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Review

Lycium Genus Polysaccharide: An Overview of Its Extraction, Structures, Pharmacological Activities and Biological Applications

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Abstract: Polysaccharide is considered to be the main active ingredient of the genus *Lycium* L., which is taken from the dried fruit of the famous Chinese herbal medicine and precious tonic known as wolfberry. Traditional uses include nourishing the liver and kidney and improving eyesight, with widespread use in the clinical practice of traditional Chinese medicine. Many studies have focused on the isolation and identification of the genus *Lycium* L. polysaccharide and its biological activities. However, the variety of raw materials and the mechanisms of polysaccharides differ. After extraction, the structure and biological activity of the obtained polysaccharides also differ. To date, approximately 58 kinds of polysaccharides have been isolated and purified from the *Lycium* genus, including water-soluble polysaccharides; homogeneous polysaccharides; pectin polysaccharides; acidic heteropolysaccharides; and arabinogalactans, which are composed of arabinose, glucosamine, galactose, glucose, xylose, mannose, fructose, ribose, galacturonic acid, and glucuronic acid. Pharmacological studies have shown that LBPs exhibit a variety of important biological activities, such as protection of nerves; promotion of reproduction; and anti-inflammatory, hepatoprotective, hypoglycemic, and eyesight-improving activities. The aim this paper is to summarize previous and current references to the isolation process, structural characteristics, and biological activities of the genus *Lycium* L. polysaccharide. This review will provide a useful reference for further research and application of the genus *Lycium* L. polysaccharide in the field of functional food and medicine

Keywords: LBP; *Lycium*; pharmacological activity; biological applications; polysaccharides

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1. Introduction

Gou qi (aka, *Lycium* fruit, Chinese wolfberry, dog's-tooth grass, or Fructus lycii) is the dried fruit from the plants *Lycium barbarum*, *Lycium chinense*, and *Lycium ruthenicum*, all of which are well-known traditional Chinese medicines and valuable tonics. This fructification is a long-recognized medical plant, the history and ethnopharmacology of which have been well-reviewed [1–4]. Owing to its nutritional properties, Gou qi has also been widely marketed as a health food, attracting European and North American interest [5–

7]. The China Food and Drug Administration (CFDA) has licensed many patented healthcare products and medicines containing *Lycium barbarum* as the active component, such as Gouqi Gao, Gouqi Yishen Jiaonang, and others. It is worth noting that these substances have the power to energize the liver and kidneys, nourish the essence, and strengthen eyesight and can be used to treat dizziness, exhaustion, lack of appetite, and poor sleep in the elderly resulting from liver and kidney deficiencies. The primary recognized active constituents are polysaccharides, composed of arabinose, glucosamine, galactose, glucose, xylose, mannose, fructose, ribose, galacturonic acid, and glucuronic acid [8–12]. Interest in the neuroprotective properties [13], as well as the reproduction-promoting [14], anti-inflammatory [15], hepatoprotective [16], and hypoglycemic activity [17], of the genus *Lycium* L. polysaccharide has been growing in recent years. Given the increased interest in the utilization of this plant, the genus *Lycium* L. polysaccharide has been used as an active ingredient in formulation development. The aim of this review is to update previous reviews in these areas, focusing on recently discovered structural features, extraction, and purification methods of the genus *Lycium* L. polysaccharide and to attract the attention of more investigators to its reliable biological functions for efficient utilization.

2. Materials and Methods

A literature review was conducted using the following databases: Web of Science (http://wokinfo.com/, accessed on 2 November 2021), Google Scholar (https://xs.scqylaw.com/news.html, accessed on 2 November 2021), PubMed (https://pubmed.ncbi.nlm.nih.gov/, accessed on 2 November 2021), Patent Hub (https://www.patenthub.cn/, accessed on 2 November 2021), Flora of China, Chinese Pharmacopoeia, the Plant List (http://www.theplantlist.org/, accessed on 2 November 2021), and other internet sources. The keywords used in the search include *Lycium* polysaccharide, LBP, *Lycium*, reproductive protection, anti-inflammatory, neuroprotective, myocardial injury, gastric, liver protection, eye protection, and diabetic. Duplicate articles were excluded from search results.

3. Botany

The genus *Lycium* L. (Solanaceae) comprises 85 species, which are widely distributed in tropical and subtropical regions of the northern and southern hemispheres, including in Asia, Africa, South America, North America, and Australia [18]. There are seven species and three varieties in China (*Lycium ruthenicum* Murr, *Lycium truncatum*, *Lycium dasystemum*, *Lycium barbarum*, *Lycium cylindricum*, *Lycium chinense*, *Lycium yunnanense*, *Lycium dasystemum* var., *Lycium barbarum* var, and *Lycium chinense* var. *potaninii*), mainly distributed in the north; those with higher medicinal value are used as medicine (Table 1).

Table 1. Characteristics and distribution of *Lycium* L. from different sources.

Scientific Name	Morphological Character	Medicament Portions	Clinical Application	Distribution	Ref.
L. barbarum L.	shrub	Fruit, root, leaf, calyx, bark, whole plant	A variety of diseases	Widely distributed in Asia, Europe, North America, and Australia; also appears in Africa and South America	[19]
L. chinense Mill.	multibranched shrub	Fruit, root, leaf, bark, whole plant	A variety of treatments	Widely distributed in Asia, Europe, North America, and Australia	[19]
L. ruthenicum Murray	spiny shrub	Fruit, leaf	Ophthalmic, blindness (veterinary), removal of blocked urine, diuretic	China, Iran, Afghanistan, India, Mexico, Pakistan, Russia, Turkmenistan, Georgia	[19]

Lycium Linn.: Single-leaf mutualism, strip cylindrical or flat, entire, with petioles. Flowers pedunculate, solitary in leaf axils; the calyx is campanulate and varies in size, with 2–5 calyx teeth or lobes arranged in petals in buds. The corolla is funnel-shaped, tubular, and campanulate, with five-lobed eaves and significantly fewer four-lobed eaves; buds are imbricated, with prominent spikes at the base. The stigma contains five stamens inserted in the middle of the corolla tube extending out of the corolla. The filament base glabrous, with oblong anthers and parallel, longitudinally fissured medicinal cells. The ovary comprised two compartments, with a filiform style and two stigmata splits, involving embryonic multiplicity. The fruit type is mainly characteristic of a berry with a fleshy peel, and the fleshy fruit contains a large number of flat seeds with dense, reticulate pits; embryos are curved into rings larger than a semicircle located on the periphery, and cotyledons are semicircular rod-shaped [19]. The physical appearance of the *Lycium* species is depicted in Figure 1.

Figure 1. Physical appearance of the studied *Lycium* species. (**a**) Wolfberry plant with red fruit; (**a-1**) characteristic red wolfberry fruit; (**a-2**) commercial red wolfberry. (**b**) Wolfberry plant with black fruit; (**b-1**) characteristic black wolfberry fruit; (**b-2**) commercial black wolfberry. (**c**) A CFDA-approved medicine, medlar kidney-tonifying capsules, is composed of the fruit of *Lycium barbarum*. It has the effect of nourishing the liver and kidneys and can be used to treat dizziness, asthenia, inappetence, and poor sleep caused by liver and kidney deficiency in the elderly.

This plant is widely planted in northwest China [20–22], growing mainly in arid and semiarid environments, rarely inhabiting coastal saline habitats [23,24]. Due to its unique characteristics of drought resistance, alkali resistance, and salt resistance, it can protect the ecological environment, prevent soil desertification, improve soil salinity, and promote agricultural development.

4. Ethnopharmacological Uses

Lycium species are widely distributed worldwide and used in traditional medicine in various countries and regions. *Lycium* species have been used as Yin strengthening agents for 2300 years, which have been used as traditional ethnomedicines to treat blurred vision, fever, night sweats, kidney deficiency, diabetes, heart disease, gynecological diseases, neurasthenia, abdominal pain, dry cough, and headache, in addition to being used to promoted prolonged life in China [25]. According to Turkish ethnobotanical research, *Lycium europaeum* is used for colds, infectious diseases, liver and kidney diseases, diabetes, and high blood pressure, in addition to being used as a diuretic and a sedative [26]. *Lycium ruthenicum* Murray, known as "Khizer" in the Ladakh region, induces remarkable immune system enhancement and has been used to treat cancer and AIDS [27]. Dried root decoction of *Lycium Intricatum* Boiss is used as a digestive aid in the southwestern region of Morocco [28]. In addition, in Argentina, it is claimed that *Lycium* can treat skin diseases, burns, and injuries, in addition to being used as an abortive [29,30]. Nineteen *Lycium*

species have been reported in traditional medicine as a folk herb. Their accepted species names, synonyms, distribution, plant parts, and ethnopharmacological uses are listed in Table 2.

Table 2. Characteristics and distribution of *Lycium* L. from different sources.

Scientific Name	Synonyms	Medicament Portions	Clinical Application	Distribution
Lycium acutifolium E. Mey. ex Dunal	*Lycium elliotii* Dammer, *Lycium pendulinum* Miers, *Lycium tenue* Willd.	Pounded bark	Promotion of good health	South Africa Madagascar Lesotho
Lycium afrum L.	*Jasminoides afrum* (L.) Medik., *Jasminoides linearifolium* Moench, *Lycium bachmannii* Dammer *Oplukion afrum* (L.) Raf.	Leaves, fruit, roots	Eye diseases, cough	South Africa France Tunisia Sweden Germany Netherlands medieval Cairo
Lycium barbarum L.	*Boberella halimifolia*, *Jasminoides flaccidum* Moench, *Lycium barbarum* var. auranticarpum, *Lycium barbarum* var. barbarum, *Lycium halimifolium*, *Lycium lanceolatum*, *Lycium turbinatum*, *Lycium vulgare* Dunal, *Teremis elliptica*	Fruit, root, leaf, calyx, bark, whole plant	A variety of diseases	Asia Europe North America Australia Africa South America
Lycium cestroides Schltdl.	-	-	Analgesic	Argentina Bolivia Uruguay Brazil Australia Germany UK
Lycium chinense Mill.	*Boberella rhombifolia* (Moench), *Jasminoides rhombifolium* Moench, *Lycium barbarum* var. *chinense* (Mill.) Aiton, *Lycium chinense* var. *chinense*, *Lycium chinense* var. *ovatum*, *Lycium chinense* var. *rhombifolium*, *Lycium megistocarpum* var. *ovatum* (poir.) Dunal, *Lycium ovatum* Poir., *Lycium rhombifolium* (Moench) Dippel, *Lycium sinense*, *Lycium trewianum*	Fruit, root, leaf, bark, whole plant	A variety of treatments	Asia Europe North America Australia
Lycium ciliatum Schltdl.	*Lycium argentinum Hie*ron., *Lycium erosum* Miers, *Salpichroa ciliata* Miers, *Withania pulvinata* Dunal	Leaf	Digestive, stomach inflammation	Argentina Brazil Bolivia
Lycium cinereum Thunb.	*Lycium arenicola* Miers, *Lycium caespitosum*, *Lycium colletioides* Dammer, *Lycium echinatum* Dunal, *Lycium kraussii* Dunal, *Lycium leptacanthum*, *Lycium minutiflorum* Dammer, *Lycium omahekense* Dammer, *Lycium oxycladum* Miers, *Lycium roridum* Miers	Root	Headache, rheumatism, anodyne, kidney disease, perfume	South Africa Botswana Namibia Lesotho
Lycium dasystemum Pojark.	*Lycium dasystemum* var. *rubricaulium*	Fruit	-	China Iran
Lycium depressum Stocks	*Lycium turcomanicum* Fisch. & C.A. Mey. ex Ledeb. *Lycium turcomanicum* Turcz. ex Miers	Leaf, fruit	Kidney problems	Iran Russia Israel Turkmenistan

				Iraq Palestinian Territory Afghanistan Turkey Pakistan Jordan
Lycium elongatum Miers	*Lycium confertum* Miers	Leaf	Digestive	Argentina
Lycium europaeum L.	-	Fruit, leaf, bark, whole plant	A variety of treatments	Spain France Israel Palestinian Territory Algeria Portugal India Tunisia Egypt Australia South Africa New Zealand Morocco Namibia US Lesotho
Lycium ferocissimum Miers	*Lycium campanulatum* E. Mey. ex C.H. Wright, *Lycium campanulatum* E. Mey. ex C. H. Wr., *Lycium macrocalyx* Dammer	-	Detoxication of narcotic poisoning	Spain Norfolk Island
Lycium intricatum Boiss.	-	Seed, fruit	Helminthiasis, digestive, eye diseases	Tunisia Spain, Morocco Portugal Mauritania Algeria Egypt Saudi Arabia Tunisia
Lycium pallidum Miers	*Lycium pallidum* var. *pallidum*	Plant, root	Toothache, chickenpox	Tunisia Italy US, Mexico
Lycium ruthenicum Murray	*Lycium foliosum* Stocks, *Lycium tataricum* Pall.	Fruit, leaf	Ophthalmic, blindness (veterinary), removal of blocked urine, diuretic	China Iran Afghanistan India Mexico Pakistan Russian Turkmenistan Georgia
Lycium schweinfurthii Dammer	-	Leaf, fruit	Stomach ulcers	Spain Israel Morocco Greece Portugal Algeria Egypt Tunisia Mauritania

Lycium shawii Roem. & Schult.	*Lycium albiflorum* Phil., *Lycium arabicum* Schweinf. ex Boiss.	Leaf, fruit, aerial part, stem	A variety of treatments	Cyprus Israel Palestinian Territory Saudi Arabia Ethiopia Oman Egypt Jordan South Africa, Botswana Yemen
Lycium torreyi A. Gray	*Lycium torreyi* var. *filiforme* M.E. Jones	Whole plant, root	Chickenpox, toothache	US Mexico
Lycium truncatum Y.C. Wang	-	Root bark	Digupi	China

Modified from Yao R, Heinrich M, Weckerle C S. The genus *Lycium* as food and medicine: A botanical, ethnobotanical and historical review [J]. Journal of ethnopharmacology, 2018, 212: 50–66.

5. Extraction and Isolation Method

Polysaccharide extraction technology provides the foundation for polysaccharide research and application. The genus *Lycium* L. polysaccharide extract have been reported [31–36]. However, present extraction and isolation methods do not produce a large yield of polysaccharides. Some examples are presented below, along with the isolated yield from each. It is worth noting that the sugar content of wolfberry depends not only on the efficiency of the extraction method but also on factors such as maturity, geography, and picking and drying methods.

5.1. Conventional Extraction Method

Water Extraction and Alcohol Precipitation

The genus *Lycium* L. polysaccharides are water-soluble but insoluble in alcohol. They are usually isolated using a combination of water extraction and alcohol precipitation. In a study by Lin et al., dried wolfberry fruit was blended with deionized water, heated, centrifuged, and filtered [37]. The material used in this study was sourced from a local drug store in Taipei, Taiwan. The extract was further centrifuged to remove impurities. The combined extracts were concentrated under vacuum, and 95% ethanol equal to five times the sample volume was added, precipitated overnight, and centrifuged to remove the supernatant. The precipitate was collected, dried under vacuum, and ground into powder. The crude extract and fraction polysaccharides were 580.00 and 57.19 mg/g, respectively. Protease and dialysis further removed the protein impurities of the crude polysaccharide fraction. The deproteinized polysaccharide solution was poured into a glass column containing DEAE-Sepharose CL-6B resin and eluted with sodium hydroxide to obtain neutral and acidic polysaccharides. The polysaccharide contents in components LPBa1, LPBa2, and LPBa3 were 9.26, 9.26, and 8.41 mg/g, respectively. This method is simple, allowing for multiple separations according to ethanol concentration. However, it is time-consuming, inefficient, and unsuitable for large-scale industrial production.

5.2. Modern Extraction Methods

5.2.1. Ultrasonic Extraction

In recent decades, ultrasonic extraction has been recognized as an efficient and environmentally friendly process for extraction of polysaccharides from Chinese herbal medicines. It can be combined with mechanical treatment, break down cell walls in plant material; facilitate mass transfer between immiscible phases through intensive agitation, especially at low frequencies; and has been widely used to extract polysaccharides. Chao and colleagues used ultrasound to extract dried goji berries with a liquid–solid ratio of

22.5 mL/g, an extraction pressure of 5 MPa, ultrasonic power of 140 W, and extraction temperature of 120 °C; the maximum yield of polysaccharides was 3.7% [38]. However, ultrasonic extraction usually requires powdered raw material, making it difficult to decompose the hygroscopic raw material, especially in industrial environments.

5.2.2. Microwave-Assisted Extraction

Microwave-assisted extraction is an innovative extraction system associated with a high extraction rate and is capable of obtaining high-yield polysaccharides in a short time with low solvent and energy consumption. Therefore, this method of extraction of bioactive compounds from the material matrix into solution is considered a promising technology for extraction of polysaccharides with significant biological activity. Wu et al. performed a 7.0-min extraction of fruits of *Lycium barbarum* at 900 W and 120 °C in a microwave extraction device. The supernatant was then evaporated to 10.0 mL using a rotary evaporator, and ethanol (95% *w*/*v*) was added to a final concentration of 80% (*v*/*v*) to obtain crude polysaccharide [39]. However, microwave extraction is only suitable for heat-stable components, and the denaturation and inactivation of heat-sensitive components, such as proteins, peptides, and enzymes, is limited by heat.

5.2.3. Enzyme-Assisted Extraction

The isolation process involves an enzyme-assisted extraction process for *Lycium barbarum* fructose with a Box–Behnken design (BBD) response surface methodology (RSM) to further optimize extraction conditions. In [40], the optimal extraction conditions were determined as the optimal concentration of compound enzymes (cellulose concentration, 2.0%; papain concentration, 1.0%): extraction time, 91 min; temperature, 59.7 °C; and pH, 5.0, 6.81 ± 0.10% by weight of crude polysaccharide extract. The plant material used in the study was purchased from an herbal medicine market in Tianjin, China. Some colored substances, lipids, and oligosaccharides were further Soxhlet-removed with petroleum ether. After vacuum drying, the defatted powder was extracted with a complex enzyme solution. The extract was concentrated, ethanol was added, and the precipitate was collected and dried to obtain crude polysaccharides. It is worth noting that enzymatic extraction is a green and efficient method that does not easily cause denaturation of macromolecular substances, with mild reaction conditions and a short duration.

6. Purification Method

Genus *Lycium* L. polysaccharides are usually crude polysaccharides containing proteins, pigments, and other impurities. Further purification is required to investigate the chemical structure of polysaccharides. Common methods for polysaccharide purification include precipitation [41], the ultrafiltration membrane method [42], and column chromatography [43]. Column chromatography is the most widely used method for classification and purification of polysaccharides. It is divided into anion-exchange chromatography and gel-filtration chromatography. Gel-filtration column chromatography, a widely used purification technique, is often used to separate polysaccharides with different molecular weights. Ion-exchange chromatography columns are mainly used to separate neutral polysaccharides by gradient salt elution. Zhang and his research team fractionated LBP using DEAE-cellulose columns eluted with 0, 0.05, 0.1, 0.15, and 0.2 M NaCl. The eluent was collected, lyophilized, and further eluted on a SephadexG-75 gel-filtration column to obtain two purified components: LBP-d and LBP-e [11]. Gong et al. used water extraction, alcohol precipitation, deproteinization, and fractional precipitation to obtain the crude polysaccharide of *Lycium barbarum*. The crude polysaccharide was further purified by Sephadex G-100 column gel-permeation chromatography to LBGP-I- 1, LBGP-I-2 and LBGP-I-3 according to molecular size. The molecular weight and monosaccharide composition were further studied [44]. After purification with an anion-exchange chromatography and

size-exclusion column (HW-65F column), LBP was obtained and identified; then, molecular weight and monosaccharide composition were further studied [45].

Therefore, in the process of purification, it is essential to select proper separation and purification methods according to the characteristics of the polysaccharides.

7. Structural Analysis of Genus *Lycium* L. Polysaccharides

Chromatography technology, spectrum analysis, and other chemical analyses have been established for the structural characterization of genus *Lycium* L. polysaccharides, including molecular weight, monosaccharide composition, type of glycosyl linkage, and type and polymerization degree of the branch.

Diverse extractions and processes differentiate the composition of genus *Lycium* L. polysaccharide monosaccharides. The structure of genus *Lycium* L. polysaccharides affect their biological activity, so it is essential to research their structural characteristics. HPGPC, FT-IR, GC-MS, HPLC, NMR, and GC (type of coupled detector: flame ionization detector) are the most commonly used methods to analyze the composition and structure of genus *Lycium* L. polysaccharides. Table 3 lists the advantages and disadvantages of instrumental analysis methods for structural characterization of genus *Lycium* L. polysaccharides.

Table 3. Advantages and disadvantages of instrumental analysis methods for polysaccharides.

Methods	Advantages	Disadvantages
HPGPC	Fast, high-resolution, and reproducible	Not suitable for separation of small molecules
HPSEC	High column efficiency and high resolution	Small sample load and poor repeatability
HPLC	Fast, high-resolution, and high-sensitivity	extra-column effect
GC	High separation efficiency, fast analysis speed, and wide application range	Difficult to analyze inorganic substances; easily decomposed high-boiling organic substances cannot directly provide qualitative analysis results
GC-MS	Sample must not contain water	Highly polar, poor volatility, thermally unstable compounds cannot be analyzed
IR	Wide range of applications, not limited by the physical state of the sample, does not destroy the sample	Not suitable for analysis of aqueous samples, high error rate in quantitative analysis, and low sensitivity
ESI-MS	High selectivity, high sensitivity	High cost
NMR	Provides the skeleton of the compound structure	Low sensitivity

The structure of polysaccharides is analyzed through the processes of "Methylation analysis, Linkage patterns analysis, Partial acid hydrolysis, FT-IR, GC-MS, NMR analysis (^{1}H-NMR, ^{13}C-NMR and (2D) NMR)" [8,17,46,47]. Sugar content is determined by phenol-sulfuric acid; uronic acid content is determined by carbazole sulfate; protein is determined by the Bradford method; molecular weight is determined by high HPSEC; and monosaccharide composition is determined by GC, HPLC, and PMP-HPLC. The periodate oxidation and Smith degradation methods, which were previously used to analyze the structure of glycosidic bonds, the existence of branches, and the composition of monosaccharides in the early stage, have been replaced by ESI-MS, FT-IR, GC, and GC-MS as the most classical and effective methods in the modern era. NMR techniques have been used to investigate the anomeric carbon arrangement, the sugar chain sequence, and the fraction of polysaccharide residue in the polysaccharide structure.

The biological activity of genus *Lycium* L. polysaccharides is closely related to its complex and multiple structural features, so it is critical to research its structural characteristics. For example, the anti-inflammatory activity of polysaccharides involves β-D-glucans [43]. The genus *Lycium* L. polysaccharides identified in recent decades, as well as their molecular weights, monosaccharide compositions, pharmacological activities, and

relevant references, are summarized in Table 4. We also focused on the physiochemical properties and structure of genus *Lycium* L. polysaccharides.

Polysaccharides are the main component of genus *Lycium* L., accounting for 75–90% of the total composition [48]. Research has confirmed that purified polysaccharides are composed of Glu and Fru a molar ratio of 1:2.1 according to HPLC [49]. Ion chromatography was used to identify the monosaccharide composition. Four polysaccharides (LBP1, LBP2, LBP3, and LBP4) were extracted by the tandem mixed membrane technique and were found to be mainly composed of D-Rha and D-Gal. LBP1, LBP2, and LBP4 consist of Rha, Gal, Glc, Man, and GalA in molar ratios of 26.9:38.1:20.7:3.8:2.2, 28.8:38.6:18.1:4.8:2.7, and 35.9:44.7:9.7:3.0, respectively; LBP3 consists of Rha, Gal, Glc, and GalA in a molar ratio of 31.3:31.6:16.5:6.7 [35]. Gong et al. made some improvements to the process, obtaining disparate results. They used a GC system to analyze the monosaccharide composition of purified LBP. LBGP-I-1 was determined to be composed of Ara (21.95%), Glu (51.22%), and Gal (17.07%); LBGP-I-2 mainly consisted of Ara (19.35%), Glu (32.26%), and Gal (35.48%); and LBGP-I-3 (9.12×10^4 Da) mainly consisted of Ara (48.15%) and Gal (44.44%) [44].

In recent decades, many polysaccharides with different structural features have been obtained from the genus *Lycium* L. It is indispensable to expound monosaccharide composition and the chaining of various monosaccharides to determine whether the polysaccharides have branching or non-branching positions. Two polysaccharides (LBP-d and LBP-e) obtained from *Lycium barbarum* via water extraction and ethanol precipitation were found to be composed of Fuc, Ribose, Rha, Ara, Xyl, Man, Gal, and Glu. Research showed that LBP-d and LBP-e had 1→6, 1→2,1→4, and 1→3-linked hexopyranose residues and 1→5, 1→2, and 1→3-linked furanose residues [11]. Some researchers used the ultrafiltration membrane method to extract and separate polysaccharides from *Lycium barbarum* into five fractions (LBP-p8, LBP-a8, LBP-a3, LBP-a1, and LBP-a4). These consist of Fuc, Rha, Ara, Xyl, Glu, Man, and Gal. It is worth noting that AFM observation revealed that LBP-p8 was mainly flocculent, whereas LBP-a4 was spherical [42].

Researchers have isolated and purified several pectic polysaccharides from the genus *Lycium* L. [50]. Pectic polysaccharides isolated from wolfberry were found to be mainly composed of Ara, Rha, Gal, and GalA. GC-MS, FT-IR and NMR data analysis showed that parts of α-GalA are methyl-esterified [51]. Zhou et al. used a DEAE Sepharose™ Fast Flow column and a Sephacryl S-300 HR column to purify pectic polysaccharides. Pectic polysaccharides were slightly modified by methylation combined with GC-MS in linkage pattern analysis and partial acid hydrolysis. The data suggest that the backbone of LBP1C-2 might be composed of 1, 2-Rha and 1, 4-GalA disaccharide repeat units. The branched chains are attached to the C-4 position of 1, 2, 4-Rha. The branched chains are composed of T-, 1, 3-, 1, 6-, and 1, 3, 6-linked Gal, T-, 1, 5- and 1, 3, 5-linked Ara, and T-linked Rha. This result was also confirmed by 1D and 2D NMR data analysis (Figure 2). Researchers purified pectic polysaccharides from *Lycium*; phenol-sulfuric acid was used to determine a sugar content of 97.5%; HPGPC determined a molecular weight of 1.37×10^5 Da; GC identified monosaccharide components, such as Rha, Ara, Xyl, Gal, and GalA, in a molar ratio of 1.0:2.2:0.5:1.2:4.7. It had a (1→4)-linked GalA backbone occasionally interrupted by (1→2)-linked Rha, and the side chains were attached to position 4 of the Rha units, including (1→3)-linked Ara, (1→3)-linked Gal, (1→3,6)-linked Gal, (1→4)-linked GalA, (1→2)-linked Rha, and (1→2,4)-linked Rha, and the termini were Ara and Rha (Figure 3) [52].

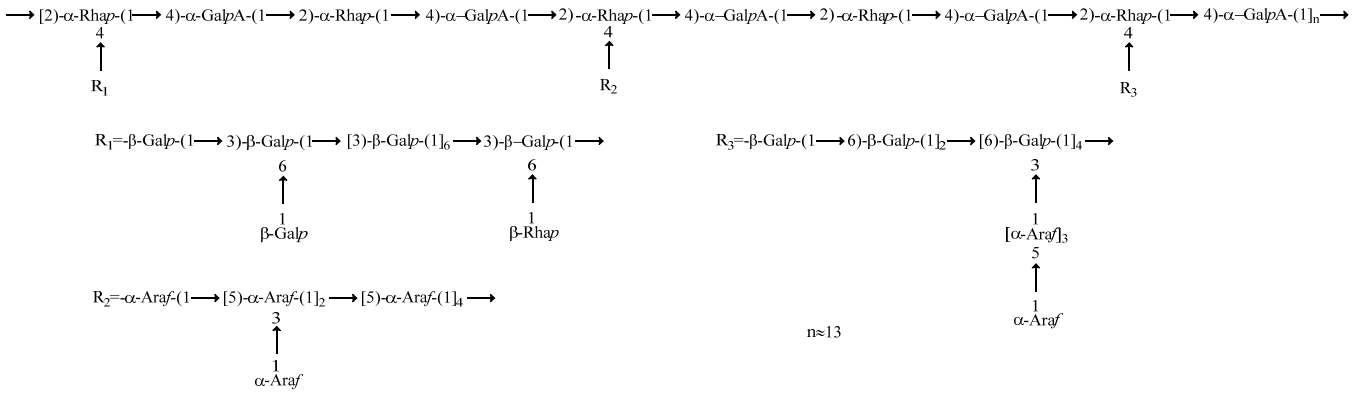

Figure 2. The proposed structure of LBP1C-2.

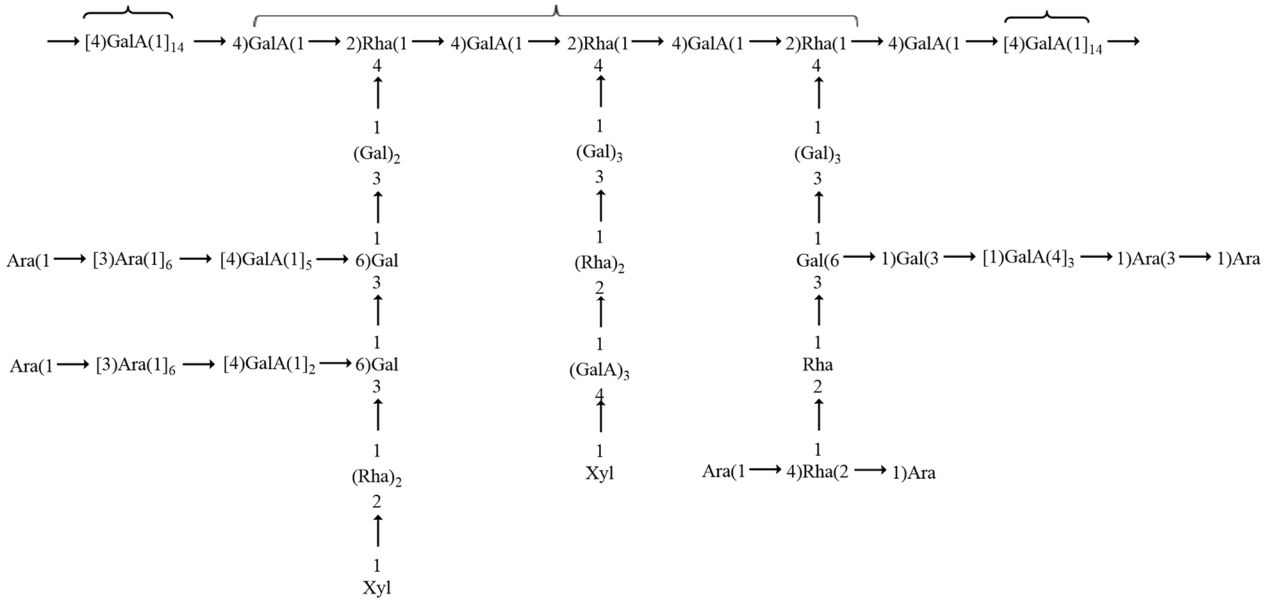

Figure 3. The hypothetical structure of the repeat unit of the glycan of LRGP5.

The composition of water-soluble polysaccharides is complex; the core structure is mainly composed of arabinose and galactose, as well as Rha, GalA, Xyl, Man, and Glu. FT-IR data show carbohydrate absorption peaks at 3400.38, 2930.49, 1629.66, 1411.40, 1151.44, 1078.24, 1032.50, 920.72, 864.33, 817.08, and 777.04 cm^{-1} [53]. Only the structures of high-purity compounds have been determined to date, but the overall structure of water-soluble polysaccharides remains unclear.

Water-soluble polysaccharide exhibit strong pharmacological activity, which is closely related to their molecular weight, composition, location, and other structural factors. In previous reports, microwave-assisted extraction and 95% ethanol precipitation were used to obtained water-soluble polysaccharides, which were hydrolyzed with trifluoroacetic acid, enzymatically digested, and analyzed by gel electrophoresis and HPTLC methods. The results showed that polysaccharides existed in β-1,3-glucosidic, α-1,4-galactosiduronic, and α-1,5-arabinoside linkages. LRGP1 has an estimated molecular weight of 56.2 kDa. GC analysis suggested that LRGP1 was composed of Rha, Ara, Xyl, Man, Glu, and Gal in a molar ratio of 0.65:10.71:0.33:0.67:1:10.41. The main chain is composed of (1→3)-linked Gal and branches joined by (1→5)-linked Ara, (1→2)-linked Ara, (1→6)-linked Gal, (1→3)-linked Gal, (1→4)-linked Gal, and (1→2,4)-linked Rha. Based on this analysis, the terminal of the branches was determined to be composed of Ara, Xyl, Man, and Glu [39]. Gong et al. isolated water-soluble glycoconjugate (LBLP5-A) from *Lycium barbarum* leaves with 93.7% carbohydrate content and 4.6% protein content.

LBLP5-A-OL1 is highly branched polysaccharide with a backbone of (1→3)-linked Gal, which was partially substituted at its O-6 position. These branches with Ara and Gal terminals were determined to be composed of (1→3)-linked Gal, (1→4)-linked Gal, (1→3)-linked Ara, (1→5)-linked Ara, and (1→2, 4)-linked Rha. LBLP5-A-OL3 and LBLP5-A-OL4 were determined to be a series of oligosaccharides that share the general structure pattern of $Aran_1$→$Galn_2$→$Rhan_3$ (n1 = 0–6, n2 = 0–8, n3 = 0–1) (Figure 4) [54]. Wang and his research team separated and purified water-soluble polysaccharides (LbGp1) extracted from the fruits of *Lycium barbarum* L. by GPC. LbGp1 has an estimated molecular weight of 49.1 KDa. Carbohydrate–peptide linkage, β-elimination, partial hydrolysis, methylation, and ESI-MS analyses suggested that LbGp1 was composed of Ara and Gal in a molar ratio of 5.6:1. LbGp1 was identified to be a highly branched polysaccharide with a backbone of Galp (1→6-linked galactose substituted at O-3 by galactosyl or arabinose groups). The branches were composed of (1→3)-linked-Galp, (1→4)-linked-Galp, (1→2)-linked-Ara, and (1→3)-linked Ara, and arabinose was located at the terminal of the branches (Figure 5) [55]. Researchers isolated and purified a water-soluble polysaccharide, LBP-3, from *Lycium barbarum* L. using hot water. HPLC determined LBP-3 to be composed of arabinose and galactose in a molar ratio of 1.00:1.56, with a molecular weight of 47.5 kDa. Fourier transform infrared spectroscopy (FT-IR), methylation, and nuclear magnetic resonance (NMR) analyses revealed that LBP-3 was a highly branched polysaccharide with a backbone of 1, 3-linked β-Galp, which is partially substituted at C-6. The branches contain 1, 5-linked α-Ara, 1, 6-linked β-Galp, 1, 3-linked α-Ara, and 1, 4-linked α-Ara (Figure 6) [56]. Liu and his research team extracted water-soluble polysaccharide LRLP4-A with the HPGPC chromatogram method with a 15% total yield, 96.6% carbohydrate content, and 2.3% protein content. The average molecular weight of LRLP4-A is 135 kDa, and it is composed of Rha, Ara, and Gal in a ratio of 1:10.3:5.3. The main chain is linked by (1→6)-linked β-glucopyranosyl residues substituted at O-3 by arabinose or galactosyl residues. The branches consisted of (1→3)-linked β-Ara and α-Arap, (1→5)-linked β-Ara, (1→3)-linked β-Galp, and (1→2, 4)-linked α-Rha with a terminal α-Ara residue (Figure 7) [57]. Lv and his team reported the structure of a water-soluble polysaccharide, LRP4-A, commonly present in plant arabinogalactan, which usually contains arabinose-3,6-galactan (type II) [58]. LRP4-A has an estimated molecular weight of 1.05×10^5 Da. GC was used to measure neutral sugars and uronic acids; 95.7% carbohydrate content was determined using phenol-sulfuric acid, and 1.4% protein components were determined using the Bradford method. It was found to mainly consist of Rha, Ara, Glu, and Gal in a molar ratio of 1:7.6:0.5:8.6, with a trace of Xyl. It had a backbone of β-(1→6)-linked galactose. The galactose residues in the backbone were partially substituted at O-3 of for (1→3)-linked Gal and Gal (1→. The branching side chain was comprised of Ara (1→, (1→3)-linked Ara, (1→5)-linked Ara, Glc (1→, and (1→2,4)-linked Rha (Figure 8). Moreover, the primary structure was easily obtained after GC-MS, FT-IR, and NMR spectral analyses, which showed that a large amount of the D-Man and a small proportion of α-D-Gal, β-D-Ara, and D-Man existed in the purified LBP [59].

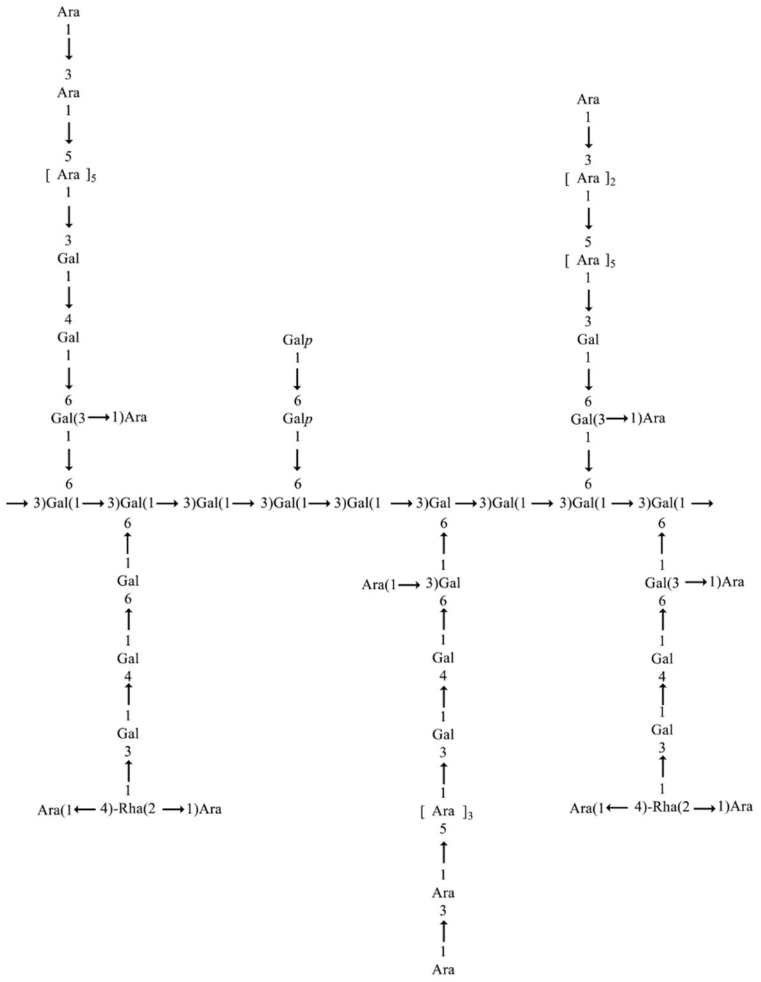

Figure 4. Schematic representation of the structural unit of LBLP5-A.

Yang and his research team reported a high-purity homogeneous polysaccharide using methylation analysis combined with FT-IR spectroscopy, GC-MS, and NMR analysis (^{1}H NMR, ^{13}C NMR, and (2D) NMR) techniques, which confirmed that it was composed of a repeated unit of→6)-*β*-Gal (1→residues and branches composed of *α*-Ara, *β*-Gal, and *α*-Rha residues at position C-3(Figure 9) [8]. RG-I-type pectin was extracted and purified from *L. ruthenicum* Murr, and its structure was identified as neutral side-chains of arabinans and type II arabinogalactan, exhibiting putative structural characteristics (Figure 10) [47]that differed from those previously reported (Figure 11) [60]. Zhang and colleagues reported an acidic heteropolysaccharide, LFP-1, composed of abundant arabinogalactan, linear homogalacturonan acid, and rhamnogalacturonan acid . Its molecular weight is 1.78 × 10^{4} kDa. According to HPGPC assay, it is composed of Rha, Ara, Xyl, Man, Glc, Gal, GlcA, and GalA in a molar ratio of 3.68: 34.88: 2.46:1.03:6.89:37.64:0.73:12.67. GC-MS and NMR data showed that its arabinogalactan is composed of a characteristic→3)-*β*-Gal (1→main chain and high content of crosslinked →6)-*β*-Gal (1→side chains substituted by branched *α*-Ara elements. The homogalacturonan linear fragments composed of the repetitive moiety of→4) GalA (1→residues alternated with short segments of rhamnogalacturonans; model structures are shown to illustrate the main structural molecules rather than explicit structures (Figure 12) [61]. An acidic polysaccharide extracted from *Lycium barbarum* has obvious differences in its monosaccharide composition. However, most of these polysaccharides consist of Rha, Xyl, Glu, and Gal, with varying molar fractions of the individual components. Notably, NMR results indicated that their furan and pyran

rings are composed of both α- and β-anomeric configurations [62]. Interestingly, ironic acid was detected in some polysaccharides. An acidic polysaccharide, LRP-S2A, isolated from *Lycium ruthenicum* Murr. was analyzed for monosaccharide composition. It was found to be composed of Rha, Ara, Gal, Glc, and GlcA in a ratio of 1.00:2.07:0.57:2.59:4.33. The backbone consists of 6-O-Me-α-(1→4)-D-GlcA, 2-O-acetyl-α-(1→4)-D-Glc, α-(1→2,4)-L-Rha, β-(1→3)-D-Gal, and α-(1→3,5)-L-Ara, with some branches consisting of 6-O-Me-α-(1→4)-D-GlcA and terminal α-L-Ara [63]. Researchers isolated an acidic polysaccharide (LBP1B-S-2) with a molecular weight of 80.00 kDa from *Lycium barbarum* L. It was found to contain rhamnose, Ara, Gal, and GluA in a molar ratio of 3.13:53.55:39.37:3.95. Partial acid hydrolysis, methylation analysis, IR, and NMR spectral analysis revealed that LBP1B-S-2 contained a backbone of 1, 3-linked β-D-Gal and 1, 6-linked β-D-Gal, with branches containing 1, 4-linked β-D-GlcA, T-linked β-D-Gal, 1, 6-linked β-D-Gal, T-linked α-L-Ara, T-linked β-L-Ara, 1, 5-linked α-L-Ara, and T-linked β-L-Rha directly or indirectly attached to the C-3 position of 1, 6-linked β-D-Gal or the C-6 position of 1, 3-linked β-D-Gal. The possible structure of LBP1B-S-2 is shown in Figure 13. On the basis of the results of FT-IR, GC-MS, ^{1}H-NMR, and ^{13}C-NMR analyses, the structures and conformations of a new polysaccharide from *Lycium barbara* L. were identified, with the backbone mainly composed of (1,5)-linkage α-L-Ara and possibly (1,4)-linkage α-D-galacturonic acid with a branch chain of-(1)-Man-(3,6)-linkage and a main terminal sugar of-(1)-Man. The polysaccharide fraction was composed of Rha, Ara, Xyl, Gal, Man, and GalA in a ratio of 1.00:7.85:0.37:0.65:3.01:8.16. Its molecular weight is 2.25×10^{6} Da [64].

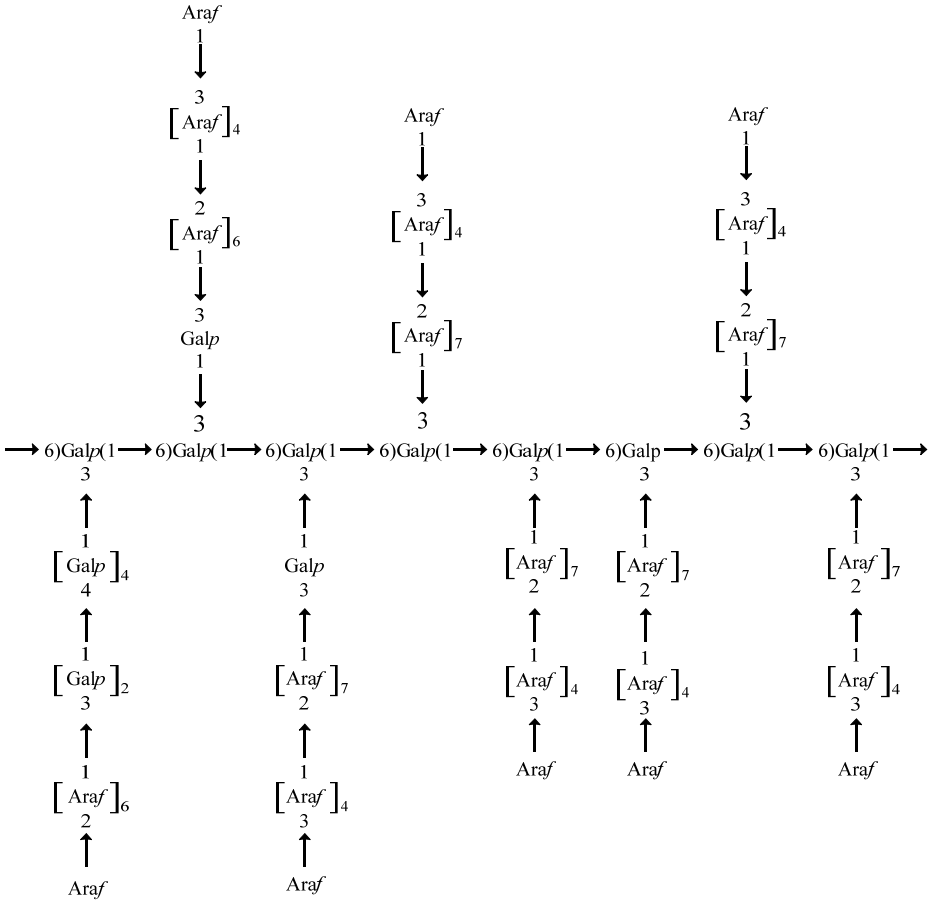

Figure 5. The hypothetical structure of the repeating unit of LbGp1.

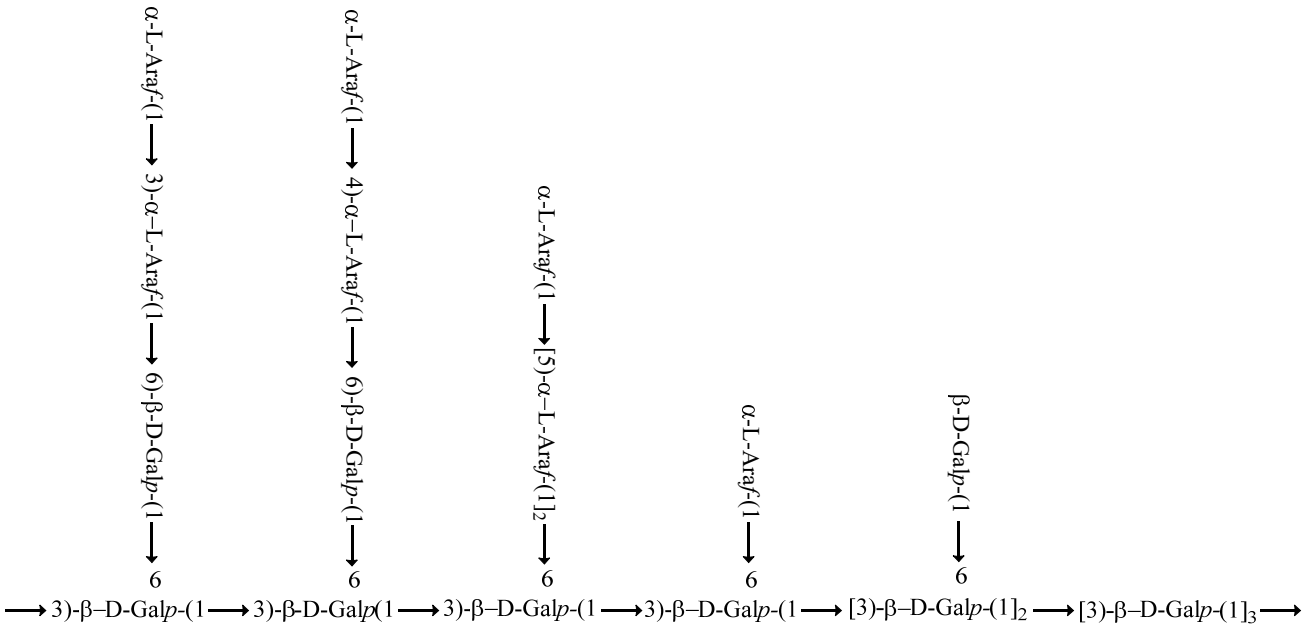

Figure 6. Possible structure of LBP-3.

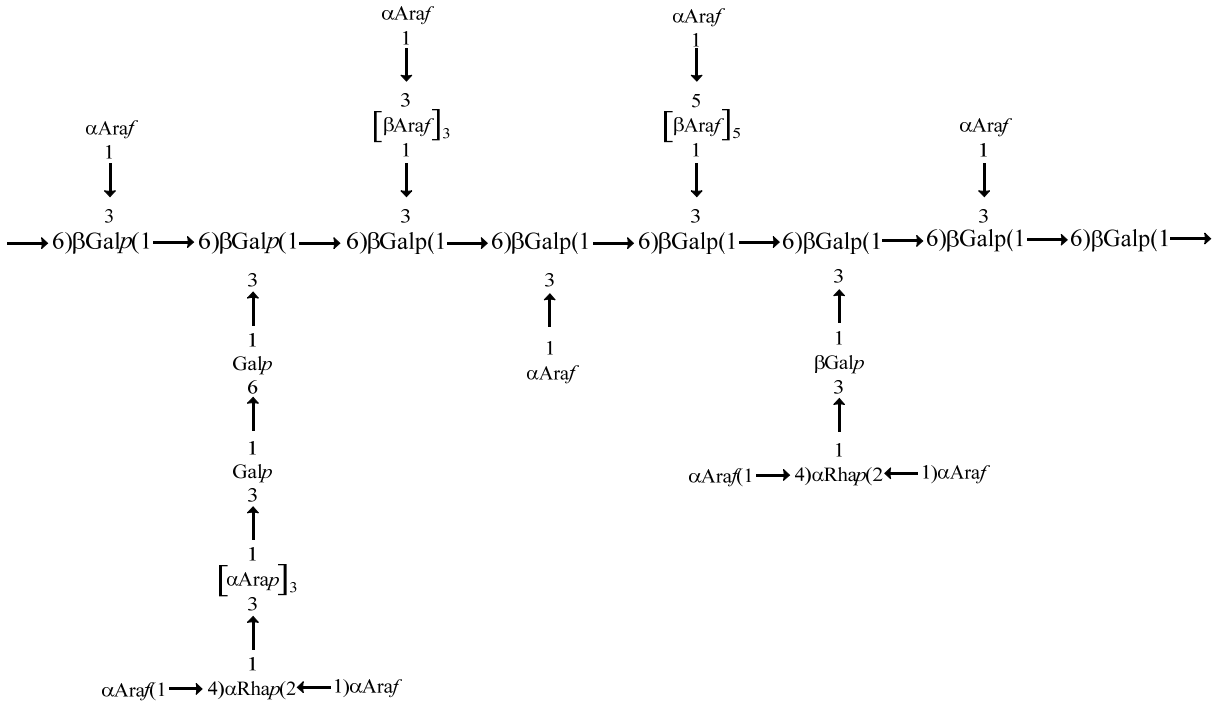

Figure 7. The hypothetical structure of the repeating unit of LRLP—A.

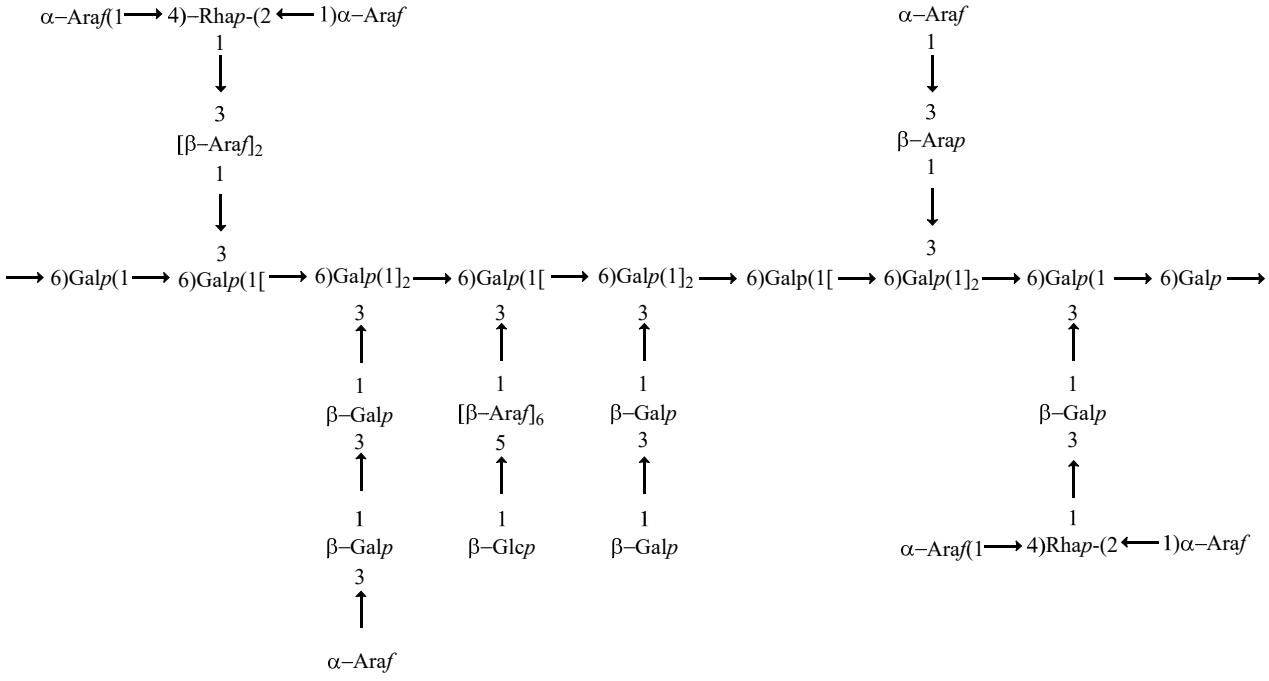

Figure 8. Schematic representation of the structural unit of LRP4-A.

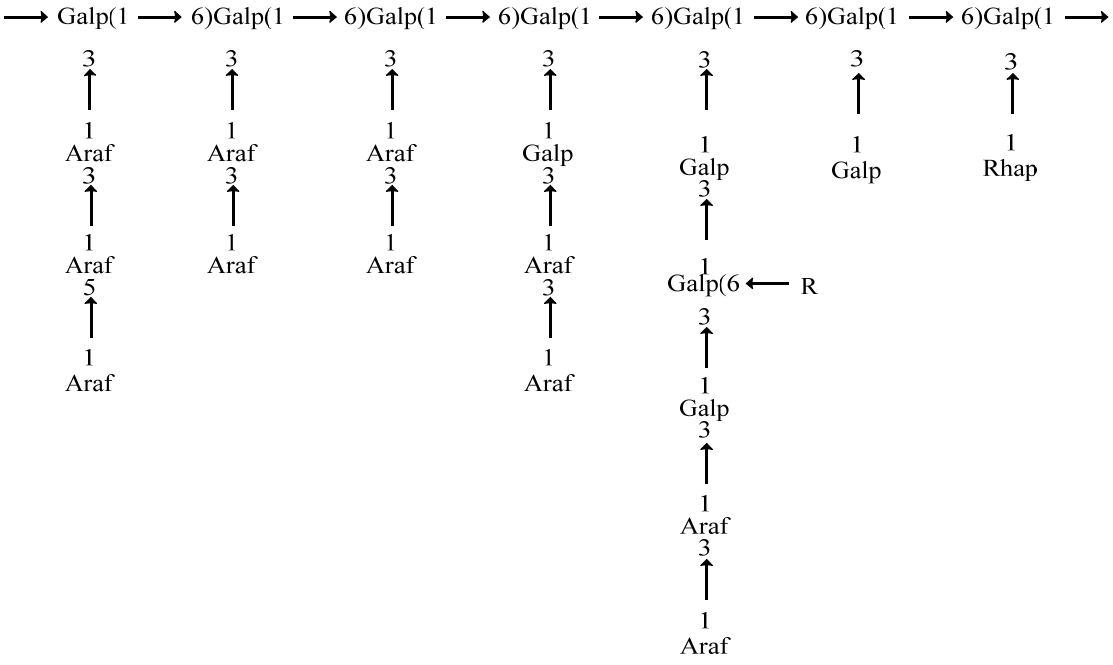

Figure 9. The presumptive structure of a homogeneous polysaccharide, LBP-W.

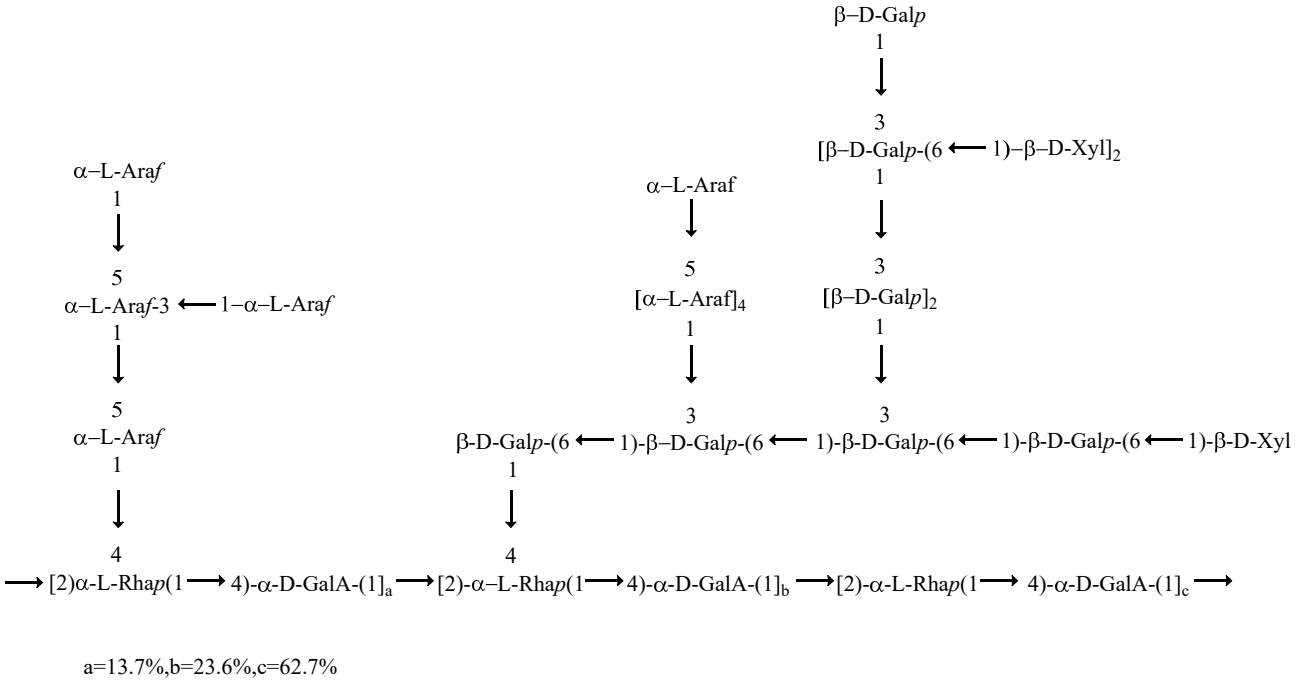

Figure 10. Putative structure of LRP3-S1.

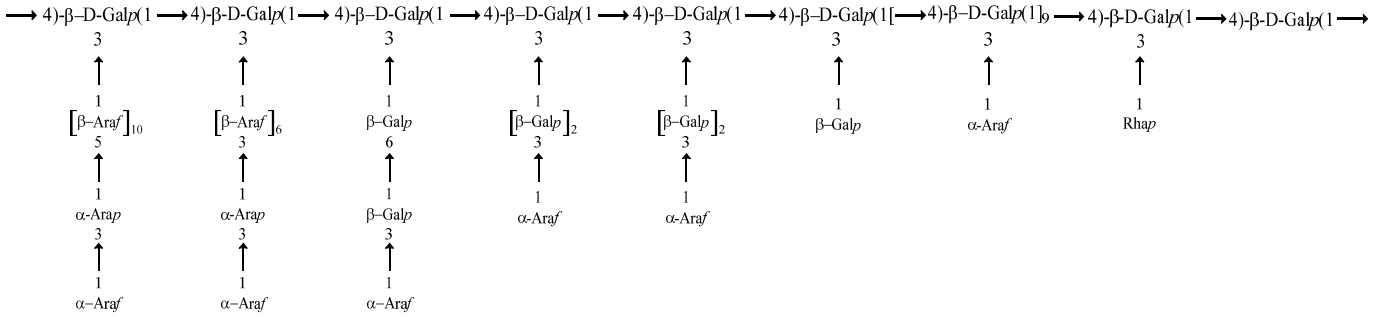

Figure 11. One of possible structure of the repeat unit of LbGp4-OL.

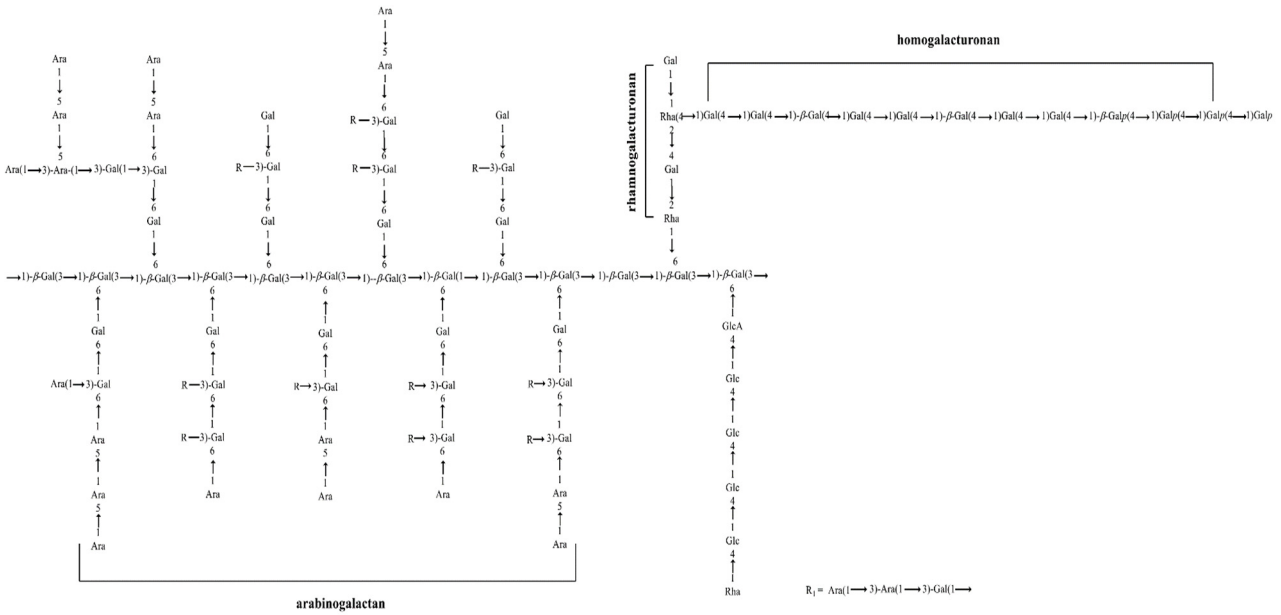

Figure 12. Model structure of LFP-1.

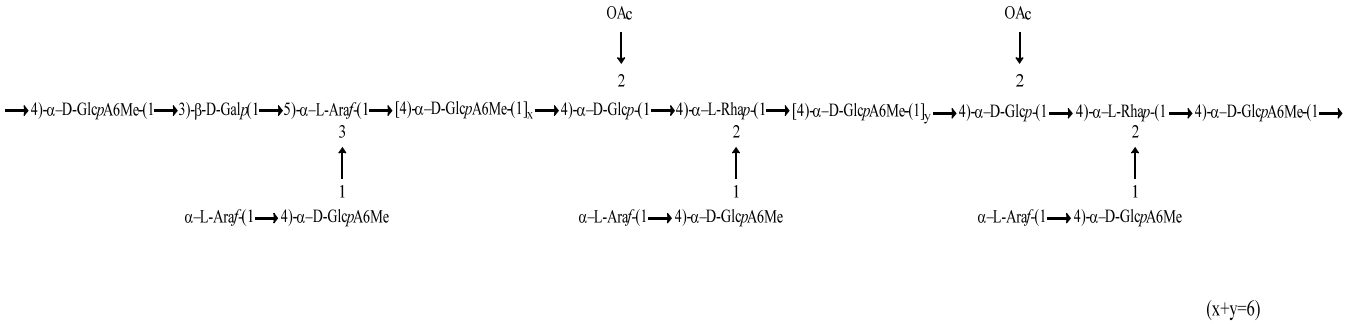

Figure 13. The possible repeat unit of LRP-S2A.

Besides the above-reported polysaccharides, some arabinogalactan polysaccharides were obtained from wolfberry, such as a rare arabinogalactan with *β*-D-(1→6)-galactan as backbone polysaccharide (LBPA). Neither type I nor type II was isolated from the *Lycium barbarium* fruit. It had a *β*-D-(1→6)-galactan backbone with branches consisting of *α*-L-Ara-(1→, *α*-L-Ara-(1→5)-*α*-L-Ara-(1→, *β*-L-Ara-(1→5)-*α*-L-Ara-(1→, and *α*-L-Rha-(1→4)-*β*-D-GlcA-(1→6)-*β*-D-Gal-(1→ was linked to *β*-D-(1→6)-galactan at O-3(Figure 14) [50]. A novel arabinogalactan polysaccharide (LBP1A1-1) was identified with a backbone of 1, 3-linked Gal, 1, 6-linked Gal, and 1, 4-linked Glc with branches of T-linked Ara, 1, 5-linked Ara, T-linked Rha, and T-linked Gal attached to the C-3 position of 1, 6-linked Gal or the C-6 position of 1, 3-linked Gal. 1D and 2D NMR data confirmed these results, and a possible structure of LBP1A1-1 was reported by Zhou and his research team (Figure 15) [65]. An arabinogalactan (LRGP3) was isolated from *Lycium ruthenicum* Murr. through acetylation and mild acid hydrolysis to obtain an acid hydrolysate (LRGP3-T) containing (1→3)-linked galactose residues (17.6%), (1→6)-linked galactose residues (23.1%), (1→3,6)-linked galactose residues (30.1%), and terminal galactose residues (29.2%) (Figure 16) [66]. The side chains (Oligo-S) consisted of Ara, Gal, and Rha in a molar ratio of 16.8:1.4:1.0. Additionally, several arabinogalactan proteins were acquired from *Lycium*. By using anion-exchange chromatography and precipitation with Yariv reagent, purified cell wall polysaccharides were separated from wolfberry fruit, which consisted of Rha (3.3):Ara (42.9):Xyl (0.3):Gal (44.3):GalA (2.4):GlcA (7.0), with a molecular weight in the range of 50–60 kDa. Linkage and NMR analysis data showed that the backbone consisted of (1→3)-linked *β*-D-galactopyranosyl residues, many of which were substituted at O-6 with side chains of 5-substituted *α*-L-arabinofuranosyl residues terminated with *α*- (and *β*-) L-arabinofuranosyl, *α*-L-rhamnopyranosyl, and *β*-D-glucopyranosyluronic acid residues. A hypothetical model of the structural features of the AGP glycan are shown in Figure 17 [46]. A polysaccharide named LbGp2 was previously obtained from *Lycium barbarum* via a Sephadex G-100 column with a molecular weight 68.2 kDa. Glycosidic bond analysis, total acid hydrolysis, partial acid hydrolysis, and ^{1}H and ^{13}C NMR spectroscopy results indicated that the glycan backbone consisted of (1→6)-*β*-galactose residues, of which approximately 50% were substituted at C-3 by galactosyl or arabinose groups, with the main nonreducing end consisting of Ara (1→. The complete structure of the repeating unit of the glycan of LbGp2 is shown in Figure 18 [67]. The glycan of glycoconjugate (LbGp3) isolated from *Lycium barbarum* in [68] has a molecular weight of 92.5 kDa in and carbohydrate content of up to 93.6%. It was found to be composed of Ara and Gal in a molar ratio of 1: 1, as well as 18 amino acids, according to component analysis. Methylation analysis, partial acid hydrolysis, and ^{1}H and ^{13}C-NMR spectroscopy of the original glycan and products of its partial hydrolysis elucidated that the linkage between the glycan and the core protein backbone may be O linkage. The anomeric configuration of the structural features of LbGp3 are shown in Figure 19. LRGP3, a water-soluble arabinogalactan protein with a molecular weight of 75.6 kDa, was extracted from *Lycium ruthenicum* by deionized water and further purified and detected using GPC and HPGPC. Its protein accounted for 1.7% of its composition, and it was found to be rich in hydroxyproline. Partial acid hydrolysis,

methylation analysis, ESI-MS, and NMR spectroscopy identified highly branched polysaccharides with a backbone of (1→3)-linked *β*-D-galactopyranosyl residues, many of which were substituted at the O-6 position by galactosyl or arabinose groups. The branches were composed of (1→5)-linked Ara, (1→2)-linked Ara, (1→6)-linked Gal, (1→3)-linked Gal, and (1→2,4)-linked Rha, and the major nonreducing termini were *α*-L-arabinofuranosyl residues (Figure 20) [69].

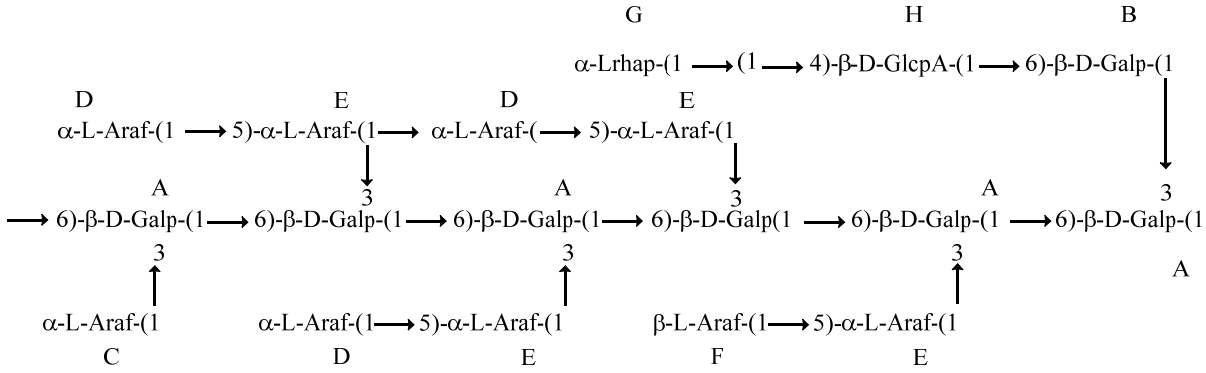

Figure 14. The chemical structure of LBPA.

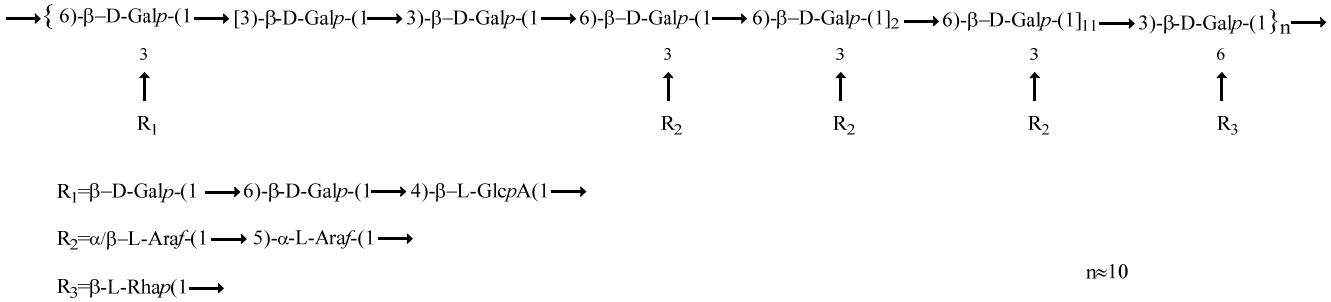

Figure 15. Possible structure of LBP1A1-1.

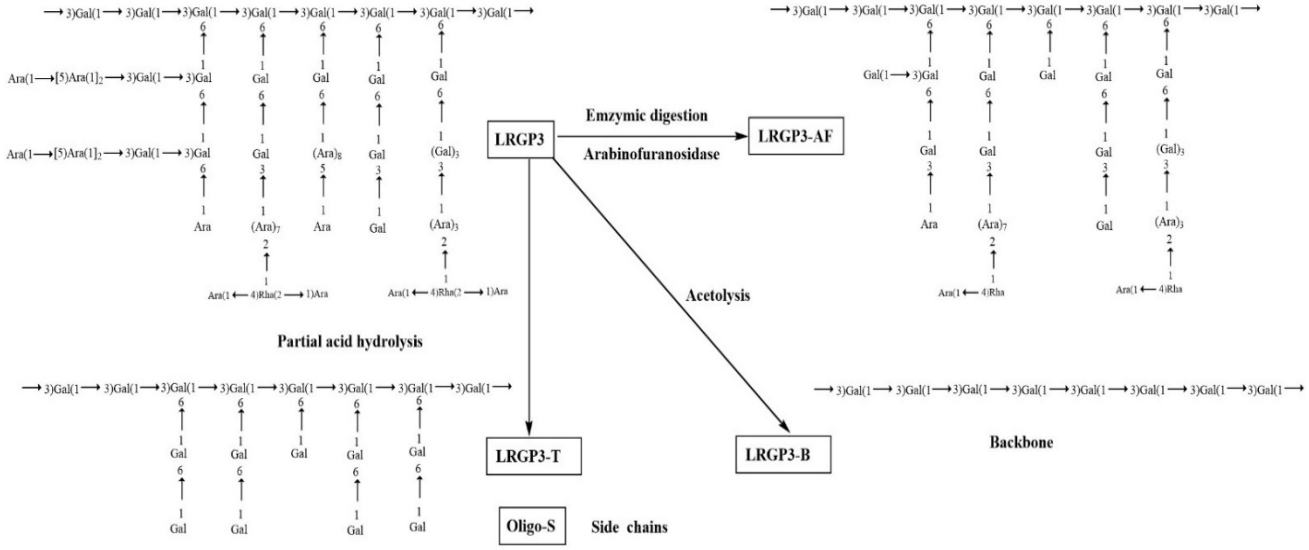

Figure 16. Schematic representation of the sequential degradation procedure of LRGP3.

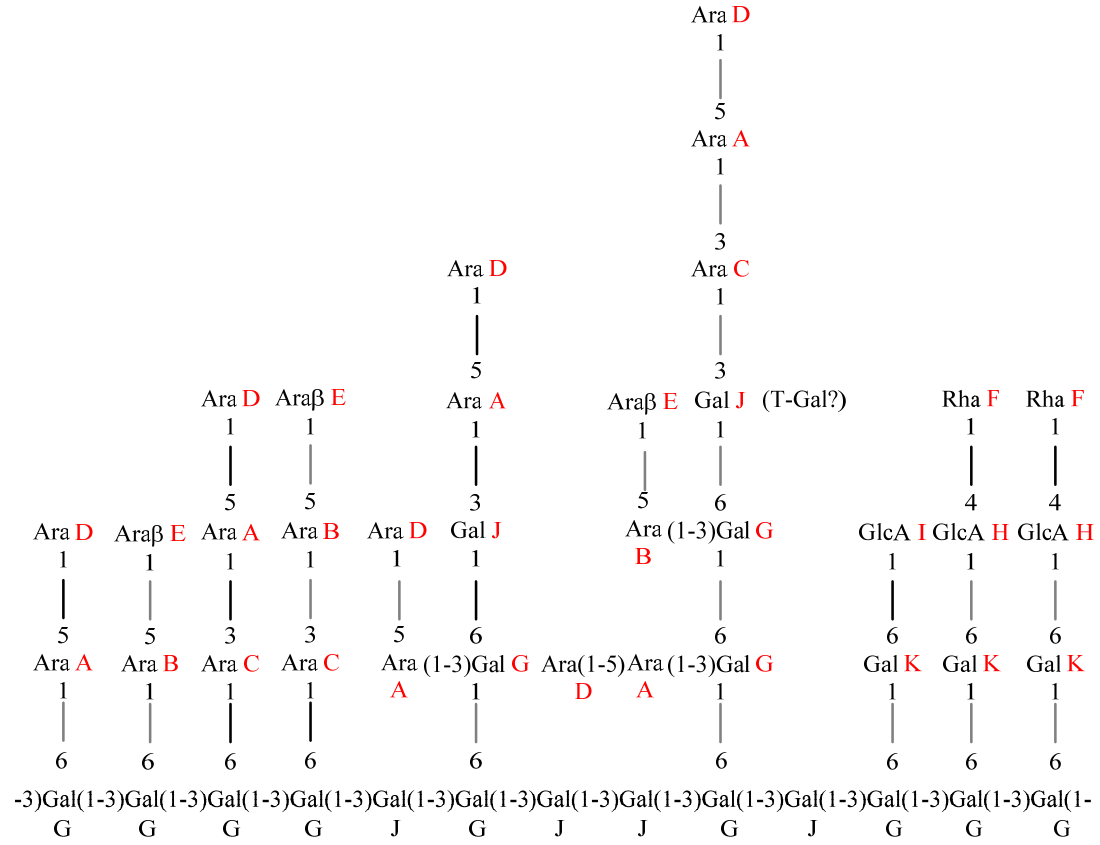

Figure 17. Hypothetical model of the structural features of the AGP glycan.

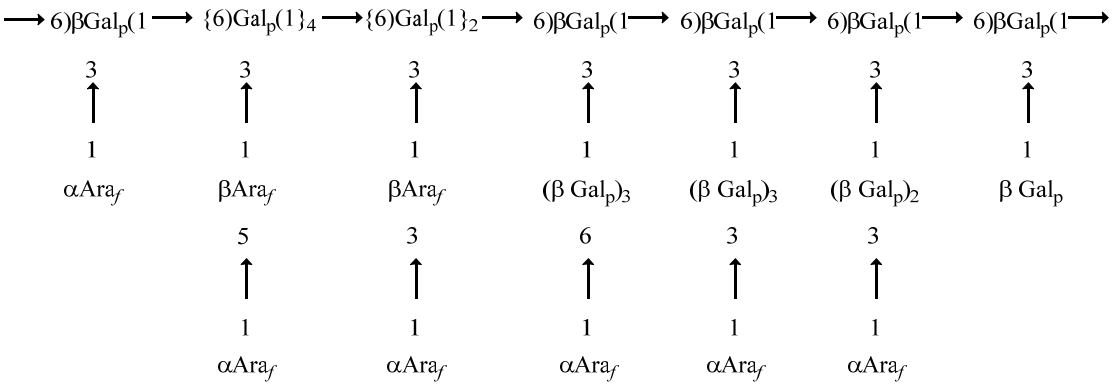

Figure 18. The complete structure of the repeat unit of the glycan of LbGp2.

In light of these results, the genus *Lycium* L. polysaccharide studied under different conditions showed remarkably variable monosaccharide composition, molecular weight, and structural characteristics, which may be dependent on raw materials and purification procedures. As a result, we cannot uniformly determine the structural characteristics of genus *Lycium* L. polysaccharides. Further studies should be conducted using advanced techniques to better comprehend the structure–bioactivity connection.

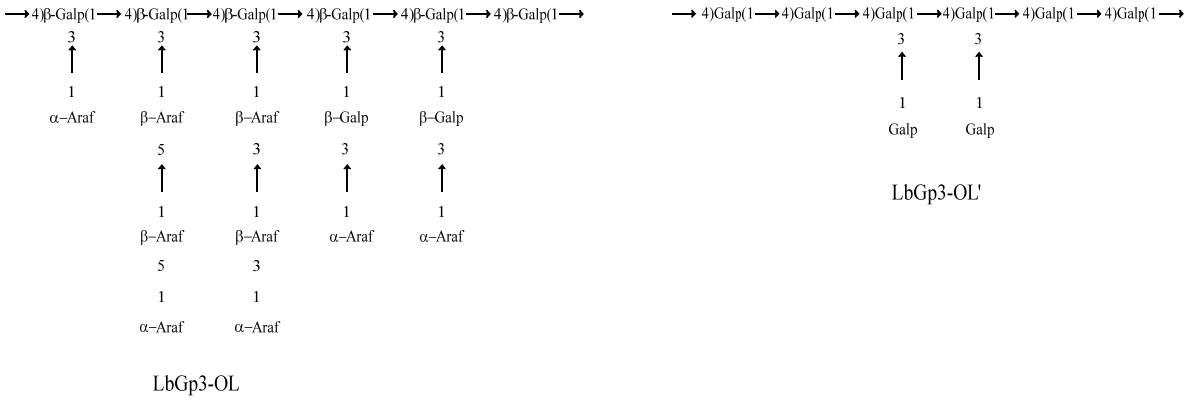

Figure 19. Possible structure of LbGp3-OL.

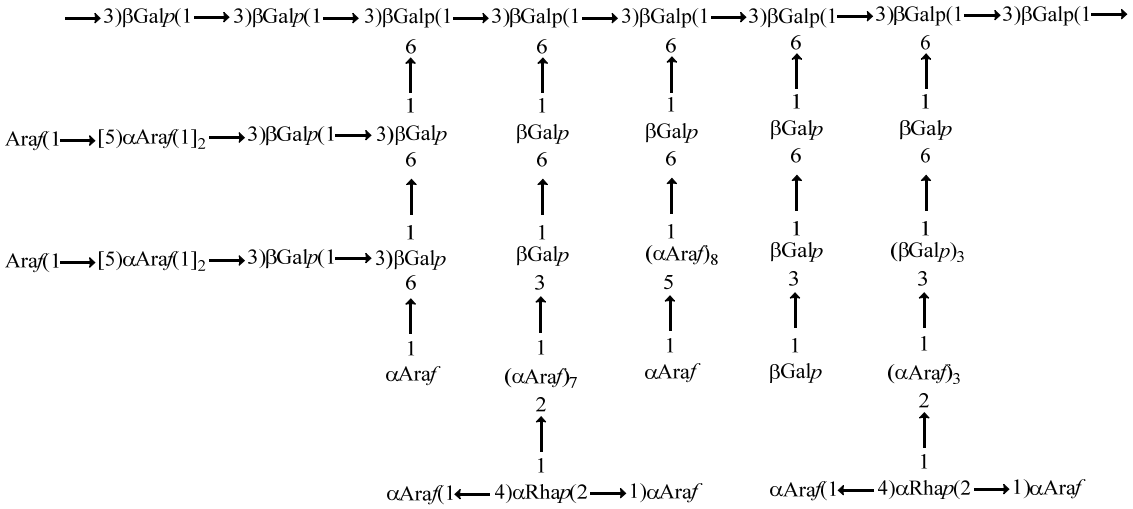

Figure 20. Hypothetical structure of the repeat unit of the glycan of LRGP3.

8. Pharmacology and Biological Applications of the Genus *Lycium* L. Polysaccharide

In China, *Lycium barbarum* is used as a beneficial medicine and herbal dietary supplement. Previous studies have proven that genus *Lycium* L. polysaccharides show various pharmacological and biological activities, including reproductive protection, anti-inflammatory and neuroprotective activity, protection against myocardial injury, gastric protection, liver protection, eye protection, and mitigation of diabetic complications.

8.1. Reproductive Protection Activity

Infertility is a common disease worldwide that is becoming a persistent global reproductive health problem. An estimate showed that by 2025, more than 186 million couples of reproductive age will be affected by infertility, with developing countries accounting for the majority or such cases [70,71]. This shocking prediction has aroused widespread concern in the scientific community. According to traditional Chinese medicine books, wolfberry has the effect of nourishing the kidneys and has been used for thousands of years. The scientific community began to conduct extensive research on the effect of wolfberry and found that the polysaccharide component of wolfberry extract can promote sexual fertility [72–74]. In one of the first reported studies [75], male rats were randomly divided into normal control group, irradiation control group 1, irradiation control group 2, irradiation control group 3, LBP irradiation group 1, LBP irradiation group 2, and LBP irradiation group 3 (n = 12 in each group). The results showed that the number of sperm in the LBP irradiation groups increased significantly by 36.84%, 30%, 82.64%, and the motility increased to 32%, 98%, 31%, and 97%, which was significantly higher than in the

irradiation control group. The results show that LBP can significantly increase male sperm counts. In rats, polysaccharides were found to increase sperm count and motility; shorten the latency of erection, capture, and ejaculation; and improve the sexual performance of males. In addition, polysaccharides restore serum testosterone levels, increase superoxide dismutase activity, reduce malondialdehyde levels, promote oxidative balance, and rescue testicular DNA damage. In an experiment investigating the effect of LBP on cyclophosphamide (CTX)-induced ovarian damage, serum indicators, Nrf2, heme oxygenase-1, and quinone oxidoreductase one protein levels were measured. LBP was found to attenuate CTX-induced ovarian damage and reverse associated adverse effects. LBP reduced oxidative stress by enhancing the potency of antioxidant enzymes and reducing the elevated levels of oxidative products after CT injection. LBP treatment upregulated the Nrf2, heme oxygenase-1, and quinone oxidoreductase one protein expression levels, indicating that LBP has a potential effect on CTX-induced ovarian injury effect by reducing oxidative stress and activating the Nrf2/ARE signaling pathway [76]. Ze-Yong Tang's team studied LBP in nonylphenol exposure-induced testicular damage in juvenile zebrafish and found that sperm density significantly increased and acellular area decreased. LBP treatment can upregulate the cyp11b gene, promote androgen secretion, inhibit cyp19a gene expression, and exert anti-estrogenic effects, mitigating the estrogenic effects of artificial endocrine disruptors [77]. It is worth noting that LBP can reduce the level of reactive oxygen species (ROS) during freezing and thawing, avoid the activation of the sperm mitochondrial apoptosis pathway, and protect the mitochondrial structure and sperm function [78].

The reproduction-promoting mechanism of LBP has also been studied [79]. LBP significantly increased the expression levels of occludin and zonula occludens-1 in a dose-dependent manner, increased the expression of androgen receptors, and activated Akt in test tissues obtained from the testis. In the Akt signaling pathway, it improves heat-stress-induced Sertoli cell and blood–testis barrier damage and reduces abnormal spermatogenesis.

Yang and his team reported that LBP is a potential new drug for the prevention of obesity-induced male infertility. In obese mice, LBP can regulate the expression levels of antioxidant molecules, SOD, GSH, and MDA; reduce blood glucose levels and insulin resistance; increase testosterone levels and insulin sensitivity; downregulate p-eIF2a in the testis tissue; and attenuate GRP78 and CHOP expression [80].

8.2. Anti-Inflammatory Activity

Inflammation is a beneficial self-protective physiological process in the body against damage to tissues and cells caused by pathogen invasion, harmful stimuli (such as chemicals), or bodily injury [81]. Extensive research has shown that natural polysaccharides containing LBP exhibit significant anti-inflammation activities [82,83]. Rjeibi et al. conducted an anti-inflammatory study with an animal model [84]. In this study, LBP was found to inhibit carrageenan-induced inflammation in mice, and the anti-inflammatory effect of LBP was comparable to that of both NSAIDs and indomethacin, which provides evidence for a new source of antioxidant and anti-inflammatory metabolites of LBP.

LBP is widely used to treat inflammation-related injuries [85]. Researchers established a collagen II-induced arthritis (CIA) mouse model and measured bone volume/tissue volume; they found that LBP can significantly ameliorate CIA-induced bone injury and bone loss and inhibit the expression of CIA-stimulated inflammatory mediators and MMPs, suggesting that LBP may protect bone integrity in CIA mice by downregulating inflammatory mediators. Another study investigated the effect of LBP on IL-1b-induced inflammatory injury in ATDC5 cells. ATDC5 cells were treated with IL-1b to establish an in vitro model of cartilage injury, and LBP was found to significantly reduce IL-1b-induced inflammation and enhance the expression of MiR-124 after treatment. The results suggested that LBP upregulates miR-124 by blocking NF-JB and JNK pathways, thereby protecting ATDC 5 cells from IL-1b-induced damage [86]. The researchers randomly

divided male rats into a control group (Con), LPS group (LPS), ulinastatin group (ULI), low-dose LBP group (LBP-1), medium-dose LBP group (LBP-2), and high-dose LBP group (LBP-3) [87]. A sepsis model (LPS group) was established by intraperitoneal injection of LPS (5 mg/kg). The ULI group was administered 10,000 u/kg ulinastatin, and the LBP-1, LBP- 2, and LBP-3 groups were administered 200, 400, and 800 mg/kg LBP, respectively. Serum levels of IL-1β, IL-6, IL-8, TNF-α, and NF-κB were detected by ELISA. PCR and Western blot analysis were used to detect the expression levels of Nrf2, Keap1, NF-κB, HO-1, and NQO1. The authors concluded that LBP attenuates renal inflammatory injury through Keap1-Nrf2/ARE signaling regulation. In the report by Cao et al. [88], the separation of LBP-3 from *Lycium barbarum* in DSS-induced chronic colitis showed that LBP-3 treatment can significantly reduce weight loss in ulcerative colitis mice, as well as histopathological injury and oversecretion of pro-inflammatory cytokines and enzymes. Furthermore, LBP-3 reversed the gut microbiota by enriching potential probiotics and inhibiting the proliferation of harmful bacteria. SCFA, a main metabolite of LBP-3 fermentation in the gut microbiota, was also promoted to maintain relatively favorable intestinal homeostasis. Therefore, LBP-3 is a potential drug candidate for the treatment of UC, given its ability to improve intestinal barrier function and partially restore the intestinal microbiota and its metabolites.

Li et al. [89] tested whether LBP has an anti-inflammatory effect on intestinal barrier dysfunction caused by proinflammatory factors and found that LBP improved TNF-α-induced intestinal barrier function by inhibiting NF-κB-mediated obstacles to the MLCK-MLC signaling pathway.

Ding and colleagues studied a model of cyclophosphamide (CTX)-induced intestinal dysbiosis in mice and found that LBP can promote the production of immunity-related cytokines (IL-2, IL-6, IL-1β, TNF-α, and IFN-γ) and prevent CTX-induced hepatotoxicity in mice [90] Furthermore, LBPS treatment promoted short-chain fatty acid production and modulated gut microbiota composition, increasing the relative abundances of Bacteroidetes, Lactobacillus, Prevotellaceae, and Verruca Bacterium, which were positively correlated with immune properties. The results suggest that LBPS may modulate immune responses by modulating gut microbiota, and LBPS can be exploited as a specialized component of immune regulation associated with gut microbiota regulation. The intestinal absorption of LBP was investigated using the $CaCO_2$ cell model. It was found that LBP was minimally absorbed in the gut, suggesting that most LBPs interact with the gut microbiota. The association of LBP-induced immune responses with the regulation of gut microbiota has also been demonstrated by other investigators [91,92].

Furthermore, researchers examined the effect of LBP against LPS-induced inflammatory response in primary bovine mammary epithelial cells, revealing a preventive role of LBP in reducing detrimental effects induced by LPS, including inhibition of NF-γB and MAPK, as well as PPARγ activation. LBP pretreatment inhibited the LPS-induced reduction in cell proliferation [93]. Furthermore, the regulatory effect of LBP on the inflammatory response of bMECs was found to be PPARγ-dependent. The data suggest that LBP reverses LPS-induced inflammatory responses in a PPARγ-activation-dependent manner via the MAPK/NF-κB signaling pathway. This provides new insights into LBP treatment of mastitis. These findings provide an accurate basis for the description of the anti-inflammatory and immune activity of LBP.

8.3. Neuroprotective Activity

An open field test (OFT), forced swimming test (FST), tail suspension test (TST), reserpine hypothermia, and ptosis were used to evaluate the effects of LBP on reserpine-induced depression in mice [94]. The results showed that LBP significantly improved the locomotor activity of reserpine-induced mice, shortened the immobility time, and inhibited hypothermia and blepharoptosis. LBP treatment reduced striatal lipid peroxidation (LPO) production and enhanced striatal antioxidant activity in depressed mice. In addition, LBP inhibited the decrease in apoptosis inhibitors Bcl-2 and PARP, which were

significantly decreased after reserpine treatment. This finding provides a background for further development of LBP as a potential dietary therapy for depression. Surprisingly, another study showed that LBP had anxiolytic effects in ovariectomized rats. The interaction also showed that HD-LBP treatment reduced anxiolytic effects in ovariectomized rats, as measured by OFT and EPM. HD-LBP treatment reduced anxious behavior by increasing antioxidant enzyme activity, as well as hippocampal SER and BDNF neurotransmitter levels, and reducing the number of TUNEL-positive cells in ovariectomized rats [95].

Alzheimer's disease is among the most common core degenerative illness and is associated with abnormal amyloid-β plaque accumulation, poor neurogenesis, and cognitive decline. In an APP/PS1 transgenic mouse model, Zhou showed that LBP can decrease Aβ levels and improve cognitive functioning. BrdU/NeuN double labeling suggested that LBP1 can boost neurogenesis and benefit from synaptic dysfunction in the CA3-CA1 circuit in the hippocampus [96].

In a study by Zhou et al. [97], a 2,4-D (75 mg/kg.b.w) exposure model was established in the colostrum of SD rats. Taking lipopolysaccharide (1 mg/kg body weight) as a positive control and LBP (50 mg/kg body weight) as an intervention factor, after 4 weeks of administration, compared with the control group and 2,4-D group, NLRP3, ASC, the expression of cleaved caspase-1, IL1β, IL-18, and p62 proteins, as well as the mRNA levels of NLRP3, IL-1β, IL18, and p62 increased, whereas the expression of LC3-II/LC3-I and Beclin 1 proteins and the expression of LC3B mRNA decreased ($p < 0.01$).

The results suggest that LBP may exert neuroprotective effects by inhibiting the activation of the NLRP3 inflammasome and upregulating the level of autophagy in vivo.

8.4. Myocardial Injury Protection

Lin et al. purified LBP from wolfberry, and the molecular weight of LBP was degraded from 4.63×10^4 Da to 3.45×10^4 Da with ascorbic acid and hydrogen peroxide [98]. In vitro experiments showed that LBP degradation significantly improved anticoagulant activity, especially antiplatelet activity ($p < 0.05$). The effect of the inhibitory activity of polysaccharides with a maximum degradation degree of 0.5 g/mL on arachidonic acid and thrombin-induced platelet aggregation was higher than that of aspirin, probably due to the reduction in uronic acid between LBP and its degradation products significantly reducing antiplatelet activity ($p < 0.05$). After further analysis, the authors concluded that the carboxyl group of polysaccharides is the main reason for their antiplatelet activity. After polysaccharides are degraded, they transforms from a compact, spherical structure to a random coil in aqueous solution, which facilitates the interaction between the polysaccharides and platelets and enhances antiplatelet activity.

Furthermore, investigators treated LBP as a potential prebiotic fiber to alleviate HFD-induced myocardial injury [45]. LBP was administered by gavage once a day for 2 months and significantly improved left ventricular function and serum trimethylamine N-oxide in HFPD mice compared to HFD mice. LBP treatment restored gut microbiota composition, improved metabolism, decreased gut permeability and inflammatory cytokine levels, maintained a healthy gut microenvironment, and attenuated myocardial injury in HFD-fed mice [99]. Nevertheless, human cardiovascular diseases are not only derived from HFD but are also affected by other long-term factors. Therefore, more clinical research is needed to provide LBP therapy for cardiovascular diseases.

8.5. Gastric Protection

Hsieh's research team investigated the potential healing effect of LBP and Spirulina C-alginic acid (CPC) on gastric ulcers in rats [100]. Male Sprague-Dawley rats were divided into five groups: normal group, aspirin (700 mg/kg body weight), LBP (aspirin + 100 mg/kg body weight/day LBP), CPC (aspirin + 50 mg/kg body weight/day CPC), and a mixed group (aspirin + 50 mg/kg body weight/day LBP + 25 mg/kg body weight/day CPC). Aspirin was administered orally for 7 weeks. Compared with the aspirin group, the levels of cyclooxygenase 1, prostaglandin E2, total nitrite, and nitrate in the mixed group

were increased by 139%, 86%, and 66%, respectively ($p < 0.05$). In addition, lipid peroxide malondialdehyde levels were reduced by 78% in the mixed group ($p < 0.05$). Compared with the aspirin group, LBP and/or CPC treatment increased the relative abundance of gastric Bifidobacterium by 2.5–4.0-fold ($p < 0.05$). The authors concluded that combining LBP and CPC can enhance gastroprotective factors, inhibit lipid peroxidation, and increase the relative abundance of gastric Bifidobacterium and that the combined application of LBP and CPC has a protective effect on aspirin-induced gastric ulcers. Nevertheless, the study lacked a group taking LBP or CPC alone and failed to address whether LBP or CPC affected gastric biochemical markers.

8.6. Liver Protection

Gao and his team investigated the effects of LBP, aerobic exercise (AE), and their combination (LBP + AE) on gut microbiota composition, the gut barrier, and liver inflammation in NAFLD patients [101]. LBP + AE showed high abundance and diversity of gut microbiota, restored gut microbiota composition, and increased some Bacteroides and SCFAs but decreased Proteobacteria and Firmicutes/Bacteroidetes. LBP, AE, and LBP + AE restored colonic and ileal tight junctions by increasing the occlusive zone-1 and occluding. They also reduced gut-derived lipopolysaccharide (LPS), hepatic LPS-binding protein, inflammatory factors, and indicators of the hepatic LPS/TLR4/NF-B signaling pathway. This finding suggests that LBP can be considered a prebiotic agent, and LBP + AE may be a promising treatment for NAFLD. Similarly, this result was validated in another randomized, double-blind, placebo-controlled trial [102]. However, due to the small sample size, there is a lack of high-quality studies for further validation.

8.7. Eye Protection

Wong investigated the efficacy of LBP solution as a pretreatment agent to reduce corneal scarring. Fibroblasts were pretreated with LBP for 24 h and incubated with transforming growth factor β1 (TGF-β1) for 24 h to induce relevant physiological events after matrix injury [103]. The investigators used immunocytochemistry and enzyme-linked immunosorbent assays to assess intracellular profibrotic proteins, extracellular matrix proteins, and proinflammatory cytokines involved in fibrosis. Compared with the positive control TGF-β1 group, LBP pretreatment significantly decreased the expression of α-smooth muscle actin, myofibroblast marker, and vimentin in cells ($p < 0.05$), as well as type II and extracellular matrix protein of type III collagen ($p < 0.05$). In addition, LBP pretreatment significantly decreased the secretion of the proinflammatory cytokines interleukin-6 and interleukin-8 ($p < 0.05$). However, the shrinkage and stiffness of the cell-loaded hydrogels did not differ significantly different between the LBP-pretreated and control groups. In addition, LBP-pretreated fibroblasts reduced the expression of angiogenic factors and suppressed undesired proliferation ($p < 0.05$). This study suggests that LBP, as Chinese natural medicine, is a potential topical pretreatment option for corneal refractive surgery.

8.8. Diabetic Complications

Diabetes is a major epidemic disease in the 21st century. Improper treatment is often accompanied by serious complications, such as retinopathy, neuropathy, and cardiovascular disease, which has become one of the major chronic diseases affecting the health of people all over the world [104,105]. However, natural polysaccharides are uniquely different from monosaccharides or oligosaccharides. Plant polysaccharides exhibit hypoglycemic activity, affect the activity of glucose metabolizing enzymes, inhibit gluconeogenesis, and promote the synthesis of the hepatic enzyme glycogen. They can promote insulin secretion through hypoglycemic activity, thereby regulating glucose disorders and insulin resistance.

In order to explore and discover novel and effective hypoglycemic drugs, the anti-diabetic effects of plant polysaccharides have been extensively studied. LBP extracted from wolfberry has been widely utilized to treat diabetes and its related complications. Yao and his team cultivated human lens epithelial cell line SRA01/04 cells in high-glucose (HG) medium after treatment with LBP or vehicle in a rat model of diabetes generated by streptozotocin injection; they found that LBP might regulate the SIRT1-p53/SIRT1-FOXO1 pathway, exerting protective effects on lens epithelial cells, upregulating Sirt1 and Bcl-2, and inhibiting cell-death-related genes to prevent diabetic cataracts in animals [106].

The researchers established a model of high-glucose-induced angiogenesis using monkey retinal vascular endothelial cells (RF/6A) and examined the effect of different doses of LBP, as well as administration time and glucose concentration, and found that 600 mg/L LBP increased apoptosis and total vascular length [107]. In addition, LBP can inhibit the expression of VEGFA, VEGFR2, and ANG2, which promote the expression of ANG1 protein. LBP can also inhibit the expression of ASM mRNA and protein. Based on the above findings, it can be concluded that LBP inhibits diabetic retinal angiogenesis by rescuing the expression of miR-15a-5p in RF/6A cells.

In addition, Liu and his research team reported that LBP can ameliorate hyperglycemia-exacerbated ischemia/reperfusion brain injury [108]. They compared neurological deficits, infarct volume, and histopathology in normoglycemic (NG) and hyperglycemic (HG) rats pretreated with LBP and insulin , respectively, and measured the expression of proteins Opa1 and Drp1. The results showed that LBP preconditioning reduced neurological deficits, infarct volume, and neuronal pyknosis at 24 h and/or 72 h of reperfusion in the HG group compared with the NG group ($p < 0.05$).

Furthermore, LBP treatment prevented mercury-induced changes in Drp-1 and Opa1 expression. The authors concluded that LBP preconditioning improves ischemic brain injury exacerbated by hyperglycemia by maintaining mitochondrial homeostasis.

8.9. Biological Applications

According to the Chinese Pharmacopoeia, *Lycium barbarum* can nourish liver and kidneys, improving vision; it is widely used to treat consumptive deficiency, waist and knee pain, tinnitus, balance loss, nocturnal emission, impotence, hypoglycemia, blood deficiency, and poor vision.

In recent years, Eastern and Western countries have favored red wolfberry and black wolfberry in high-quality food products [109], such as wolfberry candy, wolfberry wine, and wolfberry tea. Polysaccharides are the main physiological component of the genus *Lycium* L. Furthermore, the selenium nanoparticles fixed by LBP were successfully put together. In vitro studies showed that the selenium nanoparticles of LBP were found to aid in the absorption of selenium in different parts of the intestine (duodenum, jejunum, and ileum), increasing its bioavailability [110,111].

Many marketed drugs with polysaccharides as a medicinal ingredient are used to treat ailments such as insulin resistance syndrome and type 2 diabetes, as well as to relieve fatigue and improve immune function. Table 5 lists the status of health foods, drinks, skin products, and other polysaccharide-containing products that can improve health without side effects.

9. Toxicology

Rjeibi et al. conducted a toxicological study of *Lycium* water-soluble polysaccharides in male and female rats [84]. No mortality was reported during the 10-day research period with doses of 100 mg/kg bw/day.

10. Discussion and Conclusions

Chinese herbal medicine has been practiced for hundreds of years, and wolfberry is widely used in clinical practice for its relatively unique efficacy. In recent years, Goji berry

has been promoted as a superfood owing to its nutritional properties. Furthermore, it has attracted widespread attention from Eastern and Western countries as a nutritious food that can be consumed as a fruit or used as a raw material for beverages. In recent decades, polysaccharide extracts from natural medicines have been highly valued by researchers at home and abroad due to their structural diversity, low toxicity, and their essential roles in many biological processes. Polysaccharides were isolated and purified from the genus *Lycium* L. by DEAE ion-exchange cellulose, gel-permeation chromatography, and spectral analysis. Through spectral and other chemical analyses, polysaccharides have been proven to be the main component of *Lycium* plants. The polysaccharide components analyzed by GC, UHPLC-QTRAP-MS/MS, and pre-column derivatization or post-column derivatization HPLC mainly consisted of arabinoses, glucosamine, galactose, glucose, xylose, mannose, fructose, ribose, galacturonic acid, and glucuronic acid, with molecular weights ranging from 4920 Da to 7,166,000 Da. With improved separation and analysis techniques, the structure and physiological activities of genus *Lycium* L. polysaccharides have been further explored, and their physicochemical properties, structural characteristics, and potential biological activities have been further clarified.

According to many studies, genus *Lycium* L. polysaccharides have anti-inflammatory, neuroprotective, reproductive, eye protection, liver protection, and other effects. In addition, genus *Lycium* L. polysaccharides have earned considerable attention for their potential applications as tobacco substitutes, candy, health food, cosmetic products, and pharmaceuticals. In recent decades, genus *Lycium* L. polysaccharides have been used as health foods and medicines to promote immunity, antiaging, and memory activities. Polysaccharides are a promising substance for the treatment of various diseases and can promote the feasible development of pharmaceutical products. Therefore, it is necessary to review genus *Lycium* L. polysaccharide research and discuss potential future development and applications. Although larger-scale studies are needed, the results presented in this review constitute a high-level reference with respect to genus *Lycium* L. polysaccharides. However, their activities have only been demonstrated in in vitro and in vivo studies involving cells and animal models. There is also a dearth clinical applications or clinical trials involving genus *Lycium* L. polysaccharides. Only one recent study reported a randomized, double-blind clinical trial of genus *Lycium* L. polysaccharides in patients with nonalcoholic fatty liver disease.

However, the sample size of this clinical trial was limited, and more high-quality multicenter clinical investigations are needed. Nonetheless, the promising resulted reported from clinical studies and translational research should pique interest in this study area. According to current literature, the main monosaccharides present in polysaccharides are fucose, ribose, rhamnose, arabinose, xylose, mannose, galactose, and glucose, although the monosaccharide composition and glycosidic bond types are highly variable. Given the complex structure of genus *Lycium* L. polysaccharides, most researchers have not proposed a specific structure, instead only inferring a primary chemical structure model. Therefore, further research is required to elucidate the physicochemical properties of genus *Lycium* L. polysaccharides.

Moreover, there are currently no research-grade genus *Lycium* L. polysaccharides on the market. Most of experimental research on genus *Lycium* L. involves polysaccharides extracted, separated, and purified by researchers in the laboratory. Commercially available genus *Lycium* L. polysaccharides also lack uniform quality standards. Accordingly, further research is necessary to elucidate the physicochemical properties and activities of genus *Lycium* L. polysaccharides in order to establish quality standards for their preparation. This review is expected to provide a reference for researchers studying genus *Lycium* L. polysaccharides, providing a potential foundation for applications in nutrition and medicinal spheres. Focusing on the high-order structures of genus *Lycium* L. polysaccharides and their biological function in the human body is an essential area for future research.

Table 4. The summary of the structural features and biological activities of LBP.

No.	Source	Compound Name	Extraction Solvent	Purification Method	Analytical Method	Monosaccharide Composition	Molecular Weight (Da)	Structures	Pharmacological Applications	Reference
1	*Lycium barbarum*	LBP-W	95% ethanol	DEAE Fast Flow column	HPGPC, NMR	Ara:Gal:Rha = 55.6:35.5:8.0	112.97×10^3	Main chain consisting of a repeated unit of→6)-*β*-Gal (1→residues with branches composed of *α*-Ara, *β*-Gal, and *α*-Rha residues at position C-3	Weight loss	[8]
2	*Lycium barbarum* L.	LBP1C-2	Water extraction with the assistance of an enzyme	DEA, Sepharose™ Fast Flow column, Sephacryl S-300 HR column	GC-MS, partial acid hydrolysis, NMR, uronic acid reduction	Ara:Gal:Rha:GalA = 49.9:33.6:8.0:8.5	9.98×10^4	A backbone of alternate 1, 2-linked *α*-Rha and 1, 4-linked *α*-GalA with branches of the terminal (T)-, 1, 3-, 1, 6-, and 1, 3, 6-linked *β*-Gal; T-, 1, 5- and 1, 3, 5-linked *α*-Ara; and T-linked *β*-Rha substituted at C-4 of 1, 2, 4-linked *α*-Rha.	Alzheimer's disease	[9]
3	*Lycium barbarum* L.	LBP-s-1	Hot water	Microporous resin, ion-exchanged column	HPSEC, FT-IR, NMR	Rha:Ara:Xyl:Man:Glu:Gal:GalA = 1.00:8.34:1.25:1.26:1.91:7.05:15.28	1.92×10^6	Furan and pyran ring with both *α* and *β* anomeric configurations	Hypoglycemic effects and insulin-sensitizing activity	[10]
4	*Lycium barbarum* berries	LBP-d	70% EtOH	DEAE-cellulose column, Sephadex G-75 gel-filtration column	GC, periodate oxidation, Smith degradation	Fuc:Rib:Rha:Ara:Xyl:Man:Gal:Glu = 19.6:1.5:28.9:6.3:1.6:6.2:21.5:14.3	Unknown	Unknown	Anti-cancer	[11]
5	*Lycium barbarum* berries	LBP-e	70% Ethanol	DEAE-cellulose column, Sephadex G-75 gel-filtration column	GC, periodate oxidation, Smith degradation	Fuc:Rha:Ara:Man:Gal:Glu = 5.5:8.8:1.7:35.2:3.4:45.4	Unknown	Unknown	Anti-cancer	[11]
6	*Lycium barbarum*	LBP	Hot water		UHPLC-QTRAP-MS/MS	Gal:Ara:Man:Rha:Xyl:Rib:Glu	Unknown	Unknown	unknown	[12]
7	*Lycium barbarum* L.	LBP	Hot water	DEAE cellulose column, Sephadex G-150 columns	reverse-phase liquid chromatography, HPGPC, UV, FT-IR, NMR, SEM	Man:Rha:Glu:Gal:Xyl = 5.52:5.11:28.06:1.00:1.70	4.92×10^3	Furan and pyran ring, both with an *α* and β anomeric configuration	Anti-diabetic	[17]
8	*Lycium barbarum*	LBP1	Subcritical extraction technology	ITHMT	HPGPC, FT-IR	Rha:Gal:Glc:Man:GalA = 26.9:38.1:20.7:3.8:2.2	22.56×10^4	Unknown	Antioxidant	[35]
9	*Lycium barbarum*	LBP2	Subcritical extraction technology	ITHMT	HPGPC, FT-IR	Rha:Gal:Glc:Man:GalA = 28.8:38.6:18.1:4.8:2.7	14.02×10^4	Unknown	Antioxidant	[35]

10	*Lycium barbarum*	LBP3	Subcritical extraction technology	ITHMT	HPGPC, FT-IR	Rha:Gal:Glc:GalA = 31.3:31.6:16.5:6.7	6.50×10^4	Unknown	Antioxidant	[35]
11	*Lycium barbarum*	LBP4	Subcritical extraction technology	ITHMT	HPGPC, FT-IR	Rha:Gal:Glc:Man:GalA = 35.9:44.7:9.7:3.0:0.6	3.83×10^4	Unknown	Antioxidant	[35]
12	*Lycium barbarum*	LBGP-I-1	Water	GPC	GC, IR, HPGPC	Ara (21.95%):Glu (51.22%):Gal (17.07%)	3.19×10^4	Unknown	Anti-oxidant	[35]
13	*Lycium barbarum*	LBP-p8	Hot water	Ultrafiltration membranes	GC, HPLC	Fuc:Rha:Ara:Xyl:Glu:Man:Gal = 5.7:2.5:21.5:8.4:4.6:23.3:33.9	6.50×10^6	Unknown	Anti-hepatoma	[42]
14	*Lycium barbarum*	LBP-a4	Hot water	Ultrafiltration membranes	GC, HPLC	Fuc:Ara:Xyl:Glu:Man:Gal = 19:6:17.1:8.2:10.7:15.1:46.9	1.02×10^4	Unknown	Anti-hepatoma	[42]
15	*Lycium barbarium*	LBPA	80% ethanol	Semi-preparative liquid chromatography	NMR	Ara:Gal:GlcA:Rha = 9.2:6.6:1.0:0.9	4.70×10^5	An Ara with β-D-(1→6)-Gal as a backbone; branches consist of Ara, Rha, GlcA, and Gal.	unknown	[43]
16	*Lycium barbarum*	LBGP-I-2	Water	GPC	GC, IR, HPGPC	Ara (19.35%):Glu (32.26%):Gal (35.48%)	2.92×10^4	Unknown	Anti-oxidant	[44]
17	*Lycium barbarum*	LBGP-I-3	Water	GPC	GC, IR, HPGPC	Ara (48.15%):Gal (44.44%)	9.12×10^4	Unknown	Anti-oxidant	[44]
18	*Lycium barbarum*	LBPs	Water	Size-exclusion and anion-exchange chromatography	HPLC	Man:Rib:Rha:GlcA:GalA:Glc:Gal:Xyl:Ara = 3.5:3.3:3.8:1.8:22.2:11.0:20.8:3.7:29.9	12.07×10^3	Unknown	Immunosuppressed	[45]
19	Wolfberry fruit (*Lycium barbarum*)	AGP	80% ethanol	Anion-exchange chromatography, precipitation with Yariv reagent	HPLC, HPAEC, linkage analysis, NMR	Rha:Ara:Xyl:Gal:GalA:GlcA = 3.3:42.9:0.3:44.3:2.4:7.0	$(50\text{-}60) \times 10^3$	Backbone of (1→3)-linked *β*-D-galactopyranosyl residues, many of which are substituted at O-6 with side chains of 5-substituted *α*-L-arabinofuranosyl residues terminated with *α*-(and *β*-)l-arabinofuranosyl,*α*-L-rhamnopyranosyl and *β*-D-glucopyranosyluronic acid residues		[46]
20	*Lycium ruthenicum Murr.*	LRP3-S1	Boiling water	anion-exchange chromatography, DEAE Sepharose™ Fast Flow, and SephacrylS-300 HR column	FT-IR, NMR, HPGPC, GC-MS	Rha:GalA:Gal:Xyl:Ara = 14.4:17.7:26.6:16.4:24.9	11.48×10^4	A rhamnogalacturonan I (RG-I) backbone partially substituted at C-4 of Rha units by side chains, including T-linked *β*-D-Gal, 1,3-linked *β*-D-Gal, 1,6-linked *β*-D-Gal, 1,3,6-linked *β*-D-Gal, 1,5-linked *α*-L-Ara, 1,3,5-linked *α*-L-Ara, T-linked *α*-L-Ara, and T-linked *β*-D-Xyl	Anti-Pancreatic cancer	[47]

21	*Lycium barbarum*	Unknown	$CHCl_3$-MeOH	Acetone extraction	HPLC, FT-IR	Glu:Fru = 1:2.1	Unknown	Unknown	Prevented cardiovascular diseases.	[49]
22	*Lycium barbarum* L.	PLBP-I-I	Water	Anion-exchange chromatography, gel filtration.	GC, IR, NMR, size-exclusion chromatography	Ara:Rha:Xyl:Gal:GalA = 25.7:12.4:0.5:27.5:33.9	59.95×10^5	Two fractions are typical pectic polysaccharides, with an HG region, an RG-I region, and AG-I/AG-II side chains; some GalA units of both fractions are methyl-esterified	Antioxidant	[50]
23	*Lycium barbarum* L.	PLBP-II-I	Water	Anion-exchange chromatography, gel filtration.	GC, IR, NMR, Size exclusion chromatography	Ara:Rha:Xyl:Gal:GalA = 26.6:20.8:1.9:7.6:43.1	71.66×10^5	Two fractions are typical pectic polysaccharides, with an HG region, an RG-I region, and AG-I/AG-II side chains; some GalA units of both fractions are methyl-esterified	Antioxidant	[50]
24	*Xinjiang Lycium barbarum*	XLBP-I-I	Hot water	Anion-exchange chromatography, gel filtration	GC-MS, FT-IR and NMR	Ara:Rha:Xyl Gal:GlcA:GalA = 26.5:12.9:0.7:16.8:2.3:40.8	41.96×10^4	Pectic polysaccharide and portions of α-GalA are methyl-esterified	Endoplasmic reticulum stress	[51]
25	*Lycium ruthenicum* L.	LRGP5	Deionized water	DEAE-cellulose, Sephadex G-100 columns	GC, FT-IR, ESI-MS, NMR, partial acid hydrolysis, reduction in uronic acid, methylation analysis, HPGPC	Rh:Ara:Xyl:Gal:GalA = 1.0:2.2:0.5:1.2:4.7	1.37×10^5	A (1→4)- linked galacturonic acid backbone occasionally interrupted by (1→2)-linked rhamnose; the side chains are attached to position 4 of the rhamnose units, including (1→3)-linked Ara, (1→3)-linked Gal, (1→3,6)-linked Gal, (1→4)-linked GalA, (1→2)-linked Rha, and (1→2,4)-linked Rha; the termini are Ara and Rha.	Immunomodulation activity	[52]]
26	*Lycium barbarum*	PLBP	Boiling water	Column chromatography	HPSEC	Unknown	1.21×10^5	Unknown	Antioxidant	[53]
27	*Lycium barbarum leaves*	LBLP5-A	Water	DEAE-cellulose column, GPC	HPGPC, GC, ESI-MS, IR, partial acid hydrolysis	Rha:Ara:Gal = 0.5:1.9:1.0	11.33×10^4	A backbone of (1→3)-linked Gal, which is partially substituted at its O-6 position. These branches, with Ara and Gal terminals, are assigned to (1→3)-linked Gal, (1→4)-linked Gal, (1→3)-linked Ara, (1→5)-linked Ara, and (1→2, 4)-linked Rha	Anti-oxidative	[54]
28	*Lycium barbarum*	LbGp1	Water	GPC	GC, HPGPC, methylation analysis, partial acid hydrolysis, ESI-MS	Ara:Gal = 5.6:1	4.91×10^4	A backbone of→6) Gal (1→linked Gal substituted at O-3 by Gal or Ara groups. The branches are composed of (1→3)-linked-Gal, (1→4)-linked-Gal, and (1→2)-linked-Ara	unknown	[55]

29	*Lycium barbarum*	LBP-3	Hot water	DEAE-Crystarose Fast Flow column	HPLC, FT-IR, NMR, GC-MS	Ara:Gal = 1.00:1.56	6.74×10^4	(1→3)-linked Ara; Ara is located at the terminal of the branches	Alzheimer's disease (AD)	[56]
30	*Leaves of Lycium ruthenicum*	LRLP4-A	Water	DEAE-52 cellulose column, Sephadex G-100 column	GC, GC-MS, NMR, ESI-MS	Rha:Ara:Gal = 1:10.3:5.3	1.35×10^6	A backbone of 1, 3-linked β-Gal, which is partially substituted at C-6; the branches contain 1, 5-linked α-Ara, 1, 6-linked β-Gal, 1, 3-linked α-Ara, and 1, 4-linked α-Ara	Immunological active	[57]
31	*Lycium ruthenicum Murr.*	LRP4-A	Hot water	Anion-exchange chromatography and gel-filtration chromatography	GC, HPGPC, HPLC, FT-IR, partial acid hydrolysis, methylation analysis, ESI-MS	Rha:Ara:Glu:Gal = 1:7.6:0.5:8.6	Unknown	A backbone consisting of (1→6)-linked β-galactopyranosyl residues substituted at O-3 by Arab or Gal residues; the branches consist of (1→3)-linked β-Ara α-Ara, (1→5)-linked β-Ara, (1→3)-linked β-Gal, and (1→2, 4)-linked α-Rha with a terminal α-Ara residue	unknown	[58]
32	*Lycium arabicum*	LAP	Hot water	Unknown	GC-MS, FT-IR, NMR	Rha:Ara:Gal:Glu:Man = 4.7:1.5:1:8.7:16.4:5.6	Unknown	A backbone of β-(1→6)-linked galactose partially substituted at the O-3 position; the branches are composed of (1→3)-linked-Gal, (1→3)-linked-Ara, (1→5)-linked-Ara, and (1→2,4)-linked-Rha; Arab, Gal, and Glu are located at the termini of the branches	Anti-Oxidative	[59]
33	*Lycium barbarum*	LbGp4		Sephadex GlOO column and CM-Sephadex	GC, IR	Rha:Ara:Gal = 0.05:1.33:1	21.48×10^5	A glucosidic backbone linked to some branches composed mainly of D-Man, along with α-D-Gal, β-D-Ara, and D-Man in lower proportions	Immuno-modulating	[60]
34	*Lycii fructus*	LFP-1	Hot water	Ion-exchange, gel-filtration chromatography	HPGPC, NMR	Rha:Ara:Xyl:Man:Glc:Gal:GlcA:GalA = 3.68:34.88:2.46:1.03:6.89:37.64:0.73:12.67	1.78×10^4	Unknown	Immuno-modulating	[61]
35	*Lycium barbarum*	LBP-IV	Water	DEAE-Sephadex A-25 column	HPGPC, UV, IR	Rha:Ara:Xyl:Glu:Gal = 1.61:3.82:3.44:7.54:1.0	4.18×10^5	Composed of highly branched arabinogalactans, homogalacturonan, and rhamnogalacturonan moieties	Neurodegenerative Parkinson's disease (PD)	[62]
								Both α- and β-anomeric configurations in this fraction	Immunostimulating activity	

36	*Lycium ruthenicum Murr.*	LRP-S2A	Water	DEAE-cellulose anion-exchange column	GC, NMR, FT-IR, HPGPC	Rha:Ara:Gal:Glc:GlcA = 1.00:2.07:0.57:2.59:4.33	2.65×10^6	A backbone consisting of 6-O-Me-α-(1→4)-D-GlcA, 2-O-acetyl-α-(1→4)-D-Glc, α-(1→2,4)-L-Rha, β-(1→3)-D-Gal, and α-(1→3,5)-L-Ara, with some branches consisting of 6-O-Me-α-(1→4)-D-GlcA and terminal α-L-Ara	unknown	[63]
37	*Lycium barbarum* L.	LBP-1	Water	Ion-exchange column	HPLC with pre-column derivative, GC, IR, GC = MS, NMR	Rha:Ara:Xy:Gal:Man:GalA = 1.00:7.85:0.37:0.65:3.01:8.16	2.25×10^6	(1,5)-linked Ara, (1,4)-linked GalA, -(1)-Man-(3,6)-linked terminated with -(1)-Man	Hypoglycemic activity	[64]
38	*Lycium barbarum* L.	LBP1A1-1	Water extraction with the assistance of enzymes	DEAE Sepharose™ Fast Flow, Sephacryl S-200 HR column	GC, FT-IR, HPGPC, partial acid hydrolysis, GC-MS, NMR	Ara:Gal:Glu:Rha = 47.8:49.8:1.4:1.2	4.50×10^4	Backbone of 1, 3-linked β-Gal, 1, 6-linked β-Gal, and 1, 4-linked α-Glc with branches substituted at the C-3 position of 1, 6-linked β-Gal or the C-6 position of 1, 3-linked β-Gal	Alzheimer's disease (AD)	[65]
39	*Lycium chinense Mill*	AGPs	Cold water	DEAE-cellulose column chromatography,	HPLC, GLC, GC-MS, NMR	Ara:Gal = 1:1	Unknown	Unknown	unknown	[67]
40	*Lycium barbarum* L.	LbGp3	Water	Sephadex G-100 column	GC, SEC, methylation analysis, partial acid hydrolysis, NMR	Ara:Gal = 1:1	9.25×10^4	All Gal in glycan is β-pyranose	Immunoactivity	[68]
41	*Lycium ruthenicum*	LRGP3	Water	GPC	HPGPC, GC, UV, FT-IR, ESI-MS, NMR	Rha:Ara:Gal = 1.0:14.9:10.4	7.56×10^4	A backbone of (1→3)-linked β-D-galactopyranosyl residues, many of which are substituted at the O-6 position by Gal or Ara groups; the branches are composed of (1→5)-linked Ara, (1→2)-linked Ara, (1→6)-linked Gal, (1→3)-linked Gal, and (1→2,4)-linked Rha; the major nonreducing termini are α-L-arabinofuranosyl residues	unknown	[69]
42	*Lycium barbarum* L.	LbGp2	Water	Gel filtration, Sephadex G-100 column	SE, GC, HPLC, CE, NMR, IR	Ara:Gal = 4:5	6.82×10^4	Backbone consisting of (1→6)-β-galactosyl residues, about fifty percent of which are substituted at C-3 by galactosyl or arabinosyl groups; the major nonreducing end is composed of Ara (1→	unknown	[112]

43	*Lycium barbarum* L.	LP5	Water	DEAE-52 cellulose column, Sephadex G-100 column	GC, FT-IR, NMR, APC	Rib:Xyl:Man:Gal:Glu:GlcUA = 1.0:3.38:4.60:2.48:1.75:2.59	2.50×10^5	Unknown	Immunomodulatory activity	[113]
44	*Lycium ruthenicum*	LRGP1	Hot water	Ion-exchange and gel-filtration chromatography	GC, ESI-MS, HPGPC, methylation analysis	Rha:Ara:Xyl: Man:Glu:Gal = 0.65:10.71:0.33:0.67:1:10.41	5.62×10^4	A branched polysaccharide rich in arabinose and galactose with a backbone composed of (1→3)-linked Gal; the branches are composed of (1→5)-linked Ara, (1→2)-linked Ara, (1→6)-linked Gal, (1→3)-linked Gal, (1→4)-linked Gal, and (1→2,4)-linked Rha; arabinose, xylose, mannose, and glucose are located at the terminal of the branches		[114]
45	*Lycium barbarum*	LBP-4a	Chloroform/methanol solvent	DEAE-cellulose column	Sephadex G-100 gel chromatography, HPLC, UV	Gal:Glu:Rha:Ara:Man:Xyl	338.67×10^2	Unknown	Treatment of renal damage	[115]
46	*Lycium ruthenicum*	LRGP3	Water	GPC	ESI-MS, cation-exchange resin, GC-MS	Ara:Gal:Rha = 16.8:1.4:1.0	1.31×10^4	Unknown	Immunological activity	[115]
47	*Lycium barbarum*	LBP1B-S-2	Water extraction with the assistance of enzymes	DEAE SepharoseTM Fast Flow and Sephacryl S-300 HR columns, anion-exchange chromatography	PMP pre-column derivation method, FT-IR, NMR, HPGPC	Rha:Ara:Gal:GlcA = 3.13:53.55:39.37:3.95	8.00×10^4	1, 3-linked β-D-Gal, 1, 6-linked β-D-Gal, and branches containing 1, 4-linked β-D-GlcA, T-linked β-D-Gal, 1, 6-linked β-D-Gal, T-linked α-L-Ara, T-linked α-L-Ara, 1, 5-linked α-L-Ara, and T-Linked β-L-Rha directly or indirectly attached to C-3 position of 1, 6-linked β-D-Gal or the C-6 position of 1, 3-linked β-D-Gal	Anti-angiogenic activity	[116]
48	*Lycium barbarum*	p-LBP	Water	Decoloration, ion-exchange chromatography, dialysis, and gel chromatography	HPLC, HPAEC, HPSEC, FT-IR, GC-MS, and NMR	Fuc:Rha:Ara:Gal:Glc:Xyl:GalA:GlcA = 1.00:6.44:54.84:22.98:4.05:2.95:136.98:3.35	6.40×10^4	Backbone→4-α-GalA-(1→, repeatedly; a partial region connected by→4-α-GalA-(1→and→2-α-Rha-(1→, alternatively; at the C-4 position of partial→2-α-Rha-(1→residues exist with branches formed by→4-β-Gal-(1→,→3-β-Gal-(1→or→5-α-Ara-(1→, whereas at the C-6 position of partial→3-β-Gal-(1→, secondary branches	unknown	[117]

49	*Lycium barbarum*	LBP	Distilled water	Macroporous resin	GC	Ara:Rha:Xyl:Man:Gal:Glu = 0.18:0.81:0.07:2.17:0.23:6.52	Unknown	formed by terminal-α-Ara, terminal-β-Gal, or→3-α-Ara-(1→	Potential prebiotic	[118]
50	*Lycium barbarum L*	LBWP	Hot water	DEAE-cellulose ion-exchange chromatography	Gel-filtration chromatography	Man:Rha:GalUA:Glc:Gal:Ara = 2.1:0.6:1.9:86.8:3.0:5.6	Unknown	Unknown	Anti-fatigue ativity, antioxidant ativity	[119]
51	*Lycium ruthenicum Murr*	LRWP	Hot water	DEAE-cellulose ion-exchange chromatography	Gel-filtration chromatography	Man:Rha:GalUA:Glc:Gal:Xyl:Ara = 1.6:1.2:5.7:82.3:2.9:0.7:6.2	Unknown	Unknown	Anti-fatigue activity, antioxidant ativity	[119]
52	*Lycium barbarum Linnaeus*		Hot water	HPSEC	GC, HPLC	Rha:Ara:xyl:Man:Glu:Gal = 0.3:2.7:0.3:0.2:2.7:0.9	Unknown	Unknown	unknown	[120]
53	*Lycium barbarum*	LBPF5	95% Ethanol	Ion-exchange chromatography	GC, HPSEC	Ara:Man:Xyl:Glu:Rha	5.30×10^4	Unknown	Antioxidant activities	[121]
54	*Lycium barbarum*	LBP-4a	Water	DEAE cellulose and Sephadex G-100 column chromatography	Paper chromatography, UV, IR, HPLC	Gal:Glu:Rha:Ara:Man:Xyl	338.67×10^2	Unknown	Ameliorate insulin resistance	[122]
55	*Lycium barbarum* L.	LbGp5B	Water	DEAE cellulose column	GC, EMS	Rha:Ara:Glc:Gal = 0.1:1:1.2:0.3	2.37×10^5	Unknown	unknown	[123]
56	*Lycium barbarum*	LBP	Water			Rha:Xyl:Ara:Fuc:Glu:Gal = 1:1.07:2.14:2.29:3.59:10.06	241.32×10^2	Unknown	Antioxidant	[124]
57	*Lycium ruthenicum Murr.*	LRP1-S2	Boiling water	DEAE-Sepharose, Sephacryl S-100 HR	HPGPC, NMR, HPLC, GC-MS	Gal:Ara:Rha: Glu:GlcA:Man:GalA = 46.2:40.2:5.0:4.0:2.3:1.7:0.5	1.70×10^5	Linear 1, 3-β-D-Gal, linear 1, 6-β-D-Gal, and 1, 3-β-D-Man; Ara residues are attached to C-3 of 1, 3, 6-β-D-Gal; T-linked β-D-Gal and T-linked α-L-Rha are linked to C-6 of partial 1, 3, 6-β-D-Gal; the branch containing T-linked β-D-Gal, 1, 4-α-D-GalA, and 1, 2- α-L-Rha is attached to C-6 of 1, 3, 6-β-D-Gal; in addition, β-D-GlcA, and 1, 4-β-D-Glc constitute another branch attaching to C-6 of 1, 3, 6- β-D-Gal	Anti-tumor	[125]

Table 5. Patent list of products containing LBP and their claimed pharmacological properties.

Application	Main Composition	Pharmacological Properties	Publish Number
Tobacco substitutes	LBP, Tobacco	Hypolipidemic, hypoglycemic, hepatoprotective, antioxidant, antiaging	CN101692930A
Candy	LBP, κ-Carrageenan, ι-Carrageenan, xylitol, maltitol, sodium citrate, citric acid solution	Improved immunity	CN108617835A
Organ preservation solution	LBP, citric acid-disodium hydrogen phosphate buffer, potassium aspartate, magnesium aspartate, sodium adenosine triphosphate, ginsenoside Rg1, insulin	Kidney-specific preservation solution	CN103609553B
Industrial products	LBP, *Lycium ruthenicum* polysaccharides, armillaria luteo-virens polysaccharides, *Nitraria tangutorum* polysaccharides	Antioxidation	CN104530251A
Nutritious food	LBP, calcium, glucosamine hydrochloride, chondroitin sulfate sodium, colostrum alkaline protein	Increased bone density	CN111248445A
Nutritious food	LBP, polyunsaturated fat, protein, vitamin A, vitamin C, vitamin D, vitamin E, reduced glutathione, zinc, selenium, lycopene, curcumin, tea polyphenols, Lepidium meyenii walp, ostreae	Improved the nutritional structure of patients with prostatitis, improved health	CN111642739A
Beverage	LBP, vitamin C, fructo-oligosaccharides, potassium sorbate	Improved immunity, lower blood fat, lower blood sugar	CN105410257A
Beverage	LBP, *Ziziphus jujuba* Mill, honey, sugar	Improved immunity, nourishing yin and tonifying kidney, delay aging, throttle the immune system, anticancer activity	CN102948838A
Beverage	LBP, glucoraphanin, sweetener, juice powder, inulin / Konjac powder	Improved immunity, nourishing yin and tonifying kidney, delay aging, throttle the immune system, anticancer activity	CN108294211A
Beverage	LBP extract (30–50%), fish peptide hydrolysate (15–30%), levocarnitine	Antifatigue	CN102342407B
Beverage	LBP, yogurt, fermentation bacteria, flavoring agent	Nutrition and health care	CN109601622A
Healthy food	LBP, edible calcium, wolf berry powder	Prevention of hyperlipidemia and atherosclerosis and improvement of immune function	CN101032332A
Healthy food	LBP, Wheat gluten	Improved human immunity, antiradiation activity, delayed aging	CN108497027A
Healthy food	*Lycium barbarum* extract, dextrin, menthol, magnesium stearate	Antiaging, antitumor, antifatigue, antihypoxia, blood-sugar-lowering, blood-pressure-lowering, and immunity-improving activity	CN103262974A
Healthy food	LBP, Garlicin	Enhanced vascular elasticity and blood-pressure-lowering	CN1919207B

		activity, reduced platelet aggregation and heart attacks	
Healthy food	LBP, Deer blood polypeptide	Relieves fatigue	CN111820314A
Healthy food	LBP, Glycyrrhizin, oleuropein	Memory improvement	CN110693026A
Healthy food	LBP, Mangiferin, naringin, oleuropein	Liver cirrhosis cure	CN111388495A
Healthy food	Protein peptide extract from stone money turtle, LBP, Anoectochilus roxburghii	Enhanced immunity	CN107136499A
Healthy food	LBP, laver	Memory improvement	CN103637268B
Healthy food	LBP, tartary buckwheat flour, soybean protein powder, oat bran powder, sarsasapogenin, Ganoderma lucidum polysaccharide, vitamins, edible calcium carbonate	Hypoglycemic, lipid-lowering foods	CN101564163B
Cosmetics	LBP, Tremella polysaccharide, Matee extract, Fullerene, urolic acid, nicotinamide, deionized water	Moisturizing and antiaging activities	CN111920707B
Cosmetics	LBP, Brazilian cocoa fruit extract	Whitening, moisturizing	CN107822998A
Pharmaceuticals	LBP, astaxanthin, taurine acid, curcumin, ginkgo flavonoids, tea polyphenol, vitamin B_{12}, vitamin E	Prevention or treatment of Alzheimer's disease	CN106420796B
Pharmaceuticals	LBP, glycine betaine, vitamins, multi-trace elements	Liver protection	CN112957403A
Pharmaceuticals	LBP, Polygonatum cyrtonema, Hua polysaccharide, *Codonopsis pilosula* (Franch.) Nannf. Polysaccharides, Ziziphus jujuba Mill. polysaccharides	Hypoglycemic activity	CN112755044A
Pharmaceuticals	LBP, mushroom polysaccharides, Ganoderma lucidum polysaccharide	Intestinal flora regulation	CN110302210A
Pharmaceuticals	LBP, naringin, glycyrrhizin, mangiferin, oleuropein	Insulin resistance syndrome and type 2 diabetes	CN111773238A
Pharmaceuticals	LBP, chrysanthemum extract	Xerophthalmia	CN105560586A
Pharmaceutical	LBP, Atractylodes polysaccharide, Astragalus polysaccharide, Fructuszingiberis nigri polysaccharide, Tuckahoe polysaccharide	Promotes growth, improves immunity	CN113350392A
Pharmaceuticals	LBP, deer blood dry powder	Relieves fatigue, strengthening yang	CN107890473A
Pharmaceuticals	LBP, GinsenosideRh2	Antifatigue, hypoxia tolerance, heat resistance, cold resistance	CN113633657A
Pharmaceuticals	*Lycium ruthenicum* polysaccharides, Allopurinol	Lowers uric acids	CN107441241B
Pharmaceuticals	LBP, corn starch	Prevention and treatment of chronic stress, post-traumatic stress disorder, improved cognitive function	CN102283858B
Pharmaceuticals	LBP, chlorogenic acid, soybean isoflavone	Relief of depression	CN108420826A
Pharmaceuticals	LBP, chlorogenic acid, soybean isoflavone	Relief of depression	CN108420826B
Pharmaceuticals	LBP, potassium sorbate	Dry eye	CN104274484B
Pharmaceuticals	*Lycium barbarum* extracts, dextrin, menthol, magnesium stearate	Antiaging, antitumor, antifatigue, antihypoxia,	CN103262974B

	hypoglycemic, and antihypertensive activities, enhanced immunity

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Abbreviations

HPGPC, high-performance gel permeation chromatography system; GPC, gel permeation chromatography; NMR, nuclear magnetic resonance; SEM, scanning electron microscopy; HPLC, high-performance liquid chromatography; HPAEC, high-performance anion-exchange chromatography; HPSEC, high-performance size-exclusion chromatography; GC, gas chromatography; SEC, size-exclusion chromatography; CE, capillary electrophoresis; GC-MS, gas chromatography-mass spectrometry; DEAE, diethylamino ethyl cellulose; ESI-MS, electrospray ionization mass spectrometry; APC, advanced polymer chromatography; IR, infrared; UV, ultraviolet; GLC, gas-liquid chromatography; ITHMT, integrated tandem hybrid membrane technology; FT-IR, Fourier transform infrared spectroscopy; UHPLC-QTRAP-MS/MS, ultra-high-performance liquid chromatography quadrupole trap tandem mass spectrometry; AFM, atomic force microscopy; EtOH, ethanol; EMS, electrospray mass spectrometer; Ara, arabinose; Gal, galactose; Glu, glucose; Rha, rhamnose; Man, mannose; GalA, galacturonic acid; Rib, ribose; Fuc, fucose; GlcA, glucuronic acid; LBP, *Lycium barbarum* polysaccharide.

References

1. Amagase, H.; Farnsworth, N.R. A review of botanical characteristics, phytochemistry, clinical relevance in efficacy and safety of *Lycium barbarum* fruit (Goji). *Food Res. Int.* **2011**, *44*, 1702–1717. https://doi.org/10.1016/j.foodres.2011.03.027.
2. Byambasuren, S.-E.; Wang, J.; Gaudel, G. Medicinal value of wolfberry (*Lycium barbarum* L.). *J. Med. Plants Stud* **2019**, *7*, 90–97.
3. Kindscher, K.; Long, Q.; Corbett, S.; Bosnak, K.; Loring, H.; Cohen, M.; Timmermann, B.N., The ethnobotany and eth-nopharmacology of wild tomatillos, Physalis longifolia Nutt., and related Physalis species: A review. *Econ. Bot.* **2012**, *66*, 298–310.
4. Ulbricht, C.; Bryan, J.K.; Costa, D.; Culwell, S.; Giese, N.; Isaac, R.; Nummy, K.; Pham, T.; Rapp, C.; Rusie, E.; et al. An Evidence-Based Systematic Review of Goji (*Lycium* spp.) by the Natural Standard Research Collaboration. *J. Diet Suppl.* **2015**, *12*, 184–240.
5. Amagase, H.; Nance, D.M., A randomized, double-blind, placebo-controlled, clinical study of the general effects of a standardized *Lycium barbarum* (Goji) Juice, GoChi. *J. Altern. Complement. Med.* **2008**, *14*, 403–412.
6. Potterat, O. Goji (*Lycium barbarum* and *L. chinense*): Phytochemistry, pharmacology and safety in the perspective of tradi-tional uses and recent popularity. *Planta Med.* **2010**, *76*, 7–19.
7. Seeram, N.P. Berry Fruits: Compositional Elements, Biochemical Activities, and the Impact of Their Intake on Human Health, Performance, and Disease. *J. Agric. Food Chem.* **2008**, *56*, 627–629. https://doi.org/10.1021/jf071988k.
8. Yang, Y.; Chang, Y.; Wu, Y.; Liu, H.; Liu, Q.; Kang, Z.; Wu, M.; Yin, H.; Duan, J. A homogeneous polysaccharide from *Lycium barbarum*: Structural characterizations, anti-obesity effects and impacts on gut microbiota. *Int. J. Biol. Macromol.* **2021**, *183*, 2074–2087. https://doi.org/10.1016/j.ijbiomac.2021.05.209.
9. Zhou, L.; Liao, W.; Zeng, H.; Yao, Y.; Chen, X.; Ding, K. A pectin from fruits of *Lycium barbarum* L. decreases β-amyloid peptide production through modulating APP processing. *Carbohydr. Polym.* **2018**, *201*, 65–74.

10. Zhu, J.; Liu, W.; Yu, J.; Zou, S.; Wang, J.; Yao, W.; Gao, X. Characterization and hypoglycemic effect of a polysaccharide extracted from the fruit of *Lycium barbarum* L. *Carbohydr. Polym.* **2013**, *98*, 8–16. https://doi.org/10.1016/j.carbpol.2013.04.057.
11. Zhang, Q.; Lv, X.; Wu, T.; Ma, Q.; Teng, A.; Zhang, Y.; Zhang, M. Composition of *Lycium barbarum* polysaccharides and their apoptosis-inducing effect on human hepatoma SMMC-7721 cells. *Food Nutr. Res.* **2015**, *59*, 28696.
12. Xu, J.; Wang, R.; Liu, J.; Cheng, H.; Peng, D.; Xing, L.; Shi, S.; Yu, N. Determination of monosaccharides in *Lycium* barba-rum fruit polysaccharide by an efficient UHPLC-QTRAP-MS/MS method. *Phytochem. Anal* .**2021**, *32*, 785-793.
13. Po, K.K.-T.; Leung, J.W.-H.; Chan, J.N.-M.; Fung, T.K.-H.; Sánchez-Vidaña, D.I.; Sin, E.L.-L.; So, K.-F.; Lau, B.W.-M.; Siu, A.M.-H. Protective effect of *Lycium barbarum* polysaccharides on dextromethorphan-induced mood impairment and neurogenesis suppression. *Brain Res. Bull.* **2017**, *134*, 10–17. https://doi.org/10.1016/j.brainresbull.2017.06.014.
14. Qian, L. Modulation of cytokine level and sperm quality of mice by *Lycium barbarum* polysaccharides. *Int. J. Biol. Macromol.* **2019**, *126*, 475–477. https://doi.org/10.1016/j.ijbiomac.2018.12.250.
15. Peng, Q.; Liu, H.; Shi, S.; Li, M. *Lycium ruthenicum* polysaccharide attenuates inflammation through inhibiting TLR4/NF-κB signaling pathway. *Int. J. Biol. Macromol.* **2014**, *67*, 330–335.
16. Wang, F.; Tipoe, G.L.; Yang, C.; Nanji, A.A.; Hao, X.; So, K.F.; Xiao, J., *Lycium barbarum* Polysaccharide Supplementation Improves Alcoholic Liver Injury in Female Mice by Inhibiting Stearoyl-CoA Desaturase 1. *Mol. Nutr. Food Res.* **2018**, *62*, e1800144.
17. Tang, H.-L.; Chen, C.; Wang, S.-K.; Sun, G.-J. Biochemical analysis and hypoglycemic activity of a polysaccharide isolated from the fruit of *Lycium barbarum* L. *Int. J. Biol. Macromol.* **2015**, *77*, 235–242. https://doi.org/10.1016/j.ijbiomac.2015.03.026.
18. Miller, J.S.; Kamath, A.; Damashek, J.; Levin, R.A. Out of America to Africa or Asia: Inference of Dispersal Histories Using Nuclear and Plastid DNA and the S-RNase Self-incompatibility Locus. *Mol. Biol. Evol.* **2010**, *28*, 793–801. https://doi.org/10.1093/molbev/msq253.
19. Wu, C.Y.; Li, X.W. *Flora Reipublicae Popularis Sinicae*; Flora of China; Science Press: Beijing, China, 1977; Volume 66.
20. Zeng, S.; Liu, Y.; Wu, M.; Liu, X.; Shen, X.; Liu, C.; Wang, Y. Identification and Validation of Reference Genes for Quantitative Real-Time PCR Normalization and Its Applications in *Lycium*. *PLoS ONE* **2014**, *9*, e97039. https://doi.org/10.1371/journal.pone.0097039.
21. Zheng, J.; Ding, C.; Wang, L.; Li, G.; Shi, J.; Li, H.; Wang, H.; Suo, Y. Anthocyanins composition and antioxidant activity of wild *Lycium ruthenicum* Murr. from Qinghai-Tibet Plateau. *Food Chem.* **2010**, *126*, 859–865. https://doi.org/10.1016/j.foodchem.2010.11.052.
22. Wang, H.; Li, J.; Tao, W.; Zhang, X.; Gao, X.; Yong, J.; Zhao, J.; Zhang, L.; Li, Y.; Duan, J.-A. *Lycium ruthenicum* studies: Molecular biology, Phytochemistry and pharmacology. *Food Chem.* **2018**, *240*, 759–766. https://doi.org/10.1016/j.foodchem.2017.08.026.
23. Fukuda, T.; Yokoyama, J.; Ohashi, H. Phylogeny and biogeography of the genus *Lycium* (Solanaceae): Inferences from chloroplast DNA sequences. *Mol. Phylogenet. Evol.* **2001**, *19*, 246–258.
24. Levin, R.A.; Miller, J.S. Relationships within tribe Lycieae (Solanaceae): Paraphyly of *Lycium* and multiple origins of gender dimorphism. *Am. J. Bot.* **2005**, *92*, 2044–2053. https://doi.org/10.3732/ajb.92.12.2044.
25. Gao, Y.; Wei, Y.; Wang, Y.; Gao, F.; Chen, Z. *Lycium barbarum*: A Traditional Chinese Herb and A Promising Anti-Aging Agent. *Aging Dis.* **2017**, *8*, 778–791. https://doi.org/10.14336/ad.2017.0725.
26. Gulen, T.; Bayram, K.; Nazan, C.; Ahmet, G. Free radical scavenging activity and phenolic content of edible wild fruits from Kazdagi (Ida Mountains), Turkey. *J. Med. Plants Res.* **2012**, *6*, 4989–4994.
27. Dhar, P.; Tayade, A.; Ballabh, B.; Chaurasia, O.; Bhatt, R.; Srivastava, R. *Lycium ruthenicum* Murray: A less-explored but high-value medicinal plant from Trans-Himalayan cold deserts of Ladakh, India. *Plant Arch.* **2011**, *11*, 583–586.
28. Ouhaddou, H.; Boubaker, H.; Msanda, F.; El Mousadik, A. An ethnobotanical study of medicinal plants of the Agadir Ida Ou Tanane province (southwest Morocco). *J. Appl. Biosci.* **2015**, *84*, 7707. https://doi.org/10.4314/jab.v84i1.5.
29. Trillo, C.; Arias Toledo, B.; Galetto, L.; Colantonio, S. Persistence of the use of medicinal plants in rural communities of the Western Arid Chaco [Córdoba, Argentina]. *Open Complement. Med. J.* **2010**, *2*, 80–89.
30. Toledo, B.A.; Trillo, C.; Grilli, M.; Colantonio, S.; Galetto, L. Relationships between Land-Use Types and Plant Species Used by Traditional Ethno-Medical System. *Eur. J. Med. Plants* **2014**, *4*, 998–1021. https://doi.org/10.9734/ejmp/2014/6570.
31. Hao, W.; Wang, S.F.; Zhao, J.; Li, S.P., Effects of extraction methods on immunology activity and chemical profiles of Lyci-um barbarum polysaccharides. *J. Pharm. Biomed. Anal.* **2020**, *185*, 113219.
32. Luo, Q.; Yan, J.; Zhang, S. Isolation and purification of *Lycium barbarum* polysaccharides and its antifatigue effect. *J. Hyg. Res.* **2000**, *29*, 115–117.
33. Muatasim, R.; Ma, H.; Yang, X. Effect of multimode ultrasound assisted extraction on the yield of crude polysaccharides from *Lycium barbarum* (Goji). *Food Sci. Technol.* **2018**, *38*, 160–166. https://doi.org/10.1590/1678-457x.14417.
34. Zhu, M.; Jinggang, M.; ChangSheng, H.; Haiping, X.; Ning, M.; Caijiao, W. Extraction, characterization of polysaccharides from *Lycium barbarum* and its effect on bone gene expression in rats. *Carbohydr. Polym.* **2010**, *80*, 672–676. https://doi.org/10.1016/j.carbpol.2009.11.038.
35. Liu, J.; Pu, Q.; Qiu, H.; Di, D. Polysaccharides isolated from *Lycium barbarum* L. by integrated tandem hybrid membrane technology exert antioxidant activities in mitochondria. *Ind. Crop. Prod.* **2021**, *168*, 113547. https://doi.org/10.1016/j.indcrop.2021.113547.
36. Yang, R.-f.; Zhao, C.; Chen, X.; Chan, S.-w.; Wu, J.-y. Chemical properties and bioactivities of Goji (*Lycium barbarum*) polysaccharides extracted by different methods. *J. Funct. Foods* **2015**, *17*, 903–909.

37. Lin, C.; Wang, C.; Chang, S.; Inbaraj, B.S.; Chen, B. Antioxidative activity of polysaccharide fractions isolated from *Lycium barbarum* Linnaeus. *Int. J. Biol. Macromol.* **2009**, *45*, 146–151. https://doi.org/10.1016/j.ijbiomac.2009.04.014.
38. Chao, Z.; Ri-Fu, Y.; Tai-Qiu, Q. Ultrasound-enhanced subcritical water extraction of polysaccharides from *Lycium barbarum* L.. *Sep. Purif. Technol.* **2013**, *120*, 141–147. https://doi.org/10.1016/j.seppur.2013.09.044.
39. Wu, D.-T.; Cheong, K.-L.; Deng, Y.; Lin, P.-C.; Wei, F.; Lv, X.-J.; Long, Z.-R.; Zhao, J.; Ma, S.-C.; Li, S.-P. Characterization and comparison of polysaccharides from *Lycium barbarum* in China using saccharide mapping based on PACE and HPTLC. *Carbohydr. Polym.* **2015**, *134*, 12–19. https://doi.org/10.1016/j.carbpol.2015.07.052.
40. Zhang, J.; Jia, S.; Liu, Y.; Wu, S.; Ran, J. Optimization of enzyme-assisted extraction of the *Lycium barbarum* polysaccharides using response surface methodology. *Carbohydr. Polym.* **2011**, *86*, 1089–1092. https://doi.org/10.1016/j.carbpol.2011.06.027.
41. Tang, R.; Chen, X.; Dang, T.; Deng, Y.; Zou, Z.; Liu, Q.; Gong, G.; Song, S.; Ma, F.; Huang, L.; et al. *Lycium barbarum* polysaccharides extend the mean lifespan of *Drosophila melanogaster*. *Food Funct.* **2019**, *10*, 4231–4241. https://doi.org/10.1039/c8fo01751d.
42. Zhang, M.; Tang, X.; Wang, F.; Zhang, Q.; Zhang, Z. Characterization of *Lycium barbarum* polysaccharide and its effect on human hepatoma cells. *Int. J. Biol. Macromol.* **2013**, *61*, 270–275. https://doi.org/10.1016/j.ijbiomac.2013.06.031.
43. Yuan, Y.; Wang, Y.-B.; Jiang, Y.; Prasad, K.N.; Yang, J.; Qu, H.; Wang, Y.; Jia, Y.; Mo, H.; Yang, B. Structure identification of a polysaccharide purified from *Lycium* barbarium fruit. *Int. J. Biol. Macromol.* **2015**, *82*, 696–701. https://doi.org/10.1016/j.ijbiomac.2015.10.069.
44. Gong, G.; Dang, T.; Deng, Y.; Han, J.; Zou, Z.; Jing, S.; Zhang, Y.; Liu, Q.; Huang, L.; Wang, Z. Physicochemical properties and biological activities of polysaccharides from *Lycium barbarum* prepared by fractional precipitation. *Int. J. Biol. Macromol.* **2018**, *109*, 611–618. https://doi.org/10.1016/j.ijbiomac.2017.12.017.
45. Wang, Y.; Sun, M.; Jin, H.; Yang, J.; Kang, S.; Liu, Y.; Yang, S.; Ma, S.; Ni, J. Effects of *Lycium barbarum* Polysaccharides on Immunity and the Gut Microbiota in Cyclophosphamide-Induced Immunosuppressed Mice. *Front. Microbiol.* **2021**, *12*. https://doi.org/10.3389/fmicb.2021.701566.
46. Redgwell, R.J.; Curti, D.; Wang, J.; Dobruchowska, J.M.; Gerwig, G.J.; Kamerling, J.P.; Bucheli, P., Cell wall polysaccha-rides of Chinese Wolfberry (*Lycium barbarum*): Part 2. Characterisation of arabinogalactan-proteins. *Carbohydr. Polym.* **2011**, *84*, 1075–1083.
47. Zhang, S.; He, F.; Chen, X.; Ding, K. Isolation and structural characterization of a pectin from *Lycium ruthenicum* Murr and its anti-pancreatic ductal adenocarcinoma cell activity. *Carbohydr. Polym.* **2019**, *223*, 115104. https://doi.org/10.1016/j.carbpol.2019.115104.
48. Wu, H.-T.; He, X.-J.; Hong, Y.-K.; Ma, T.; Xu, Y.-P.; Li, H.-H. Chemical characterization of *Lycium barbarum* polysaccharides and its inhibition against liver oxidative injury of high-fat mice. *Int. J. Biol. Macromol.* **2010**, *46*, 540–543. https://doi.org/10.1016/j.ijbiomac.2010.02.010.
49. Lu, S.-P.; Zhao, P.-T. Chemical characterization of *Lycium barbarum* polysaccharides and their reducing myocardial injury in ischemia/reperfusion of rat heart. *Int. J. Biol. Macromol.* **2010**, *47*, 681–684. https://doi.org/10.1016/j.ijbiomac.2010.08.016.
50. Yao, R.; Huang, C.; Chen, X.; Yin, Z.; Fu, Y.; Li, L.; Feng, B.; Song, X.; He, C.; Yue, G.; et al. Two complement fixing pectic polysaccharides from pedicel of *Lycium barbarum* L. promote cellular antioxidant defense. *Int. J. Biol. Macromol.* **2018**, *112*, 356–363. https://doi.org/10.1016/j.ijbiomac.2018.01.207.
51. Huang, C.; Yao, R.; Zhu, Z.; Pang, D.; Cao, X.; Feng, B.; Paulsen, B.S.; Li, L.; Yin, Z.; Chen, X.; et al. A pectic polysaccharide from water decoction of Xinjiang *Lycium barbarum* fruit protects against in-testinal endoplasmic reticulum stress. *Int. J. Biol. Macromol.* **2019**, *130*, 508–514.
52. Peng, Q.; Xu, Q.; Yin, H.; Huang, L.; Du, Y. Characterization of an immunologically active pectin from the fruits of *Lycium ruthenicum*. *Int. J. Biol. Macromol.* **2013**, *64*, 69–75. https://doi.org/10.1016/j.ijbiomac.2013.11.030.
53. Liang, B.; Jin, M.; Liu, H. Water-soluble polysaccharide from dried *Lycium barbarum* fruits: Isolation, structural features and antioxidant activity. *Carbohydr. Polym.* **2011**, *83*, 1947–1951. https://doi.org/10.1016/j.carbpol.2010.10.066.
54. Gong, G.; Fan, J.; Sun, Y.; Wu, Y.; Liu, Y.; Sun, W.; Zhang, Y.; Wang, Z. Isolation, structural characterization, and antioxidativity of polysaccharide LBLP5-A from *Lycium barbarum* leaves. *Process. Biochem.* **2016**, *51*, 314–324.
55. Wang, Z.; Liu, Y.; Sun, Y.; Mou, Q.; Wang, B.; Zhang, Y.; Huang, L. Structural characterization of LbGp1 from the fruits of *Lycium barbarum* L.. *Food Chem.* **2014**, *159*, 137–142. https://doi.org/10.1016/j.foodchem.2014.02.171.
56. Wu, J.; Chen, T.; Wan, F.; Wang, J.; Li, X.; Li, W.; Ma, L. Structural characterization of a polysaccharide from *Lycium* bar-barum and its neuroprotective effect against β-amyloid peptide neurotoxicity. *Int. J. Biol. Macromol.* **2021**, *176*, 352–363.
57. Liu, Y.; Gong, G.; Sun, Y.; Gu, X.; Huang, L.; Wang, Z. Isolation, structural characterization, and immunological activity of a polysaccharide LRLP4-A from the leaves of *Lycium ruthenicum*. *J. Carbohydr. Chem.* **2016**, *35*, 40–56.
58. Lv, X.; Wang, C.; Cheng, Y.; Huang, L.; Wang, Z. Isolation and structural characterization of a polysaccharide LRP4-A from *Lycium ruthenicum* Murr.. *Carbohydr. Res.* **2012**, *365*, 20–25. https://doi.org/10.1016/j.carres.2012.10.013.
59. Fakhfakh, J.; Athmouni, K.; Mallek-Fakhfakh, H.; Ayedi, H.; Allouche, N. Polysaccharide from *Lycium* arabicum: Structural Features, in Vitro Antioxidant Activities and Protective Effect against Oxidative Damage in Human Erythrocytes. *Chem. Biodivers.* **2020**, *17*, e2000614.
60. Peng, X.-M.; Huang, L.-J.; Qi, C.-H.; Zhang, Y.-X.; Tian, G.-Y. Studies on chemistry and immuno- modulating mechanism of a glycoconjugate from *Lycium barbarum* L.. *Chin. J. Chem.* **2010**, *19*, 1190–1197. https://doi.org/10.1002/cjoc.20010191206.

61. Zhang, F.; Zhang, X.; Guo, S.; Cao, F.; Zhang, X.; Wang, Y.; Liu, J.; Qian, B.; Yan, Y.; Chen, P.; et al. An acidic heteropolysaccharide from Lycii fructus: Purification, characterization, neurotrophic and neuroprotective activities in vitro. *Carbohydr. Polym.* **2020**, *249*, 116894. https://doi.org/10.1016/j.carbpol.2020.116894.
62. Liu, H.; Fan, Y.; Wang, W.; Liu, N.; Zhang, H.; Zhu, Z.; Liu, A. Polysaccharides from *Lycium barbarum* leaves: Isolation, characterization and splenocyte proliferation activity. *Int. J. Biol. Macromol.* **2012**, *51*, 417–422. https://doi.org/10.1016/j.ijbiomac.2012.05.025.
63. Wang, S.Q.; Liu, B.; Liu, S.; Xie, S.Z.; Pan, L.H.; Zha, X.Q.; Li, Q.M.; Luo, J.P., Structural features of an acidic polysaccha-ride with the potential of promoting osteoblast differentiation from *Lycium ruthenicum* Murr. *Nat. Prod. Res.* **2020**, *34*, 2249–2254.
64. Zou, S.; Zhang, X.; Yao, W.; Niu, Y.; Gao, X. Structure characterization and hypoglycemic activity of a polysaccharide iso-lated from the fruit of *Lycium barbarum* L. *Carbohydr. Polym.* **2010**, *80*, 1161–1167.
65. Zhou, L.; Liao, W.; Chen, X.; Yue, H.; Li, S.; Ding, K. An arabinogalactan from fruits of *Lycium barbarum* L. inhibits production and aggregation of Aβ42. *Carbohydr. Polym.* **2018**, *195*, 643–651. https://doi.org/10.1016/j.carbpol.2018.05.022.
66. Peng, Q.; Liu, H.; Lei, H.; Wang, X. Relationship between structure and immunological activity of an arabinogalactan from *Lycium ruthenicum*. *Food Chem.* **2015**, *194*, 595–600. https://doi.org/10.1016/j.foodchem.2015.08.087.
67. Qin, X.; Yamauchi, R.; Aizawa, K.; Inakuma, T.; Kato, K. Structural features of arabinogalactan–proteins from the fruit of *Lycium chinense* Mill.. *Carbohydr. Res.* **2001**, *333*, 79–85. https://doi.org/10.1016/s0008-6215(01)00118-5.
68. Huang, L.J.; Tian, G.Y.; Ji, G.Z. Structure Elucidation of Glycan of Glycoconjugate LbGp3 Isolated from the Fruit of *Lycium barbarum* L. *J. Asian Nat. Prod. Res.* **1999**, *1*, 259–267. https://doi.org/10.1080/10286029908039874.
69. Peng, Q.; Song, J.; Lv, X.; Wang, Z.; Huang, L.; Du, Y. Structural Characterization of an Arabinogalactan-Protein from the Fruits of *Lycium ruthenicum*. *J. Agric. Food Chem.* **2012**, *60*, 9424–9429. https://doi.org/10.1021/jf302619c.
70. Vander Borght, M.; Wyns, C. Fertility and infertility: Definition and epidemiology. *Clin. Biochem.* **2018**, *62*, 2–10. https://doi.org/10.1016/j.clinbiochem.2018.03.012.
71. Inhorn, M.C.; Patrizio, P. Infertility around the globe: New thinking on gender, reproductive technologies and global movements in the 21st century. *Hum. Reprod. Update* **2015**, *21*, 411–426.
72. Luo, Q.; Li, Z.; Huang, X.; Yan, J.; Zhang, S.; Cai, Y.-Z. *Lycium barbarum* polysaccharides: Protective effects against heat-induced damage of rat testes and H2O2-induced DNA damage in mouse testicular cells and beneficial effect on sexual behavior and reproductive function of hemicastrated rats. *Life Sci.* **2006**, *79*, 613–621. https://doi.org/10.1016/j.lfs.2006.02.012.
73. Yang, L.; Lei, L.; Zhao, Q.; Gao, Z.; Xu, X. *Lycium barbarum* polysaccharide improves the development of mouse oocytes vitrified at the germinal vesicle stage. *Cryobiology* **2018**, *85*, 7–11. https://doi.org/10.1016/j.cryobiol.2018.10.265.
74. Lau, B.W.; Lee, J.C.; Li, Y.; Fung, S.M.; Sang, Y.H.; Shen, J.; Chang, R.C.; So, K.F., Polysaccharides from wolfberry pre-vents corticosterone-induced inhibition of sexual behavior and increases neurogenesis. *PLoS ONE* **2012**, *7*, e33374.
75. Luo, Q.; Cui, X.; Yan, J.; Yang, M.; Liu, J.; Jiang, Y.; Li, J.; Zhou, Y. Antagonistic effects of *Lycium barbarum* polysaccharides on the impaired reproductive system of male rats induced by local subchronic exposure to 60Co-γ irradiation. *Phytother. Res.* **2011**, *25*, 694–701.
76. Yang, D.-M.; Zhang, J.-Q.; Fei, Y.-F. *Lycium barbarum* polysaccharide attenuates chemotherapy-induced ovarian injury by reducing oxidative stress. *J. Obstet. Gynaecol. Res.* **2017**, *43*, 1621–1628. https://doi.org/10.1111/jog.13416.
77. Tang, Z.-Y.; Sun, D.; Qian, C.-W.; Chen, Q.; Duan, S.-S.; Sun, S.-Y. *Lycium barbarum* polysaccharide alleviates nonylphenol exposure induced testicular injury in juvenile zebrafish. *Int. J. Biol. Macromol.* **2017**, *104*, 618–623. https://doi.org/10.1016/j.ijbiomac.2017.06.035.
78. Yan, B.; Zhang, X.; Wang, J.; Jia, S.; Zhou, Y.; Tian, J.; Wang, H.; Tang, Y. Inhibitory effect of *Lycium barbarum* polysaccha-ride on sperm damage during cryopreservation. *Exp. Ther. Med.* **2020**, *20*, 3051–3063.
79. Hu, S.; Liu, D.; Liu, S.; Li, C.; Guo, J. *Lycium barbarum* Polysaccharide Ameliorates Heat-Stress-Induced Impairment of Pri-mary Sertoli Cells and the Blood-Testis Barrier in Rat via Androgen Receptor and Akt Phosphorylation. *Evid. Based Complement Alternat. Med.* **2021**, *2021*, 5574202.
80. Yang, F.-L.; Wei, Y.-X.; Liao, B.-Y.; Wei, G.-J.; Qin, H.-M.; Pang, X.-X.; Wang, J.-L. Effects of *Lycium barbarum* Polysaccharide on Endoplasmic Reticulum Stress and Oxidative Stress in Obese Mice. *Front. Pharmacol.* **2020**, *11*. https://doi.org/10.3389/fphar.2020.00742.
81. Weiss, U. Inflammation. *Nature* **2008**, *454*, 427.
82. de Souza Zanchet, M.Z.; Nardi, G.M.; de Oliveira Souza Bratti, L.; Filippin-Monteiro, F.B.; Locatelli, C. *Lycium barbarum* Reduces Abdominal Fat and Improves Lipid Profile and Antioxidant Status in Patients with Metabolic Syndrome. *Oxidative Med. Cell. Longev.* **2017**, *2017*, 9763210. https://doi.org/10.1155/2017/9763210.
83. Chang, J.-S.; Lee, Y.-J.; Wilkie, D.A.; Lin, C.-T. The Neuroprotective and antioxidative effects of submicron and blended *Lycium barbarum* in experimental retinal degeneration in rats. *J. Veter.-Med. Sci.* **2018**, *80*, 1108–1115. https://doi.org/10.1292/jvms.17-0623.
84. Rjeibi, I.; Feriani, A.; Ben Saad, A.; Ncib, S.; Sdayria, J.; Hfaiedh, N.; Allagui, M.S. *Lycium* europaeum Linn as a source of polysaccharide with in vitro antioxidant activities and in vivo anti-inflammatory and hepato-nephroprotective potentials. *J. Ethnopharmacol.* **2018**, *225*, 116–127. https://doi.org/10.1016/j.jep.2018.06.036.
85. Liu, Y.; Lv, J.; Yang, B.; Liu, F.; Tian, Z.; Cai, Y.; Yang, D.; Ouyang, J.; Sun, F.; Shi, Y.; et al. *Lycium barbarum* polysaccha-ride attenuates type II collagen-induced arthritis in mice. *Int. J. Biol. Macromol.* **2015**, *78*, 318–323.

86. Ni, H.; Wang, G.; Xu, Y.; Gu, X.; Sun, C.; Li, H. RETRACTED ARTICLE: *Lycium barbarum* polysaccharide alleviates IL-1β-evoked chondrogenic ATDC5 cell inflammatory injury through mediation of microRNA-124. *Artif. Cells Nanomed. Biotechnol.* **2019**, *47*, 4046–4052. https://doi.org/10.1080/21691401.2019.1673765.
87. Wu, Q.; Liu, L.T.; Wang, X.Y.; Lang, Z.F.; Meng, X.H.; Guo, S.F.; Yan, B.; Zhan, T.; Zheng, H.Z.; Wang, H.W., *Lycium barbarum* polysaccharides attenuate kidney injury in septic rats by regulating Keap1-Nrf2/ARE pathway. *Life Sci.* **2020**, *242*, 117240.
88. Cao, C.; Zhu, B.; Liu, Z.; Wang, X.; Ai, C.; Gong, G.; Hu, M.; Huang, L.; Song, S. An arabinogalactan from *Lycium barbarum* attenuates DSS-induced chronic colitis in C57BL/6J mice associated with the modulation of intestinal barrier function and gut microbiota. *Food Funct.* **2021**, *12*, 9829–9843. https://doi.org/10.1039/d1fo01200b.
89. Li, W.; Gao, M.; Han, T. *Lycium barbarum* polysaccharides ameliorate intestinal barrier dysfunction and inflammation through the MLCK-MLC signaling pathway in Caco-2 cells. *Food Funct.* **2020**, *11*, 3741–3748. https://doi.org/10.1039/d0fo00030b.
90. Ding, Y.; Yan, Y.; Chen, D.; Ran, L.; Mi, J.; Lu, L.; Jing, B.; Li, X.; Zeng, X.; Cao, Y. Modulating effects of polysaccharides from the fruits of *Lycium barbarum* on the immune response and gut microbiota in cyclophosphamide-treated mice. *Food Funct.* **2019**, *10*, 3671–3683.
91. Ding, Y.; Yan, Y.; Peng, Y.; Chen, D.; Mi, J.; Lu, L.; Luo, Q.; Li, X.; Zeng, X.; Cao, Y. In vitro digestion under simulated saliva, gastric and small intestinal conditions and fermentation by human gut microbiota of polysaccharides from the fruits of *Lycium barbarum*. *Int. J. Biol. Macromol.* **2018**, *125*, 751–760. https://doi.org/10.1016/j.ijbiomac.2018.12.081.
92. Zhu, W.; Zhou, S.; Liu, J.; McLean, R.J.; Chu, W. Prebiotic, immuno-stimulating and gut microbiota-modulating effects of *Lycium barbarum* polysaccharide. *Biomed. Pharmacother.* **2019**, *121*, 109591. https://doi.org/10.1016/j.biopha.2019.109591.
93. Xu, T.; Liu, R.; Lu, X.; Wu, X.; Heneberg, P.; Mao, Y.; Jiang, Q.; Loor, J.; Yang, Z. *Lycium barbarum* polysaccharides alleviate LPS-induced inflammatory responses through PPARγ/MAPK/NF-κB pathway in bovine mammary epithelial cells. *J. Anim. Sci.* **2022**, *100*, skab345.
94. Zhao, R.; Master, B.Q.; Master, B.M.; Cai, Y. Improving Activity of *Lycium barbarum*. Polysaccharide on Depressive Mice Induced by Reserpine. *Iran. J. Pharm. Res.* **2019,** *18*, 1556–1565.
95. Karakaş, F.P.; Coşkun, H.; Soytürk, H.; Bozat, B.G. Anxiolytic, antioxidant, and neuroprotective effects of goji berry polysaccharides in ovariectomized rats: Experimental evidence from behavioral, biochemical, and immunohistochemical analyses. *Turk. J. Biol.* **2020**, *44*, 238–251. https://doi.org/10.3906/biy-2003-8.
96. Zhou, Y.; Duan, Y.; Huang, S.; Zhou, X.; Zhou, L.; Hu, T.; Yang, Y.; Lu, J.; Ding, K.; Guo, D.; et al. Polysaccharides from *Lycium barbarum* ameliorate amyloid pathology and cognitive functions in APP/PS1 transgenic mice. *Int. J. Biol. Macromol.* **2019**, *144*, 1004–1012. https://doi.org/10.1016/j.ijbiomac.2019.09.177.
97. Zhou, J.; Li, H.; Wang, F.; Wang, H.; Chai, R.; Li, J.; Jia, L.; Wang, K.; Zhang, P.; Zhu, L.; et al. Effects of 2,4-dichlorophenoxyacetic acid on the expression of NLRP3 inflammasome and autophagy-related proteins as well as the protective effect of *Lycium barbarum* polysaccharide in neonatal rats. *Environ. Toxicol.* **2021**, *36*, 2454–2466. https://doi.org/10.1002/tox.23358.
98. Lin, S.; Al-Wraikat, M.; Niu, L.; Zhou, F.; Zhang, Y.; Wang, M.; Ren, J.; Fan, J.; Zhang, B.; Wang, L. Degradation enhances the anticoagulant and antiplatelet activities of polysaccharides from *Lycium barbarum* L. leaves. *Int. J. Biol. Macromol.* **2019**, *133*, 674–682. https://doi.org/10.1016/j.ijbiomac.2019.04.147.
99. Zhang, Z.; Liu, H.; Yu, B.; Tao, H.; Li, J.; Wu, Z.; Liu, G.; Yuan, C.; Guo, L.; Cui, B. *Lycium barbarum* polysaccharide attenuates myocardial injury in high-fat diet-fed mice through manipulating the gut microbiome and fecal metabolome. *Food Res. Int.* **2020**, *138*, 109778. https://doi.org/10.1016/j.foodres.2020.109778.
100. Hsieh, S.Y.; Lian, Y.Z.; Lin, I.H.; Yang, Y.C.; Tinkov, A.A.; Skalny, A.V.; Chao, J.C., Combined *Lycium* babarum poly-saccharides and C-phycocyanin increase gastric Bifidobacterium relative abundance and protect against gastric ulcer caused by aspirin in rats. *Nutr. Metab.* **2021**, *18*, 4.
101. Gao, L.-L.; Ma, J.-M.; Fan, Y.-N.; Zhang, Y.-N.; Ge, R.; Tao, X.-J.; Zhang, M.-W.; Gao, Q.-H.; Yang, J.-J. *Lycium barbarum* polysaccharide combined with aerobic exercise ameliorated nonalcoholic fatty liver disease through restoring gut microbiota, intestinal barrier and inhibiting hepatic inflammation. *Int. J. Biol. Macromol.* **2021**, *183*, 1379–1392. https://doi.org/10.1016/j.ijbiomac.2021.05.066.
102. Gao, L.L.; Li, Y.X.; Ma, J.M.; Guo, Y.Q.; Li, L.; Gao, Q.H.; Fan, Y.N.; Zhang, M.W.; Tao, X.J.; Yu, J.Q.; et al. Effect of *Lycium barbarum* polysaccharide supplementation in non-alcoholic fatty liver disease patients: Study protocol for a ran-domized controlled trial. *Trials* **2021**, *22*, 566.
103. Wong, H.L.; Hung, L.T.; Kwok, S.S.; Bu, Y.; Lin, Y.; Shum, H.C.; Wang, H.; Lo, A.C.Y.; Yam, G.H.F.; Jhanji, V.; et al. The anti-scarring role of *Lycium barbarum* polysaccharide on cornea epithelial-stromal injury. *Exp. Eye Res.* **2021**, *211*, 108747. https://doi.org/10.1016/j.exer.2021.108747.
104. Guariguata, L.; Whiting, D.R.; Hambleton, I.; Beagley, J.; Linnenkamp, U.; Shaw, J.E., Global estimates of diabetes preva-lence for 2013 and projections for 2035. *Diabetes Res. Clin. Pract.* **2014**, *103*, 137–149.
105. Zheng, Y.; Ley, S.H.; Hu, F.B. Global aetiology and epidemiology of type 2 diabetes mellitus and its complications. *Nat. Rev. Endocrinol.* **2018**, *14*, 88–98. https://doi.org/10.1038/nrendo.2017.151.
106. Yao, Q.; Zhou, Y.; Yang, Y.; Cai, L.; Xu, L.; Han, X.; Guo, Y.; Li, P.A., Activation of Sirtuin1 by lyceum barbarum polysac-charides in protection against diabetic cataract. *J. Ethnopharmacol.* **2020**, *261*, 113165.
107. Zhu, Y.; Zhao, Q.; Jiang, Y. *Lycium barbarum* polysaccharides attenuates high glucose-induced diabetic retinal angiogenesis by rescuing the expression of miR-15a-5p in RF/6A cells. *J. Ethnopharmacol.* **2021**, *283*, 114652. https://doi.org/10.1016/j.jep.2021.114652.

108. Liu, W.J.; Jiang, H.F.; Rehman, F.U.; Zhang, J.W.; Chang, Y.; Jing, L.; Zhang, J.Z., *Lycium barbarum* Polysaccharides De-crease Hyperglycemia-Aggravated Ischemic Brain Injury through Maintaining Mitochondrial Fission and Fusion Balance. *Int. J. Biol. Sci.* **2017**, *13*, 901–910.
109. Amagase, H. Comparison of *Lycium barbarum*-containing Liquid Dietary Supplements to Caffeinated Beverages on Ener-gy/Caloric Metabolism Activity and Salivary Adrenocortical Hormone levels in Healthy Human Adults. *FASEB J.* **2010**, *24*, 540.13.
110. Liu, G.; Yang, X.; Zhang, J.; Liang, L.; Miao, F.; Ji, T.; Ye, Z.; Chu, M.; Ren, J.; Xu, X. Synthesis, stability and anti-fatigue ac-tivity of selenium nanoparticles stabilized by *Lycium barbarum* polysaccharides. *Int. J. Biol. Macromol.* **2021**, *179*, 418–428.
111. Zhang, J.; Yang, X.; Ji, T.; Wen, C.; Ye, Z.; Liu, X.; Liang, L.; Liu, G.; Xu, X. Digestion and absorption properties of *Lycium barbarum* polysaccharides stabilized selenium nanoparticles. *Food Chem.* **2021**, *373*, 131637. https://doi.org/10.1016/j.foodchem.2021.131637.
112. Peng, X.; Tian, G. Structural characterization of the glycan part of glycoconjugate LbGp2 from *Lycium barbarum* L.. *Carbohydr. Res.* **2001**, *331*, 95–99. https://doi.org/10.1016/s0008-6215(00)00321-9.
113. Zhang, B.; Wang, M.; Wang, C.; Yu, T.; Wu, Q.; Li, Y.; Lv, Z.; Fan, J.; Wang, L.; Zhang, B. Endogenous calcium attenuates the immunomodulatory activity of a polysaccharide from *Lycium barbarum* L. leaves by altering the global molecular conformation. *Int. J. Biol. Macromol.* **2018**, *123*, 182–188. https://doi.org/10.1016/j.ijbiomac.2018.11.067.
114. Peng, Q.; Lv, X.; Xu, Q.; Li, Y.; Huang, L.; Du, Y. Isolation and structural characterization of the polysaccharide LRGP1 from *Lycium ruthenicum*. *Carbohydr. Polym.* **2012**, *90*, 95–101. https://doi.org/10.1016/j.carbpol.2012.04.067.
115. Li, J.; Shi, M.; Ma, B.; Zheng, Y.; Niu, R.; Li, K. Protective effects of fraction 4a of polysaccharides isolated from *Lycium* barbarum against KBrO(3)-induced renal damage in rats. *Food Funct.* **2017**, *8*, 2566–2572.
116. Zhou, L.; Huang, L.; Yue, H.; Ding, K. Structure analysis of a heteropolysaccharide from fruits of *Lycium barbarum* L. and anti-angiogenic activity of its sulfated derivative. *Int. J. Biol. Macromol.* **2018**, *108*, 47–55. https://doi.org/10.1016/j.ijbiomac.2017.11.111.
117. Liu, W.; Liu, Y.; Zhu, R.; Yu, J.; Lu, W.; Pan, C.; Yao, W.; Gao, X. Structure characterization, chemical and enzymatic degradation, and chain conformation of an acidic polysaccharide from *Lycium barbarum* L.. *Carbohydr. Polym.* **2016**, *147*, 114–124. https://doi.org/10.1016/j.carbpol.2016.03.087.
118. Zhou, F.; Jiang, X.; Wang, T.; Zhang, B.; Zhao, H. *Lycium*barbarum Polysaccharide (LBP): A Novel Prebiotics Candidate for Bifidobacterium and Lactobacillus. *Front. Microbiol.* **2018**, *9*, 1034. https://doi.org/10.3389/fmicb.2018.01034.
119. Ni, W.; Gao, T.; Wang, H.; Du, Y.; Li, J.; Li, C.; Wei, L.; Bi, H. Anti-fatigue activity of polysaccharides from the fruits of four Tibetan plateau indigenous medicinal plants. *J. Ethnopharmacol.* **2013**, *150*, 529–535. https://doi.org/10.1016/j.jep.2013.08.055.
120. Wang, C.C.; Chang, S.C.; Chen, B.H. Chromatographic determination of polysaccharides in *Lycium barbarum* Linnaeus. *Food Chem.* **2009**, *116*, 595–603. https://doi.org/10.1016/j.foodchem.2009.03.015.
121. Ke, M.; Zhang, X.-J.; Han, Z.-H.; Yu, H.-Y.; Lin, Y.; Zhang, W.-G.; Sun, F.-H.; Wang, T.-J. Extraction, purification of *Lycium barbarum* polysaccharides and bioactivity of purified fraction. *Carbohydr. Polym.* **2011**, *86*, 136–141. https://doi.org/10.1016/j.carbpol.2011.04.023.
122. Zhao, R.; Qiu, B.; Li, Q.; Zhang, T.; Zhao, H.; Chen, Z.; Cai, Y.; Ruan, H.; Ge, W.; Zheng, X. LBP-4a improves insulin re-sistance via translocation and activation of GLUT4 in OLETF rats. *Food Funct* **2014**, *5*, 811–820.
123. Peng, X.-M. Physico-chemical Properties and Bioactivities of a Glycoconjugate LbGpSB from *Lycium barbarum* L. *Chin. J. Chem.* **2001**, *19*, 842–846.
124. Li, X.-M. Protective effect of *Lycium barbarum* polysaccharides on streptozotocin-induced oxidative stress in rats. *Int. J. Biol. Macromol.* **2007**, *40*, 461–465. https://doi.org/10.1016/j.ijbiomac.2006.11.002.
125. He, F.; Zhang, S.; Li, Y.; Chen, X.; Du, Z.; Shao, C.; Ding, K. The structure elucidation of novel arabinogalactan LRP1-S2 against pancreatic cancer cells growth in vitro and in vivo. *Carbohydr. Polym.* **2021**, *267*, 118172. https://doi.org/10.1016/j.carbpol.2021.118172.