



OPEN ACCESS

EDITED BY

Bhaskar R. Sathe,
Dr. Babasaheb Ambedkar Marathwada
University, India

REVIEWED BY

Venkata Reddy Udumula,
Emory University, United States
Kunming Qin,
Jiangsu Ocean University, China
Zhenhua Liu,
Henan University, China

*CORRESPONDENCE

Cheng-Ting Zi,
✉ zichengting@126.com

RECEIVED 03 March 2024

ACCEPTED 03 June 2024

PUBLISHED 02 July 2024

CITATION

Yang L, Qin S-H and Zi C-T (2024), Research progress of *Gastrodia elata* Blume polysaccharides: a review of chemical structures and biological activities. *Front. Chem.* 12:1395222. doi: 10.3389/fchem.2024.1395222

COPYRIGHT

© 2024 Yang, Qin and Zi. This is an open-access article distributed under the terms of the [Creative Commons Attribution License \(CC BY\)](https://creativecommons.org/licenses/by/4.0/). The use, distribution or reproduction in other forums is permitted, provided the original author(s) and the copyright owner(s) are credited and that the original publication in this journal is cited, in accordance with accepted academic practice. No use, distribution or reproduction is permitted which does not comply with these terms.

Research progress of *Gastrodia elata* Blume polysaccharides: a review of chemical structures and biological activities

Liu Yang^{1,2}, Shi-Hui Qin² and Cheng-Ting Zi^{3,4*}

¹State Key Laboratory of Quality Research in Chinese Medicine, Macau Institute for Applied Research in Medicine and Health, Macau University of Science and Technology, Taipa, Macao SAR, China, ²State Key Laboratory of Phytochemistry and Plant Resources in West China, Kunming Institute of Botany, Chinese Academy of Sciences, Kunming, China, ³Research Center for Agricultural Chemistry, College of Science, Yunnan Agricultural University, Kunming, China, ⁴Key Laboratory of Pu-erh Tea Science, Ministry of Education, College of Food Science and Technology, Yunnan Agricultural University, Kunming, China

Gastrodia elata Blume (*G. elata*), listed as one of the 34 precious Chinese medicines, serves a dual purpose as both a medicinal herb and a food source. Polysaccharide is the main active ingredient in *G. elata*, which has pharmacological activities such as immune regulation, anti-oxidation, anti-cancer, anti-aging, neuroprotection and antibacterial activity and so on. The biological activities of *G. elata* polysaccharide (GPs) is closely related to its chemical structures. However, no a review has synthetically summarized the chemical structures and pharmacological activities of GPs. This study delves into the chemical structures, pharmacological action of GPs, offering insights for the future development an application of these compounds.

KEYWORDS

Gastrodia elata, polysaccharides, chemical structure, pharmacological activity, mechanism

1 Introduction

Gastrodiae Rhizoma (known as *Tianma* in China) is the dry tubers of *G. elata* Blume (*G. elata*), which was first mentioned in the *Shen Nong's Herbal Classic* and was widely distributed in Sichuan, Guangdong, Yunnan and Guizhou provinces (Wang et al., 2022). According to the theory of Traditional Chinese Medicine (TCM), *G. elata* nature is naturally warm and tastes sweet, returns to the liver meridian, which has the function of calming wind and stopping convulsive seizures, suppressing liver yang, expelling wind and clearing collateral. In clinical practice, *G. elata* is widely used in the prevention and treatment of childhood convulsions, memory loss, sciatic neuropathy, epilepsy and other diseases, and is also widely used in health products and food fields (Zhang et al., 2007). Modern pharmacology recognizes that *G. elata* and its extracts have anti-tumor, anti-oxidation and anti-aging effects, regulating immunity, sedation, hypoglycemia, hypolipidemia, anti-depression, anti-viral, and anti-convulsant effects (Liu and Huang, 2017).

Studies have shown that 134 bioactive compounds originate from *G. elata*, including phenolic compounds, polysaccharides, organic acids and sterols (Feng et al., 1979; Yang et al., 2007; Duan et al., 2013; Zhu et al., 2019). Some of these molecules showed activity against migraines, hypertension, and other neurological diseases (Hayashi et al., 2002; Zhu et al., 2019). It has been suggested that *G. elata* polysaccharides (GPs) are active compounds

TABLE 1 The chemical structures of *Gastrodia elata* Blume polysaccharides.

Compound name	Molecular weight (Da)	Monosaccharide composition and molar ratio	Backbone	Ref.
WGEW	1.00×10^5	Glc	α -1,4-Glcp α -1,4,6-Glcp	Qiu et al. (2007)
AGEW	2.80×10^5	Glc	α -1,4-Glcp α -1,4,6-Glcp	Qiu et al. (2007)
GPs	2.71×10^5	Glc	α -1,4-Glcp	Bao et al. (2017)
GPSa	4.97×10^5	Rha: Man: Glc: 1: 1.07: 67.24	α -1,4-Glcp	Zhu et al. (2010)
WTMA	7.00×10^5	Glc	α -1,4-Glcp α -1,4,6-Glcp	Chen et al. (2011)
PGEB-3H	2.88×10^4	Glc	α -1,4-Glcp α -1,4,6-Glcp	Ming et al. (2012)
Acidic polysaccharides	–	Xyl: Glc: GlcA: GlaA	–	Lee et al. (2012)
RGP-1a	1.93×10^4	Glc: Fru: 10.68: 1	–	Chen et al. (2016)
RGP-1b	3.92×10^3	Glc	–	
PGE	1.54×10^6	Glc	α -1,4-Glcp α -1,4,6-Glcp α -1,3-Glcp	Zhu et al. (2018)
GEP	8.75×10^6	Glc	–	Chen et al. (2018a)
GEP-3	2.52×10^4	Glc	α -1,4-Glcp β -1,4-Glcp β -1,6-Glcp α -1,3,4-Glcp	Huo et al. (2021)
GEP-1	2.01×10^5	Glc	α -1,4-Glcp α -1,4,6-Glcp β -1,6-Glcp β -1,3-Glcp p-hydroxybenzyl alcohol	Huo et al. (2021)
GEP-1	7.64×10^4	Ara: Gal: Glc: Man: 2.189: 4.791: 92.035: 0.342	α -1,4-Glcp	Guan et al. (2022)
GEPs	2.90×10^5	Glc: Gal: GlcA: 88.21: 4.48: 4.40	α -1,4-Glcp	Li N. et al. (2023)
GaE-B	2.15×10^5	Man: Rha: Glc: Gal: Xyl: 5.36: 2.64: 77.35: 5.33: 9.34	–	Ji et al. (2022)
GaE-R	1.49×10^5	Man: Rha: Glc: Gal: Xyl: 5.07: 3.18: 71.01: 6.41: 14.32	–	Ji et al. (2022)
GaE-Hyb	1.95×10^5	Man: Rha: Glc: Gal: Xyl: 4.83: 3.02: 77.58: 4.76: 9.81	–	Ji et al. (2022)
GaE-G	2.51×10^5	Man: Rha: Glc: Gal: Xyl: 3.64: 2.96: 81.88: 3.11: 8.40	–	Ji et al. (2022)
GEP2-6	2.71×10^6	Glc	α -1,4-Glcp α -1,6-Glcp	Chen et al. (2024)

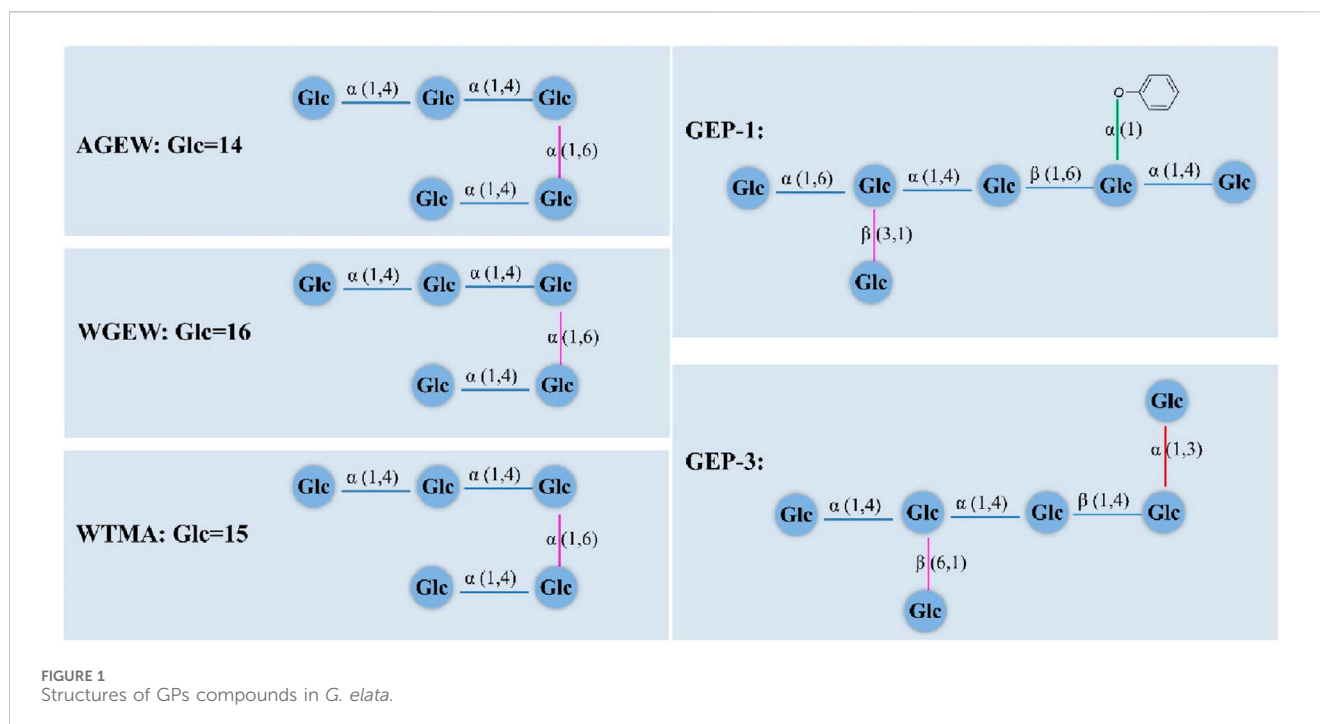
Notes:–Indicates that the item is not detected; Glc: glucose, Man: mannose, Rha: rhamnose, Gal: galactose, Xyl: xylose, Fru: fructose, GlcA: glucuronic acid, GlaA: galacturonic acid.

with a wide range of pharmacological effects, such as anti-oxidant, anti-cancer, anti-virus, anti-osteoporosis, immunomodulatory, and neuroprotective effects and so on (Qiu et al., 2007; Chen et al., 2015; Liu and Mori, 1992; Liu et al., 2015; Bao et al., 2017). Due to its great medical and health value, more and more researchers are paying attention to the pharmacological activities of GPs. Furthermore, many studies have attested that the biological activities of GPs are closely related to their chemical structures. However, no previous articles have synthetically summarized the chemical structures and pharmacological activities of GPs. In this article, we review the structural characteristics, biological activities and structure-activity

relationships of GPs, to aid in providing a theoretical basis and data for the research, development and utilization of GPs.

2 The structural features of GPs

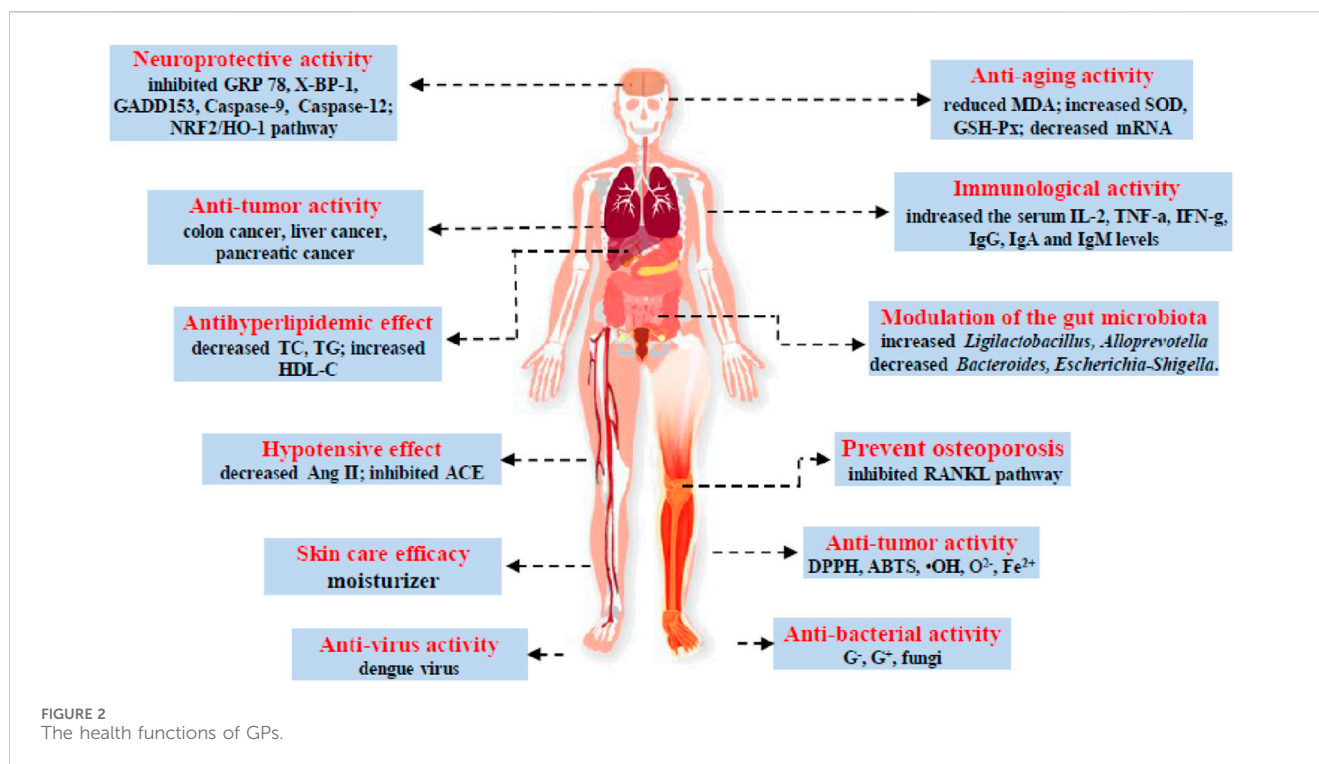
The structures of polysaccharides can be divided into primary structure and high-level structure. The primary structure includes molecular weight, monosaccharide composition, glycosidic bond configuration, repeating structural units and branching degree. The high-level structure (secondary, tertiary and quaternary structures)



is mainly the spatial conformation of polysaccharides (Zhang et al., 2018). To date, more than 20 GPs with known structures have been extracted and separated. The primary structural characteristics of the GPs, including molecular weight, monosaccharide composition, molar ratio, and backbone, are summarized in Table 1. The structures of the some GPs are shown in Figure 1.

Qiu et al. (2007) obtained two glucans (WGEW and AGEW) from *G. elata* Blume, with molecular weight of AGEW and WGEW was 2.80×10^5 Da and 1.00×10^5 Da, respectively. Their structures have an α -(1 \rightarrow 4)-linked glucosyl backbone. Methylation analysis showed that two polysaccharides have terminal Glc, 1,4- and 1,4,6-linked Glc, the ratio of Glc:1,4-:1,4,6-linked Glc in WGEW was 1:16:1, and the ratio of it in AGEW was 1:14:1. Zhu et al. (2010) obtained *G. elata* polysaccharide (GPSa), with a molecular weight of 4.97×10^5 Da. Structural analysis revealed that GPSa was composed mainly of glucose, but also contained small amounts of rhamnose and mannose. The molar ratio of GPSa is rhamnose: mannose: glucose: 1: 1.07: 67.24. IR and NMR analysis indicated GPSa chain was α -(1 \rightarrow 4) glucan with α -(1 \rightarrow 4) glucosyl branches. Chen et al. (2011) also obtained water-soluble glucan (WTMA) from the rhizome of *Gastrodia elata* Bl. The mean molecular weight of WTMA was 7.0×10^5 Da, with the results showed that WTMA was an α -(1 \rightarrow 4) glucan with α -(1 \rightarrow 4) glucosyl branches attached to O-6 of the branch points. Ming et al. (2012) purified *G. elata* polysaccharide (PGEB-3H), was found to be a glucan with a molecular weight of 2.88×10^5 Da. Structural analysis showed that PGEB-3H was consisted of 1,4-linked glucose and 1,4,6-linked glucose with an approximate molar ratio of 20: 1. FT-IR analysis indicated a pyranose form of the glucosyl residue, absorption at 1027.0 cm^{-1} , 1079.6 cm^{-1} , and 1153.2 cm^{-1} . Lee et al. (2012) obtained an acidic polysaccharide. It was purified from the crude polysaccharides by DEAE-Sephacel CL-6B. The analysis was shown that the fraction of acidic polysaccharide included xylose, glucose, galacturonic acid, and

glucuronic acid (Table 1). Chen et al. (2016) separated two homogeneous polysaccharides (RGP-1a and RGP-1b) from the residue of *Rhizoma gastrodiae*. The results showed that RGP-1a was composed of fructose and glucose in a molar ratio of 1:10.68, and RGP-1b was mainly consisted of glucose. Bao et al. (2017) obtained a homogeneous polysaccharide (GPs), with a molecular weight of 2.71×10^5 Da. Analysis of the monosaccharide composition of GPs showed that GPs was composed of glucose. Zhu et al. (2018) yielded a polysaccharide (PGE) with hot water and purified it with Sephadex G-200 followed by ultra-filtration. This study indicated that PGE had a molecular weight of 1.54×10^6 Da, the backbone of PGE composed of (1 \rightarrow 4)-linked-D-Glcp and the branches are (1 \rightarrow 3)-linked-D-Glcp, (1 \rightarrow 4,6)-linked-d-Glcp and (1 \rightarrow)-linked-glucose terminal. Further detailed data are shown in Table 1. Chen et al. (2018a) isolated a *G. elata* Blume polysaccharide (GEP), with a molecular weight of 8.75×10^6 Da. IR and NMR showed that GEP was consists of glucose. Huo et al. (2018) obtained a homogeneous polysaccharide which was named GEP-1. It was isolated and purified from *G. elata* by hot-water extraction, ethanol precipitation, and membrane separator. The structural analysis showed that the backbone of GEP-1 consisted of 1,3,6-linked- α -Glcp, 1,4-linked- α -Glcp, 1,4-linked- α -Glcp and 1,4,6-linked- α -Glcp, with a molecular weight of 2.01×10^5 Da, and contained a citric acid and repeating the p-hydroxybenzyl alcohol as a branch. Guan et al. (2022) isolated a polysaccharide from *G. elata* (named GEP-1), with a molecular weight of 7.64×10^5 Da. NMR and methylation analyses revealed that the main chain structure of GEP-1 was α -(1 \rightarrow 4)-glucans. Li F. et al. (2013) obtained a polysaccharide named GEPs, with a molecular weight of 2.92×10^5 Da, which consists of glucose, galactose and galacturonic acid was in the ratio of 88.21: 4.48: 4.40. Ji et al. (2022) obtained four components of GaE-B (*G. elata* Bl. f. *glaucua* S. chow polysaccharides), GaE-R (*G. elata* Bl. f. *elata* polysaccharides),



GaE-Hyb (hybridization of *G. elata* Bl. f. *glauca* S. chow and *G. elata* Bl. f. *elata* polysaccharides), and GaE-G (*G. elata* Bl. f. *viridis* Makino polysaccharides). Based on HPGPC analysis, their average molecular weight are 2.15×10^5 Da, 1.49×10^5 Da, 1.95×10^5 Da, 2.51×10^5 Da, respectively. GC analysis showed that these GaE polysaccharides were heteropolysaccharides, and the polysaccharides comprised Man, Rha, Glc, Gal, and Xyl. The detail more ratio shown in Table 1. Chen et al. (2024) obtained a water-soluble polysaccharide (GEP2-6), with a molecular weight of 2.71×10^6 Da, which consists of only glucose. NMR and methylation analyses revealed that the main chain structure of GEP2-6 consists of α -(1 \rightarrow 4) and α -(1 \rightarrow 6) glycosidic bonds.

3 Biological activities

In recent years, research has focused on the pharmacodynamics of GPs. Many references point out that GPs showed that significant pharmacological activities, such as anti-oxidation, anti-tumor, immune regulation, anti-aging, improve memory, improve cerebral ischemia, reduce blood pressure, anti-bacterial effect and reduce blood lipid (Figure 2) (Zhu et al., 2019; Wang et al., 2022). The biological activities of GPs are summarized in Table 2.

3.1 Anti-oxidation activities

Free radicals can accelerate the oxidation process *in vivo* and lead to cell aging. Previous studies have shown that GPs can effectively remove free radicals including 1,1-diphenyl-2-picrylhydrazyl (DPPH), oxygen radicals ($\text{O}_2^{\cdot-}$), and hydroxyl radicals ($\cdot\text{OH}$). GPs has good antioxidant activity, as evaluated by DPPH, $\text{O}_2^{\cdot-}$ -and- OH assays. The clearance rate

of DPPH, $\text{O}_2^{\cdot-}$ -and OH was around 50%, when the concentration of GPs was 1–3.5 mg/mL (Hou and Hou, 2018; Chen et al., 2018b; Zhang et al., 2021; Chen et al., 2024; Liu et al., 2009; Wang, et al., 2022). Xu et al. (2015) reported that GPs had the best removal effect on hydrogen peroxide (H_2O_2), the clearance rates was 25.80%, and the scavenging power of other free radicals as following DPPH (22.37%) > ONOO $^-$ (20.52%) > $\text{O}_2^{\cdot-}$ (12.23%) > $\cdot\text{OH}$ (4.85%). Chen et al. (2018a) found GEP had high radical-scavenging activities. At concentration of 200 mg/mL, the HRSA and DRSA of the GEP were 94.56% and 84.21%, respectively. In addition, GPs have a strong scavenging effects on ABTS radicals, superoxide radicals, ferrous ion chelating capacity, and reducing power (Hou and Hou, 2018; Zhang et al., 2019; Ji et al., 2022; Wang, et al., 2022). The above studies showed that GPs had a strong antioxidant effect. The antioxidant range of heteropolysaccharides is wider than that of glucan from *G. elata*.

3.2 Anti-aging activities

Many studies have shown that GPs can improve the expression of peroxidase and slow down the aging of organs and tissue. Li N. et al. (2023) reported that GPs had anti-aging effects in D-galactose-induced senescence mice. GPs significantly increased SOD and GSH-Px activity and decreased MDA and NO contents in aging mice, and showed a good dose-dependent relationship. Xie et al. (2010) found that GPs can improve the learning and memory ability of D-galactose-induced aging mice, its mechanism is mainly related to oxidative metabolism in the body. The finding of Kong et al. (2005) displayed that GPs significantly increased the activities of SOD and CAT in the serum, liver, brain and heart tissue of aging mice, significantly inhibited the formation of MDA in the serum, liver, brain and heart tissue of aging mice, and significantly increased

TABLE 2 Biological activities of GPs isolated from the *Gastrodia elata*.

Biological activities	Name	Description	<i>In vivo/In vitro</i>	Ref.
Anti-oxidative activity	GP	evaluated the scavenging activity of DPPH and ABTS.	<i>In vitro</i>	Hou and Hou (2018)
	heteropolysaccharides	tested the activities of DPPH radicals, ABTS radicals, superoxide radicals, hydroxyl radicals, ferrous ion chelating capacity, and reducing power	<i>In vitro</i>	Ji et al. (2022)
	GPs	The scavenging rate of DPPH and ABTS was higher, and the antioxidant capacity was lower than that of Vc	<i>In vitro</i>	Wang et al. (2022)
	GEP1-G GEP2-G	The clearance rates of DPPH were 44.5% and 25.6%, the clearance rates of O ^{2·-} were 33.32% and 21.55%, the clearance rates of ·OH were 39.5% and 22.8%	<i>In vitro</i>	Chen et al. (2018b)
	GPs	the clearance rate of DPPH and ·OH was 40.52% and 36.52%	<i>In vitro</i>	Zhang et al. (2021)
	GPs	has the best removal effect on hydrogen peroxide (H ₂ O ₂), the clearance rates was 25.80%	<i>In vitro</i>	Xu et al. (2015)
	GPs	the concentration IC ₅₀ were 1.18 mg/mL (·OH), 1.62 mg/mL (O ^{2·-})	<i>In vitro</i>	Liu et al. (2009)
	GPs	has a certain scavenging effect on ferrous ions, ABTS free radicals, hydroxyl free radicals and DPPH free radicals	<i>In vitro</i>	Zhang et al. (2019)
	GEP2-6	scavenged DPPH and hydroxyl radicals	<i>In vitro</i>	Chen et al. (2024)
Anti-aging activity	GEP	reduced the MDA level, increased the SOD and GSH-Px activities	<i>In vivo</i>	Chen et al. (2018c)
	GPs	increased SOD and GSH-Px activity and decreased MDA and NO content	<i>In vivo</i>	Li F. et al. (2013)
	GPs	related to oxidative metabolism in the body	<i>In vivo</i>	Xie et al. (2010)
	GPs	increased the activities of SOD and CAT in serum, liver, brain and heart	<i>In vivo</i>	Kong et al. (2005)
	GPs	decreased the mRNA expression and protein level of caspase-3, MURF-1 and MAFbX	<i>In vivo</i>	Wang et al. (2019)
Anti-tumor activity	WTMA	inhibited PANC-1 cell growth, showed no effect on PANC-1 cells growth	<i>In vitro</i>	Chen et al. (2011)
	GPs	inhibited at 90 mg/kg, and the inhibition rate was 27.6%	<i>In vitro</i>	Wang et al. (2014)
	GPs	increased G0/G1 phase and decrease G2/M phase	<i>In vitro</i>	Liu et al. (2015)
	WSS25	blocked of BMP/Smad signaling pathway	<i>In vitro</i>	Qiu et al. (2010)
	PGEs	promoted late apoptosis and arrested at G2/M phase	<i>In vitro</i>	Dai et al. (2021)
Immunological activity	RGP-1a RGP-1b	effected the NO production and phagocytic activity	<i>In vitro</i>	Chen et al. (2016)
	GPs	increased the serum IL-2, TNF-α, IFN-γ, IgG, IgA, IgM levels, and the spleen and thymus indexes	<i>In vivo</i>	Bao et al. (2017)
	GEP-1	induced TNF-α, IL1-β and NO release	<i>In vitro</i>	Guan et al. (2022)
	GEPs	increased content of SCFAs	<i>In vitro</i>	Li N. et al. (2023)
	GPs	regulated the levels of IgA, IgG, IgM and hemolysin in mice, increased the index of thymus and spleen	<i>In vitro</i> <i>In vivo</i>	Dai et al. (2021)
	GPs	reduced the activity of ALT, AST, NO and the contents of TNF-α and IL-1 in serum of mice, inhibited MAD, increased SOD.	<i>In vitro</i> <i>In vivo</i>	Li et al. (2015)
	GPs	stimulated IL-2, TNF-α, IFN-γ, IgG, IgA and IgM	<i>In vivo</i>	Li et al. (2016)

(Continued on following page)

TABLE 2 (Continued) Biological activities of GPs isolated from the *Gastrodia elata*.

Biological activities	Name	Description	<i>In vivo/In vitro</i>	Ref.
Neuroprotective activity	GPs	decreased BCL-12 and BAX protein, inhibited the expression of caspase-3 protein	<i>In vitro</i>	Zhou et al. (2013)
	GPs	reduced the level of intracellular toxic reactive oxygen species, reduced the release of LDH, inhibited the expression of GRP 78, X-BP-1, GADD153, caspase-9 and caspase-12	<i>In vitro</i>	Zhou et al. (2017)
	NPGE	attenuated ferroptosis-mediated neuroinflammation via the NRF2/HO-1 signaling pathway	<i>In vitro</i>	Zhang et al. (2023)
	GPs	increased Bcl-2 expression in brain tissue, reduced the expression of Bax	<i>In vitro</i>	Wang et al. (2019)
Hypotensive effects	GPs	reduced systolic blood pressure in SHR fed a high-fat diet	<i>In vitro</i>	Lee et al. (2012)
	PGE	exhibited ACE-inhibitory activity	<i>In vitro</i>	Zhu et al. (2018)
	GPs	decreased the levels of Ang II, and increased the levels of NO were increased	<i>In vitro</i>	Wang et al. (2019)
Antihyperlipidemic effects	PGEB-3H	caused 29% increase in HDL-C	<i>In vitro</i>	Ming et al. (2012)
	GPs	decreased hypolipidemic indexes (total cholesterol, triglyceride and low-density lipoprotein cholesterol levels)	<i>In vivo</i>	Lee et al. (2012)
	PGEB-3-H	decreased the content of TC and TG and increased HDL-C, had no significant effect on the content of LDL-C	<i>In vitro</i>	Miao and Shen (2006)

the activity of GSH-Px in the serum of aging mice. The results indicated that GPs had better scavenging free radicals, decreasing MDA content and delaying cell aging. Chen et al. (2018b) found that intragastric administration of GEP significantly decreased the MDA levels but significantly increased SOD and GSH-Px activities in the sera and brains of D-galactose-induced aging mice as compared with those of the model group, indicated that GEP can effectively suppress oxidation-induced damage to the sera and brain tissues of D-galactose-induced aging mice. Wang and Liu (2019) found that GPs could delay skeletal muscle aging in mice by reducing the mRNA expression and protein levels of caspase-3, MURF-1 and MAFbX in muscle tissue. However, the molecular mechanism of anti-aging is not been clarified.

3.3 Anti-tumor activities

Numerous cell and animal model studies have shown that GPs can significantly inhibit the development of various types of cancer, such as colon cancer, liver cancer, pancreatic cancer, etc. Wang et al. (2014) found that the tumor growth of GPs was significantly inhibited at 90 mg/kg, and the inhibition rate was 27.6%. Liu et al. (2015) reported that GPs have a significant anti-cancer effect on H22 tumor-bearing mice, the results showed that the GPs inhibition rate on H22 cells was 44.7%. The mechanism is mainly related to GPs could increase the cell percentage in the G0/G1 phase and decrease cell percentage in the G2/M phase. Qiu et al. (2010) reported that WSS25 could inhibit the growth of xenografted hepatocellular cancer cells in nude mice, its mechanism is related to the blocking of BMP/Smad signaling by WSS25, as shown in Figure 3. Dai et al. (2021) investigated the anti-tumor activities of *G. elata* polysaccharides (PGEs) against MCF-7 cells *in vitro*. The results

showed that the PGEs could inhibit the growth of MCF-7 cells by promoting late apoptosis and arresting at G2/M phase. Chen et al. (2011) investigated the anti-pancreatic cancer activities of WTMA against PANC-1 cell lines and showed no effect on the growth of PANC-1 cells.

3.4 Immunological activities

Numerous *in vitro* and *in vivo* studies have demonstrated the immunological activities of GPs. Li et al. (2016) found that GPs can regulate the levels of immunoglobulin (IgA, IgG, IgM) and hemolysin in mice, and increase the index of thymus and spleen. Li et al. (2015) reported that GPs significantly reduced the activity of ALT, AST, NO and the content of TNF- α and IL-1 in the serum of mice, inhibited the level of MAD in the liver, increased the activity of SOD and the concentration could significantly increase the proliferation ability of T and B lymphocytes in the spleen. The results indicated that GPs had a good protective effect against immunological liver injury in mice. Li F. et al. (2013) found that GEPs can effectively alleviate immunosuppression, the potential mechanism was related to the modulation of gut microbiota composition by GEPs and the resulting increased content of SCFAs. Chen et al. (2016) found that the two polysaccharides (RGP-1a and RGP-1b) have a significant impact on NO production and phagocytic activity of RAW264.7 macrophages. Compared to RGP-1a, RGP-1b, which has a smaller molecular weight and a uniform monosaccharide composition, exhibits superior immunological activities in RAW264.7 macrophages. Molecular weight and homogeneous composition may be key factors affecting the immunological activity of GPs. Bao et al. (2017) found that GPs can increase serum IL-2, TNF- α , IFN- γ , IgG, IgA and IgM levels, as well as spleen and thymus indices of Kunming mice, showing that GPs could improve the immune function of immunosuppression model mice.

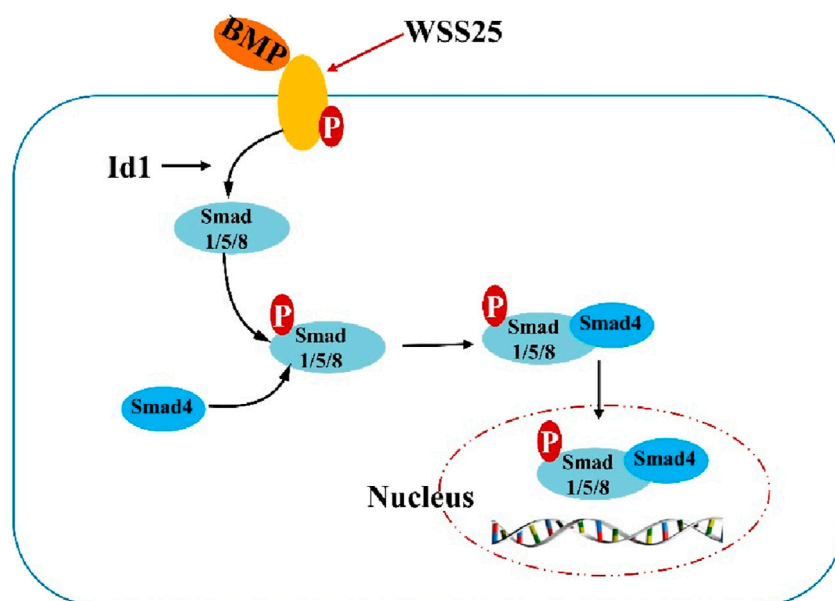


FIGURE 3 The mechanism of WSS25 in hepatocellular cancer cell lines.

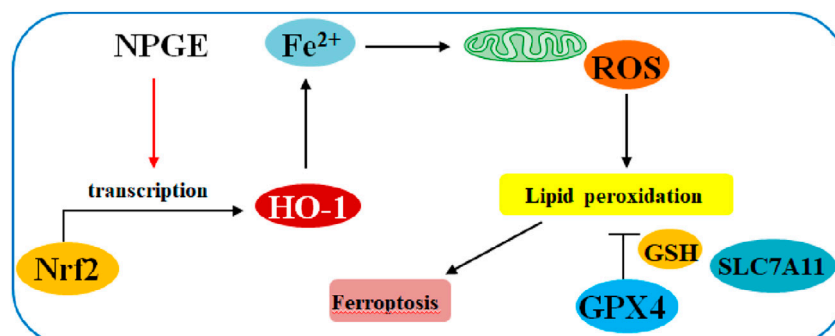


FIGURE 4 Schematic illustration of NPGE in BC cells through of the NRF2/HO-1 pathway.

Guan et al. (2022) observed the effect of GEP-1 on immune function by increasing phagocytic activities and induced release of cytokines (TNF- α , IL1- β) and nitric oxide (NO) in macrophages.

3.5 Neuroprotective activities

The neuroprotective effect of GPs on rat pheochromocytoma nerve cells (PC12) has recently attracted great attention. Zhou et al. (2013) found that GPs significantly could improve corticosterone (CORT)-induced injury and cell morphology of PC12 cells, reduce the expression of BCL-12 and BAX protein, and inhibit the expression of caspase-3 protein. Zhou et al. (2017) reported that GPs play a protective role in nerve cells by reducing the level of intracellular toxic reactive oxygen species, reducing the release of LDH, and inhibiting the expression of GRP 78, X-BP-1, GADD153, caspase-9 and caspase-12.

Zhang et al. (2023) reported that neutral polysaccharide from *G. elata* (NPGE) had potential effects on the neuropathology of cerebral ischemia-reperfusion injury (CIRI). Its mechanism is related to that NPGE alleviates CIRI by attenuating ferroptosis-mediated neuroinflammation via the NRF2/HO-1 signaling pathway, the relevant mechanism is shown in Figure 4. In addition, GPs could increase the expression of anti-apoptotic gene Bcl-2 in brain tissue reduce expression of apoptosis gene Bax, alleviating cerebral palsy, apoptosis of brain tissue, exerting neuroprotective activity (Wang et al., 2019).

3.6 Hypotensive effects

Numerous studies have demonstrated the blood pressure lowering effect of GPs. Angiotensin-converting enzyme (ACE) plays a significant role in the development of hypertension in the body.

Miao and Shen (2006) observed the effect of GPs on angiotensin II (Ang II) level, the results showed that Ang II levels were decreased and the NO levels were increased. Zhu et al. (2018) found that PGE had ACE inhibitory activity, the inhibition rate of PGE on ACE was calculated to be 74.40% and the IC₅₀ value was 0.66 mg/mL. Lee et al. (2012) reported that the acidic polysaccharide fraction from *Gastrodia* rhizome significantly reduced blood pressure in SHR fed a high-fat diet.

3.7 Antihyperlipidemic effect

Ming et al. (2012) reported effects of PGEB-3-H on total cholesterol (TC), triglycerides (TG), low-density lipoprotein cholesterol (LDL-C) and high-density lipoprotein cholesterol (HDL-C). The results showed that PGEB-3-H could reduce the content of TC and TG and increase the level of HDL-C, but had no significant effect on the LDL-C content. It can be seen that PGEB-3-H has a potential effect on lowering blood lipids and is related to the regulation of cholesterol content. Lee et al. (2012) studies showed that the hypolipidemic indexes (total cholesterol, triglyceride and low-density lipoprotein cholesterol levels) of the acidic polysaccharide groups were lower than those in the control group. These results indicated that acidic polysaccharide improve serum lipid levels.

3.8 Other activities

GPs has various structures and diverse pharmacological effects. A large number of studies have shown that GPs play an effective role in anti-bacterial activity, osteoporosis prevention, liver protective effects, memory improvement and skin care effectiveness. Chen et al. (2018c) found that GPs had an inhibitory effect on G⁻, G⁺ and fungi. Chen et al. (2015) investigated that a sulfated polysaccharide (WSS25) extracted from the rhizome of *G. elata* inhibited RANKL-induced osteoclast formation in RAW264.7 cells and BMMs by blocking the BMP-2/Smad/Id1 signaling pathway. Shi et al. (2017) reported that GPs could improve the memory of rats with cerebral palsy by regulating neurotransmitter in the brain. A number of studies have applied GPs to develop a skin care product (Wang et al., 2016; Du and Chen, 2018; Zheng et al., 2018). Qiu et al. (2007) reported that WGEW and AGEW showed strong anti-dengue virus bioactivity. Chen et al. (2024) found that four heteropolysaccharides had an inhibitory effect on the anti-hyperglycaemic activity of α -amylase and α -glucosidase. Xu et al. (2023) reported that GPs had modulation of gut microbiota and improvement in metabolic disorders.

References

- Bao, Q. W., Qian, L., Gong, C., and Shen, X. Z. (2017). Immune-enhancing activity of polysaccharides from *Gastrodia elata*. *J. Food. Process. Pres.* 41, 13016. doi:10.1111/jfpp.13016
- Chen, C., Qin, Y., Fang, J. P., Ni, X. Y., Yao, J., Wang, H. Y., et al. (2015). WSS25, a sulfated polysaccharide, inhibits RANKL-induced mouse osteoclast formation by blocking SMAD/ID1 signaling. *Acta Pharmacol. Sin.* 36, 1053–1064. doi:10.1038/aps.2015.65
- Chen, J. C., Tian, S., Shu, X. Y., Du, H. T., Li, N., and Wang, J. R. (2016). Extraction, characterization and immunological activity of polysaccharides from *Rhizoma gastrodiae*. *Int. J. Mol. Sci.* 17, 1011. doi:10.3390/ijms17071011
- Chen, J. Q., Miao, W., Liu, Y., Zhou, J., Han, J., Zhang, L., et al. (2024). Structural characterization, molecular dynamic simulation, and conformational visualization of a water-soluble glucan with high molecular weight from *Gastrodia elata* Blume. *Int. J. Biol. Macromol.* 263, 130207. doi:10.1016/j.ijbiomac.2024.130207
- Chen, L., Zhang, Y. P., and Jin, L. X. (2018a). Preparation, characterization and anti-ageing activity of *Gastrodia elata* Blume polysaccharide. *Acta Aliment.* 47 (2), 210–219. doi:10.1556/066.2018.47.2.10
- Chen, S., Li, X. X., Fu, Y. D., Liu, X., Zheng, H. X., Wu, S. Q., et al. (2018b). Study on antibacterial activity of *Gastrodia* polysaccharides from Hanzhong. *Jiangsu Agri. Sci.* 46 (11), 156–159. doi:10.15889/j.issn.1002-1302.2018.11.041

4 Conclusion

In conclusion, as a traditional Chinese medicine, *G. elata* is widely used in medicine, food and health products. *G. elata* polysaccharides are one of the main components of *G. elata*. Due to its pharmacological effects such as anti-oxidation, anti-tumor, immune regulation and memory improvement, it has attracted great attention from scientists in medicine and healthcare fields. In this paper, structural analysis and pharmacological activities of related research, further study of *G. elata* polysaccharides and rational application for reference.

Author contributions

LY: Writing–original draft, Writing–review and editing. S-HQ: Writing–original draft. C-TZ: Writing–original draft, Writing–review and editing.

Funding

The author(s) declare that financial support was received for the research, authorship, and/or publication of this article. This work was supported by the National Natural Science Foundation of China (31960075 and 21602196), the Yunnan Province Agricultural Basic Research Joint Foundation (202101BD070001-028), and the Yunnan Ten Thousand Talents Plan Young and Elite Talents Project (YNWR-QNB J-2020-178).

Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Publisher's note

All claims expressed in this article are solely those of the authors and do not necessarily represent those of their affiliated organizations, or those of the publisher, the editors and the reviewers. Any product that may be evaluated in this article, or claim that may be made by its manufacturer, is not guaranteed or endorsed by the publisher.

- Chen, S., Li, X. X., Xu, Y. M., Lin, B. B., Zhou, T. H., Liu, X., et al. (2018c). Extraction, purification and antioxidant activity of polysaccharides from *Gastrodia elata* Bl. *Chin. J. Clin. Pharmacol.* 34 (18), 2203–2206. doi:10.13699/j.cnki.1001-6821.2018.18.020
- Chen, X., Cao, D. X., Zhou, L., Jin, H. Y., Dong, D., Yao, J., et al. (2011). Structure of a polysaccharide from *Gastrodia elata* Bl., and oligosaccharides prepared thereof with anti-pancreatic cancer cell growth activities. *Carbohydr. Res.* 342, 1300–1305. doi:10.1016/j.carbpol.2011.06.029
- Dai, S. S., Zhang, W. H., Dou, Y. W., Liu, H. M., Chen, X., Shi, J. H., et al. (2021). Towards a better understanding of the relationships between the structure and antitumor activity of *Gastrodia elata* polysaccharides by asymmetrical flow field-flow fractionation. *Food Res. Int.* 149, 110673. doi:10.1016/j.foodres.2021.110673
- Du, S. J., and Chen, D. L. (2018). Extraction of polysaccharides from Tianma stem and preparation of moisturizer. *Yunnan Chem. Tech.* 45, 102–104.
- Duan, X. H., Li, Z. L., Yang, D. S., Zhang, F. L., Lin, Q., and Dai, R. (2013). Study on the chemical constituents of *Gastrodia elata*. *J. Chin. Med. Mater.* 36 (10), 1608–1611. doi:10.13863/j.issn1001-4454.2013.10.022
- Feng, X. Z., Chen, Y. W., and Yang, J. S. (1979). Study on the chemical composition of *Tianma*. *Hua Hsueh Hsueh Pao* 37, 175–182.
- Guan, H., Ling, X., Xu, J., Zhu, Y. Q., Zhang, J. Y., and Liu, X. Y. (2022). Structural characterization of polysaccharide derived from *Gastrodia elata* and its immunostimulatory effect on RAW264.7 cells. *Molecules* 27, 8059. doi:10.3390/molecules27228059
- Hayashi, J., Sekine, T., Deguchi, S., Lin, Q., Horie, S., Tsuchiya, S., et al. (2002). Phenolic compounds from *Gastrodia* rhizome and relaxant effects of related compounds on isolated smooth muscle preparation. *Phytochem* 59, 513–519. doi:10.1016/S0031-9422(02)00008-0
- Hou, M. N., and Hou, S. P. (2018). Experimental study on antioxidant activity of *Gastrodia* polysaccharides from Shaanxi Province. *Shaanxi J. Agr. Sci.* 64 (6), 31–32.
- Huo, J. J., Lei, M., Li, F. F., Hou, J. J., Zhang, Z. J., Long, H. L., et al. (2021). Structural characterization of a polysaccharide from *Gastrodia elata* and its bioactivity on gut Microbiota Available. *Int. J. Biol. Macromol.* 186, 501–509. doi:10.1016/j.ijbiomac.2021.06.157
- Ji, N., Liu, P., Zhang, N., Yang, S. Y., and Zhang, M. S. (2022). Comparison on bioactivities and characteristics of polysaccharides from four varieties of *Gastrodia elata* Blume. *Front. Chem.* 10, 956724. doi:10.3389/fchem.2022.956724
- Kong, X. W., Liu, T. Y., and Guan, J. (2005). Effect of polysaccharide from the *Gastrodia elata* Blume on metabolism of free radicals in subacute aging model mice. *J. Anhui Univ. Nat. Sci. Ed.* 29 (2), 95–99.
- Lee, O. H., Kim, K. I., Han, C. K., Kim, Y. C., and Hong, H. D. (2012). Effects of acidic polysaccharides from *Gastrodia* rhizome on systolic blood pressure and serum lipid concentrations in spontaneously hypertensive rats fed a high-fat diet. *Int. J. Mol. Sci.* 13, 698–709. doi:10.3390/ijms13010698
- Li, F., Zhu, J. P., Wang, Y. M., and Shen, Y. S. (2013). Study on anti-senility effect of polysaccharide from *Gastrodia elata* Bl. *J. West Anhui Univ.* 29 (5), 12–14.
- Li, F., Zhu, J. P., Wang, Y. M., Zhou, E. H., and Shen, Y. S. (2015). Protection effect of polysaccharides from *Gastrodia elata* Bl. on the immunological liver injury in mice. *Pharmacol. Clin. Chin. Med.* 31 (1), 111–113.
- Li, N., Wang, D., Wen, X. J., Chu, R., Fan, J. Y., Chen, Y. L., et al. (2023). Effects of polysaccharides from *Gastrodia elata* on the immunomodulatory activity and gut microbiota regulation in cyclophosphamide-treated mice. *J. Sci. Food Agric.* 103, 3390–3401. doi:10.1002/jsfa.12491
- Li, X. B., Zhan, J. P., Zhang, Y. T., Xie, Z. L., Zhu, Y. Q., Chen, Y. L., et al. (2016). Effect of polysaccharide from *Gastrodia elata* Bl on humoral immune function in immunosuppressed mice induced by cyclophosphamide. *Chin. J. Gerontol.* 36 (5), 1027–1028.
- Liu, J., and Mori, A. (1992). Antioxidant and free radical scavenging activities of *Gastrodia elata* Bl. and *Uncaria rhynchophylla* (Miq.) Jacks. *Neuropharmacology* 31, 1287–1298. doi:10.1016/0028-3908(92)90058-W
- Liu, M. X., Li, Q. F., Liu, Q., Huang, Z. Q., and Qiu, F. (2009). Study on extraction technology, structure and free radical scavenging activity of polysaccharides from *Gastrodia elata* Bl. *Food Sci.* 30 (3), 29–32. doi:10.1360/972009-1551
- Liu, X. H., Guo, X. N., Zhan, J. P., Xie, Z. L., Wang, J. M., Zhang, Y. T., et al. (2015). The effects of polysaccharide from *Gastrodia elata* Bl on cell cycle and caspase proteins activity in H22 tumor bearing mice. *Chin. J. Gerontol.* 20, 5681–5682.
- Liu, Y., and Huang, G. L. (2017). The chemical composition, pharmacological effects, clinical applications and market analysis of *Gastrodia elata*. *Pharm. Chem. J.* 51, 211–215. doi:10.1007/s11094-017-1584-5
- Miao, H. C., and Shen, Y. S. (2006). Antihypertensive effect of polysaccharides substracted from *Gastrodia elata* Blume. *Chin. J. Hypertens.* 4 (7), 531–534. doi:10.1016/S1872-2040(06)60020-0
- Ming, J., Liu, J., Wu, S., Guo, X., Chen, Z., and Zhao, G. (2012). Structural characterization and hypolipidemic activity of a polysaccharide PGEB-3H from the fruiting bodies of *Gastrodia elata* Blume. *Procedia. Eng.* 37, 169–173. doi:10.1016/j.proeng.2012.04.221
- Qiu, H., Tang, W., Tong, X. K., Ding, K., and Zuo, J. P. (2007). Structure elucidation and sulfated derivatives preparation of two α -D-glucans from *Gastrodia elata*, and their anti-dengue virus bioactivities. *Carbohydr. Res.* 342, 2230–2236. doi:10.1016/j.carres.2007.06.021
- Qiu, H., Yang, B., Pei, Z. C., Zhang, Z., and Ding, K. (2010). WSS25 inhibits growth of xenografted hepatocellular cancer cells in nude mice by disrupting angiogenesis via blocking bone morphogenetic protein (BMP)/Smad/Id1 signaling. *J. Biol. Chem.* 285 (42), 32638–32646. doi:10.1074/jbc.M110.105544
- Shi, H., He, Q., Lou, Y. J., and Shao, S. J. (2017). Effect of *Gastrodia* rhizoma polysaccharide on brain neutral transmitter in immature rats with cerebral palsy. *Chin. J. Exp. Tradit. Med. Formulae.* 23 (23), 140–145.
- Wang, C. Q., Yang, Y., Tang, C., and He, X. R. (2022). Research progress on extraction, separation and pharmacological activities of rhizoma *Gastrodia* polysaccharide. *Chin. Pharm. Aff.* 36 (4), 417–428. doi:10.16153/j.1002-7777.2022.04.007
- Wang, Q., Zhang, Y., Li, J., and Re, T. L. (2014). The inhibition effect of polysaccharides from *Gastrodia elata* Bl on tumor growth through immune system. *Immunol. J.* 30 (6), 566–568. doi:10.13431/j.cnki.immunol.j.2014.01.24
- Wang, X. L., Liu, P. D., Zhang, L., Xie, Y., Yang, C., and Yu, Q. (2019). Effect of *Gastrodia* rhizoma polysaccharide on neuronal apoptosis gene expression in brain tissue of cerebral palsy newborn rats. *Clin. Basic Bridg. Res.* 35 (18), 2062–2064. doi:10.13699/j.cnki.1001-6821.2019.18.027
- Wang, X. M., and Liu, K. X. (2019). Experimental study of the effects of *Gastrodia elata* polysaccharide on delay in skeletal muscle aging. *J. Zunyi Med. Univers.* 42 (2), 135–140. doi:10.14169/j.cnki.zunyiuebao.2019.0027
- Wang, Y., Zan, L. X., Hu, L. L., Xu, H., Yang, P. J., Zhao, H., et al. (2016). Formulation study of O/W creams cosmetics *Tianma* crude extract. *Asia-Pac. Tradit. Med.* 12, 21–23. doi:10.11954/ytctuu.201617009
- Xie, X. Y., Chao, Y. M., Du, Z., and Zhang, Y. (2010). Effects of polysaccharides from *Gastrodia elata* Bl on anti-aging of ageing Mice. *Pharm. J. Chin. PLA.* 26, 206–209. doi:10.3969/j.issn.1008-9926.2010.03.06
- Xu, D., Wu, Q. Y., Liu, W. Y., Hu, G. M., Meng, H. H., and Wang, J. S. (2023). Therapeutic efficacy and underlying mechanisms of *Gastrodia elata* polysaccharides on dextran sulfate sodium-induced inflammatory bowel disease in mice: modulation of the gut microbiota and improvement of metabolic disorders. *Int. J. Biol. Macromol.* 248, 125919. doi:10.1016/j.ijbiomac.2023.125919
- Xu, L., Huang, Y. S., Zhu, Q. J., Wang, R. M., and Ye, C. (2015). Extraction and scavenging free radical effects of polysaccharides from *Gastrodia elata*. *Guangdong Agri. Sci.* 42 (21), 117–123. doi:10.16768/j.issn.1004-874x.2015.21.029
- Yang, X. D., Zhu, J., Yang, R., Liu, J. P., Li, L., and Zhang, H. B. (2007). Phenolic constituents from the rhizomes of *Gastrodia elata*. *Nat. Prod. Res.* 21, 180–186. doi:10.1080/14786410601081997
- Zhang, G., Xu, C. Y., Xu, M., and Zhang, X. F. (2019). Study on extraction and antioxidant activity of *Gastrodia* polysaccharide. *Agri. Dev. Equip.* 6, 118–119.
- Zhang, M. J., Xu, H. D., and An, X. G. (2007). Research on ultrasonic wave extraction of *Gastrodia elata* Bl. *Polysaccharides. J. Nat. Sci. Ed.* 35 (4), 91–95.
- Zhang, R. X., Zhang, Y. H., Zhou, Y. C., and Qi, Y. (2018). Research progress on the chemical structure and pharmacological effects of polysaccharides from traditional Chinese medicine. *Heilongjiang J. Tradit. Chin. Med.* 47 (1), 88–89.
- Zhang, S. Q., Liu, L., He, N. W., and Zhao, Y. (2021). *Gastrodia elata* polysaccharide from Shaanxi by ultrasound-assisted hot water extraction: process optimization and antioxidant activity. *Chin. Agri. Sci. Bull.* 37 (9), 131–136.
- Zhang, Y. G., Ye, P., Zhu, H., Gu, L. J., Li, Y. T., Feng, S., et al. (2023). Neutral polysaccharide from *Gastrodia elata* alleviates cerebral ischemia-reperfusion injury by inhibiting ferroptosis-mediated neuroinflammation via the NRF2/HO-1 signaling pathway. *CNS Neurosci. Ther.* 30, 14456–e14514. doi:10.1111/cns.14456
- Zheng, J., Sun, M. M., Hu, A. J., Hu, X. H., Ren, Y. Y., and Yu, S. Y. (2018). Extraction of polysaccharide from *Gastrodia elata* Blume and preparation of its drinks. *Food Res. Dev.* 39, 123–128. doi:10.3969/j.issn.1005-6521.2018.04.022
- Zhou, B. H., Liang, Y. X., Shen, H., Liu, G., and Tu, J. (2013). Study on the protective mechanism of *Gastrodia* polysaccharide on PC12 cells damaged by corticosterone. *J. Chin. Med. Mater.* 36 (4), 630–633.
- Zhou, B. H., Tan, J., Zhang, C., and Wu, Y. (2017). Neuroprotective effect of polysaccharides from *Gastrodia elata* Blume against corticosterone induced apoptosis in PC12 cells via inhibition of the endoplasmic reticulum stress mediated pathway. *Mol. Med. Rep.* 28 (17), 1182–1190. doi:10.3892/mmr.2017.7948
- Zhu, H., Liu, C., Hou, J., Long, H., Wang, B., Guo, D., et al. (2019). *Gastrodia elata* Blume polysaccharides: a review of their acquisition, analysis, modification, and pharmacological activities. *Molecules* 24, 2436. doi:10.3390/molecules24132436
- Zhu, X. X., Zhang, Y., and Luo, X. G. (2010). Studies on structure characterization of *Gastrodia elata* Bl polysaccharides. *Food Res. Dev.* 31 (09), 52–56.
- Zhu, Z. Y., Chen, C. J., Sun, H. Q., and Chen, L. J. (2018). Structural characterization and ACE-inhibitory activities of polysaccharide from *Gastrodia elata* Blume. *Nat. Prod. Res.* 33 (12), 1721–1726. doi:10.1080/14786419.2018.1434643