DOI: 10.66069/ojspub.27450815

Research Progress on the Pharmacological Effects of Active Components of Traditional Chinese Medicine Astragalus in the Treatment of Heart Failure

Qiuhong Wu[1], Dezhi Ren[2,*]

[1]Shaanxi University of Chinese Medicine, Xianyang 712046, Shaanxi, China
[2]Shaanxi Provincial Hospital of Chinese Medicine, Xi'an 710003, Shaanxi, China
**Correspondence Author*

Abstract: ***Heart failure, referred to as HF for short, is a complex clinical syndrome caused by changes in cardiac structure and function, leading to impaired ejection function or ventricular filling. In recent years, its mortality rate has ranked first among the total death causes of urban and rural residents in China. Traditional Chinese medicine (TCM) has always had rich experience in the prevention and treatment of heart failure. Nowadays, with the vigorous development of modern TCM, the research, development and application of effective active components of traditional Chinese medicine have attracted increasing attention. As a drug for benefiting qi, warming yang and activating blood circulation, Astragalus has the effects of benefiting qi and activating blood circulation, strengthening healthy qi and eliminating pathogenic factors. It also has the functions of improving myocardial energy metabolism, hemodynamics, protecting myocardium and promoting angiogenesis.In clinical practice, Astragalus is commonly used to treat patients with various types of heart failure with good efficacy. In recent years, studies have found that the active components of Astragalus, such as astragaloside IV, astragalus polysaccharides and flavonoids, can improve cardiac function and treat heart failure through multiple pathways, including inhibiting inflammatory response, cardiomyocyte apoptosis and myocardial fibrosis.***

Keywords: Astragalus, Astragaloside IV, Astragalus polysaccharides, Active components, Inflammatory response**.**

1. Introduction

Heart failure is a clinical syndrome characterized by typical symptoms such as dyspnea, ankle swelling and fatigue, which may be accompanied by signs caused by abnormal cardiac structure and/or function (such as elevated jugular venous pressure), leading to reduced cardiac output and/or elevated intracardiac pressure at rest or under stress [1]. According to the data released in the Summary of China Cardiovascular Health and Disease Report 2020, cardiovascular disease deaths rank first among the total death causes of urban and rural residents in China, with 8.9 million heart failure patients [2]. In the treatment of heart failure, TCM has been widely used and plays an important role with significant efficacy, multi-target effects, low cost and few side effects. The field of bioactive components of traditional Chinese medicine has also attracted increasing attention. Astragalus (Radix Astragali, RA), a commonly used drug for the treatment of heart failure in TCM, is derived from the dried roots of Astragalus membranaceus (Fisch.) Bge. var. mongholicus (Bge.) Hsiao, Astragalus membranaceus (Fisch.) Bge. and related plants of the same genus. First recorded in Shennong's Classic of Materia Medica, it is a representative sweet-warm tonic with the effects of tonifying qi and elevating yang, reinforcing defensive qi to consolidate the exterior, and inducing diuresis to reduce edema. It is often used for strengthening the body resistance and tonifying middle-jiao and qi, known as "Astragalus is used in eight out of ten prescriptions". Modern pharmacological studies have shown that Astragalus has the effects of improving cardiac function, regulating blood pressure and reducing inflammatory response [3]. This paper reviews the relevant research reports on the application of Astragalus active components in the treatment of heart failure, providing new ideas and theoretical basis for the treatment of heart failure.

2. Astragalus Active Components Can Resist Oxidative Stress

Current studies believe that excessive reactive oxygen species (ROS) will be produced when cells and tissues are stimulated by internal and external environmental factors. When the intracellular antioxidant system cannot completely neutralize ROS, cells will be damaged. Oxidative stress is an important link in chronic inflammation and plays a crucial role in cardiovascular diseases. Nowadays, oxidative stress has been identified as an important pathophysiological pathway in the occurrence and progression of heart failure [4]. The effects of active components of Astragalus on this process have also been gradually confirmed. In a study by Sui et al. [5], it was found that astragaloside IV can resist oxidative stress through the Nrf2/HO-1 pathway to prevent heart failure. Yang et al. [6] also confirmed that astragaloside IV regulates the expression of nuclear factor erythroid 2-related factor 2 (Nrf2) and transcription factor BTB-CNC homology 1 (BACH1) in the nucleus through the PI3K/Akt/HO-1 signaling pathway, and jointly regulates heme oxygenase-1 (HO-1) protein and promotes its expression, exerting a protective effect on myocardial ischemia-reperfusion injury. PI3K/Akt is the upstream of Nrf2, and Keap1 is the negative regulator of Nrf2. In the nucleus, Nrf2 promotes the expression of p62 gene, and the interaction among p62, Keap1 and Nrf2 leads to the interaction of apoptosis, autophagy and oxidative stress. Astragaloside IV reverses the above expression by inhibiting the PI3K/Akt pathway to prevent cardiac damage [7]. Liu et al. [8] found that astragaloside IV can reduce mitochondrial

damage by lowering the level of heart failure-induced oxidative stress, inhibit ventricular remodeling, and thus improve cardiac function. In a study on the effect of astragalus polysaccharides on myocardial oxidative stress in diabetes mellitus by Sun Qilin et al. [9], it was found that after treatment with astragalus polysaccharides, blood glucose was significantly reduced, myocardial oxidative stress was significantly inhibited, and cardiac function was significantly improved in mice, suggesting that astragalus polysaccharides can improve blood glucose and block myocardial oxidative stress. Therefore, it is concluded that astragalus polysaccharides can protect the myocardium of diabetic mice and inhibit the development of diabetic cardiomyopathy, which may be achieved by regulating the expression level of myocardial superoxide dismutase to inhibit the production of ROS. Among flavonoids, quercetin has antioxidant effects [10]. A study by Tang Xilan et al. [11] suggested that the mechanism of quercetin may be to inhibit the renin-angiotensin-aldosterone system, reduce the expression of TGF-β1 and CTGF, inhibit the phosphorylation and activation of NF-κB p65 and Akt, and reduce the secretion of inflammatory factors such as tumor necrosis factor (TNF)-α, interleukin (IL)-6 and IL-1 by cardiac fibroblasts (CF).

3. Astragalus Active Components Can Improve Hemodynamics

The core mechanism of the occurrence and development of heart failure is myocardial remodeling, which is a typical pathological state causing abnormal hemodynamics and sympathetic nerve excitation in the body, including changes in cardiac structure and function, with decreased LVEF and increased LVEFDD [12]. Most heart failure patients are of qi deficiency and blood stasis type in clinical practice. Astragalus flavonoids may improve hemodynamics by inducing the accumulation of hypoxia-inducible factor-1α to mediate signals, promoting the expression of erythropoietin, stimulating blood regeneration and increasing the number of erythrocytes [13]. Astragaloside IV (AS) can improve hemodynamic indicators by reducing left ventricular end-diastolic pressure and exerting a cardiotonic effect to a certain extent [14]. In addition, in a study on astragaloside IV, total saponins and total flavonoids by Jin Liyan [15], the data from the experimental groups showed that Astragalus could significantly improve myocardial injury and promote the recovery of myocardial function according to the changes in electrocardiogram and cardiac hemodynamic indicators. Lv Wenwei et al. [16] found that astragalus polysaccharides can improve myocardial contractility, reduce myocardial injury, and significantly improve hemodynamic indicators, indicating that astragalus polysaccharides have a positive inotropic effect. In addition, Zhang Zhuo et al. [17] conducted a study on the effect of astragalus polysaccharides on cardiac hemodynamics after reperfusion, its mechanism and its relationship with oxygen free radicals, and found that astragalus polysaccharides have a significant protective effect on myocardial diastolic function, which is of great significance for maintaining normal cardiac pump function. Moreover, this anti-oxygen free radical effect may be an important mechanism for improving cardiac hemodynamics and resisting myocardial ischemia-reperfusion injury.

4. Astragalus Active Components Can Inhibit Inflammatory Response

Inflammatory response is one of the important pathophysiological mechanisms of heart failure, and various inflammatory mediators produced in the inflammatory response can promote the progression and deterioration of heart failure [18]. Under physiological conditions, the expression of inflammatory factors in the inflammatory response is related to whether an inflammatory response will be triggered. When the dynamic balance between pro-inflammatory factors and anti-inflammatory factors in the body is broken, an inflammatory response will occur. Current studies [19] have shown that astragaloside IV can inhibit the TLR4/MyD88/NF-κB pathway and inflammatory response in exhausted exercise rats, which is a potential reason for its protection against myocardial injury, indicating that it has a certain application prospect in the prevention and treatment of exercise-induced myocardial injury. The results of this study [19] also confirmed that the iNOS activity and the contents of NO, IL-1β, IL-6 and TNF-α were significantly decreased, while the content of IL-10 was significantly increased in the exhausted exercise model + low-dose astragaloside IV group and exhausted exercise model + high-dose astragaloside IV group, suggesting that inhibiting inflammatory response is a potential reason for astragaloside IV to protect against myocardial injury. In addition, in an experiment exploring the effects of Astragalus and its active component astragalus polysaccharides on the levels of homocysteine (Hcy), nuclear factor-κB (NF-κB) and D-dimer (D-D) in heart failure model mice by Chai Lianhai et al. [20], the results showed that Astragalus and its active component astragalus polysaccharides could significantly reduce the plasma levels of Hcy, NF-κB and D-D in heart failure model mice, and astragalus polysaccharides had the best effect. The values of the three indicators after treatment were basically close to those of the normal group. It is considered that astragalus polysaccharides have the advantages of enhancing efficacy and reducing toxicity in the treatment of heart diseases, and are often regarded as ideal immunopotentiators in clinical practice. Studies have shown that luteolin, quercetin and genistein among flavonoids can significantly reduce the expression of cyclooxygenase-2 (COX-2), and protect H9c2 cardiomyocytes from LPS-induced inflammatory damage by regulating the NF-κB and MAPK pathways [21]. In a review on the research progress of the protective effects and mechanisms of flavonoids on cardiomyocytes through inflammatory pathways by Feng Bailin et al. [22], it was summarized that flavonoids mainly reduce myocardial cell apoptosis and other injuries by lowering the levels of TNF-α, IL-1, IL-6, COX-2 and iNOS, up-regulating Nrf2 expression, and inhibiting inflammatory pathways such as NF-κB and MAPK signaling pathways, thereby inhibiting myocardial fibrosis and remodeling, reducing cardiac toxicity and improving cardiac function.

5. Astragalus Active Components Can Regulate Energy Metabolism

Abnormal cardiac energy metabolism will lead to cardiac hypertrophy and participate in energy metabolism damage in

the early stage of ischemia. Pretreatment with astragaloside IV can significantly reduce the surface area and protein content in neonatal rat ventricular myocytes (NRVM), down-regulate the mRNA expression of atrial natriuretic peptide (ANP) and brain natriuretic peptide (BNP), increase ATP/AMP, and reduce the content of free fatty acids (FFA). It also increases the protein expression of ATP5D, ATP synthase and PGC-1α subunits in rats and NRVM, and inhibits the translocation of p65 and nuclear translocation of NF-κB subunits, indicating that astragaloside IV prevents isoproterenol-induced cardiac hypertrophy by regulating energy synthesis mediated by the NF-κB/PGC-1α signal [23]. In an experiment exploring the effects and mechanisms of astragaloside IV, total saponins and total flavonoids on cardiac function in mice with myocardial ischemia-reperfusion injury by Jin Liyan [15], it was found that the content of Na+-K+-ATPase in the astragaloside IV group, total saponins group and total flavonoids group was lower than that in the control group ($P<0.05$). This indicates that the three Astragalus extracts can provide more energy supply for cardiomyocytes by enhancing the activity of Na+-K+-ATPase in cardiomyocytes, thereby exerting a positive inotropic effect. In a study by Jiang et al. [24], it was found that astragaloside IV can enhance skeletal muscle energy metabolism to reduce cell apoptosis, which significantly improves skeletal muscle energy metabolism disorders. Wang Tianbao et al. [25] used astragaloside IV to treat rats with acute heart failure (AHF). The myocardial and mitochondrial structure of the rats was significantly alleviated, the serum ATP level was increased, the AMP and ADP levels were decreased, and the contents of myocardial tissue fatty acids (FFA) and triglycerides (TG) were reduced, suggesting that astragaloside IV can improve myocardial energy metabolism, alleviate AHF symptoms and delay disease progression. Therefore, it is believed that astragaloside IV can significantly improve AHF in rats, and its mechanism may be to improve myocardial energy metabolism and cardiac function by activating the AMPK/ PPARα signaling pathway. Another study showed that astragalus polysaccharides can improve cardiac function and myocardial cell energy metabolism in rats with chronic heart failure, reduce mitochondrial structural damage and pathological changes of myocardial tissue, and reduce myocardial cell apoptosis. It is speculated that its mechanism is related to activating the AMPK/PGC-1α signaling pathway [26].

6. Astragalus Active Components Can Inhibit Cardiomyocyte Apoptosis

At present, scholars believe that cell apoptosis is the main pathological process of massive cell death in heart failure. Myocardial infarction, myocardial ischemia-reperfusion injury and other conditions will promote progressive cell necrosis and apoptosis, aggravating cardiac function damage [27]. Lu Xinlun et al. [28] believed that when cardiovascular diseases develop to the advanced stage, cardiomyocyte apoptosis may be one of the important causes of cardiac insufficiency, and cardiomyocyte apoptosis also plays a key role in the occurrence and development of heart failure. Song Aixin et al. [29] believed that astragaloside IV can improve myocardial function, reduce myocardial fibrosis, decrease cardiomyocyte apoptosis rate and reverse ventricular remodeling in rats with chronic heart failure, and its mechanism may be to exert effects by inhibiting the TGF-β1/Smad3 signaling pathway, providing a certain theoretical basis for the clinical treatment of chronic heart failure. Zhao Yan et al. [30] believed that astragaloside IV may significantly improve cardiac function and hemodynamic indicators and inhibit cardiomyocyte apoptosis in rats with chronic heart failure by down-regulating the expression of P-Cx43 in myocardial tissue. In addition, studies have shown that astragaloside IV can reduce cardiomyocyte apoptosis by up-regulating Bcl-2 expression and down-regulating cleaved-caspase-3 protein expression [31]. Hu Mingxu et al. [32] found that astragaloside IV can inhibit cardiomyocyte apoptosis by improving telomere activity of cardiomyocytes, regulating energy metabolism and promoting the expression of telomerase reverse transcriptase. Studies have also shown that total astragalus saponins can reduce oxidative stress-induced cardiomyocyte apoptosis by interfering with the p38MAPK and AKT signaling pathways [33]. It has been found that the mechanism by which astragalus polysaccharides reduce lipopolysaccharide (LPS)-induced cardiomyocyte apoptosis may be related to inhibiting the NF-κB and JNK signaling pathways [34].

7. Astragalus Active Components Can Inhibit Myocardial Fibrosis

Studies believe that myocardial fibrosis will increase ventricular wall stiffness, reduce the proportion of cardiomyocytes and decrease ventricular compliance, which will lead to systolic dysfunction, affect the normal diastolic and systolic function of myocardium, and thus cause heart failure [35]. Astragaloside IV can inhibit myocardial fibrosis in rats with chronic heart failure, and its mechanism may be achieved by up-regulating LCAD, down-regulating PFK1 and correcting abnormal energy metabolism [36]. In a study by Wei Lan et al. [37], the expression of CD31 protein in myocardial tissue of mice in the astragaloside IV group was significantly up-regulated, while the expression of AKT, GSK3-β, p-GSK3-β, SNAIL and α-SMA proteins was significantly down-regulated, which proved that astragaloside IV may inhibit the activation of fibroblasts and myofibroblasts by End MT through the AKT/GSK3-β/SNAIL signaling pathway, so as to alleviate myocardial fibrosis in mice with heart failure. Han Dong et al. [38] found that astragaloside IV can regulate the expression of SNAIL by regulating the AKT/GSK3-β/SNAIL signaling pathway, inhibit the transformation of endothelial cells into mesenchymal cells, and avoid the production of fibroblasts, myofibroblasts and smooth muscle cells, thereby inhibiting myocardial fibrosis in mice. Jiang Zhengkui et al. [39] found that astragalus polysaccharides can improve cardiac function and myocardial fibrosis in spontaneously hypertensive rats to a certain extent, and its mechanism may be related to down-regulating the expression of TGF-β1 gene and up-regulating the expression of PPAR-γ gene. Quercetin can significantly improve cardiac function, reduce compensatory ventricular enlargement, decrease collagen fiber deposition and inhibit ventricular remodeling in rats with chronic heart failure (CHF), and its mechanism may be related to regulating the TGF-β1/Smad3 signaling pathway [40].

8. Conclusion

Heart failure is the late stage of most cardiovascular diseases and one of the main causes of cardiovascular death in most developed and developing countries, which seriously threatens the life and health of patients. Therefore, it is very important to prevent the occurrence of heart failure or provide appropriate treatment after diagnosis. Traditional Chinese medicine Astragalus is often used in the treatment of cardiovascular diseases. Current studies have shown that the active components of Astragalus can reduce myocardial damage and protect cardiac function through multiple pathways, including alleviating oxidative stress, improving hemodynamics, inhibiting inflammatory response, regulating cardiomyocyte energy metabolism, reducing cardiomyocyte apoptosis and inhibiting myocardial fibrosis. However, the research on the application of Astragalus active components in heart failure is mainly based on cell and animal experiments, and their mechanism of action in humans needs further research and confirmation. In addition, there are many active components in Astragalus, and whether the interaction of various components is beneficial to delaying the progression of heart failure needs to be confirmed. Researchers still need to increase the research on pharmaceutical preparations of Astragalus active components, so as to develop drugs mainly composed of Astragalus active components as soon as possible and lay a foundation for human experiments. In conclusion, the active components of Astragalus have broad prospects in the prevention and treatment of heart failure, and it is worthy of increasing clinical investment in human and material resources to benefit more patients with heart failure.

References

[1] HEIDENREICH P A, BOZKURT B, AGUILAR D, et al. 2022 AHA/ACC/HFSA guideline for the management of heart failure: A report of the American college of cardiology/American heart association joint committee on clinical practice guidelines [J]. Circulation, 2022, 145(18):e895-e1032.

[2] Editorial Board of China Cardiovascular Health and Disease Report. Summary of China Cardiovascular Health and Disease Report 2022 [J]. Chinese Circulation Journal, 2023, 38(6):583-612.

[3] YANG Q, CHEN K, LU S, et al. Research progress on mechanism of action of Radix Astragalus in the treatment of heart failure [J]. Chinese Journal of Integrative Medicine, 2012, 18(3):235-240.

[4] VAN DERPOL A, VAN GILST W H, VOORS A A, et al. Treating oxidative stress in heart failure: past, present and future [J]. Eur J Heart Fail, 2019, 21(4):425-435.

[5] SUI Y B, ZHANG K K, REN Y K, et al. The role of Nrf2 in astragaloside IV-mediated antioxidative protection on heart failure [J]. Pharm Biol, 2020, 58(1):1192-1198.

[6] Yang P, Zhou Y, Xia Q, et al. Astragaloside IV regulates the PI3K/Akt/HO-1 signaling pathway and inhibits H9c2 cardiomyocyte injury induced by hypoxia-reoxygenation [J]. Biol Pharm Bull, 2019, 42(5):721-727.

[7] Luo L F, Qin L Y, Wang J X, et al. Astragaloside IV attenuates the myocardial injury caused by Adriamycin by inhibiting autophagy [J]. Front Pharmacol, 2021, 12:669782.

[8] LIU J, LI Y, BIAN X, et al. Astragaloside IV alleviates heart failure by regulating SUMO-specific protease 1 [J]. Exp Ther Med, 2021, 22(4):1076.

[9] Sun Q L, Ju J, Wang H, et al. Experimental study on astragalus polysaccharides intervening myocardial oxidative stress in diabetes mellitus [J]. Chinese Journal of Integrated Traditional and Western Medicine, 2020(02):196-203.

[10] Li M, Jiang Y, Jing W, et al. Quercetin provides greater cardioprotective effect than its glycoside derivative rutin on isoproterenol-induced cardiac fibrosis in the rat [J]. Canad J Physiol Pharmacol, 2013, 91(11):951-959.

[11] Tang X L, Liu J X, Dong W, et al. Intervention effect of quercetin on inflammatory secretion of rat neonatal cardiac fibroblasts [J]. China Journal of Chinese Materia Medica, 2014, 39(12):2314-2317.

[12] Li B B. Observation on the efficacy of sacubitril valsartan in the treatment of acute decompensated heart failure after hemodynamic stabilization [J]. Heilongjiang Medical Journal, 2021(21):2320-2321.

[13] ZHENG K Y, CHOI C, CHEUNG A W, et al. Flavonoids from radix astragali induce the expression of erythropoietin in cultured cells: a signaling mediated via the accumulation of hypoxia-inducible factor-1α [J]. J Agric Food Chem, 2011, 59(5):1697-1704.

[14] Cui D M, Chen Y J, Liu D H, et al. Effects of astragaloside IV on hemodynamics and neuroendocrine in rats with heart failure after myocardial infarction [J]. Journal of Naval Medicine, 2013, 34(1):18-20.

[15] Jin L Y. Effects and mechanisms of astragaloside IV, total saponins and total flavonoids on cardiac function in mice with myocardial ischemia-reperfusion injury [J]. Chinese Journal of Drugs and Clinics, 2019(15): 2544-2547.

[16] Lv W W, Liu S J, Wang Q J, et al. Effects of astragalus polysaccharides on hemodynamics and oxygen metabolism in anesthetized dogs with acute cardiogenic shock [J]. Chinese Traditional and Herbal Drugs, 2006, 37(10):1547-1548.

[17] Zhang Z, Chen L X, Song C S, et al. Protective effect of astragalus polysaccharides on myocardial ischemia - reperfusion injury in rats [J]. Chinese Journal of Information on Traditional Chinese Medicine, 2007, 14(2):33-34.

[18] HAJJAR R J, LEOPOLD J A. Inflammation and Heart Failure: Friend or Foe [J]. Circulation, 2021, 144(15): 1241-1243.

[19] Wang G J, Zhao Y. Effects of astragaloside IV on myocardial injury and inflammatory response in exhausted exercise rats [J]. Acta Ecologiae Animalis Domastici, 2022(09):43-47.

[20] Chai L H, Wang L L, Chen W S. Effects of astragalus and its active component astragalus polysaccharides on levels of homocysteine, nuclear factor-κB and D-dimer in heart failure model mice [J]. Chinese Journal of Experimental Traditional Medical Formulae, 2015(17): 142-145.

[21] Gutiérrez-Venegas G, Torras-Ceballos A, Gómez-Mora J A, et al. Luteolin, quercetin, genistein and quercetagetin inhibit the effects of lipopolysaccharide obtained from Porphyromonas gingivalis in H9c2 cardiomyoblasts [J]. Cellular & Molecular Biology Letters, 2017(1):1-12.

[22] Feng B L, Qin Q, Bai L, et al. Research progress on protective effects and mechanisms of flavonoids on cardiomyocytes through inflammatory pathways [J]. Global Traditional Chinese Medicine, 2022(02): 349-356.
[23] ZHANG S, TANG F, YANG Y, et al. Astragaloside IV protects against isoproterenol-induced cardiac hypertrophy by regulating NF-κB/PGC-1α signaling mediated energy biosynthesis [J]. PLoS One, 2015, 10:e0118759.
[24] JIANG B, YANG Y J, DANG W Z, et al. Astragaloside IV reverses simvastatin-induced skeletal muscle injury by activating the AMPK-PGC-1α signaling pathway [J]. Phytother Res, 2020, 34(5):1175-1184.
[25] Wang T B, Ma D P, Liu Y, et al. Effect of astragaloside IV on myocardial mitochondrial energy metabolism in rats with acute heart failure [J]. Journal of Guangzhou University of Traditional Chinese Medicine, 2022(04): 884-891.
[26] Liu L L, Wang G L. Effect of astragalus polysaccharides on myocardial cell energy metabolism in rats with chronic heart failure [J]. Chinese Journal of Integrative Medicine on Cardio-Cerebrovascular Disease, 2022(03): 420-426.
[27] Aimo A, Castiglione V, Borrelli C, et al. Oxidative stress and inflammation in the evolution of heart failure: from pathophysiology to therapeutic strategies [J]. Eur J Prev Cardiol, 2020, 27(5):494-510.
[28] Lu X L, Hu C Y, Zhang Y M. Research progress on the mechanism of heart failure [J]. Shanxi Medical Journal, 2011, 40(8):766-767.
[29] Song A X, Wang L, Zhang Y Y. Effect and mechanism of astragaloside IV on cardiomyocyte apoptosis in rats with chronic heart failure via TGF-β1/Smad3 signaling pathway [J]. Chinese Journal of Integrative Medicine on Cardio-Cerebrovascular Disease, 2021(10):1645-1651.
[30] Zhao Y, Yang D, Yu S S. Effect of astragaloside IV on cardiomyocyte apoptosis and P-Cx43 expression in rats with chronic heart failure [J]. Journal of Clinical and Experimental Medicine, 2018(20):2143-2147.
[31] Ren L Y, Huang X K, Chen N, et al. Clinical research progress of astragalus and its compound in the treatment of chronic heart failure [J]. Practical Journal of Traditional Chinese Medicine, 2019, 35(10):1292-1294.
[32] Hu M X, Liu L. Effect of astragaloside IV on cardiomyocyte apoptosis in rats with heart failure [J]. Chinese Journal of Information on Traditional Chinese Medicine, 2014, 21(1):40-42.
[33] You X, Zhu X F, Hu Y P, et al. Effect of total astragalus saponins on cardiomyocyte apoptosis and mitochondrial membrane potential in heart failure rats [J]. Basic & Clinical Medicine, 2020, 40(9):1218-1223.
[34] Han L, Wang H X, Lu M L. Astragalus polysaccharides attenuate LPS-induced cardiomyocyte apoptosis in mice by inhibiting NF-κB and JNK signaling pathways [J]. Chinese Pharmacological Bulletin, 2018(02):243-249.
[35] GONZÁLEZ A, SCHELBERT E B, DÍEZ J, et al. Myocardial interstitial fibrosis in heart failure: Biological and translational perspectives [J]. J Am Coll Cardiol, 2018, 71(15):1696-1706.
[36] Tang B, Zhang J G, Tan H Y, et al. Effect of astragaloside IV on myocardial fibrosis and energy metabolism in rats with chronic heart failure [J]. Chinese Journal of Pathophysiology, 2017(03):411-416.
[37] Wei L, Wang L J, He J Q, et al. Protective effect of astragaloside IV on mice with myocardial fibrosis in heart failure based on AKT/GSK3-β/SNAIL pathway [J]. Traditional Chinese Drug Research & Clinical Pharmacology, 2021, 32(9):1231-1237.
[38] Han D. Study on hypoglycemic, lipid-regulating and antioxidant effects of astragaloside IV on experimental diabetic rats [J]. Modern Journal of Integrated Traditional Chinese and Western Medicine, 2016, 25: 360-364.
[39] Jiang Z K, Li X, Tian F Q, et al. Effect of astragalus polysaccharides on cardiac function and myocardial fibrosis in spontaneously hypertensive rats and its mechanism [J]. China Pharmacy, 2016, 27(25): 3505-3508.
[40] Jiao M, Zhong H Y, Chen K Y, et al. Quercetin improves myocardial fibrosis in chronic heart failure rats via TGF-β1/Smad3 signaling pathway [J]. Progress of Anatomical Sciences, 2020(04):391-395.