

Research Progress of Xuefu Zhuyu Decoction and Its Single Herbs in the Treatment of Coronary Heart Disease

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Abstract: *Coronary atherosclerotic heart disease, abbreviated as coronary heart disease (CHD), is a chronic cardiovascular disease and one of the major diseases threatening the life and health of populations worldwide. Its morbidity and mortality rates are on the rise. In recent years, CHD has also shown a trend of affecting younger individuals, making long-term treatment and management critically important. In traditional Chinese medicine (TCM), CHD falls under the category of "chest stuffiness and heart pain" (xiongbi xintong). Xuefu Zhuyu Decoction is a classic TCM formula used in clinical practice for promoting blood circulation and removing blood stasis, first recorded in the Qing dynasty medical text Yilin Gaicuo (Corrections on Medical Errors). The formula is rigorously composed, consisting primarily of eleven medicinal herbs: Persicae Semen (Taoren), Carthami Flos (Honghua), Angelicae Sinensis Radix (Danggui), Rehmanniae Radix (Shengdi), Chuanxiong Rhizoma (Chuanxiong), Paeoniae Radix Rubra (Chishao), Achyranthis Bidentatae Radix (Niuxi), Platycodi Radix (Jiegeng), Bupleuri Radix (Chaihu), Aurantii Fructus (Zhiqiao), and Glycyrrhizae Radix (Gancao). When combined, these herbs exert the core actions of promoting blood circulation, removing blood stasis, regulating qi flow, and alleviating pain. Clinically, it is widely used for various conditions caused by internal blood stasis and qi obstruction. Studies have found that Xuefu Zhuyu Decoction contains volatile oils, alkaloids, flavonoids, and other components, which exhibit anti-myocardial ischemia effects, improve blood circulation, resist atherosclerosis, and influence angiogenesis, thereby demonstrating the advantages of TCM in the clinical diagnosis and treatment of CHD.*

Keywords: Coronary heart disease, Xuefu Zhuyu Decoction, Pharmacological research, Traditional Chinese medicine therapy.

1. Introduction

CHD is a cardiac disease caused by coronary atherosclerosis, which narrows or even occludes the vascular lumen, reducing or eliminating blood supply to the heart, leading to ischemia, hypoxia, and even necrosis of corresponding cardiomyocytes, thereby triggering a series of symptoms. In mild cases, patients experience chest tightness and chest pain after physical activity or emotional agitation, which may be relieved by rest or medication; in severe cases, the chest pain is intractable, leading to myocardial infarction and life-threatening consequences [1]. Globally, CHD has become a major cardiovascular disease that endangers physical and mental health, causes mortality, and increases the societal disease burden, and it is currently a key public health concern. In TCM, CHD is classified as xiongbi xintong (chest stuffiness and heart pain). Most TCM practitioners believe that the pathological nature of CHD is generally characterized by "phlegm turbidity" (tanzhuo), "blood stasis" (xueyu), and "heat toxin" (redu) as the manifestations, with "qi deficiency" (qixu), "yang deficiency" (yangxu), and "yin deficiency" (yinxu) as the root causes [2]. Blood stasis in the vessels runs through the entire course of the disease [3], with varying intrinsic pathological changes at different stages.

2. Clinical Observations and Experimental Studies of Xuefu Zhuyu Decoction in Treating CHD

2.1 Protection of Cardiomyocytes

He Li et al. [4] demonstrated through observation of mitochondrial ultrastructure that the pathological state of

myocardial tissue could be regulated by Xuefu Zhuyu Decoction, which also alleviated the degree of myocardial mitochondrial damage. By continuously regulating the level of mitophagy, the decoction ultimately exerted a protective effect on cardiomyocytes. Further research focusing on the NLRP3 signaling pathway has confirmed that the therapeutic effect of Xuefu Zhuyu Decoction is dose-dependent and can block the progression of myocardial injury by enhancing mitophagy and reducing the proportion of damaged cardiomyocytes. This mechanism provides a new research direction and theoretical basis for the prevention and treatment of myocardial ischemic diseases with TCM, and also identifies novel therapeutic targets for clinical myocardial protection. Chen Yuchun [5] conducted a study involving 120 patients with ischemic cardiomyopathy complicated by heart failure, setting up a control group and a combined treatment group, of which 60 patients received a clinical intervention combining trimetazidine and Xuefu Zhuyu Decoction. The results showed that the combination of trimetazidine and Xuefu Zhuyu Decoction yielded ideal therapeutic effects and high clinical application value, suggesting its potential for clinical promotion. Li Lei [6] observed mitochondrial ultrastructure using transmission electron microscopy, and the results showed that cardiomyocytes in the Xuefu Zhuyu Decoction intervention group exhibited only mild edema, with less severe and limited mitochondrial structural damage, and a small number of autophagosomes were observed. These findings fully demonstrated that Xuefu Zhuyu Decoction could alleviate the pathological injury of cardiomyocytes, reduce mitochondrial structural and functional damage, positively regulate mitophagy, and thereby achieve myocardial protection. Chang Bing [7] also confirmed in an animal model

experiment that Xuefu Zhuyu Decoction effectively inhibited vascular remodeling in CHD model rats and exerted significant cardioprotective effects, with the mechanism likely closely related to the regulation of the PI3K-AKT signaling pathway.

2.2 Improvement of Cardiac Function

Miao Yuli [8] found that the left ventricular ejection fraction and left ventricular fractional shortening in patients receiving Xuefu Zhuyu Decoction were higher than those in the control group, confirming that this formula could effectively optimize cardiac function indicators and alleviate the clinical symptoms of angina pectoris in CHD patients. Li Jing [9] verified through animal experiments that Xuefu Zhuyu Decoction significantly improved myocardial injury, repaired vascular endothelial damage, and induced angiogenesis in CHD model rats with the syndrome of blood stasis obstructing the heart vessels. The pharmacological mechanism may be closely related to the upregulation of HIF-1 α , VEGF-A, and VEGFR-2 protein expression in myocardial tissue. From the perspective of TCM pharmacology, Xuefu Zhuyu Decoction promotes blood circulation, removes blood stasis, unblocks blood vessels, and improves microcirculation, thereby facilitating the repair of impaired cardiac function. Relevant studies have confirmed that the combination of this formula with metoprolol sustained-release tablets exerts synergistic therapeutic effects, effectively regulating blood pressure, reducing heart rate, decreasing cardiac workload, further improving cardiac function, and enhancing clinical efficacy [10].

2.3 Inhibition of Inflammatory Responses

Li Guangzhi et al. [11] found that using Xuefu Zhuyu Decoction as an adjunctive therapy for CHD effectively alleviated the micro-inflammatory state in patients, while inhibiting thrombosis, which had a positive impact on improving long-term prognosis. It could optimize various lipid parameters in CHD patients and downregulate the expression levels of inflammatory factors such as MCP-1, TXB2, and hs-CRP, thereby improving overall therapeutic efficacy and effectively reducing the dosage of nitroglycerin used by patients. Ren Xiaoqing et al. [12] confirmed that, on the basis of conventional Western medical treatment, the combined intervention of Xuefu Zhuyu Decoction and modified Shixiao San could, through regulating fatty acid metabolism and inhibiting the activation of NLRP3 inflammasomes, significantly suppress the release of inflammatory factors, correct lipid metabolism disorders, and ultimately achieve improved myocardial function and enhanced therapeutic outcomes for CHD. Lai Xiaoyan et al. [13] conducted a study on patients with angina pectoris of the phlegm-stasis intermingling type and found that modified Xuefu Zhuyu Decoction effectively reduced systemic inflammatory responses, optimized cardiac function indicators, and alleviated the clinical symptoms of angina pectoris, with good safety and no significant adverse reactions. Li Shujing [14] also confirmed in a clinical observation that Xuefu Zhuyu Decoction had significant efficacy in patients with angina pectoris of the heart-vessel stasis obstruction type, markedly improving clinical response rates, enhancing

cardiac function, and effectively reducing the levels of inflammatory factors and alleviating inflammatory damage.

3. Pharmacological Studies of Xuefu Zhuyu Decoction in Treating CHD

3.1 Screening of Core Active Ingredients and Molecular Docking Validation

Kuang Huifang et al. [15], using network pharmacology approaches, confirmed that the active components in Xuefu Zhuyu Decoction could form stable and potent binding interactions with core therapeutic targets for CHD and ischemic stroke. Among them, quercetin, luteolin, and kaempferol were identified as the primary material bases for the formula's pharmacological effects. These active components regulate core targets including ALB, IL-6, TNF, Akt1, and INS, and mediate multiple signaling pathways such as lipid metabolism disorders, atherosclerosis, HIF-1, relaxin, NF- κ B, and insulin resistance, thereby participating in the regulation of various pathological processes including inflammatory responses, oxidative stress injury, aberrant angiogenesis, vascular dysfunction, cell apoptosis, and lipid metabolism disorders. Through the synergistic regulation of multiple components, multiple targets, and multiple pathways, they inhibit inflammatory progression, improve hemorheological status, and ultimately exert therapeutic effects on CHD and ischemic stroke.

Ma Shuhui et al. [16] systematically investigated the material basis and mechanism of action of Xuefu Zhuyu Decoction in treating CHD by constructing drug-disease intersection target networks and component-target networks. This study screened 170 common targets shared between Xuefu Zhuyu Decoction and CHD and performed visualization network analysis using Cytoscape software. According to degree value ranking, the top five core active components were quercetin, luteolin, kaempferol, wogonin, and naringenin, with degree values of 102, 40, 37, 30, and 28, respectively, clearly identifying the aforementioned components as the key pharmacologically active substances of Xuefu Zhuyu Decoction in the treatment of CHD.

3.2 Overall Pharmacological Effects in Treating CHD

Studies [17-19] have found that the pharmacological effects of Xuefu Zhuyu Decoction in treating CHD are characterized by multi-pathway and multi-target actions. This formula not only protects vascular endothelial structure and function and optimizes cardiac function but also effectively inhibits abnormal platelet aggregation and alleviates myocardial injury caused by ischemia-reperfusion. Furthermore, Xuefu Zhuyu Decoction exerts protective effects on ischemic myocardial tissue by blocking cardiomyocyte apoptosis, reducing myocardial ischemic lesions, and suppressing local inflammatory infiltration. In addition, it alleviates myocardial oxidative stress injury, ameliorates the pathological state of myocardial tissue, induces the migration of endothelial progenitor cells and endothelial cells, and promotes neovascularization, thereby improving the pathological damage of CHD from multiple aspects and exerting therapeutic effects.

3.3 Studies on the Active Components of Individual Herbs in Xuefu Zhuyu Decoction for Treating CHD

Studies have shown that the active components of the individual herbs in Xuefu Zhuyu Decoction mainly include amygdalin, quercetin, luteolin, β -sitosterol, stigmasterol,

tetramethylpyrazine, ferulic acid, monoterpenoids, polysaccharides, organic acids, saikosaponins, platycodin, and glycyrrhizin, among others. A summary of the specific targets of these active components and their mechanisms of action in treating CHD is presented in Table 1.

Table 1: Mechanisms of action of active components from individual herbs in Xuefu Zhuyu Decoction for treating CHD				
Herb	Active Components	Targets	Effects	References
Persicae Semen (Taoren)	Amygdalin	TNF- α , IL-6, CRP $\downarrow$; TC, TG, LDL-C $\downarrow$; HDL-C $\uparrow$; NF- κ B p65, COX-2 mRNA $\downarrow$; p-NF- κ B p65, COX-2 protein $\downarrow$	Anti-atherosclerosis, anti-inflammatory, anti-tumor, immunomodulation	[20-21]
Carthami Flos (Honghua)	Quercetin, luteolin, kaempferol, baicalein, β -carotene, β -sitosterol, stigmasterol	VEGF-A $\uparrow$; MMP-9 $\uparrow$; cTnI, 8-OHdG $\downarrow$	Myocardial protection, anti-thrombosis, anti-inflammatory	[22-23]
Angelicae Sinensis Radix (Danggui)	β -sitosterol, stigmasterol	Bcl-2 $\downarrow$; Caspase-3 $\uparrow$; (NF)- κ B, IL-6, TNF- α $\uparrow$	Anti-inflammatory, antioxidant, immunoregulation, anti-aging	[24]
Chuanxiong Rhizoma (Chuanxiong)	Tetramethylpyrazine, ferulic acid	HO-1, VEGF $\uparrow$	Antioxidant, anti-inflammatory, anticoagulant, pro-angiogenesis, vasodilation, blood pressure regulation	[25]
Paeoniae Radix Rubra (Chishao)	Monoterpenoids, polysaccharides, organic acids	VEGF, bFGF $\uparrow$; vascular cell adhesion molecule-1 $\uparrow$; serum IL-2, CRP, TNF- α $\downarrow$; NF- κ B p65, VEGF $\downarrow$	Anti-platelet aggregation, anti-inflammatory, anti-thrombosis, anti-atherosclerosis, lipid-lowering, glucose-lowering	[26-27]
Rehmanniae Radix (Shengdi/Shudi)	Sitosterol/stigmasterol, catalpol, iridoids, ionone-like and phenylethanoid compounds	IL-6, TNF- α $\downarrow$	Anti-inflammatory, antioxidant, vascular endothelial protection, reduction of inflammatory response, myocardial protection	[28-30]
Bupleuri Radix (Chaihu)	Saikosaponin D	BDNF-TrkB $\uparrow$; IL-1 β , IL-6, TNF- α $\downarrow$	Anti-cancer, anti-depressant, anti-inflammatory, cardioprotective	[31]
Aurantii Fructus (Zhiqiao)	Flavonoids, synephrine, N-methyltyramine	NF- κ B $\downarrow$; TNF- α $\downarrow$; IL-6 $\downarrow$; IL-1 β $\downarrow$; HIF-1 α $\uparrow$; GSK-3 β $\downarrow$	Increased cardiac output, elevated left ventricular pressure and arterial blood pressure; reduced vascular fragility, shortened bleeding time, prevention of atherosclerosis	[32-33]
Platycodi Radix (Jiegeng)	Platycodin D	VCAM-1 $\downarrow$; ICAM-1 $\downarrow$ (mRNA $\downarrow$); NF- κ B $\downarrow$; iNOS $\downarrow$; COX-2 $\downarrow$	Anti-tumor, immunomodulation, anti-inflammatory, hepatoprotective, anti-atherosclerosis	[34]
Achyranthis Bidentatae Radix (Niuxi)	Steroids, triterpenoid saponins, polysaccharides	PTEN $\downarrow$; Akt $\uparrow$	Anti-inflammatory analgesia, cardiovascular system protection, effective reduction of myocardial ischemia	[35]
Glycyrrhizae Radix (Gancao)	Glycyrrhizin	TNF- α $\downarrow$; IL-6 $\downarrow$; SIRT1 $\uparrow$	Anti-oxidative stress, anti-inflammatory, inhibition of apoptosis	[36]

Note: $\uparrow$ indicates promotion/elevation; $\downarrow$ indicates inhibition/reduction.

4. Conclusions and Prospects

At present, the prevalence of CHD is increasing annually, commonly affecting middle-aged and elderly populations, with a trend toward younger age groups. The symptoms commonly seen in CHD patients, such as chest tightness, chest pain, and palpitations, closely correspond to the “blood stasis in the chest” pattern targeted by this formula. Through the blood-activating and collateral-unblocking actions of core herbs such as Persicae Semen, Carthami Flos, and Chuanxiong Rhizoma, the formula directly alleviates the blood supply insufficiency caused by vascular obstruction, with significant clinical efficacy in symptom relief. Xuefu Zhuyu Decoction is currently an effective TCM formula for the treatment of CHD. Its compound formulation can be tailored according to the patient’s actual condition, allowing flexible modifications in herbal composition. The overall incidence of adverse reactions is relatively low, the safety profile is favorable, and patient compliance is high. In clinical practice, the combination of Xuefu Zhuyu Decoction with conventional Western medical therapies (including antiplatelet agents and statin lipid-lowering drugs) can further reduce the frequency of angina attacks, enhance exercise tolerance, and alleviate some of the gastrointestinal side

effects of Western medications, thereby improving treatment adherence. Pharmacological studies indicate that Xuefu Zhuyu Decoction offers advantages in CHD treatment, including broad-spectrum activity, multi-target actions, and a relatively safe therapeutic profile. However, the following issues remain to be addressed: First, most studies employ relatively simple control groups, making it difficult to comprehensively and systematically reveal the overall therapeutic characteristics and mechanistic basis of Xuefu Zhuyu Decoction in CHD treatment. Second, existing clinical studies predominantly focus on the combination of the formula with Western drugs, while the standalone effects of the pure TCM formula or individual herbs in the formula lack sufficient supporting data and require further investigation and validation. Third, current research mostly concentrates on the separate targets of individual active components, without in-depth exploration of the interconnections and regulatory relationships among different targets, leaving the relevant mechanistic studies still relatively superficial. In view of these limitations, future research may focus on exploring new targets and deeper mechanistic levels of Xuefu Zhuyu Decoction in treating CHD, or adopt network pharmacology approaches combined with data mining techniques to investigate the correlations among targets of various active components, thereby providing a reliable theoretical basis for

TCM treatment of CHD in the future.

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