Research advances on antioxidation, neuroprotection, and molecular mechanisms of *Lycium barbarum* polysaccharides

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**ABSTRACT**

*Lycium barbarum* polysaccharides (LBPs) are the major polysaccharides extracted from *L. barbarum*, which is used in traditional Chinese medicine (TCM) for treating diseases. Studies have shown that LBPs have important biological activities, such as antioxidation, anti-aging, neuroprotection, immune regulation. LBPs inhibit oxidative stress, improve neurodegeneration and stroke-induced neural injury, increase proliferation and differentiation of neural stem cell, and promote neural regeneration. Here we have reviewed latest advances in the biomedical activities of LBPs and improved methods for the isolation, extraction, and purification of LBPs. Then, new discoveries to decrease oxidative stress and cell apoptosis, inhibit aging progress, and improve neural repair in neurodegeneration and ischemic brain injury have been discussed in detail through *in vitro* cell culture and *in vivo* animal studies. Importantly, the molecular mechanisms of LBPs in playing neuroprotective roles are further explored. Lastly, we discuss the perspective of LBPs as biomedical compounds in TCM and modern medicine and provide the experimental and theoretical evidence to use LBPs for the treatment of aging-related neurological diseases and stroke-induced neural injuries.

**1 Introduction**

*Lycium barbarum* polysaccharides (LBPs) are the main biologically active components of *L. barbarum*, which belongs to the Solanaceae family. The commonly found *L. barbarum* is used in food and traditional Chinese medicine (TCM) and mainly includes Ningxia *L. barbarum*, Chinese *L. barbarum*, and *L. ruthenicum* Murr. *L. barbarum* wolfberry is used in TCM for nourishing the
liver, kidney, lung, and brain to improve blood circulation and organ function, etc. Wolfberry is used as functional food in China [1, 2]. Wolfberry contains more than 200 components, including total saponins, phenylpropanes, flavonoids, polyphenols, and polysaccharides. Studies have shown that polysaccharides, vitamins, betaine, and mixed extracts of wolfberry have biomedical effects in anti-aging, improving vision, increasing immunomodulation, and other biomedical functions [3].

*L. barbarum* polysaccharides (LBPs) are the main chemical components of wolfberry extract and account for 5%–8% of wolfberry dry weight. LBPs are mainly composed of glucose, arabinose, rhamnose, mannose, xylose, and galactose. Studies on the chemical structures and biological functions of LBPs revealed that LBPs have various biological functions, including antioxidation, anti-aging, neuroprotection, and immunomodulation [3, 4]. To fully understand the medicinal application and functional mechanisms of LBPs, we first summarize the extraction methods used for LBPs and then analyze the neuroprotective functions of LBPs. We have also explored mechanisms of neuroprotection mediated by LBPs for developing the LBP-related products to improve neurodegeneration and neural damage in neurological diseases.

2 **Isolation, extraction, and identification of LBPs**

2.1 **Techniques for the isolation and extraction of LBPs**

Several methods are used for the isolation of LBPs, which include hot water extraction, enzyme-assisted extraction, microwave-assisted extraction, and ultrasound-assisted extraction. The pretreatment method of *L. barbarum* raw materials involves drying and crushing raw materials into small particles of different sizes. In recent years, the development of new isolation methods has overcome the shortcomings of traditional extraction methods [5]. To select a suitable extraction method, high extraction rates and the maintenance of high biological activity of LBPs are mainly considered. These methods are briefly discussed here.

Hot water extraction is a traditional method for the isolation of polysaccharide compounds, but the long-term and high temperature used in this method may degrade polysaccharides and affect their biological activity. The productivity of LBPs using this extraction method ranges from 1.14% to 18.56% [2].

Enzyme-assisted extraction involves the use of alkaline proteases to hydrolyze *L. barbarum* and centrifuge the digested supernatant to purify LBPs. The commonly include papain, cellulase, and pectinase. When LBPs are extracted by the enzymatic method, factors, such as the type and dosage of enzymes, ratio of raw material to liquid, time, pH, and temperature of enzymatic hydrolysis, which affect their productivity, should be considered. The product yield of LBPs extracted by enzymatic method varies between 2.9498% and 23.68% [6]. This method has the advantages of high efficiency, easy operation, low cost, and energy saving; however, the selection of enzyme is specific, and factors, such as enzyme concentration, temperature, time, and pH, also affect the biological functions of extracted LBPs.

Microwave-assisted extraction is a physical approach that uses the crushing effect of electromagnetic waves to extract LBPs. Advantages include short extraction time, high production rate, and lower cost. The raw material to liquid ratio, temperature, time, and microwave power used in this method have a great influence on the extraction rate. The temperature used for microwave extraction is usually between 50 and
100 °C and the extraction time varies in different studies. The most commonly used temperature is approximately 1 h which can avoid the decomposition and destruction of thermally unstable substances caused by long-term high temperature. Under the above conditions, the yield of LBPs is between 6.6% and 19.1%, which is a significant improvement when compared with traditional hot water extraction [7].

Ultrasonic-assisted extraction utilizes the thermal and mechanical effects of ultrasonic waves to instantly extract *L. barbarum*. This method can significantly improve the extraction efficiency of polysaccharides. However, ultrasonic treatment may affect the structure and molecular weight of polysaccharides, thereby affecting their biological activity. The extraction temperature used for ultrasonic-assisted extraction is 60–90 °C, and the ratio of raw material to liquid during extraction is between 1:20 and 1:30. Due to the assistance of ultrasound, the extraction time is between 15 and 50 min, significantly shorter than that of other extraction methods. Most studies have reported the use of ultrasonic power between 60 and 250 W. Under the above conditions, the yield of LBPs is between 4.28% and 14.48% [8, 9]. The major advantages of ultrasonic microwave extraction include fast extraction speed, low energy consumption, and short time. This method has been widely used in the extraction of active ingredients of natural products [8, 10].

### 2.2 Purification and identification

Many studies evaluating the chemical composition and structure of LBPs have revealed that LBPs are mainly composed of polysaccharides, with some polypeptides and proteins. The molecular weight of LBPs is 10–2300 kDa. Approaches for purifying LBPs from *L. barbarum* include DEAE ion exchange cellulose, gel permeation chromatography, and high-performance liquid chromatography (HPLC). It was shown that glycoconjugates are composed of monosaccharides and amino acid residues are the main structure of LBPs by analyzing glycosidic bond of the glycan backbone. More than 30 types of LBPs have been purified and identified, which mainly consist of arabinose, glucose, galactose, mannose, xylose, rhamnose, and other monosaccharides. Its monosaccharide is mainly composed of rhamnosyl, arabinosyl, xylose, mannosyl, glucosyl, and galactosyl. Their molar ratio in LBPs is 2.07:2.38:3.11:1.00:1.12:2.86. However, other factors, such as the regions of origin of *L. barbarum*, may affect the formation of the sugar ring, type of glycosidic bonds, monosaccharide composition, and the amount of individual components [11].

Some studies have indicated that crude LBPs can be purified using the DEAE-52 cellulose (OH-) column and Sephadex G-50 column chromatography to isolate LBP1 and LBP2 [12, 13]. Analysis using ultraviolet spectrum scanning and column chromatography revealed that both LBP1 and LBP2 have a relatively uniform molecular mass. Infrared spectroscopy showed that both LBP1 and LBP2 are mainly composed of pyranose. The relative molecular masses of LBP1 and LBP2 detected by HPLC were 367 and 358, respectively. Gas chromatographic analysis determined that the molar ratio of monosaccharide components of LBP1 is galactose:mannose:glucose = 1.79:1.00:3.08 and that for LBP2 is galactose:mannose:glucose = 1.32:1.00:7.38 [2].

### 3 Antioxidative damage function and molecular mechanism of LBP action

Several studies have given evidence on the potential antioxidant activities of LBPs in many tissues and cells. LBPs can significantly increase levels of SOD and GSH-Px in the serum of mice.
and significantly reduce oxidative damage MDA after skin fibroblasts cultured from newborn Kunming mice were treated with LBPs. In this study [14], LBPs were divided into high, medium, and low dose groups and the control group. Cell proliferation was examined using the tetramethylazozale blue method (MTT assay). LBPs were shown to promote the growth of fibroblast cells and delay cell apoptosis to increase cell survival. LBPs significantly increased the activity of antioxidant enzymes in exercise-trained mice and reduced lipid peroxidation in a rabbit model of atherosclerosis. The exercising ability of aging mice was found to be significantly reduced compared with young mice; however, after the aging mice drank water containing LBPs, the continuous running time of mice was prolonged, indicating that the exercise ability of mice had increased. It also showed that LBPs could enhance the animal’s antifatigue ability. After 24 h of treatment with LBPs, LBPs were found to protect CoCl2-induced apoptosis of retinal ganglion cells in mice, and inhibited the production of reactive oxygen species (ROS) by improving mitochondrial function. ROS include oxygen free radicals, hydroxyl radicals, superoxide anion, hydrogen peroxide, and nitric oxide. In the CoCl2-induced oxidative stress model of rat retinal ganglion cells (RGCs), LBPs were found to exert an antioxidative damage effect. After pretreatment of RGCs with LBPs for 24 h, LBPs were found to effectively reduce the occurrence of CoCl2-induced hypoxia in the RGC model, reduce cell apoptosis of RGCs, inhibit oxidative stress response, and improve the potential function of mitochondria to produce antioxidant protection on RGC cells [15].

Studies have also shown that the antioxidant activity of LBPs has a protective effect on oxidative damage of the skin, can delay cell entry into senescence and apoptosis, indicating the antioxidative damage function of LBPs [16]. LBPs can also enhance the phagocytic ability of macrophages by increasing the production of NO and acid phosphatase in macrophages, and thus, produce significant antioxidant activity. LBPs can significantly inhibit the damage mediated by oxidative toxic substances to neural cells and regulate oxidative stress by inhibiting the caspase-3 activation and ROS production. On stressed retinal pigment epithelium (RPE), LBPs can reduce ROS production to prevent ROS-induced apoptosis by scavenging free radicals and regulating the expression of downstream genes. After the rats were fed LBPs, the activity of the antioxidant enzymes manganese superoxide dismutase (MnSOD) and glutathione peroxidase and GSH expression significantly increased [17]. LBPs can regulate ROS activation and the expression of transcription factors, such as Nrf2 and NF-κB. LBPs can also affect the transcription and expression of various genes in the body and participate in the regulation of important biological processes, such as inflammation, development, immunity, cell growth, and stem cell regeneration. SOD plays an important role in maintaining the dynamic balance of ROS. Studies have shown that the exogenous supplementation of LBPs significantly increased SOD activity in the retina after 3 months [18, 19].

A recent study indicated that pretreatment of the human retinal epithelial cell line (ARPE-19) with LBPs showed that LBPs are highly efficient in reducing oxidative damage and inhibiting cell apoptosis. Furthermore, LBPs may regulate the expression of proteins involved in the apoptotic pathway and activate the Nrf2 signaling pathway [20].

Many studies have shown that the antioxidant and antiaging functions of LBPs are performed mainly through three pathways mediated by the NF-κB pathway (the intracellular mitochondrial pathway), endoplasmic reticulum pathway, and extracellular receptor pathway to protect cells
from oxidative stress and apoptosis. NF-κB is an important transcriptional regulator in cells. In addition to participating in antioxidative stress, it also regulates the expression of apoptosis-related genes. NF-κB plays functions in the mitochondrial pathway through the transcriptional regulation of X-linked inhibitor of apoptosis protein (XIAP), c-IAP-1, and c-IAP-2, members of the inhibitor of apoptosis protein (IAP) family. XIAP is a key factor for NF-κB to inhibit apoptosis. XIAP can specifically inhibit the activation of the apoptotic effector caspase (GSH), thereby blocking the release of cytochrome c (cyt c) in cells, and subsequently, inhibiting cell apoptosis [21]. In the endoplasmic reticulum signaling pathway, the transcription factor NF-κB plays a role through the endoplasmic reticulum stress-mediated Jun N-terminal kinase (JNK) signaling pathway. After the cell is stimulated by calcium homeostasis disorder and oxidative stress, the accumulation of unfolded or misfolded proteins in the endoplasmic reticulum eventually leads to apoptosis. Endoplasmic reticulum stress initiates cell apoptosis mainly through protein transcription activation, protease activation, and c-JNK signal activation. Studies have shown that NF-κB activation can inhibit cell apoptosis caused by the Fas/FasL signaling pathway. Treating cells with monoethylhexyl phthalate can cause cell apoptosis through NF-κB activation. After knocking out genes related to the death region, the number of NF-κB accumulating in the FasL promoter region is reduced, causing Fas/FasL increased gene expression promotes cell apoptosis. LBPs inhibit the NF-κB signaling pathway, thereby activating cell function and antiaging [22, 23].

4 Neuroprotective effect and mechanism of LBPs

*L. barbarum* has been used in several decoctions of TCM for the treatment of neural injury and neurological diseases for a long time. In recent years, a large number of studies have shown that LBPs have neuroprotective effects on neurodegenerative diseases, cerebral ischemia, brain injury, and other neurological diseases.

4.1 Mechanism of neuroprotection in neurodegenerative diseases

Neurodegenerative diseases are mainly caused by the degeneration and apoptosis of neurons in the brain. Alzheimer’s disease (AD) is the most common neurodegenerative disease; its characteristic pathology involves the deposition of beta amyloid (Aβ) to form Aβ plaques, which are mainly formed in the cerebral cortex and hippocampus. Studies have shown that LBPs can reduce the formation of Aβ plaques, and thus, protect neural cells from degeneration. Moreover, the mechanism of preventing Aβ deposits depends on the solvents used to extract LBP. The LBPs extracted by hot water mainly inhibit the apoptosis-related XIAP pathway and reduce the production of Aβ deposits. The LBPs extracted from alkaline solutions mainly activate the Akt pathway to have neuroprotective effects and promote neural cell survival. Some studies also showed that LBPs can improve the effect on memory impairment in AD at cellular and molecular levels [24].

Parkinson’s disease (PD) is the second largest neurodegenerative disease after AD. PD is mainly caused by environmental factors and genetic mutations that produce protein aggregates of Lewy body with α-synuclein as the main component, causing moderate apoptosis and necrosis of dopamine neurons in the substantia nigra. Studies have reported that LBPs can significantly improve MPTP (1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine)-induced dyskinesia in a mouse model with PD. Using fluorescence quantitative real time PCR (qRT-PCR) and western
blot analysis, LBPs were found to significantly increase the gene expression of SOD2, CAT, and GPX1 in dopamine neurons in the midbrain of PD mice and inhibited MPTP-induced α-synuclein deposition. At the same time, LBPs are found to mainly strengthen the phosphorylation of Akt and mTOR signaling molecules and play a neuroprotective effect by activating the PTEN/ AKT/mTOR signaling pathway, suggesting that LBPs can be used compatibly with TCM for treating PD and other neurodegenerative diseases [25]. Other studies have found that both low- and high-dose LBP can inhibit the apoptosis of dopamine neurons in the mouse and rat PD model induced by MPTP, reduce motor defects in PD mice and rats, and improve some aspects of memory deficits in PD mice. Further studies showed that the expression of PTEN, p-Akt, and p-mTOR proteins significantly increased in the MPTP-induced mouse PD model. After LBP treatment, the expression of these proteins was effectively reduced, indicating that LBPs act mainly by regulating the PTEN/ AKT/mTOR signaling pathway to exert neuroprotective effects [26]. The mechanisms by which LBP inhibits the PTEN/ AKT/mTOR signaling pathway are shown in Fig. 1.

Elderly visual impairment and blindness are mainly caused by the aging and degeneration of the retina and optic nerves. Treatment with LBPs can significantly reduce these injuries by enhancing the autophagic ability of endogenous microglia in the body. Ultrastructural alterations of the optic nerves in retinal degenerative diseases are the most common pathological changes that reflect the degeneration and apoptosis of optic nerve cells. Optic nerve degeneration reduced axon formation in RGCs and the injured axons then triggers RGC death. After LBPs were administered to rats with optic nerve degeneration for 3 months, the density of the optic nerve was found to increase, the number of microfilaments and microtubules in axons also increased, and axonal demyelination improved. After treatment with LBPs, the morphology of the myelin sheath almost returned to normal, even though a small part of the axons remained demyelinated [27]. The increase in intraocular pressure caused by senile glaucoma gradually damages the optic nerve and causes loss of vision. In the acute ocular hypertension model of rats, LBPs were administered before and after the model was established. Both the thickness of the retina and electrophysiological function of the optic nerve improved significantly, indicating that LBPs can promote the regeneration of retinal neural stem cells and prevent the degeneration of the optic nerve and retina. The optic nerve transection model is often used to study RGC degeneration. In this model, obvious pathological alterations of the microglia and macrophages can be found and autophagy of the optic nerve can also be

![Fig. 1](image-url)
observed. Studies have shown that LBPs can increase the survival of RGCs, promote the polar response of the microglia and macrophages, and delay the degenerative changes of RGCs, thereby improving optic nerve degeneration. Thus LBPs have both preventive and therapeutic effects on optic nerve injuries caused by retinal diseases, such as glaucoma [28, 29].

4.2 Mechanism of neuroprotection in ischemic brain injury

Cerebrovascular diseases mainly affect the elderly. Ischemic stroke accounts for the most cases of cerebrovascular diseases. An effective treatment for ischemic stroke involves selectively blocking the excitotoxic effects of neuronal cells and maintain the normal physiological functions of glutamate neurons. Three N-methyl-D-aspartate receptors (NMDAR) subunits—NR1, NR2 (A–D), NR3 (A, B)—are located on glutamate neurons. The functional NMDAR is a tetrameric structure composed of two NR1 subunits with two NR2 and/or NR3 subunits [30]. NR2 subunit isomers (NR1/NR2A, NR1/NR2B) exhibit different physiological and pharmacological functions. From a functional analysis, the NR2A subunit produces stronger neuroprotection by activating the CREB or Akt signaling pathway [31]. Activating NR2A can induce the phosphorylation of CREB and induce overexpression of brain-derived neurotrophic factor (BDNF), thereby enhancing the survival of neuronal cells. Studies have shown that certain drugs can produce neuroprotective effects by enhancing CREB activity. By contrast, activation of the NR2B receptor outside the synapses can initiate apoptosis in neural cells by promoting ROS production and inhibiting CREB expression [32]. The mechanism by which certain drugs can produce neuroprotection through NR2A or NR2B subunits is unclear.

Studies have shown that the neuroprotective effect of LBPs on ischemic brain injury is mainly through the activation of the NR2A subunit and inhibition of signal transduction of the NR2B subunit. In a rat model of cerebral ischemic injury, LBPs can improve the memory impairment caused by cerebral ischemia and increase the tolerance of cerebral cortex neurons to hypoxia injury. Further analysis indicated that LBPs enhance the expression of major related proteins in the NR2B and NR2A signaling pathways, such as NR2B, nNOS, Bcl-2-associated death promoter (BAD), cyt c, and cleaved caspase-3. Moreover, LBPs can reduce hypoxia-induced ROS response, cell calcium influx, and mitochondrial permeability. LBPs were shown to produce neuroprotection for ischemic brain injury by increasing NR2A expression and inhibiting the bidirectional effect of the NR2B signaling pathway. In addition, LBPs can improve memory loss and motor dysfunction of neurological disorders caused by focal cerebral ischemia. Thus, LBPs can be used as a preventive and therapeutic drug for ischemic stroke [33].

Recent studies reported that the mechanism of LBP producing neuroprotection is mediated through in vitro and in vivo studies [34]. To evaluate whether LBPs induce neuroprotection through the NR2A-Akt-CREB signaling pathway, one study showed that the expression of NR2A remained at a normal level within 2 h of exposure to hypoxic glucose depletion (OGD) [35]; however, after 4 and 8 h of OGD exposure, the expression of NR2A decreased to 66.5% and 33.5% of the normal level, respectively. The expression of Akt protein was decreased to 59.5% after 30 min of OGD treatment. The expression of CREB protein remained unchanged after 1 h of OGD treatment, but decreased to 66.5% and 33.5% of the normal level, respectively. The expression of Akt protein was decreased to 59.5% after 30 min of OGD treatment. The expression of CREB protein remained unchanged after 1 h of OGD treatment, but decreased to 50.8%, 46.2%, and 32.1% after 2, 4, and 8 h of OGD treatment, respectively. Further analysis of the effect of LBPs on the expression of the main proteins in the NR2A signaling pathway showed that even
though the expression of NR2A, Akt, and CREB did not change after 1 h of OGD treatment, after 4 h, LBP significantly improved the expression of NR2A, Akt, and CREB. This study indicated that LBPs protected the CA1 neurons from OGD damage, and reduced apoptosis in injured neural cells in the cerebral cortex, thereby producing neuroprotective effects. Other studies have shown that the neuroprotection induced by LBPs is mainly through the inhibition of related proteins in the NR2B signaling pathway, including NR2B, BAD, and cyt c and by the removal of caspase-3, mitochondrial stress, and Ca²⁺ influx [34]. Recent studies have also reported that LBPs can increase the expression of Nrf2 and inhibit the expression of HO-1 through the Nrf2/HO-1 signaling pathway to inhibit Nrf2-induced cell apoptosis, thereby reducing oxidative damage and protecting cell function [20, 33]. The mechanism by which LBPs neuroprotect against ischemic nerve injury is shown in Fig. 2.

4.3 LBPs promote neural regeneration and prevent aging

Recent studies have shown that neural stem cells located in the brain and spinal cord play a key role in delaying aging and neurodegeneration. With increasing age, a gradual decrease of neurons occurs in the brain, which is the main cause for neurodegeneration and aging. Latest studies have reported that Cxcl13 increases the functions of the aging brain significantly through the CXCR5/5/CXCL13 signaling pathway, whereas the gradual decrease of Cxcr5 leads to a reduction in the number of neuroblasts, which causes aging with a combination of inflammatory factors [31]. During normal aging, due to the decline in the metabolic function of neurons and astrocytes, accumulation of abnormal proteins and DNA breakage, lipids and other macromolecular substances are gradually oxidized and cannot be degraded by the lysosomes. In addition, the destruction of proteins during aging increases and affects the phagocytosis of cells, which leads to the accumulation of denatured proteins in lysosomes [35, 36]. Several studies have shown that LBPs can promote the neural differentiation of neural stem cells and inhibit the abnormal differentiation of glial cells, thereby improving brain function during aging and in neurodegenerative diseases, such as AD and macular degeneration. This neuroprotection of LBPs has good potential in clinical application [37, 38].

The retina is highly sensitive to chronic oxidative stress. Due to the mitochondrial metabolism of retinal pigment epithelial cells and light-sensitive cells, ROS, such as oxygen free radicals, are generated, which eventually leads to the degeneration of light-sensitive cells and apoptosis of retinal neural cells. Through the antioxidative effect of their active ingredients, LBPs play important roles in neuroprotection by removing superoxide anions and free hydroxyl groups;

Fig. 2  LBPs inhibit the NR2B signaling pathway and activate the NR2A signaling pathway to induce neuroprotection against stroke and hemorrhage-induced hypoxia injury [33].
increasing the activities of antioxidative enzymes, superoxidase, and glutathione oxidase; and promoting the neural differentiation of retinal neural stem cells [18, 39].

Diabetic retinopathy is mainly caused by dysfunction of the Rho/ROCK signaling pathway. Studies in diabetic rats revealed that after LBP treatment, levels of blood sugar and lipids significantly reduced, body weight significantly increased, and the retina thickened [40]. Further studies revealed that LBPs play these roles by potentiating signaling pathways involving ROCK and P-MLC [41]. Using LBPs to treat a rat model with optic nerve transverse defect, revealed that LBPs delayed the degeneration of optic nerve stem cells (RGCs), increased the activity of microglia, and improved the autophagy effect of optic nerve stem cells [29].

Through the rat model of nerve injury, it was found that LBPs can reduce the toxic effects of scopolamine on the central nervous system, increase the regeneration of neural stem cells, and improve the memory and cognitive ability of rats. LBPs can promote the neural differentiation of neural stem cells to generate more neurons [42, 43]. In addition, in rats, LBPs can prevent hippocampal-dependent spatial memory loss caused by hypoxia, promote the regeneration of hippocampal neurons, and decrease the apoptosis of neurons and astrocytes. Several animal studies have revealed that LBPs can improve memory and cognitive abilities in transgenic APP/PS1 mice. LBP1 was reported to enhance neurogenesis and restore synaptic dysfunction in the hippocampus CA3-CA1 pathway [44, 45]. In addition to improving the neural regeneration of the central nervous system, LBP was incorporated into the nanofibrous scaffolds via coaxial electrospinning and was also showed to promote the proliferation and neural differentiation of both PC12 cells and Schwann cells cultured on the scaffolds. Furthermore, the myelination of Schwann cells and neurite outgrowth of dorsal root ganglion (DRG) sensory neurons were increased on LBP loaded scaffolds. This study indicated that LBP can be used as a drug encapsulated into electrospun nanofibers as tissue engineered scaffold for peripheral nerve regeneration [46]. Studies have found that LBPs mainly inhibit protein aggregation and promote autophagy in glial cells, improve nerve cell activity and nerve regeneration, and exert inhibitory effects on nerve degeneration and antiaging [25, 29]. Single-cell proteomics can provide new research ideas for revealing its molecular mechanism and the antineural degeneration and aging mechanism of TCM ingredients.

5 Conclusions and prospect

As a traditional Chinese herbal medicine, *L. barbarum* is widely used to treat many diseases. As one of the main components of *L. barbarum*, LBPs have been shown to have antioxidation, antiaging, and neuroprotective effects in *in vitro* and *in vivo* animal studies. LBPs also have other biological activities, such as antitumor, immunomodulation, enhancing cell activity, and reducing tissue damage, caused by toxic substances, such as CCl4, which induces fibrosis. Using the rabbit model with diabetes, LBPs were found to inhibit the expression of NF-κB and Ang II signaling genes, and played an important protective role in renal dysfunction caused by diabetes [46]. Recent studies have found that LBPs can improve the functions of vascular endothelial cells caused by oxidative stress by inhibiting the expression of apoptosis-related proteins, thereby having a protective effect on cardiovascular and cerebrovascular diseases [16]. In recent years, researchers from outside China, e.g. America and some European countries, have also begun to explore the biological activities of LBPs.
With the continuous improvement in extraction methods and functional studies of LBPs, clinical application of active ingredients and biological functions of LBPs will increase.

Recent progress in proteomics, metabolomics, and genomics and other new technologies have been used to study the different activities of LBPs. Future research work should focus on the new biological functions and relationship between structure and biological activity of LBPs to promote the development and clinical application of LBPs. Because of aging and neurodegenerative diseases, a large number of lysosomal proteins, abnormal endophagosomes, and denatured protein aggregates appear in neural cells of the brain, leading to degeneration and apoptosis of neural cells. Studies have shown that LBPs can increase the activity of neural cells and the ability of neural regeneration by inhibiting protein aggregation and strengthening the autophagy of glial cells. For understanding the mechanism of LBPs on antiaging and neurodegenerative diseases, it is necessary to use integrated transcriptomics, metabolomics, and optogenetic technology to uncover the expression of the key genes responsible for aging and degeneration. Therefore, the development and utilization of LBPs and other active ingredients used in TCM, and comprehensive studies on the molecular mechanisms on neuroprotection will be a hot research topic, with important applications in the future.

Conflict of interests

All contributing authors have no conflict of interests to declare.

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