ISSN 2706-6819 Vol.3, Issue 5: 46-51, DOI: 10.25236/IJFM.2021.030507

Current Situation of Protective Effect of Lycium Barbarum Polysaccharide on Cardiac

Shaopeng Wang[a], Guangyuan Yang[*]

Department of Cardiology, First Affiliated Hospital of Jiamusi University, Jiamusi, Heilongjiang, 154000, China
**Corresponding author: ygy665@126.com, [a]wangshaopeng8546@163.com*

Abstract: *Lycium barbarum is a kind of traditional Chinese medicine. Lycium barbarum tastes sweet and juicy with many benefits such as nourishing liver and kidney, improving eyesight, delaying aging, etc. Lycium barbarum polysaccharide (LBP) is the main active ingredient of Lycium barbarum which has been widely used in the treatment of cardiovascular diseases in China. It has many biological activities such as anti-oxidation, anti-aging, relieving body fatigue, regulating blood lipid and blood glucose. Recent studies on LBP have shown that LBP is involved in cardiac protection through various mechanisms such as blocking l-type calcium channel, antioxidant reaction, improving myocardial fibrosis, inhibiting apoptosis, and anti-cytotoxicity. In this paper, the relevant research contents are summarized in order to provide reference for clinical research.*

Keywords: *Lycium barbarum polysaccharide, Cardiomyocytes, Cardiacprotection, Apoptosis, Fibrosis, Signaling pathways*

1. Introduction

Lycium Barbarum, also known as Lycium Barbarum, is a very hard, prickly, shrubby vine belonging to solanaceae [1]. Lycium Barbarum has a history of more than 2000 years in China as a major medicinal material for both food and medicine [2]. The chemical components of Lycium barbarum polysaccharide mainly included Lycium barbarum polysaccharide, flavonoids, carotenoids, betaine, brain glycosides, β -sterols, amino acids, vitamins, trace elements, etc. [1-3], in which Lycium barbarum polysaccharide was the main chemical component of Lycium barbarum polysaccharide. It is also the main active ingredient of Wolfberry, with a variety of biological activities such as anti-aging [4], anti-oxidation [5], hypoglycemic [6], anti-tumor [7], neuroprotection [8] and immune regulation [9]. Among many pharmacological effects, the protective effect on the heart is very important, mainly manifested in improving the function of vascular endothelial cells, protecting myocardial ischemia, inhibiting myocardial apoptosis and inhibiting myocardial fibrosis. This paper reviews the protective effect and mechanism of LBP on heart.

2. Protective effect of Lycium barbarum Polysaccharide on hypoxia heart

Li et al. [10] treated H9c2 cardiomyocytes with LYcium barbarum polysaccharide (300μg/ mL) for 24 h under hypoxia, evaluated the changes of cell viability, migration and apoptosis, established an animal model of myocardial infarction (MI), and further studied the effects of LYcium barbarum polysaccharide in vivo. The results showed that lycium barbarum polysaccharide increased cell viability and improved migration. It inhibited the apoptosis of hypoxia-damaged H9c2 cardiomyocytes, reduced the size of myocardial infarction and improved cardiac function in rats, possibly by down-regulating mir-122 pathway in vitro and in vivo. Studies have shown that "calcium overload" caused by accumulation of calcium ions in cells caused by various injuries may be the final pathway leading to cell damage and death [11-12]. Xu Shunlin et al. [13] cultured myocardial cells of SD Suckling rats two or three days old to establish myocardial hypoxia model, and pretreated with 50 mg/L LBP. By observing cell activity, morphology and [Ca2+] I fluorescence density, the results showed that LBP had protective effect on hypoxia myocardial cells. The mechanism may be related to the reduction of intracellular calcium overload by LBP. Liu Miao et al. [14], based on the results of previous experiments, further recorded calcium channel currents by using single rat cardiomyocytes and standard whole-cell patch clamp technique, and showed that LBP inhibited L-type calcium channels in a concentration-dependent manner,

ISSN 2706-6819 Vol.3, Issue 5: 46-51, DOI: 10.25236/IJFM.2021.030507

mainly affecting the activation and recovery of calcium channels. It can not only reduce intracellular calcium ion concentration, reduce the occurrence of calcium overload, reduce the activation and release of degradation enzymes caused by myocardial ischemia and hypoxia injury; It can also shorten the action potential duration (APD), reduce the early and late depolarization caused by excitatory reentry, and reduce the occurrence of arrhythmias. These studies indicate that LBP has a certain protective effect on hypoxia heart, and LBP may achieve the protective effect on hypoxia heart through different mechanisms. The literatures can be summarized as Table 1.

Table 1: Protective effect and mechanism of Lycium barbarum Polysaccharide on hypoxic.

Cardioprotective effect	mechanism	dose	The experimental model	The experimental type	reference
Increase cell viability, improve migration, inhibit apoptosis and reduce infarct area	Down-regulation of mir-122 pathway	300ug/mL	Cells, rats	In vitro and in vivo	10
Increase cell vitality and improve cell hypoxia morphology	Reduce calcium overload	25, 50, 100ug/L	cells	In vitro	13
Regulate cell excitation and contraction, reduce arrhythmia	Inhibits l-type calcium channels	25, 50, 100ug/L	cells	In vitro	14

3. Protective effect of Lycium barbarum Polysaccharide on heart after ischemia/reperfusion (I/R)

Zhou Xin et al. [15] established myocardial infarction rat model by coronary ligation, and gave lycium barbarum polysaccharide (100 mg/kg) intragastric administration for 4 consecutive weeks. Cardiac structural parameters of each group were collected at 3d, 1, 3 and 4 weeks after operation, respectively. The results showed that LBP can significantly improve myocardial ischemia injury in rats after myocardial infarction. The mechanism may be related to activating endothelial cell function, promoting neovascularization and blood perfusion by increasing the expression of CD133 and VEGFR2 proteins. Lu et al. [16] observed the effects of LBP on myocardial cell injury in rats with myocardial I/R injury, and the results showed that LBP could significantly reduce the LD level of I/R rats and improve the activities of Na+-K+ -ATpase and Ca2+ -ATpase. In addition, LBP could significantly down-regulate Bax level and inhibit apoptosis. In addition, the expression level of Bcl-2 increased in a dose-dependent manner, which was consistent with the experimental conclusion of Hou et al. [17]. Wang Yucai et al. [18] also used myocardial I/R animal model to prove the protective effect of LBP on rat myocardial I/R, and its mechanism was related to the reduction of SOD content, promotion of Bcl-2 expression and inhibition of Fas protein expression by LBP after scavenging oxygen free radicals in serum after I/R. This experimental conclusion is consistent with that of Li Lifang et al. [19]. Pan H et al. [20] reported that LBP can also activate Nrf2 by inhibiting autophagy, thus exerting its protective effect on I/ R-induced heart injury.

Table 2: Protective effect and mechanism of Lycium barbarum polysaccharide on myocardial

Cardioprotective effect	**mechanism**	**dose**	**The experimental model**	**The experimental type**	**reference**
Increase EF, FS and decrease myocardial cell damage	Increased CD133 and VEGFR2 protein expression	100mg/kg	The rat	In the body	15
Decreased LD level and increased Na^+-K^+- atpase and Ca^{2+}- atpase activity	Bax level was down-regulated and bcl-2 expression level was increased	150, 300 mg/kg	The rat	In the body	16 or 17
Inhibit apoptosis and oxidative stress	Promote bcl-2 expression and inhibit Fas expression	1mg/kg	The rat	In the body	18th and 19th
Increase cell viability, inhibit apoptosis, inflammation, oxidative stress	Nrf2 expression was activated and autophagy was inhibited	15, 30, 60ug/ml	cells	In vitro	20

In addition, Chinese wolfberry polysaccharides can also sympathetic nerve plays a protective role of ischemic myocardium, can maintain the stability of the cardiac electrophysiology, reduce the incidence of arrhythmia after myocardial infarction, its mechanism may be related to LBP effectively reduce inflammatory factor levels in the body, reduce the excitability of infarction myocardial tissue, inhibiting sympathetic nerve regeneration after myocardial infarction (mi), Reduction of NGF release is related[21].

ISSN 2706-6819 Vol.3, Issue 5: 46-51, DOI: 10.25236/IJFM.2021.030507

In addition, Qi G X et al. [22] found that LBP has a protective effect on myocardium during er stress (ERS) in homocysteine (Hcy) mediated apoptosis of APOE mouse and H9C2 rat myocardium, and its mechanism may be related to reducing ERS and decreasing Hcy-mediated apoptosis of myocardium. The literatures can be summarized as Table 2.

4. Lycium barbarum polysaccharide (LBP) inhibits myocardial fibrosis and protects the heart from heart failure

Meng Lili [23] established rat models of chronic heart failure (CHF) by abdominal aortic constriction method (ACC), and treated with LBP. The results showed that LBP could significantly improve cardiac systolic and diastolic functions, reduce myocardial cell damage, and improve ventricular structural changes and progression of myocardial fibrosis in CHF rats. The mechanism may be related to the down-regulation of TGFβ1/Smad3 signaling pathway and the reduction of collagen fiber deposition in myocardial tissue. Liu Xinyan et al. [24] established isO-induced heart failure rats as models and administered LBP for 30d, and found that LBP could significantly reduce heart weight/body weight in heart failure rats (P< 0.01), decreased serum CTN-I, improved cardiac function, increased SOD level in serum and myocardium, and decreased MDA content, suggesting that LBP has protective effect on myocardium hypertrophy and heart failure induced by ISO in rats. The mechanism may be related to increasing antioxidant enzyme activity and decreasing lipid peroxides. Pop C et al. [25] also proved the anti-inflammatory and antioxidant effects of LBP in HF animal models, improving heart failure and thus protecting the heart. Zang R et al. [26] found that LBP improved abnormal electrocardiogram and cardiac function indicators, restored sarcomere assembly, disc and intervertebral disc junction morphological changes, and reversed the decrease of CaM and cMLCK (Mir-1-targeted proteins) in PV ring detection of Mir-1-overexpressed transgenic (Tg) mice. The results showed that LBP restored adverse structural remodeling and improved cardiac systolic dysfunction, which may be related to down-regulation of Mir-1 expression. In addition, LBP can also reduce the level of oxidative stress in the heart of diabetic rats, which has a protective effect on diabetic cardiomyopathy rats. The mechanism may be related to the inhibition of calpain-1 activity and NF-κB activation [27]. The literatures can be summarized as Table 3.

Table 3: Protective effect and mechanism of Lycium barbarum polysaccharide on myocardial fibrosis and heart failure

Cardioprotective effect	mechanism	dose	The experimental model	The experimental type	reference
Improve cardiac systolic and diastolic function, improve ventricular structure change and myocardial fibrosis progression	TGF beta 1 / Smad 3 Signal pathway	100mg/kg	The rat	In the body	23
Reduce cardiac hypertrophy and improve cardiac function	Increase antioxidant enzyme activity and decrease lipid peroxides	50, 100, 200mg/kg	The rat	In the body	24
Improve myocardial systolic function	Anti-inflammatory and antioxidant	100, 200 mg/kg	The rat	In the body	25
Restore adverse structural remodeling and improve cardiac systolic function	Down-regulation of Mir-1 expression	200 mg/kg/d	The rat	In the body	26

5. Protective effect of Lycium barbarum Polysaccharide on cardiac injury induced by Doxorubicin

Zhou Guoliang et al. [28] detected the survival rate, SOD activity and MDA content of H9c2 cells damaged by DOxorubicin (DOX) by adjusting the concentration of LYcium barbarum polysaccharide. The results showed that the survival rate of H9c2 cells reached the maximum when the concentration of Lycium barbarum polysaccharide reached 1.85μg/mL. At the same time, DOX induced decreased SOD activity and increased MDA concentration in myocardial cells, and the protective mechanism may be related to LBP alleviating oxidative stress injury. Xin YF et al. [29] also confirmed the typical protective effect of LBP on DOX induced acute cardiotoxicity by inhibiting oxidative stress in rats. On this basis, Xin Y et al. [30] treated male beagles with Lycium barbarum polysaccharide (20mg/kg, orally) for 7 days.

ISSN 2706-6819 Vol.3, Issue 5: 46-51, DOI: 10.25236/IJFM.2021.030507

The protective effect of LYcium barbarum polysaccharide (LBP) on DOX-induced acute cardiotoxicity in beagle dogs was then investigated by intravenous injection of DOX(1.5 mg/kg). It was found that pretreatment with LBP effectively alleviated DOx-related conduction abnormalities and increased serum CK and AST. Confirm and extend previous observations on the efficacy of LBP against DOX-induced cardiomyopathy in rats. The literatures can be summarized as Table 4.

Table 4: Protective effect and mechanism of Lycium barbarum Polysaccharide on cardiac injury induced by Doxorubicin

Cardioprotective effect	mechanism	dose	The experimental model	The experimental type	reference
Reduce cardiotoxicity and increase cell viability	Reduce oxidative stress damage	1.85 mu g/mL	cells	In vitro	28
Reduce cardiotoxicity and increase cell viability	Reduce oxidative stress damage	200mg/kg	The rat	In the body	29
Alleviates conduction abnormalities and reduces CK and AST	Reduce oxidative stress damage	20mg/kg	beagle	In the body	30

6. Protective effect of Lycium barbarum polysaccharide on ovariectomized rat myocardium

Yu NING et al. [31] used ovariectomized SD rats and administered lycium barbarum polysaccharide (250, 125mg/kg) orally for 12 weeks continuously. The results showed that LBP high-dose group increased serum estradiol content, increased myocardial H2S content, GSH-Px activity, eNOS protein and Akt phosphorylation levels, decreased myocardial ROS activity and MDA content, decreased serum LDH and CK activities, and improved the changes of myocardial morphology. These results indicate that LBP has protective effect on myocardium of ovariectomized rats, and its mechanism may be related to the regulation of PI3K/Akt/eNOS pathway. Yu N et al. [32] also used ovariectomized SD rats as a model to prove that LBP can improve the heart injury of ovariectomized rats caused by oxidative stress, and the mechanism may be that the improvement of antioxidant status is related to the Akt signaling pathway in the ovariectomized rats. It provides a new therapeutic idea for the treatment of postmenopausal cardiovascular disease. Table 5.

Table 5: Protective effect of Lycium barbarum Polysaccharide on ovariectomized rat myocardium

Cardioprotective effect	mechanism	dose	The experimental model	The experimental type	reference
Improve oxidative stress damage	Regulation of PI3K/Akt/eNOS pathway	250, 125 mg/kg	The rat	In the body	31
Improve oxidative stress damage	Activation of Akt signaling pathway	125, 300 mg/kg	The rat	In the body	32

7. Conclusion

In conclusion, LBP has a certain protective effect on the heart, but the mechanism is not completely clear.

Lycium barbarum polysaccharides (LBP) may protect the heart through multiple pathways, which may be due to its simultaneous action on multiple targets. As these studies continue to deepen, the results will provide more references for clinical work and provide a reliable theoretical basis for screening more effective drugs to treat heart disease.

References

[1] Wenli S, Shahrajabian MH, Qi C. Health benefits of wolfberry (Gou Qi Zi, Fructus barbarum L.) on the basis of ancient Chineseherbalism and Western modern medicine [J]. Avicenna J Phytomed, 2021, 11 (2): 109-119.
[2] Tian X, Liang T, Liu Y, et al. Extraction, Structural Characterization, Studies on Polysaccharides from Lycium Barbarum [J]. Biomolecules, 2019, 9(9): 389-406.
[3] Jin M, Huang Q, Zhao K, et al. Biological activities and potential health benefit effects of polysaccharides isolated from Lycium barbarum L [J]. Int J Macromol, 2013, 54(1):16-23.

ISSN 2706-6819 Vol.3, Issue 5: 46-51, DOI: 10.25236/IJFM.2021.030507

[4] Xia G, Xin N, Liu W. Inhibitory effect of Lycium barbarum polysaccharides on cell apoptosis and senescence is potentially mediated by the p53 signaling pathway [J]. Mol Med Rep, 2014, 9(4): 1237-1241.

[5] Varoni MV, Pasciu V, Gadau SD, et al. Possible antioxidant effect of Lycium barbarum polysaccharides on hepatic cadmium-induced oxidative stress in rats [J]. Environ Sci Pollut Res Int, 2017, 24(3): 2946-2955.

[6] Zhu J, Liu W, Yu J, et al. Characterization and hypoglycemic effect of a polysaccharide extracted from the fruit of Lycium barbarum L [J]. Carbohydr Polym, 2013, 98 (1): 8 to 16.

[7] Tang WM, Chan E, Kwok CY, et al. A review of the anticancer and immunomodulatory effects of Lycium barbarum fruit [J]. Inflammopharmacology, 2012, 20 (6): 307-314.

[8] Li SY, Yang D, Yeung CM, et al. Lycium barbarum polysaccharides reduce neuronal damage, blood-retinal barrier disruption and oxidative stress in retinal ischemia/reperfusion injury [J]. PLoS One, 2011, 6 (1): e16380.

[9] Bo R, Zheng S, Xing J, et al. The immunological activity of Lycium barbarum polysaccharides liposome in vitro and adjuvanticity against PCV2 in Int J Macromol, 2016, 85(1): 294-301.

[10] Li Q, Zhang Z, Li H, et al. Lycium barbarum polysaccharides protects H9c2 cells from hypoxia-induced injury by down-regulation of miR-122 [J]. Biomed Pharmacother, 2019, 110(1): 20-28.

[11] Liang Q, Zhang Y, Zeng M, et al. The role of IP3R-SOCCs in Cr(vi)-induced cytosolic Ca2+ overload and apoptosis in L-02 hepatocytes [J]. Toxicol Res (Camb), 2018, 7 (3): 521-528.

[12] Xiao Yuanyuan, Yin Xiaochen, Zeng Ming. Research progress on molecular mechanism of heavy metal induced calcium overload and apoptosis [J]. Practical Preventive Medicine, 2020, 27(02): 252-257.

[13] XU Shunlin, Huang Jun, TIAN Gengyuan, et al. Effects of lycium wolfberry peptide on free calcium concentration in neonatal myocardial cells of hypoxia rats [J]. Chinese Journal of Clinical Rehabilitation, 2005, 9(11): 62-64.

[14] LIU Miao, TANG Qizhu, Wang Xiaoling, et al. Effects of lycium barbarum polysaccharide (LBP) on l-type calcium current in rat ventricular myocytes [J]. J Wuhan univ med, 2009, 30(01): 57-60.

[15] Zhou Xin, YU Rui, Lin Ping. Effects of lycium barbarum polysaccharide (LBP) on myocardial ischemia in rats with myocardial infarction [J]. Chinese Journal of Traditional Chinese Medicine, 201, 39(04): 219-223.

[16] Lu SP, Zhao PT. Chemical characterization of Lycium barbarum polysaccharides and their reducing myocardial injury in ischemia/reperfusion of rat heart [J]. Int J Biol Macromol, 2010, 47(5): 681-684.

[17] Hou YM, Wang J, Zhang XZ. Lycium barbarum polysaccharide exhibits cardioprotection in an experimental model of ischemia-reperfusion damage [J]. Mol Med Rep, 2017, 15(5):2653-2658.

[18] Wang Yucai, Zhang Yutao, Wang Jiajun. Effects of lycium barbarum polysaccharide on myocardial ischemia reperfusion injury in rats [J]. Shandong medicine, 2013, 53(05): 34-35. (In Chinese)

[19] Li Lifang, DU Juan, Xue Hua, et al. Effects of lycium barbarum polysaccharide on myocardial apoptosis in rats with myocardial infarction [J]. Journal of guangxi medical university, 2018, 40(02): 97-99.

[20] Pan H, Niu L, Wu Y, et al. Lycium barbarum polysaccharide protects rats and cardiomyocytes against ischemia/reperfusion injury via Nrf2 Activation through inhibition by autophagy [J]. Mol Med Rep, 2021, 24(5): 778-792.

[21] Han Bing, Wu Qi, Chen Ying. Effects of Lycium barbarum polysaccharide on sympathetic nerve remodeling after myocardial infarction [J]. Journal of Heze Medical College, 201, 33(02): 3-4.

[22] QI Guoxue, Cui Ying, Yan Ning, et al. Homocysteine mediated apoptosis of APOE-/- mouse myocardial cells by endoplasmic reticulum stress and the intervention of Lycium barbarum polysaccharide [J]. Journal of ningxia medical university, 2019, 41(02): 109-113.

[23] Meng Lili. Lycium barbarum polysaccharide improves myocardial fibrosis in chronic heart failure rats by TGFβ1/Smad3 signaling pathway [J]. Chinese Journal of Experimental Diagnostics, 201, 25(02): 242-247.

[24] LIU Xinyan, ZHENG Ping, Yan Lin, et al. Protective effect of Lycium barbarum Polysaccharide on isoprenaline induced heart failure in rats and its mechanism [J]. Journal of ningxia medical university, 2011, 33(7): 601-604.

[25] Pop C, Berce C, Ghibu S, et al. Effects of Lycium barbarum L. Polysaccharides on Inflammation and Oxidative Stress Markers in a Pressure Overload-Induced Heart Failure Rat Model [J]. Molecules, 2020, 25(3):466-477.

[26] Zhang R, Xu Y, Niu H, et al. Lycium barbarum polysaccharides restore adverse structural remodelling and cardiac contractile dysfunction Study on the expression of micrornA-1 [J]. Cell Mol Med, 2018, 22(10):4830-4839.

ISSN 2706-6819 Vol.3, Issue 5: 46-51, DOI: 10.25236/IJFM.2021.030507

[27] Liu Qianqian. Effects of lycium barbarum polysaccharide (LBP) on diabetic cardiomyopathy in rats [J]. Jinzhou Medical University, 2019.

[28] Zhou Guoliang, XIN Yanfei, Xie Fang, et al. Protective effect of lycium barbarum polysaccharide on H9c2 injury induced by doxorubicin [J]. China journal of traditional Chinese medicine, 2011, 29(07): 1500-1502.

[29] Xin YF, Wan LL, Peng JL, et al. Alleviation of the acute doxorubicin-induced cardiotoxicity by Lycium barbarum polysaccharides through the suppression of oxidative stress [J]. Food Chem Toxicol, 2011, 49(1):259-264.

[30] Xin Y, Zhang S, Gu L, et al. Electrocardiographic and biochemical evidence for the cardioprotective effect of antioxidants in acute Biol Pharm Bull, 2011, 34(10):1523-1526. (In Chinese with English abstract)

[31] Yu Ning, Yang Fang, Leng Xue, et al. Lycium barbarum polysaccharide (LBP) regulates PI3K/Akt/eNOS signaling pathway to promote antioxidant activity in ovariectomized rat myocardium [J]. Chinese journal of pathophysiology, 2016, 32(08): 1370-1375.

[32] Yu N, Song N, Liu CY, et al. The estrogen like protective effect of Lycium barbarum polysaccharides in reducing oxidative stress on myocardial Study on the influence of different treatments on the apoptosis of rats [J]. Mol Med Rep, 2019, 19(3):2271-2278.