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Research Article
Evaluation of Some Active Nutrients, Biological Compounds and Health Benefits of Reishi Mushroom (*Ganoderma lucidum*)

[1]Yugandhar Parepalli, [2,3]Murthy Chavali, [4]Rokayya Sami, [4]Ebtihal Khojah, [5]Abeer Elhakem, [6]Ahmad El Askary, [7]Meenakshi Singh, [8]Surabhi Sinha and [9]Ghadir El-Chaghaby

[1]Division of Chemistry, Department of Sciences and Humanities, VFSTR, Vadlamudi, District Guntur, 522 213, Andhra Pradesh, India
[2]Office of Dean (Research), Department of Chemistry, Alliance College of Engineering and Design, Faculty of Science and Technology, Alliance University (Central Campus), Chikkahagade Cross, Chandapura-Anekal Main Road, Bengaluru 562 106 Karnataka, India
[3]NTRC-MCETRC and Aarshanano Composite Technologies Pvt. Ltd., District Guntur, Andhra Pradesh, 522201, India
[4]Department of Food Science and Nutrition, College of Sciences, Taif University, P.O. 11099, Taif, 21944, Saudi Arabia
[5]Department of Biology, College of Science and humanities in Al-Kharj, Prince Sattam Bin Abdulaziz University, Al-Kharj 11942, Saudi Arabia
[6]Department of Clinical Laboratory Sciences, College of Applied Medical Sciences, Taif University, Taif, Saudi Arabia
[7]Department of Botany, The Maharaja Sayajirao University of Baroda, Vadodara, 390002, Gujarat, India
[8]Amity Institute of Biotechnology, Amity University, Noida, 201303, Uttar Pradesh, India
[9]Regional Center for Food and Feed (RCFF), Agricultural Research Center (ARC), 9 Algamaa Street, Giza 12511 Egypt

Abstract

Background and Objective: *Ganoderma lucidum*, a therapeutic mushroom, its extract holds several bioactive compounds include polysaccharides, triterpenes, peptidoglycans are the three main physiologically active ingredients in *G. lucidum*. Triterpenoids and polysaccharides are the prime bioactive constituents that are responsible for their medicinal properties and have numerous health properties as an immune booster and a health supplement. The primary objective is to evaluate the biologically active compounds of Reishi Mushroom (*Ganoderma lucidum*). **Materials and Methods:** In this study, we have extracted and quantified some of the polysaccharides, triterpenes and peptidoglycans, via ethanol and water extracts. **Results:** A comparison of polysaccharide and triterpenes contents from fruit body extracts in the three commercial variants were made polysaccharides from fruit body extracts in all variants varied between 4.48-16.85% and triterpenes 0.90-2.56%, respectively. **Conclusion:** Also, the therapeutic and biological applications of polysaccharide NPs, Chitosan-GLP NPs, the nutritional profile and health benefits of the mushroom were mentioned.

Key words: *Ganoderma lucidum*, bio-active compounds, polysaccharides, triterpenes, therapeutic, nutrition profile

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Corresponding Author: Murthy Chavali, NTRC-MCETRC and Aarshanano Composite Technologies Pvt. Ltd., District Guntur, Andhra Pradesh, 522201, India
Tel: +91-8309337736

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Data Availability: All relevant data are within the paper and its supporting information files.

INTRODUCTION

Miracle Chinese herb, *Ganoderma lucidum* or *reishi* or *lingzhi*, is a massive and unpleasant medicinal mushroom with a brilliant outshining exterior that contains a high amount of active biological molecules[1]. *Ganoderma lucidum*, a therapeutic mushroom, its extract holds several bioactive compounds include polysaccharides, triterpenes, peptidoglycans are the three main physiologically active ingredients in *G. lucidum*[2]. *Ganoderma lucidum* touted as a top source of antioxidants is a natural medicine that is widely used and recommended by Asian physicians and naturopaths for its supporting effects on the immune system[3]. Oriental medicinal mushrooms over the decade gained popularity for their application in the deterrence and remedy of innumerable diseases. More than two thousand years of steady use in China and Japan and the current clinical trial studies have revealed that *Ganoderma lucidum* is an all-cure herb, an effective medicine of life that cannot make a person deathless or even ageless can save him from many living deaths such as AIDS, cancer and other deadly ailments making man's life a terrifying situation, worse than bereavement[4]. Triterpenoids and polysaccharides are the prime bioactive constituents that are responsible for their medicinal properties and have numerous health properties as an immune booster and a health supplement. The best essential thing is that it is harmless to consume for extensive periods without any side effects and nothing even happens when not taken excessively. *Ganoderma lucidum* is one of the popular medicinal mushrooms; many of its species are found over the globe with diverse characteristics[5], for example, shape and colour (reddish, black, bluish to greenish, brownish red, snowy white, buttery yellow and dark purple) of the fruit body, specific to the host and geographical source. *Ganoderma lucidum* belongs to basidiomycetous and allocated to the family *Polyporaceae* and popularly applied in Chinese traditional medicine for more than 4000 years. The Ganodermataceae family designates polypore basidiomycete's fungi that are dual-walled basidiospore to comprise around 219 species under the genus Ganoderma.

Ganoderma lucidum has been studied for its vast active biological compounds[4], say, pure polysaccharides, triterpenes peptidoglycans, etc. In this research work, the authors discussed an overview of the *Ganoderma lucidum* polysaccharide (and their nanoparticles), triterpenes analysis, bioactive peptidoglycans and biological applications[5] and their advantages[6]. Also discussed are the nutrient profile and health benefits of the mushroom. The research attempted to quantify the available content that carries promising anticancer and immunomodulatory properties. The primary objective is to evaluate the biologically active compounds of reishi mushroom (*Ganoderma lucidum*).

MATERIALS AND METHODS

Study area: This study was carried out at the Microbiology Division of N. I. University and VFSTR University, India from March, 2018-February, 2020.

Chemicals and solutions: All the chemicals and reagents that were used in this research study were obtained from Sigma Chemicals (USA), Fisher Scientific (Mumbai, India), Gujarat Research Chemicals (India) and Merck Co. (Germany) are of AR grade. Water used in these experiments is of Millipore quality. Laboratory feed water was distilled and deionized (DI) using Milli-Q® Reference Water Purification System (Millipore Corp.; https://www.merckmillipore.com/). Ultrapure, Type-1 water has a resistivity of 18.2 M cm^{-1} (@ 25°C) was obtained from Q-POD® dispenser. Thus, obtained ultrapure (Type-1) water was used for solution preparations.

Extract preparation: In the present work, characterized commercially available samples of mycelia and finely powdered fruiting body of *G. lucidum* was acquired from commercial growers and suppliers of mushrooms from Hyderabad, India. Aqueous extracts of *G. lucidum* were prepared through the ASE system furnished with a solvent unit to control. The 3 types of extracts (GLM, GLF and GLMF) were undone from the mycelia, fruiting body and their combined mixture (1:1 ratio; mycelium to the fruiting body of *G. lucidum*), respectively, as described elsewhere[7].

Preparation of *Ganoderma lucidum* polysaccharide (GLP) NPs: A large number of studies were conducted on polysaccharides and their derivatives in the past understanding their probable applications in nanoparticle-based drug delivery systems. Innumerable polysaccharides that were investigated for the research of nanoparticles appropriate as delivery systems are tremendously great. Consequently, the main attention has been concentrated on immediate studies and utilizations related to such systems, plus some of the maximum polysaccharides, a short description of their structural features and some of the techniques carried out towards polysaccharide-based nanoparticles in preparing was mentioned. Nanoparticle drug delivery systems have outstanding advantages[8]:

- Move-in via the minutest capillary vessels due to their ultra-tiny volume and evade quick clearance by phagocytes prolonging their duration in the bloodstream
- Shall penetrate (through cells and tissue gaps) reaching targeted organs-liver, spleen, lung, spinal cord and lymph
- Show various control-release properties-biodegrad ability, pH, ion and/or materials temperature sensibility
- Improves the drug utility and toxic side effects shall be reduced etc.

Currently, nanoparticles were widely applied to deliver drugs, polypeptides, proteins, vaccines, nucleic acids, genes and so on. Over the years, nanoparticle drug delivery systems have shown huge potential in biological, medical and pharmaceutical applications. At present, the research on the nanoparticle drug delivery system focuses on:

- Selectiveness and carrier materials combination towards suitable drug release speed
- Surface amendment of NPs to increase their ability to target
- Optimization of NPs preparation to increase their drug delivery capability, an application in hospitals and the possibility of industrial production
- Investigation of *in vivo* dynamic process disclosing the collaboration of NPs with blood and target tissues and organs, etc.

Materials used for preparing NPs (especially polymers) for drug delivery must be biocompatible and biodegradable. With this objective, many like PLA PGA, polysaccharides (mainly chitosan) [2], poly (acrylic acid) family, proteins or polypeptides (gelatin), etc. Amongst them, polysaccharides are the polymeric materials to develop nanoparticles targeting drug delivery.

Preparation of Chitosan-GLP nanoparticles: Chitosan-GLP nanoparticles were prepared by adding 10 mL GLP solution to the chitosan solution (2.5 mg mL^{-1}; 100 mL) obtained by dissolving chitosan in 1% (v/v) acetic acid solution for one hour under magnetic stirring[3]. Then by using 1 mol L^{-1} NaOH the pH of the solution was attuned to 5.0 and the solution was stirred for 1 hr at room temperature. Lastly, counter ion TPP solution, which was prepared by dissolving 1 mg mL^{-1} in pure water was mixed to the chitosan-GLP solution while mildly stirring at 75 rpm for 1 hr forming chitosan-GLPNPs. Then centrifuged at 22000 rpm at 4-5°C for 30 min, nanoparticles at the bottom were collected and the supernatant was discarded, thoroughly washed with warm water and to end lyophilized.

GLP entrapment efficiency and NPs loading capacity: The GLP entrapped in the NPs quantity was calculated using DEAE weak anion exchange method. The entrapment efficiency of the NPs was intended as[3]:

$$\text{Entrapment efficiency (\%)} = \frac{\text{Total GLP-Free GLP}}{\text{Total GLP (mg)}}$$

GLP loading capacity was intended as:

$$\text{Loading capacity (\%)} = \frac{\text{Total GLP-Free GLP}}{\text{Weight of nanoparticles}}$$

RESULTS AND DISCUSSION

In this section, the identified active biological compounds in *Ganoderma lucidum* were discussed and a comparison of polysaccharide and triterpenes content in 3 commercially available lingzhi variants were discussed along with their nutritional content per gram of mushroom. Lastly therapeutic and biological applications of mushroom and GLP based NPs were also mentioned.

Active biological compounds: The three major physiologically active constituents in *G. lucidum* Polysaccharides, peptidoglycans and triterpenes have varied and diversified content. Fungi are extraordinary for the assortment of high-molecular-weight polysaccharide structures, bioactive polysaccharides, triterpenes, peptidoglycans and polyglucans (bioactive) were found in the mushroom parts. *Ganoderma lucidum* polysaccharide (and their nanoparticles), Triterpene's analysis, bioactive peptidoglycans and biological applications and their advantages were discussed alongside their nutrient profile and health benefits of the mushroom.

Polysaccharides: Polysaccharides signify structurally varied biological macromolecules with a range of novel physiochemical properties. In the design of drug delivery systems polysaccharides are regularly used materials as they are largely viewed for their properties-biocompatibility and biodegradability and also enjoy additional anticipated properties, the adhering ability to mucosal linings. Polysaccharide based Nps might embrace the positive features of both NPs and polysaccharides suitable for drug administration both via parenteral and mucosal. Designing NPs that deliver drugs at a required rate to the targeted body sites in the right dosage forms for a specific treatment is one of the most vital goals of drug delivery research.

Polysaccharides a class of natural polymers are extremely bioactive and biocompatible with an intelligent method for drug delivery by coupling the drug to a carrier particle as microspheres, NPs, liposomes, etc., modulating the drug release and absorption characteristics. With their small size and efficient carrier characteristics, NPs based particulate drug delivery systems establish as an authoritative part. Extractions of polysaccharides from mushrooms are regularly done via hot water followed by precipitation with EtOH or MeOH, or simply with water and alkali with certain conditions.

Triterpenes: Naturally occurring class of compounds with one or more isoprene C_5 units are terpenes, a major constituent of essential oils. These are classified as monoterpenes ($C_{10,}$ menthol, α-pinene), diterpenes (C_{20}), triterpene (squalene), tetraterpene (β-carotene), sesquiterpenes (C_{15}), etc. Terpenes possess anti-inflammatory, antifeedant, anti-tumorigenic, anti-cancer and hypolipidemic activities. Numerous plant species (prokaryotes as well as eukaryotes) produce triterpenes for their regular growth and development, but some species produce large amounts of triterpenes (latex and resins), believed to contribute to disease resistance. Triterpenes (a subclass of terpenes) are with a C_{30} simple skeleton. Among the many triterpenes isolated from various plants having beneficial effects and with fewer therapeutic applications known; the molecular weights of these triterpenoids range between 400 and 600 kDa[4]. Triterpene's chemical structure in *G. lucidum* is created on lanostane. Lanostane is a metabolite of lanosterol; its biological synthesis is established on the squalene cyclization.

Ganoderic acids A and B are the first isolated two new lanostane type bitter triterpenes from *G. lucidum*[4].To date nearly 100 triterpenes (majority are ganoderic and lucidenic acids, others like ganoderals, ganoderiols and ganodermic acids) were reported; of which over 50 compositions are very unique to the fungus, *G. lucidum.* Triterpene's extractions were usually done with is usually done using CH_3OH, C_2H_5OH, CH_3COCH_3, $CHCl_3$, R-O-R, or a mixture of these solvents, further purified with several separation methods, including normal HPLC and RP- HPLC[5]. *Ganoderma lucidum* is high in triterpene concentrations and responsible for its bitter taste and believed for its health benefits, mainly lipid content lowering and antioxidant properties. Nevertheless, the triterpene content is dissimilar in diverse parts of the mushroom and also varies with countless mushroom growth stages. With the triterpenes in different species, the triterpenes profile was made to distinguish from several taxonomically connected species serving as auxiliary evidence for classification. The triterpene content is also a measure of quality in a diverse range of mushroom samples.

Table 1: Comparison of polysaccharide and triterpenes content in 3 commercially available lingzhi (*G. lucidum*) variants

		Polysaccharides (%)		Triterpenes (%)	
Variants	n*	Min.	Max.	Min.	Max.
GL-1	3	1.25	2.56	4.48	16.84
GL-2	3	0.90	2.41	3.84	15.42
GL-3	3	1.11	2.36	3.96	15.68

*Average of 3 values

Peptidoglycans, polysaccharides and triterpenes from the three main physiologically active ingredients in *G. lucidum*[5]. Polysaccharides extracted from the fruiting body, spores and mycelia of lingzhi; are formed by the fungal mycelia further cultivated in fermenters, but duly differ in their molecular weights, sugar content and peptide compositions (e.g., ganoderans A, B and C) known for anti-inflammatory, antiulcer, hypoglycemic, anti-tumorigenic and immune-stimulating properties. A comparison of polysaccharide and triterpenes contents from fruit body extracts in the three commercial Lingzhi (*G. lucidum*) variants were listed in Table 1. Polysaccharides from fruit body extract in Lingzhi variants varied, GL-2 variant found to be the lowest with 0.90% and GL-1 variant with 2.56% as the highest. Triterpenes, on the other hand, the variant GL-2 variant found to be the lowest with 3.84% and GL-1 variant with 16.84% as the highest.

Peptidoglycans: Literature reports show numerous bioactive peptidoglycans isolated from *G. lucidum*, say, proteoglycan (GLPG) known for its antiviral activity[5], G. *lucidum* Immune-modulating Substance (GLIS), water-soluble glycopeptide[6], PGY is thoroughly fractionated and refined from aqueous extracts of *G. lucidum* fruiting bodies, GL-PS peptide (GL-PP)[6] and a fucose-containing glycoprotein fraction F3. Identified active biological compounds in *Ganoderma lucidum* are listed in Table 2.

Nutritional profile: A variety of bioactive molecules are widely present in mushrooms, steroids, phenols, terpenoids, nucleotides and their derivatives, glycoproteins and polysaccharides. Most mushrooms contain 88-92% water by weight[21]. The remaining 08-12% contains carbohydrate, fibre, ash, protein, fat and some vitamins and minerals. In addition to these, minerals like K, P, Ca, Mg, Fe, Zn, Cu Se, etc account for most of the mineral content. Non-volatile components of *G. lucidum* account for ash, carbohydrate, crude fat, fibre and protein etc.,[21].

All the essential amino acids are seen in mushroom proteins, particularly rich in lysine and leucine. The lower protein present in dried *G. lucidum* is lower than that of many other mushrooms. Bioactive proteins are attributed to the therapeutic properties of *G. lucidum*, with LZ-8, an

Table 2: Identified active biological compounds in *Ganoderma lucidum*

Compound	Function/outcome	References
Polysaccharides		
(1→3)-β-D-glucans	Growth inhibition of sarcoma S 180 tumour in mice	Y. Yang *et al.*[7]
PS-G, protein-bound polysaccharides (95.5% polysaccharides and 4.5% peptides)	Immune response activation, IL-1β, IL-6, TNF-α and IFN-γ (stimulation), Produced by macrophages and T lymphocytes, Neutrophil apoptosis inhibition, neutrophil phagocytosis and GST induction	M.J. Hsu *et al.*[8,9]
G009, amino polysaccharides	Antioxidant	J.M. Lee *et al.*[10]
Glycoproteins (with fructose)	IL-1, IL-2 and IFN-γ expression in spleen cells (stimulation)	Y.Y. Wang *et al.*[11]
GLIS, proteoglycans	Activation of β-lymphocytes	J. Zhang *et al.*[12]
Cerebrosides	DNA-polymerase inhibition	B. Boh *et al.*[13]
Triterpenes		
Ganoderic acids (U, V, W, X, Y)	Cytotoxic for hepatoma cells	M.S. Shiao *et al.*[14]
Ganoderic acids (A and C)	Farnesyl protein transferase inhibition	C.R. Cheng *et al.*[15]
Lucidimol (A and B), Ganoderiol F, ganodermanondiol, ganodermanontriol	Cytotoxic for sarcoma and lung carcinoma cells	Fernandes, P.D.T. and B.S. Min *et al.*[16,17]
Ganoderic acid F	Angiogenesis inhibition	Y. Kimura *et al.*[18]
Phenols	Antioxidants	J.L. Mau *et al.*[19]
Lipids	Hepatoma, sarcoma S-180 and reticulocyte sarcoma L-II *in vivo* (growth inhibition)	X. Liu *et al.*[20]

Table 3: Nutritional content per gram of mushroom, *Ganoderma lucidum* (n = 3)

Content	Amount (% g^{-1})
Total fat	5.8
Carbohydrates	42.8
Proteins	23.6
Ash	18.7
Water	7.5

*Average of 3 values

immunosuppressive protein refined from the mycelia exhibiting hepatoprotective, antioxidant activities and ganodermin (15 kDa; antifungal protein), thoroughly isolated from fruiting bodies of *G. lucidum*[21].

The mushrooms total fatty acids are substantial contributors as health boosters. The dried mushroom sample was examined for the carbohydrate and crude fibre content and the nutritional content per gram of mushroom *Ganoderma lucidum* is given in Table 3.

Health benefits: Many regions of Asia have used many parts of the Ganoderma species in traditional medicine. *Ganoderma lucidum*, a large, dark mushroom with a glossy exterior contains diverse phytochemicals with unclear properties *in vivo*, triterpenoids and polysaccharides, an area of inquiry still under elementary research. Ganoderma mushrooms have been promoting health used for a long time in Japan, China and other Asian countries known to stimulate immunity and fight cancer, thereby boosting longevity[22]. *Ganoderma lucidum* proteins and lectins may contribute to most of the stated medicinal effects. Other compounds that have been isolated from *G. lucidum* include enzymes are:

- Metalloprotease, an anticoagulant
- Ergosterol (pro-vitamin D_2)
- Nucleosides
- Nucleotides (adenosine and guanosine)

Therapeutic and biological applications: *Ganoderma lucidum* was used for more than hundreds of years in treatment strategies aiding in health care advancement, which was also evidenced with reported literature studies. These studies were based on several cellular models and limited animal models, *in vitro* assessments and very few human trials. Therapeutic interventions towards applications of *G. lucidum* include the effective development of benefits without any toxicity levels. With no division in the research unit for investigation towards an unbiased evaluation of human health that remains to be established. The studies on the properties of *G. lucidum* about cancer, viral and bacterial infection, diabetes and liver injury attracted a lot of interest. For example, *G. lucidum* as a prevalent nutritional supplement when taken proves to boost the immunity of a healthy individual also properties shown to work against cancer upon the combination with conventional therapies. Using biologically active *G. lucidum* towards cancer treatment was built on cancer and immune cells investigations from numerous laboratories and preclinical studies on animal models demonstrating various biological activities *in vitro* and *in vivo*. In future, this method may lead to the expansion of consistent *G. lucidum* preparations with precise anti-cancer properties and other associated activities[23].

Table 4: Significant active biological compound applications of GLP based NPs

Applications	References
Cytotoxicity of GLP-nanoparticles on tumour cells	Sohretoglu, D. and S. Huang[25]
Effects on growth promotion in mouse spleen cells	N. Li *et al.*[26]
Nasal delivery of drugs with nanoparticulate systems: a real enhancement over modest systems	L. Illum[27]
Role of curcuminoids in addressing plentiful chronic ailments- colon cancer, lung cancer, breast cancer, inflammatory bowel diseases	A. Amalraj *et al.*[28]
Epigallocatechin gallate-loaded polysaccharide nanoparticles for prostate cancer chemoprevention	S. Rocha *et al.*[29]
Cellular and molecular mechanisms of immuno-modulation	Z.B. Lin[30]
Efficiency of NPs as a carrier system for antiviral agents in HIV infected human oncocytes/macrophages *in vitro*	Seo, D.J. and C. Choi[31]
Ganoderma lucidum: a potential for biotechnological production of anti-cancer and immunomodulatory drugs	B. Boh[32]
Antitumor and anti-inflammatory activities of polysaccharides	S. Joseph[33]
Main compounds in rat bile after oral administration of complete triterpenoids	X.Y. Guo *et al.*[34]

Nanomedicine applications concern precisely engineered nanomaterials towards developing novel therapeutic and diagnostic modalities[23]. Nanomaterials have unique physicochemical properties, such as ultra-small size, large aspect ratios and high reactivity, mainly different from bulk materials. Most properties can overcome limitations found in traditional therapeutic and diagnostic agents. These nanoscale materials provide unparalleled degrees of freedom to change fundamental properties say solubility, drug release features, diffusivity, blood circulation half-life and immunogenicity. In the past 20-30 years, several NP-based therapeutic and diagnostic agents have been produced to treat cancer, aching, diabetes, asthma, allergy, infections and others[24]. These nanoscale agents are highly effective and/or more appropriate means for administration, lessen therapeutic toxicity, prolong the product life cycle and eventually diminish healthcare charges. As therapeutic delivery systems, NPs allow both targeted and controlled delivery/release. For diagnostic applications, NPs allow detection on the molecular scale they help identify abnormalities such as fragments of viruses, precancerous cells and disease markers that cannot be detected with traditional diagnostics. NP-based contrast agents for imaging have also exposed the improvement in sensitivity and specificity of MRI. The active biological compound applications of GLP based nanoparticles were given in Table 4.

Ganoderma lucidum used in traditional Chinese medicine for centuries as a nutritional supplement and herbal medication. This work summarizes some of the active substances of *Ganoderma lucidum*. Polysaccharides and triterpenoids are the major secondary metabolites of *G. lucidum*. The triterpenoids and polysaccharides have attracted considerable attention because of their high content and significant bioactivities. Modern studies may show that *G. lucidum* contains several active compounds, along with the triterpenoids, polysaccharides, steroids, fatty acids, amino acids, nucleosides, proteins and alkaloids, known to have over 400 bioactive compounds. *Ganoderma lucidum* is a decent homologous medicinal and immune booster material, receiving more attention in the food health care, biotechnology, medicine and cosmetics industry with modern-day technological advances. Several applications related to the food sector, human health and cosmetics have immense potential for further exploration.

CONCLUSION

Ganoderma lucidum is a well-known remedy for several impressive ranges of submissions. Universal consumption of *G. lucidum* is enormous with the growing sequence of products as an active food supplement and some of the extracts and isolated compositions used in several various formulations as capsules, creams, hair tonics and syrups that are sold worldwide. With certain varied amounts, the three major physiologically active constituents in *G. lucidum,* polysaccharides, peptidoglycans and triterpenes are present. With its growing sales and consumption, while increasing applications of the *G. lucidum* extracts like antioxidant, anticancer, antiulcer, anti-tumorigenic, antibacterial, organ protection, antiviral effects, attracted more relevant studies than ever. So far done are animal studies or cellular models gave any supportive *in vitro* findings.

SIGNIFICANCE STATEMENT

With fewer human studies a great amount of data is required to generate evidence of the effects of *G. lucidum* complementing valid experimental and significant clinical data are required. Several challenges and an assortment of factors still exist to address, numerous strategies must be intended for standard quality control procedures in preparing *G. lucidum* formulations are desirable to decide mechanisms of action and to support characterize the bio-active compounds.

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REFERENCES

1. Reis, C.P., R.J. Neufeld, A.J. Ribeiro and F. Veiga, 2006. Nanoencapsulation I. Methods for preparation of drug-loaded polymeric nanoparticles. Nanomedicine, 2: 8-21.
2. Parepalli, Y., M. Chavali, S. Rokayya, T. Fouzia, S. Surabhi and S. Meenakshi, 2021. *Ganoderma lucidum*: Extraction and characterization of polysaccharides, yields and their bioapplications. Algerian J. Res. Tech., 5: 30-43.
3. Koo, H., M.S. Huh, I.C. Sun, S.H. Yuk, K. Choi, K. Kim and I.C. Kwon, 2011. *In vivo* targeted delivery of nanoparticles for theranosis. Acc. Chem. Res., 44: 1018-1028.
4. Cör, D., Ž. Knez and M.K. Hrnčič, 2018. Antitumour, antimicrobial, antioxidant and antiacetylcholinesterase effect of *Ganoderma lucidum* terpenoids and polysaccharides: A review. Molecules, 23: 649-662.
5. Ji, Z., Q. Tang, J. Zhang, Y. Yang, W. Jia and Y. Pan, 2007. Immunomodulation of RAW264.7 macrophages by GLIS, a proteopolysaccharide from *Ganoderma lucidum*. J. Ethnopharmacol., 112: 445-450.
6. Chien, C.M., J.L. Cheng, W.T. Chang, M.H. Tien and C.M. Tsao *et al*., 2004. Polysaccharides of *Ganoderma lucidum* alter cell immunophenotypic expression and enhance $CD56^+$ NK-cell cytotoxicity in cord blood. Bioorg. Med. Chem., 12: 5603-5609.
7. Yang, Y., H. Zhang, J. Zuo, X. Gong, F. Yi, W. Zhu and L. Li, 2019. Advances in research on the active constituents and physiological effects of *Ganoderma lucidum*. Biomed. Dermatol., Vol. 3. 10.1186/s41702-019-0044-0.
8. Hsu, M.J., S.S. Lee and W.W. Lin, 2002. Polysaccharide purified from *Ganoderma lucidum* inhibits spontaneous and Fas-mediated apoptosis in human neutrophils through activation of the phosphatidylinositol-3 kinase/Akt pathways. J. Leuokoc. Biol., 72: 207-216.
9. Hsu, M.J., S.S. Lee, S.T. Lee and W.W. Lin, 2003. Signaling mechanisms of enhanced neutrophil phagocytosis and chemotaxis by the polysaccharide purified from *Ganoderma lucidum*. Br. J. Pharmacol., 139: 289-298.
10. Lee, J.M., H. Kwon, H. Jeong, J.W. Lee, S.Y. Lee, S.J. Baek and Y.J. Surh, 2001. Inhibition of lipid peroxidation and oxidative DNA damage by *Ganoderma lucidum*. Phytother. Res., 15: 245-249.
11. Wang, Y.Y., K.H. Khoo, S.T. Chen, C.C. Lin, C.H. Wong and C.H. Lin, 2002. 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., 10: 1057-1062.
12. Zhang, J., Q. Tang, M. Zimmerman-Kordmann, W. Reutter and H. Fan, 2002. Activation of B lymphocytes by GLIS, a bioactive proteoglycan from *Ganoderma lucidum*. Life Sci., 71: 623-638.
13. Boh, B., M. Berovic, J. Zhang and L. Zhi-Bin, 2007. *Ganoderma lucidum* and its pharmaceutically active compounds. Biotechnol. Annu. Rev., 13: 265-301.
14. Shiao, M.S., 2003. Natural products of the medicinal fungus *Ganoderma lucidum*: Occurrence, biological activities and pharmacological functions. Chem. Rec., 3: 172-180.
15. Cheng, C.R., Q.X. Yue, Z.Y. Wu, X.Y. Song and S.J. Tao *et al*., 2010. Cytotoxic triterpenoids from *Ganoderma lucidum*. Phytochemistry, 71: 1579-1585.
16. Fernandes, P.D.T., E. Chaquisse and J. Ferrão, 2020. HIV and the antiviral role of mushroom nutraceuticals. Eur. J Appl. Sci., 8: 64-100.
17. Min, B.S., J.J. Gao, N. Nakamura and M. Hattori, 2000. Triterpenes from the spores of *Ganoderma lucidum* and their cytotoxicity against meth-A and LLC tumor cells. Chem. Pharm. Bull., 48: 1026-1033.
18. Kimura, Y., M. Taniguchi and K. Baba, 2002. Antitumor and antimetastic effects on liver triterpenoid fractions of *Ganoderma lucidum*: Mechanism of action and isolation of an active substance. Anticancer. Res., 22: 3309-3318.
19. Mau, J.L., H.C. Lin and C.C. Chen, 2002. Antioxidant properties of several medicinal mushrooms. J. Agric. Food Chem., 50: 6072-6077.
20. Liu, X., J.P. Yuan, C.K. Chung and X.J. Chen, 2002. Antitumor activity of the sporoderm-broken germinating spores of *Ganoderma lucidum*. Cancer Lett., 182: 155-161.
21. González, A., V. Atienza, A. Montoro and J.M. Soriano, 2020. Use of *Ganoderma lucidum* (ganodermataceae, basidiomycota) as radioprotector. Nutrients, 12: 1143-1149.
22. Cheng, S. and D. Sliva, 2015. *Ganoderma lucidum* for cancer treatment: We are close but still not there. Integr. Cancer Ther., 14: 249-257.
23. Liu, Y., H. Miyoshi and M. Nakamura, 2007. Nanomedicine for drug delivery and imaging: A promising avenue for cancer therapy and diagnosis using targeted functional nanoparticles. Int. J. Cancer, 120: 2527-2537.
24. Kawasaki, E.S. and A. Player, 2005. Audrey Player. Nanotechnology, nanomedicine and the development of new, effective therapies for cancer. Nanomedicine, 1: 101-109.
25. Sohretoglu, D. and S. Huang, 2018. *Ganoderma lucidum* polysaccharides as an anti-cancer agent. Anti-Cancer Agents Med. Chem., 18: 667-674.
26. Li, N., Y.L. Hu, C.X. He, C.J. Hu, J. Zhou, G.P. Tang and J.Q. Gao, 2010. Preparation, characterisation and anti-tumour activity of *Ganoderma lucidum* polysaccharide nanoparticles. J. Pharm. Pharmacol., 62: 139-144.
27. Illum, L., 2007. Nanoparticulate systems for nasal delivery of drugs: A real improvement over simple systems? J. Pharm. Sci., 96: 473-483.

28. Amalraj, A., A. Pius, S. Gopi and S. Gopi, 2017. Biological activities of curcuminoids, other biomolecules from turmeric and their derivatives-a review. Afr. J. Traditional Compl. Alt. Med., 7: 205-233.
29. Rocha, S., R. Generalov, M. do Carmo Pereira, I. Peres, P. Juzenas and M.A.N. Coelho, 2011. Epigallocatechin gallate-loaded polysaccharide nanoparticles for prostate cancer chemoprevention. Nanomedicine, 6: 79-87.
30. Lin, Z.B., 2005. Cellular and molecular mechanisms of immuno-modulation by *Ganoderma lucidum*. J. Pharmacol. Sci., 99: 144-153.
31. Seo, D.J. and C. Choi, 2021. Antiviral bioactive compounds of mushrooms and their antiviral mechanisms: A review. Viruses, Vol. 13. 10.3390/v13020350.
32. Boh, B., 2013. *Ganoderma lucidum*: A potential for biotechnological production of anti-cancer and immunomodulatory drugs. Recent Pat. Anti-Cancer Drug Discovery, 8: 255-287.
33. Joseph, S., B. Sabulal, V. George, K.R. Antony and K.K. Janardhanan, 2011. Antitumor and anti-inflammatory activities of polysaccharides isolated from *Ganoderma lucidum*. Acta Pharm., 61: 335-342.
34. Guo, X.Y., J. Han, M. Ye, X.C. Ma, X. Shen, B.B. Xue and Q.M. Che, 2012. Identification of major compounds in rat bile after oral administration of total triterpenoids of *Ganoderma lucidum* by high-performance liquid chromatography with electrospray ionization tandem mass spectrometry J. Pharm. Biomed. Anal., 63: 29-39.