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Review

Overview of *Ganoderma sinense* polysaccharide–an adjunctive drug used during concurrent Chemo/Radiation therapy for cancer treatment in China

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ABSTRACT

Ganoderma sinense or “Chinese Lingzhi” is a well-known medicinal fungus in China for more than 2000 years. Polysaccharide is the main immunomodulatory and antitumor component in *G. sinense*. In 2010, *G. sinense* polysaccharide (GSP) tablet is approved as an adjunctive therapeutic drug in China for treating leukopenia and hematopoietic injury caused by concurrent chemo/radiation therapy during cancer treatment by the State Food and Drug Administration (SFDA). β-glucan, an established immunostimulant, is one of the components in GSP. Based on CNKI (China National Knowledge Infrastructure), VIP (Chongqing VIP Chinese Scientific Journals Database), Wanfang database, and PubMed searches, we have not only summarized but also translated all the basic and preclinical studies about GSP published in Chinese into English in this review article. Unfortunately, all the clinical studies about GSP tablet could not be found during the search or by contacting the drug manufacturers. However, both basic and preclinical studies showed that GSP has antitumor, antioxidant, anticytopenia, and unique mushroom-poison detoxification properties that are different from that of *G. lucidum* polysaccharide, another “Lingzhi” polysaccharide. The structure and molecular mechanisms of GSP are also discussed. This article urges availability of clinical study results of GSP tablet that would allow in-depth evaluation if the tablet is appropriate to serve as an immunomodulatory drug during cancer therapy at world stage.

1. Introduction

Ganoderma, which is known as “Lingzhi” in Chinese, have used widely in China and other oriental countries for over two thousand years. “Lingzhi” includes both *G. lucidum* and *G. sinense* as recorded in Chinese Pharmacopoeia of 2010 [1,2].

G. sinense is a special species of “Lingzhi” named “Chinese Lingzhi” for it is mainly found in certain regions of China. The fruiting body of *G. sinense* has a purplish color (Fig. 1), which is enriched in polysaccharides, ergosterol, coumarin, organic acids, glucosamine, mannitol, polysaccharide alcohol, fatty acids, alkaloids, water-soluble proteins, and a variety of enzymes. Since *G. sinense* is traditionally used in the form of decoction, the water-soluble polysaccharides are considered to be the major pharmaceutical ingredients of *G. sinense*. Indeed, the *G. sinense* polysaccharide (GSP) has immune-balancing, anti-tumor [3], antioxidant [4,5], anti-cytopenia [6], mushroom-poison detoxification properties [7]. So far, high-performance liquid chromatography (HPLC), gas chromatography (GC), mass spectrometry (MS), nuclear magnetic resonance (NMR) and high-performance thin-layer chromatography (HPTLC) have been used to determine chemical structures of polysaccharides from “Lingzhi” [8–10]. Previous studies showed that polysaccharides from both *G. lucidum* and *G. sinense* consist of arabinose, galactose, glucose, xylose, and mannose, which indicates that their monosaccharide compositions are similar [11,12]. Among different fractions of polysaccharides obtained, a polysaccharide named GSP-2 isolated from the fruiting bodies of *G. sinense* has a molecular weight of 32 kDa. By a combined chemical and spectroscopic analytical approaches, GSP-2 is proved to be a β-glucan with a backbone of (1 → 4)–and (1 → 6)–Glc*p*, bearing terminal- and (1 → 3)–Glc*p* side-chains at O-3 position of (1 → 6)–Glc*p* [13–15] (Fig. 2). In addition, another polysaccharide named GS-A-1 isolated and identified by Niu et al. from *G. sinense* turns out to be a totally different polysaccharide consisting of α-L-mannopyranose and α-L-galactopyranose with (1 → 2) or (1 → 6) linkages [16]. Based on the monosaccharide composition data for both

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Fig. 1. The fruiting body of *G. sinense* or Chinese Lingzhi [2].

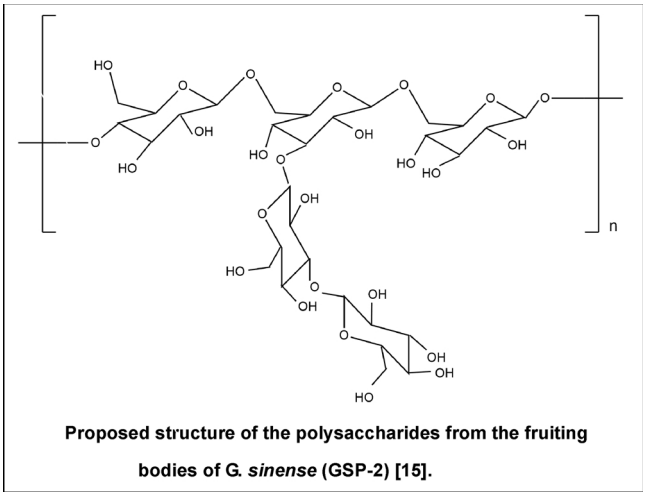


Fig. 2. Proposed structure of the polysaccharides from the fruiting bodies of G. *sinense* (GSP-2) [15].

G. lucidum and *G. sinense* [11,12], most of GSP structures that also contain arabinose and xylose have not been characterized.

G. sinense Polysaccharide Tablet (GSPT), whose active constituent is *G. sinense* polysaccharide (GSP), has already been approved for marketing by China Food and Drug Administration (SFDA) since 2010. So far, GSPT is produced by two pharmaceutical companies in China including Jilin Tonghua Zhenguo Pharmaceutical Company and Jiangxi Zezhong Pharmaceutical Company with SFDA approval numbers of Z22022112 and Z36021232, respectively.

Based on CNKI (China National Knowledge Infrastructure), Wanfang database, and PubMed searches by using keyword *Ganoderma sinense polysaccharide*; we pulled out all of the publications. After reviewing the description about the GSP used; the methods; data; results and conclusions; we found 21 relevant studies of GSP both in English and Chinese spanning from 1979 to 2016. A summary of the major biological activities of GSP is shown in Fig. 3; which will discussed in detail in the next section. Unfortunately; all the clinical studies about GSP tablet could not be found in the public database or obtained by contacting the two drug manufacturers.

Fig. 4 is a summary of reported molecular mechanisms that explain the biological activities of GSP. It is well known that the activities of polysaccharides are related to their molecular weight, chemical composition, configuration, chain conformation, as well as their physicochemical properties. As shown in Fig. 4, GSP has an obvious effect on regulating immune function by activating macrophages, T lymphocytes, and B lymphocytes to promote antibody formation and complement system activation [15,17]. Macrophages of the innate immune system plays critical roles in bacteria destruction, antigen presentation, tumor cell destruction, and wound healing. It is also the first group of immune cells that interacts with the exogenous polysaccharides in that macrophages in the intestine engulf those polysaccharides survived both chemical and enzymatic digestion when passing through stomach. Macrophages then degrade these polysaccharides into oligosaccharides, which will be further presented to the T and B lymphocytes for adaptive immune responses [18,19]. Meanwhile, GSP induces the synthesis of cytokines such as interleukin-1β (IL-1β), IL-2, IL-6, IL-10, IL-12, granulocyte-macrophage colony stimulating factor (GM-CSF), transforming growth factor-β (TGF-β) and tumor necrosis factor-α (TNF-α). IL-12 is a typical Th1 cytokine, which indicates that GSP has the ability to induce Th1-dependent immune response [17]. At the same time, GSP inhibits cancer cell proliferation both *in vivo* and *in vitro* [3,20].

2. The biological activities of GSP both *in vitro and in vivo*

2.1. Anti-oxidation

A range of chronic diseases such as cancer, diabetes, and cardiovascular disease and human aging are closely related to excessive reactive oxygen species (ROS). Interestingly, most polysaccharides have anti-oxidative activities through their radical-scavenging and immune regulatory activities [21,22].The anti-oxidative activities of GSP have been evaluated both in animal and cell models during the past.

It was reported that GSP up-regulates both the activity and quantity of the super oxide dismutase (SOD) in an animal model [23]. As a result, it enhances the body's ability to scavenge free radicals and also reduces radical-induced organ injury by inhibiting the peroxidation of lipids to protect body cells and to delay senescence of cells [23]. The anti-oxidative properties of GSP are also investigated by using four different assay systems and the results are summarized in Table 1. GSP scavenges all four oxidative species including OH, DPPH, O_2^-, and H_2O_2 in a dose-dependent manner (Table 1). It is speculated that the hydroxyl groups increase the affinities between free radicals and GSP that is directly responsible for the anti-oxidative activity [20]. Tang et al. also reported that GSP has antioxidant activities against DPPH, FRAP, and ABTS [24].

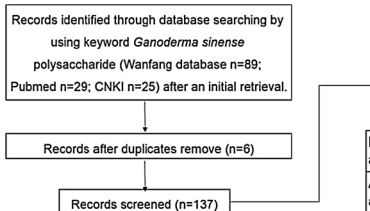
2.2. Anti-tumor

As shown in Fig. 4, both innate and acquired immunities are enhanced by GSP through activating T-cells, B-cells, dendritic cells, monocytes and macrophages by releasing a variety of chemokines, cytokines, and growth factors, which leads to cancer cell destruction. In addition, GSP inhibits cancer cell growth directly in cultured conditions. In the published reports, different fractions of GSP or *G. sinense* powder have been prepared by different research groups and used to study the anti-tumor effect of GSP compared to *G. sinense* powder both *in vitro* (Table 2) and *in vivo* (Table 3). The data in Table 2 show that GSP inhibits cultured cancer cell growth in general (A549, LoVo, QGY-7703, CEM cell lines [20] and EC-109 [3]), indicating GSP has direct cytotoxicity against cancer cells.

Most importantly, different GSP fractions also inhibit the growth of both hepatoma and Lewis lung tumors (Table 3) in a mouse model [20], which confirm the results of the *in vitro* studies (Table 2).

2.3. Anti-inflammatory, analgesic and immune regulation

GSP regulates B cell, T cell, and macrophage activities. Different structures of GSP from different *G. sinense* species stimulate the expression of different cytokines and growth factors. In general, GSP can induce synthesis of cytokines such as IL-1β, IL-2, IL-6, IL-10, IL-12, GM-CSF, TGF-β and TNF-α and regulate the expression of CD4, CD8, CD14 in PBMC [15,17,23,25,26]. IL-12 is a typical Th1 cytokine, which indicates that GSP has the ability to induce Th1 immune response [25,26]. Fig. 4 is a summary of molecular mechanisms of GSP. Anti-inflammatory and analgesic results in animal models are shown in Table 4. Compared with GSP isolated from the extraction of *G. sinense* mycelia by batch fermentation, GSP from fruiting body of *G. sinense* has better anti-inflammatory effect on preventing joint swelling. However



Biological activities	Article numbers	Models
Anti-inflammatory and analgesia	2	Wistar Rats
		Kun Ming Mice
Anti-oxidation	2	Colorimetric method
Anti-tumor	4	A549 (human lung cancer cells)
		LoVo (human hepatocellular carcinoma cells)
		CEM (human T cell leukemia cells)
		QGY-7703 (human hepatocellular carcinoma cells)
		EC-109 (human esophageal cancer cells)
		Lewis Lung Cancer Mouse Model
		Hepatoma H22 Mouse Model
Detoxication	3	Poisoned patients
Liver protection	1	Kun Ming Mice
Radiation protection	2	LACA Mouse Model
Anti-ulcer effect	1	Wistar Rats and Kun Ming Mice
Anti-fatigue effect	1	SD Rats
Immunomodulating Activity	4	RAW 264.7 mouse macrophage cells
Anti-diabetic	1	α-glycosidase inhibition assay

Flow chart of literature review process. Based on CNKI (China National Knowledge Infrastructure), Wanfang database, and PubMed searches by using keyword *Ganoderma sinense* polysaccharide, we pulled out all of the publications. After reviewing the description about the GSP used, the methods, data, results and conclusions, we found 21 qualified studies of GSP both in English and Chinese spanning from 1979 to 2016.

Fig. 3. Flow chart of literature review process. Based on CNKI (China National Knowledge Infrastructure), Wanfang database, and PubMed searches by using keyword *Ganoderma sinense* polysaccharide, we pulled out all of the publications. After reviewing the description about the GSP used, the methods, data, results and conclusions, we found 21 qualified studies of GSP both in English and Chinese spanning from 1979 to 2016.

GSP from the extraction of *G. sinense* mycelia has better analgesic effect on pain caused by blanching and acetic acid, suggesting the GSP structures from mycelia and fruiting body might not be the same. In addition, GSP reduces capillary permeability, the effect is similar to that of indomethacin [27].

2.4. Other effects

2.4.1. Radiation protection

Liu et al. [28] delivered GSP to LACA mice by ip, which revealed that GSP protects the mice from ^{60}Coγ radiation-induced damage. They speculated that GSP increases the hematopoietic cells directly or indirectly in the mouse model. Meanwhile, GSP has the ability to reduce ^{60}Coγ radiation damage to the mice compared to that of the control [28,29].

2.4.2. Anti-fatigue

Zhu et al. [30] administered different doses of GSP to the exhausted rats and reported that GSP improves running time of the SD rats significantly, suggesting GSP had anti-fatigue effect in a dose-dependent manner. They speculated that GSP has ability to maintain the concentration of blood glucose and amount of hepatic glycogen in the rat model.

2.4.3. Increasing leukocyte production and bone marrow function

Niu et al. [16] found that GS-A-1, isolated from *G. sinense* mycelium submerged culture, has anti-cytopenia effect in mice. When compared with the combination of Lentinan and Cytoxan, GS-A-1 combined with Cytoxan has better effect in increasing the numbers of leukocytes, platelets, and hemoglobin ($P < 0.05$) in the mouse model [16].

2.4.4. Liver protection

Liu et al. [31] reported that GSP has various pharmaceutical effects in a mouse liver injury model. When liver cell injury is induced by CCl_4, which is accompanied with increased serum glutamic-pyruvic transaminase (SGPT) concentration ($P < 0.05$), GSP not only reduces SGPT concentration significantly but also reduces the liver damage caused by CCl_4.

GSP reduces the side effects of digitoxin and indomethacin as well. Moreover, when mouse liver is partially resected, GSP promotes liver regeneration significantly ($P < 0.01$). Furthermore, GSP shortens the pentobarbital sleep time after administrating GSP three times in a row [31].

2.4.5. Anti-diabetic effect

Tang et al. [24] found that GSP has remarkable antidiabetic effect with almost no side effect. GSP has the ability to promote the recovery and proliferation of islet B cells, to stimulate the secretion of insulin, and to increase the rate of glucose metabolism rather than by inhabiting α-glycosidase activity [4].

2.4.6. Detoxification against mushroom poisoning in patients

Even though *G. lucidum* and *G. sinense* polysaccharides have similar monosaccharide compositions, the detoxification mechanism of GSP is different from that of *G. lucidum* polysaccharide [11,12]. Table 5 summarizes the data from three independent studies when the decoctions enriched in either GSP or *G. lucidum* polysaccharides are used to treat poisoned patients caused by toxic mushrooms. The data show that the decoction from *G. sinense* but not *G. lucidum* has detoxification effect against mushroom poisoning in patients with a curing rate above 90% [6,32,33].

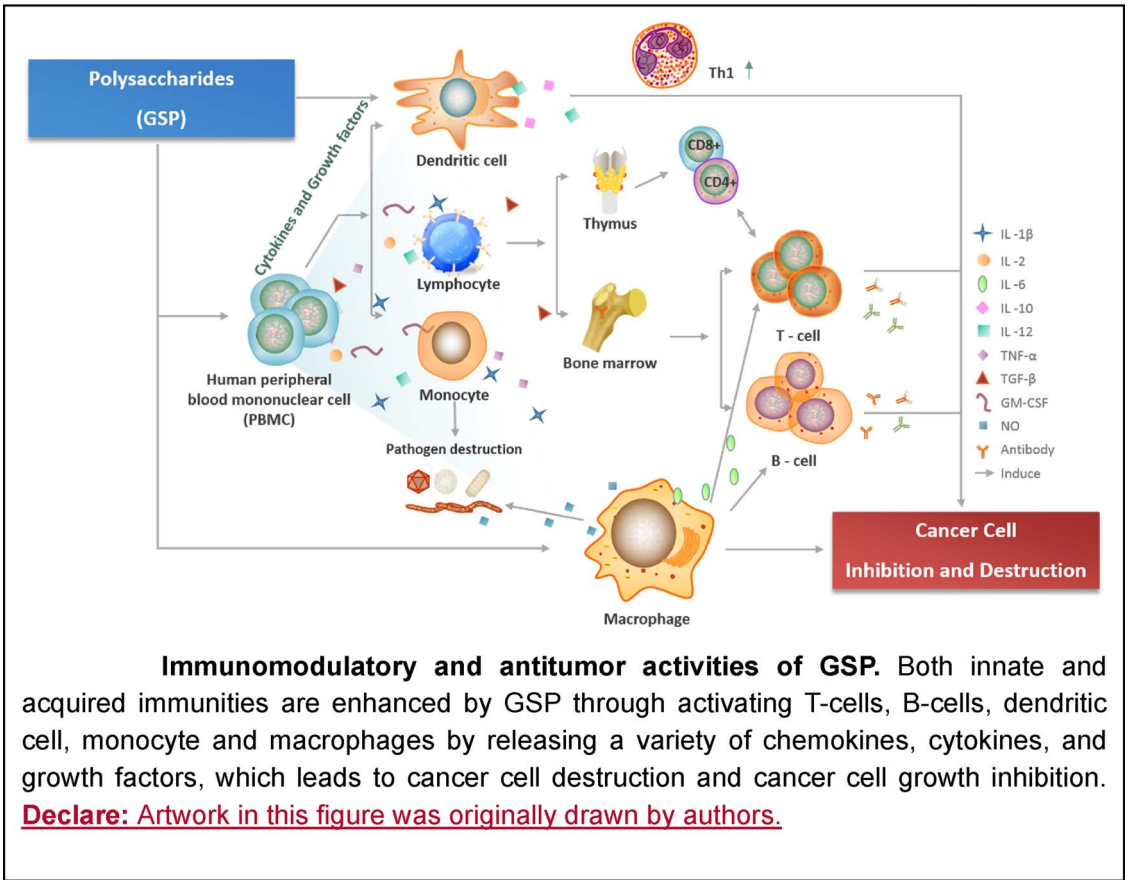


Fig. 4. Immunomodulatory and antitumor activities of GSP. Both innate and acquired immunities are enhanced by GSP through activating T-cells, B-cells, dendritic cell, monocyte and macrophages by releasing a variety of chemokines, cytokines, and growth factors, which leads to cancer cell destruction and cancer cell growth inhibition. **Declare:** Artwork in this figure was originally drawn by authors.

Table 1
Anti-oxidative effect of GSP.

Models	Component	Dosage (mg/ml)	Clearance (%)	References
-OH	GSPI	2.5	94.76	[3]
DPPH			87.76	
- OH	GSP1	5	39.46	[7]
	GSP2		81.50	
DPPH	GSP1	1.6	76.30	
O_2^-	GSP1	9	3.29	
	GSP2		47.40	
	GSP3		21.70	
H_2O_2	GSP1	10	22.31	
	GSP2		48.12	
	GSP3		26.81	

Abbreviations: GSP, *G. sinense* polysaccharide; DPPH, 1, 1-diphenyl-2-picrylhydrazyl; GSPI, fraction I of GSP; GSP1, fraction 1 of GSP; GSP2, fraction 2 of GSP; GSP3, fraction 3 of GSP.

3. Discussions and conclusion

This article briefly summarized the published data about the structure (Fig. 3), molecular mechanisms (Fig. 4), and biological activities (Table 1–5) of GSP. Since GSP is a mixture of polysaccharides, the fractionation methods and the raw materials used for GSP preparations should be important factors to consider in future studies. The analysis and evaluation of different polysaccharide components and molecular mechanisms of GSP are expected in near future. Moreover, the pharmaceutical active ingredient for making GSP tablets should be obtainable for research purposes.

Conventional cancer treatments include surgery, chemotherapy, and radiation therapy, which are associated with either surgical risk or severe side effects. In recent years, the impact of immunotherapy on clinical cancer care is growing rapidly. Developing immunotherapeutics, especially from existing drugs, are highly expected.

Table 2
In vitro anti-cancer effects of GSP.

Cell Comp	IC_{50}/μg·mL^{-1}				Inhibitory Rate (%)	References
	A549	LoVo	QGY-7703	CEM	EC-109	
B	160.00 ± 4.25	29.28 ± 3.78	45.06 ± 4.36	37.38 ± 2.75	/	[20]
CGLE	100.00 ± 2.26	100.00 ± 4.33	100.00 ± 3.98	100.00 ± 3.55	/	
GSPI	/	/	/	/	48.31	[3]
GSPII	/	/	/	/	25.33	

Abbreviations: GSP, *G. sinense* polysaccharide; B, fraction B of GSP; CGLE, Ganoderma powder; Comp, component; GSPI, fraction I of GSP; GSPII, fraction II of GSP.
EC-109, human esophageal cancer cells; A549, human lung cancer cells A549; LoVo, human hepatocellular carcinoma cells ; CEM, human T cell leukemia cells; and QGY-7703, human hepatocellular carcinoma cells.

Table 3
In vivo anti-tumor effect of GSP.

Model	GSP fractions	Drug delivery	Dosage (mg/kg)	Animal amount	Inhibitory rate (%)	P-value	CGLE group	Dosage (mg/kg)	Inhibitory rate (%)	P-value	References
Hepatoma H22 Mouse	GSPa	ig	1383	10	40.80	< 0.01	CGLE	250	57.85	< 0.01	[20]
		ip	691.5		55.11	< 0.01					
	GSPb	ig	442	10	29.55	< 0.05					
		ip	221		50.16	< 0.01					
	GSPc	ig	135	10	58.22	< 0.01					
		ip	67.5		58.07	< 0.01					
	GSPd	ig	692	10	57.11	< 0.01					
		ip	346		56.50	< 0.01					
	A	ig	78	10	41.59	< 0.01	CGLE	250	33.73	< 0.01	
	B		40.5		63.94	< 0.01					
	C		37.5		38.73	< 0.01					
Lewis Lung Cancer Mouse	A	ig	78	10	33.22	< 0.05	CGLE	250	44.90	< 0.01	
	B		40.5		58.32	< 0.01					
	C		37.5		22.52	< 0.01					

Abbreviations: GSP, *G. sinense* polysaccharide; GSPa, component a from *G. sinense* fermentation supernatant; GSPb, component b from *G. sinense* fermentation supernatant; GSPc, component c from *G. sinense* fermentation precipitation; GSPd, component c from *G. sinense* fermentation precipitation; ig, irrigation; ip, intraperitoneal injection; CGLE, Ganoderma complex powder; A, fraction A of GSP; B, fraction B of GSP; C, fraction C of GSP.
CGLE (Ganoderma complex powder) is used as a positive control. P-values are obtained by comparing the efficacy data of GSP fractions or CGLE to the no-treatment control [20].

Table 4
Anti-inflammatory and analgesic effects of GSP.

Experimental group								Control group			
Model	Animal amount (M/F)	Item	GSP source	Drug delivery	Dosage (g/kg)	Inhibitory rate (%)	P-value	Positive and negative controls	Dosage of control (g/kg)	Inhibitory rate of control (%)	References
Wistar Rats	50 (25/25)	JSP	AGSP	ig	2.5	38.6	< 0.01	Indomethacin	0.05	95.7	[27]
					5.0	55.0					
			NGS		5.0	70.2	< 0.01				
	40 (20/20)	JST	AGSP		2.5	51.0	< 0.01	Physiological saline	/	/	
					5.0	64.7					
			NGSP		5.0	70.5	< 0.01				
Kun Ming Mice	51 (N/A)	ES	AGSP	ig	2.5	20.0	< 0.05	Physiological saline	/	/	[27]
	50 (25/25)	PBM	AGSP		3.0	64.2	< 0.01	Indomethacin	0.01	57.1	
					5.0	57.1	< 0.05				
			NGSP		5.0	50.0	< 0.05				
	55 (N/A)	PAA	AGSP		2.5	40.4	< 0.01	Indomethacin	0.01	47.7	
					5.0	58.2					
			NGSP		5.0	42.0	< 0.01				

Abbreviations: GSP, *G. sinense* polysaccharide; AGSP, fermentation production of cultured *G. sinense*; NGSP, fermentation production of natural *G. sinense*; JSP, swelling of joint prevention; JST, swelling of joint treatment; ES, ear swelling; SCP, skin capillary permeability; CBG, cotton pellet granuloma; PBM, pain caused by blanching method; PAA, pain caused by acetic acid; N/A, not available.
Indomethacin is used as positive control and physiological saline is used as a negative control. P-value was obtained by comparing the efficacy data of GSPs to that of physiological saline group.

Table 5
Detoxification of mushroom poisoning effect of G. sinense.

Treatment	Case (M/F)	Poisonous Mushroom Species	Recovery rate (%)	References
Ganoderma decoction and treated with hemodialysis	37 (29/8)	Lepiota brunneo-incarna	91.8	[33]
Ganoderma decoction and treated with traditional Chinese and Western medicine	25 (N/A)	Amanita virosa Lam	90.9	[32]
		Amanita solitaria (Bull.: Fr.) Karst.	100	
		Amanita pantherina (DC.: Fr.) Schrmm	100	
Ganoderma decoction treated with traditional Chinese and Western medicine	28 (N/A)	Amanita virosa Lam	96.4	[6]
		Amanita solitaria (Bull.: Fr.) Karst.	96.4	
		Amanita pantherina (DC.: Fr.) Schrmm	96.4	

Abbreviations: GSP, *G. sinense* polysaccharide; M/F, numbers of male /numbers of female; N/A, not available.

Impressively, China is the only country that has approved eight polysaccharide-based drugs as immunotherapeutics, where GSP tablet is one of them [2].

There are many issues needed to be addressed before GSP is considered as drug or drug candidates at world stage, such as how to standardize the β-glucan contents in GSP, how to describe other GSP structure and biological functions in the GSP tablets, how to comprehend the pharmacodynamics of GSP at molecular level, how to elaborate the immunomodulatory mechanisms of GSP.

Conflict of interest

None

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References

[1] L.Z. Meng, J. Xie, G.P. Lv, D.J. Hu, J. Zhao, J.A. Duan, S.P. Li, A comparative study on immunomodulatory activity of polysaccharides from two official species of Ganoderma (Lingzhi), Nutr. Cancer 66 (2014) 1124–1131.
[2] Z.J. Zhou, Z.R. Han, Y.Y. Zeng, M. Zhang, Y.D. Cui, L.L. Xu, L.J. Zhang, Chinese FDA approved fungal glycan-Based drugs: an overview of structures, mechanisms and clinical related studies, Transl. Med. 4 (2014) 1–11.
[3] M.L. Zhao, Study on Extraction, Purification, and the Primary Efficacy Activity of the Polysaccharides Isolated from Ganoderma Sinense, Hebei North University, China, 2013.
[4] T. Wu, B. Xu, Antidiabetic and antioxidant activities of eight medicinal mushroom species from China, Int. J. Med. Mushrooms 17 (2015) 129–140.
[5] N. Chen, Study on the Liquid Fermentation of Ganderma Lucidum and Antioxidant Activity of the Polysaccharide, South China University of Technology, China, 2012.
[6] X.L. He, J.Y. He, Efficacy analysis of Ganoderma lucidum mushroom poisoning treatment, Shi Yong Jun Xue Bao. 3 (1999) 47–48.
[7] Y.M. Qi, T. Chen, Purification and antioxidant activity in vitro of exopolysaccharides from fermentation liquid of Ganoderma Sinense, Sci. Technol. Food Ind. 34 (2013) 105–113.
[8] Y.W. Chang, T.J. Lu, Molecular characterization of polysaccharides in hot-water extracts of Ganoderma lucidum fruiting bodies, J. Food Drug Anal. 12 (2003) 59–67.
[9] S.Q. Huang, J.W. Li, Y.Q. Li, Z. Wang, Purification and structural characterization of a new water-soluble neutral polysaccharide GLP-F1-1 from Ganoderma lucidum, Int. J. Biol. Macromol. 48 (2011) 165–169.
[10] X. Di, K.K. Chan, H.W. Leung, C.W. Huie, Fingerprint profiling of acid hydrolyzates of polysaccharides extracted from the fruiting bodies and spores of Lingzhi by high-performance thin-layer chromatography, J. Chromatogr. A 1018 (2003) 85–95.
[11] A.O. Tzianabos, Polysaccharide immunomodulators as therapeutic agents: structural aspects and biologic function, Clin. Microbiol. Rev. 13 (2000) 523–533.
[12] J. Xie, J. Zhao, D.J. Hu, J.A. Duan, Y.P. Tang, S.P. Li, Comparison of polysaccharides from two species of Ganoderma, Molecules 17 (2012) 740–752.
[13] P. Lin, H.P. Yang, L. Huang, D.S. Wei, J. Wu, Y. Wang, Y.K. Yong, Isolation, purification and structural comparison investigation polysaccharides of G. Japonicum Mycelium, Food Res. Dev. 28 (2007) 66–70.
[14] Y.G. Yu, J. Zhang, J.L. Zhang, Advances on structure and pharmacological effects of Ganoderma lucidum polysaccharde, J. Traditional Chin. Vet. Med. 4 (2012) 20–21.
[15] X.Q. Han, G.L. Yue, R.Q. Yue, C.X. Dong, C.L. Chan, C.H. Ko, W.S. Cheung, K.W. Luo, H. Dai, C.K. Wong, Structure elucidation and immunomodulatory activity of a beta glucan from the fruiting bodies of Ganoderma sinense, PLoS One 9 (2014) 1–10.
[16] L..X. Niu, Y.F. Yang, Z,B. Zhao, Identification and biological activity research of GS-A-1 polysaccharide from Ganoderma, Chinese Traditional Patent Medicine 34 (2012) 968–971.
[17] X.Q. Han, B.C. Chan, H. Yu, Y.H. Yang, S.Q. Hu, C.H. Ko, C.X. Dong, C.K. Wong, P.C. Shaw, K.P. Fung, P.C. Leung, W.L. Hsiao, P.F. Tu, Q.B. Han, Structural characterization and immuno-modulating activities of a polysaccharide from Ganoderma sinense, Int. J. Biol. Macromol. 51 (2012) 597–603.
[18] Chan GC-F, W.K. Chan, Sze DM-Y, The effects of β−glucan on human immune and cancer cells, J. Hematol. Oncol. 25 (2009) 1–11.
[19] J.Z. Chen, R. Seviour, Medicinal importance of fungal β-(1→3), (1→6)-glucans, Mycol. Res. 111 (2007) 635–652.
[20] G. Yang, Y. Yang, J. Jin, Antitumor fraction from liquid submerged fermentation of Ganoderma Sinense, Chin. Traditional Herbal Drugs 39 (2008) 877–880.
[21] Z.J. Wang, J.H. Xie, S.P. Nie, M.Y. Xie, Review on cell models to evaluate the potential antioxidant activity of polysaccharides, Food Funct. 8 (2017) 915–926.
[22] J. Wang, S. Hu, S. Nie, Q. Yu, M. Xie, Reviews on mechanisms of In vitro antioxidant activity of polysaccharides, Oxid. Med. Cell Longev. 2016 (2016) 5692852.
[23] Y.F. Qiu, D.S. Xing, W. Deng, G.Q. Xing, X.F. Qiao, Experimental study of ganoderma lucidum polysaccharide oral liquid's effects on immunologic function in mice, J. Taishan Med. Coll. 6 (2004) 586–588.
[24] X. Tang, W. Cai, B. Xu, Comparison of the chemical profiles and antioxidant and antidiabetic activities of extracts from two ganoderma species (Agaricomycetes), Int. J. Med. Mushrooms 18 (2016) 609–620.
[25] G.G. Yue, B.C. Chan, X.Q. Han, L. Cheng, E.C. Wong, P.C. Leung, K.P. Fung, M.C. Ng, K. Fan, D.M. Sze, C.B. Lau, Immunomodulatory activities of Ganoderma sinense polysaccharides in human immune cells, Nutr. Cancer 65 (2013) 765–774.
[26] X.Q. Han, L.C.B. Chung, C.X. Dong, Y.H. Yang, C.H. Ko, Y.G. Gar-Lee, D. Chen, C.K. Wong, L.C. Bik-San, P.F. Tu, P.C. Shaw, K.P. Fung, P.C. Leung, W.L. Hsiao, Q.B. Han, Isolation, structure characterization, and immunomodulating activity of a hyperbranched polysaccharide from the fruiting bodies of Ganoderma sinense, J. Agric. Food Chem. 60 (2012) 4276–4281.
[27] F.C. Wan, D.Z. Huang, Studies of anti-inflammatory and analgesic actions of artificial and fermentative Ganoderma Sinense, China J. Chin. Mater. Med. 10 (1992) 619–622.
[28] Z.F. Liu, S.L. Chen, F. Chu, M.G. Yin, Influence of Ganoderma polysaccharide on hematopoietic cells in bone marrow on LACA mice and its radiation sensitivity, Jiangxi Med. J. 2 (1983) 9–12.
[29] F. Chu, H.L. Luo, G. Luo, S.L. Chen, Z.F. Liu, Ganoderma polysaccharide on micronucleus in bone marrow nucleated cells of mice induced by radiation effect of protective effects, Radiat. Prot. 8 (1988) 16–20.
[30] Z.X. Zhu, The Ganoderma Sinensis effect in the exhaustive rat of resistant sport fatigue and resisitant tissue damage, China Sport Sci. 32 (2012) 75–80.
[31] G.T. Liu, T.T. Bao, H.L. Wei, Z.Y. Song, Some pharmacological actions of Ganoderma Lucidum and G.Japonicum (Fr) Llyod on mouse liver, Acta Pharma. Sin. 14 (1979) 284–287.
[32] J.Y. He, Three kinds of poisonous mushroom poisoning clinical and treatment effect of Ganoderma.Information on epidemic prevention in Guangdong, Guangdong J. Health Epidemic Prevention 1 (1984) 102–105.
[33] R.Y. Qiao, Y. Guo, Y.H. Zhang, Ganoderma decoction combined with hemodialysis in the treatment of 37 cases of mushroom poisoning, Shanxi J. Traditional Chin. Med. 29 (2008) 1028–1029.