**International Journal of Research Studies in Biosciences (IJRSB)**
*Volume 9, Issue 1, 2021, PP 1-15*
*ISSN No. (Online) 2349-0365*
*DOI: https://doi.org/10.20431/2349-0365.0901001*
*www.arcjournals.org*

# Overview on the Pharmacological Functions of Polysaccharides from *Lycium Barbarum*

**Xiaoxia Zhang, Xiaohan Gao, Shuang Liang, Zichen Guo, Yaxuan Sun, Zhaolan Gao, Xueling Dai ***

*Beijing Key Laboratory of Bioactive Substances and Functional Food, Research Institute for Science and Technology of Functional Food, Beijing Union University, Beijing 100191, China*

***Corresponding Author:** ***Xueling Dai,*** *Beijing Key Laboratory of Bioactive Substances and Functional Food, Research Institute for Science and Technology of Functional Food, Beijing Union University, Beijing*

**Abstract:** *In the last decades, the bioactivity of natural products and health benefits has drawn much attention. Lycium barbarum has long been deemed as anti-inflammatory, antipyretic, and anti-ageing Chinese herbal medicine and nutritious supplements. The major constituents of Lycium barbarum are polysaccharides named Lycium barbarum polysaccharides (LBPs) that have plenty of biological effects such as antioxidant activity, anti-tumor, anti-inflammatory and neuroprotective effect, etc. In recent years, LBPs tend to be a new research focus. Here, we summarized the pharmacological activities of LBPs, aiming to provide a reference for further research as well as application of LBPs in food and pharmaceutical industry.*

**Keywords:** *Lycium barbarum polysaccharides; pharmacological activities; neuroprotective; antioxidant*

## 1. INTRODUCTION

Traditional Chinese herb *Lycium barbarum* (also called Goji berries, wolfberry), popular for its biological and pharmacological functions, is widely grown in the dry or semidry regions of China (such as Gansu province, Ningxia province, etc.), Korea, Japan, as well as Europe. High soil and air temperature, low latitude, strong light intensity, and moderate soil moisture are favorable geographical and climatic conditions for the production of nutrient-rich Goji berries [1]. It was estimated that there were eighty species of *Lycium barbarum*, of which seven species were found in China [2]. *Lycium barbarum* has long been used as medicine in China that could be traced back to the Tang Dynasty. According to Chinese traditional medicine, *Lycium barbarum* berries were considered to have the ability of improving the function of eyes, the activity of liver and kidneys, as well as enhancing the endurance/physical energy [3]. Moreover, its novel applications were explored such as *Lycium barbarum* was cultivated and consumed as nutritious supplements. Particularly, adding juice concentrate or extract of *Lycium barbarum* fruit to beverages could effectively improve liver function and reduce oxidative stress [4]. Due to the potential health benefits, ingredients from *Lycium barbarum* were extensively identified and analyzed, including but not limited to polysaccharides, flavonoids, carotenoids and polyphenols, of which *Lycium barbarum* polysaccharides (LBPs) were among the most bioactive ingredients. LBPs were composed of a bunch of water-soluble monosaccharides and glycoconjugates [5], including arabinose (Ara), rhamnose (Rha), glucose (Glc), xylose (Xyl), fucose (Fuc), glucuronic acid (GlcA), etc [6].

LBPs were supposed to have a variety of biological effects, including antioxidant, anti-tumor effects,

blood glucose and lipids metabolism regulation, anti-ageing, immune regulation, anti-radiation, etc [7-12]. Further, we summarized and updated pharmacological functions of LBPs according to recent studies, to provide theoretical basis for extensive comprehension and making full use of LBPs.

## 2. PHARMACOLOGICAL ACTIVITIES AND POTENTIAL HEALTH BENEFITS OF LBPS

In line with other polysaccharides, LBPs have a variety of biological activities. At present, the biological functions of LBPs has covered anti-oxidation, neuroprotection, anti-tumor, anti-inflammation, anti-apoptotic effects, etc (as shown in **Figure. 1**).

### 2.1 The neuroprotective effect of LBPs

According to former studies, LBPs exhibited great neuroprotective effects on *in vivo* and *in vitro* models of neurological diseases such as Alzheimer's disease (AD), Parkinson's disease (PD), stroke, and so on [13-15].

AD, a neurodegenerative disease with characteristics of gradual memory loss and cognitive disorders, is the most common cause of dementia [16]. The neuropathological features of AD contained progressive hippocampal and cortical atrophy, the presence of neurofibrillary tangles and the aggregation of β-amyloid (Aβ) in extracellular senile plaques [17]. Evidence from genetics and biochemical studies proved that excessive production of cytotoxic Aβ generated via amyloid precursor protein (APP) hydrolysis was responsible for the development and progression of AD [18]. The proteolytic processing of APP was comprised of amyloidogenic and non-amyloidogenic ways, where the former was mediated by β- and γ-secretase resulting in the generation of Aβ, while the latter was mediated by α- and γ-secretase leading to the production of a non-Aβ fragment termed p3 [19, 20]. One prospective strategy for AD prevention is to suppress the generation or assembly of Aβ [21]. Some study demonstrated that LBP1C-2 could reduce the production of Aβ42 by decreasing the expression of APP cleavage enzyme 1 (BACE1) and upregulating the expression of ADAM10 [22-24].

Several studies indicated that crude LBPs could significantly attenuate cytotoxicity triggered by Aβ *in vitro*, and their sulfated derivatives were proved to possess anti-angiogenic activity [22, 23, 25]. LBPs pretreatment could markedly protect neurons from Aß-mediated cellular apoptosis possibly via depressing the activity of caspase-2 and -3, underlining the potential beneficial role of LBPs in AD [26].

One of the vital clinical features and standards for AD diagnosis is cognitive dysfunction [27]. In APP/PS1 double-transgenic mice, LBPs drastically improved the cognitive functions as determined by novel object recognition test and Morris water maze (MWM), as well as enhanced neurogenesis and proliferation, restored hippocampal synaptic plasticity. Moreover, LBPs decreased Aβ levels, amyloid plaque burden *in vivo* [28]. Similarly, LBPs treatment could significantly enhance cognitive and memory ability according to MWM and NORT, and prevent the decrease of cell proliferation and differentiation in scopolamine-treated rats [29].

PD is also known as dyskinesia, with the prevalence secondary to AD among neurodegenerative diseases. The protective effect of LBPs on pathological alterations and neurobehavioral defects was confirmed in a PD mouse model mediated by methyl-4-phenyl-1,2,3,6- tetrahydropyridine (MPTP). LBPs could enhance the expression of SOD2, GSH-Px, CAT as well as repress MPTP-mediated aberrant α-synuclein aggregation. Moreover, phosphorylation of AKT and mTOR could also be upregulated by LBPs treatment, indicating the protective effect of LBPs on attenuating MPTP-induced nigrostriatal degeneration was probably due to the activation of PTEN/AKT/mTOR

signaling pathway [30]. Besides, LBPs could dose-dependently decrease cell apoptosis, impede amassing of ROS and NO, as well as suppress the expression of NF-κB and iNOS mediated by 6-hydroxydopamine exposure, and the mechanism was found to be associated with the regulatory effect of LBPs on ROS-NO pathway [31].

The protective effect of LBPs on neurobehavioral defects mediated by cerebral ischemia was also sufficiently studied. A study reported that LBPs pretreatment could significantly ameliorate regional cortical blood flow, enhance motor coordination ability and memory, and repress microglia and astrocytes activation after perfusion in middle cerebral artery occlusion (MCAO) mice. The results further implied that LBPs could inhibit MCAO-mediated stimulation of NF-κB and p38 pathway, as well as decrease the expression of proinflammatory mediators in the hippocampus [32]. LBPs could also protect primary cultured hippocampal neurons from cerebral ischemia/ reperfusion injury possibly due to the activation of PI3K/Akt/mTOR signaling pathway [33]. Similarly, Wu et al. conducted a study on investigating the potential effect of LBPs on MCAO mice, where LBPs were administered prophylactically to MCAO mice by intragastric administration for 7 days, followed by cerebral ischemia for 2 hours and reperfusion for 24 hours. Consequent results suggested that neuronal morphological damage and neuronal apoptosis were markedly reduced, and caspase-3 activity and Bax protein expression was significantly decreased while Bcl-2 expression was increased with LBPs pretreatment [34].

LBPs pretreatment could also effectively protect retinal nerves and photoreceptor cells from light-induced retinal damage [35]. Li et al. reported that LBP could obviously retard the secondary degeneration of retinal ganglion cells, ameliorate the polarization of microglia/ macrophages, as well as decrease the autophagy level upon partial optic nerves injury [36]. Similarly, in an electric stimulation-induced microglial injury system, pretreatment with LBPs dramatically restored the appearance of cells, as well as attenuated inflammatory response, oxidative damage, and cell apoptosis possibly due to the modulation on endogenous autophagy and MAPK signaling pathway [37]. Another study demonstrated that LBPs could dose-dependently reduce the expression of Bax and Caspase-3 in hippocampal neurons exposed to sevoflurane, as well as promote the phosphorylation of ERK1/2 and the expression of Bcl-2 [38]. Furthermore, LBPs treatment could also exert neuroprotective effects against hypoxia, as manifested by reduced brain apoptosis, improved performance in MWM test in $CoCl_2$-exposed rats [39]. Similarly, Deng et al. obtained *Lycium ruthenicum* polysaccharide 3 (LRP3) from crude polysaccharide through using ion exchange and gel permeation chromatography approaches. They found that LRP3 also exhibited neuroprotective effect on rat primary cortical neurons against oxygen-glucose deprivation/reoxygenation (OGD/R)-induced neuronal damage [40].

### 2.2 The antioxidant property of LBPs

Former reports suggest that LBPs and related glycoconjugates could effectively scavenge superoxide anions, 1,1-diphenyl-2-picrylhydrazyl (DPPH)-, hydroxyl-, and ABTS radicals, as well as improve the level of antioxidant enzymes [41-44]. Free radicals could be dose-dependently eliminated by LBPs, and the clearance rate reached a plateau as the concentration of LBPs increased [44].

LBPs could exert antioxidant effects by increasing enzymatic activity and expression of anti-oxidative enzymes including glutathione peroxidase (GSH-Px), superoxide dismutase (SOD) and catalase (CAT) and decreasing malondialdehyde (MDA) *in vivo* and *in vitro* [45, 46]. LBPs could also repress hydrogen peroxide-induced embryonic stem cell death, MDA and caspase-3 expression, as well as improve Bcl-2 expression [47]. Similarly, Li et al. proposed that LBPs inhibited hydrogen

peroxide-induced oxidative stress by lowering reactive oxygen species (ROS) and lactate dehydrogenase (LDH) levels while increasing SOD activity in trophoblast HTR8/SV cells [48]. Moreover, LBPs could effectively ameliorate cellular damage, cell apoptosis as well as autophagy induced by hydrogen peroxide via down-regulating miR-194 in PC-12 cells [49]. Chen et al. fed weaned piglets with different concentrations of LBPs and found that LBPs could effectively promote antioxidant properties through improving antioxidant enzyme activities including CAT, SOD, and GSH-Px, etc., as well as decreasing the MDA content in serum and liver of piglets [50]. Tang et al. extracted LBPs to obtain LBP-1 and LBP-2, where LBP-2 was acquired by deproteinating LBP-1 using Sevag method. Consequent supplementation of *Drosophila melanogaster* with dietary LBP-1 or LBP-2 resulted in increased SOD and CAT activities but reduced MDA levels [51].

Nuclear factor E2-related factor 2 (Nrf2) played a significant role in the endogenous antioxidant system. Nrf2 could bind to antioxidant response element (ARE) thus upregulate downstream genes with antioxidant activities, such as heme oxygenase1 (HO-1), SOD and GSP-Px [52, 53]. LBPs were supposed to inhibit hydrogen peroxide-induced Nrf2 and HO-1 decrease and facilitate the binding of Nrf2 to HO-1 promoter [39]. Similar research implied that LBPs could decrease the level of ROS and lipid peroxide, while increase cell viability, SOD and GSP-Px levels mediated by silencing Nrf2 gene in fibroblastic HSF cells [12]. *In vivo* and *in vitro* studies indicated that LBPs could markedly attenuated high fat-mediated insulin resistance, manifested by improved expression of antioxidant and detoxifying enzymes, upregulated phosphorylation of Nrf2 and GSK3β, whereas ROS levels as well as phospho-JNK levels were decreased possibly due to the activation of PI3K/AKT/Nrf2 signaling pathway. Besides, LBPs dramatically attenuated expression of glycolytic and gluconeogenic genes by activating Nrf2 [54]. Similarly, Tang et al. proposed that LBPs pretreatment could markedly protect photoreceptor cells from light-mediated injury possibly via enhancing the expression of Nrf2 and TrxR1, eliminating oxygen free radicals, and decreasing resultant oxidative stress [35].

Antioxidants strongly related to ageing, and LBPs were identified as efficient antioxidants and anti-ageing agents according to former studies [55]. The expression of antioxidant enzymes including SOD, GSH-Px and CAT was markedly upregulated in senile mice treated with LBPs intragastrically (200, 350 and 500 mg/kg respectively), whereas the formation of MDA (metabolite of lipid peroxidation products) was significantly decreased [56]. Another study showed that hydrogen peroxide-induced apoptosis, ROS and MDA production, as well as loss of $\Delta\psi m$ were markedly attenuated in the human lens epithelial cells upon LBPs treatment. Further, LBPs also upregulated the expression of Bcl-2, downregulated the expression of Bax, attenuated cellular senescence, as well as improved the enzyme activity of SOD and GSH in human lens epithelial cells [57].

### 2.3 The immunomodulatory effect of LBPs

Previous studies indicated that inflammatory reactions were involved in numerous diseases. The nuclear factor κB (NF-κB) plays an important role in cell survival and inflammation, where abnormally elevated NF-κB level was deemed as a key indicator of inflammatory or autoimmune diseases. NF-κB pathway could be stimulated by translocation of NF-κB to nucleus in response to various irritative substances including IL-1β, TNF-α, growth factors, TLR4, etc [58, 59]. Ni et al. established an *in vitro* cartilage inflammation injury model by exposing ATDC5 cells to IL-1β. Subsequent results suggested that either COX-2 elevation or the activation of NF-kB signaling pathway mediated by IL-1β was significantly suppressed by LBPs treatment [60]. Another study indicated that LBPs treatment could suppress hepatotoxicity, mitigate immune organ injury, improve immune indexes, as well as increase the generation or secretion of cytokines including IL-1β, IL-2,

TNF-α, IL-6, and IFN-γ in cyclophosphamide- mediated mice [61]. Moreover, LBPs significantly repressed the increase of IL-1β, IL-6, IL-8, NF-κB and TNF-α mediated by lipopolysaccharide (LPS) exposure in a dose-dependent manner, as well as upregulated the mRNA levels of HO-1, NQO1 and Nrf2 but downregulated the expression of NF-κB and Keap1 [62]. Peng et al. purified LRGP3 from *L. ruthenicum Murr.* using hot water extraction method followed by Savage method for purification. Subsequent results showed that LRGP3 could significantly decrease NO production, prevent IκBα from degradation, as well as repressed pro-inflammatory cytokines like IL-1α, TNF-α, IL-6 in mouse macrophage cells exposed to LPS. Meanwhile, LRGP3 could also decrease the expression of Toll-like receptor 4 (TLR4) and the phosphorylation of NF-κB p65, suggesting the anti-inflammatory effect of LRGP3 might be relevant to TLR4/NF-κB signaling pathway [63]. Similarly, Zhang et al. purified a fraction named LBPF4-OL from LBPs by hot water extraction and Savage method. They stated that LBPF4-OL could significantly facilitate the expression of TLR4/MD2 and phospho-p38 MAPK though depressing the expression of phospho-JNK and phospho-ERK1/2, suggesting a potential role of LBPF4-OL as an inducer or activator in TLR4/MD2/MAPK signal pathway [64]. Analogously, LBPs markedly decreased the expression of IL-1β and TNF-α, and restored the lung morphology in hyperoxia-mediated mice, possibly due to the inhibitory effect of LBPs on SIRT1-mediated stimulation of NLRP3 inflammasome [65]. Furthermore, LBPs could facilitate the activation and multiplication of immune cells including B cells, T cells, macrophagocytes, NK cells and dendritic cells [66-69]. Studies indicated that LBPs could stimulate the maturation of dendritic cells both phenotypically and functionally, as manifested by enhanced expression of CD-40, -80, -86, decreased ingestion of Ag, up-regulated allostimulatory effect, as well as improved Th1/Th2 response, implying the potential role of LBPs as an adjuvant for dendritic cells associated vaccines [70].

### 2.4 The anti-apoptotic activity of LBPs

Apoptosis is automatically controlled to maintain a stable internal environment [71]. LBPs were deemed to have bidirectional regulation effects, i.e. promoting apoptosis of tumor cells or tumor volume shrinkage, as well as repressing apoptosis in normal cells or tissues. Hydrogen peroxide was frequently used in establishing oxidative damage cell models, while oxidative stress could lead to apoptosis [72, 73]. One study demonstrated that LBPs repressed Δψm decrease and cell apoptosis mediated by hydrogen peroxide via enhancing the expression of Bcl-2, survivin, and HIF1-α, but inhibiting the expression of Bax [48]. The accumulation of excessive ROS could exacerbate damage of retinal tissue, since free radicals trigger lipid peroxidation, protein damage and DNA breakage. LBPs could also protect retinal ganglion cells from $CoCl_2$-induced apoptosis by increasing Δψm and decreasing ROS [74]. Moreover, LBPs significantly protected human retinal pigment epithelial cells from hydrogen peroxide-induced cell apoptosis as manifested by increased expression of Bcl-2 and decreased expression of Bax [75].

Excessive apoptosis is increasingly associated with ageing and ageing-related diseases [76]. One study carried out in a zebrafish model implied the protective effect of LBPs against ageing and cell apoptosis, with the level of ageing-related genes including p53, p21 as well as Bax was downregulated, while the expression of anti-ageing genes like Mdm2 and TERT was upregulated upon LBPs treatment [77]. Chen et al. reported that LBPs could significantly reduce cell death induced by LPS and repress the activation of caspase-3 *in vitro* [78]. LBPs could also dose-dependently suppress osteoblast apoptosis mediated by palmitate (PA), which was relevant to the inhibition of endoplasmic reticulum stress (ERS)-mediated JNK phosphorylation [79]. Similarly, Yang et al. reported that LBPs could inhibit cisplatin-mediated cell apoptosis in MLTC-1 cells through downregulating the expression of caspase-3, -7 and -12 [80]. Another study showed that LBPs

treatment could greatly downregulate the expression of pro-caspase and cleaved caspase, while upregulate the expression of PARP as well as cleaved PARP in photoreceptor cells exposed to N-methyl-N-nitrosourea [81].

### 2.5 The anti-cancer effect of LBPs

Apoptosis played an indispensable role in preventing canceration by eliminating damaged cells or abnormally excessive cells. A series of studies suggested that LBPs had favorable anti-tumor activity and stimulated apoptosis of cancer cells [82]. One study demonstrated that LBPs could inhibit proliferation and mediate apoptosis in human hepatoma cells [83]. Deng et al. separated four water-soluble LBPs fractions (i.e. LBP-2, LBP-3, LBP-4, and LBP-5) with different MW. *In vitro* experiments suggested that all of the LBPs fractions exhibited great inhibitory effect on murine hepatoma H22 cell line viability, but cell apoptosis, S-phase arrest and mitochondrial dysfunction were only observed in cells treated with LBP-3 [84]. Furthermore, LBP-3 repressed transplanted tumor growth by 37.97% as well as prolonged survival time in tumor-bearing mice. Similar studies reported that LBPF5 obtained from purification of LBPs with ion-exchange chromatography could notably suppress the multiplication and migration of BIU87 cells originated from bladder cancer [85] via downregulating PI3K/AKT pathway [86]. Similarly, studies on primary human hemangioma endothelial cells (HemEC) indicated that LBPs could effectively inhibit the proliferation of HemECs and induce apoptosis of HemECs through PI3K/AKT signaling pathway [87]. Shen and Du demonstrated that LBPs could dose-dependently stimulate Erk1/2 activity and S phase cell cycle arrest in MCF-7 cells [88]. Analogously, combined usage of LBPs and recombinant interferon (IFN-α2b) significantly promoted cell cycle arrest, facilitated cell apoptosis, as well as repressed cell multiplication in mouse Renca cells. Further, tumor volume and the ratio of myeloid-derived suppressor cells were significantly decreased in mice with transplanted tumor upon LBPs and IFN-α2b combined treatment [89].

### 2.6 The Hypoglycemic activity of LBPs

A significant decrease in serum glucose and increase in proinsulin indexes was uncovered after 3 months oral administration of LBPs at a dose of 300 mg/day according to a clinical trial on 67 patients with type II diabetes. Moreover, high-density lipoprotein levels in diabetic patients were increased upon LBPs treatment, suggesting the potential role of LBPs as therapeutic adjuvants for type II diabetes [90]. Tang et al. obtained crude LBPs using hot water extraction method at the optimum temperature of 30°C and working pressure of 0.25 MPa, and further purified and obtained four components named LBP1, LBP2, LBP3 and LBP4 respectively. Two components LBP3a and LBP3b were purified from LBP3 using Sephadex G-150 columns (2.5 cm × 60 cm), and the hypoglycemic activity of LBP3b was studied. LBP3b repressed the uptake of glucose in a dose-dependent manner *in vitro*, possibly due to the combination of LBP3b with bit points of glucose absorption, thus delayed the absorption of glucose, and finally decreased postprandial blood glucose [91]. Li also proposed that oral administration of LBPs could effectively improve oxidative indexes of blood, kidney and liver in streptozotocin-induced diabetic rats [92]. Moreover, LBPs were always used in treating certain diabetic complications, such as diabetic peripheral neuropathy, testicular dysfunction, vascular disease, and diabetic retinopathy, etc [93-95]. LBPs were found to slightly reduce blood glucose, partly relieve hyperalgesia, and greatly ameliorate nerve fiber myelin structural damage in diabetic rats, suggesting the protective effect of LBPs against diabetic peripheral neuropathy [96]. Besides, LBPs played a protective role by increasing cell proliferation, inhibiting apoptosis, regulating the expression of sirtuin 1 (SIRT1) and hypoxia-inducible factor 1-alpha (HIF-1α) in diabetic rats [97]. Testicular

dysfunction was regarded as a serious secondary complication to diabetes. Shi et al. reported that LBPs could inhibit excessive testicular autophagy via activating PI3K/AKT signaling pathway, thereby protect diabetic mice against testicular dysfunction [98].

### 2.7 Other Biological Activities

In addition to above mentioned bioactivities, LBPs were reported to have the ability of radioresistance [99], anti-fatigue [100], intestinal microbiota regulation [101, 102], cardioprotection [103], protecting male reproductive organs [104, 105] as well as kidney and liver from damage [106-110]. As bioactive ingredients, LBPs exhibited versatile biological activities as well as benefits for human health.

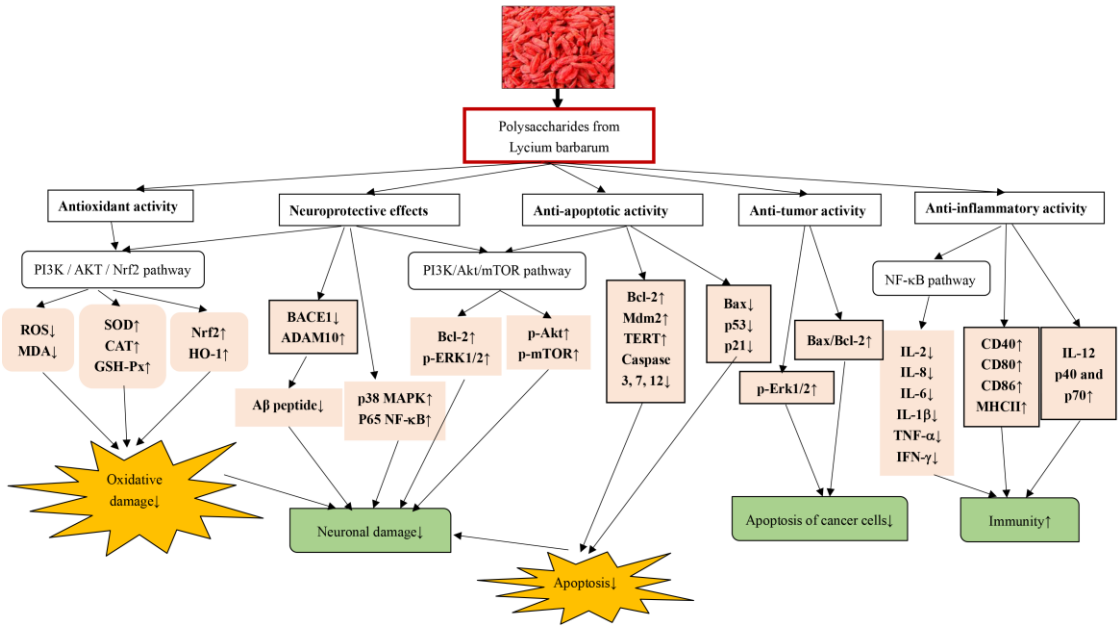


**Figure1.** *Summary of biological effects of polysaccharides from Lycium barbarum (LBPs). LBPs exerted a remarkable protective effect on in vitro and in vivo models. LBPs treatment increased the activity of SOD, CAT and GSH-Px but decrease the expression level of ROS and MDA via PI3K/AKT/Nrf2 pathway, and reduced apoptosis by inhibiting the generation of oxidative stress. LBPs decreased the expression of genes related to aging like p53, p21, and decreased the expression of apoptosis-related protein caspase 3, caspase 7 and caspase 12. Moreover, LBPs exerted neuroprotective effects via inhibiting the production of Aβ by reducing the expression of β-APP cleavage enzyme 1 (BACE1) and up-regulating the expression of ADAM10. Besides, LBPs also enhanced neuroprotective function by inhibiting the generation of oxidative stress. LBPs could also down-regulated the expression of proinflammatory mediators and chemokines like IL-2, 8 IL-6, IL-1β, TNF-α and IFN-γ via NF-κB pathway.*

## 3. PERSPECTIVES

In conclusion, *Lycium barbarum* has been explored both medically and nutritionally so far. Particularly, it has been used to improve the function of liver, kidney and lung as Chinese traditional medicine for a long time. *Lycium barbarum* berries were edible either fresh or dried, or could be processed into jam, juice, wine and tea. At present, *Lycium barbarum* berries were widely used in food supplements and Chinese herbal medicine, such as Goji Yishen Capsule, Goji Cream Formula, Compound Goji Granules, and Wolfberry pulp, etc. What's more, *Lycium barbarum* has a variety of physiological activities, which is highly related to its abundant content of polysaccharides i.e. LBPs. Studies suggest that LBPs possessed plenty of biological functions, including anti-oxidation, neuroprotective effect, anti-tumor, immunomodulation, anti-apoptosis, anti-inflammation,

hypoglycemic effect, etc, though the mechanism involved in biological activities of LBPs was yet to be clarified. Thus, further studies using systematic pharmacology approaches such as proteomic and metabolomic analysis are required to uncover the molecular target networks of LBPs. Besides, researchers acquired good effect by using LBPs in clinical trials for patients with type II diabetes, though clinical safety data on LBPs are still lacking. Moreover, the safe and effective use of herbal medicines like LBPs requires a full understanding of their side effects and mechanism of action. Therefore, it is necessary to establish a relationship between dose response and dose toxicity of LBP in animal and human studies to provide effective evidence for further development of LBPs-related health products. Last but not least, the relation between LBPs bioactivities and chemical structures was not properly established. Accordingly, further study on relationship between structure and bioactivity, could be one of the research priorities on LBPs.

## AUTHOR CONTRIBUTIONS

X.Z. wrote the first draft of this manuscript and drew Tables 1, 2 and Figures 1. S.L., X.G., Z. G., `Y.S., Z.G. and X.D. revised the manuscript. X.D. designed this review and checked the draft as the final version before submission.

## ACKNOWLEDGEMENTS

This research was supported by grants from the Beijing Natural Science Foundation (6164030), Beijing Municipal Outstanding Talent Training Funding (2015000020124G049), 2019 Basic Research Projects of Beijing Union University, Beijing Key Laboratory of Bioactive Substances and Functional Foods Research Project, the Academic Research Projects of Beijing Union University (No. XP202007), and Graduate Funding Project in Beijing Union University.

## REFERENCES

[1] Y.J. Wang, X.J. Liang, Y.K. Li, Y.F. Fan, Y.L. Li, Y.L. Cao, W. An, Z.K. Shi, J.H. Zhao, S.J. Guo,(2020). Changes in Metabolome and Nutritional Quality of Lycium barbarum Fruits from Three Typical Growing Areas of China as Revealed by Widely Targeted Metabolomics, Metabolites 10(2), 46.

[2] R.A. Levin, J.S. Miller,(2005). Relationships within tribe Lycieae (Solanaceae): paraphyly of Lycium and multiple origins of gender dimorphism, Am J Bot. 92, 2044-2053.

[3] R.Y. Yao, M. Heinrich, C.S. Weckerle,(2018). The genus Lycium as food and medicine: A botanical, ethnobotanical and historical review, J. Ethnopharmacol. 212, 50-66.

[4] J. Cheng, Z.W. Zhou, H.P. Sheng, L.J. He, X.W. Fan, Z.X. He, T. Sun, X.J. Zhang, R.J. Zhao, L. Gu, C.H. Cao, S.F. Zhou,(2015). An evidence-based update on the pharmacological activities and possible molecular targets of Lycium barbarum polysaccharides, Drug Des. Dev. Ther. 9, 33-78.

[5] M.L. Jin, Q.S. Huang, K. Zhao, P. Shang,(2013). Biological activities and potential health benefit effects of polysaccharides isolated from Lycium barbarum L, Int. J. Biol. Macromol. 54, 16-23.

[6] H. Amagase, N.R. Farnsworth,(2011). A review of botanical characteristics, phytochemistry, clinical relevance in efficacy and safety of Lycium barbarum fruit (Goji), Food Res. Int. 44, 1702-1717.

[7] R.Y. Yao, C. Huang, X.F. Chen, Z.Q. Yin, Y.P. Fu, L.X. Li, B. Feng, X. Song, C.L. He, G.Z. Yue, B. Jing, C. Lv, G. Su, G. Ye, Y.F. Zou,(2018). Two complement fixing pectic polysaccharides from pedicel of Lycium barbarum L. promote cellular antioxidant defense, Int. J. Biol. Macromol. 112, 356-363.

[8] B.K. Cui, Y.F. Chen, S. Liu, J. Wang, S.H. Li, Q.B. Wang, S.P. Li, M.S. Chen, X.J. Lin,(2012). Antitumour activity of Lycium chinensis polysaccharides in liver cancer rats, Int. J. Biol. Macromol. 51, 314-318.

[9] R. Zhao, R. Jin, Y. Chen, F.M. Han,(2015). Hypoglycemic and Hypolipidemic Effects of Lycium barbarum Polysaccharide in Diabetic Rats, Chinese Herbal Medicines 7, 310-315.

[10] Y.J. Gao, Y.F. Wei, Y.Q. Wang, G. Fang, Z.G. Chen,(2017). Lycium Barbarum: A Traditional Chinese Herb and A Promising Anti-Aging Agent, Aging Dis. 8, 778-791.

[11] X.R. Zhang, C.H. Qi, J.P. Cheng, G. Liu, L.J. Huang, Z.F. Wang, W.X. Zhou, Y.X. Zhang,(2014). Immune activities comparison of polysaccharide and polysaccharide-protein complex from Lycium barbarum L, Int. J. Biol. Macromol. 65(5), 441-445.

[12] B.H. Liang, L.Q. Peng, R.X. Li, H.P. Li, Z.Y. Mo, X.Y. Dai, N. Jiang, Q. Liu, E.T. Zhang, H.Y. Deng, Z.J. Li, H.L. Zhu,(2018). Lycium barbarum polysaccharide protects HSF cells against ultraviolet-induced damage through the activation of Nrf2, Cell Mol Biol Lett. 23(1), 18.

[13] Y.S. Ho, M.S. Yu, S.Y. Yik, K.F. So, W.H. Yuen, R.C.C. Chang,(2009). Polysaccharides from wolfberry antagonizes glutamate excitotoxicity in rat cortical neurons, Cell. Mol. Neurobiol. 29(8), 1233-44.

[14] Y. Lakshmanan, F.S.Y. Wong, B. Zuo, K.F. So, B.V. Bui, H.H.L. Chan,(2019). Posttreatment Intervention With Lycium Barbarum Polysaccharides is Neuroprotective in a Rat Model of Chronic Ocular Hypertension, Invest. Ophthalmol. Vis. Sci. 60(14), 4606-4618.

[15] D. Yang, S.Y. Li, C.M. Yeung, R.C.C. Chang, K.F. So, D. Wong, A.C.Y. Lo,(2012). Lycium barbarum extracts protect the brain from blood-brain barrier disruption and cerebral edema in experimental stroke, PLoS One 7(3), e33596.

[16] K. Blennow, J. Mony, H. Zetterberg,(2006). Alzheimer's Disease, Lancet 368(9533), 387-403.

[17] K. Govindpani, L.G. McNamara, N.R. Smith, C. Vinnakota, H.J. Waldvogel, R.L. Faull, A. Kwakowsky,(2019). Vascular Dysfunction in Alzheimer's Disease: A Prelude to the Pathological Process or a Consequence of It?, J. Clin. Med. 8(5), 651.

[18] H.C. Rice, G. Marcassa, I. Chrysidou, K. Horré, T.L. Young-Pearse, U.C. Müller, T. Saito, T.C. Saido, R. Vassar, J.d. Wit, B.D. Strooper,(2020). Contribution of GABAergic interneurons to amyloid-β plaque pathology in an APP knock-in mouse model, Mol. Neurodegener. 15(1), 3.

[19] N.M. Moussa-Pacha, S. Abdin, H. Omar, H.Y. Alniss, T.H. Al-Tel,(2020). BACE1 inhibitors: Current status and future directions in treating Alzheimer's disease, Med. Res. Rev. 40(1), 339-384.

[20] U. Neumann, R. Machauer, D.R. Shimshek,(2019). The β-secretase (BACE) inhibitor NB-360 in preclinical models: From amyloid-β reduction to downstream disease-relevant effects, Br J Pharmacol 176(18), 3435-3446.

[21] F. Panza, M. Lozupone, G. Logroscino, B.P. Imbimbo,(2019). A critical appraisal of amyloid-β-targeting therapies for Alzheimer disease, Nat. Rev. Neurol. 15(2), 73-88.

[22] L.S. Zhou, W.F. Liao, H. Zeng, Y.L. Yao, X. Chen, K. Ding,(2018). A pectin from fruits of Lycium barbarum L. decreases β-amyloid peptide production through modulating APP processing, Carbohydr. Polym. 201, 65-74.

[23] L.S. Zhou, L.L. Huang, H. Yue, K. Ding,(2018). Structure analysis of a heteropolysaccharide from fruits of Lycium barbarum L. and anti-angiogenic activity of its sulfated derivative, Int. J. Biol. Macromol. 108, 47-55.

[24] L.S. Zhou, W.F. Liao, X. Chen, H. Yue, S.J. Li, K. Ding,(2018). An arabinogalactan from fruits of Lycium barbarum L. inhibits production and aggregation of Aβ42, Carbohydr. Polym. 195, 643.

[25] M.S. Yu, S.K.Y. Leung, S.W. Lai, C.M. Che, S.Y. Zee, K.F. So, W.H. Yuen, R.C.C. Chang,(2005). Neuroprotective effects of anti-aging oriental medicine Lycium barbarum against beta-amyloid peptide neurotoxicity, Exp. Gerontol. 40(8-9), 716-727.

[26] M.S. Yu, C.S.W. Lai, Y.S. Ho, S.Y. Zee, K.F. So, W.H. Yuen, R.C.C. Chang,(2007). Characterization of the effects of anti-aging medicine Fructus lycii on β-amyloid peptide neurotoxicity, Int. J. Mol. Med. 20(2), 261-268.

[27] X.W. Xing, F.Y. Liu, J. Xiao, K.F. So,(2016). Neuro-protective Mechanisms of Lycium barbarum, Neuromol. Med. 18(3), 253-263.

[28] Y. Zhou, Y.H. Duan, S.C. Huang, X. Zhou, L.S. Zhou, T.T. Hu, Y.F. Yang, J. Lu, K. Ding, D.A. Guo, X.H. Cao, G. Pei,(2020). Polysaccharides from Lycium barbarum ameliorate amyloid pathology and cognitive functions in APP/PS1 transgenic mice, Int. J. Biol. Macromol. S0141-8130, 35538-2.

[29] W.W. Chen, X. Cheng, J.Z. Chen, X. Yi, D.K. Nie, X.H. Sun, J.B. Qin, M.L. Tian, G.H. Jin, X.H. Zhang,(2014). Lycium barbarum polysaccharides prevent memory and neurogenesis impairments in scopolamine-treated rats, PLoS One 9(2), e88076.

[30] X.H. Wang, L. Pang, Y.Q. Zhang, J. Xu, D.Y. Ding, T.L. Yang, Q. Zhao, F. Wu, F. Li, H.W. Meng, D.N. Yu,(2018). Lycium barbarum Polysaccharide Promotes Nigrostriatal Dopamine Function by Modulating PTEN/AKT/mTOR Pathway in a Methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP) Murine Model of Parkinson's Disease, Neurochem. Res. 43(4), 938-947.

[31] K. Gao, M.Y. Liu, J.Y. Cao, M.N. Yao, Y.Y. Lu, J.K. Li, X.H. Zhu, Z.F. Yang, A.D. Wen,(2014). Protective effects of Lycium barbarum polysaccharide on 6-OHDA-induced apoptosis in PC12 cells through the ROS-NO pathway, Molecules 20(1), 293-308.

[32] P. Zhao, R. Zhou, X.Y. Zhu, G. Liu, Y.P. Zhao, P.S. Ma, W. Wu, Y. Niu, T. Sun, Y.X. Li, J.Q. Yu, Z.M. Qian,(2017). Neuroprotective Effects of Lycium barbarum Polysaccharide on Focal Cerebral Ischemic Injury in Mice, Neurochem. Res. 42(2), 1-16.

[33] Y. Yu, X.Q. Wu, J.N. Pu, P. Luo, W.K. Ma, J. Wang, J.L. Wei, Y.X. Wang, Z. Fei,(2018). Lycium barbarum polysaccharide protects against oxygen glucose deprivation/reoxygenation-induced apoptosis and autophagic cell death via the PI3K/Akt/mTOR signaling pathway in primary cultured hippocampal neurons, Biochem. Biophys. Res. Commun. 495(1), 1187-1194.

[34] C. Wu, T. Wang, J. Yu,(2015). Lycium barbarum Polysaccharide Pretreatment Attenuates Cerebral Ischemic Reperfusion Injury by Inhibiting Apoptosis in Mice, Zhong Yao Cai 38(7), 1454-1459.

[35] L.J. Tang, S.Y. Bao, Y. Du, Z.Y. Jiang, W.L.i.J. Ao, X. Ren, C.H. Zhang, H.Y. Chu, L. Kong, H.Y. Ma,(2018). Antioxidant effects of Lycium barbarum polysaccharides on photoreceptor degeneration in the light-exposed mouse retina, Biomed. Pharmacother. 103, 829-837.

[36] H.Y. Li, M. Huang, Q.Y. Luo, X. Hong, S. Ramakrishna, K.F. So,(2019). Lycium barbarum (Wolfberry) Increases Retinal Ganglion Cell Survival and Affects both Microglia/Macrophage Polarization and Autophagy after Rat Partial Optic Nerve Transection, Cell Transplant. 6, 963689719835181.

[37] M. Bie, Y. Lv, C.R. Ren, F.Y. Xing, Q. Cui, J. Xiao, K.F. So,(2015). Lycium barbarum polysaccharide improves bipolar pulse current-induced microglia cell injury through modulating autophagy, Cell Transplant. 24(3), 419-428.

[38] Y.H. Xie, X.J. Wang,(2018). Lycium barbarum polysaccharides attenuates the apoptosis of hippocampal neurons induced by sevoflurane, Exp. Ther. Med. 16(3), 1834-1840.

[39] S.M. Cao, J.L. Du, Q.H. Hei,(2017). Lycium barbarum polysaccharide protects against neurotoxicity via the Nrf2-HO-1 pathway, Exp. Ther. Med. 14(5), 4919-4927.

[40] K.W. Deng, Y.L. Li, M. Xiao, F.H. Wang, P. Zhou, W. Zhang, A. Heep, X.Q. Li,(2020). Lycium ruthenicum Murr polysaccharide protects cortical neurons against oxygen-glucose deprivation/reperfusion in neonatal hypoxic-ischemic encephalopathy, International Journal of Biological Macromolecules 158, 562-568.

[41] S.L. Qiu, J. Chen, X. Chen, Q. Fan, C.S. Zhang, D.Y. Wang, X.P. Li, X.Y. Chen, X.L. Chen, C. Liu, Z.Z. Gao, H.Q. Li, Y.L. Hu,(2014). Optimization of selenylation conditions for lycium barbarum polysaccharide based on antioxidant activity, Carbohydr. Polym. 103(1), 148-153.

[42] G.P. Gong, J.B. Fan, Y.J. Sun, Y.M. Wu, Y. Liu, W. Sun, Y. Zhang, Z.F. Wang,(2015). Isolation, structural characterization, and antioxidativity of polysaccharide LBLP5-A from Lycium barbarum leaves, Process Biochem. 51(2), 314-324.

[43] C.L. Lin, C.C. Wang, S.C. Chang, B.S. Inbaraj, B.H. Chen,(2009). Antioxidative activity of polysaccharide fractions isolated from Lycium barbarum Linnaeus, Int. J. Biol. Macromol. 45(2), 146-151.

[44] L.L. Zhang, J.X. Gu, Y.J. Chen, L. Zhang,(2013). A study on four antioxidation effects of Lycium Barbarum polysaccharides In vitro, Afr J Tradit Complement Altern Med. 10(6), 494-498.

[45] D.M. Yang, J.Q. Zhang, Y.F. Fei,(2017). Lycium barbarum polysaccharide attenuates chemotherapy-induced ovarian injury by reducing oxidative stress: LBP attenuates ovarian injury, J. Obstet. Gynaecol. Res. 43(10), 1621-1628.

[46] L.N. Long, B.J. Kang, Q. Jiang, J.S. Chen,(2020). Effects of dietary Lycium barbarum polysaccharides on growth performance, digestive enzyme activities, antioxidant status, and immunity of broiler chickens, Poult Sci 99(2), 744-751.

[47] T.Y. Shan, T.Q. Shan, F.L. Liu, H.P. Zheng, G.Y. Li,(2016). Effects of Lycium barbarum polysaccharides on the damage to human endometrial stromal cells induced by hydrogen peroxide, Mol. Med. Rep. 15(2), 879-884.

[48] J. Li, Z.J. Ding, Y. Yang, B.H. Mao, Y.X. Wang, X.Y. Xu,(2018). Lycium barbarum polysaccharides protect human trophoblast HTR8/SVneo cells from hydrogen peroxide‑induced oxidative stress and apoptosis, Mol. Med. Rep. 18(3), 2581-2588.

[49] T. Niu, L.Z. Jin, S.Z. Niu, C.Q. Gong, H. Wang,(2018). Lycium Barbarum Polysaccharides Alleviates Oxidative Damage Induced by H2O2 Through Down-Regulating MicroRNA-194 in PC-12 and SH-SY5Y Cells, Cell. Physiol. Biochem. 50(2), 460-472.

[50] J.S. Chen, L.N. Long, Q. Jiang, B.J. Kang, Y.H. Li, J. Yin,(2019). Effects of dietary supplementation of Lycium barbarum polysaccharides on growth performance, immune status, antioxidant capacity and selected microbial populations of weaned piglets, J. Anim. Physiol. Anim. Nutr.

[51] R. Tang, X.Y. Chen, T.T. Dang, Y.N. Deng, Z.H. Zou, Q. Liu, G.P. Gong, S. Song, F.L. Ma, L.J. Huang, Z.F. Wang,(2019). Lycium barbarum polysaccharides extend the mean lifespan of Drosophila melanogaster, Food Funct 10(7), 4231-4241.

[52] A. Loboda, M. Damulewicz, E. Pyza, A. Jozkowicz, J. Dulak,(2016). Role of Nrf2/HO-1 system in development, oxidative stress response and diseases: an evolutionarily conserved mechanism, Cell. Mol. Life Sci. 73(17), 3221-3247.

[53] P.F. Surai, I.I. Kochish, V.I. Fisinin, M.T. Kidd,(2019). Antioxidant Defence Systems and Oxidative Stress in Poultry Biology: An Update, Antioxidants (Basel) 8(7).

[54] Y. Yang, W. Li, Y. Li, Q. Wang, L. Gao, J.J. Zhao,(2016). Dietary Lycium barbarum Polysaccharide Induces Nrf2/ARE Pathway and Ameliorates Insulin Resistance Induced by High-Fat via Activation of PI3K/AKT Signaling, Oxidative Med. Cell. Longev. 2014(1), 145641.

[55] Z.K. Zhang, Y.N. Zhou, H.T. Fan, K.J. Billy, Y.J. Zhao, X. Zhan, L.J. Yang, Y. Jia,(2019). Effects of Lycium barbarum Polysaccharides on Health and Aging of C. elegans Depend on daf-12/daf-16, Oxid Med Cell Longev 2019, 6379493.

[56] X.M. Li, Y.L. Ma, X.J. Liu,(2007). Effect of the Lycium barbarum polysaccharides on age-related oxidative stress in aged mice, J. Ethnopharmacol. 111(3), 504-511.

[57] B. Qi, Q.S. Ji, Y.C. Wen, L. Liu, X.L. Guo, G.H. Hou, G.F. Wang, J.X. Zhong,(2014). Lycium barbarum Polysaccharides Protect Human Lens Epithelial Cells against Oxidative Stress–Induced Apoptosis and Senescence, PLoS One 9(10), e110275.

[58] Z.L. Hu, B. Song, L. Xu, Y.L. Zhong, F. Peng, X.Y. Ji, F. Zhu, C.K. Yang, J.Y. Zhou, Y.Y. Su, S.N. Chen, Y. He, S.D. He,(2016). Aqueous synthesized quantum dots interfere with the NF-κB pathway and confer anti-tumor, anti-viral and anti-inflammatory effects, Biomaterials 108, 187-196.

[59] W. Li, M.B. Gao, T. Han,(2020). Lycium Barbarum Polysaccharides Ameliorate Intestinal Barrier Dysfunction and Inflammation Through the MLCK-MLC Signaling Pathway in Caco-2 Cells., Food Funct. 11(4), 3741-3748.

[60] H.W. Ni, G.X. Wang, Y. Xu, X.M. Gu, C.Z. Sun, H.B. Li,(2019). Lycium barbarum polysaccharide alleviates IL-1beta-evoked chondrogenic ATDC5 cell inflammatory injury through mediation of microRNA-124, Artif Cells Nanomed Biotechnol 47(1), 4046-4052.

[61] Y. Ding, Y.M. Yan, D. Chen, L.W. Ran, J. Mi, L. Lu, B. Jing, X.Y. Li, X.X. Zeng, Y.L. Cao,(2019). Modulating effects of polysaccharides from the fruits of Lycium barbarum on the immune response and gut microbiota in cyclophosphamide-treated mice, Food Funct. 10(6), 3671-3683.

[62] Q. Wu, L.T. Liu, X.Y. Wang, Z.F. Lang, X.H. Meng, S.F. Guo, B. Yan, T. Zhan, H.Z. Zheng, H.W. Wang,(2020). Lycium barbarum polysaccharides attenuate kidney injury in septic rats by regulating Keap1-Nrf2/ARE pathway, Life Sci 242, 117240.

[63] Q. Peng, H.J. Liu, S.H. Shi, M. Li,(2014). Lycium ruthenicum polysaccharide attenuates inflammation through inhibiting TLR4/NF-κB signaling pathway, Int. J. Biol. Macromol. 67, 330-335.

[64] X.R. Zhang, C.H. Qi, J.P. Cheng, G. Liu, L.J. Huang, Z.F. Wang, W.X. Zhou, Y.X. Zhang,(2014). Lycium barbarum polysaccharide LBPF4-OL may be a new Toll-like receptor 4/MD2-MAPK signaling pathway activator and inducer, Int. Immunopharmacol. 19(1), 132-141.

[65] C.Y. Hong, H.D. Zhang, X.Y. Liu, Y. Xu,(2019). Attenuation of hyperoxic acute lung injury by Lycium barbarum polysaccharide via inhibiting NLRP3 inflammasome, Arch. Pharm. Res. 42(10), 902-908.

[66] Z. Chen, B.K.H. Tan, S.H. Chan,(2008). Activation of T lymphocytes by polysaccharide–protein complex from Lycium barbarum L, Int. Immunopharmacol. 8(12), 1663-1671.

[67] H.Y. Ting, Q. Li, H. Yang, M.L. Jin, M.J. Zhang, L.J. Ye, Q.S. Huang, D.C. Yin,(2014). Protective effect of polysaccharides on simulated microgravity-induced functional inhibition of human NK cells, Carbohydr. Polym. 101(1), 819-827.

[68] R.N. Bo, S.S. Zheng, J. Xing, L. Luo, Y.L. Niu, Y.E. Huang, Z.G. Liu, Y.L. Hu, J.G. Liu, Y. Wu, D.Y. Wang,(2016). The immunological activity of Lycium barbarum polysaccharides liposome in vitro and adjuvanticity against PCV2 in vivo, Int. J. Biol. Macromol. 85, 294-301.

[69] L. Feng, X. Xiao, J. Liu, J.Y. Wang, N. Zhang, T. Bing, X.J. Liu, Z.P. Zhang, D.H. Shangguan,(2020). Immunomodulatory Effects of Lycium barbarum Polysaccharide Extract and Its Uptake Behaviors at the Cellular Level, Molecules 25(6), 1351.

[70] Z.S. Chen, J.H. Lu, N. Srinivasan, B.K.H. Tan, S.H. Chan,(2009). Polysaccharide-Protein Complex from Lycium barbarum L. Is a Novel Stimulus of Dendritic Cell Immunogenicity, J. Immunol. 182(6), 3503-3509.

[71] M.S. D'Arcy,(2019). Cell death: a review of the major forms of apoptosis, necrosis and autophagy, Cell Biol. Int. 43(6), 582-592.

[72] M. Giorgio, M. Trinei, E. Migliaccio, P.G. Pelicci,(2007). Hydrogen peroxide: a metabolic by-product or a common mediator of ageing signals?, Nat. Rev. Mol. Cell Biol. 8(9), 722-728.

[73] X. Zhang, K. Huang, H. Zhong, Y.Q. Ma, Z.B. Guo, Z.Y. Tang, J.N. Liang, Y.J. Luo, Z.J. Su, L.Q. Wang,(2020). Effects of Lycium barbarum polysaccharides on immunological parameters, apoptosis, and growth performance of Nile tilapia (Oreochromis niloticus), Fish Shellfish Immunol 97, 509-514.

[74] L. Liu, X.Y. Sha, Y.N. Wu, M.T. Chen, J.X. Zhong,(2020). Lycium barbarum polysaccharides protects

retinal ganglion cells against oxidative stress injury, Neural Regeneration Research 15(8).

[75] L. Liu, W. Lao, Q.S. Ji, Z.B. Yang, G.C. Yu, J.X. Zhong,(2015). Lycium barbarum polysaccharides protected human retinal pigment epithelial cells against oxidative stress-induced apoptosis, Int. J. Ophthalmol. 8(1), 11-16.

[76] M.A. Petr, T. Tulika, L.M. Carmona-Marin, M. Scheibye-Knudsen,(2020). Protecting the Aging Genome, Trends Cell Biol.

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

[78] L. Chen, W. Li, D. Qi, D.X. Wang,(2018). Lycium barbarum polysaccharide protects against LPS-induced ARDS by inhibiting apoptosis, oxidative stress and inflammation in pulmonary endothelial cells, Free Radic. Res. 52(4), 480-489.

[79] L. Jing, X.W. Jia,(2018). Lycium barbarum polysaccharide arbitrates palmitate-induced apoptosis in MC3T3-E1 cells through decreasing the activation of ERS-mediated apoptosis pathway, Mol. Med. Rep. 17(2), 2415-2421.

[80] F.L. Yang, Y.W. Wei, B.Y. Liao, G.J. Wei, H.M. Qin, X.X. Pang, J.L. Wang,(2018). Lycium barbarum polysaccharide prevents cisplatin-induced MLTC- I cell apoptosis and autophagy via regulating endoplasmic reticulum stress pathway, Drug Des. Dev. Ther. 12, 3211-3219.

[81] Y.F. Zhu, Q.P. Zhao, H. Gao, X.D. Peng, Y.M. Wen, G.D. Dai,(2016). Lycium barbarum polysaccharides attenuates N-methy-N-nitrosourea-induced photoreceptor cell apoptosis in rats through regulation of poly (ADP-ribose) polymerase and caspase expression, J. Ethnopharmacol. 191, 125-134.

[82] Y. Wang, Q.Q. Han, F. Bai, Q. Luo, M.L. Wu, G. Song, H.M. Zhang, Y.Q. Wang,(2020). The assembly and antitumor activity of lycium barbarum polysaccharide-platinum-based conjugates, J Inorg Biochem 205, 111001.

[83] M. Zhang, H.X. Chen, J. Huang, Z. Li, C.P. Zhu, S.H. Zhang,(2005). Effect of lycium barbarum polysaccharide on human hepatoma QGY7703 cells: inhibition of proliferation and induction of apoptosis, Life Sci. 76(18), 2115-2124.

[84] X.L. Deng, X.L. Li, S. Luo, Y.Y. Zheng, X. Luo, L. Zhou,(2017). Antitumor activity of Lycium barbarum polysaccharides with different molecular weights: an in vitro and in vivo study, Food Nutr. Res. 61(1), 1399770.

[85] M. Ke, X.J. Zhang, Z.H. Han, H.H. Yu, Y. Lin, W.G. Zhang, F.H. Sun, T.J. Wang,(2011). Extraction, purification of Lycium barbarum polysaccharides and bioactivity of purified fraction, Carbohydr. Polym. 86(1), 136-141.

[86] X.J. Zhang, H.Y. Yu, Y.J. Cai, M. Ke,(2017). Lycium barbarum polysaccharides inhibit proliferation and migration of bladder cancer cell lines BIU87 by suppressing Pi3K/AKT pathway, Oncotarget 8(4), 5936-5942.

[87] L. Lou, G. Chen, B. Zhong, F. Liu,(2019). Lycium barbarum polysaccharide induced apoptosis and inhibited proliferation in infantile hemangioma endothelial cells via down-regulation of PI3K/AKT signaling pathway, Biosci Rep 39(8), BSR20191182.

[88] L.L. Shen, G. Du,(2012). Lycium barbarum polysaccharide stimulates proliferation of MCF-7 cells by the ERK pathway, Life Sci. 91(9-10), 353-357.

[89] S.Y. Chen, L.N. Liang, Y. Wang, J.H. Diao, Z.C. Xiong, G. Chen, Y.F. He, C.L. Luo, X.H. Wu, Y. Zhang,(2015). Synergistic immunotherapeutic effects of Lycium barbarum polysaccharide and interferon-α2b on the murine Renca renal cell carcinoma cell line in vitro and in vivo, Mol. Med. Rep. 12(5), 6727-6737.

[90] H.Z. Cai, F.K. Liu, P.G. Zuo, G.L. Huang, Z.X. Song, T.T. Wang, H.X. Lu, F. Guo, C. Han, G.J. Sun,(2015).

Practical Application of Antidiabetic Efficacy of Lycium barbarum Polysaccharide in Patients with Type 2 Diabetes, Med. Chem. 11(4), 383-390.

[91] H.L. Tang, C. Chen, S.K. Wang, G.J. Sun,(2015). Biochemical analysis and hypoglycemic activity of a polysaccharide isolated from the fruit of Lycium barbarum L, Int. J. Biol. Macromol. 77, 235-242.

[92] X.M. Li,(2007). Protective effect of Lycium barbarum polysaccharides on streptozotocin-induced oxidative stress in rats, Int. J. Biol. Macromol. 40(5), 461-465.

[93] G.J. Shi, J. Zheng, J. Wu, H.Q. Qiao, Q. Chang, Y. Niu, T. Sun, Y.X. Li, J.Q. Yu,(2017). Beneficial effects of Lycium barbarum polysaccharide on spermatogenesis by improving antioxidant activity and inhibiting apoptosis in streptozotocin-induced diabetic male mice, Food Funct. 8(3), 1215-1226.

[94] Q. Yao, Y. Yang, X.H. Lu, Q. Zhang, M.X. Luo, P.A. Li, Y. Pan,(2018). Lycium Barbarum Polysaccharides Improve Retinopathy in Diabetic Sprague-Dawley Rats, Evid.-based Complement Altern. Med. 2018, 7943212.

[95] J.H. Wang, Y. Yao, X.Z. Liu, K.L. Wang, Q.Q. Zhou, Y. Tang,(2019). Protective effects of lycium barbarum polysaccharides on blood-retinal barrier via ROCK1 pathway in diabetic rats., Am J Transl Res 11(10), 6304-6315.

[96] S.Y. Liu, L. Chen, X.C. Li, Q.K. Hu, L.J. He,(2017). Lycium barbarum polysaccharide protects diabetic peripheral neuropathy by enhancing autophagy via mTOR/p70S6K inhibition in Streptozotocin-induced diabetic rats, J. Chem. Neuroanat. 89, 37-42.

[97] X.C. Lei, P. Huo, Y.H. Wang, Y.J. Xie, Q.X. Shi, H.Y. Tu, J. Yao, Z.C. Mo, S. Zhang,(2020). Lycium barbarum Polysaccharides Improve Testicular Spermatogenic Function in Streptozotocin-Induced Diabetic Rats, Front Endocrinol (Lausanne) 11, 164.

[98] G.J. Shi, J. Zheng, X.X. Han, Y.P. Jiang, Z.M. Li, J. Wu, Q. Chang, Y. Niu, T. Sun, Y.X. Li, Z. Chen, J.Q. Yu,(2018). Lycium barbarum polysaccharide attenuates diabetic testicular dysfunction via inhibition of the PI3K/Akt pathway-mediated abnormal autophagy in male mice, Cell Tissue Res. 374, 653-666.

[99] H.P. Li, Z.J. Li, L.Q. Peng, N. Jiang, Q. Liu, E.T. Zhang, B.H. Liang, R.X. Li, H.L. Zhu,(2017). Lycium barbarum polysaccharide protects human keratinocytes against UVB-induced photo-damage, Free Radic. Res. 51(2), 200-210.

[100] R. Zhao, Y.P. Cai, X.Y. Shao, B.L. Ma,(2015). Improving the activity of Lycium barbarum polysaccharide on sub-health mice, Food Funct. 6(6), 2033-2040.

[101] W. Zhu, S. Zhou, J. Liu, R.J.C. McLean, W. Chu,(2020). Prebiotic, immuno-stimulating and gut microbiota-modulating effects of Lycium barbarum polysaccharide, Biomed Pharmacother 121, 109591.

[102] M.Z. Wang, J. Wang, L.L. Fu, M. Al-Wraikat, S.Z. Lin, P.P. Lu, L.W. Shan, J.F. Fan, B.L. Zhang,(2020). Degradation of polysaccharides from Lycium barbarum L. leaves improves bioaccessibility and gastrointestinal transport of endogenous minerals., Int J Biol Macromol. 143, 76-84.

[103] C. Pop, C. Berce, S. Ghibu, I. Scurtu, O. Soritau, C. Login, B. Kiss, M.G. Stefan, I. Fizesan, H. Silaghi, A. Mocan, G. Crisan, F. Loghin, C. Mogosan,(2020). Effects of Lycium barbarum L. Polysaccharides on Inflammation and Oxidative Stress Markers in a Pressure Overload-Induced Heart Failure Rat Model, Molecules 25(3).

[104] L. Qian, S.J. Yu,(2016). Protective effect of polysaccharides from Lycium barbarum on spermatogenesis of mice with impaired reproduction system induced by cyclophosphamide, Am. J. Reprod. Immunol. 76(5), 383-385.

[105] C.L. Liu, J.W. Gu, W.Q. Ma, Q. Zhang, M.L. Song, L.X. Ha, X. Xu, H.Y. Jiao, Z.H. Huo,(2020). Lycium barbarum polysaccharide protects against ethanol-induced spermiotoxicity and testicular degeneration in Immp2l(+/-) mice, Andrologia 52(4), e13554.

[106] F. Gan, Q. Liu, Y.H. Liu, D. Huang, C.L. Pan, S.Q. Song, K.H. Huang,(2017). Lycium barbarum polysaccharides improve CCl4-induced liver fibrosis, inflammatory response and TLRs/NF-kB signaling pathway expression in wistar rats, Life Sci. 192, 205-212.

[107] J. Li, M. Shi, B.L. Ma, Y. Zheng, R.X. Niu, K. Li,(2017). Protective Effects of Fraction 4a of Polysaccharides Isolated from Lycium barbarum Against KBrO3-induced Renal Damage in Rats, Food Funct. 8(7), 2566-2572.

[108] J. Liao, B. Liu, W. Zhong, G.D. Wang, Y.L. Xu, X. Chen,(2019). Protective effect of polysaccharides against high-fat diet-induced renal injury and lipid deposition in rat kidneys, J. Biol. Regul. Homeost. Agents 33(1), 7-17.

[109] T. Lu, W.E. Zhao, F. Zhang, X.H. Qi, Y. Yang, C.Y. Gu,(2019). Lycium barbarum polysaccharides attenuate rat anti-Thy-1 glomerulonephritis through mediating pyruvate dehydrogenase, Biomed Pharmacother 116, 109020.

[110] Y. Yan, W.Q. Wu, L. Lu, J. Ren, J. Mi, X.B. Liu, Y.L. Cao,(2019). Study on the synergistic protective effect of Lycium barbarum L. polysaccharides and zinc sulfate on chronic alcoholic liver injury in rats, Food Sci Nutr 7(11), 3435-3442.

**Citation:** *Xueling Dai, et.al., Overview on the Pharmacological Functions of Polysaccharides from Lycium Barbarum. International Journal of Research Studies in Biosciences. 2021; 9(1): 1-15. DOI: https://doi.org/10.20431/2349-0365.0901001.*