

Research Progress of Tonifying Qi and Activating Blood and Promoting Diuresis Formula in Treating Chronic Heart Failure

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Abstract: Chronic heart failure (CHF) is the end-stage manifestation of cardiovascular disease and the most important cause of death, which is one of the two major challenges in the neighborhood of cardiovascular disease in the 21st century. Currently, Western medicine is more mature in treating CHF, but its improvement of clinical symptoms of CHF still has some limitations and adverse effects. Traditional Chinese medicine has a long history of recognizing CHF, and it is believed that heart failure is an evidence of deficiency, and the key to its pathogenesis is the interplay of "deficiency, silt, and water". Based on the clinical literature of Yiqi, Blood and Water Formula for chronic heart failure, this paper analyzes the etiology, application, mechanism and commonly used formulas, so as to comprehensively discuss the research progress of Yiqi, Blood and Water Formula for the treatment of chronic heart failure.

Chronic Heart Failure (CHF) is a complex clinical condition resulting from various underlying factors that impair the heart's ability to fill and pump efficiently. Characterized by fluid retention, fatigue, and breathing difficulties, it remains a major global health challenge despite therapeutic advancements in recent decades. Mortality rates continue to climb, underscoring the urgent need for more effective interventions. Traditional medical systems offer valuable perspectives in CHF management. Historical medical literature describes similar presentations under different pathological concepts, including symptoms like irregular heartbeats, labored breathing, edema, and systemic fluid accumulation. These manifestations typically emerge in advanced stages of cardiac or

systemic disorders. Early signs include exertional fatigue and shortness of breath, progressing to severe respiratory distress even at rest, decreased urine output, and pronounced swelling in extremities. Contemporary research has demonstrated significant progress in botanical medicine approaches for CHF, particularly regarding formulas designed to enhance cardiac function through multiple therapeutic pathways. This review examines current evidence supporting the use of a specific herbal strategy that combines three therapeutic actions: energy enhancement, circulatory improvement, and fluid regulation in CHF management.

1. Etiology and Pathogenesis

The occurrence of heart failure is often caused by external pathogens such as wind, cold, dampness, and heat invading the heart, first damaging the heart body and then impairing heart function; or heart diseases themselves, such as long-term illnesses like palpitation, heartache due to chest impediment, and heart impediment, which damage heart qi; or diseases of other zang-organs affecting the heart, such as chronic lung diseases like cough, asthma, wheezing, and consumption, leading to obstruction of lung qi, inability to assist the heart in moving blood and facing all vessels, thus impairing the heart. Chronic damage to the spleen and stomach results in insufficient production of qi and blood, leading to gradual decline of heart qi, or spleen deficiency failing to resolve dampness, dysfunction of the vessel pathways, and prolonged condition affecting the heart. Chronic liver disease with abnormal dispersion and conveyance affects the circulation of qi and blood, thereby impairing the heart. Chronic kidney disease with decline of original yin and original yang leads to the heart losing nourishment and warmth, resulting in weak(heart's propelling function), or kidney deficiency with qi failing to transform water, causing water-fluid to assail the heart and shoot the lung, thus leading to heart failure. Heart failure caused by heart diseases themselves and diseases of other zang-organs affecting the heart, accompanied by additional contraction of external pathogens, can lead to failure of the lung to diffuse and descend, and inability to exercise governance and regulation[1]; excessive overstrain, leading to qi consumption due to overstrain; emotional stimulation, resulting in disorder of zang-qi; as well as childbirth, which consumes blood and injures qi, leaving all vessels empty, all of which are common etiologies of heart failure. In recent years, the discussions on the pathogenesis of heart failure in traditional Chinese medicine have basically reached a consensus. For example, the "Expert Consensus on Integrated Traditional Chinese and Western Medicine Diagnosis and Treatment of Chronic Heart Failure" [2] points out that the root cause of heart failure is deficiency of heart qi, and its pathogenesis can be summarized as "deficiency", "blood stasis" and "water retention", belonging to a syndrome of root deficiency and branch excess, which is the most recognized statement. According to its clinical manifestations, physicians of past dynasties have proposed that heart failure is a syndrome of root deficiency and branch excess, with deficiency as the main aspect, often involving deficiency complicated with excess. Deficiency refers to deficiency of qi, blood, yin and yang, mainly insufficiency of heart qi. Excess refers to the trouble of blood stasis and fluid retention, affecting the five zang-organs. It is often caused by deficiency leading to excess: insufficient heart qi failing to circulate blood results in blood stasis; deficiency of heart, lung, spleen and kidney leads to internal retention of fluid. Professor Hu Yebin [3] believes that heart failure is often caused by long-

term deficiency of yang qi, which leads to inability to circulate blood, or qi stagnation and blood stasis, resulting in blood stasis and water retention. Yuan Guoqiang et al [4] explored from the perspective of collaterals and concluded that collateral stasis with water retention, deficiency of yang-qi, and collateral stagnation forming accumulation are the pathological mechanisms of heart failure, and the mutual influence of the pathological products of "qi, blood, and water" can promote the development of heart failure.

2. Qi-Boosting, Blood-Activating, and Water-Draining Formula for Treating Heart Failure

2.1 The Application of the Qi-Invigorating, Blood-Activating, and Water-Draining Formula in Treating Heart Failure

Traditional Chinese Medicine (TCM) identifies the fundamental pathogenesis of heart failure as qi deficiency, blood stasis, and water retention. Among these, blood stasis is considered a consistent pathological factor throughout the progression of the disease. Heart qi deficiency serves as the underlying basis, blood stasis represents the primary pathological process, and fluid retention is the resulting pathological product. The key therapeutic principles for treating heart failure involve tonifying qi, promoting blood circulation, and facilitating water excretion. In a study conducted by Chen Zhengyu et al. [5], Chinese herbal medicine aimed at tonifying qi, promoting blood circulation, and facilitating diuresis was used to treat chronic heart failure. A total of 80 patients with chronic heart failure were enrolled and randomly assigned to two groups. The control group, consisting of 40 patients, received conventional treatment. The observation group, also comprising 40 patients, received the same conventional treatment supplemented with the aforementioned Chinese herbal medicine. Following treatment, both groups showed an improvement in overall efficacy, with the observation group demonstrating a higher total effective rate compared to the control group. Therefore, the use of traditional Chinese medicine (TCM) with functions of tonifying Qi, promoting blood circulation, and inducing diuresis has shown favorable therapeutic effects in patients with chronic heart failure (CHF) caused by coronary heart disease. A relatively high overall efficacy rate has been observed, along with improvements in cardiac function indices, increased 6-minute walking distance, and enhanced quality of life. Pan Chao et al. [6] suggested that combining Qi-tonifying, blood-activating, and diuresis-promoting TCM with Western medicine can further improve relevant signs and symptoms in CHF patients and enhance clinical outcomes. Deng Kun [7] proposed that TCM therapies aimed at tonifying Qi, warming Yang, promoting blood circulation, and inducing diuresis are effective in improving cardiac function and can serve as a foundational treatment approach for CHF. Liu Guanwei et al. [8], based on the theory of "tonifying Qi assisted by warming Yang, and promoting blood circulation to aid diuresis," developed a self-formulated prescription named the "Qi-tonifying, blood-activating, diuresis-promoting, and heart-strengthening formula" for the treatment of CHF. This formula includes traditional Chinese medicinal herbs such as Tinglizi (Semen Lepidii), Baizhu (*Atractylodes macrocephala*), Fuling (*Poria*), Zexie (*Alisma*), Yimucao (*Leonurus japonicus*), Huangqi (*Astragalus*), Dangshen (*Codonopsis*), Sanqi (*Panax notoginseng*), Hongshen (Red Ginseng), Danshen (*Salvia miltiorrhiza*), Baishao (*Paeonia lactiflora*), Chuanxiong

(*Ligusticum chuanxiong*), and *Cheqianzi* (*Plantago asiatica*). These herbs work synergistically to promote blood circulation, induce diuresis, and tonify heart Qi, thereby alleviating symptoms such as palpitations, chest tightness, fatigue, shortness of breath, and lower limb edema, and improving patients' exercise tolerance. Wang Shaobing [9] noted that the Yiqi Huoxue Lishui formula is highly effective in treating chronic heart failure. Its efficacy and advantages have been well demonstrated through its application by various physicians.

2.2 The Mechanism of the Yi Qi Huo Xue Li Shui Formula in Treating Heart Failure

The Yiqi Huoxue Lishui formula for the treatment of chronic heart failure (CHF) is associated with minimal adverse effects, features a complex composition of medicinal ingredients, and has the potential to improve cardiac function, alleviate clinical symptoms, and slow disease progression. Numerous researchers have been exploring its underlying mechanisms. Current experimental studies have shown that traditional Chinese medicine treats CHF through multi-targeted actions, including anti-fibrotic, anti-inflammatory, vascular remodeling, antioxidant effects, regulation of mitochondrial function and energy metabolism, inhibition of apoptosis, and suppression of renin-angiotensin-aldosterone system (RAAS) activation. These mechanisms are closely interconnected [10]. He Xiaofang et al. investigated the effects of this formula on inflammatory factors in CHF. Based on the *Xinshengmai San* formula, they modified it by removing qi-consuming and blood-breaking components such as *Curcuma zedoaria* and *Sparganium*, and adding *Astragalus membranaceus*, which tonifies qi and promotes diuresis. A total of 47 patients were assigned to the treatment group, receiving the Yiqi Huoxue Lishui formula in addition to standard Western medical therapy for a duration of four weeks. After treatment, LVEF levels in both groups increased significantly compared to baseline, with the treatment group showing greater improvement than the control group; the difference was statistically significant. It was concluded that the Yiqi Huoxue Lishui formula improves cardiac function and clinical symptoms in patients with chronic heart failure (CHF) characterized by Qi deficiency, blood stasis, and fluid retention by inhibiting inflammatory responses and thereby delaying ventricular remodeling. Modern pharmacological studies of traditional Chinese medicine have demonstrated that Qi-tonifying and Yang-warming herbs in the formula, such as red ginseng and aconite, can enhance myocardial contractility and improve myocardial tolerance to hypoxia. Meanwhile, blood-activating and diuretic herbs such as *Salvia miltiorrhiza*, red peony root, *Alisma*, *Lepidium seed*, and bamboo leaf help dilate cardiac and renal blood vessels, improve heart and kidney function, and reduce cardiac workload. Yang Zhen et al. [11] suggested that traditional Chinese medicines with functions of tonifying Qi, promoting blood circulation, and inducing diuresis exert vasodilatory effects on coronary arteries. These effects can effectively increase coronary blood flow, alleviate symptoms of myocardial ischemia and hypoxia, protect the myocardium, and enhance myocardial contractility. Qiao Yu et al. [12] demonstrated through their research that *Shenli Jia* granules can improve myocardial fibrosis and protect the hearts of rats with heart failure by regulating the expression of endocrine gland-derived vascular endothelial growth factor (EG-VEGF) in the myocardium of CHF rats. The underlying mechanism may involve the activation of signaling pathways by EG-VEGF, which promotes endothelial cell proliferation, migration, and survival,

thereby inducing angiogenesis, increasing myocardial perfusion, alleviating myocardial ischemia, and ultimately protecting the myocardium. The renin-angiotensin-aldosterone system (RAAS) plays a role in maintaining homeostasis and is involved in the processes of cell proliferation and apoptosis. Excessive activation can result in water and sodium retention, increased cardiac preload, and other effects, and is considered a key factor in the onset and progression of congestive heart failure (CHF) [13]. In a study conducted by Liu Xueli et al. [14], it was found that traditional Chinese medicine (TCM) formulations designed to tonify Qi, promote blood circulation, and induce diuresis regulate the renin-angiotensin-aldosterone system (RAAS) through multiple targets, primarily by downregulating renin. Modulating a single target within this system can inhibit the impact of RAAS on cardiac function, thereby producing therapeutic effects mainly by reducing cardiac preload and afterload. These findings suggest that the therapeutic mechanism may be associated with the RAAS-mediated regulation of the cardiovascular system.

3. Clinically Commonly Used Prescriptions

In the treatment of heart failure, physicians throughout history have followed the principles of tonifying Qi, activating blood circulation, and promoting diuresis, leading to the development of numerous classical prescriptions. Zhenwu Decoction, originating from the **Synopsis of Prescriptions of the Golden Chamber** (**Jin Gui Yao Lue**), is a representative formula for warming Yang and promoting diuresis. In this formula, *Aconiti Lateralis Radix Praeparata* (Fuzi), *Zingiberis Rhizoma Recens* (Shengjiang), and *Cinnamomi Ramulus* (Guizhi) are used to warm and activate the Heart and Kidney; *Poria* (Fuling) and *Atractylodis Macrocephalae Rhizoma* (Baizhu) to strengthen the Spleen and promote diuresis; *Alismatis Rhizoma* (Zexie) and *Polyporus* (Zhuling) to promote diuresis and reduce edema; and *Salviae Miltiorrhizae Radix et Rhizoma* (Danshen), *Chuanxiong Rhizoma* (Chuanxiong), and *Achyranthis Bidentatae Radix* (Niuxi) to activate blood circulation and promote diuresis. This formula is known for its cardiotonic and diuretic effects. Wang Jian et al. [15] reported that the modified Zhenwu Decoction can reduce serum levels of profibrotic growth factors, inhibit myocardial fibrosis, and delay myocardial remodeling, thereby helping to slow disease progression. Lingui Zhugan Decoction, a commonly used prescription from the **Treatise on Cold Damage** (**Shang Han Lun**), is composed of four traditional Chinese medicines: *Poria* (Fuling), *Cinnamomi Ramulus* (Guizhi), *Atractylodis Macrocephalae Rhizoma* (Baizhu), and *Glycyrrhizae Radix et Rhizoma* (Gancao). It is a classical and well-established formula for resolving fluid retention, promoting diuresis, strengthening the Spleen, and eliminating dampness. In this formula, *Poria* is prominently used as the chief herb to promote urination through its bland and percolating properties, thereby eliminating pre-existing fluid retention. It is supported by *Ramulus Cinnamomi* (Guizhi), which warms yang and regulates qi. The combination of *Poria* and *Guizhi* is well known for its effectiveness in warming yang and promoting water metabolism, and is a commonly used pairing in the treatment of yang deficiency with fluid accumulation. Zhang Yu et al. [16] have suggested that Lingui Zhugan Decoction, as a representative classical formula in Traditional Chinese Medicine, is suitable for the clinical treatment of various cardiovascular diseases involving heart-spleen yang deficiency and fluid retention with counterflow of qi, and holds significant clinical promise. Currently,

Linggui Zhugan Decoction and its modified versions are commonly prescribed for cardiovascular diseases and are frequently used in combination with Western medicine for the prevention and treatment of chronic heart failure. Shi Zhenzhen et al. [17] investigated the use of a modified Linggui Zhugan Decoction, in which additional herbs such as *Salvia miltiorrhiza* (Danshen), processed *Aconitum carmichaeli* (Zhi Fuzi), *Semen Persicae* (Taoren), and *Allium macrostemon* (Xiebai) were incorporated into the original formula for the treatment of chronic heart failure. The results showed that the modified decoction could alleviate clinical symptoms, effectively reduce serum levels of N-terminal pro-B-type natriuretic peptide (NT-proBNP), enhance cardiac function, and demonstrated good safety. Since blood stasis is involved throughout the progression of heart failure, Xuefu Zhuyu Decoction has been widely used by physicians throughout history for its treatment. The formula originates from Wang Qingren's **Yilin Gaicuo** and is primarily composed of Taohong Siwu Decoction and Sini San, with the addition of Niu Xi to promote downward movement and Jie Geng to facilitate upward movement. In clinical practice, Professor Ji Zhongqiang has adopted Xuefu Zhuyu Decoction as the core prescription. For patients with qi deficiency, it is combined with Shengxian Decoction; for those experiencing fatigue, the dosage of *Astragalus membranaceus* is increased; for palpitations, *Cinnamomi Ramulus*, *Schisandra chinensis*, and *Nardostachys jatamansi* are added; for severe chest oppression, *Allium macrostemon* is included to relieve chest discomfort; and for pronounced edema, Wupi Yin is combined. The formula is adjusted based on individual symptoms, resulting in significant therapeutic effects in the treatment of heart failure [18]. Through clinical observation, Tan Jielong [19] found that Xuefu Zhuyu Decoction can improve cardiac function classification in patients with chronic heart failure (CHF), help prevent adverse reactions, and enhance quality of life, demonstrating clear advantages and potential for broader application. Heart qi deficiency is considered the pathological basis of heart failure. In clinical practice, Baoyuan Decoction is commonly used to treat heart failure characterized by yuan-qi deficiency. This formula contains four traditional Chinese medicinal herbs: *Astragalus membranaceus* (Huangqi), *Panax ginseng* (Renshen), *Cinnamomum cassia* (Rougui), and *Glycyrrhiza uralensis* (Gancao). *Panax ginseng* and *Astragalus membranaceus* are used to strongly tonify yuan-qi, *Cinnamomum cassia* warms yang and promotes circulation through the meridians, and *Glycyrrhiza uralensis* augments qi, making the formula a representative prescription for tonifying qi and warming yang. Baoyuan Decoction is recommended for Stage C heart failure in the "Expert Consensus on Integrated Traditional Chinese and Western Medicine Diagnosis and Treatment of Chronic Heart Failure" and is widely used in clinical practice. Huo Li et al. [20], through a meta-analysis, concluded that Baoyuan Decoction is safe and effective in the treatment of chronic heart failure (CHF), and that it can further improve clinical outcomes compared to conventional treatment alone. Ma Xuezhu et al. [21] reported that, when added to standard Western medical treatment for chronic heart failure, Baoyuan Decoction and its modified forms are more effective than Western medicine alone in improving clinical efficacy, increasing left ventricular ejection fraction, relieving symptoms, enhancing quality of life, and reducing hospitalization rates. Many practitioners also regard Tingli Dazao Xiefei Decoction as a representative prescription for the treatment of heart failure. Tinglizi (*Semen Lepidii*) is often combined with Qi-tonifying and blood-activating herbs. Tonifying Qi promotes its circulation, which

in turn facilitates blood flow; when the meridians are unblocked, water metabolism is regulated. These herbs work synergistically to treat heart failure. Zeng Li et al. [22] divided 80 patients with heart failure into two groups. The group receiving traditional Chinese medicine (TCM) was treated with a modified Tingli Dazao Xiefei Decoction in addition to the standard therapy given to the control group. After 20 days of treatment, the TCM group showed significantly better therapeutic outcomes than the control group. The research team also suggested that, in clinical practice, Tingli Dazao Xiefei Decoction should be decocted to a high concentration and administered one hour after meals for optimal efficacy, with the duration of treatment kept within a reasonable limit. Li Yuming et al. [23] demonstrated that treatment with a modified Tingli Dazao Xiefei Decoction produced significant therapeutic effects in patients with chronic heart failure (CHF).

4. Conclusion

In summary, in recent years, the understanding of the etiology and pathogenesis of chronic heart failure (CHF) has become increasingly refined. The formula aimed at tonifying Qi, promoting blood circulation, and inducing diuresis has been widely adopted in clinical practice for the treatment of CHF and has gradually gained broad public acceptance. In clinical applications, effective prescriptions can be flexibly employed based on accurate syndrome differentiation according to specific symptoms, thereby alleviating patient discomfort, improving quality of life, and reducing hospitalization rates. However, due to the complex composition of traditional Chinese medicine, the mechanisms by which the Qi-tonifying, blood-activating, and diuresis-promoting formula exerts therapeutic effects on CHF remain insufficiently understood and lack standardization. Further research is needed to elucidate these mechanisms from multiple perspectives, with the aim of achieving significant breakthroughs in understanding the therapeutic mechanisms of traditional Chinese medicine in the treatment of CHF.

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