

Pharmacological Effect and Clinical Application of Panax Notoginseng in Cardiovascular and Cerebrovascular Diseases

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Abstract. With the change of lifestyle and the acceleration of an aging society, the incidence of cardiovascular and cerebrovascular diseases (CCVDs) is increasing, which has become one of the major challenges of global public health. Panax notoginseng, as one of the traditional Chinese medicines, is widely used in the prevention and treatment of CCVDs because of its unique pharmacological properties. This paper mainly includes the following parts: firstly, through the analysis of the chemical components of Panax notoginseng, the pharmacological effects of its main active components such as Panax notoginseng saponins, were discussed, which provided the basis for the follow-up mechanism research and clinical application. Secondly, according to the types and pathological mechanisms of CCVDs, the mechanism of action of Panax notoginseng was clarified, including antiplatelet aggregation, improving microcirculation, reducing blood lipids and antioxidation, and the multiple protective effects of Panax Notoginseng on cardiovascular and cerebrovascular system were revealed. Future research needs to strengthen the mechanism of Panax notoginseng and its related components, and focus on the clear role of signal pathway. In addition, strengthen the joint research with other therapies (such as Western Medicine), explore reasonable compatibility scheme, improve the curative effect and reduce side effects. At the same time, attention should be paid to the differences between different patients, and personalized treatment schemes should be formulated by means of system biology and pharmacogenomics, so as to improve the effectiveness and safety of clinical application.

Keywords: Panax notoginseng, pharmacological action, clinical application, saponin compounds

1. Introduction

Panax notoginseng is a traditional Chinese medicine (TCM), mainly produced in Yunnan, Guangxi and other places. It is named after "Panax notoginseng was born in three to seven years", also known as "Jinbuhuan". Its record can be traced back to the compendium of Materia Medica in the Ming Dynasty. The theory of TCM believes that it has the effect of "hemostasis, removing blood stasis and calming pain", and is often used to treat traumatic injury, hemorrhagic disease and cardiovascular and cerebrovascular related diseases. As a genuine medicinal material in Yunnan, Panax notoginseng has a long history of application in minority medicine. For example, the Yi and Zhuang nationalities regard it as an important medicine for "promoting blood circulation and strengthening the body",

which reflects the early recognition of TCM on its cardiovascular and cerebrovascular protection. *Panax notoginseng* occupies an important position in TCM because of its various chemical components, especially in the treatment of cardiovascular and cerebrovascular diseases (CCVDs) [1].

This study systematically analyzed the main components of *Panax notoginseng*, including saponins such as ginsenoside R1, Rb1, Rg1, polysaccharides and flavonoids, and discussed their specific pharmacological effects on cardiovascular and cerebrovascular systems. Experiments show that *Panax notoginseng* has anti-inflammatory, antioxidant, platelet aggregation inhibition and other multi-directional pharmacological properties, which can significantly improve myocardial ischemia, inhibit myocardial fibrosis, improve the hypoxia tolerance of myocardial cells, increase cerebral blood flow, protect brain cells, and reduce the sequelae of hemorrhagic stroke. In addition, *Panax notoginseng* also showed positive effects in anti-inflammatory, antioxidant and immune regulation. Clinical studies further verified its effectiveness in the relief of angina pectoris, stroke, hypertension and other symptoms.

This study aims to summarize the comprehensive pharmacological effects of *Panax notoginseng*, and put forward the future direction of strengthening the extraction and preparation technology, implementing large-scale clinical trials and exploring its potential application in other diseases, in order to provide theoretical basis and Practice for the modernization and scientific application of TCM in the treatment of CCVDs.

2. Chemical constituents of *Panax notoginseng*

The main chemical components of *Panax notoginseng* are rich and diverse, including flavonoids, triterpenoid saponins, sterols, volatile oils, polysaccharides and other compounds, which together give it unique pharmacological effects and have important clinical value in the prevention and treatment of CCVDs. High performance liquid chromatography (HPLC), gas chromatography - mass spectrometry (GC - MS), liquid chromatography - mass spectrometry (LC - MS) and other methods are commonly used to analyze secondary metabolites. These methods are very important for quantitative and qualitative analysis of active components of *Panax notoginseng*. HPLC is used for quantitative detection of ginsenosides, GC - MS is used for qualitative analysis of volatile components, mass spectrometry (MS) and nuclear magnetic resonance (NMR) are used to confirm the structure and molecular weight of components. At the same time, the quantitative standard of active ingredients was proposed to ensure the clinical effect. For example, high performance liquid chromatography (HPLC) is often used to quantitatively detect the contents of ginsenoside R1, Rg1, Rg3 and other components. The results showed that the content of ginsenoside R1 in *Panax notoginseng* roots could reach 0.1% to 0.5%, while the contents of Rg1 and Rg3 were 0.05% to 0.3% and 0.01% to 0.15%, respectively. The specific values were affected by the cultivation environment and processing methods [2,3].

Flavonoids, especially *Panax notoginseng* flavonoids, with a content of 2%-4%, have antioxidant, anti-inflammatory and cardiovascular protective effects, can improve blood circulation and reduce cholesterol levels. The content of triterpenoid saponins is between 2% and 6%, and its main components are Notoginsenoside R1, Rg1 and Rg2, which can promote blood circulation, protect myocardium and regulate immune function. Sterols, mainly β - sitosterol, have significant anti-inflammatory effects, can regulate cell signal transduction and improve vascular endothelial health. The content of volatile oil is 0.1% -0.5%, which has antibacterial and analgesic effects, and can improve the cardiovascular and cerebrovascular microenvironment and protect the heart.

Polysaccharide content is 5% -10%, which can regulate immunity and anti-tumor, and play a role by improving the activity of macrophages.

The main secondary metabolites of *Panax notoginseng* include flavonoids, saponins, phenolic acids, amino acids and polysaccharides, which have significant pharmacological effects in the prevention and treatment of CCVDs. The content of flavonoids is about 1.2% -3.5%, which has the effects of antioxidant, anti-inflammatory, improving microcirculation, reducing blood lipids and scavenging free radicals. Saponins include ginsenosides and *Panax notoginseng* saponins, which can promote blood circulation and anti thrombosis. *Panax notoginseng* saponins can reduce cholesterol and inhibit arteriosclerosis. The total amount of phenolic acids is about 1.8% -2.2%, which has antioxidant activity and can reduce pathological damage. Polysaccharide has immune regulation and other functions, with a molecular weight of 1000-50000 da. The total content of amino acids is about 9% -12%, which can promote insulin secretion and improve metabolism. In addition, *Panax notoginseng* also contains trace elements such as zinc and selenium, which help maintain cardiovascular and cerebrovascular health.

3. Overview of CCVDs

3.1. Pathogenesis

The pathogenesis of CCVDs is complex, which is affected by many factors such as heredity, environment, lifestyle and metabolism. Atherosclerosis is the basic pathological change of the disease, and its pathogenesis covers endothelial cell function damage, lipid deposition and fat plaque formation.

Hypertension, hyperglycemia, smoking and inflammation can cause endothelial cell damage, increase vascular permeability, release inflammatory mediators, and then promote the proliferation of smooth muscle cells. During the formation of atherosclerosis, low density lipoprotein (LDL) will accumulate in the intima of the artery, trigger local inflammation and oxidative stress, and form foam cells and lipid cores. This process involves the interaction between cytokines and immune cells, such as the transformation of monocytes into macrophages, thereby changing the structure and function of the arterial wall. Inflammatory factors promote smooth muscle cells to migrate to the intima and form fibrous caps [4].

Thrombosis is the key factor inducing cardiovascular and cerebrovascular events, which usually occurs in the rupture of atherosclerotic plaque. Plaque rupture can lead to platelet aggregation and coagulation reaction, leading to thrombosis, and ultimately induce myocardial infarction and ischemic stroke. Platelet activating factor (PAF) and thrombin play an important role in this process.

CCVDs are closely related to metabolic syndrome such as systemic inflammation, diabetes, obesity and hyperlipidemia. These factors affect endothelial function and aggravate atherosclerosis by regulating biomarkers such as C-reactive protein (CRP) and tumor necrosis factor - α (TNF - α). Changes in cellular signaling pathways, such as abnormal activation of phosphatidylinositol 3-kinase (PI3K) and mitogen activated protein kinase (MAPK) pathways, are also associated with CCVDs [5].

3.2. Clinical symptoms

The clinical symptoms of CCVDs are various, including headache, dizziness, fatigue and so on. Headache is usually caused by cerebral ischemia or increased intracranial pressure, and may be accompanied by nausea, vomiting and other symptoms; Vertigo is related to cerebral blood supply

insufficiency, and patients may have physical imbalance or spatial orientation disorder; Palpitation is a manifestation of arrhythmia, which may be accompanied by chest discomfort and affect daily life; Chest pain is common in patients with coronary heart disease, which is manifested as a sense of oppression or tingling. The symptoms will be aggravated when they are active or emotional. Typical angina pectoris can be relieved after rest or nitroglycerin; Dyspnea is related to heart or lung lesions. The symptoms are aggravated when lying flat or moving, often accompanied by cough and expectoration. If edema is caused by heart lesions, the symptoms will be further aggravated [6].

Electrocardiography (ECG) and echocardiography (echo) are important means to evaluate CCVDs. ECG can identify arrhythmia, myocardial ischemia and other conditions. Echo can be used to evaluate the structure and function of the heart. CT or MRI can help early identify high-risk atherosclerotic plaques and timely intervene [7].

These clinical symptoms and pathological mechanisms provide an important basis for the early diagnosis and treatment of CCVDs. Further research can point out the direction for exploring more effective intervention measures. At the same time, it is necessary to conduct regular physical examination and health monitoring in order to discover and manage potential risks in time.

3.3. Common treatment methods

The treatment methods of CCVDs mainly include drugs, intervention, surgery and other treatments, as well as the adjuvant treatment of TCM. In drug therapy, antihypertensive drugs (such as ACE inhibitors, calcium channel blockers, diuretics) are used in patients with hypertension, and the drugs are selected according to the specific situation; Statins (such as amlodipine and lovastatin) are used in patients with atherosclerosis and coronary heart disease, and the recommended LDL-C (low-density lipoprotein cholesterol) reduction target is <2.6 mmol/L; Nitrates (such as nitroglycerin) and β - receptor antagonists (such as metoprolol) can relieve symptoms and reduce cardiac load in patients with angina pectoris.

In terms of interventional therapy, cardiovascular interventional technology has developed rapidly. Percutaneous coronary intervention (PCI) is the main treatment for coronary heart disease, and it is recommended for patients with acute myocardial infarction within 120 minutes after onset. Drug eluting stent (DES) can reduce the restenosis rate. Aspirin and clopidogrel are used to prevent thrombosis 3-12 months after stent implantation. Carotid endarterectomy (CEA) can reduce the risk of stroke in patients with severe cerebrovascular stenosis.

Surgical treatment includes bypass surgery (CABG), which is used for patients with severe coronary artery disease to improve the blood supply to the heart. Usually, 1-4 vascular bridges are implanted. Long term management of heart failure and new arrhythmias is required after operation. For ischemic stroke, robot assisted surgery has been developed in recent years, which has improved the accuracy and safety [8,9].

In general, the treatment of CCVDs should be set according to the individual patient and the type of disease. Active intervention, early diagnosis and personalized treatment are the key to improve the prognosis and reduce the disability and mortality rate.

4. Pharmacological effects of *Panax notoginseng*

4.1. Effect on heart

The effects of *Panax Notoginseng* on the heart are mainly reflected in improving myocardial ischemia, reducing blood lipids, antioxidation, regulating cardiovascular function and so on. Studies

have shown that it can inhibit cardiomyocyte apoptosis and oxidative stress, promote myocardial repair and enhance cardiac function. Relevant experiments showed that Panax notoginseng saponins could increase cardiac output and reduce the area of cardiac necrosis after myocardial infarction. In clinical trials, the use of 3-9 g/day of Panax notoginseng routine administration can reduce the frequency of angina pectoris and improve ECG. The experimental data showed that Panax notoginseng could reduce LDL-C level, increase HDL - C level and improve plasma lipid metabolism. In addition, it inhibits platelet aggregation, reduces the risk of thrombosis, and promotes cardiovascular health [10].

In terms of antioxidation, Panax notoginseng increased the activities of superoxide dismutase (SOD) and glutathione peroxidase (GSH - PX), reduced the production of free radicals and reduced the damage of heart cells. Related experiments show that it can improve the activity of antioxidant enzymes in myocardial tissue and reduce the content of malondialdehyde (MDA), which has an important protective role in cardiac oxidative stress.

In the study of ventricular remodeling, Panax notoginseng improves ventricular structure, reduces ventricular hypertrophy and dilation, and improves cardiac diastolic function. In patients with long-term application of Panax notoginseng, the heart diameter and quality indexes were significantly improved, and the cardiac function score was improved. The regulation of Panax Notoginseng on cardiac physiological function may be related to cardiac autonomic nerve function, and the specific mechanism needs to be studied.

In general, Panax notoginseng can improve the pathological state of cardiovascular disease by acting on the heart through multiple targets and pathways, which has a good prospect of clinical application. Further research on its pharmacology and clinical application will provide theoretical and clinical basis for the prevention and treatment of cardiovascular diseases [11,12].

4.2. Effect on cerebral vessels

The effects of Panax Notoginseng on cerebral vessels are mainly reflected in anti ischemia, improving microcirculation and protecting neurons. Studies have shown that the effective components of Panax notoginseng, such as ginsenosides, ginsenosides and glycans, have significant protective effects on cerebral ischemia model. Taking rats as the object, the administration of Panax notoginseng extract after the induction of local cerebral ischemia can significantly reduce the neurological deficit and cerebral infarction volume. In terms of dose, Panax notoginseng extract as low as 10 mg/kg can significantly improve cerebral blood flow perfusion, with an improvement rate of 30%. Panax notoginseng has obvious protective effect on endothelial cells, which can promote the synthesis of nitric oxide (no) and improve the ability of vascular expansion. After acute ischemia, Panax notoginseng can inhibit inflammatory reaction and reduce brain tissue damage. In diet, Panax notoginseng combined with common drugs can enhance the therapeutic effect, for example, combined with aspirin can improve the hemodynamic parameters. Clinical observation found that Panax notoginseng had obvious curative effect on patients with mild to moderate stroke. After treatment with Panax notoginseng soft capsule (each capsule containing 150 mg of Panax notoginseng extract) for 4 weeks, the proportion of patients' symptoms improved was 65%. Experimental results show that Panax notoginseng can reduce the activation of apoptotic proteins and promote the release of growth factors by regulating the pathway of cell apoptosis, which contributes to the survival and functional recovery of neurons. At the same time, Panax notoginseng has strong anticoagulant effect in reducing cerebral thrombosis, and can reduce the platelet aggregation rate by more than 30%. In general, Panax notoginseng has a broad application prospect

in the prevention and treatment of cerebrovascular diseases, and its multi-target mechanism is worthy of further study [13].

4.3. Other pharmacological effects

Panax notoginseng is a TCM, which has multiple pharmacological effects in addition to significant curative effects on CCVDs. Its active ingredients are mainly ginsenosides, such as Rb1, Rg1, Rg3, etc., with antioxidant, anti-inflammatory, immune regulation and other biological activities.

The study found that *Panax notoginseng* extract can reduce the level of oxidative stress, promote the activity of antioxidant enzymes, improve the antioxidant capacity of cells, and reduce the cell damage induced by H₂O₂ in vitro. At the same time, *Panax notoginseng* has anti-inflammatory effect, can inhibit the release of inflammatory factors by macrophages, inhibit the activation of NF- κ B signaling pathway, and reduce inflammatory reaction, which has been verified in the chronic disease model.

In addition, *Panax notoginseng* can promote blood circulation, improve microcirculation and other ways to prevent thrombosis. Animal experiments show that it can improve hemorheological indexes in mice. In terms of immune regulation, it can enhance the proliferation of lymphocytes, promote the production of cytokines, and promote humoral and cellular immunity in mice.

In the anti-tumor research, *Panax notoginseng* saponins can inhibit the proliferation of tumor cells, regulate the expression of apoptosis related proteins, and have good anti-cancer effect, which is suitable for a variety of tumor research. Moreover, *Panax notoginseng* has neuroprotective effect, which can reduce neuronal apoptosis and prevent the occurrence of neurodegenerative diseases. In conclusion, *notoginseng* not only plays an important role in the treatment of CCVDs, but also has a wide range of pharmacological effects, and has application potential in the field of modern medicine [14,15].

5. Conclusion

Panax notoginseng, the scientific name of *Panax notoginseng*, has attracted much attention because of its significant pharmacological effect in the prevention and treatment of CCVDs. Many studies have shown that *Panax notoginseng* has multiple cardiovascular and cerebrovascular protection mechanisms, such as anticoagulation, anti-inflammatory, vasodilation, reducing blood lipids, and protecting the myocardium. The relevant literature showed that *Panax notoginseng* saponins could significantly improve the release of PGI₂ in hippocampal cells by inhibiting platelet aggregation, and its main component, *Panax notoginseng* saponins Rh2, could reduce myocardial ischemia-reperfusion injury in animal experiments, and the ECG indexes were significantly improved. In a recent clinical study, the application of *Panax notoginseng* extract (400 mg/day) compared with the placebo group showed a significant effect in improving the symptoms of coronary heart disease, and the frequency of angina pectoris was reduced by 35%.

The regulating effect of *Panax Notoginseng* on blood lipids has also been widely recognized. Studies have shown that *Panax notoginseng* extract can reduce total cholesterol and LDL-C by regulating lipid metabolism in the liver and reducing cholesterol levels. A follow-up study in 2023 pointed out that in the *Panax notoginseng* intervention group, the average reduction of LDL-C was 20.2%, and the average reduction of total cholesterol was 15.8%. In addition, the anti-inflammatory effect of *Panax notoginseng* is mainly attributed to its inhibition of NF- κ B signaling pathway, thereby reducing the release of inflammatory factors, preventing and improving the occurrence of atherosclerosis.

In terms of myocardial protection, the alkaloids of *Panax notoginseng* can significantly reduce the level of oxidative stress, improve mitochondrial function, and then affect cardiac contractility and diastolic function under myocardial ischemia. The experimental data showed that the heart rate variability index of *Panax notoginseng* extract treatment group increased, indicating that it has a positive effect on cardiac autonomic nerve function.

The future research direction can focus on the molecular mechanism of the active ingredients of *Panax notoginseng* and the clinical efficacy evaluation of its combination. Multi center large-scale clinical trials will help to further verify the effectiveness and safety of *Panax notoginseng* in the field of CCVDs. In addition, we should explore the appropriate preparation form and route of administration to improve the bioavailability of *Panax notoginseng* and promote its wide clinical application.

References

- [1] Wen, Q. (2022). Study on quality standard of *Panax notoginseng* saponins sustained release nanocapsules.
- [2] Huang, Y. W., Luo, F., Zhang, M., et al. (2024). 20(S)-Protopanaxatriol improves atherosclerosis by inhibiting low-density lipoprotein receptor degradation in ApoE KO mice. *Journal of Cardiovascular Pharmacology*.
- [3] Xu, X. (2022). Research on quality evaluation of ginseng traditional Chinese medicine and related Chinese patent medicine based on multidimensional "one method and multiple uses" strategy.
- [4] Cui, Z., Liang, Y., Li, Q., et al. (2023). Experience of self-made Shenqi Tangluo Decoction in the prevention and treatment of vascular complications of type 2 diabetes mellitus based on the theory of "Tangluo disease". *Clinical Research of Traditional Chinese Medicine*.
- [5] Jiang, H., Huang, X., Xian, B., et al. (2023). Chinese herbal injection for cardio-cerebrovascular disease: Overview and challenges. *Frontiers in Pharmacology*.
- [6] None. (2020). Three points tell you: Why does *Panax notoginseng* become a member of the "new coronavirus pneumonia"! *Ginseng Research*.
- [7] Wang, X., Zhang, L., & Wang, J. W. L. (2023). Improvement on renal interstitial fibrosis in rats with renal failure via TLR4/NF- κ B signaling pathway by means of *Panax notoginseng* saponins. *Materials Express: An International Journal on Multidisciplinary Materials Research*, 13(11), 1875–1881.
- [8] Xie, Q. (2020). *Bidens bipinnata*. Happy: Kangleshou.
- [9] Zhou, J. (2020). Study on the structural modification and diastolic cardiocerebral vascular activity of *Panax notoginseng* saponins and analogues.
- [10] Liu, Y., Zhu, L., Tang, J., et al. (2024). Research progress on chemical constituents and pharmacological effects of *Sedum notoginseng*. *Journal of Shaanxi University of Traditional Chinese Medicine*.
- [11] Chen, K. (2022). Simultaneous determination of 28 *Panax notoginseng* saponins by UPLC-MS/MS and preliminary study on pharmacokinetics in vivo.
- [12] Lv, D. (2022). Quality evaluation of new *Panax notoginseng* decoction pieces based on pharmacological activity and metabonomics.
- [13] Li, Z. (2022). Pharmacological effects of *Panax notoginseng* saponins on cardiovascular and cerebrovascular diseases. *Chinese Science and Technology Journal Database (Full Text Version) Medical and Health*.
- [14] Liu, P. (2020). Regulation mechanism of potassium on pnpme1 gene of *Panax notoginseng* under cadmium stress through brassinolide signaling pathway.
- [15] Hui, X. (2022). *Panax notoginseng* regulates miR-370-3p/IRAK2/NF- κ B pathway to improve vascular endothelial function injury in hyperlipidemia.