

SECTION 4

Documents regarding a Chinese Patent of the herbal formulation

The herbal formulation has been patented in China since 2000. The patent name is *a drug for treating atherosclerosis*. **File #3** is the translated version and **File# 4** is a copy of the original version.

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**File #3 Translated English Version of the Patent
(From page 3 to 12)**

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Certificate of Patent for Invention

Certificate No. 58347

Name of Invention: A medicine for treating atherosclerosis ailment

Inventor: Liu Yanzhu

Patent Number: ZL 98 1 17984.3

International Master Class Number of Patent: A61K 35/78

Date of Application: September 11, 1998

Patentee: Liu Yanzhu

After examination in accordance with Patent Law of the People's Republic of China, the office hereby grant the patent right to the invention.

After examination in accordance with Patent Law of the People's Republic of China, the office decides to grant the patent right to the invention and issues the certificate and registers the patent on the patent register on August 12, 2000. The patent right goes into effect from the issuing date of the certificate.

The duration of the patent right is 20 years, which starts from the date of application. The patentee shall pay the yearly fee in accordance with Patent Law and the enforcement regulations. The fee shall be paid within one month before the 11th day of September every year. If the patentee fails to pay the yearly fee, the patent right shall terminate from the expiry date of the payment.

The patent certificate records the legal conditions on the date of registration. The assignment, inheritance, cancellation, nullification and termination of the patent and the alternation of the name, nationality, address and etc. of the patentee shall be recorded on the patent register.

Jiang Ying

Director General

Seal of State Intellectual Property Office of the People's Republic of China

August 12, 2000

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Office for Local Taxes Administration of Haidian District Beijing

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[19] China Patent Office

[51] Int. Cl⁶

A61K 35/78

[12] Disclosure of an Invention Patent

[21] Application No. 98117984.3

[43] Disclosure Date: April 28, 1999

[11] Disclosure Number: CN1214931A

[22] Application Date: September 11, 1998

[21] Application Number: 98117984.3

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Agent: Tao Zhang

Note: one page for the Claim; 5 pages for the Description; none for the Appendix

[54] Name of the invention: A drug for treating atherosclerosis.

[57] Abstract: An invention relates to a drug for atherosclerosis treatment. The herb components and their parts in the formulation are listed as follows:

Raw Radix Ginseng (5.8%), Radix Polygoni Multiflori (17.6%), Pollen Typhae (17.6%), Radix et Rhizoma rhei (8.8%), Fructus Crataegi (17.6%), Resina Ferulae (5.8%), Rhizoma Alismatis (17.6%), Sargassum (8.8%)

This drug invigorates kidneys, nourishes spleen, promotes blood circulation and expels blood

Claims

What is claimed is:

1. A drug for treating atherosclerosis comprising the following herbs in parts of the total composition:

Raw Radix Ginseng (5.8%), Radix Polygoni Multiflori (17.6%), Pollen Typhae (17.6%), Radix et Rhizoma rhei (8.8%), Fructus Crataegi (17.6%), Resina Ferulae (5.8%), Rhizoma Alismatis (17.6%), Sargassum (8.8%)

2. A drug for treating atherosclerotic diseases according to claim 1 comprising the following herbs in weight, which could be used 3 days for one patient.

Extract from 10g of Raw Radix Ginseng, extract from 30g of Radix Polygoni Multiflori, extract from 30g of Pollen Typhae, extract from 15g of Radix et Rhizoma rhei, extract from 30g of Fructus Crataegi, extract from 10g of Resina Ferulae, extract from 30g of Rhizoma Alismatis, extract from 15g of Sargassum.

3. A drug on claim 1 or 2, wherein the Radix Polygoni Multiflori is salt-processed.

4. A drug on claim 1 or 2, wherein the Radix et Rhizoma rhei is processed by alcohol.

5. A drug on claim 1 or 2, wherein the Fructus Crataegi is used in raw form.

6. A drug according to claim 1 or 2, wherein the Rhizoma Alismatis is salt-processed.

7. A drug on claim 1 or 2, wherein the Pollen Typhae is in raw form.

8. A drug on claim 1 or 2, wherein the composition is used in the form of granules.

9. A method of the preparation of a drug for treating atherosclerosis comprising herbal components and procedures are followed.

Herbal components:

Raw Radix Ginseng (5.8%), Radix Polygoni Multiflori (17.6%), Pollen Typhae (17.6%), Radix et Rhizoma rhei (8.8%), Fructus Crataegi (17.6%), Resina Ferulae (5.8%), Rhizoma Alismatis (17.6%), Sargassum (8.8%)

Procedures for preparation:

The oil-components of Resina Ferulae are first extracted. The residues left from the extracted Resina Ferulae are mixed with the remaining seven herbs and boiled with eight volumes of water twice with one hour for each boiling. The gross liquid extractions are condensed to a suspensor with a one-to-one solid-to-liquid ratio, into which ethanol is added to the final concentration of 70% ethanol. After being cooled, soak 24 hours at room temperature, a paste is formed by further condensing the filtrate. The paste is finally processed to form granules after mixing homogeneously with cyclones and the oil-components from Resina Ferulae.

Description

A drug for treating atherosclerosis

This invention is a drug for treating atherosclerosis that is made from Chinese herbs. The invention belongs to the field of Chinese Medicine.

Background

Diseases due to atherosclerosis, such as coronary artery diseases and stroke, are arguably the most serious diseases that threaten the health and life of human beings. The treatment of atherosclerosis (AS) has been focused on clinic endpoint event, including coronary disease and stroke. Recently, however, many clinical trials aimed at providing effective treatments for patients who have developed atherosclerotic plaques, the initial form of AS without clinical symptoms, have been carried out from drugs and operations to gene therapy. Nevertheless, no ideal therapeutic approach has been found yet.

Although the exact mechanisms of AS are unclear, among a number of biochemical, physiological and environmental risk factors, hyperlipidemia and hypertension have been proven to be the most critical ones. The incidence of hyperlipidemia is more than 60% in Western countries, whereas in China, the incidence has reached 40% due to the improvement of living standards. It has been reported that 30% of the hyperlipidemia patients develop atherosclerotic plaques. The incidence of hypertension is about 10-20% in Western countries compared to about 7.8% in China. The possibility of developing AS among hypertension patients is about 4 times greater than among normal people.

Over the past 20 years, there has been a constant exploration of new therapies for AS. Western medicine has gained considerable achievements in treating AS. However, the issues of side effects and safety concerns have always compromised these efforts. Angioplasty surgery has been practiced for over forty years; however, there is a high possibility of thrombosis following the operation. Ultrasonic therapy is still in clinical trials. Currently, with the development of modern molecular biology, more people put high expectations on gene therapy. However, due to the nature of abnormal expression of multigenes in AS and the difficulty of identifying a specific gene for the occurrence of AS, plus the deficiency of persistent expression of the transferred gene, it will be a long time for gene therapy to achieve any real clinical application.

The treatment of AS by Chinese medicine is now largely restricted to laboratory studies and a few clinical trials. Therefore, inventing an effective herbal formulation for treating AS is, without a doubt, a large contribution to this field. The inventor has been studying the preventions and treatments of AS by Chinese medicine since 1992. Simultaneously, he also participates in clinic practices for treating AS as well. Based on his constant studies and clinic observations, he invented this herbal formulation for treating AS, which has been proven effective clinically.

The purpose of this invention is to provide an effective Chinese medicine for treating AS

The inventor established his unique theory about AS based on his deep comprehension of Chinese medicine. He believes that the occurrence of AS is the result of the weakness of the

spleen, which is expressed as the accumulation of sputum resulting from accumulation of body fluid due to the dysfunction of lung, spleen or kidneys, and the blockage of blood circulation. Risk factors include the damage of spleen either by inappropriate diet or over exertions, or by depletion of the kidney essence inside. The spleen and stomach can malfunction by eating a high fat diet and over exertions as well. Once these happen, food cannot be fully digested so that the balance of "Qi" (the important substance for the body function) will be disturbed. The resulting "bad Qi" will influence the movement of the blood and the "normal Qi" after it enters the circulation, thus forming clots within the circulatory system. The undigested food can also lead to the formation of phlegm that will influence the circulation over a long period of time. Aging as one inside-factor which is natural stage of life, could not be altered. Others include inherited deficiency or early exhaustion of the essence in the kidneys, anemia, and the malfunction of the blood circulation. From another point of view, the weakness of spleen in a long term will affect the kidney function which will then accelerate the symptoms of phlegm accumulation and blood stasis that first resulted from the deficiency of Qi in the spleen and the depletion of the kidney essence as well.

Under his theory about AS, the inventor achieved the formulation by following the principle of invigorating the spleen, strengthening the kidneys, improving blood circulation, dispersing blood stasis, softening and breaking down atherosclerotic plaques.

The invention comprises the following herbs in parts of the total composition

Raw Radix Ginseng (5.8%), Radix Polygoni Multiflori (17.6%), Pollen Typhae (17.6%), Radix et Rhizoma rhei (8.8%), Fructus Crataegi (17.6%), Resina Ferulae (5.8%), Rhizoma Alismatis (17.6%), Sargassum (8.8%)

The invention comprises the following herbs in weight, which could be used 3 days for or patient.

Extract from 10g of Raw Radix Ginseng, Extract from 30g of Radix Polygoni Multiflori, Extract from 30g of Pollen Typhae, Extract from 15g of Radix et Rhizoma rhei, Extract from 30g of Fructus Crataegi, Extract from 10g of Resina Ferulae, Extract from 30g of Rhizoma Alismatis, Extract from 15g of Sargassum.

Among the components in this invented formulation, the Radix Polygoni Multiflori is salt-prepared, the Radix et Rhizoma rhei is alcohol-processed, the Fructus Crataegi is used in raw, the Resina Ferulae is salt-processed, and the cattail pollen is used in raw.

The principal (which is directed against, and has the greatest effect upon, the principal pattern or disease) herbs of the formulation are Ginseng and Polygonum multiflorum. Ginseng invigorates the primary Qi, promotes the production of blood and disperses the stagnant. Radix Polygoni Multiflori nourishes both liver and kidneys, tonifies blood, and invigorates the essence. The minister herbs (which aid the principal herb in treating the principal pattern or disease) of the formulation are Pollen Typhae and Radix et Rhizoma rhei. They both promote blood circulation, dissipate stasis, assist the movement of the bowels, and reduce cholesterol level, which all contribute to the smooth blood circulation throughout the whole body. Fructus Crataegi, Resina Ferulae, Rhizoma Alismatis, Sargassum are the adjuvant herbs in the formulation. Fructus Crataegi can promote the secretion of spleen and the movement of the stomach so that it can assist digestion.

Alismatis, has the functions of promoting urination, transforming phlegm, and clearing the channel of "sanjiao" (which is located inside the body, its main functions are to govern various forms of Qi). Sargassum has the function of transforming phlegm, leaching out dampness, softening and breaking down the plaques. All components combined together to form the drug that invigorates the spleen, strengthens the kidneys, promotes blood circulation, expels stasis, softens and breaks down the plaques.

The amount of each ingredient in the formulation can be increased or reduced based on the symptoms manifested at different disease situations. Some examples are given as following.

To a patient with a relatively serious condition of blood blockage, extracts from 3-60g of Salvia Miltiorrhiza should be added to the formulation.

To a patient with a relatively light blood stasis, extracts from and Pollen Typhae can be eliminated. or extracts from 3-60g of Salvia Miltiorrhiza and 6-60g of Semen Cassiae should be added.

To a patient with serious kidney weakness, back, shoulder, and chest pain, Radix Polygoni Multiflori, Pollen Typhae, and Fructus Crataegi can be eliminated, while 3-60g of the Fructus Ligustri Lucidi, 3-60g of Herba Epimedii, and 3-60g of Rhizoma Curcumae Longae should be added.

The herbal components of this invention can be dried and broken down directly into forms of powder or capsules. The common processing procedure can also be adapted as first, extracting each herbal component and then, making into whatever drug forms, such as tablet, capsule, liquid paste, granule, or pill.

The best preparation of this invention is a granular form produced by the following procedure:

The oil-components of Resina Ferulae are first extracted. The residues left from the extracted Resina Ferulae are mixed with the remaining seven herbs and boiled with eight volumes of water twice with one hour for each boiling. The gross liquid extractions are condensed to a suspension with a one-to-one solid-to-liquid ratio, into which ethanol is added to the final concentration of 70% ethanol after being cooled. Soaking 24 hours at room temperature, a paste is formed by further condensing the filtrate. The paste is finally processed to form granules after mixing homogeneously with cyclones and the oil-components from Resina Ferulae.

The major indications for this invention are listed below:

This drug can be used to treat other clinically defined disorders, such as hyperlipidemia, an obesity, in addition to atherosclerosis.

Based on Chinese Medicine, the phlegm accumulation and blood stasis, which are caused by the deficiency of spleen Qi and the weakness of kidney essence, are manifested through the following symptoms: Palpitation, distention and a stifling sensation in the chest, anorexia, distention in abdomen, obesity and lassitude, soreness and weakness in the lower back, vertigo, tinnitus, floating tongue with tooth marks, dark blue tongue or dark spots on the sides of the tongue, rolling pulse.

This invention has been clinically proven having significant therapeutic effects in treating diseases resulting from atherosclerosis.

Clinical trial: Therapeutic effects of this invention in treating atherosclerotic diseases

Methods and Materials

1. General description of the method

17 patients were chosen based on the diagnosis of color-Doppler. Overall 30 blood vessels were detected to be AS and totally 20 plaques were found in all patients. - The patients were randomized into two groups. One group was treated with granules of *VasoCleaner*TM (the drug name of the invention for clinical trial); the other group was treated with the herbal formulation that has been shown to have the functions of promoting blood circulation and dispersing stasis.

2. Case selection

- Cases included:

Patients with either one or two of the following:

AS plaques diagnosed by the B-ultrasound

Abnormal intimal-medial thickness (more than 0.13cm) of carotid artery.

- Cases not included:

Patients under 18 or above 65 years of age.

Patients suffering from acute angina, stroke, serious injury, or who has major surgical operation within the past six months.

Patients whose AS were resulted from the complication of kidney diseases, malfunction of thyroid, migratory arthralgia, acute liver and gallbladder diseases, and diabetes.

Patients using heparin and other drugs to treat thyroid diseases, or other drugs that influence either lipid metabolisms or anticoagulant, or using other lipid-lowering drugs within two weeks.

Patients with serious diseases in liver, kidney and hemopoiesis.

Patients with psychological diseases.

Other situations, including patients, who did not use drugs following the doctor's recommendations, or lack of enough data to evaluate the effectiveness and safety.

3. The diagnostic criteria of AS by Chinese medicine:

A stifling sensation in the chest, palpitation, vertigo, tinnitus, poor memory, soreness and weakness in the lower back, sweating, floating tongue with tooth marks, dark blue tongue, deep

4. Method of administration

The granules of *VasoCleaner*TM was given three times a day with two bags of the fomulation each time to the group for the clinical trial. The same dosage of the commonly used herbal fomulation for promoting blood circulation and dispersing phlegm was given to the control group. The clinical trial lasted for two months for every patient.

5. Clinical Diagnosis

- Color-Doppler was used for detecting Intimal-medial thickness (IMT), and the characteristics and size of the plaque.
- The levels of blood lipids, including TC, TG, HDL-C, LDL-C, apoA-1, and apoB-100, were also measured.

6. Statistic Process

The AS degree was presented by both the size of the plaque and the IMT of the carotid artery. The blood lipid level was compared between control and experimental group before and after treatment.

Results**1. The IMT observation of the carotid artery**

In the *VasoCleaner*TM treated group, there were 6 blood vessels with IMT more than 1.3mm before treatment. After treatment, the IMT of three vessels was reduced to 0.1 to 0.3mm. The effective rate is 50%. In the control group, there were 9 blood vessels with IMT greater than 1.3mm before treatment. After treatment, only one vessel showed reduced thickness of 0.1 to 0.3mm. The effective rate is only 11.1%.

Table 1 The change of IMT of carotid artery before and after treatment

Group	Vessels N	IMT ≥ 1.3mm		IMT reduce 0.1-0.3mm		No change vessels	
		N	Effective rate %	N	Effective rate %	N	%
<i>Vasocleaner</i>	16	6	50	3	50	3	50
Control	14	9	11.1	1	11.1	8	88.9

N represents the number of examined vessels.

2. The size of the plaque

The size of the plaque before and after the treatment was carefully recorded. In the *VasoCleaner*TM group, which includes 14 plaques, 7 of them reduced 0.2 to 6.4 mm² in size. The effective rate is 50%. In the control group, among the 15 plaques, only 5 of them reduced the size in the above range. The effective rate is 33.3%. It can be predicted that *VasoCleaner*TM treatment is more effective in reducing the plaque size than the control treatment.

Table 2 The change of the plaque size

Group	Characteristic of plaque			Plaque		Decrease		Increase		No change	
	Soften	Harden	Mixture	N	N	%	N	%	N	%	
<i>VasoCleaner</i>	7	3	2	14	7	50	3	21.4	4	28.6	
Control	1	7	7	15	5	33.3	4	26.7	6	40	

3. Serum lipid profile

The profile of serum lipids, including TC, TG, LDL, HDL, apoA and apoB, was recorded. In *VasoCleaner*TM group, there is a significant reduction in TC level after treatment compared with the control group. The levels of both TG and LDL have decreased. No significant change has been observed in either apoA or apoB level. In the control group, no significant change has been observed in the profile of serum lipids. It is noteworthy that the levels of TC and TG in *VasoCleaner*TM group have been significantly reduced after treatment compared with those in the control group.

Table 3 The change of TC, TG and LDL before and after treatment

Group	TC		TG		LDL	
	Before	After	Before	After	Before	After
<i>VasoCleaner</i>	237.46±42.25	203.15±31.42*##	129.14±53.71	110.18±53.13##	133.27±24.98	126.90±36.68
Control	237.14±40.59	260.57±53.90	145.00±14.17	188.57±14.32	154.27±38.25	176.03±48.58

P<0.05 vs before treatment; ## P<0.01 vs control group.

Table 4 The change of HDL-cholesterol, apoA and apoB before and after treatment

Group	HDL		apoA		apoB	
	Before	After	Before	After	Before	After
<i>VasoCleaner</i>	54.14±14.29	48.00±14.70	145.75±16.52	149.12±37.02	111.51±23.29	125.53±36.43
Control	47.28±22.37	46.57±18.15	117.58±21.44	149.28±37.25	100.11±34.31	140.34±33.49

Discussion

Data from the clinical trial indicate that this invention is effective in reducing IMT of carotid arteries and the plaque size. The effective rate is about 50%. The formulation also has the potential to reduce TC, TG, and LDL-C, and the potential to increase apoA. The clinical results are very impressive compared with the commonly used formulation of promoting blood circulation and reducing stasis (since no drug for treating AS has been invented yet, this invention can only be compared with the commonly applied Chinese medicine for promoting blood circulation and

reducing stasis). Due to its apparent therapeutic advantage, this invention is the first effective drug invented for directly targeting AS.

Formulation clinically used

Herbal components:

Raw Radix Ginseng (5.8%), Radix Polygoni Multiflori(17.6%), Fructus Crataegi (17.6%), Rhizoma Alismatis (17.6%), Radix et Rhizoma rhei (8.8%), Pollen Typhae (17.6%), Resina Ferulae (5.8%), Sargassum (8.8%) .

Method of preparation

The oil-components of Resina Ferulae are first extracted. The residues left from the extracted Resina Ferulae are mixed with the remaining seven herbs and boiled with eight volumes of water twice with one hour for each boiling. The gross liquid extractions are condensed to a suspension with a one-to-one solid-to-liquid ratio, into which ethanol is added to the final concentration of 70% ethanol after being cooled. Soaking 24 hours at room temperature, a paste is formed by further condensing the filtrate. The paste is finally processed to form granules after mixing homogeneously with cyclones and the oil-components from Resina Ferulae.

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File #4 A Copy of Original Version of the Patent
(8 pages)

发明专利证书



证书号 第 58347 号

发明名称: 一种治疗动脉粥样硬化性疾病的药物

本发明已由本局依照专利法进行审查, 决定于 2000 年 8 月 12 日授予专利权, 颁发本证书并在专利登记簿上予以登记。专利权自证书颁发之日起生效。

发明人: 刘彦珠

本专利的专利权期限为二十年, 自申请日起算。专利权人应当依照专利法及其实施细则规定缴纳年费。缴纳本专利年费的期限是每年 9 月 11 日前一个月内。未按照规定缴纳年费的, 专利权自应当缴纳年费期满之日起终止。

专利号: ZL 98 1 17984.3 国际专利主分类号: A61K 35/78

专利申请日: 1998 年 9 月 11 日

专利书记载专利权登记时的法律状况。专利权的转让、继承、撤销、无效、终止和专利权人的姓名或名称、国籍、地址变更等事项记载在专利登记簿上。

专利权人: 刘彦珠

专利号

该发明已由本局依照中华人民共和国专利法进行审查, 决定授予专利权。

局长 姜颖



[12] 发明专利申请公开说明书

[21] 申请号 98117984.3

[43]公开日 1999年4月28日

[11]公开号 CN 1214931A

[22]申请日 98.9.11 [21]申请号 98117984.3
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 代理人 张 韬

权利要求书 1 页 说明书 5 页 附图页数 0 页

[54]发明名称 一种治疗动脉粥样硬化性疾病的药物

[57]摘要

本发明公开了一种治疗动脉粥样硬化的药物,制备该药物的原料组成及重量份数为:

生晒参 3—30 份 何首乌 6—60 份 蒲黄 6—60 份;

大黄 3—30 份 山楂 6—60 份 阿魏 1—30 份;

泽泻 6—60 份 海藻 3—60 份;

该药物具有健脾滋肾,活血化瘀,软坚散结的作用。

ISSN 1008-4274

权利要求书

1、一种治疗动脉粥样硬化的药物，其特征在于制备该药物的原料组成及重量份数为：

生晒参 3-30 份	何首乌 6-60 份	蒲黄 6-60 份
大黄 3-30 份	山楂 6-60 份	阿魏 1-30 份
泽泻 6-60 份	海藻 3-60 份	

2、根据权利要求 1 的药物，其特征在于各组份的重量份为：

生晒参 10g	何首乌 30g	蒲黄 30g
大黄 15g	山楂 30g	阿魏 10g
泽泻 30g	海藻 15g	

3、根据权利要求 1 或 2 的药物，其特征在于所说的何首乌是制何首乌。

4、根据权利要求 1 或 2 的药物，其特征在于所说的大黄是酒制大黄。

5、根据权利要求 1 或 2 的药物，其特征在于所说的山楂为生山楂。

6、根据权利要求 1 或 2 的药物，其特征在于所说的泽泻为盐泽泻。

7、根据权利要求 1 或 2 的药物，其特征在于所说的蒲黄为生蒲黄。

8、根据权利要求 1 或 2 的药物，其特征在于该药物的剂型为颗粒剂。

9、一种治疗动脉粥样硬化药物的制备方法，其特征在于制备该药物的原料配方及制法如下：

配方

生晒参 3-30 份	何首乌 6-60 份	蒲黄 6-60 份
大黄 3-30 份	山楂 6-60 份	阿魏 1-30 份
泽泻 6-60 份	海藻 3-60 份	

制法

取阿魏提取挥发油后，残渣与其它七味药一起放入提取灌，加水 8 倍量，水煮 2 次，每次 1 小时，合并滤液，浓缩至 1：1 混悬液，放冷，加醇至含醇量为 70%，混匀放置 24 小时，过滤，滤液浓缩成流浸膏，加糊精混匀，将所提挥发油均匀喷到表面，混匀，制粒分装。

一种治疗动脉粥样硬化性疾病的药物

本发明是一种一种治疗动脉粥样硬化性疾病的药物，具体说是一种以中草药制成的中成药，属于中药领域。

动脉粥样硬化性疾病，如冠心病、脑血管病已成为危害人类健康和生命的最主要疾病，但对动脉粥样硬化的治疗还局限在临床终点事件(冠心病、脑血栓)的处理上。近年来医学界从药物、手术、基因治疗等方面进行了不少探索，以期对动脉粥样硬化斑块已形成但尚未表现出临床症状患者进行有效的治疗，但一直未找到有效的治疗方法。

动脉粥样硬化(AS)发病机制仍不十分清楚，但在诸多因素(高脂血症、高血压、遗传、生活习惯、外界环境等)中，高脂血症及高血压作为其主要发病原因已得到证实。在西方发达国家，中老年人高脂血症发病率为60%以上；我国近年来，随着物质生活水平的提高，高脂血症发病率也已达到40%。其中高脂血症患者，动脉粥样硬化斑块发生率达30%。另一方面，欧美等国高血压病的发病率为10-20%，在我国发病率为7.8%，其中高血压患者动脉粥样硬化的发病率为血压正常人的4倍。

近20年来，由于对动脉粥样硬化治疗的重视，人们不断探索新疗法。西药在治疗动脉粥样硬化方面取得不少进步，但西药的副作用、疗效的持久性及长期服用的安全性一直是本病治疗的难题，至今未找到有效的药物；动脉内膜剥脱术已有40余年的历史，由于存在术后再栓的可能性，难以应用于临床；介入超声疗法还仅处于实验阶段；近年来，随着分子生物学的发展，人们将动脉粥样硬化的治疗寄希望于基因治疗上，但由于动脉粥样硬化为多基因表达异常，特异性治疗基因难以确定，基因转移途径还处于探索阶段。再者，转移基因的表达难以持久，故基因治疗要真正运用到临床上还是很遥远的事。总之目前仍未找出有效的方法来治疗本病。

中药治疗动脉粥样硬化多局限在动脉实验研究，仍很少用于临床动脉粥样硬化的治疗。发明一种有效治疗动脉粥样硬化的中药无疑是对当今医学领域的一大贡献。发明人自1992年起开展动脉粥样硬化的中药临床及实验防治研究，在先期研究的基础上，又通过临床研究验证，开发研制成一种有效的中药制剂

本发明目的是提供一种能够有效治疗动脉粥样硬化性疾病的中药。

动脉粥样硬化的发病病机，脾虚亏虚为本，痰瘀阻脉为标。发

病原因外因为饮食、劳倦伤脾，内因为肾精亏虚。过食肥甘、劳倦，损伤脾胃，脾胃运化不利，水谷难化，化为浊气，注入脉中，碍脉中气血运行，瘀血内生；水湿不化，痰湿内生，日久注入脉中。内因为增龄因素。内因为先天肾精不足或肾精过早消耗，精血不充，血脉不利，瘀血内生。另一方面脾虚日久又可及肾，终致脾气不足，肾精亏虚，痰瘀阻脉之病证。

基于上述发病机理，制定了健脾滋肾，活血化瘀，软坚散结的治疗原则，组成方剂，制成药物制剂。

本发明的药物以下述重量份的组合物为原料配方制成制剂：

生晒参 3-30 份	何首乌 6-60 份	蒲黄 6-60 份
大黄 3-30 份	山楂 6-60 份	阿魏 1-30 份
泽泻 6-60 份	海藻 3-60 份	

本发明的上述药物组合物各组份优选重量配比为：

生晒参 10g	何首乌 30g	蒲黄 30g
大黄 15g	山楂 30g	阿魏 10g
泽泻 30g	海藻 15g	

本发明上述药物组合物中何首乌优选制何首乌，大黄优选酒制大黄，山楂优选生山楂，泽泻优选盐泽泻，蒲黄优选生蒲黄。

本发明药物组合物以人参、首乌为君药，人参大补元气，生血行滞，首乌滋补肝肾，补血填精；以蒲黄、大黄为臣药，活血化瘀，通腑降浊，通达血脉；以山楂、阿魏、泽泻、海藻为佐使药，山楂运脾和胃，消食化滞，阿魏消积散结，泽泻淡渗利湿，化痰涤饮，通利三焦，海藻，化痰利湿，软坚散结。共同达到健脾滋肾，活血化瘀，软坚散结的作用。

对于上述药物组合物，可以针对不同的疾病兼症进行加减，例如

如果瘀血较重者，加用丹参 3-60g；

如果瘀血症状较轻者，减去阿魏、生蒲黄；

如果阻滞较轻者，减去阿魏、生蒲黄加用丹参 3-60g、决明子 6-60g；

如果肾虚重，有肩背疼痛，胸痹等，去何首乌（制）、生蒲黄、生山楂后，加用女贞子 3-60g、淫羊藿 3-60g、姜黄 3-60g；

本发明药物组合物可以直接干燥、粉碎，制成散剂或胶囊剂，也可以采用常规的制剂工艺，以上述配方的组份为原料，分别进行提取后，制成常规药剂，如，片剂、胶囊剂、口服液、膏剂、颗粒剂、丸剂等。

本发明药物制剂优选是以下述方法制备的颗粒剂：

取阿魏提取挥发油后，残渣与其它七味药一起放入提取灌，加

水 8 倍量，水煮 2 次，每次 1 小时，合并滤液，浓缩至 1:1 混悬液，放冷，加醇至含醇量为 70%，混匀放置 24 小时，过滤，滤液浓缩成流浸膏，加糊精混匀。将所提挥发油均匀喷到表面，混匀，制粒分装。

本发明药物的主治病证及适应症为：

适用于脾气不足，肾精亏虚，痰瘀阻脉。动脉粥样硬化、高脂血症，心悸胸闷，食少腹胀，肥胖乏力，腰膝酸软，眩晕耳鸣，舌体胖大有齿痕，舌质淡暗有瘀斑，脉弦滑。

经过临床证实，本发明药物对动脉粥样硬化具有明显的治疗效果。

实验例 本发明药物治疗脉粥样硬化的临床药效观察

资料和方法

一、一般资料

从门诊选择经彩色多普勒检查诊为动脉粥样硬化患者 17 例，其中检查血管 30 根，动脉粥样硬化斑块 29 块，分为洁脉冲剂组（洁脉冲剂为本发明药物的临床商品名，下同）及活血化瘀组。

二、病例选择

（一）纳入病例标准：具备任一项，或同时具有两项

颈动脉 B 超检验：动脉粥样硬化斑块；或者颈内动脉内一中膜厚度 $>0.13\text{cm}$ 。

（二）排除病例标准：①年龄在 18 岁以下或 65 岁以上；②半年内曾患急性心肌梗塞、脑血管意外、严重创伤或重大手术后患者；③因肾病综合征、甲状腺机能减退、痛风、急性肝胆疾病、糖尿病等所致的动脉粥样硬化性疾病；正在使用肝素、甲状腺素治疗药和其化影响血脂代谢和防凝药物者，及近两周曾采用其他降脂措施的患者；④合半肝、肾及造血系统等严重原发性疾病、精神病患者；⑤不符合纳入标准，未按规定用药，无法判断疗效，或资料不全等影响疗效或安全性判断者。

（三）中医诊断标准：胸闷、心悸、头晕、记忆力减退、腰膝酸软、自汗、舌体胖大，舌质暗，脉沉无力或脉滑等

三、观察服药方法：采用常规活血化瘀法进行对照，洁脉冲剂组服用洁脉冲剂一次二袋，每日三次；活血化瘀组服用冲剂（由丹参、水蛭、蒲黄、山楂组成，与洁脉冲剂相同工艺制成冲剂），用量与用法与洁脉冲剂组同。

四、观察指标

（一）治疗前后作双侧彩色多普勒检查，详细记悄血管内膜厚

度、斑块性质及面积大小。

(二) 血脂含量测定: 胆固醇 (TC)、甘油三酯 (TG)、高密度脂蛋白胆固醇 (HDL-C)、低密度脂蛋白胆固醇 (LDL-C), 载脂蛋白 A (apoA-1), 载脂蛋白 B (apoB-100)

五、统计学处理: 动脉粥样硬化指标 (斑块及动脉内膜厚度) 用百分比、血脂指标用前后比较, 组间比较。

结果

一、颈动脉内膜厚度观察

洁脉冲剂组内膜增厚血管 $\geq 1.3\text{mm}$ 者 6 根, 治疗后下降 0.1-0.3mm 者有 3 根, 占 50%, 而活血化瘀组内膜增厚血管 9 根, 治疗后下降 0.1-0.3mm 者只有 1 根, 占 11.1%。

表 1 治疗前后颈动脉内膜厚度

分组	血管总数 根数	$\geq 1.3\text{mm}$ 血管		治疗后厚度减少 0.1-0.3mm		治疗后无变化	
		根数	根数	根数	%	根数	%
洁脉冲剂	16	6	3	50	3	50	
活血化瘀组	14	9	1	11.1	8	88.9	

二、颈动脉斑块观察

治疗前后颈动脉斑块变化, 斑块面积缩小幅度在 0.2-6.4 之间, 洁脉冲剂组为 14 块斑块, 治疗后有减少者 7 块, 占 50%, 而活血化瘀组 15 块, 治疗后面积只有 5 块减少, 占 33.3%, 从趋势上洁脉冲剂组优于活血化瘀组。

表 2 治疗前后颈动脉斑块变化

分组	斑块性质			斑块总数	疗后面积缩小		疗后面积增大		疗后面积无变化	
	软斑	硬斑	混合斑		块数	%	块数	%	块数	%
洁脉冲剂	7	3	2	14	7	50	3	21.4	4	28.6
活血化瘀法	1	7	7	15	5	33.3	4	26.7	6	40

三、血脂观察

观察 TC、TG、LDL、HDL、apoA 和 apoB 六项指标治疗前后的变化。洁脉冲剂组 TC 治疗后明显降低, 有显著性差异; TG、LDL 治疗后有下降趋势, apoA 和 apoB 无变化。而活血化瘀组治疗前后各项血脂指标变化均不明显。TC、TG 治疗后洁脉冲剂组均明显低于活血化瘀组。

表 3 治疗前后 TC、TG 和 LDL 的变化

	TC		TG		LDL	
	前	后	前	后	前	后
洁脉冲剂	237.46 \pm 42.25	203.15 \pm 31.42**	129.14 \pm 53.71	110.19 \pm 53.13**	133.27 \pm 24.99	126.90 \pm 36.68
活血化瘀法	237.14 \pm 40.59	260.57 \pm 53.90	145.00 \pm 14.17	168.57 \pm 14.32	154.27 \pm 38.25	176.03 \pm 48.58

*表示与治疗前比较, $P < 0.05$; **与活血化瘀组比较 $P < 0.01$ 。

表 4 治疗前后 HDL、apoA 和 apoB 的变化

	HDL		apoA		apoB	
	前	后	前	后	前	后
活血冲剂	54.14±14.29	48.00±14.70	145.75±16.52	149.12±37.02	111.51±23.29	125.53±36.43
活血化瘀法	47.28±22.37	46.57±18.15	117.58±21.44	143.28±37.25	100.11±34.31	140.34±33.49

讨论

本发明药物对颈动脉内膜厚度及粥样化斑块减少有一定的疗效，减少程度均占病变血管和斑块的 50%，此药物又有降低 TC、TG、LDL-C、升高 apoA 的趋势，经与常规活血化瘀药剂比较，效果较为满意。由于目前还没有治疗动脉粥样硬化药物的问世，故与人们普遍采用活血化瘀中药制剂相比较，本发明药物有明显的优势，可以填补动脉粥样硬化治疗的空白。

实施例

处方：

生晒参 10g	何首乌 30g	蒲黄 30g
大黄 15g	山楂 30g	阿魏 10g
泽泻 30g	海藻 15g	

制法：

取阿魏提取挥发油后，残渣与其它七味药一起放入提取灌，加水 8 倍量，水煮 2 次，每次 1 小时，合并滤液，浓缩至 1：1 混悬液，放冷，加醇至含醇量为 70%，混匀放置 24 小时，过滤，滤液浓缩成流浸膏，加糊精混匀。将所提挥发油均匀喷到表面，混匀，制粒分装。