ASIAN JOURNAL OF PHARMACEUTICAL AND CLINICAL RESEARCH

INNOVARE ACADEMIC SCIENCES
Knowledge to Innovation

Vol 14, Issue 3, 2021

Online - 2455-3891
Print - 0974-2441

Review Article

MAJOR BIOACTIVE PROPERTIES OF *GANODERMA* POLYSACCHARIDES: A REVIEW

ZAHOOR AHMAD BHAT*, ABDUL HAMID WANI, JOHN MOHD WAR, MOHD YAQUB BHAT

Department of Botany, Section of Plant Pathology and Mycology, University of Kashmir, Hazaratbal, Srinagar, India.
Email: zahoorbht20@gmail.com

Received: 27 November 2020, Revised and Accepted: 31 December 2020

ABSTRACT

Ganoderma a white rot fungus has been used as a folk remedy for promoting health and longevity for centuries. The vast amount of study has been performed on the medicinal properties of *Ganoderma* in general and *Ganoderma lucidum* in particular. The bioactivities of the metabolites reported from *G. lucidum* are immense. The main bioactive metabolites of *G. lucidum* consist of mainly polysaccharides and triterpenoids. The major bioactive polysaccharides isolated from *Ganoderma* species are β (1→3), β (1→4), and β (1→6)-D glucans. With respect to the pure chemical and structural points of view, *G. lucidum* polysaccharides are mostly composed of β-glucans, heteropolysaccharides, and glycoptoteins. The major component of this sugar molecule is glucose together with xylose, mannose, galactose, and fructose in different conformations. Many of these bioactive polysaccharides have shown activities against the major diseases of our time and the list of effects shown is huge. Various important bioactivities, namely, antitumor, antioxidant, cytotoxic, immunomodulatory, antibacterial, anti-inflammation, neuroprotective, hepatoprotective, anti-HIV, and so on have been shown by these bioactive polysaccharides. The main purpose of this review is to report the most bioactive polysaccharides from *G. lucidum* and other species of *Ganoderma* and to report their potential health benefits.

Keywords: *Ganoderma lucidum*, β-glucans, Bioactive metabolites, Antitumor, Antioxidant.

 DOI: http://dx.doi.org/10.22159/ajpcr.2021v14i3.40390. Journal homepage: https://innovareacademics.in/journals/index.php/ajpcr

INTRODUCTION

The mushroom is a macrofungus with a distinctive fruiting body that can be either epigeous (aboveground) or hypogeous (underground) and large enough to be seen with the naked eye and to be picked by hand [1]. Mostly mushrooms belong to class Ascomycetes and Basidiomycetes of the fungal kingdom. It is estimated that out of 1.5 million species of fungi existing on this biosphere 140,000 species are considered as mushrooms [2]. Only 14,000 species are known to man, which would account for 10% of the estimated mushroom species [3]. About 7000 species are considered to possess varying degree of edibility and more than 3000 species from 31 genera are regarded as prime edible mushrooms. About 2000 medicinal mushrooms are known with a variety of health attributes [4]. These mushrooms possess enormous metabolites with nutraceutical and therapeutic significance [5].

Ganoderma belongs to wood rotting mushroom having hard fruiting body which grows on decaying logs of wood. Taxonomic studies have reported about 300 species in the genus *Ganoderma* and majority of which are mostly distributed in tropical regions [6,7]. The fruiting bodies of *Ganoderma* species are thick, corky, and tough and do not have the fleshy texture and are therefore not listed among edible mushrooms [8,9]. Some of the important species of *Ganoderma* on which most of the research work on medicinal aspects have been carried out are: *Ganoderma lucidum*, *Ganoderma applanatum, Ganoderma pfeifferi, Ganoderma sinensis, Ganoderma theaecolum, Ganoderma colossum, Ganoderma zonatum, Ganoderma australe, Ganoderma tsugae, Ganoderma amboinense, Ganoderma resinaceum, Ganoderma formosanum,* and *Ganoderma atrum. G. lucidum* is the most commonly characterized medicinal mushroom of the genus *Ganoderma* [10-15]. It is commonly known as "Reishi" in Japan, "Lingzhi" in China, and "Yeongji" in Korea. The highly ranked *G. lucidum* in oriental traditional medicine has been used as a remedy for number of chronic diseases such as hypertension, insomnia, asthma, arthritis, diabetes, hepatopathy, nephritis, bronchitis, and cancer [16-19]. For the promotion of longevity and the maintenance of vitality, the crude extract of *G. lucidum* has been used in Traditional Chinese Medicine [20,21]. *G. lucidum* was considered as an "elixir that could revive the dead" [10,22]. Mizuno *et al*., 1995 [23], have reported the composition of *G. lucidum* extract (% of dry weight), which consisted of Folin-positive material (68.9%), glucose (11.1%), protein (7.3%), and metals (10.2%) (K, Mg, and Ca are the major components with Ge having the 5th highest metal concentration at 489 mg/g). However, there are qualitative and quantitative differences in the chemical composition of *G. lucidum* products depending on the strain, origin, extracting process, and cultivation conditions.

As per traditional Chinese medicine, *G. lucidum* supports numerous health benefits and studies through animal models and molecular based research techniques have demonstrated vast array of pharmacological effects [8,13,24]. *G. lucidum*, more specifically has shown tremendous potential in the treatment of modern deadly diseases such as antitumor [25,26], antioxidant [27], immunoregulation [28], hepatoprotection [29], hypoglycemic effect [30,31], antibacterial activity [32], reduction of blood cholesterol [33,34], inhibition of angiogenesis [35,36], antifibrotic activity [37], anti-HIV activity [38], and reduction of lower urinary tract symptoms [39]. These bioactivities of *Ganoderma* have been considered due to the main bioactive compounds: Terpenoids and polysaccharides. In addition, other bioactive metabolites such as lectins, proteins, adenosine, peptides, and sterols have also been found to play an important role in these functions [40-46]. The mechanisms of action of different active components of *G. lucidum* and other *Ganoderma* species have remained poorly defined, despite the numerous reported medicinal properties of *G. lucidum*. Due to the advancement in modern research techniques, detailed insights into these mechanisms of action in which *G. lucidum* can influence the observed health benefits are becoming increasingly possible. Understanding the mechanisms of action may lead to more vigorous use of *Ganoderma* as an anti-carcinogenic agent. Due to the improvement in techniques, better separation and purification techniques have proved beneficial for the isolation and identification of some of the active components in *G. lucidum*. However, modern researchers have primarily focused more on two active components,

namely, triterpenes and polysaccharides. In this review, emphasis has been given on the work carried on bioactive polysaccharides found in *G. lucidum* and other species of *Ganoderma.*

POLYSACCHARIDES

Polysaccharide is a polymer of long chain sugar molecules which are joined together by glycosidic bonds. Several studies have revealed that mushrooms possess biologically active polysaccharides with several medicinal benefits [23,28,47-53]. In this review; however, emphasis will be given on the studies carried out on the medicinal properties of various biologically active polysaccharide molecules from species of *Ganoderma* (Table 1). Vast array of polysaccharides with molecular weights ranging from 4×10^5 to 1×10^6 Da has been identified from *G. lucidum* [13]. Sanodiya *et al*., 2009 [13], also reported that irrespective of the molecular weights of the identified polysaccharides, number of them have positive impacts on reducing cancer progression. About 200 polysaccharides have been reported from *G. lucidum*. The major bioactive polysaccharides isolated from *Ganoderma* species are β (1→3), β (1→4), and β (1→6)-D-glucans. Structural analysis of the identified polysaccharides has shown that these polysaccharides are all heteropolysaccharides [54]. The major component of this sugar molecule is glucose together with xylose, mannose, galactose, and fructose in different conformations. It is believed that the polysaccharides extracted and identified from different parts of *G. lucidum* can induce different immune responses with varying degree of immune potential activities [54]. According to recent studies by Chow-Chin *et al*., 2008 [55], β-D-glucan of polysaccharide from *G*. *lucidum* was found to be carcinostatic substance. *G*. *lucidum* contains glycans as a large group of polysaccharide. Glycans consists of mannose, fucose, arabinose, glucuronic acid, xylose, glucose, and galactose [56]. In addition, the other pharmacological properties of polysaccharides were reported such as neuroprotective effect [57], hepatoprotective [58], anticancer effect [59,60], anti-amnesic effect [61], anti-epileptic effect [62], anti-obesity effect [63], antimicrobial [64-66], antidiabetic [67], and anti-depressant [68]. Recently Li *et al*., 2018 [69], carried an extensive work on comparison of polysaccharides from *G. lucidum* and *G. sinense* and these two species showed antitumor, immunomodulatory, and gut microbiota modulatory activities. The polysaccharides from these two mushroom species have been compared systematically through a series of biological and chemical experiments. This study revealed that the polysaccharides from these two mushroom species shared the same structural features with respect to mono-/oligo-saccharide composition, molecular weight, sugar linkages, and NMR/IR spectra. The polysaccharides from these two species showed similar tumor-suppressive property in mice (4T1 breast cancer in BALB/C mice). The study on RAW264.7 cells showed that these polysaccharides exhibit similar inducing effects to macrophages, as evaluated in the phagocytosis function, nitric oxide (NO)/cytokines production, inhibition against the viability and migration of cancer cells. Mechanistic investigation revealed the identical activation through toll-like receptor (TLR)-4 related MAPK/NF-κB signaling pathway and gut-microbiota modulatory effects.

The solubility characteristics and different branching conformation affect the anti-tumorigenic properties of these polysaccharides [70]. Polysaccharides having structure β-D-glucans consisting of (1→3), (1→4), and (1→6)-β-D linkages are known to have robust antitumor potential and better absorption than other polysaccharides identified from *G. lucidum* [70]. The polysaccharides from *Ganoderma* which is the prominent component of water extracts have been studied and investigated very recently. The branched polysaccharide arabinoxyloglucan from *G. lucidum* was first isolated by Miyazaki and Nishijima in 1981 [71] and it was demonstrated to possess antitumor activity. Since after this study, various kinds of biologically active polysaccharides have been isolated and studied from different species of *Ganoderma* [72-79]. Further, the spores and mycelium of *Ganoderma* can also produce various polysaccharides with significant biological activities [80,81]. Research on bioactive polysaccharides has shown a considerable progress with the development of advanced molecular biology tools, therefore the scope of prebiotics and other related benefits research has now shifted from basic to applied science [82-84]. The research which has been carried out revealed that numerous mushrooms possess different biologically active polysaccharides with prebiotic, antimicrobial, anti-oxidant, and immunomodulating properties. With respect to the pure chemical and structural points of view, *G. lucidum* polysaccharides are mostly composed of β-glucans, heteropolysaccharides, and glycoptoteins [85-87]

CHEMICAL FEATURES OF THE MOST COMMON *GANODERMA* POLYSACCHARIDES

Various biologically active polysaccharides from the fruiting bodies of *G. lucidum* have been isolated and these are considered as one of the main and robust bioactive metabolites present in the *Ganoderma* genus. Various researchers have reported on the islolation, structural elucidiation, and bioactivities of *Ganoderma* polysaccharides. The results from these researches have indicated about structural characterization that α or β (1→3), (1→6)-glucans, and other heteropolysaccharides conjugated to galactose, glucose, mannose, arabinose, xylose, and fucose were the most predominant. Various polysaccharides have been isolated and structurally characterized from *G. lucidum;* however, various new polysaccharides from *G. lucidum* are being revealed by modern analytical chemistry [88]. The major polysaccharides which have been isolated and structurally characterized from the *G. lucidum* showed to have a backbone of β-(1→3)-linked-D-glucopyranosyl residues, with branches of mono, di, and oligosaccharide side chains substituting at the C-6 of the glucosyl residues in the main chain. The studies which have been investigated on these polysaccharides have suggested an important finding that the degree of substitution of the backbone chain and the length of the branching chain might be having some important role in determining the bioactivities of β-(1-3)-linked glucans [75,89]. The polysaccharides isolated from *Ganoderma* by different researchers are composed of glucose, galactose, mannose, arabinose, xylose, and fucose, having different types of combinations and glycosidic linkages and which can bind to peptide or protein residues (polysaccharide-protein or peptide complexes) [46,70,90-93]. These polysaccharides are characterized by their molecular weight, degree of branching, and higher tertiary structures [46] and these polysaccharides are having different compositions, constituted by β-glucans, hetero-β-glucans, and heteroglycans or α-manno-β-glucan complexes [94]. *Ganoderma* polysaccharides such as homo-glucans are linear or branched biopolymers which possess backbone consisting of α or β-linked glucose units (1→3), (1→6)-β-glucans, and (1→3)-α-glucans and may possess side-chains attached at different positions. Out of the all homo-glucans, β-glucans are glucose polymers that exist as non-branched (1→3)-β-linked backbone or as (1→3)-β-linked backbone with (1→6)-β-branches [46,94]. These polysaccharides of *Ganoderma* contain either linear or branched molecules with backbone composed of α or β-linked glucose units, with side chains that are attached in various ways. The Hetero-glucan side chains contain glucuronic acid, galactose, xylose, mannose, arabinose or ribose moieties as main component or in different combinations [28,46].

The other polysaccharides found in *Ganoderma* are Glycans. In general, these glycans contain units other than glucose in their backbone which are classified as galactans, xylans, mannans, and fucans by the individual sugar components in the backbone [94]. The Hetero-glycan side chains possess glucuronic acid, glucose, xylose, galactose, mannose, arabinose, and fucose as the main component or in various other combinations [28,94]. *Ganoderma* polysaccharides are also covalently bound to peptides or proteins as polysaccharide-protein or peptide complexes, which show antitumor and antioxidant activities [46,95]. *G. lucidum* immunomodulating substance (GLIS) example of proteoglycan is a bioactive proteoglycan isolated from *G. lucidum* fruiting bodies. GLIS possesses carbohydrate and protein in the ration of 11.5:1, the carbohydrate portion being formed by seven different monosaccharide's, predominantly D-glucose, D-galactose, and

Table 1: Polysaccharides from *Ganoderma* and their bioactivity

Mushroom	Source	Bioactive Polysaccharide with main glycosidic bonds	Sugar composition	Extraction/isolation Procedure	Bioactivity	References
G. lucidum	Fruiting body (cultivated)	Branched Hetero-glucan Arabinoxyloglucan β-D-(1→3)-, β-D-(1→6)-, β-D (1→4), α-(1→4)	Glucose, Xylose, arabinose	Hot-water extraction; ethanol precipitation; Sevag method; DEAE-cellulose column chromatography with sodium hydrogen carbonate	Antitumor activity against Sarcoma 180 solid tumor	[71]
G. lucidum	Fruiting body	Branched homo-glucan (GLP0; GLP1) (1→3)-β-D-glucan with (1→6)-β-D branches	Glucose	Hot-water followed by ethanol precipitation	Antitumor activity which induced a cascade of immunomodulatory cytokines against Sarcoma 180 solid tumor	[106]
G. tsugae	Mycelium (cultivated)	Hetero-glucans (GTM3; GTM4; GTM5; GTM6) (1→3)-β-D-glucans and (1→4)-α-D-glucans: and (1→6)-branched (1→3)-β-D-glucan	Rhamnose, fucose, xylose, mannose, galactose, N-acetylglucosamine	Immersion in 0.2 M sodium phosphate buffer (pH 7.0); Sevag method; H_2O_2; dialysis; isolation with phosphate buffer, distilled water and 0.5 NaOH	Antitumor activity against Sarcoma 180 solid tumor	[80]
G. lucidum	Fruiting body (cultivated)	Heteropolysaccharide de (GP1 and GP2) Main glycosidic bonds (na)	Glucose, galactose, mannose, rhamnose, fucose	Extraction with 95% ethanol; ultrasonic-acid extraction (UAE);DEAE cellose-52 chromatography and Sephadex G-100 size-exclusion chromatography	Antitumor activity against Human breast cancer cell line (MDA-MB-231)	[100]
G. lucidum	Mycelium (cultivated)	Heteropolysaccharide α-D-Glc (1→6), α-D-Glc,α-D-Man (rhamnoseand arabinose residues in the side chain)	Rhamnose, arabinose, mannose, glucose, galactose	Hot water; ethanol precipitation; Sevag method; dialysis	Antitumor activity against Human hepatocarcinoma cell line (HepG2) and tumor xenografts in ICR mice	[99,108]
G. lucidum	Fruiting body (cultivated)	Heteroglycans GLP, GLP1, GLP2, GLP3, GLP4) Main glycosidic bond (Na)	Mannose, rhamnose, glucose, galactose	Pretreatment with ethanol; Sevag method; Ultrasonic cell disruption; ultrafiltration	Antitumor activity against adrenal gland from rat-PC12 cell line	[109]
G. lucidum	Fruiting body (cultivated)	Water soluble Heteropolysaccharides Water-insoluble glucans (1→3)-β-D-glucan with a few short (1→4)-linked glucosyl units	Glucose, galactose, mannose, arabinose, xylose, fucose, glucose	First extraction with cold PBS (separation of soluble and insoluble fractions). Hot water, cold and hot 1M NaOH; treatment with cetyl pyridinium chloride and glucoamylase; acid hydrolysis	Antitumor activity against Sarcoma 180 solid tumor	[70]
G. lucidum	Mycelium (cultivated)	Branched Homoglucan (1→3)-β-D-glucan	Glucose	Ethanol precipitation/ Toyopearl HW-65S column chromatography	Antitumor activity against Sarcoma 180 solid tumor	[70]
G. lucidum	Fruiting body (cultivated)	Na	Na	Hot water followed by ethanol precipitation/ DEAE-cellulose column chromatography	Antimicrobial activity *in vitro* by Microdilution method	[180]
G. lucidum	Fruiting body (Wild)	Na	Na	Hot water	Antimicrobial activity *in vitro* by agar diffusion method	[139]
G. applanatum	Fruiting body (Wild)	Na	Na	Na	Antimirobial activity *in vitro* by cup diffusion method	[136]
G. formosanum	Mycelium (cultivated)	Branched homoglucan (1→3)-β-D-glucan with (1→6)-β-D- branches	Mannose, galactose, glucose, arabinose, fucose, fructose, rhamnose	Ethanol extraction followed by fractionation on a Sepharose CL-6B gel filtration column	Antimicrobial activity *in vitro*	[181]

(Contd...)

Table 1: (*Continued*)

Mushroom	Source	Bioactive Polysaccharide with main glycosidic bonds	Sugar composition	Extraction/isolation Procedure	Bioactivity	References
G. lucidum	Fruiting body cultivated	Heteroglucans (GLP, GLP1, GLP2, GLP3, GLP4) Main glycosidic bond (na)	Mannose, rhamnose, glucose, galactose	Ultrasonic extraction; Sevag method; ethanol precipitation; ultrafiltration membranes	Antioxidant activity *in vitro* by DPPH scavenging activity; Reducing power; Fe^{2+}chelating activity; ORAC	[109]
G. lucidum	Fruiting body (cultivated)	Na	Na	Hot water extraction; ethanol precipitation; Sevag method; dialysis	Antioxidant activity *in vivo* by SOD activity; GSH-Px activity; CAT activity; MDA levels	[121]
G. lucidum	Mycelium (cultivated)	Heteroglycans (GLPI, GLPII, GLPIII, GLPIV) Main glycosidic bond (na)	GLPI-arabinose, rhamnose, xylose, mannose, glucose, GLPII- arabinose, xylose, glucose GLPIII-arabinose, rhamnose, xylose galactose, mannose, glucose GLPIV-arabinose, rhamnose, fucose, xylose, mannose, glucose	Ultrasonic assisted extraction; hydrolysis; Sevag method; ethanol precipitation; anion exchange DEAE Sephadex A-50 column; regenerated cellulose bag filter; dialysis	Antioxidant activity *in vitro* by DPPH scavenging activity; Reducing power; Fe^{2+}chelating activity; HO scavenging activity; ABTS scavenging activity; SOD-like activity	[118]
G. lucidum	Fruiting body	LMG: Homoglucan β-1,3	Glucose	Alkaline extraction; hydrolysis; size-exclusion chromatography	Antioxidant activity *in vitro* by MTT assay (RAW264.7 cells); ROS formation; nSMase and aSMase activities	[119]
G. lucidum	Fruiting body	GLP_L1: Homoglucan GLP_L2: Heteroglucan β-(1→3) (1→4) (1→6)	GLP_L1: Glucose GLP_L2: Glucose; galactose; mannose	Hot water extraction; D301R macroporous adsorption/ion exchange resin column; DEAE-Cellulose-32 column; gel filtration chromatography	Antioxidant activity *in vitro* by Reducing power; Fe^{2+}chelating activity; HO scavenging activity; O_2 scavenging activity; H_2O_2 scavenging activity	[112]
G. lucidum	Fruiting body (cultivated)	Homopolysaccharide Main glycosidic bond (na)	Mannose	Hot water extraction; ethanol precipitation; Sevag method; dialysis precipitation with cetyl trimethyl ammonium hydroxide; DEAE cellulose column; anion exchange column of DEAE –sepharose fast flow	Antioxidant activity *in vivo* by SOD activity; CAT activity; GSH-Px activity; TAOC level; TBARS (MDA levels)	[182]
G. lucidum	Fruiting body (cultivated)	Homopolysaccharide Main glycosidic bond (na)	Mannose	Hot water extraction; ethanol precipitation; Sevag method; dialysis precipitation with cetyl trimethyl ammonium hydroxide; DEAE cellulose column; anion exchange column of DEAE –sepharose fast flow	Antioxidant activity *in vitro* by HO scavenging activity; O_2 scavenging activity; DPPH scavenging activity *in vivo* by SOD activity; CAT activity; GSH-Px activity	[114]
G. lucidum	Fruiting body (cultivated)	Heteroglucan β-	Rhamnose; xylose; fructose; galactose; mannose; Glucose	Hot water extraction; ethanol precipitation; Sevag method; dialysis	Antioxidant activity *in vitro* by TBARS; LOOH; Protein carbonyls formation; Protein thiols formation; SOD activity; CAT activity; GSH-Px activity	[122]

(Contd...)

Table 1: (*Continued*)

Mushroom	Source	Bioactive Polysaccharide with main glycosidic bonds	Sugar composition	Extraction/isolation Procedure	Bioactivity	References
G. lucidum	Fruiting body (cultivated)	Water insoluble glucans (GL4-1; GL4-2) (1→3)-α-D-glucans	Glucose	PBS; Ethanol precipitations; 1N NaOH	Unreported	[175]
G. japonicum	Fruiting body (wild)	Alkali soluble glucan β-(1→3)-linked D-glucopyranosyl residues with side chains of single, β-(1→6)-linked D-glucopyranosyl groups	Glucose; laminarabiose	Hot dichloromethane and hot methanol hot water; dialysis; gel filtration on sepharose CL-4B	Unreported	[72]
G. lucidum	Spores (cultivated)	Water soluble Polysaccharides (1→3)-linked-Glc (1→6)-linked-Gal (1→4)-linked-Gal (1→6)-linked-Glc	Glucose; galactose	Hot water followed by ethanol precipitation	Unreported	[174]
G. lucidum	Germinating spores (cultivated)	Heteropolysaccharide Main glycosidic bond (na)	Glucose; galactose	Deproteinization by Sevag method and frozen-thaw method, fractionation by ultrafiltration and gel chromatography on CL-6B column	Unreported	[177]
G. lucidum	Fruiting body (cultivated)	Water soluble Hetero Polysaccharide (GL-1; GL-V) (1→4)-galactan hetero- polysaccharide, (1→3)- glucan: 1,4,6 glucan,(1→3)-galactan, (1→6)-galactan, (1→4)-grabinan	Glucose; galactose; mannose; arabinose	Ethyl-acetate; Sevag method; Dialysis	Unreported	[137]
G. resinaceum	Fruiting body (wild)	Water soluble glucan High branched (1→3)-linked β-glucan	Glucose; galactose; mannose; Xylose	Chloroform-methanol; Hot water; dialysis; Freeze-thawing; ultrafiltration	Unreported	[179]
G. lucidum	Fruiting body (wild)	Water soluble polysaccharide α-(1→6)-, (1→2,6) Galactose β-(1→3)-, (1→4,6) Glucose	Fucose; glucose; galactose	Hot water followed by ethanol precipitation; ultrafiltration; DEAE-Sepharose Fast Flow and Sephacryl S-300	Unreported	[76]
G. lucidum	Fruiting body (cultivated)	Water soluble neutral polysaccharide β-(1→4)-Glucose	Glucose; galactose	Ultrasonic/microwave assisted extraction; DEAE Sepharose Fast Flow and Sephacryl S-500	Unreported	[176]
G. lucidum	Spores (cultivated)	Neutral water soluble polysaccharide (GLSA50-1B) β-(1→6)-Glucan	Glucose	Hot-water extraction; graded ethanol precipitation; anion exchange chromatography	Unreported	[178]
G. lucidum	Fruiting body	α-(1→6)-, (1→2,6) Galactose β-(1→3)-, (1→4,6) Glucose	Fucose; galactose; glucose	Hot-water extraction	Immunostimulating Potential	[183]
G. atrum	Fruiting body	β-(1→3)-, (1→6) Glucose, with α-(1→4) galactose, α-(1→2)-, α(1→4)-mannose	Mannose; glucose; galactose	Hot-water extraction; Gel-filtration chromatography with Superdex-G 200	Antioxidant	[79,91]
G. lucidum	Spores	Branched β-D-(1→3)-glucan	Glucose	Hot-water extraction; DEAE-cellulose and Sephacryl S-200HR	Proliferation of T and B lymphocytes and production of antibodies against sheep red blood cells	[81]
G. lucidum	Fruiting body	Heteroglycan α-(1→4), β-(1→6)	Glucose; galactose; rhamnose	Hot-water extraction	Immunologically active (Proliferation of T and B lymphocytes), immune-stimulating activity in mice	[75]

(Contd...)

Table 1: (*Continued*)

Mushroom	Source	Bioactive Polysaccharide with main glycosidic bonds	Sugar composition	Extraction/isolation Procedure	Bioactivity	References
G. tsugae	Mycelium	Heteropolysaccharides (EPF1 and EPF2) β-D-Galacto-α- D-mannan	Mannose; xylose; fucose; galactose; glucosamine	DEAE-Sepharose CL-6B	Potential antitumour drug	[184]
G. lucidum	Extracellular	Galactose rich extracellular polysaccharide GLP-2 α-(1→4)-D-Galactose	Galactose; glucose; mannose; rhamnose; arabinose	DEAE-Sephacel and Sephadex G200	Enhancement of T and B lymphocyte proliferation hepatoprotective activity	[185]
G. lucidum	Fruiting body	Glycopeptide GLPCW-II (90% carbohydrate and 8% protein) α-(1→6)-Galactose α-(1→3)-Glucose	Galactose; glucose; fucose	Hot-water extraction; DEAE-Sepharose Fast-Flow and Sephacryl S-300	Stimulated the proliferation of mouse spleen lymphocytes	[186]
G. tsugae	Fruiting body	Protein containing glucuronolactone and β-(1→3)-glucans	Galactose; glucose; mannose; fucose	Extracted by hot-water, 1% ammonium oxalate solution and 5% NaOH solution in order. DEAE-cellulose and Toyopearl HW-65F gel chromatography	Antitumor active	[74]
G. lucidum	Mycelium	Polysaccharide (WEGL–G1 subfraction)	Arabinose, fucose, galactose, galactosamine, glucose, glucosamine mannose, rhamnose	Extracted by water, 95% ethanol, centrifugation, vacuum concentrator, filtration by Spectrum KrosFlo system	Anti-obesity	[63]

Na: Data not available, *G. lucidum*: *Ganoderma lucidum*, *G. tsugae*: *Ganoderma tsugae*, *G. applanatum*: *Ganoderma applanatum*, *G. formosanum*: *Ganoderma formosanum*, *G. japonicum*: *Ganoderma japonicum*, *G. resinaceum*: *Ganoderma resinaceum*

D-mannose in the molar ratio of 3:1:1 [96]. Therefore, polysaccharides from *Ganoderma* have been under special consideration and attention as they have robust capability for carrying biological information, because they show great potential for structural variability [28].

Ganoderma has been most widely used in medicine and functional foods to promote health. The polysaccharides identified from *Ganoderma* have attracted considerable attention of scientists due to the potentially significant bioactivities such as antitumor, immunomodulatory, antioxidant, antimicrobial, antihypertensive, and hepatoprotective activities (Table 1). The bioactivities of *Ganoderma* polysaccharides as reported by several workers are summarized below:

ANTITUMOR ACTIVITIES

The traditional Chinese medicine has used the crude water soluble extracts of *Ganoderma* species as immunomodulating and antitumor agents [97]. The antitumor activity of polysaccharides of *Ganoderma* has been found to be mainly related to the host-mediated immune function [11,20,98,99]. Liew *et al*., 1992 [20], observed the effect of *G. lucidum* on induction of differentiation in Leukemic U937-cells. The polysaccharides from the *Ganoderma* in general and *G. lucidum* in particular have received special attention from the scientific world and the polysaccharides from *Ganoderma* have been demonstrated to have robust antitumor activity both under *in vivo* and *in vitro* conditions [25]. Polysaccharides from *G. lucidum* with bioactivity have been isolated from the fruiting body [75,100] and also from the mycelium cultivated in liquid culture medium [80,99,101]. Extracellular polysaccharides have also been isolated from the culture medium of growing mycelium [70]. Polysaccharides from *G. lucidum* with antitumor properties such as the branched heteroglucan and arabinoxyloglucan (GL-1) have been observed initially in subcutaneously transplanted sarcoma-180 ascites growing in mice [71]. This heteroglucan inhibited significantly the growth of sarcoma-180 solid-type tumor (Inhibition ratio, 95.6–98.5%) after intra-peritoneal injection (20 mg/kg) for 10 days in imprinting control regions of mice [71]. The *G. lucidum* polysaccharides (GLP) of *G. lucidum* also exhibited antitumor activity against solid tumor induced by Ehrlichs ascites carcinoma cells. These polysaccharides of *G. lucidum* showed 81.2% and 79.5% inhibition of tumor mass and tumor volume, respectively, when administered before tumor inoculation at the dose of 100 mg/g. However, these polysaccharides at the same dose showed 80.8% and 77.6% reduction in tumor volume and tumor mass, respectively, when administered 24 h after tumor cell implantation [102]. The *G. lucidum* polysaccharide peptide (GLPP) of *G. lucidum* when added to the cultured medium did not showed inhibition of human lung carcinoma (PG cell line) proliferation *in vitro;* however, GLPP-treated serum significantly inhibited PG cell line proliferation *in vitro* and reduced the xenograft (PG cell line) in BALB/c nude mice *in vivo* [103]. The antitumor activity of polysaccharides of *Ganoderma* fruiting body and mycelium with (1→3)-β-D-glucan bonds has also been reported by Sone *et al*., 1985 [70]. The antitumor property of *Ganoderma* polysaccharides is mostly related to their immunomodulatory activity. These polysaccharides cannot penetrate the host cells because of large molecular weight however they bind to immune cell receptors. It is widely known that there are fungal pattern-recognition molecules for the innate immune system. The mechanism through innate immune system recognizes and responds to the polysaccharides of the fungal cell wall is a very complex and multifactorial process [104]. The activity of polysaccharides from *G. lucidum* has been found to be mediated through the compliment receptor Type 3 (CR3 receptor), which binds β-glucan polysaccharides [105]. *Ganoderma* polysaccharides exert their bioactivity through the activation of the immune response of the host, thereby enhancing the defense system of host [23]. The water-soluble antitumor polysaccharide-enriched fractions from *Ganoderma* are believed to be related to the stimulation of interleukin (IL)-1β, tumor necrosis factor (TNF)-α, IL-6 from human monocyte-macrophages, and interferon (INF)-γ from T lymphocytes [25]. The polysaccharides from *G. lucidum* (Homo-glucan) are known to exert its antitumor activity in sarcoma-180 solid tumor by inducing a cascade of immunomodulatory cytokines. It also resulted in the significant increase in the gene expression levels of IL-1α, IL-1β, TNF-α, IL12 p35, and IL-12 p40 in the splenocytes. Polysaccharides from *G. lucidum* are also known to promote a remarkable increase in the gene expression levels of IL-β, TMF-α, and granulocyte-macrophage colony-stimulating factor in the macrophages [106]. Polysaccharides

from *G. lucidum* not only have(1→3)-β-D-glucan bonds but also has (1→6)-β-D branches. The structural features such as (1→3)-β-linkages in the main chain of the glucan and additional (1→6)-β-branch points are considered important factors to be responsible for the antitumor activity. The similar results were studied for the heteroglucan from *G. tsugae*, which were composed of (1→3)-β-D-glucans and (1→4)-α-D-glucans having antitumor property against sarcoma-180 solid tumor [80]. Pan *et al*., 2013 [107], have isolated polysaccharide (GLP) from *G. lucidum* which was optimized by response surface method (RSM). The results showed that the GLP reduced the levels of serum IL-6 and TNF-α level significantly and caused increase in the levels of serum IL-2, IL-4, and IL-10 in GLP-treated rats as compared to gastric cancer model rats. Various other heteropolysaccharides from *Ganoderma* have been studied very recently both *in vitro* and *in vivo* conditions, with inhibitory activity in tumor cell lines, inhibition of tumors transplanted in mice, and induction of apoptosis [99,108,109]. Polysaccharides from *G. lucidum* have been found to suppress growth of lung cancer cells and prostate cancer cells [35,110]. In a recent study by Kumar *et al*., 2017 [111], the authors reported that gold nanoparticles (Au-NPs) which were synthesized from *G. lucidum* and conjugated with doxorubicin drug showed significant anticancer drug accumulation and cytotoxic activity against MCF-7-doxbreast cancer cell line. Au-NPs reduced 97% growth of MCF-7-doxbreast cancer cell line at higher concentration (400 μ M/ml). The mRNA expression of ABCB1 gene and CDNA synthesized from human breast cancer cell line (MCF-7) showed reduced expression. It is, thus, necessary to conclude that the pharmacological activity of *G. lucidum* exhibits the anticancer activity of newly synthesized Au-NPs conjugated with drug doxorubicin [111].

ANTIOXIDANT ACTIVITIES

Antioxidant activities include free-radical scavenging properties, chelating effects on ferrous ions, and reducing power [112,113]. The radical scavenging activity seems to be related with an increase in the activities of antioxidant enzymes, catalase (CAT) which causes the detoxification of hydrogen peroxide and converts lipid hydroperoxides (LOOH) into less or non-toxic substances, superoxide dismutase (SOD) which help in the catalysis of superoxide anion to hydrogen peroxide and glutathione peroxidase (GSH-Px) which maintains the levels of reduced GSH [114]. Polysaccharides from *Ganoderma* have been found to exhibit strong antioxidant activity [115-117]. *Ganoderma* polysaccharides have shown antioxidant activity both *in vivo* and *in vitro* activities, which suggested that they act as novel antioxidant agents in the promotion of human health and therefore improve oxidative stress associated pathologies. Homo-glucans and hetero-glucans of *G. lucidum* have shown very much promising radical scavenging activities, as evaluated by various antioxidant methods, such as 2,2-diphenyl-1-picrylhydrazyl (DPPH) scavenging assay, chelating ability, reducing power, hydroxyl radical scavenging activity, superoxide, and hydrogen peroxide scavenging activity [109,112-118]. The low molecular weight polysaccharide isolated from *G. lucidum* such as β-1, 3-glucan was able to increase the viability from 40% to 80%, of a mouse leukemic monocyte macrophage cell line (RAW 264.7) with H_2O_2-induced oxidative stress. This low molecular weight, β-1, 3-glucan, is known to reduce the reactive oxygen species formation and it also suppressed the activities of acidic and neutral sphingomyelinases (SMases) [119]. Kan *et al*., 2015 [120], reported antioxidant activity of polysaccharides extracted from *G. lucidum* using response surface methodology. The homo-polysaccharide composed of mannose isolated from *Ganoderma* displayed very high radical scavenging activity by increasing the activity of antioxidant enzymes, SOD, CAT, GSH-Px, and decreasing malondialdehyde (MDA) levels in rats with cervical and ovarian cancer [114]. The antioxidant activity of *G. lucidum* polysaccharide (GLPS) against exercise induced oxidative stress significantly increased the activity of antioxidant enzymes; SOD, CAT, and GSH-Px and decreased the levels of MDA [121]. The hetero-glucan also isolated from *G. lucidum* showed significant antioxidant activity against mitochondria oxidative injury induced by γ-irradiation, which caused an enormous decrease in MDA levels, LOOH and formation of carbonyl protein, while the formation of thiol protein increased. This hetero-glucan also resulted in the increased activities of antioxidant enzymes, SOD, CAT, and GSH-Px [122]. The main linkages which were present in the homo-glucans were β-(1-3), (1-4), and (1-6) glycosidic bonds, as also in the hetero-glucans were, composition of different sugars is, mannose, galactose, glucose, rhamnose, xylose, arabinose, and fucose in varying proportions. The polysaccharides such as homo-glucans and hetero-glucans were isolated by Liu *et al*. [112] and reported higher antioxidant activity of the homo-glucan due to its comparatively low molecular weight. However, hetero-glucans isolated with different molecular weights showed highest anti-oxidant activities for the polysaccharide with the highest molecular weight [109]. Pan *et al*., 2013 [107], isolated polysaccharide (GLP) from *G. lucidum* which was optimized by RSM. The results showed that the GLP reduced the levels of serum IL-6 and TNF-α levels significantly and caused increase in the levels of serum IL-2, IL-4, and IL-10 in GLP-treated rats as compared to gastric cancer model rats. Further, the administration of *G. lucidum* polysaccharides to GLP-treated group of rats increased the levels of CAT, SOD, and GSH-Px in serum and gastric tissue against the control values in dose dependent manner. This experiment showed that the *G. lucidum* polysaccharide can enhance immunity and antioxidant activities in gastric cancer rats.

Chen and Wu 2014 [123] designed a novel and very efficient technique for extracting the crude antioxidant polysaccharides. In this technique, dried fruiting bodies of *G. lucidum* were finely pulverized into ultrafine powder, subsequently to extract the crude antioxidant polysaccharides by ultrasonic circulating extraction. Various extraction factors were investigated by single factor analysis with the help of DPPH radical scavenging activity as an index. After this, multiple regression equations were worked out through which optimal processing conditions can be predicted and therefore predicted model was verified experimentally. The highest polysaccharide concentration, that is, 47.87 mg/ml, along with highest DPPH scavenging rate 53.63% was achieved at 671 W ultrasonic powder, 48°C extraction temperature, 5.5/1 of intermit-running ratio (s/s), 1:12.5 of solid-liquid ratio (w/v), and 45 min extraction time. The results showed that this novel technique proved to be very efficient for high extract yield of crude antioxidant polysaccharide from *G. lucidum.*

IMMUNOMODULATION

The polysaccharides of *Ganoderma* are known for significant immunomodulating properties, which enhanced the function of mononuclear phagocyte system, antigen presenting cells, humoral immunity, and cellular immunity [28,48]. The isolated and identified polysaccharides from *Ganoderma* have been demonstrated to modulate and improve immune function both in human studies and mouse models [124]. During the administration of polysaccharide extracts of *G. lucidum*, there was increase in the secretion of cytokines from immune cells which lead to increased cellular activity and survival of immune cells related to adaptive immunity (Lymphocytes) and innate immunity (Macrophages) [125,126]. Chang *et al*., 2004 [3], and Pan *et al*., 2013 [107], have also reported that these polysaccharides have been found to improve the activity of cytotoxic T-lymphocytes and natural killer cells. The polysaccharide peptide (GLPP) from *G. lucidum* when administered intraperitoneally significantly increased the survival rate of macrophages which were injured by tert-butylhydroperoxide under *in vitro* and *in vivo* conditions [127]. Zhu *et al*., 2007 [128], reported that the phagocytosis and cytotoxicity of macrophages were increased significantly in cyclophosphamide (Cy)-treated mice after the treatment with polysaccharides from *G. lucidum* at low dose (2.5 mg/kg) for 12 days. The *Ganoderma* polysaccharides have also been reported to enhance the expression of major histocompatibility complex in a melanoma cell line, which improves antigen presentation thereby promoting cancer and viral immunity [129]. Sun *et al*., 2011 [129], have reported the promoting effects of the polysaccharides from *G. lucidum* on B16F10 cells which help in the activation of lymphocytes. The treatment of T lymphocyte or macrophage culture medium with *G. lucidum* polysaccharides increased the TNF-α and IFN-γ release in dose-

dependent and time-dependent instances [130]. Cao and Lin 2002 [131] have reported that the polysaccharides from *G. lucidum* promoted the maturation of cultured murine bone marrow derived dendritic cells. The effects of *Ganoderma* polysaccharides on the immune functions of the patients with the advanced cancer stages were also investigated and the results showed that the *Ganoderma* polysaccharides significantly lead to the increase in the concentration of IL-2, IL-6, IFF-γ, the absolute number of CD56+ cells, and the NK activity also showed increase from the baselines after 12-week treatment. However, it was observed that the levels of IL-1 and TNF-α decreased significantly. When compared to pretreatment baselines after 12-week treatment with *Ganoderma* polysaccharides, it was reported that the phytohemagglutinin responses were enhanced in most patients. Thus, these results showed that the *Ganoderma* polysaccharides could significantly enhance the immune responses in patients with advanced cancer stages [124,132]. Huang and Ning [133] isolated polysaccharide from *G. lucidum* by RSM to optimize the ultrasonic/microwave-assisted extraction conditions. The immunological studies showed that *G. lucidum* polysaccharides extracted by ultrasonic/microwave (UMP) could improve the weight of immune organ of immunocompromised mice, improve hemolysis antibody level, restore delayed-type hypersensitivity reaction to DFNB, and natural killer cell activity at high doses. However, UMP did not seem to be had any noticeable effect on phagocytosis of monocytes at the tested dose ranges. It is, thus, clear that the polysaccharides of *Ganoderma* have robust immunomodulatory properties both *in vivo* and *in vitro* conditions. The polysaccharides from *Ganoderma* enhanced the immune responses of the human body during the experiments on advanced cancer stage patients to exhibit the antitumor effects.

ANTIMICROBIAL PROPERTIES

Fungi are known for the production of very important antibiotics, such as penicillin. However, the search for the presence of antibiotics in mushrooms is less documented [134]. Mushrooms have been thought to possess weak antifungal activity [23,33] and thus have not been scrutinized for their antifungal activity. Very recently mushrooms have become of interest due to the occurrence of secondary metabolites which possess wide range of antimicrobial activities. *Ganoderma* mushroom has been studied for their therapeutic properties as antiviral and antitumor agents but have been far less studied for their antimicrobial property [135-137]. Majority of the antibacterial studies on *Ganoderma* species have been carried out on the fruiting body and there are relatively few studies which have been performed on extracts from the liquid cultivated mycelium. Wasser 2011 [85] has reported that eastern and western medicine system has adopted various regulatory systems for mushroom and herbal preparations. As per the studies of Sullivan *et al*., 2006 [138], western medicine has made much little use of medicinal mushroom products partly because of their complex structure and lack of acceptable pharmacological purity. Researchers working on the active compounds from *Ganoderma* have worked on extracts from the mycelium and fruiting body, and there only few reports on antimicrobial activity of isolated polysaccharides. It is, therefore, quite obvious, that there are a number of biologically active compounds to be found in the fruiting body and mycelium, but the antimicrobial activity evaluation of chemically characterized polysaccharides is very much limited. It has also been found that the (1→3)-β-D- glucan with (1→6)-β-D branches could act as antimicrobial agents. Bhattacharyya *et al*., 2006 [136], have reported that the polysaccharides from the basidiocarp and mycelia of *G. applanatum* were found to possess antimicrobial activity against *Bacillus brevis, Bacillus subtilis, Acrobacter aerogenes, Arthrobacter citreus, Acetobacter aerogenes, Escherichia coli, Corynebacterium insidiosum, Proteus vulgaris, Clostridium pasteurianum, Micrococcus roseus, Mycobacterium phlei, Staphylococcus aureus,* and *Sarcina lute.* In another study by Bai *et al*., 2008 [139], polysaccharides from *G. lucidum* were tested for antimicrobial activity against three plant pathogens, namely (*Penicillium digitatum, Erwinia carotovora,* and *Botrytis cinerea*), and five food harmful microorganisms (*B. subtilis, Bacillus cereus, E. coli, Rhizopus nigricans, and Aspergillus niger).* After the investigation, the results showed that the polysaccharides had inhibitory effect on *E. carotovora*, weak inhibitory on *P. digitatum* and nearly non-inhibitory effect on *B. cinerea* for the plant pathogens. With respect to the harmful food microorganisms, the polysaccharides showed strong inhibitory effect on *B. subtilis and B. cereus*, weak inhibitory effect on *E. coli and A. niger* and nearly non-inhibitory effect on *R. nigricans* [139].

The polysaccharides from *Ganoderma* have been much investigated against several pathogenic bacteria [32,140]. So far various authors have reported antimicrobial activity of different extracts of *G. lucidum* but not of isolated polysaccharides [141,142]. The extracts from *G. lucidum* have shown strong antifungal, antibacterial, demelanizing properties even better than the standard streptomycin (STZ), and ampicillin in few cases. Therefore, the polysaccharides of *Ganoderma* in general and *G. lucidum* in particular should be investigated, since they have strong participation in antimicrobial properties. Paul *et al*., 2015 [143], synthesized silver nanoparticles (AgNPs) from *G. lucidum* and impregnated the cotton fabrics with these synthesized AgNPs to check the antimicrobial activity. The antibacterial activity of silver impregnated cotton was investigated and results showed strong and robust activity against three pathogens, *Streptococcus aureus*, *Pseudomonas* species, and *Proteus* species. Hence, it is revealed that dressing material incorporated with AgNPs can be used as sterile fabric that could be used commercially against infections and wounds. Very recently the antimicrobial activity of *G. lucidum* against *Candida* Biofilms has been evaluated [144]. In this study, the mycelial aqueous extracts of *G. lucidum* demonstrated higher anti-*Candida* activity and ascorbic acid (potent antioxidant) content among all the extracts and fractions. This study further reveals the preventive effect against *Candida albicans* and *Candida glabrata* biofilms due to the activity of *G. lucidum* extracts which will prove very beneficial for humanity as *Candida* is potent pathogen.

NEUROPROTECTIVE EFFECT

The constituents of *G. lucidum* include triterpenoids, polysaccharides, unsaturated fatty acids, and ergosterol. Among these, polysaccharides are, however, the major pharmacologically active compound. The effects of polysaccharide extracts of *G. lucidum* have been related to promote suppression of cancer cell migration, innate immune responses, and modulations of cell proliferations [57,145-147]. In last few years, studies have shown that the *G. lucidum* show neuroprotective activity and significantly weakened amyloid beta (Aβ) peptide-induced neurotoxicity [148]. Zhou *et al*., 2012 [149], have reported that the pre-administration of spores of *G. lucidum* to rats may also protect the hippocampus from the oxidative damages. All of these results showed positive implications for *G. lucidum* in the treatment of Alzheimer's disease (AD). However, there are very less reports in the biochemical mechanism to which polysaccharides of *G. lucidum* might target AD. The cause of AD is very complex mechanisms and has not been fully resolved yet. Two important distinguishing characteristics which characterize this neurodegenerative disease are the aggregation of Aβ which leads to senile plaques and the progressive cognitive impairments [150]. The deposition of Aβ results into the activation of microglia, the resident immune cells and therefore causes neuroinflammation in the central nervous system (CNS) [151]. The activation of microglia results in the release of pro-inflammatory cytokines and neurotoxic mediators with altered cell behaviors, which may be characterized by the microglial morphology, migration, and phagocytosis [152]. The positive feedback from microglial phagocytosis is the removal of dead neurons and neuronal debris that helps in the reduction of inflammatory stress. Nevertheless, extended activation by TLR agonists, such as lipopolysaccharides (LPS), Aβ, and lipoteichoic acid might result into aberrant phagocytosis process [153,154]. Under these conditions, microglia target on live neurons, neuronal progenitor cells, and glioma cells, all of which leads to neuronal loss in the CNS [153]. Other than the pro-inflammatory mediators, chemokines such as MCP-1 also accumulate as a result of neuroinflammation. The over-expression of MCP-1 has been observed in many neurodegenerative

diseases [155-157]. In the AD brain, the function of MCP-1 is related to cell movement and to initiate the accumulation of monocytes at the site of Aβ deposition [158-160]. Upregulation of MCP-1 expression might contribute to the chronic inflammation [161].

Very recently, Cai *et al*., 2017 [162], provided a view into the regulatory roles of polysaccharides from *G. lucidum* in LPS and Aβ-induced microglial behavior and pro-inflammatory responses. These authors revealed that the polysaccharides from *G. lucidum* reduced the pro-inflammatory cytokines and MCP-1 expressions with a tendency to promote anti-inflammatory cytokine levels. They also demonstrated that the polysaccharide from *G. lucidum* modulation of microglial behavioral changes *in vitro* was associated to MCP-1 expressions. Finally, it was also confirmed that the polysaccharides from *G. lucidum* modulated microglial behavioral changes *in vivo*. These observations indirectly reveal that polysaccharides from *G. lucidum* show a neuroprotective function in the treatment of AD. In association with the neurogenesis effect Huang *et al*., 2017 [163], polysaccharides from *G. lucidum* represents a dual functional cocktail-like natural product, which bears a great and robust potential in the early prevention and treatment of AD.

HYPOGLYCEMIC ACTIVITIES

The hypoglycemic property of *Ganoderma* polysaccharides has been widely studied and the studies on animals have suggested that polysaccharides from *Ganoderma* might help in the prevention of diabetes and slow down the progression of diabetes once it has developed. It has been found that polysaccharides from *G. lucidum* could significantly increase the levels of insulin and decrease blood glucose in STZ-induced diabetic mice [164,165]. The hypoglycemic activities of *G. lucidum* polysaccharides have been determined in patients having Type II diabetes mellitus and the results demonstrated that these polysaccharides of *G. lucidum* were efficient and safe in lowering concentration of glucose in blood [166]. Polysaccharides from *G. lucidum* could also significantly reverse alloxan-induced islets viability loss by inhibiting the free radical production, reducing serum glucose levels, and increasing serum insulin in alloxan-induced diabetic mice dose-dependently [167]. This study suggested that polysaccharides of *G. lucidum* had a protective effect on alloxan-induced pancreatic islets damage under *in vivo* and *in vitro* conditions [167]. Further, polysaccharides from *G. lucidum* have also been investigated to possess potential beneficial effects on diabetic complications. The polysaccharides from *G. lucidum* exhibited renal protective effect in mice with diabetic nephropathy through the amelioration of metabolic disorders, renal dysfunction associated with renal lesions, and oxidative stress [164]. He *et al*., 2006 [164], reported that the treatment of polysaccharides of *G. lucidum* reduced the levels of blood urea nitrogen, serum creatinine, serum glucose, and urine albumin excretion in a dose-dependent manner compared with diabetic model mice. He *et al*., 2006 [164], also reported that the polysaccharides from *G. lucidum* could be used in the treatment of myocardial fibrosis of diabetes. The polysaccharides from *G. lucidum* weakened the myocardial collagen cross-linking in diabetic rats which was related to the decreased level of advanced glycation endproducts and increased the activities of the antioxidant enzymes. Meng *et al*., 2011 [165], reported that the polysaccharides from *G. lucidum* have the capacity to weaken the renal morphometric changes and oxidative stress of diabetic mice. Pan *et al*., 2012 [168], isolated a neutral polysaccharide (FYGL-1) which was fractionated from the hypoglycemic extract FYGL by DEAE-52 cellulose column chromatography of *G. lucidum*. The molecular weight of FYGL-1 was found to be 78 KDa. Furthermore, the monosaccharide analysis showed that FYGL-1 was a heteropolysaccharide consisting of galactose, rhamnose, and glucose residues in the molar ratio of 1.00:1.15:3.22. The backbone structure of FYGL-1 consisted mainly of 1,2-linked-β-L-Rhap, 1,3,6-linked-α-D-Galp, 1,2,6-linked-α-D-Glcp, and 1-linked-α-D-Glcp, based on the analysis of methylation, periodate oxidation, smith degradation, and 1D and 2D NMR. The previous studies on *G. lucidum* had shown beneficial effects on Type 2 diabetes mellitus in murine molds; however, the effects of this mushroom on the gut microbiota, inflammation, and obesity had not been investigated. Recent study by Chang *et al*., 2015 [63], on mice investigated that water extract of *G. lucidum* mycelium (WEGL) prevents dietary-induced obesity and alleviates inflammation by modulating the gut microbiota composition and maintaining intestinal barrier integrity. Chang *et al*., 2015 [63], concluded that WEGL showed significant changes in the gut microbiota composition and the anti-obesity activity of WEGL is transferrable through fecal transplantation support the concept that obesity is associated with an altered gut microbiota composition (e.g., reduction of *Escherichia fergusonii*).

HEPATOPROTECTIVE ACTIVITY

Hepatoprotective activity of *G. lucidum* polysaccharides against Bacillus of Calmette Guerin (BCG)-induced immune injury of liver was studied in mice by determining the activity of alanine aminotransferase (ALT) in serum and hepatocytes cultured supernatant, NO production in the cultured supernatant, histological examination, and liver weight changes [169]. These observations showed that *G. lucidum* polysaccharides significantly mitigated hepatic tumefaction, decreased ALT enzyme release and NO production in the serum/supernatant, and improved the pathological changes of acute and chronic inflammation induced by BCG-stimuli in mice. In addition, it was further reported that the polysaccharides of *G. lucidum* inhibited iNOS protein expression in BCG-immune hepatic damage model. This finding by Zhang *et al*., 2002 [169], also revealed that the NO participation in immune liver injury induced by *Mycobacterium bovis* BCG infection and the mechanism of protective roles by *G. lucidum* polysaccharides for BCG-induced immune liver injury might be because of the influencing NO production in mice. Gao *et al*., 2003 [170], and Pham *et al*., 2016 [171], also observed hepatoprotective activity of *G. lucidum* with respect to cyclophosphamide induced liver injury in mice. Zhu *et al*., 2016 [172], reported the beneficial effects of polysaccharide isolated from *G. atrum* (PSG-1) on the liver function in diabetic rats (Type 2). The results revealed that the polysaccharide (PSG-1) reduced the activities of serum ALT and aspartate aminotransferase, while increasing the hepatic glycogen levels. Polysaccharide PSG-1 also exhibited very strong antioxidant activities, together with the upregulation of mRNA expression of peroxisome proliferator-activated receptor-γ, glucose transporter-4 (GLUT4), phosphoinositide 3-kinase (PI3K), and phosphorylated-Akt (p-Akt) in the liver of diabetic rats. Furthermore, after treating diabetic rats with PSG-1 for 4 weeks, the concentrations of short-chain fatty acids (SCFA) were significantly higher in the liver, serum, and feces. These results recommended that the improvement of PSG-1 on liver function in Type 2 diabetic rats might be due to its antioxidant property, SCFA excretion in the colon from PSG-1, and regulation of hepatic glucose uptake by inducing GLUT4 translocation through PI3K/Akt signaling pathways. Very recently, Yu *et al*., 2017 [173], studied that *G. lucidum* polysaccharides have a therapeutic effect on hepatocellular carcinoma (HCC) cells exposed to radiation. The authors concluded that the GLP enhances the radiosensitivity of HCC cell lines through the regulation of Akt signaling pathways, implying a potential therapeutic effect of GLP as a radiation sensitizer in HCC treatment.

In some studies, it has been found that the bioactivity of *Ganoderma* polysaccharides may be due to the alkali soluble polysaccharides and/or water insoluble polysaccharides and water-soluble polysaccharides. The water insoluble, but alkali-soluble glucan G-A has been isolated from *Ganoderma japonicum* [72]. A water soluble and low branched polysaccharide (SGL-III) has been isolated from the spores of *G. lucidum* [174]. A water-soluble polysaccharide, heteropolysaccharide LZC-1 has been isolated from *G. lucidum* [76]. The water-insoluble glucans, namely, GL4-1 and GL4-2 have been isolated from the fruiting bodies of *G. lucidum* [175]. Neutral polysaccharide, soluble in water was isolated by Huang *et al*., 2011 [176], from *G. lucidum* fruiting body. Neutral, water soluble, and hetero-polysaccharide (GLPS3) have been isolated from germinating spores *of G. lucidum* [177]. A novel water soluble and neutral β-D-glucan (GLSA50-1B) have been isolated from

the spores of *G. lucidum* [178]. A water-soluble b-glucan (DESSK5) was reported in the basidiocarp of *G. resinaceum* [179]. Novel hetero-polysaccharides (GL-1 to GL-5) have also been isolated from the fruiting bodies of *G. lucidum* [137]. However, these polysaccharides need further evaluation for their potential bioactivities, as their chemical properties are very much promising.

CONCLUSION

The beneficial health properties of *Ganoderma* species have been attributed to the variety of bioactive compounds. *Ganoderma* genus in general and *G. lucidum* in particular can be considered as a natures pharmaceutical store due to the presence of various bioactive compounds isolated till date and demonstrated to have numerous therapeutic activities. *G. lucidum* has been extensively used for centuries for numerous pharmacological benefits, including immune-modulating, anticancer, anti-oxidant, anti-aging, antimicrobial, anti-inflammatory effects, and only very recently these claims have been accepted due to the scientific information that has become available. Certainly and from the enormous work carried out, *Ganoderma* species offers concrete promises for the development of therapeutic drugs, nutraceuticals, and novel functional foods. Extensive literature has been reported on bioactive compounds of *G. lucidum*, but further clinical studies are still needed to demonstrate their therapeutic efficacy. Furthermore, there is need of more studies regarding the safety and application of these bioactive metabolites for providing more convincing evidence to shift to application stage from just clinical trials. The future studies should also focus more on the mechanisms of action of *G. lucidum* and related species of *Ganoderma*, because most of them are not very well known and thus need to be understood properly. Moreover, various polysaccharides isolated from *Ganoderma* species have unknown sugar composition and unreported bioactivity, thus more work is needed to identify these polysaccharides and work on their bioactivity. Therefore, *G. lucidum* can represent practical and promising approach for cancer prevention and cancer treatment and other ailments based on current data available from *in vivo* and *in vitro* studies. However, further experimental, epidemiological and clinical studies are needed to identify the molecular targets, to resolve the relationships between different ailments and uptake of *Ganoderma* and to explore the dosing, efficacy and safety along with chemotherapy and radiotherapy.

AUTHORS' CONTRIBUTIONS

All authors contributed to this work. Zahoor Ahmad Bhat initiated this work and drafted the original manuscript. Abdul Hamid Wani, John Mohd War, and Mohd Yaqub Bhat participated in writing, editing and revision of the manuscript. Abdul Hamid Wani and Mohd Yaqub Bhat supervised the overall work.

CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

REFERENCES

1. Chang ST, Miles PG. Mushrooms biology a new discipline. Mycologist 1992;6:64-5.
2. Hawksworth DL. The magnitude of fungal diversity. The 1.5 million species estimate revisited. Mycol Res 2001;105:1422-32.
3. Chang ST, Miles PG. Mushroom's Cultivation, Nutritional Value, Medicinal Effect, and Environmental Impact. Boca Raton, London: CRC Press; 2004.
4. Chang ST, Mshigeni KE. Mushroom and their Human Health: Their Growing Significance as Potent Dietary Supplements. Windhoek: The University of Namibia; 2001. p. 1-79.
5. Rahi DK, Malik D. Diversity of mushrooms and their metabolites of nutraceuticals and therapeutic significance. J Mycol 2016;2016:7654123.
6. Seo GS, Kirk PM. *Ganodermataceae*: Nomenclature and classification. In: Flood J, Bridge PD, Holderness P, editors. *Ganoderma* Disease of Perennial Crops. Wallingford, UK: CABI Publishing; 2000. p. 3-22.
7. Richter C, Wittstein K, Kirk PM, Stadler M. An assessment of the taxonomy and chemotaxonomy of *Ganoderma*. Fungal Divers 2015;71:1-15.
8. Jong SC, Birmingham JM. Medicinal benefits of the mushroom *Ganoderma.* Adv Appl Microbiol 1992;37:101-34.
9. Jonathan SG, Kigigha LT, Ohimain E. Evaluation of the inhibitory potentials of eight higher Nigerian fungi against pathogenic microorganisms. Afr J Biomed Res 2008;11:197-202.
10. Leung SW, Yeung KY, Ricky YL, Man YK. Lingzhi (*Ganoderma*) research: The past, present and future perspectives. In: Lin ZB, editor. *Ganoderma*: Genetics, Chemistry, Pharmacology and Therapeutics. Beijing: Beijing Medical University Press; 2002. p. 1-9.
11. Paterson RR. *Ganoderma* a therapeutic fungal biofactory. Phytochemistry 2006;67:1985-2001.
12. Ziegenbein FC, Hanssen HP, Konig WA. Secondary metabolites from *Ganoderma lucidum* and *Spongiporus leucomallellus*. Phytochemistry 2006;67:202-21.
13. Sanodiya BS, Thakur GS, Baghel RK, Prasad GB, Bisen PS. *Ganoderma lucidum*: A potent pharmacological macrofungus. Curr Pharm Biotechnol 2009;10:717-42.
14. Ríos JL, Andújar I, Recio MC, Giner RM. Lanostanoids from fungi: A group of potential anticancer compounds. J Nat Prod 2012;75:2016-44.
15. Rios JL, Andujar I. Lanostanoids from fungi as potential medicinal agents. In: Fungal Metabolites. Cham: Springer; 2017. p. 931-64.
16. Nishitoba T, Oda K, Sato H, Sakamura S. Novel triterpenoids from the fungus *Ganoderma lucidum*. Agri Biol Chem 1988;52:367-72.
17. Mizushina Y, Hanashima L, Yamaguchi T, Takemura M. A mushroom fruiting body inducing substance inhibits activities of replicative DNA polymerases. Biochem Biophys Res Commun 1988;249:17-22.
18. Wasser SP, Weis AL. Therapeutic effects of substance occurring in higher basidiomycete mushrooms: A modern perspective. Crit Rev Immunol 1999;19:65-96.
19. Wasser SP. Reishi or Ling Zhi (*Ganoderma lucidum*), Encyclopedia of Dietary Supplements. New York, USA: Marcel Dekker; 2005. p. 603-22.
20. Liew CW, Lee SS, Wang SY. The Effect of *Ganoderma lucidum* on induction of differentiation in leukemic U937-cells. Anticancer Res 1992;12:1211-6.
21. Adams M, Christen M, Plitzko I, Zimmermann S, Brun R, Kaiser M, *et al.* Antiplasmodial lanostanes from the *Ganoderma lucidum* mushroom. J Nat Prod 2010;73;897-900.
22. Cheng CR, Yue QX, Wu ZY, Song XY, Tao SJ, Wu XH, *et al.* Cytotoxic triterpenoids from *Ganoderma lucidum*. Phytochemistry 2010;71:1579-85.
23. Mizuno T, Saito H, Nishitoba T, Kawagashi H. Antitumor active substances from mushrooms. Food Rev Int 1995;11:23-61.
24. Wachtel-Galor S, Yuen J, Buswell JA, Benzie IFF. *Ganoderma lucidum* (Lingzhi or Reishi): A medicinal mushroom. In: Herbal Medicine: Bimolecular and Clinical Aspects. Boca Raton, USA: CRC Press Taylor and Francis; 2011.
25. Wang SY, Hsu ML, Hsu HC, Tzeng CH, Lee SS, Shiao MS, *et al.* The anti-tumor effect of *Ganoderma lucidum* is mediated by cytokines released from activated macrophages and T-lymphocytes. Int J Cancer 1997;70:699-705.
26. Yuen JW, Gohel MD. Anticancer effects of *Ganoderma lucidum*: A review of scientific evidence. Nutr Cancer 2005;53:11-7.
27. Yen GC, Wu JY. Antioxidant and radical scavenging properties of extracts from *Ganoderma tsugae*. Food Chem 1999;65:375-9.
28. Wasser SP. Medicinal mushrooms as a source of antitumor and immunomodulating polysaccharides. Appl Microbiol Biotechnol 2002;60:258-74.
29. Kim DH, Shim SB, Kim NJ, Jang NJ. Beta glucuronidase-inhibitory activity and hepatoprotective effect of *Ganoderma lucidum*. Biol Pharm Bull 1999;22:162-4.
30. Hikino H, Konno C, Mirin Y, Hayashi T. Isolation and hypoglycemic activity of ganoderans A and B, glycans of *Ganoderma lucidum* fruit bodies. Plant Med 1985;4:339-40.
31. Seto SW, Lam TY, Tam HL, Au AL, Chan SW, Wu JH, *et al.* Novel hypoglycemic effects of *Ganoderma lucidum* water-extract in obese/diabetic (+db/+db) mice. Phytomedicine 2009;16:426-36.
32. Gao Y, Tang W, Gao H, Chan E, Lan J, Li X, *et al.* Antimicrobial activity of the medicinal mushroom *Ganoderma.* J Food Rev Int 2005;21:211-29.
33. Mizuno T, Wang G, Zhang J, Kawagishi H, Nishitoba T, Li J. Reishi, *Ganoderma lucidum* and *Ganoderma tsugae*: Bioactive substances and medicinal effects. Food Rev Int 1995;11:151-66.
34. Berger A, Rein D, Kratky E, Monnard I, Hajjaj H, Meirim I, *et al.* Cholesterol-lowering properties of *Ganoderma lucidum in vitro*, *ex vivo*, and in hamsters and minipigs. Lipids Health Dis 2004;3:2.

35. Stanley G, Harvey K, Slivova V, Jiang J. *Ganoderma lucidum* suppresses angiogenesis through the inhibition of secretion of VEGF and TGF-beta1 from prostate cancer cells. Biochem biophys res commun 2005;330:46-52.
36. Hsu SC, Ou CC, Chuang TC, Li JW, Lee YJ, Wang V, *et al. Ganoderma tsugae* extract inhibits expression of epidermal growth factor receptor and angiogenesis in human epidermoid carcinoma cells: *In vitro* and *in vivo*. Cancer Lett 2009;281:108-16.
37. Park EJ, Ko G, Kim J, Sohn DH. Anti-fibrotic effects of a polysaccharide extracted from *Ganoderma lucidum*, glycyrrhizin, and pentoxifylline in rats with cirrhosis induced by biliary obstruction. Biol Pharm Bull 1997;20:417-20.
38. El-Mekkawy S, Meselhy MR, Nakamura N, Tezuka Y, Hattori M, Kakiuchi N, *et al.* Anti-HIV-1 and anti-HIV-1- protease substances from *Ganoderma lucidum*. Phytochemistry 1988;49:1651-7.
39. Noguchi M, Kakuma T, Tomiyasu K, Kurita Y, Kukihara H, Konishi F, *et al.* Effect of an extract of *Ganoderma lucidum* in men with lower urinary tract symptoms: A double- blind, placebo-controlled randomized and dose-ranging study. Asian J Androl 2008;10:651-8.
40. Kawagishi H, Fukuhara F, Sazuka M, Kawashima A, Mitsubori T, Tomita T. 50-Deoxy-50-methylsulphinyladenosine, a platelet aggregation inhibitor from *Ganoderma lucidum*. Phytochemistry 1993;32:239-41.
41. Shiao MS, Lee Kuan R, Lin LJ, Wang CT. Natural products and biological activities of the Chinese medicinal fungus *Ganoderma lucidum*. In: Food Phytochemicals for Cancer Prevention II. Vol. 547. Springer; 1994. p. 342-54.
42. Wang YY, Khoo KH, Chen ST, Lin CC, Wong CH, Lin CH. Studies on the immuno-modulating and antitumor activities of *Ganoderma lucidum* (Reishi) polysaccharides: Functional and proteomic analyses of a fucose-containing glycoprotein fraction responsible for the activities. Bioorg Med Chem 2002;10:1057-62.
43. Smania EFA, Monache FD, Smania A Jr., Yunes RA, Cuneo RS. Antifungal activity of sterols and triterpenes isolated from *Ganoderma annulare*. Fitoterapia 2003;74:375-7.
44. Sun J, He H, Xie BJ. Novel antioxidant peptides from fermented mushroom *Ganoderma lucidum*. J Agric Food Chem 2004;52:6646-52.
45. Akihisa T, Nakamura Y, Tagata M, Tokuda H, Yasukawa K, Uchiyama E, *et al.* Anti-inflammatory and anti-tumor-promoting effects of triterpene acids and sterols from the fungus *Ganoderma lucidum*. Chem Biodivers 2007;4:224-31.
46. Ferreira I, Vaz J, Vasconcelos MH, Martins A. Compounds from wild mushrooms with antitumor potential. Anticancer Agents Med Chem 2010;10:424-36.
47. Ooi VE, Liu F. A review of pharmacological activities of mushroom polysaccharides. Int J Med Mushrooms 1999;1:195-206.
48. Ooi VE, Liu F. Immunomodulation and anti-cancer activity of polysaccharide protein complexes. Curr Med Chem 2000;7:715-29.
49. Konno S, Aynehchi S, Dolin DJ, Schwartz AM, Choudhury MS, Tazaki H. Anticancer and hypoglycemic effects of polysaccharides in edible and medicinal Maitake mushroom (Grifola frondosa (Dicks.:Fr.) S.F.Gray). Int J Med Mushrooms 2002;4:185-95.
50. Ohno N, Harada T, Masuzawa S, Miura NN. Antitumor activity and hematopoietic response of a β-glucan extracted from an edible and medicinal mushroom *Sparassis crispa* Wulf.:Fr. Int J Med Mushrooms 2002;4:13-26.
51. Cai X, Pi Y, Zhou X, Tian L, Qiao S, Lin J. Hepatoma cell growth inhibition by inducing apoptosis with polysaccharide isolated from Turkey tail medicinal mushroom, *Trametes versicolor* (L.: Fr.) Lloyd (Aphyllophoromycetideae). Int J Med Mushrooms 2010;12:257-63.
52. Ren L, Hemar Y, Perera CO, Buchanan PK. Antibacterial and antioxidant activities of aqueous extracts of eight edible mushrooms. Bioact Carbohydr Diet Fibre 2014;3:41-51.
53. Ferreira IC, Heleno SA, Reis FS, Stojkovic D, Queiroz MJ, Vasconcelos MH, *et al.* Chemical features of *Ganoderma* polysaccharides with antioxidant, antitumor and antimicrobial activities. Phytochemistry 2015;114:38-55.
54. Chan WK, Law HK, Lin ZB, Lau YL, Chan GC. Response of human dendritic cells to different immunomodulatory polysaccharides derived from mushroom and barley. Int Immunol 2007;19, 891-9.
55. Chow-Chin T, Yew-Keong C, Mohamed S, Mustapha NM, Umar NA. Efficacy of *G. lucidum* on plasma lipids and lipoproteins in rats fed with high cholesterol diet. Nutr Food Sci 2008;38:229-38.
56. Lemieszek M, Rzeski W. Anticancer properties of polysaccharides isolated from fungi of the basidiomycetes class. Wspolczesna Onkol 2012;16:285-9.
57. Zhang W, Zhang Q, Deng W, Li Y, Xing G, Shi X, *et al*. Neuroprotective effect of pre-treatment with *G. lucidum* in cerebral ischemia/reperfusion injury in rat hippocampus. Neural Regen Res 2014;9:1446-52.
58. Jang SH, Cho SW, Yoon HM, Jang KJ, Song CH, Kim CH. Hepatoprotective evaluation of *G. lucidum* pharmacopuncture: *In vivo* studies of ethanol-induced acute liver injury. J Pharmacopuncture 2014;17:16-24.
59. Liu X, Yuan JP, Chung CK, Chen XJ. Antitumor activity of the sporoderm-broken germinating spores of *G. lucidum*. Cancer Lett 2002;182:155-61.
60. Sun LX, Lin ZB, Duan XS, Qi HH, Yang N, Li M, *et al.* Suppression of the production of transforming growth factor b1, interleukin-10, and vascular endothelial growth factor in the B16F10 cells by *G. lucidum* polysaccharides. J Interferon Cytokine Res 2014;34:667-75.
61. Choi YJ, Yang HS, Jo JH, Lee SC, Park TY, Choi BS, *et al.* Anti-amnesic effect of fermented *G. lucidum* water extracts by lactic acid bacteria on scopolamine-induced memory impairment in rats. Prev Nutr Food Sci 2015;20:126-32.
62. Wang SQ, Li XJ, Qiu HB, Jiang ZM, Simon M, Ma XR, *et al.* Anti-epileptic effect of *G. lucidum* Polysaccharides by inhibition of intracellular calcium accumulation and stimulation of expression of CaMKII a in epileptic hippocampal neurons. PLoS One 2014;9:e102161.
63. Chang CJ, Lin CS, Lu CC, Martel J, Ko YF, Ojcius DM, *et al. G. lucidum* reduces obesity in mice by modulating the composition of the gut microbiota. Nat Commun 2015;6:74-89.
64. Nithya M, Ambikapathy V, Panneerselvam A. Studies on antimicrobial potential of different strains of *G. lucidum* (Curt..: Fr.) P. Karst. Int J Pharm Sci Rev Res 2013;21:317-20.
65. Celik GY, Onbasli D, Altinsoy B, Alli H. *In vitro* antimicrobial and antioxidant properties of *G. lucidum* extracts grown in Turkey. Phys Med 2014;4:709-22.
66. Nayak RN, Dixitraj PT, Nayak A, Bhat K. Evaluation of antimicrobial activity of spore powder of *G. lucidum* on clinical isolates of *Prevotella intermedia*: A pilot study. Contemp Clin Dent 2015;6:248-52.
67. Pan D, Zhang D, Wu J, Chen C, Xu Z, Yang H, *et al.* Antidiabetic, antihyperlipidemic and antioxidant activities of a novel proteoglycan from *G. lucidum* fruiting bodies on db/db mice and the possible mechanism. PLoS One 2013;8:e68332.
68. Matsuzaki H, Shimizu Y, Iwata N, Kamiuchi S, Suzuki F, Iizuka H, *et al.* Antidepressant-like effects of a water-soluble extract from the culture medium of *G. lucidum* mycelia in rats. BMC Complement Altern Med 2013;13:1-8.
69. Li LF, Liu HB, Zhang QW, Li ZP, Wong TL, Fung HY, *et al.* Comprehensive comparison of polysaccharides from *Ganoderma lucidum* and *G. sinense*: Chemical, antitumor, immunomodulating and gut-microbiota modulatory properties. Sci Rep 2018;8:1-12.
70. Sone Y, Okuda R, Wada N, Kishida E, Misaki A. Structure and antitumor activities of polysaccharides isolated from fruiting body and the growing culture of mycelium of *Ganoderma lucidum*. Agric Biol Chem 1985;49:2641-53.
71. Miyazaki T, Nishijima M. Studies on fungal polysaccharides. XXVII. Structural examination of water-soluble, anti tumor polysaccharide of *Ganoderma lucidum.* Chem Pharm Bull 1981;29:3611-6.
72. Ukai S, Yokoyama S, Hara C, Kiho T. Structure of an alkali soluble polysaccharide from the fruit body of *Ganoderma japonicum* Lloyd. Carbohy Res 1982;105:237-45.
73. Gao B, Yang GZ. Immunoregulatory effect and antitumor, antiviral, antivirus activity of *Ganoderma applanatum* polysaccharide. Int J Immunopharmacol 1991;13:731.
74. Wang G, Zhang J, Mizuno T, Zhuang C. Antitumor active polysaccharides from the Chinese mushroom Songshan lingzhi, the fruiting body of *Ganoderma tsugae*. Biosci Biotechnol Biochem 1993;57:894-900.
75. Bao XF, Wang XS, Dong Q, Fang JN, Li XY. Structural features of immunologically active polysaccharides from *Ganoderma lucidum*. Phytochemistry 2002;59:175-81.
76. Ye LB, Zhang JS, Yang Y, Zhou S, Liu Y, Tang Q, *et al.* Structural characterisation of a heteropolysaccharide by NMR spectra. Food Chem 2009;112:962-6.
77. Pan Y, Hao Y, Chu TW, Li CQ. Ultrasonic-assisted extraction, chemical characterization of polysaccharides fromYunzhi mushroom and its effect on osteoblast cells. Carbohydr Polym 2010;80:922-6.
78. Kozarski M, Klaus A, Niksic M, Vrvic MM, Todorovic N, Jakovljevic D, *et al.* Antioxidative activities and chemical characterization of polysaccharide extracts from the widely used mushrooms *Ganoderma applanatum*, *Ganoderma lucidum*, *Lentinus edodes* and *Trametes versicolor.* J Food Composit Anal 2012;26:144-53.

79. Zhang H, Li WJ, Nie SP, Chen Y, Wang YX, Xie MY. Structural characterisation of a novel bioactive polysaccharide from *Ganoderma atrum*. Carbohydr Polym 2012;88:1047-54.
80. Peng Y, Zhang L, Zeng F, Kennedy JF. Structure and antitumor activities of the water-soluble polysaccharides from *Ganoderma tsugae* mycelium. Carbohydr Polym 2005;59:385-92.
81. Bao XF, Liu CP, Fang JN, Li XY. Structural and immunological studies of a major polysaccharide from spores of *Ganoderma lucidum* (Fr.) Karst. Carbohydr Res 2001;332:67-74.
82. Duggan C, Gannon J, Walker WA. Protective nutrients and functional foods for the gastrointestinal tracts. Am J Clin Nutr 2002;75:789-808.
83. Benkeblia N. Polysaccharides: Natural Fibers in Food and Nutrition. London, Boca Raton, (FL): CRC Press, Taylor and Francis Group; 2014.
84. Giavasis I. Bioactive fungal polysaccharides as potential functional ingredients in food and nutraceuticals. Curr Opin Biotechnol 2014;26:162-73.
85. Wasser SP. Current findings, future trends, and unsolved problems in studies of medicinal mushrooms. Appl Microbiol Biotechnol 2011;89:1323-32.
86. Chang ST, Wasser SP. The role of culinary-medicinal mushrooms on human welfare with a pyramid model for human health. Int J Med Mushrooms 2012;14:95-134.
87. Mizuno M, Nishitani Y. Immunomodulating compounds in basidiomycetes. J Clin Biochem Nutr 2013;52:202-7.
88. Shaoping N, Zhang H, Li W, Xie M. Current development of polysaccharides from *Ganoderma*: Isolation, structure and bioactivities. Bioact Carbohydr Diet Fibre 2013;1:10-20.
89. Lin YL, Liang YC, Lee SS, Chiang BL. Polysaccharide purified from *Ganoderma lucidum* induced activation and maturation of human monocyte-derived dendritic cells by the NF-κB and p38 mitogen activated protein kinase pathways. J Leukoc Biol 2005;78:533-43.
90. Zhang M, Cui SW, Cheung PC, Wang Q. Antitumor polysaccharides from mushrooms: A review on their isolation process, structural characteristics and antitumor activity. Trends Food Sci Technol 2007;18:4-19.
91. Chen Y, Xie MY, Nie SP, Li C, Wang YX. Purification, composition analysis and antioxidant activity of a polysaccharide from the fruiting bodies of *Ganoderma atrum*. Food Chem 2008;107:231-41.
92. Wang JG, Zhang LN. Structure and chain conformation of five water soluble derivatives of a b-D-glucan isolated from *Ganoderma lucidum*. Carbohydr Res 2009;344:105-12.
93. Nie S, Zhang H, Li W, Xie M. Current development of polysaccharides from *Ganoderma*: Isolation, structure and bioactivities. Bioact Carbohydr Diet Fibre 2013;1:10-20.
94. Moradali MF, Mostafavi H, Ghods S, Hedjaroude GA. Immunomodulating and anticancer agents in the realm of macromycetes fungi (macrofungi). Int Immunopharmacol 2007;7:701-24.
95. Jia J, Zhang X, Hu YS, Wu Y, Wang QZ, Li NN, *et al.* Evaluation of *in vivo* antioxidant activities of *Ganoderma lucidum* polysaccharides in STZ diabetic rats. Food Chem 2009;115:32-6.
96. Zhang J, Tang Q, Zimmerman-Kordmann M, Reutter W, Fan H. Activation of B lymphocytes by GLIS, a bioactive proteoglycan from *Ganoderma lucidum*. Life Sci 2002;71:623-38.
97. Zong A, Cao H, Wang F. Anticancer polysaccharides from natural resources: A review of recent research. Carbohydr Polym 2012;90:1395-410.
98. Gao YH, Gao H, Chan E, Tang WB, Xu A, Yang H, *et al.* Antitumor activity and underlying mechanisms of ganopoly, the refined polysaccharides extracted from *Ganoderma lucidum*, in mice. Immunol Invest 2005;34:171-98.
99. Liu YJ, Shena J, Xia YM, Zhang J. The polysaccharides from *Ganoderma lucidum*: Are they always inhibitors on human hepatocarcinoma cells? Carbohydr Polym 2012;90:1210-5.
100. Zhao L, Dong Y, Chen G, Hu Q. Extraction, purification, characterization and antitumor activity of polysaccharides from *Ganoderma lucidum.* Carbohydr Polym 2010;80:783-9.
101. Kim BK, Cho HY, Kim JS, Kim HW, Choi EC. Studies on constituents of higher fungi of Korea (LXVIII). Antitumor components of the cultured mycelia of *Ganoderma lucidum*. Korean J Pharmacol 1993;24:203-12.
102. Joseph S, Sabulal B, George V, Antony K, Janardhanan K. Antitumor and anti-inflammatory activities of polysaccharidesisolatedfrom *Ganoderma lucidum*. Acta Pharm 2011;61:335-42.
103. Cao QZ, Lin ZB. Antitumor and anti-angiogenic activity of *Ganoderma lucidum* polysaccharides peptide. Acta Pharmacol Sin 2004;25:833-8.
104. Lowe E, Rice P, Ha T. A(1-->3)-b-D-linked heptasaccharide is the unitligand for glucan pattern recognition receptors on human monocytes. Microbes Infect 2001;3:789-97.
105. Yan J, Vetvicka V, Xia Y, Coxon A, Carrol MC, Mayadas TN, *et al.* Beta-glucan, a "specific" biologic response modifier that uses antibodies to target tumors for cytotoxic recognition by leukocyte complement receptor Type 3 (CD11b/CD18). J Immunol 1999;163:3045-52.
106. Ooi LS, Ooi VEC, Fung MC. Induction of gene expression of immunomodulatory cytokines in the mouse by a polysaccharide from *Ganoderma lucidum* (Curt.: Fr.) P. Karst. (Aphyllophoromycetideae). Int J Med Mushrooms 2002;4:27-35.
107. Pan K, Jiang Q, Liu G, Miao X, Zhong D. Optimization extraction of *Ganoderma lucidum* polysaccharides and its immunity and antioxidant activities. Int J Biol Macromol 2013;55:301-6.
108. Zhang J, Liu YJ, Park HS, Xia YM. Antitumor activity of sulfated extracellular polysaccharides of *Ganoderma lucidum* from the submerged fermentation broth. Carbohydr Polym 2012;87:1539-44.
109. Ma CW, Feng M, Zhai X, Hu M. Optimization for the extraction of polysaccharides from *Ganoderma lucidum* and their antioxidant and antiproliferative activities. J Taiwan Inst Chem Eng 2013;44:886-94.
110. Cao QZ, Lin ZB. *Ganoderma lucidum* polysaccharides peptide inhibits the growth of vascular endothelial cell and the induction of VEGF in human lung cancer cell. Life Sci 2006;78:1457-63.
111. Kumar DS, Senthilkumar P, Surendran L, Sudhagar B. *Ganoderma lucidum* oriental mushroom mediated synthesis of gold nanoparticles conjugated with doxorubicin and evaluation of its anticancer potential on human breast cancer MCF-7/DOX cells. Int J Pharm Pharm Sci 2017;9:267-74.
112. Liu W, Wang HY, Pang XB, Yao WB. Characterization and antioxidant activity of two low- molecular-weight polysaccharides purified from the fruiting bodies of *Ganoderma lucidum*. Int J Biol Macromol 2010;46:451-7.
113. Kozarski M, Klaus A, Niksic M, Jakovljevic S, Helsper JP, Van Griensven LJ. Antioxidative and immunomodulating activities of polysaccharide extract of the medicinal mushrooms *Agaricus bisporus*, *Agaricus brasiliensis*, *Ganoderma lucidum* and *Phellinus linteus*. Food Chem 2011;129:1667-75.
114. Ping CX, Yan C, Shuibing L, YouGou C. Free radical scavenging of *Ganoderma lucidum* polysaccharides and its effect on antioxidant enzymes and immunity activities in cervical carcinoma rats. Carbohydr Polym 2009;77:389-93.
115. Mau JL, Tsai SY, Tseng YH, Huang SJ. Antioxidant properties of hot water extracts from *Ganoderma tsugae* Murrill. LWT Food Sci Technol 2005;38:589-97.
116. Mau JL, Tsai SY, Tseng YH, Huang SJ. Antioxidant properties of methanolic extracts from *Ganoderma tsugae.* Food Chem 2005;93:641-9.
117. Tseng YH, Yang JH, Mau JL. Antioxidant properties of polysaccharides from Ganoderma tsugae. Food Chem 2008;107:732-8/
118. Shi M, Zhang Z, Yang Y. Antioxidant and immunoregulatory activity of *Ganoderma lucidum* polysaccharide. Carbohydr Polym 2013;95:200-6.
119. Kao PF, Wang SH, Hung WT, Liao YH, Lin CM, Yang WB. Structural characterization and antioxidative activity of low-molecular-weights Beta-1,3-glucan from the residue of extracted *Ganoderma lucidum* fruiting bodies. J Biomed Biotechnol 2012;2012:1-8.
120. Kan Y, Chen T, Wu Y, Wu J. Antioxidant activity of polysaccharide extracted from *Ganoderma lucidum* using response surface methodology. Int J Biol Macromol 2015;72:151-7.
121. Zhonghui Z, Xiaowei Z, Fang F. *Ganoderma lucidum* polysaccharides supplementation attenuates exercise-induced oxidative stress in skeletal muscle of mice. Saudi J Biol Sci 2014;21:119-23.
122. Li XL, Zhou AG, Li XM. Inhibition of *Lycium barbarium* polysaccharides and *Ganoderma lucidum* polysaccharides against oxidative injury induced by γ- irradiation in rat liver mitochondria. Carbohydr Polym 2007;69:172-8.
123. Chen TQ, Wu JZ. Efficient extraction technology of antioxidant crude polysaccharides from *Ganoderma lucidum* (Linghzi), ultrasonic-circulating extraction integrating with superfine-pulverisation. J Taiwan Inst Cheml Eng 2014;45:57-62.
124. Gao Y, Zhou S, Jiang W, Huang M, Dai X. Effects of Ganopoly (a *Ganoderma lucidum* polysaccharide extract) on the immune functions in advanced-stage cancer patients. Immunol Invest 2003;32:201-15.
125. Bach JP, Deuster O, Balzer-Geldsetzer M, Meyer B, Dodel R, Bacher M. The role of macrophage inhibitory factor in tumorigenesis

and central nervous system tumors. Cancer 2009;115:2031-40.
126. Mantovani A, Sica A. Macrophages, innate immunity and cancer: Balance, tolerance, and diversity. Curr Opin Immunol 2010;22:231-7.
127. You YH, Lin ZB. Protective effects of *Ganoderma lucidum* polysaccharides peptide on injury of macrophages induced by reactive oxygen species. Acta Pharmacol Sin 2002;23:789-91.
128. Zhu XL, Chen AF, Lin ZB. *Ganoderma lucidum* polysaccharides enhance the function of immunological effect or cells in immune-suppressed mice. J Ethnopharmacol 2007;111:219-26.
129. Sun LX, Lin ZB, Li XJ, Li M, Lu J, Duan XS, *et al.* Promoting effects of *Ganoderma lucidum* polysaccharides on B16F10 cells to activate lymphocytes. Basic Clin Pharmacol Toxicol 2011;108:149-54.
130. Zhang QH, Lin ZB. The antitumor activity of *Ganoderma lucidum* (Curt Fr) P Karst (Ling Zhi) (Aphyllophoromycetideae) polysaccharides sis related to tumor necrosis factor-a and interferon-g. Int J Med Mushrooms 1999;1:207-15.
131. Cao LZ, Lin ZB. Regulation on maturation and function of dendritic cells by *Ganoderma lucidum* polysaccharides. Immunol Lett 2002;83:163-9.
132. Gao YH, Tang WB, Dai XH, Gao H, Chen G, Ye J, *et al.* Effects of water-soluble *Ganoderma lucidum* polysaccharides on the immune functions of patients with advanced lung cancer. J Med Food 2005;8:159-68.
133. Huang SQ, Ning ZX. Extraction of polysaccharide from *Ganoderma lucidum* and its immune enhancement activity. Int J Biol Macromol 2010;47: 336-41.
134. Miles PG, Chang ST. Mushroom Biology: Concise Basics and Current Developments. Singapore: World Scientific; 1997. p. 194.
135. Gao Y, Zhou S, Huang M, Xu A. Antibacterial and antiviral value of the genus *Ganoderma* P. Karst species (Aphyllophoromycetideae): A review. Int J Med Mushrooms 2003;5:235-46.
136. Bhattacharyya C, De S, Basak A, Banerjee M, Snigdha M, Samajpati N. Antimicrobial activities of some basidiomycetous fungi. J Mycopathol Res 2006;44:129-35.
137. Wang JG, Ma ZC, Zhang LN, Fang YP, Jiang F, Phillips GO. Structure and chain conformation of water-soluble heteropolysaccharides from *Ganoderma lucidum*. Carbohydr Polym 2011;86:844-51.
138. Sullivan R, Smith JE Rowan NJ. Medicinal mushrooms and cancer therapy. Translating a traditional practice into Western medicine. Perspect Biol Med 2006;49:159-70.
139. Bai D, Chang NT, Li DH, Liu JX, You XY. Antiblastic activity of *Ganoderma lucidum* polysaccharides. Acta Agric Boreali Sin 2008;23:282-5.
140. Yoon SY, Eo SK, Kim YS, Lee CK, Han SS. Antimicrobial activity of *Ganoderma lucidum* extract alone and in combination with some antibiotics. Arch Pharm Res 1994;17:438-42.
141. Quereshi S, Pandey AK, Sandhu SS. Evaluation of antibacterial activity of different *Ganoderma lucidum* extracts. J Sci Res 2010;3:9-13.
142. Sheena N, Ajith TA, Mathew AT, Janardhanan KK. Antibacterial activity of three macrofungi, *Ganoderma lucidum*, *Navesporus floccosa* and *Phellinus rimosus* occurring in South India. Pharm Biol 2003;41:564-7.
143. Paul S, Sasikumar CS, Singh AR. Fabrication of silver nanoparticles synthesized from *Ganoderma lucidum* into the cotton fabric and its antimicrobial property. Int J Pharm Pharm Sci 2015;7:53-56.
144. Bhardwaj A, Gupta P, Kumar N, Mishra J, Kumar A, Misra K. Lingzhi or reishi mushroom, *Ganoderma lucidum* (Agaricomycetes), inhibits *Candida* biofilms: A metabolic approach. Int J Med Mushrooms 2017;19:685-96.
145. Cheung WM, Hui WS, Chu PW, Chiu SW, Ip NY. *Ganoderma* extract activates MAP kinases and induces the neuronal differentiation of rat pheochromocytoma PC12 cells. FEBS Lett 2000;486:291-6.
146. Zhao HB, Lin SQ, Liu JH, Lin ZB. Polysaccharide extract isolated from *Ganoderma lucidum* protects rat cerebral cortical neurons from hypoxia/reoxygenation injury. J Pharmacol Sci 2004;95:294-8.
147. Zhang J, Tang Q, Zhou C, Jia W, Da Silva L, Nguyen LD, *et al.* GLIS, a bioactive proteoglycan fraction from *Ganoderma lucidum*, displays antitumour activity by increasing both humoral and cellular immune response. Life Sci 2010;87:628-37.
148. Lai CS, Yu MS, Yuen WH, So KF, Zee SY, Chang RC. Antagonizing β-amyloid peptide neurotoxicity of the anti-aging fungus *Ganoderma lucidum.* Brain Res 2008;1190:215-24.
149. Zhou Y, Qu ZQ, Zeng YS, Lin YK. Neuroprotective effect of preadministration with *Ganoderma lucidum* spore on rat hippocampus. Exp Toxicol Pathol 2012;64:673-80.
150. Selkoe DJ. Alzheimer's disease: Genotypes, phenotypes, and treatments. Science 1997;275:630-1.
151. Heneka MT, O'Banion MK. Inflammatory processes in Alzheimer's disease. J Neuroimmunol 2007;184:69-91.
152. Perry VH, Nicoll JA, Holmes C. Microglia in neurodegenerative disease. Nat Rev Neurol 2010;6:193-201.
153. Brown GC, Neher JJ. Microglial phagocytosis of live neurons. Nat Rev Neurosci 2014;15:209-16.
154. Fu R, Shen Q, Xu P, Luo JJ, Tang Y. Phagocytosis of microglia in the central nervous system diseases. Mol Neurobiol 2014;49:1422-34.
155. Gerard C, Rollins BJ. Chemokines and disease. Nat Immunol 2001;2:108-15.
156. Nagata T, Nagano I, Shiote M, Narai H, Murakami T, Hayashi T, *et al.* Elevation of MCP-1 and MCP-1/VEGF ratio in cerebrospinal fluid of amyotrophic lateral sclerosis patients. Neurol Res 2007;29:772-6.
157. Gao L, Tang H, Nie K, Wang L, Zhao J, Gan R, *et al.* MCP-1 and CCR2 gene polymorphisms in Parkinson's disease in a Han Chinese cohort. Neurol Sci 2015;36:571-6.
158. El Khoury JB, Moore KJ, Means TK, Leung J, Terada K, Toft M, *et al.* CD36 mediates the innate host response to beta-amyloid. J Exp Med 2003;197:1657-66.
159. Hickman SE, El Khoury J. Mechanisms of mononuclear phagocyte recruitment in Alzheimer's disease. CNS Neuro Disord Drug Targets 2010;9:168-73.
160. Selenica ML, Alvarez JA, Nash KR, Lee DC, Cao C, Lin X, *et al.* Diverse activation of microglia by chemokine (C-C motif) ligand 2 overexpression in brain. J Neuroinflammation 2013;10:856.
161. Ishizuka K, Kimura T, Igata-yi R, Katsuragi S, Takamatsu J, Miyakawa T. Identification of monocyte chemoattractant protein-1 in senile plaques and reactive microglia of Alzheimer's disease. Psychiatry Clin Neurosci 1997;51:135-8.
162. Cai Q, Li Y, Pei G. Polysaccharides from *Ganoderma lucidum* attenuate microglia mediated neuroinflammation and modulate microglial phagocytosis and behavioural response. J Neuroinflammation 2017;14:63.
163. Huang S, Mao J, Ding K, Zhou Y, Zeng X, Yang W, *et al.* Polysaccharides from *Ganoderma lucidum* promotes cognitive function and neural progenitor proliferation in mouse model of Alzheimer's disease. Stem Cell Rep 2017;8:84-94.
164. He CY, Li WD, Guo SX, Lin SQ, Lin ZB. Effect of polysaccharides from *Ganoderma lucidum* on streptozotocin- induced diabetic nephropathy in mice. J Asian Nat Prod Res 2006;8:705-11.
165. Meng G, Zhlu H, Yang S, Wu F, Zheng H, Chen E, *et al.* Attenuating effects of *Ganoderma lucidum* polysaccharides on myocardial collagen cross-linking relates to advanced glycation end product and antioxidant tenzymes in high-fat-diet and streptozotocin-induced diabetic rats. Carbohydr Polym 2011;84:180-5.
166. Gao YH, Lan J, Dai XH, Ye JX, *et al.* Aphase I/II study of Lingzhi mushroom *Ganoderma lucidum* (W.Curt:Fr.) Lloyd (Aphyllophoromycetideae) extract in patients with Type II diabetes mellitus. Int J Med Mushrooms 2004;6:33-9.
167. Zhang HN, He JH, Yuan L, Lin ZB. *In vitro* and *in vivo* protective effect of *Ganoderma lucidum* polysaccharides on alloxan-induced pancreatic islets damage. Life Sci 2003;73:2307-19.
168. Pan D, Wang L, Chen C, Teng B. Structure characterization of a novel neutral polysaccharide isolated from *Ganoderma lucidum* fruiting bodies. Food Chem 2012;135:1097-103.
169. Zhang GL, Wang YH, Ni W, Teng H, Lin ZB. Hepatoprotective role of *Ganoderma lucidum* polysaccharide against BCG-induced immune liver injury in mice. World J Gastroenterol 2002;15:728-33.
170. Gao Y, Huang M, Lin ZB, Zhou S. Hepatoprotective activity and the mechanisms of action of *Ganoderma lucidum* (Curt.:Fr.) P. Karst. (Ling Zhi, Reishi Mushroom). Int J Med Mushrooms 2003;5:27-35.
171. Pham HN, Hoang LS, Phung VT, Hsu TC. Hepatoprotective activity of *Ganoderma lucidium* (Curtis) P. Karst against cyclophosphamide-induced liver injury in mice. Cogent Biol 2016;2:1267421.
172. Zhu KX, Nie SP, Tan LH, Li C, Gong DM, Xie MY. Polysaccharide from *Ganoderma atrum* improves liver function in Type 2 diabetic rats via antioxidant action and short-chain fatty acids excretion. J Agric Food Chem 2016;64:1938-44.
173. Yu Y, Qian L, Du N, Liu Y, Zhao X. *Ganoderma lucidum* polysaccharide enhances radiosensitivity of hepatocellular carcinoma cell line HepG2 through Akt signaling pathway. Exp Ther Med 2017;14:5903-7.
174. Zhao GM, Zhang LX, Yu TM, Liu SM, Zhang LP. Chemical structure of water soluble polysaccharide from spores of *Ganoderma lucidum*. J Clin Pharmacol 2005;41:902-04.
175. Chen JH, Zhou JP, Zhang LN. Chemical structure of the water-insoluble polysaccharide isolated from the fruiting body of

Ganoderma lucidum. Polym J 1998;30:838-42.

176. Huang SQ, Li JW, Li YQ, Wang Z. Purification and structural characterization of water-soluble neutral polysaccharide GLP-F1-1from *Ganoderma lucidum*. Int J Biol Macromol 2011;48:165-9.
177. Zhang LX, Zhao GM, Wu MJ, Cao PY. Purification and characterization of water soluble polysaccharide GLPS 3 from sporderm-unbroken germinting spores of *Ganoderma lucidum.* J Clin Pharm 2006;41:230-2.
178. Dong Q, Wang Y, Shi L, Yao J, Li J, Ma F, *et al.* A novel water-soluble β-D-glucan isolated from the spores of *Ganoderma lucidum*. Carbohydr Res 2012;353:100-5.
179. Amaral AE, Carbonero ER, Simao CG, Kadowaki MK, Sassaki GL, Osaku CA, *et al.* An unusual water-soluble b- glucan from the basidiocarp of the fungus *Ganoderma resinaceum.* Carbohydr Polym 2008;72:473-8.
180. Skalicka-Wozniak K, Szypowski J, Łos R, Siwulski M, Sobieralski K, Glowniak K, *et al.* Evaluation of polysaccharides content in fruit bodies and their antimicrobial activity of four *Ganoderma lucidum* (W Curt.: Fr.) P. Karst strains cultivated on different wood type substrates. Acta Soc Bot Pol 2012;81:17-21.
181. Wang CL, Pi CC, Kuo CW, Zhuang YJ, Khoo KH, Liu WH, *et al.* Polysaccharides purified from the submerged culture of *Ganoderma formosanum* stimulate macrophage activation and protect mice against Listeria monocytogenes infection. Biotechnol Lett 2011;33:2271-8.
182. YouGuo C, Zongji S, XiaoPing C. Modulatory effect of *Ganoderma lucidum* polysaccharides on serum antioxidant enzymes activities in ovarian cancer rats. Carbohydr Polym 2009;78:258-62.
183. Ye LB, Li JR, Zhang JS, Pan YJ. NMR characterization for polysaccharide moiety of a glycopeptide. Fitoterapia 2010;81:93-6.
184. Peng YF, Zhang LN, Zeng FB, Xu YX. Structure and antitumor activity of extracellular polysaccharides from mycelium. Carbohydr Polym 2003;54:297-303.
185. Li YQ, Fang L, Zhang KC. Structure and bioactivities of a galactoseric extracellular polysaccharide from submergedly cultured *Ganoderma lucidum.* Carbohydr Polym 2007;68:323-8.
186. Ye LB, Zhang JS, Ye XJ, Tang QJ, Liu Y, Gong C, *et al.* Structural elucidation of the polysaccharide moiety of a glycopeptides (GLPCW-II) from *Ganoderma lucidum* fruiting bodies. Carbohydr Res 2008;343:746-52.