Bletilla striata Polysaccharides: Structures and Functional Activities

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Abstract *Bletilla striata* (Thunb.) Reichb.f. is a species of genus *Bletilla* (Family Orchidaceae) and it is a commonly used traditional Chinese medicine. *Bletilla striata* polysaccharides (BSPs) were extracted from the tuber of *Bletilla striata*. Herein, we reviewed the extraction and purification methods of BSPs, compared the advantages and disadvantages of different methods comprehensively, and analyzed molecular weights and structural characterization of BSPs systematically. In addition, we analyzed hemostasis, anti-oxidation, anti-aging and other functional activities of BSPs to provide scientific basis for further study of BSPs.

Keywords *Bletilla striata* polysaccharides, structures, functional activities

Introduction

Bletilla striata (Thunb.) Reichb.f. is a kind of Chinese traditional medicine widely distributed in East Asia. Its dried tubers are widely used as a hemostatic agent.^[1] It is reported that these polysaccharides are the most important biologically active components of *B. striata* with various bioactivities.^[2] Clinically, it is mainly used to treat hemoptysis, traumatic hemorrhage, gastrointestinal mucosal injury, ulcers, bruises and burns, anorectal diseases, gynecological fibroma, tumor embolization and prostate surgery, etc.^[3-6] Polysaccharides were extracted from *B. striata*. In the pharmaceutical industry, BSPs have been widely applied as biomaterials with good mechanical properties and unique biological functions.^[7] Most of BSP are water-soluble polysaccharides, which are considered as the main active ingredients with the above-mentioned medicinal functions. As a promising natural anti-oxidant or excellent moisturizer, they are widely used in cosmetics and chemical industries.

Pharmacological research on *B. striata* shows that BSPs are a glucomannan formed from glucose and mannose (1 : 4) polymerized with β -glycosidic bonds.^[8] As a natural polymer material, BSPs have the characteristics of functional slow-release, local retention, self-degradability and non-irritating. It is increasingly valued in the process of pharmaceutical preparation and application^[9] with wide application prospects.^[10,11] BSPs have high safety as food additives or ingredients, and they are widely used in food processing industry due to their unique properties.^[12] Herein, we summarized extraction, purification, structural characterization and functional activities of BSPs for more reference values in future.

Extraction, Separation and Purification of BSPs

Extraction of BSPs

At present, the extraction methods of BSPs include traditional extraction methods and new extraction techniques.

In the traditional method, the extraction of polysaccharides mainly uses the reflux method, and the conventional method requires longer processing time and lower efficiency. The reflux temperature is not easy to control, and it is easy to consume a lot of volatiles and harmful organic solvents, causing environmental pollution. At the same time, the reflux process is likely to cause deformation and degradation of polysaccharides, resulting in the reduction of sample purity.^[13] At present, the most commonly used method to extract BSPs is water extraction and alcohol precipitation. Kong *et al.*^[14] reported that the dried tubers of *B. striata* were ground into powder and the ratio of material to liquid (V/V) was controlled. Then, they were extracted for 4 h at 80 °C, filtrated, adsorbed with 0.5% activated carbon at 60 °C for 2 h, and precipitated for 2 h with 75% ethyl alcohol. After that, the precipitate was centrifugated, dissolved and freeze-dried. Under this condition, the extraction rate of BSPs is 28.96%. Nowadays, various methods have been developed for extraction of BSPs. Table 1 shows the advantages and disadvantages of various extraction methods of BSPs.

Separation and purification of BSPs

The crude polysaccharides obtained by extraction needs to be further purified by separation and purification. Seavage is a common method for removing free protein from polysaccharides. It is relatively mild and has a little effect on the structures of polysaccharides. It can effectively avoid protein residue after repeated use.^[22] Column chromatography is widely used in the purification of BSPs due to its simple operation and good purification performance. Anion exchange chromatography is suitable for separation of various polysaccharides, while gel permeation chromatography is generally not suitable for separation of mucopolysaccharides.^[22] As a kind of mucopolysaccharide, BSPs should be loaded into anion exchange chromatography firstly, and then DEAE-cellulose exchanger was used for chromatography to obtain separated components.

Table 1 Comparison of extraction methods of BSPs.

Method	Advantage	Disadvantage	Ref.
Hot water extraction	The most widely used; easy to operate	This method took long time	[17, 18]
Ultrasonic extraction	Widely used; no heating; high efficiency	High yield energy	[15—19]
Infrared assisted extraction	Short extraction time; low extraction temperature	High yield energy	[16]
Enzyme-assisted method	High extraction	Rarely used alone, usually combined with other method	[20]
Dilute alkaline water extraction	Mild reaction conditions and high efficiency	—	[21]

In the subsequent purification process, each component of BSPs can be separated more carefully according to different molecular weights. With the monitoring of the phenol sulfuric acid method, the two chromatographic methods can be used interchangeably, and the product can be further purified. After concentration, the purified BSPs were obtained from eluent.^[2] Finally, purified BSPs have been widely studied in many aspects (Figure 1).

Figure 1 Schematic representation of the extraction, purification and bioactivity of BSPs.^[2]

Portion weights of BSPs

BSPs are a kind of compound polymerized by many monosaccharides linked by glycoside bond. BSPs were a glucomannan consisting of 4 molecules of mannose and 1 molecule of glucose. There are also a few metal ions in the molecule. At the same time, there are three kinds of residues including β -1,4-mannose, β -1,4-glucose and α -1,6-glucose.^[23,24] The relative molecular weights of BSPs range from tens of thousands to millions.^[25,26,28] The relative molecular weights of polysaccharides only represent the average distribution of a certain range of relative molecular weights. Even if the same batch of polysaccharides, different relative molecular weights are often measured by different methods. Chen *et al.*^[23] used high performance liquid gel permeation chromatography (HPGPC) to measure the molecular weights of BSPs (9.9658×10^4). Lu *et al.*^[27] measured the average molecular weights of BSPs were 183,000 by Sephadex G-200 gel filtration method. Liu *et al.*^[28] used *B. striata* tuber as material, which was extracted three times at 80 °C with ultrasonic method, ethanol precipitated, removed of protein by Seavage method. Finally, two polysaccharide samples were obtained by ultrafiltration treatment and gel column (Sephadex G-200) chromatography. The relative molecular weight is 460 kDa and 390 kDa, respectively.

Structural characterization of BSPs

The primary structure of polysaccharide refers to the composition and sequence of monosaccharide residues,

adjacent glycosyl connections, anomeric configuration, and the location and length of branches. Though the reports on the structural fractions of BSPs have been in update, all the results indicated that BSPs were a sort of glucomannan (Table 2). An early publication in 1973 reported firstly that BSPs contained a mannose to glucose in a molar ratio of 3 : 1, and its skeleton is composed of (1→4) linked aldonic sugar residues.^[30] In 2006, 2010, 2014 and 2017, more new BSPs components were extracted with different molecular weights and monosaccharide compositions.^[29,31-33] The skeleton of BSPs is mainly composed of 1,4 linked mannose residues and 1,4 linked glucose residues. In addition, the monosaccharide composition of BSPs is mainly mannose and glucose, only bsp2 contains a small amount of galactose units.^[1,29-33] In 2015, it could be referred to as glucomannan polymer.^[34] In addition, there is a certain diversity in the molecular weight of each BSP component, which remains in the range of $1-3 \times 10^5$. The hypothesized structure of BSPs fractions consists of two tapes, linear chain and branched chain. Generally, branched polysaccharides consisting of mannose and glucose are widely recognized as drug carriers in the ratio of 2.4 : 1, because the curved structure is conducive to drug encapsulation. Based on the information, it could be speculated that there probably existed other fractions of BSPs. Thus, the structure of rest fractions remained to be further explored. The two kinds of repeating motifs of BSPs are shown in Figures 2 and 3.

Functional Activities of BSPs

A book on traditional Chinese medicine *Compendium of Materia Medica* mentioned: “*B. striata* is astringent and condensation, so it can enter the lung to stop bleeding, muscles and treat sores.”

B. striata plays a very important clinical role as a traditional Chinese medicine. The main component of *B. striata* is polysaccharides, which plays an irreplaceable role in medical, chemical industry, health care, beauty and moisturization.^[43]

Hemostatic activity

Animal experiments showed that the water extract of polar solvent alcohol extract of *Bletilla* tuber had good hemostasis and coagulation effects on animal organs such as liver, spleen, muscle and blood vessel bleeding. In the study of platelet aggregation and coagulation function in rats, it was found that BSPs exerted hemostatic function, which may activate endogenous and exogenous coagulation system, promote platelet aggregation and achieve hemostasis in rats.^[44] The water-soluble part and the alcohol-soluble part of *B. striata* are main effective components of *B. striata* hemostasis, which can significantly improve the maximum platelet aggregation rate and promote platelet aggregation. Guo *et al.*^[45] found that freeze-dried powder absorbed 2—3 times water of its own weight, the degradation rate is positively related to the content of BSPs, and the bacteriostasis is positively related to the

Table 2 *Bletilla striata* structure characterization^[42]

BSPs type	Monosaccharide	Relative molecular weight	Purity/%	Connection type	Ref.
i	Man : Glc = 3 : 1	2.6×10^5	98.5	→4)-D-Man-(1→	[35]
ii	Man : Glc = 2.4 : 1	ca. 1.35×10^5	95.7	→4)-D-Glc-(1→	[1, 36]
iii	—	—	—	→4)-D-Man-(1→	[37]
iv	Man : Glc = 3.5 : 1	0.2×10^5	96	→6)-D-Glc-(1→ →4)-D-Man-(1→ →4)-D-Glc-(1→	[38]
v	—	—	—	—	[33]
vi	Man : Glc = 2.8 : 1.23	1.68×10^5	—	→4)-D-Man-(1→ →4)-D-Glc-(1→	[39]
vii	Man : Glc = 2.4 : 1	—	90	—	[40]
viii	—	1.383×10^5	—	—	[41]

Abbreviations: Glc, glucose; Man, mannose

Figure 2 BSPb Man : Glc = 3 : 1^[22] **Figure 3** BSP Man : Glc = 2.4 : 1^[22]

content of *N*-alkylated chitosan. When the ratio of *N*-alkylated chitosan to BSPs is 4 : 1, the composite freeze-drying powder has the best performance and potential as hemostatic material. *B. striata* can shorten the bleeding time and coagulation time of normal rats and mice. It may be that *B. striata* can make blood cells agglutinate, activate, deform, and aggregate blood platelets. Zhang *et al.*^[46] found that BSPs could promote hematopoiesis in mice with low hematopoietic function. The bioactivity of BSPs is related to its viscosity and solubility.^[47] BSPs have promoting effects on hemostasis and coagulation.^[48]

Anti-oxidant and anti-aging activities

Anti-oxidant is any substance that can effectively inhibit the oxidation reaction of free radicals when it exists in a low

concentration. Its mechanism of action can directly act on free radicals or indirectly consume substances that are prone to free radicals to prevent further reactions. While human body produces free radicals inevitably, it also naturally produces antioxidants that are resistant to free radicals, so as to counteract the oxidative attack of free radicals on human cells.^[49]

Senescence usually refers to the senescence of cells, which is a short period of near death when cells are subjected to oxidative stress, oncogene activation and DNA damage.^[50] Senescence cells can secrete a variety of soluble factors to produce inflammation, accelerate the aging of the body and make the body sick. Some studies showed that promoting the apoptosis of senescence cell can inhibit the senescence of organism.^[51]

BSPs have anti-aging effects, but their effects cannot be separated from the ability of scavenging free radicals and antioxidants. He *et al.*^[52] studied the antioxidant activity of wild BSPs *in vitro*. They concluded that BSPs had scavenging effects on O_2^- , $\cdot OH$ and $DPPH\cdot$, and the scavenging capacity was different. Rui *et al.*^[24] conducted antioxidant study of neutral polysaccharides from *B. striata* *in vitro*. The result showed that BSPs inhibited the production of hydroxyl radicals significantly. Based on the anti-oxidation effect *in vitro*, the anti-oxidation effect *in vivo* was studied. The aging model of mice was established by injecting *D*-galactose and the neutral polysaccharides of *B. striata* were given. It can be seen that the neutral polysaccharides of *B. striata* increased the SOD activity of various organs of aging mice induced by *D*-galactose significantly.

Other activities

BSPs had significant antitumor activities *in vivo* and *in vitro*.^[2] Li *et al.*^[53] found that previously investigated the *in vivo* and *in vitro* effects of paclitaxel nanoparticle- (PTX-) loaded BSPs on human gastric cancer cells. The results suggested that BSP-loaded paclitaxel nanoparticles could realize enhanced drug delivery and exert an antiproliferative effect on the human gastric gland cancer cell line (MKN45) effectively and safely both *in vivo* and *in vitro*. Wu *et al.*^[54] found that BSPs had an obvious anti-stress gastric ulcer effect. Shi *et al.*^[55] found that BSPs have certain immunomodulatory ability on macrophages and can alleviate colitis in mice. In the food field, the polysaccharides of *B. striata* have no toxic side effect and has high application value. Chen *et al.*^[56] pointed out that *B. striata* can be used for brewing wine or stewing soup for medicinal meals, with unique aroma and strong edibility.

Li et al.^[57] prepared a compound preservation solution using *B. striata* and applied it on the surface of mango, disclosing that it could effectively delay the weight loss, yellowing and decay of mango, reduce the respiratory strength of mango, inhibit the decline of titrable acid, vitamin C, and soluble total solids content, maintain the good quality of the fruit and extend the storage life of the fruit.

Conclusions

BSPs are a neutral heteropolysaccharide polymerized by glucose and mannose in a certain proportion. In the past years, a variety of BSPs have been isolated and their diverse structures make the research more challenging. Herein, the structure of BSPs was characterized, which showed that BSPs were a kind of glucomannan. The monosaccharide of BSPs is mainly composed of mannose and glucose, which provides a better scientific basis for further research on BSPs. In addition, BSPs have astringent hemostasis, antioxidant, anti-aging and other active functions. Polysaccharides from *B. striata* have obvious scavenging effects on $\cdot\text{OH}$ and $\text{DPPH}\cdot$, but they have no obvious scavenging effect on $\text{O}_2^{\cdot-}$. Polysaccharides can be used as natural food antioxidants. It has low toxicity, high safety and good biocompatibility, and has great potential in medicine and food.

Conflict of Interest

The authors declare no conflict of interest.

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