

# *Research Progress on Traditional Chinese Medicine Treatment of Viral Myocarditis*

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**Abstract:** Viral Myocarditis (VMC) is an inflammatory condition of the myocardium caused by infections such as Coxsackie B viruses. Traditional Chinese Medicine classifies it under categories such as "palpitations" and "heart-related disorders," with "deficiency, toxin, and stasis" as the core pathogenesis. This paper systematically reviews the research progress on the treatment of VMC with traditional Chinese medicine: active components of Chinese herbal medicines, such as puerarin, astragaloside I, total saponins of Panax notoginseng, and berberine, can protect the myocardium through antiviral, antioxidant, and anti-inflammatory mechanisms; Compound formulas such as Shengmai San and Yiqu Jiedu Tang, as well as proprietary Chinese medicines like Shenmai Injection and Xiaochaihu Granules, have demonstrated definite efficacy in improving clinical symptoms and regulating immune function; external therapies such as acupuncture and acupoint plaster application have also shown unique advantages, providing important references for the comprehensive prevention and treatment of VMC.

## 1. Introduction

Viral myocarditis (VMC) is one of the common diseases of the cardiovascular system, referring to localized or diffuse inflammatory lesions of the myocardium caused by infections such as Coxsackie B viruses and influenza viruses<sup>[1]</sup>. Clinically, VMC is primarily characterized by palpitations, chest tightness, fatigue, and arrhythmias; in severe cases, it can progress to dilated cardiomyopathy or even sudden cardiac death. The disease is most common in children and adolescents and is one of the leading causes of sudden cardiac death in young and middle-aged adults. Epidemiological data indicate that 4 to 14 people per 100,000 are affected by this disease globally each year<sup>[2]</sup>. With changes in environmental factors and advances in diagnostic methods, the incidence of VMC has been rising annually, making it a significant global public health challenge. Therefore, the prevention and treatment of VMC are of urgent importance. Traditional Chinese Medicine (TCM) has demonstrated significant efficacy in managing VMC and slowing disease progression. This article aims to summarize the recent research landscape on the treatment of VMC with TCM.

## 2. Traditional Chinese Medicine's Understanding of VMC

### 2.1. Understanding of Etiology and Pathogenesis

Although the term “viral myocarditis” does not appear in classical TCM texts, based on its clinical manifestations, the condition is often classified under categories such as “palpitations”, “cardiac agitation”, “chest obstruction”, and “anxiety”. The Huangdi Neijing states: “ ‘The heart trembles as if someone were about to seize it,’ and ‘If chest obstruction persists and one is further affected by pathogenic factors, they will lodge within the heart,’ these passages already demonstrate an understanding of the etiology and pathogenesis of this disease<sup>[3]</sup>. The modern TCM community generally holds that the onset of viral myocarditis is the result of the interaction between internal and external factors, with the primary site of pathology being the heart, though it often involves other organs such as the lungs, spleen, and kidneys<sup>[4]</sup>.

Regarding internal factors, a constitutional deficiency of vital energy (zhengqi) serves as a crucial foundation for the onset of this disease<sup>[5]</sup>. The Suwen: Treatise on the Evaluation of Feverish Diseases states, “Where pathogenic factors gather, the vital energy must be deficient.” This deficiency of vital energy may stem from constitutional insufficiency or result from excessive fatigue, prolonged illness leading to physical debility, and the depletion of vital energy. Regarding external factors, the primary cause is the invasion of warm-heat toxins. These toxins typically enter through the skin and hair or the mouth and nose, then progress from the exterior to the interior, where they linger and fail to dissipate, ultimately lodging in the heart. Ye Tianshi's theory that “when warm pathogens are received from above, they first attack the lungs and then reverse to the pericardium” aptly elucidates the pattern of transmission from the lungs to the heart in this disease<sup>[6]</sup>. Regarding the progression of the pathogenesis, the acute phase is characterized by the proliferation of pathogenic toxins, where warm-heat toxins invade the heart internally, depleting heart qi and obstructing the heart meridians; the recovery phase is often marked by deficiency of both qi and yin, with residual toxins remaining, as the heat toxins scorch the ying yin, resulting in damage to both qi and yin of the heart; In the chronic phase, qi deficiency and yang depletion lead to impaired blood circulation; body fluids condense into phlegm, and heat-toxin scorches these fluids, transforming them into stasis, ultimately resulting in the mutual entanglement of phlegm and stasis that obstructs the heart vessels. As emphasized by medical scholars such as Ding Shuwen and others in their “stasis-toxin” theory, the persistent development of stasis-toxin is a critical factor in the protracted course and worsening of viral myocarditis. In summary, the pathogenesis of this disease can be summarized by the three characters “deficiency, toxin, and stasis.” Insufficient vital energy is the root cause of the disease, invasion by pathogenic toxins is the causative factor, and the mutual entanglement of phlegm and stasis is the result of the pathological changes. These three elements are intertwined and persist throughout the entire course of the disease.

### 2.2. Understanding of Syndrome Differentiation and Classification

Based on an in-depth understanding of the etiology and pathogenesis, modern Traditional Chinese Medicine (TCM) has developed a relatively unified understanding of the syndrome differentiation and classification of viral myocarditis, which is primarily divided into three stages for diagnosis: the acute phase, the recovery phase, and the chronic phase<sup>[7]</sup>. The acute phase is commonly characterized by the pattern of pathogenic toxins invading the heart, presenting with symptoms such as persistent fever, red throat with nasal discharge, cough with phlegm, palpitations and shortness of breath, chest tightness and chest pain, a red tongue with a yellow coating, and a slippery, rapid, or intermittent pulse. Treatment should focus on clearing heat, resolving toxins, calming the heart, and soothing the mind. The recovery phase is primarily characterized by

deficiency of both qi and yin, with symptoms including palpitations and anxiety, chest tightness and shortness of breath, low-grade fever, restlessness, dry mouth and throat, night sweats or spontaneous sweating, and mental and physical fatigue. The tongue is pale red or slightly red with little saliva, and the pulse is fine, weak, rapid, or intermittent. Treatment should focus on tonifying qi, nourishing yin, calming the heart, and soothing the spirit. In the chronic phase, the pattern of phlegm and blood stasis obstructing the meridians is common. Symptoms include chest tightness and stabbing pain, palpitations and restlessness, and cyanosis of the lips and nails. The tongue may appear dark or have ecchymoses, with a greasy coating, and the pulse may be thready or intermittent. Treatment should focus on resolving phlegm, removing blood stasis, unblocking the meridians, and relieving pain.

In addition, some clinicians have proposed other patterns of differentiation based on clinical practice. For example, the pattern of damp-heat invading the heart presents with palpitations, chest tightness, fluctuating chills and fever, generalized muscle aches, and abdominal pain with diarrhea; treatment should focus on clearing heat and resolving dampness<sup>[8]</sup>. The pattern of deficient heart yang presents with palpitations and anxiety, aversion to cold with cold limbs, pale complexion, and limb edema; treatment should aim to warm and invigorate heart yang<sup>[8]</sup>. The syndrome of deficiency of both the heart and spleen, characterized by palpitations, shortness of breath, poor appetite, abdominal distension, loose stools, and a sallow complexion, which should be treated by tonifying the heart and spleen<sup>[9]</sup>. In recent years, with in-depth research into the theories of latent pathogens and stasis-toxin, some scholars have proposed new insights into pathogenesis, such as “latent pathogens concealed within the heart” and “internal accumulation of stasis-toxin,” providing new perspectives for pattern differentiation. Overall, TCM pattern differentiation for viral myocarditis emphasizes the integration of disease staging and pattern classification. Only by grasping the evolutionary patterns of “deficiency, toxin, and stasis” and dynamically observing the fluctuations in the balance between pathogenic factors and the body’s defensive energy can one accurately differentiate patterns and administer precise treatment.

### 3. Traditional Chinese Medicine Treatment for VCM

Modern medicine currently lacks specific antiviral drugs for treating VCM; clinical management primarily focuses on rest, myocardial nutrition, control of arrhythmias, and the prevention and treatment of complications. Leveraging its multi-targeted and holistic regulatory advantages, TCM has demonstrated unique value in alleviating symptoms, promoting myocardial repair, and reducing long-term sequelae, and is gaining increasing recognition. Current research primarily covers two major areas: active components of Chinese herbal medicines and compound formulas. Both focus on the core pathogenesis of VCM—characterized by “deficiency, toxin, and stasis”—and exert therapeutic effects through mechanisms such as antiviral action, myocardial protection, and immune regulation, collectively forming a comprehensive system for TCM intervention in VCM.

#### 3.1. Active Ingredients in Traditional Chinese Medicine

Active ingredients in traditional Chinese medicine refer to components extracted from single-herb preparations that possess well-defined chemical structures and pharmacological activities. Research on these ingredients helps elucidate the material basis and mechanisms of action underlying the treatment of VMC with traditional Chinese medicine. In recent years, with advances in molecular biology techniques, the roles of various active ingredients—including flavonoids, saponins, and alkaloids—in the treatment of VMC have been thoroughly elucidated.

### 3.1.1. Flavonoids

Flavonoids are important active components in the treatment of VMC with TCM, with puerarin being a representative example. Puerarin is an isoflavonoid compound extracted from the leguminous plant *Pueraria lobata*, and it possesses multiple pharmacological effects, including antioxidant, anti-inflammatory, and cardioprotective properties. Yang Kai et al.<sup>[10]</sup> found that puerarin inhibits the progression of VMC by activating the CSE/H<sub>2</sub>S and IL-10/STAT3 pathways and inhibiting the NF- $\kappa$ B signaling pathway. Using a mouse model of VMC induced by Cocksackievirus B3 (CVB3), the study confirmed that puerarin treatment reduces serum tumor necrosis factor- $\alpha$  (TNF- $\alpha$ ), high-sensitivity C-reactive protein (hs-CRP), and cardiac troponin I (cTnI) levels, reduced the phosphorylation levels of phosphoinositide 3-kinase (PI3K) and protein kinase B (AKT) in cardiac tissue, downregulated the expression levels of nuclear factor  $\kappa$ B p65 (NF- $\kappa$ B p65) and NF- $\kappa$ B p50, upregulate the expression of interleukin-10 (IL-10) and signal transducer and activator of transcription 3 (STAT3), increase serum hydrogen sulfide (H<sub>2</sub>S) levels, and elevate the expression of nuclear factor  $\kappa$ B inhibitor  $\alpha$  (I $\kappa$ B $\alpha$ ) in cardiac tissue, thereby effectively delaying VMC.

### 3.1.2. Saponins

Saponins are the core active compounds in traditional Chinese medicines such as *Astragalus* and *Panax notoginseng*, primarily comprising astragaloside I and total saponins from *Panax notoginseng*. Astragaloside I, the main active component of *Astragalus*, has been widely demonstrated to possess cardioprotective effects<sup>[11]</sup>. Studies have shown<sup>[12]</sup> that astragaloside IV, by regulating the IRF7/NLRP3 pathway, reduces NLRP3 expression and the formation of neutrophil extracellular traps (NETs) in CVB3-induced VMC mice, thereby improving myocardial fibrosis and inflammatory responses. Li et al.<sup>[13]</sup> found that astragaloside IV reduces serum CK-MB, LDH, and NT-proBNP levels in CVB3-induced VMC mice, thereby exerting a cardioprotective effect by alleviating the degree of myocardial fibrosis, inflammatory response, and apoptosis.

Total *Panax notoginseng* saponins, as the primary active components of *Panax notoginseng*, also exhibit significant cardioprotective effects. Rong Xing et al.<sup>[14]</sup> found that total *Panax notoginseng* saponins can reduce CVB3-induced iNOS expression in cardiomyocytes, serum NO levels, and inflammatory scores in VMC mice, thereby alleviating inflammatory cell infiltration and ultrastructural damage in the myocardium, and consequently improving VMC. Experiments by Cheng Zhiqing et al.<sup>[15]</sup> demonstrated that in a mouse model of chronic VMC, intervention with total *Panax notoginseng* saponins significantly reduced the degree of myocardial fibrosis, as evidenced by decreases in collagen volume fraction (CVF), perivascular collagen area (PVCA), and both protein and mRNA levels of platelet-derived growth factor-B (PDGF-B). These results suggest that total *Panax notoginseng* saponins may exert their protective effects in improving myocardial fibrosis by regulating PDGF-B expression, thereby inhibiting excessive collagen deposition.

### 3.1.3. Alkaloid Components

Alkaloid compounds, as important active ingredients in traditional Chinese medicine, have demonstrated significant efficacy in the treatment of VMC. Berberine is a representative compound of this class; it is an isoquinoline alkaloid primarily derived from traditional Chinese medicines such as *Coptis chinensis*, which are used to clear heat. A study by Dai et al.<sup>[16]</sup> demonstrated that berberine significantly improves survival rates in CVB3-induced VMC mice, increases ejection fraction (EF) and short-axis shortening fraction (FS), and reduces levels of creatine kinase isoenzyme (CK-MB), aspartate aminotransferase (AST), lactate dehydrogenase (LDH), and creatine kinase (CK). Mechanistic studies indicate that berberine exerts its protective effects through a dual

pathway: on the one hand, it directly inhibits CVB3 viral replication, reducing myocardial viral titers and viral protein 1 (vp1) mRNA expression levels; on the other hand, it suppresses the host inflammatory response, reducing the production of pro-inflammatory factors such as TNF- $\alpha$ , IL-6, and IL-1 $\beta$ , as well as chemokines such as CCL5, CCL2, and CXCL10, and inhibiting the infiltration of CD68<sup>+</sup> macrophages, without affecting the antiviral activity of CD4<sup>+</sup>/CD8<sup>+</sup> T cells.

### 3.2. Traditional Chinese Medicine Formulations and Patent Medicines

Traditional Chinese medicine formulations and patent medicines, based on the holistic concept and syndrome differentiation and treatment, regulate the body's immune balance, suppress inflammatory responses, and improve myocardial energy metabolism through the synergistic action of multiple components and targets, offering unique advantages in the treatment of VMC. In clinical studies, Jiang Zhiyong et al.<sup>[17]</sup> found that among 94 patients with VMC, those who received Yiqie Jiedu Decoction (composed of ginseng, schisandra, biota seed, salvia, safflower, honeysuckle, forsythia, Mentha, Ejiao, Arctium, Fried Glycyrrhiza, Ophiopogon, Schizonepeta, and Fermented Soybean), combined with conventional treatment, had significantly lower CK, AST, and LDH levels, as well as lower TCM syndrome scores, compared to patients receiving conventional treatment alone. This indicates that Yiqie Jiedu Decoction demonstrates superior clinical efficacy in treating VMC. Zhong Bin<sup>[18]</sup> found in a study of 76 patients with VMC that Shengmai San with modifications (composed of Radix Pseudostellariae, Ophiopogon, Schisandra, Astragalus, and Angelica) combined with conventional Western medical treatment could increase the overall response rate. Li Wen et al.<sup>[19]</sup> found that Yinqiao San with modifications (composed of Lonicera japonica, Forsythia suspensa, Isatis root, Platycodon grandiflorus, Mentha haplocalyx, Arctium lappa, Schizonepeta tenuifolia, and Bambusa vulgaris leaves) combined with conventional Western medical treatment can increase the overall response rate and improve TCM syndrome patterns, ventricular premature beats, and cardiac function in patients with acute VMC. Wang Bei et al.<sup>[20]</sup> found that modified Chaihu Guizhi Decoction (composed of Bupleurum, Cinnamomum twig, Scutellaria, Pinellia, Paeonia alba, Codonopsis, fried Glycyrrhiza, jujube, and ginger) combined with conventional treatment can reduce the TCM syndrome score and improve electrocardiogram (ECG) findings in patients with VMC. Shi Zhiling et al.<sup>[21]</sup> found that Shenmai Injection combined with dexamethasone can improve T-lymphocyte subsets in patients with VMC, reduce myocardial enzymes and serum inflammatory markers, indicating that the combination of Shenmai Injection and dexamethasone can suppress inflammatory responses, alleviate oxidative stress, and maintain cellular immune balance. Zhao Yanling<sup>[22]</sup> found that, compared with conventional Western medical treatment alone, Xiaochaihu Granules (composed of Bupleurum, Scutellaria, Ginseng, Fried Licorice, Pinellia, Ginger, and Jujube) combined with conventional Western medical therapy can effectively increase ejection fraction (EF), cardiac index (CI), stroke volume (SV), and cardiac output (CO); increase CD3<sup>+</sup>, CD4<sup>+</sup>, CD8<sup>+</sup>, and NK cell counts; and reduce LDH, CK, CK-MB,  $\alpha$ -hydroxybutyrate dehydrogenase ( $\alpha$ -HBDH), cTnl, and cTnT levels. This indicates that Xiaochaihu Granules can reduce myocardial damage, enhance immune function, and improve VMC. Shang Wei<sup>[23]</sup> found that Re-Du-Ning Injection (composed of Artemisia annua, Lonicera japonica, and Gardenia jasminoides, among others) combined with ribavirin can improve clinical efficacy and myocardial enzyme levels, indicating that Re-Du-Ning Injection is highly effective in treating pediatric VMC with minimal adverse reactions.

Furthermore, animal studies have shown<sup>[24]</sup> that the Qi-tonifying and Blood-activating Formula (composed of Astragalus, Salvia miltiorrhiza, Ophiopogon, Curcuma, and Imperata cylindrica, among others) can improve VMC by upregulating the expression of the ribosomal protein S20 gene in VMC rats. Research by He Junzheng et al.<sup>[25]</sup> indicates that Compound Astragalus Granules

(composed of Astragalus, Scrophularia, Salvia miltiorrhiza, and Oyster shell) can increase serum superoxide dismutase (SOD) levels in VMC mice, reduce serum TNF- $\alpha$  and IL-2 levels, and alleviate myocardial pathological damage, indicating that Compound Astragalus Granules have a significant therapeutic effect on CVB3-induced VMC. Research by Wu Zhihuan<sup>[26]</sup> indicates that Panax notoginseng and Salvia miltiorrhiza Tablets (composed of Panax notoginseng and Salvia miltiorrhiza) can reduce the expression of markers associated with myocardial injury, myocardial cell apoptosis rate, CD4<sup>+</sup>/CD8<sup>+</sup> ratio, and the expression of proteins such as IL-17, IL-10, Toll-like receptor 4 (TLR4), and Notch1, suggesting that Panax notoginseng and Salvia miltiorrhiza Tablets may improve myocardial injury and apoptosis in VMC-infected mice by regulating immune function, inhibiting the activation of the Notch1/TLR4 pathway, and reducing inflammatory responses. A study by Meng Lin et al.<sup>[27]</sup> demonstrated that Guihuang Granules (composed of Angelica sinensis and Panax notoginseng) can reduce mortality, myocardial viral titers, histopathological damage scores, LDH activity, and CK levels in VMC mice, indicating that Guihuang Granules have a protective effect against myocardial damage in VMC mice. Liu Xiong et al.<sup>[28]</sup> found that Xinjiekang (composed of Panax ginseng, Astragalus membranaceus, Isatis indigotica, Salvia miltiorrhiza, Ophiopogon japonicus, Sophora flavescens, and Trichosanthes kirilowii) can increase serum SOD activity in VMC mice and reduce malondialdehyde (MDA) levels in myocardial tissue, indicating that Xinjiekang's antioxidant enzyme activity and rapid clearance of oxygen free radicals in the body are among its mechanisms for treating VMC.

#### 4. External Treatment Methods in Traditional Chinese Medicine for VMC

Acupuncture and acupoint plaster application, as core methods of external treatment in Traditional Chinese Medicine, regulate the flow of qi and blood and balance the yin and yang of the internal organs by stimulating meridians and acupoints; each has its own distinct characteristics in the treatment of VMC. Regarding acupuncture, Hu Zhongchun<sup>[29]</sup> used acupuncture on the Eight Extra Meridian Intersection Points to treat VMC, selecting the Neiguan and Gongsun points in combination, with significant therapeutic effects. The Neiguan point connects to the Yin Wei Meridian and can regulate the heart's qi and blood, nourish the heart and calm the spirit, and promote blood circulation to relieve pain; the Gongsun point belongs to the Foot Taiyin Spleen Meridian and can strengthen the spleen and boost qi, generate blood and nourish the body's vital fluids, and distribute nourishment throughout the body. The synergistic action of these two points enhances the effects of boosting qi and promoting blood circulation, thereby nourishing the heart meridian and calming the mind, leading to spontaneous recovery. Regarding herbal plaster therapy, Li Jianping et al.<sup>[30]</sup> ground Chinese herbs into powder to formulate plasters, which were applied to acupoints for the treatment of VMC patients. The results showed that herbal acupoint plaster therapy was as effective as Western medical treatment.

#### 5. Conclusion

Traditional Chinese Medicine (TCM) treats VMC based on the core pathogenesis of "deficiency, toxin, and stasis." During the acute phase, it focuses on clearing heat and detoxifying; during the recovery phase, on tonifying qi and nourishing yin; and during the chronic phase, on resolving phlegm and removing stasis. This approach offers the advantages of multi-targeted and holistic regulation. Active components of Chinese herbal medicines, such as puerarin, astragaloside I, total saponins of Panax notoginseng, and berberine, exert antiviral, anti-inflammatory, and cardioprotective effects by regulating pathways such as NF- $\kappa$ B and IRF7/NLRP3; Compound formulas such as Shengmai San and Yiqu Jiedu Tang, as well as proprietary Chinese medicines like Shenmai Injection and Xiaochaihu Granules, have demonstrated definite efficacy in improving

overall response rates, enhancing cardiac function, and regulating immunity; acupuncture at acupoints such as Neiguan and Gongsun, along with herbal acupoint plasters, regulate qi, blood, and yin-yang through meridian pathways, providing non-invasive adjunctive therapies. However, current research still has limitations: most studies remain at the stage of animal experiments or small-sample clinical observations, lacking large-scale, multicenter randomized controlled trials; TCM formulas have complex compositions, and the specific active substances and target networks have not yet been fully elucidated, with inconsistent quality control standards; research on external therapies such as acupuncture is scarce, and exploration of their mechanisms of action is insufficient. Future efforts should focus on conducting high-quality clinical studies to validate efficacy and safety, thoroughly investigating the mechanisms of action of active ingredients and advancing formulation development, and strengthening standardized research on external therapies to promote the clinical translation and application of TCM in the treatment of VMC.

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