAPSULE FOR TREATING AND PREVENTING CEREBRAL STROKE AND PREPARATION METHOD THEREOF.**

(57) The invention relates to the technical field of medicines, and in particular to a Mongolian medicine composition capsule for treating and preventing cerebral stroke and a preparation method thereof; the Mongolian medicine composition capsule comprises a capsule shell and contents, wherein the contents comprise the following raw materials in parts by weight: 30-40 parts of Panax notoginseng, 36-44 parts of Roselle Thistle, 15-20 parts of Fructus Choerospondiatis, 20-30 parts of Clematis, 25-32 parts of Ginseng, 20-30 parts of synergist, and 8-12 parts of promoter. The invention also provides a preparation method of the Mongolian medicine composition capsule for treating and preventing cerebral stroke. The raw materials are easily available, the process is simple, and a variety of Mongolian medicines are combined to achieve synergistic enhancement. The prepared capsule can effectively treat and prevent cerebral stroke caused by various causes without toxic side effects. The synergist and promoter can enhance the therapeutic effect and improve the absorption and utilization rate of the drug.

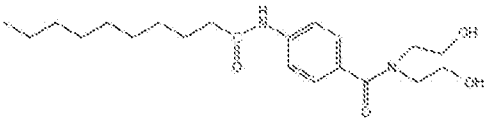

FIG. 1

MONGOLIAN MEDICINE COMPOSITION CAPSULE FOR TREATING AND PREVENTING CEREBRAL STROKE AND PREPARATION METHOD THEREOF

TECHNICAL FIELD

The invention relates to the technical field of medicines, and in particular to a Mongolian medicine composition capsule for treating and preventing cerebral stroke and a preparation method thereof.

BACKGROUND ART

Cerebral stroke is a common and serious neurological disease. Risk factors for cerebral stroke (hypertension, hyperglycemia, etc.) and ischemia can lead to the activation of reactive oxygen species (ROS)-related enzyme systems, produce a large amount of ROS, and cause oxidative stress. After the onset of cerebral stroke, superoxide dismutase (SOD), reduced glutathione (GSH), catalase (CAT), glutathione peroxidase (GSH Px), and total antioxidant capacity (TAC) are significantly reduced, and malondialdehyde (MDA) is significantly increased. The high morbidity and mortality of stroke has placed a huge burden on patients. Therefore, the treatment and prevention of stroke are crucial to the life and quality of life of patients. Early acute treatment and comprehensive rehabilitation treatment can minimize brain damage, restore function, and improve the quality of life and prognosis of patients. Mongolian medicine is a type of traditional Chinese medicine, which is believed to have the effects of harmonizing qi and blood, promoting blood circulation and removing blood stasis, and dispelling wind and unblocking collaterals in traditional Chinese medicine theory. In recent years, more and more studies have shown that the active ingredients in Mongolian medicine have biological activities such as anti-inflammatory, antioxidant, anticoagulant, and angiogenesis promotion, and may have potential effects on the treatment and prevention of stroke. At present, drugs for the treatment of stroke mainly include thrombolytic drugs and anticoagulant drugs. However, thrombolytic drugs need to be used within a few hours after the occurrence of stroke and cannot play a preventive effect. In addition, these drug

compositions often have a single efficacy, or poor safety and low bioavailability.

SUMMARY OF THE INVENTION

In view of the above technical problems, the invention provides a Mongolian medicine composition capsule for treating and preventing cerebral stroke and a preparation method thereof.

The invention is achieved by the following technical solutions.

A Mongolian medicine composition capsule for treating and preventing cerebral stroke, comprising a capsule shell and contents, wherein the contents comprise the following raw materials in parts by weight: 30-40 parts of Panax notoginseng, 36-44 parts of Roselle Thistle, 15-20 parts of Fructus Choerospondiatis, 20-30 parts of Clematis, 25-32 parts of Ginseng, 20-30 parts of synergist, and 8-12 parts of promoter;

further, the preparation method of the synergist includes the following steps:

(1) mixing Spirulina platensis, Staurastrum crenulatum, and water evenly with a mass ratio of 1:1:30 to obtain a mixed algae solution, adjusting the pH value to 5-6, adding a biological enzyme, stirring at 80 rpm for 3-5 hours, and heating to 95℃ and maintaining 20 minutes to obtain a hydrolyzate;

(2) centrifuging the hydrolyzate obtained in step (1) at 4000 r/min for 10 minutes, concentrating the supernatant at 0.01 MPa and 60℃ for 4 hours and then freeze-drying it to obtain the synergist.

Further, the biological enzyme in step (2) is a mixture of acidic cellulase, neutral cellulase, and papain in a mass ratio of 2:1:1.2.

Further, in step (2), the mass ratio of the biological enzyme to the mixed algae liquid is 1:1000.

Further, the preparation method of the promoter includes the following steps:

I. in an ice-water bath, adding diethanolamine and p-aminobenzoyl chloride to a dimethylformamide solvent, and then adding pyridine and triethylamine, stirring at 100 rpm for 15-20 minutes, and stirring to react at 25℃ for 24 hours to obtain a reaction mixture I;

II. adding decanoic acid to the reaction mixture I obtained in step I, and the molar ratio of decanoic acid to p-aminobenzoyl chloride is 1:1; then adding dimethyl carbonate, and the

mass ratio of dimethyl carbonate to p-aminobenzoyl chloride is 9:13; stirring at 25℃ and 60 rpm for 6-8 hours to obtain a reaction mixture II;

III. concentrating the reaction mixture II obtained in step II under reduced pressure to 30% of the original volume; washing with acetone three times, recrystallizing in tetrahydrofuran, filtering, washing with 95wt% ethanol solution and deionized water three times in sequence, and drying in vacuum at 40-50℃ for 2-3 hours to obtain the promoter.

Further, in step I, the amount ratio of diethanolamine, p-aminobenzoyl chloride, dimethylformamide, pyridine and triethylamine is 2 g:3 g:4 mL:0.6 g:0.3 g.

Further, the capsule is a hard capsule or a soft capsule.

Further, the capsule shell is prepared from gastric-soluble capsule excipients or enteric-soluble capsule excipients.

Further, the material of the capsule shell comprises but is not limited to one or more of gelatin, glycerol, sodium alginate, and starch.

The invention also provides a preparation method of the Mongolian medicine composition capsule for treating and preventing cerebral stroke, including the following steps:

S1: washing and drying Panax notoginseng, Fructus Choerospondiatis, Ginseng, Clematis, and Roselle Thistle, crushing through an 80-mesh sieve to obtain a Mongolian medicine mixture, heating to 60°C in a 1 mol/L citric acid solution and soaking for 2 hours; after filtering, rotating to evaporate the filtrate at 60°C for 1-2 hours and spraying to dry to obtain Mongolian medicine granules;

S2: mixing the Mongolian medicine granules, the promoter, and the synergist evenly, grinding through a 500-mesh sieve, sterilizing by ultraviolet light for 1 hour, and filling into capsules with each capsule containing 0.5 g to obtain a Mongolian medicine composition capsule for treating and preventing cerebral stroke.

Further, in step S1, the dosage ratio of the Mongolian medicine mixture to the citric acid solution is 1 g:8 mL.

Compared with the prior art, the invention has the following beneficial effects:

The invention selects and combines a variety of Mongolian medicines with the effect of treating and preventing cerebral stroke, creates a unique drug combination, can synergize, effectively treat and prevent cerebral stroke. Algae is a kind of plant rich in nutrients and

bioactive compounds. The invention uses Spirulina platensis and Staurastrum crenulatum to prepare a synergist, which has anti-thrombotic and neuroprotective effects, can improve cerebrovascular function, reduce the risk of cerebral stroke, and prevent the occurrence of cerebral stroke. The promoter of the invention can improve the solubility of the drug, enhance the bioaffinity of the drug, promote the absorption and utilization of the drug, and thus enhance the drug effect. The Mongolian medicine granules prepared by the invention have good biocompatibility and are more easily absorbed by the human body. The invention uses citric acid solution to extract Mongolian medicine, which can neutralize or degrade toxic substances in the medicinal materials, reduce the toxicity of the drug, and improve the safety of the drug.

BRIEF DESCRIPTION OF THE DRAWINGS

FIG. 1 is a chemical structure diagram of the promoter in Embodiment 1 according to the invention;

FIG. 2 is a nuclear magnetic resonance spectrum of the promoter in Embodiment 1 according to the invention, wherein a is a ^{1}H spectrum and b is a ^{13}C spectrum;

FIG. 3 is a scanning electron microscope image of the Mongolian medicine preparation in Embodiment 1 according to the invention;

FIG. 4 is a graph showing the cytotoxicity test of the contents of the capsules in Embodiments 1-2 and Comparative Embodiments 1-3 according to the invention;

FIG. 5 is a graph showing the effects of the contents of the capsules in Embodiments 1-2 and Comparative Embodiments 1-3 according to the invention on oxidative stress in rats;

FIG. 6 is a test graph of the dissolution rate of the capsule contents of in Embodiments 1-2 and Comparative Embodiments 1-3 according to the invention.

SPECIFIC EMBODIMENT OF THE INVENTION

In order to make the purpose, technical solutions and advantages of the invention more clearly understood, the invention will be further described in detail hereinafter with reference to specific embodiments, but the invention is not limited to the following embodiments.

It should be noted that, unless otherwise specified, the chemical reagents involved in the invention are purchased through commercial channels.

Embodiment 1: the embodiment provides Mongolian medicine composition capsule contents for treating and preventing cerebral stroke, comprising the following raw materials in parts by weight: 40 parts of Panax notoginseng, 44 parts of Roselle Thistle, 20 parts of Fructus Choerospondiatis, 30 parts of Clematis, 32 parts of Ginseng, 30 parts of synergist, and 12 parts of promoter;

the preparation method of the synergist includes the following steps:

(1) mixing Spirulina platensis, Staurastrum crenulatum, and water evenly with a mass ratio of 1:1:30 to obtain a mixed algae solution, adjusting the pH value to 6, adding a biological enzyme, and the mass ratio of the biological enzyme to the mixed algae liquid is 1:1000; the biological enzyme is a mixture of acidic cellulase, neutral cellulase, and papain in a mass ratio of 2:1:1.2; stirring at 80 rpm for 5 hours, and heating to 95℃ and maintaining 20 minutes to obtain a hydrolyzate;

(2) centrifuging the hydrolyzate obtained at 4000 r/min for 10 minutes, concentrating the supernatant at 0.01 MPa and 60 ℃ for 4 hours and then freeze-drying it to obtain the synergist.

the preparation method of the promoter includes the following steps:

I. in an ice-water bath, adding diethanolamine and p-aminobenzoyl chloride to a dimethylformamide solvent, and then adding pyridine and triethylamine, and the amount ratio of diethanolamine, p-aminobenzoyl chloride, dimethylformamide, pyridine and triethylamine is 2 g:3 g:4 mL:0.6 g:0.3 g; stirring at 100 rpm for 20 minutes, and stirring to react at 25℃ for 24 hours to obtain a reaction mixture I;

II. adding decanoic acid to the reaction mixture I obtained in step I, and the molar ratio of decanoic acid to p-aminobenzoyl chloride is 1:1; then adding dimethyl carbonate, and the mass ratio of dimethyl carbonate to p-aminobenzoyl chloride is 9:13; stirring at 25℃ and 60 rpm for 8 hours to obtain a reaction mixture II;

III. concentrating the reaction mixture II obtained in step II under reduced pressure to 30% of the original volume; washing with acetone three times, recrystallizing in tetrahydrofuran, filtering, washing with 95wt% ethanol solution and deionized water three times in sequence, and drying in vacuum at 50 ℃ for 3 hours to obtain the promoter; the chemical structure is shown in FIG. 1, the nuclear magnetic resonance spectrum is shown in

FIG. 2, and the molecular formula is $C_{21}H_{34}O_4N_2$.

The embodiment also provides a preparation method of the Mongolian medicine composition capsule for treating and preventing cerebral stroke, including the following steps:

S1: washing and drying Panax notoginseng, Fructus Choerospondiatis, Ginseng, Clematis, and Roselle Thistle, crushing through an 80-mesh sieve to obtain a Mongolian medicine mixture, heating to 60°C in a 1 mol/L citric acid solution and soaking for 2 hours, and the dosage ratio of the Mongolian medicine mixture to the citric acid solution is 1 g:8 mL; after filtering, rotating to evaporate the filtrate at 60°C for 2 hours and spraying to dry to obtain Mongolian medicine granules; the scanning electron microscope image of Mongolian medicine particles is shown in FIG. 3; the particle size is small, the shape is approximately spherical, and it is in a well-dispersed state, indicating that it has good stability and is easy to absorb and utilize;

S2: mixing the Mongolian medicine granules, the promoter, and the synergist evenly, grinding through a 500-mesh sieve, sterilizing by ultraviolet light for 1 hour to obtain a Mongolian medicine composition capsule for treating and preventing cerebral stroke.

Embodiment 2: the embodiment provides Mongolian medicine composition capsule contents for treating and preventing cerebral stroke, comprising the following raw materials in parts by weight: 30 parts of Panax notoginseng, 36 parts of Roselle Thistle, 15 parts of Fructus Choerospondiatis, 20 parts of Clematis, 25 parts of Ginseng, 20 parts of synergist, and 8 parts of promoter;

the preparation method of the synergist includes the following steps:

(1) mixing Spirulina platensis, Staurastrum crenulatum, and water evenly with a mass ratio of 1:1:30 to obtain a mixed algae solution, adjusting the pH value to 5, adding a biological enzyme, and the mass ratio of the biological enzyme to the mixed algae liquid is 1:1000; the biological enzyme is a mixture of acidic cellulase, neutral cellulase, and papain in a mass ratio of 2:1:1.2; stirring at 80 rpm for 3 hours, and heating to 95℃ and maintaining 20 minutes to obtain a hydrolyzate;

(2) centrifuging the hydrolyzate obtained at 4000 r/min for 10 minutes, concentrating the supernatant at 0.01 MPa and 60 ℃ for 4 hours and then freeze-drying it to obtain the synergist.

the preparation method of the promoter includes the following steps:

I. in an ice-water bath, adding diethanolamine and p-aminobenzoyl chloride to a dimethylformamide solvent, and then adding pyridine and triethylamine, and the amount ratio of diethanolamine, p-aminobenzoyl chloride, dimethylformamide, pyridine and triethylamine is 2 g:3 g:4 mL:0.6 g:0.3 g; stirring at 100 rpm for 15 minutes, and stirring to react at 25℃ for 24 hours to obtain a reaction mixture I;

II. adding decanoic acid to the reaction mixture I obtained in step I, and the molar ratio of decanoic acid to p-aminobenzoyl chloride is 1:1; then adding dimethyl carbonate, and the mass ratio of dimethyl carbonate to p-aminobenzoyl chloride is 9:13; stirring at 25℃ and 60 rpm for 6 hours to obtain a reaction mixture II;

III. concentrating the reaction mixture II obtained in step II under reduced pressure to 30% of the original volume; washing with acetone three times, recrystallizing in tetrahydrofuran, filtering, washing with 95wt% ethanol solution and deionized water three times in sequence, and drying in vacuum at 40℃ for 2 hours to obtain the promoter.

The embodiment also provides a preparation method of the Mongolian medicine composition capsule for treating and preventing cerebral stroke, including the following steps:

S1: washing and drying Panax notoginseng, Fructus Choerospondiatis, Ginseng, Clematis, and Roselle Thistle, crushing through an 80-mesh sieve to obtain a Mongolian medicine mixture, heating to 60°C in a 1 mol/L citric acid solution and soaking for 2 hours, and the dosage ratio of the Mongolian medicine mixture to the citric acid solution is 1 g:8 mL; after filtering, rotating to evaporate the filtrate at 60°C for 1 hour and spraying to dry to obtain Mongolian medicine granules;

S2: mixing the Mongolian medicine granules, the promoter, and the synergist evenly, grinding through a 500-mesh sieve, sterilizing by ultraviolet light for 1 hour to obtain a Mongolian medicine composition capsule for treating and preventing cerebral stroke.

The difference between Comparative Embodiment 1 and Embodiment 1 is that no synergist is added.

The only difference between Comparative Embodiment 2 and Embodiment 1 is that no promoter is added.

The only difference between Comparative Embodiment 3 and Embodiment 1 is that the

preparation method of the Mongolian medicine granules comprises the following steps: washing and drying Panax notoginseng, Fructus Choerospondiatis, Ginseng, Clematis, and Roselle Thistle, crushing through an 80-mesh sieve to obtain a Mongolian medicine mixture, adding the Mongolian medicine mixture into deionized water, and the dosage ratio of the Mongolian medicine mixture to the citric acid solution is 1 g:8 mL; heating to 60°C and soaking for 2 hours, after filtering, rotating to evaporate the filtrate at 60°C for 2 hours and spraying to dry to obtain Mongolian medicine granules.

Experimental Embodiment 1: determine cytotoxicity by the MTT method. Immerse the contents of the capsules sterilized by ultraviolet light for 1 hour in complete medium at a ratio of m capsule contents/v complete medium=50 mg/mL, to obtain the extract by leaching in a 37°C water bath for 24 hours. Take L 929 in the logarithmic growth phase, adjust the concentration of L 929 to 2×10^4 cells/mL, and inoculate 100 μL into a 96-well plate per well. After the cells adhered to the wall at 37°C and 5% CO_2, add 100 μL of the extract to each well as the experimental group. A well with only 200 μL of complete medium is set as the blank control group, and a well with 100 μL of complete medium + 100 μL of cells is set as the negative control. After adding the extract, continue to culture for 5 days, add 20 μL MTT (5 mg/mL in PBS) to each well in the dark every day, and continue to culture for 4 hours after adding MTT on the last day. After removing all the liquid in the well, add 150 μL DMSO solution to each well, shake at low speed for 15 minutes in the microplate reader, and measure the absorbance value at λ=490 nm. Determine the cytotoxicity by calculating the relative growth rate (RGR, %): RGR=(OD experimental group-OD blank group)/(OD negative control group-OD blank group). The specific toxicity classification standard is: Level 0: RGR ⩾100%; Level 1: 99%⩾RGR⩾75; Level 2: 74⩾RGR⩾50; Level 3: 49⩾RGR⩾25; Level 4: 24⩾RGR⩾1; Level 5=0. Level 2 or above can be regarded as a cytotoxic reaction. The results are shown in FIG. 4.

The results in FIG. 4 show that the RGR of Comparative Embodiments 1-3 is smaller than that of Embodiment 1-2, but the toxicity levels of the contents of the capsules prepared in Embodiments 1-2 and Comparative Embodiments 1-3 are both 0-1, indicating that the Mongolian medicine composition capsules of the invention are non-cytotoxic and safe and reliable.

Experimental Embodiment 2: randomly divide 160 male SD rats (weight 240 ± 20 g) into 8 groups after adaptive feeding for 1 week, each group of 20 rats, namely sham operation group, model group, Embodiments 1-2 groups, Comparative Embodiments 1-3 groups. Suspend the capsule contents prepared in each Embodiment and Comparative Embodiment with sodium carboxymethyl cellulase solution to prepare suspension, shake well before administration, and gavage the corresponding drugs to each group of mice every day. Administrate the rats in Embodiments 1-2 groups and Comparative Embodiments 1-3 groups respectively at 50 mg content/kg body weight, and administrate the rats in the sham operation group and model group the same amount of sodium carboxymethyl cellulase solution, and both for 4 weeks. Prepare the rat cerebral ischemia-reperfusion model on the second day after the end of administration. The rats are fasted for 12 hours before the operation and have free access to water. Anesthetize the rats in each group by intraperitoneal injection of 10% chloral hydrate solution (0.3 mL/100 g), fix on the operating table in a lateral position, shave, and disinfect. The length of the midline incision in the neck is about 20 mm, and the common carotid artery is exposed. Bluntly separate the internal carotid artery, clamp the common carotid artery and the internal carotid artery, and slowly and gently advance the nylon thread to the direction of the internal carotid artery entering the skull through the incision of the external carotid artery. The common carotid artery bifurcation is used as a mark, and advance the nylon thread 18±0.5 mm and encounter slight resistance, that is, it reaches the thinner middle cerebral artery and stops. The middle cerebral artery is ligated and blocked to fully block the local cerebral blood flow. Suture the wound, leave a nylon thread of about 3 cm outside the body, and disinfect the surgical area with iodine. After 1 hour of ischemia, gently pull out the thread for 10 minutes to achieve reperfusion. Sham operation group: ligate with no thread inserting, and the rest of the treatment is the same as the model group, the embodiment groups, and the comparative embodiment groups. During the operation, a transcranial Doppler blood flow analyzer is used to monitor cerebral blood flow.

The rats in each group are observed within 24 hours of ischemia-reperfusion, and behavioral defects are evaluated according to the ZeaLonga scoring standard, where 0 means normal, with no neurological damage symptoms; 1 means the contralateral forelimb cannot be fully extended; 2 means turning in circles to the contralateral side when crawling; 3 means the

body falls to the contralateral side when walking; 4 means the body cannot walk spontaneously and loses consciousness. The results are shown in Table 1.

Table 1

	Behavioral Score (Points)
Sham Operation Group	0
Model Group	3.42±0.23
Embodiment 1	2.20±0.18**
Embodiment 2	2.21±0.2**
Comparative Embodiment 1	2.63±0.31*
Comparative Embodiment 2	2.57±0.37*
Comparative Embodiment 3	2.39±0.37*

The results in Table 1 show that compared with the model group, the behavioral scores of rats in the embodiment groups and comparative embodiment groups are significantly reduced, and the scores of the embodiment 1-2 groups are lower than those of the comparative embodiment groups 1-3, indicating that the Mongolian medicine composition capsule according to the invention can improve neurological deficits.

After 24 hours of reperfusion after drug administration, kill the rats in each group. Take the whole brains of 10 rats in each group randomly, and weigh the wet weight of brain tissue, slice, stain in 2% triphenyltetrazolium chloride (TTC) solution for 30 minutes, fix, and separate the pale area (infarction area, not stained) and non-pale area (normal area). The volume of cerebral infarction (%) = (wet weight of infarction area/wet weight of brain tissue) × 100%. The results are shown in Table 2.

Table 2

	Cerebral Infarction Volume (%)	Brain Water Content (%)
Sham Operation Group		67.12±2.12**
Model Group	23.91±0.34	79.42±1.14
Embodiment 1	20.89±0.35**	71.31±1.21**
Embodiment 2	21.04±0.78**	71.55±2.64**

Comparative Embodiment 1	22.73±0.33*	75.51±1.1*
Comparative Embodiment 2	22.37±0.55*	74.07±1.82*
Comparative Embodiment 3	22.16±0.45**	73.14±1.49**

The results in Table 2 show that compared with the model group, the cerebral infarction volume and brain water content of rats in the embodiment groups and comparative embodiment groups are significantly reduced, indicating that the Mongolian medicine composition capsule for treating and preventing cerebral stroke according to the invention can improve and reduce the degree of cerebral edema and reduce the area of cerebral infarction.

After 24 hours of reperfusion after administration, kill the remaining 10 rats in each group, and quickly take out the brains and weigh, and prepare a 10wt% brain tissue homogenate with normal saline. After low-temperature centrifugation, take the supernatant. Detect the malondialdehyde (MDA), reduce glutathione (GSH) content and superoxide dismutase (SOD) activity in the brain tissue according to the method in the kit instructions. The results are shown in FIG. 5.

The results in FIG. 5 show that compared with the model group, the MDA content in the brain tissue of rats in the embodiment groups and comparative embodiment groups is significantly reduced, and the GSH content and SOD activity are significantly increased. The embodiment group has the best effect, indicating that the Mongolian medicine composition capsule according to the invention can reduce oxidative stress, protect brain tissue from damage by oxygen free radicals, and protect brain tissue, and is suitable for the prevention and treatment of cerebral stroke.

Experimental Embodiment 3: prepare 100 mL of hydrochloric acid solution with a pH of 1.2 and 100 mL of phosphate buffer solution with a pH of 6.8, add the contents of the Mongolian medicine composition capsule prepared in Embodiments 1-2 and Comparative Embodiments 1-3, add 0.3 g/100 mL, and record the weight as m_1. Stir at 200 rpm for 3 hours at room temperature, filter with 0.22 μm filter paper, and dry the precipitate to constant

weight, and record the weight as m_2. Calculate the dissolution rate of each group of contents in hydrochloric acid solution and phosphate buffer solution, dissolution rate (%) = $[(m_1-m_2)/m_1] \times 100\%$, and the results are shown in FIG. 6.

The results in FIG. 6 show that the dissolution rates of Embodiments 1-2 groups are higher than those of Comparative Embodiments 1-3, especially higher than Comparative Embodiment 2, indicating that the Mongolian medicine composition capsules according to the invention have good biocompatibility, high absorption rate, are more easily absorbed and utilized by the human body, have high bioavailability, and can improve the effect of treating and preventing cerebral stroke.

Experimental Embodiment 4: randomly divide 80 male SD rats (weight 240 ± 20 g) into 8 groups after adaptive feeding for 1 week, each group of 10 rats, namely sham operation group, model group, Embodiments 1-2 groups, Comparative Embodiments 1-3 groups. After adaptive feeding for 1 week, prepare the rat cerebral ischemia-reperfusion model according to the method of Experimental Embodiment 2. After the operation, suspend the capsule contents prepared in each Embodiment and Comparative Embodiment with sodium carboxymethyl cellulase solution to prepare suspension, shake well before administration, and gavage the corresponding drugs to each group of mice every day. Administrate the rats in Embodiments 1-2 groups and Comparative Embodiments 1-3 groups respectively at 50 mg content/kg body weight, and administrate the rats in the sham operation group and model group the same amount of sodium carboxymethyl cellulase solution. After 2 weeks of administration, perform behavioral scores according to the method of Experimental Embodiment 2, and calculate the cerebral infarction volume and brain water content. The results are shown in Table 3.

Table 3

	Behavioral Score (Points)	Cerebral Infarction Volume (%)	Brain Water Content (%)
Sham Operation Group	0	-	68.01±0.89**
Model Group	3.91±0.31	22.78±1.21	81.04±1.81

Embodiment 1	2.08±0.25**	17.56±0.77**	72.36±1.24**
Embodiment 2	2.03±0.23**	17.43±1.24**	72.19±0.98**
Comparative Embodiment 1	2.71±0.29**	18.98±1.75*	77.17±0.71*
Comparative Embodiment 2	2.58±0.33**	18.21±1.09**	76.51±1.28*
Comparative Embodiment 3	2.51±0.31**	18.02±0.54**	75.42±1.31*

The results in Table 3 show that compared with the model group, the behavioral scores, cerebral infarction volume and brain water content of rats in the embodiment groups and comparative embodiment groups are significantly reduced, and those in the Embodiments 1-2 groups are lower than that in the Comparative Embodiments 1-3 groups, indicating that the Mongolian medicine composition capsule according to the invention can improve neurological deficits, reduce the degree of brain edema, reduce the area of cerebral infarction, and has the effect of treating cerebral stroke.

CLAIMS

1. A Mongolian medicine composition capsule for treating and preventing cerebral stroke, comprising a capsule shell and contents, wherein the contents comprise the following raw materials in parts by weight: 30-40 parts of Panax notoginseng, 36-44 parts of Roselle Thistle, 15-20 parts of Fructus Choerospondiatis, 20-30 parts of Clematis, 25-32 parts of Ginseng, 20-30 parts of synergist, and 8-12 parts of promoter;

the preparation method of the synergist includes the following steps:

(1) mixing Spirulina platensis, Staurastrum crenulatum, and water evenly to obtain a mixed algae solution, adjusting the pH value, adding a biological enzyme, stirring, and heating to obtain a hydrolyzate;

(2) centrifuging the hydrolyzate obtained in step (1), concentrating the supernatant and then freeze-drying it to obtain the synergist;

the preparation method of the promoter includes the following steps:

I. in an ice-water bath, adding diethanolamine and p-aminobenzoyl chloride to a dimethylformamide solvent, and then adding pyridine and triethylamine, and stirring the mixture to react to obtain a reaction mixture I;

II. adding decanoic acid to the reaction mixture I obtained in step I, and the molar ratio of decanoic acid to p-aminobenzoyl chloride is 1:1; then adding dimethyl carbonate, and the mass ratio of dimethyl carbonate to p-aminobenzoyl chloride is 9:13; stirring to obtain a reaction mixture II;

III. concentrating the reaction mixture II obtained in step II; washing, recrystallizing in tetrahydrofuran, filtering, washing, and drying in vacuum to obtain the promoter.

2. The Mongolian medicine composition capsule for treating and preventing cerebral stroke according to claim 1, wherein the mass ratio of the Spirulina platensis, Staurastrum crenulatum, and water is 1:1:30.

3. The Mongolian medicine composition capsule for treating and preventing cerebral stroke according to claim 2, wherein the biological enzyme is a mixture of acidic cellulase, neutral cellulase, and papain in a mass ratio of 2:1:1.2; the mass ratio of the biological enzyme to the mixed algae liquid is 1:1000.

4. The Mongolian medicine composition capsule for treating and preventing cerebral stroke according to claim 3, wherein in step I, the amount ratio of diethanolamine, p-aminobenzoyl chloride, dimethylformamide, pyridine and triethylamine is 2 g:3 g:4 mL:0.6 g:0.3 g.

5. A preparation method of the Mongolian medicine composition capsule for treating and preventing cerebral stroke according to any one of claims 1-4, including the following steps:

S1: washing and drying Panax notoginseng, Fructus Choerospondiatis, Ginseng, Clematis, and Roselle Thistle, crushing and sieving, heating and soaking in citric acid solution; after filtering, rotating to evaporate and spraying to dry to obtain Mongolian medicine granules;

S2: mixing the Mongolian medicine granules, the promoter, and the synergist evenly, grinding and sieving, sterilizing, and filling into capsules to obtain a Mongolian medicine composition capsule for treating and preventing cerebral stroke.

Schutzansprüche

1. Kapsel mit mongolischer Arzneimittelzusammensetzung zur Behandlung und Vorbeugung von Schlaganfall, wobei sie eine Kapselhülle und einen Inhalt umfasst, wobei der Inhalt die folgenden Rohmaterialien in Gewichtsteilen umfasst: 30-40 Teile Panax notoginseng, 36-44 Teile Roselle Thistle, 15-20 Teile Fructus Choerospondiatis, 20-30 Teile Clematis, 25-32 Teile Ginseng, 20-30 Teile Synergist und 8-12 Teile Promotor;

das Verfahren zur Herstellung des Synergisten umfasst die folgenden Schritte:

(1) gleichmäßiges Mischen von Spirulina platensis, Staurastrum crenulatum und Wasser, um eine gemischte Algenlösung zu erhalten, Einstellen des pH-Wertes, Hinzufügen eines biologischen Enzyms, Rühren und Erhitzen, um ein Hydrolysat zu erhalten;

(2) Zentrifugieren des in Schritt (1) erhaltenen Hydrolysats, Konzentrieren des Überstandes und anschließendes Gefriertrocknen, um den Synergisten zu erhalten;

das Verfahren zur Herstellung des Promotors umfasst die folgenden Schritte:

I. Zugabe von Diethanolamin und p-Aminobenzoylchlorid zu einem Dimethylformamid-Lösungsmittel in einem Eiswasserbad, dann Zugabe von Pyridin und Triethylamin und Rühren der Mischung zur Reaktion, um eine Reaktionsmischung I zu erhalten;

II. Zugabe von Decansäure zu der in Schritt I erhaltenen Reaktionsmischung I, wobei das molare Verhältnis von Decansäure zu p-Aminobenzoylchlorid 1:1 beträgt; anschließend Zugabe von Dimethylcarbonat, wobei das Massenverhältnis von Dimethylcarbonat zu p-Aminobenzoylchlorid 9:13 beträgt; Rühren, um eine Reaktionsmischung II zu erhalten;

III. Konzentrieren der in Schritt II erhaltenen Reaktionsmischung II; Waschen, Umkristallisieren in Tetrahydrofuran, Filtrieren, Waschen und Trocknen im Vakuum, um den Promotor zu erhalten.

2. Kapsel mit mongolischer Arzneimittelzusammensetzung zur Behandlung und Vorbeugung von Schlaganfall nach Anspruch 1, wobei das Massenverhältnis von

Spirulina platensis, Staurastrum crenulatum und Wasser 1:1:30 beträgt.

3. Kapsel mit mongolischer Arzneimittelzusammensetzung zur Behandlung und Vorbeugung von Schlaganfall nach Anspruch 2, wobei das biologische Enzym eine Mischung aus saurer Cellulase, neutraler Cellulase und Papain in einem Massenverhältnis von 2:1:1,2 ist; das Massenverhältnis des biologischen Enzyms zu der gemischten Algenlösung ist 1:1000.

4. Kapsel mit mongolischer Arzneimittelzusammensetzung zur Behandlung und Vorbeugung von Schlaganfall nach Anspruch 3, wobei in Schritt I das Mengenverhältnis von Diethanolamin, p-Aminobenzoylchlorid, Dimethylformamid, Pyridin und Triethylamin 2 g:3 g:4 mL:0,6 g:0,3 g beträgt.

5. Verfahren zur Herstellung der Kapsel mit mongolischer Arzneimittelzusammensetzung zur Behandlung und Vorbeugung von Schlaganfall nach einem der Ansprüche 1-4, wobei es die folgenden Schritte umfasst:

S1: Waschen und Trocknen von Panax notoginseng, Fructus Choerospondiatis, Ginseng, Clematis und Roselle Thistle, Zerkleinern und Sieben, Erhitzen und Einweichen in Zitronensäurelösung; nach dem Filtern, Drehen zum Verdampfen und Sprühen zum Trocknen, um Granulat der mongolischen Medizin zu erhalten;

S2: gleichmäßiges Mischen des Granulats der mongolischen Medizin, des Promotors und des Synergisten, Zerkleinern und Sieben, Sterilisieren und Füllen in Kapseln, um eine Kapsel mit mongolischer Arzneimittelzusammensetzung zur Behandlung und Vorbeugung von Schlaganfall zu erhalten.

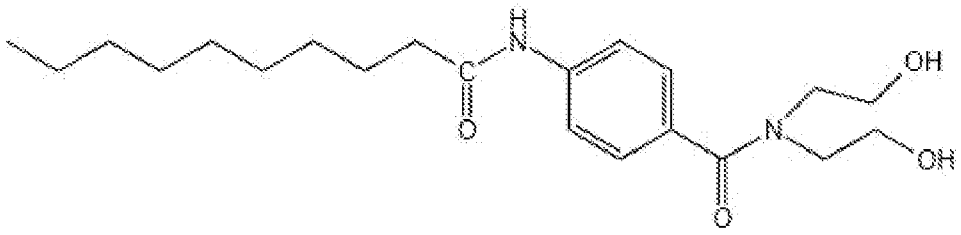

FIG. 1

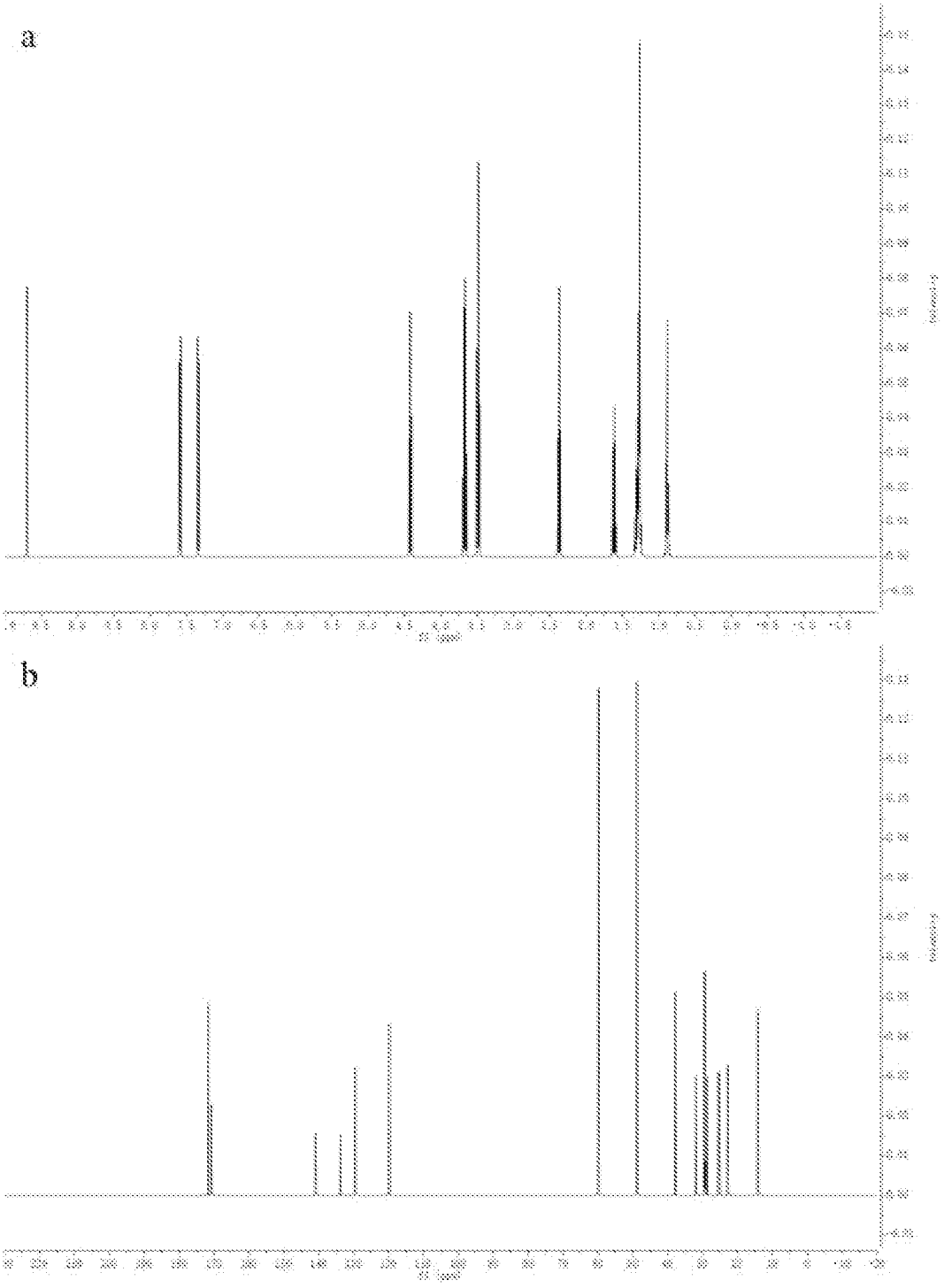

FIG. 2

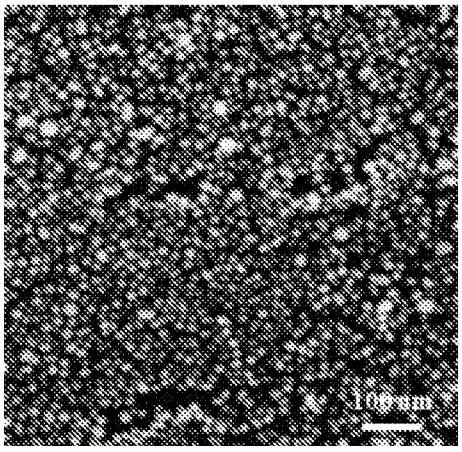
100nm

FIG. 3

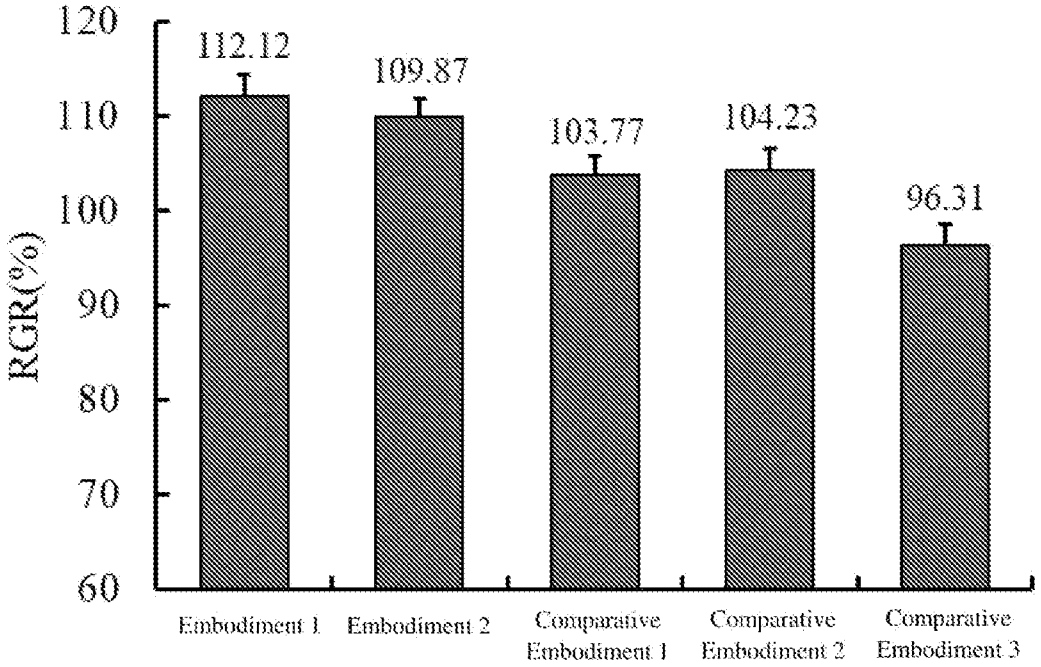
120
110
100
90
80
70
60
RGR(%)
112.12
109.87
103.77
104.23
96.31
Embodiment 1
Embodiment 2
Comparative Embodiment 1
Comparative Embodiment 2
Comparative Embodiment 3

FIG. 4

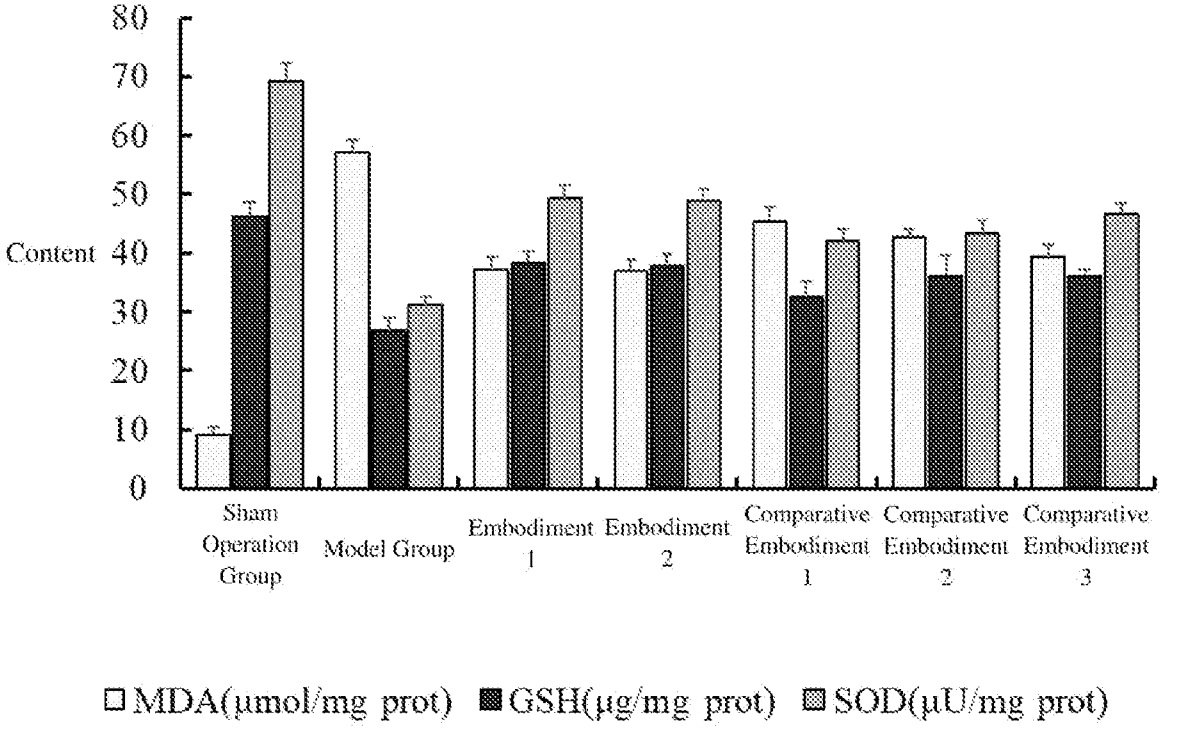
80
70
60
50
Content 40
30
20
10
0
Sham Operation Group
Model Group
Embodiment 1
Embodiment 2
Comparative Embodiment 1
Comparative Embodiment 2
Comparative Embodiment 3
MDA(μmol/mg prot)
GSH(μg/mg prot)
SOD(μU/mg prot)

FIG. 5

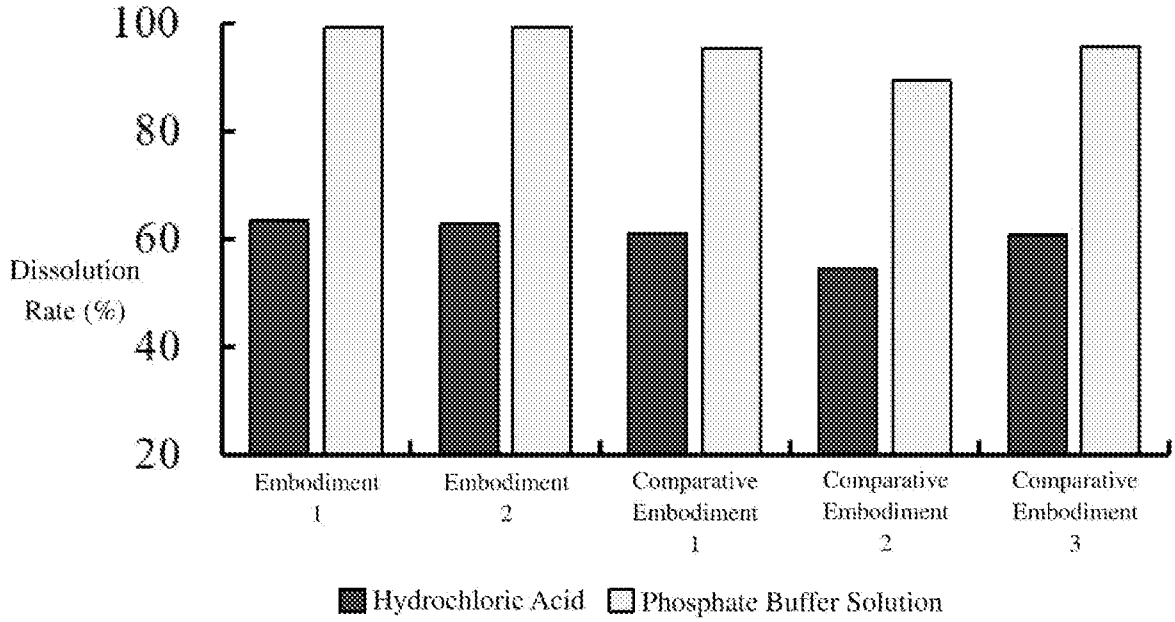
100
80
60
40
20
Dissolution Rate (%)
Embodiment 1
Embodiment 2
Comparative Embodiment 1
Comparative Embodiment 2
Comparative Embodiment 3
Hydrochloric Acid
Phosphate Buffer Solution

FIG. 6