International Journal of Science and Research Archive

eISSN: 2582-8185

Cross Ref DOI: 10.30574/ijsra

Journal homepage: https://ijsra.net/

(REVIEW ARTICLE)

Check for updates

# Medicinal Benefits of *Ganoderma lucidum* (Reishi) in Cancer Treatment: A review of current evidence and future directions

Sunidhi Kachari *

*Infectious Diseases and Cancer Epidemiology, Faculty of Cancer Biology, ICMR- Regional Medical Research Centre, NE, Assam-786001, India.*

International Journal of Science and Research Archive, 2024, 13(01), 2206–2215

Publication history: Received on 12 August 2024; revised on 02 October 2024; accepted on 05 October 2024

Article DOI: https://doi.org/10.30574/ijsra.2024.13.1.1789

## Abstract

In the ancient practice of Asian medicine, *Ganoderma lucidum* popularly known as Reishi or Lingzhi, has assumed enormous respect for its potential health benefits. In the past years, however, more studies have focused on its anticancer effects specifically due to its bioactive components including triterpenes, polysaccharides, and proteins. This article reviews the properties and mechanisms of various active compounds in *G. lucidum* against cancer. Strong anticancer effects typical of triterpenes are gained by promoting cell apoptosis and suppressing tumor metastasis by ganoderic acids. Most polysaccharides enhance immune response and possess anti-tumor activity while proteins such as Ling Zhi-8 have immuno-modulatory effects. Out of the nature of research and some clinical data, most researches to date include small samples and short durations. Efforts geared towards the assessment show the need to carry out more precise thorough clinical studies in order to establish the various benefits and risks of *G. lucidum* as a cancer treatment method. At this time, it is likely that *G. lucidum* will be used to augment such treatment however there should be more fundamental evidence to support this claim towards improvement or even substitution of such therapy without compromising efficacy and safety measures of *G. lucidum.*

**Keywords:** *Ganoderma lucidum*; Reishi mushroom; Anticancer activity; Bioactive compounds; Polysaccharides; Triterpenoids; Immunomodulation

## 1. Introduction

In both China and Japan, *G. lucidum* which is commonly known as Reishi or Lingzhi, is also termed. *G. lucidum* is unique and valuable in the Ganodermataceae family which is well known as the all-healed mushroom. This wood rooting mushroom grows on dead and live woody stems and branches in humid quiet areas mostly found in subtropical and temperate forest of Asia, Europe and North and South America [1]. Broad-leafed tree species such as *Acacia, poplar, oak, Maple, Melia, Eucalyptus, Hevea, Tectona,* and *Grewia* are favored. Of the estimated more than 3 million species of fungi known to exist, only about 150,000 species have been documented, 2000 species are known to be edible, and 200 species of wild mushrooms are recognized to have therapeutic effects on the body [2]. Traditionally, it is the culinary and nutritional assessment that has dominated research focusing on mushrooms. Recently, mushrooms are becoming more and more appreciated for their positive health impacts, including but not limited to: nutritional supplements, nutraceuticals, and mycotherapy products [3]. Some common examples of medicinal mushrooms are *G. lucidum* (reishi), *Trametes versicolor* or *Coriolus versicolor* (turkey tail), *Lentinus edodes* (shiitake), *Grifola frondosa* (maitake) [4]. This mushroom has distinctive bioactive compounds consisting of polysaccharides, triterpenes, sterols, proteins and polyphenols that have antioxidant, anti-inflammatory, anti-cancer liver protecting, antidiabetic and several different properties [5]. In India, yet, the ability, capacity of the fungus is still under investigation. Triterpenes, which are present in *G. lucidum* (Reishi mushroom), are a subclass of terpenes composed of six isoprene units, forming intricate ring structures. It has multiple health benefits, comprising anti-inflammatory, antitumor, anti-HIV, and hypolipidemic

* Corresponding author: Sunidhi Kachari

activities, with significant compounds such as ganoderic acids. A long chain of monosaccharides linked by glycosidic bonds, including D-glucans, and D-glucans are known as polysaccharides. They are isolated from the fruiting bodies, spores, and mycelia of *G. lucidum* and are widely recognized for their immunomodulatory effects and anticancer activity, contributing to multiple biological functions. Sterols are lipid compounds present in *G. lucidum*, exhibit antiviral activity, and can offer protective effects against multiple diseases, comprising antihepatotoxic properties. Proteins are made up of specific polypeptides like LZ-8 found in the mycelium of *G. lucidum*. Its immunomodulatory effects of LZ-8 enhance immune responses in the body. Phenolic compounds are known for their antioxidant properties as well as their anti-inflammatory and antimicrobial activities [6].

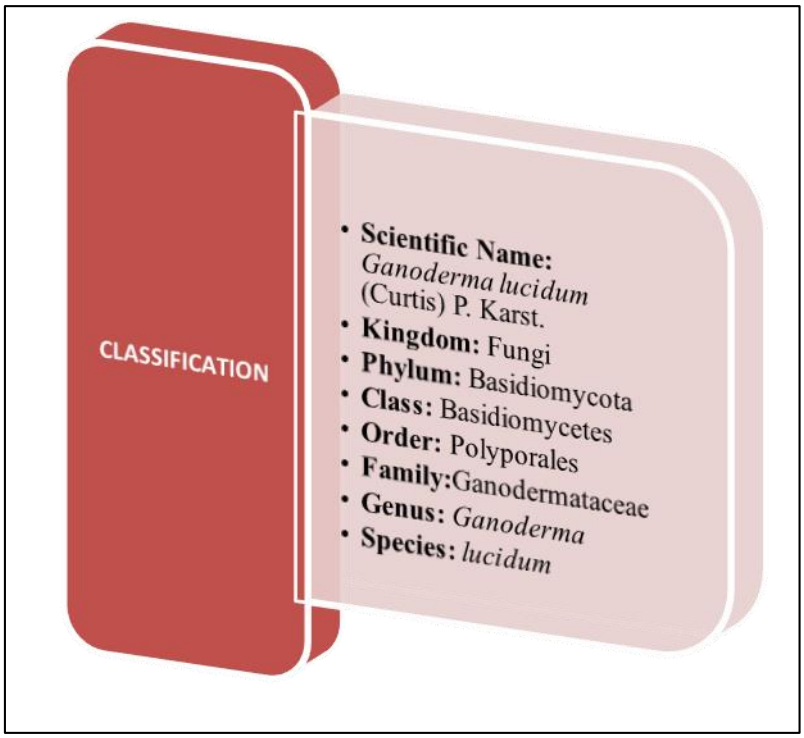


**Figure 1** Classification of *G. lucidum*

The fact that *G. lucidum* has a long history of traditional application, coupled with positive preclinical results, does not imply that its adjunctive use in chemotherapy is justified without comprehensive investigation of its therapeutic potential and safety. The objective of this review is to focus on the anticancer properties of *G. lucidum* and its active constituents, including the modes of action and the levels of clinical evidence available. The emphasis of the review is also the further investigation in order to prove these findings and fill in the gap of studies done.

## 2. Materials and Method

This review was made on scientific literature about *Ganoderma lucidum*, also called Reishi mushroom, and it was found out if it presented therapeutic value in the treatment process of cancer. For this study, different databases used for searching for literature involved PubMed, Scopus, Google Scholar, and Web of Science. The key words adopted included "*Ganoderma lucidum*," "Reishi mushroom, anticancer activity," "bioactive compounds," "polysaccharides," "triterpenoids," and "immunomodulation."

The review focused on peer-reviewed articles published in English, specifically those that explore the bioactive compounds of *G. lucidum* and their anticancer properties. Both preclinical and clinical studies were included, particularly those examining the mechanism of action, therapeutic efficacy, and safety of *G. lucidum* in cancer treatment. To ensure relevance and currency, only articles published between 1999 and 2024 were considered. Those studies were excluded wherein no experimental evidence related to the treatment of cancer was found in them.

Data relevant to this review from the selected articles involved types of cancers studied, *Ganoderma lucidum's* bioactive compounds especially examples of polysaccharides and triterpenoids, and the mechanisms in anticancer activities such

as inducing apoptosis and immunomodulation. The findings were then organized and synthesized to provide an overview of the therapeutic potential of *Ganoderma lucidum* in cancer treatment.

### 2.1. Bioactive Compounds

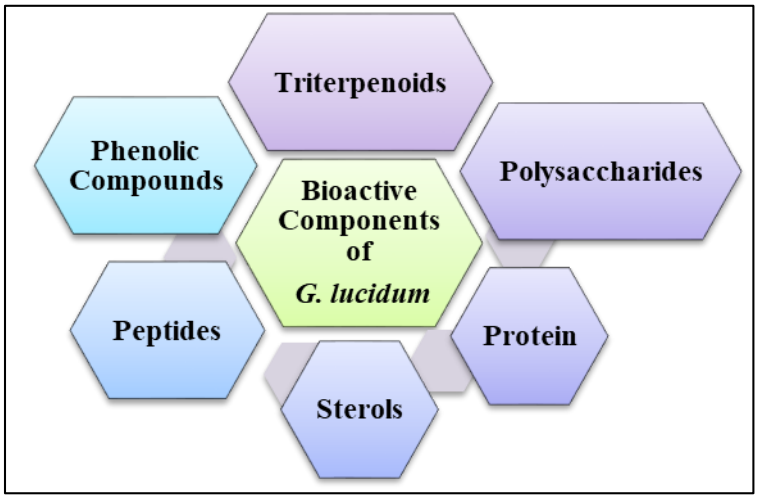


**Figure 2** Overview of key bioactive components of *G. lucidum*

There are more than 200 medicinal mushroom species among the more than 2000 classes of Reishi mushroom (*G. lucidum*), known to date, only six mushrooms are red, black, blue, white, yellow and purple Reishi. Black Reishi (*G. sinensis*) and red Reishi (*G. lucidum*) have listed the highly important health-enhancing effects. *G. lucidum* has been reported to generate miraculous health benefits and encompasses over 400 bioactive compounds, comprising triterpenoids, polysaccharides, nucleotides, sterols, steroids, fatty acids and proteins/peptides [7], which have a variety of medicinal effects such as antitumor, antimicrobial, ant atherosclerotic, anti-inflammatory, hypolipidemic, antidiabetic, antioxidative and radical scavenging [8, 9,10].

#### *2.1.1. Triterpenes:*

Triterpene is an organic compound composed of six isoprene units. Triterpene is known for its anti-inflammatory and low lipid properties, and can form a linear chain or a ring-like structure [11]. They have listed significant pharmacological activity, including cancer cell apoptosis inducers, cell cycle degradation, and antioxidant effects. Triterpenoids are a variety of bioactive compounds in *G. lucidum*, with intricate structures and important health benefits. They have an extensive range of biological effects, including an anti-inflammatory and immunomodulatory effect, and are very convenient in the handling of various health conditions. Triterpenoids, such as ganoderic acids, have illustrated cytotoxic properties against cancer cells and can boost immune functions, while suggesting the advantages of hypolipidemia, antihypertensive and hepatoprotection. With more than 150 triterpenes identified in *G. lucidum* [12], these compounds are mainly extracted primarily for therapeutic purposes in complementary and alternative medicines, emphasizing the potential for cancer treatment and general health promotion. Ganoderic acid A (GA-A) has been demonstrated to greatly reduce the feasibility of cancer cells through numerous mechanisms; facilitated by various studies, GA-A has been proven to induce apoptosis in cancer cell lines. For example, triterpenoids, including GA-A, activate inherent apoptotic pathways, leading to programmed cell death in cancer cells [13]. Research shows that GA-A can cause cell cycle arrest, notoriously in the G1/S phase, which is crucial for DNA synthesis. This effect was highlighted in studies in which GA-A inhibited cancer cell proliferation by stopping their progression through the cell cycle. GA-A has been shown to inhibit the invasion and migration. GA-A suppresses the expression of matrix metalloproteinases (MMPs), which are necessary for cancer cell invasion, thus reducing metastatic potential [14]. GA-A affects multiple signaling pathways associated with cancer progression. For example, it has been reported to prevent the NF-B pathway, which is related to inflammation and cancer cell survival, consequently contributing to its anti-cancer effects [15]. The antioxidant properties of GA-A help alleviate oxidative stress, which can lead to DNA damage and promote cancer cell survival. This was mentioned in studies that highlighted the function of GA-A in mitigating oxidative stress in cancer cells [16].

#### *2.1.2. Polysaccharides:*

Polysaccharides in *Ganoderma lucidum* are complex carbohydrates that play an important role in its medicinal properties. More than 200 different polysaccharides are isolated from *Ganoderma lucidum*. The major is classified into

two main categories that are lucans and heteropolysaccharides. The bioactive classes, which are known in particular for cancer prevention and immune enhancement, include β-1,3 and β-1,6-D- glucans [17]. The structural variability of *G. lucidum* polysaccharides is critical for their biological activity, particularly their antitumorigenic properties and immune response. The molecular weight of the *G. lucidum* polysaccharide ranges from 4 × 10^5 to 1 × 10^6 Daltons [18]. Molecular weight, degree of branching, and solubility in water are key features that impact their functionality. For example, higher molecular weight polysaccharides tend to show stronger biological activities, including enhanced immune responses and antioxidant effects [19]. Polysaccharides of *G. lucidum* have been shown to scavenge free radicals and alleviate oxidative stress. This activity is attributed to their capacity to enhance the activity of antioxidant enzymes such as superoxide dismutase and catalase, which help protect cells from oxidative damage [20].

Research indicates that *G. lucidum* polysaccharides can regulate the maturation and function of dendritic cells, which are essential for initiating immune responses. They also have a regulatory effect on cytotoxic T lymphocytes, enhancing their ability to target and destroy cancer cells [21].

#### *2.1.3. Protein*

The protein content in this mushroom has a wide range, while in some other species it contains more than 20% proteins [22]. Fungal immunomodulatory protein (FIP) is involved in innate immunity and can activate the expression of gene coding for proteins related to the immune response [23]. Some proteins have a cytotoxic characteristic against cancer. Lectin in *G. lucidum* is a type of glycoprotein that binds with carbohydrate on the surface of the cell, it can activate the immune system and shows a chemo preventive effect against cancer [24,25]. Ling Zhi-8, is a protein that can exhibit anti-diabetic activities by modulating the immune response and decrease the plasma glucose concentration [26,27].

#### *2.1.4. Sterol*

Sterols are 20 types, ergosterol is commonly found in fungi. It plays an important role in the maintenance of the structure and function of cells. When exposed to UV radiation, ergosterol undergoes photolysis and produces vitamin D2. It has been shown to be cytotoxic to particular cancer cells, such as acute promyelocytic leukemia and liver cancer cells, as well as having some antibacterial action against some bacteria and fungus [28,29]. Some sterols found in *G. lucidum* have antiviral properties against viruses such as the Epstein-Barr virus. Sterols in *G. lucidum* have been associated with a variety of pharmacological actions, including anti-HIV-1 and anti-aging properties, as well as neuroprotective benefits against hypoxia or reoxygenation damage [30].

#### *2.1.5. Peptides*

*G. lucidum* contains a range of peptides, such as polysaccharide peptides, that are well known for their biological effects. Peptide can be generated from the polysaccharides present in the mushroom [31]. Polysaccharide peptides have been shown to boost immune reactions. These substances may enhance the activation of genes linked to the immune system's response and encourage the growth of immune cells, such as macrophages. Certain peptides have shown cytotoxic properties against cancer cells and can prevent the growth of tumor cells. They might also improve the function of immune cells that attack tumors [32].

### 2.2. Phenolic Compounds

The phenolic compounds found in *Ganoderma lucidum* possess powerful antioxidant properties such as restraining free radicals [33], controlling peroxide decomposition [34], removing reactive oxygen species, and obstructing the activity of metals that accelerate oxidation reactions [35]. These compounds prevent mutations in cellular DNA and decrease carcinogenesis processes [36]. The main phenolic compounds found in mushrooms are gallic, caffeic, and p-coumaric acids, along with various others [37]. Furthermore, phenolic compounds exhibit various advantageous effects on the human body, such as anticancer, antioxidant, hypoglycemic qualities, and the capacity to decelerate aging mechanisms.

The presence of p-coumaric acid, a hydroxycinnamic acid and one of the phenolic compounds that has been identified in various studies, was also detected. They are said to have antioxidant properties which, of course, improve and enhance the general health benefits of the mushroom. Studies have shown that p-coumaric acid also contributes to the antimicrobial and anti-inflammatory properties of the species, along with other phenolic acids [38]. Similarly, the composition of *G. lucidum* extracts significantly differs according to varied extraction method and conditions, especially regarding the p-coumaric acid content in this compound.

Another phenolic compound polyphenols in *G. lucidum* are gallic acid. This is reported to hold potent antioxidant, antibacterial and anticancer activities. The presence of the main active ingredient residing in *G. lucidum* extracts were mentioned aside the gallic acid concentrations that varied, reporting for example 1103 μg/g in few instances.

**Table 1** The bioactive components of *Ganoderma lucidum* and their therapeutic mechanisms

| Bioactive components | Specific compounds | Parts of mushroom that is used to extract | Extraction method | Anti-cancer mechanisms | Key effects | References |
|---|---|---|---|---|---|---|
| Triterpenoids | Ganoderic acid T, ganoderic acid Me, lucidone | Fruiting body and spores | Supercritical CO2 extraction, Ethanol extraction | Antimetastatic, activate apoptosis, blocks angiogenesis | Cytoxicity, anti-angiogenesis, anti-metastatis | [39,40,41] |
| Polysaccharides | β-D-Glucan, Ganoderan A, B | Fruiting body and mycelium | Ethanol precipitation, hot water extraction | Boost immune system, activate apoptosis and NK cells | Tumor suppression, immune modulation | [42,43] |
| Protein | LZ-8 (Ling Zhi-8) | mycelium | Ammonium sulfate precipitation, Ion-exchange chromatography | Boost immune system, anti-metastatic | Reduces metastatis, regulate immune system | [44,45] |
| Sterols | Ergosterol peroxide | Fruiting body | Organic solvent extraction (Hexane Methanol,) | Supress tumor growth, induces cell cycle arrest | Tumor growth suppression, anti-proliferative | [46,47] |
| Peptides | *Ganoderma* peptide | Fruiting body | Gel filtration chromatography Ammonium sulfate precipitation, | Induces cancer cell death, antimicrobial activity | Apoptosis induction, antimicrobial | [48] |
| Phenolic Compounds | p-Coumaric acid, Gallic acid | Fruiting body and spores | Solvent partitioning, Ethanol extraction | Prevent oxidative stress, activate apoptosis | Antiproliferate, pro-apoptotic, antioxidant | [49,50] |

### 2.3. Mechanisms of action

*G. lucidum* enhances the immune response against cancer by inducing a self-triggered immune response and increasing the activity of natural killer cells. Specifically, *G. lucidum* has been shown to alter cell immunophenotypic expression and enhance the cytotoxicity of CD56 and NK cells, which plays a crucial role in the targeting and destroying cancer cells [51]. Furthermore, the general effects of *G. lucidum* for instance, antioxidant properties and the rest, work to help the body during treatment of cancer to boost the immune system [52]. *G. lucidum* promotes programmed cell death (apoptosis) in cancer cells through various mechanisms. For example, lucidenic acid B is capable of performing an apoptotic reaction in leukaemia cells by down-regulation of the Bcl-2 protein and through caspases-9 and 3, which are a fundamental protein in the apoptotic process [53]. Additionally, *G. lucidum* non-triol is recorded to work in invasive and metastatic breast cancer cell lines by inhibiting protein molecules in cell cycle regulation leading to a process referred to as apoptosis [54]. Altogether, the bioactive compounds of *G. lucidum* contribute to the apoptotic pathways of cancer cells, which result in the execution of program cell death. It plays a role in inhibiting the formation of new blood vessels (angiogenesis) in tumors through its bioactive compounds. For example, ganoderic acids have been found to induce apoptosis and prevent angiogenesis in cancer cells by regulating scores of signaling pathways, such as the inhibition of matrix metalloproteinases (MMPs) and other factors involved in angiogenesis [55]. Furthermore, research shows that certain compounds from *G. lucidum* can reduce the expression of pro-angiogenic factors, thus contributing to the inhibition of tumor vascularization [56].

*G. lucidum* exhibits anti-inflammatory effects by modulating various inflammatory pathways, which can contribute to its overall health benefits. Additionally, its antiproliferative effects are primarily attributed to its bioactive compounds, such as triterpenes and polysaccharides, which inhibit cancer cell proliferation mechanisms that include modulation of cell cycle regulatory proteins and induction of apoptosis [57].

These findings highlight the potential of *G. lucidum* as a therapeutic agent in cancer treatment and its protective effects against chemotherapy-induced toxicity:

*G. lucidum* shows anticancer effects, inhibiting the growth of different tumor cells in mice such as S180, Heps, and EAC tumor cells [58]. Studies indicate that *G. lucidum* can enhance the activities of antioxidant enzymes and reduce inflammatory cytokines such as IL-1b, IL-6, and TNF-α in cancer models [59]. It also promotes the proliferation of immune cells and the production of cytokines that inhibit tumor growth [60]. *G. lucidum* has been used in combination with chemotherapy drugs, such as cisplatin, to reduce side effects and enhance therapeutic efficacy [61]. Preliminary analyses suggest that there are generally no serious side effects associated with the use of *G. lucidum,* indicating a favorable safety profile in the studies reviewed. Research involving cisplatin-induced nephrotoxicity, *G. lucidum* extracts markedly reduced serum creatinine and urea levels, restoring renal antioxidant defense systems [62]. Some clinical evidence from human studies on *G. lucidum* indicates that:

Some human studies suggest that the antitumor effects of *G. lucidum* may be mediated through the immune system. However, it is important to note that all these studies were conducted by the same research group, and other direct antitumor effects of *G. lucidum* have not yet been studied in humans in vivo [63]. Clinical trials involving *G. lucidum* preparations have reported successful outcomes. However, the validity of these results is undermined by several factors, including small sample sizes, lack of placebo control groups, and insufficient information regarding long-term treatment effects, demographics (age and gender), and side effects [64]. The findings highlight the needs for systematic translational research programs that utilize standardized, preclinically evaluated, and biologically active *G. lucidum* extracts in clinical treatments. This would improve scientific rigor and reproducibility of future studies [65].

In summary, while there is some evidence supporting the antitumor potential of *G. lucidum* in humans, current studies have limitations that require further research to validate these findings.

### 2.4. Safety and Toxicity

The known safety and toxicity data for *G.lucidum* indicate that this mushroom is considered to have low toxicity and is widely used as an anticancer immunotherapy agent. However, patients should be monitored for possible side effects, which may include liver toxicity and chronic watery diarrhea. Some studies have reported that this may exhibit toxicity in vitro [66], and treatment with powdered *G. lucidum* spores has been associated with hepatotoxic effects. More comprehensive studies to better understand the safety and potential toxicity of *G. lucidum* in humans, as current data is insufficient.

In summary, while the fruiting body of *G. lucidum* is tough and rigid in general it is not considered safe to consume, meanwhile it is a highly valued medicinal mushroom [67]. There are concerns about specific side effects and the need for further investigation of its safety profile.

There is a strong emphasis on the need for systematic translational research programmed that utilizes standardized, preclinically evaluated, and biologically active *G. lucidum* extracts in clinical treatments to improve scientific rigor and reproducibility. Most clinical trials involving preparation for *G. lucidum have* reported successful outcomes; however, factors such as small sample sizes, lack of placebo control groups, and insufficient information on long-term treatment effects undermine the validity of these results. More studies on the isolated compounds of *G. lucidum* compounds, focusing on specific components of bioactive compounds to determine their exact amounts for further clinical studies. Although *G. lucidum* has potential health benefits, it should not be used as first-line therapy for cancer, indicating the need for caution in its clinical application.

### 2.5. Research Gaps and Future Directions

Most of the clinical investigation of *G. lucidum* are conducted by the same research group and are immune-mediated; therefore, there are limited studies examining the direct antitumor effects of *G. lucidum* on humans in vivo. In this regard, more home clinical studies should be conducted on the direct antitumor actions of *G. lucidum* in patients, as now most studies are concentrating mainly on immune-mediated actions. Many clinical parties have shown successful results, but lack of little detail or follow-up on the long-term effects of *G. lucidum* treatments places a limitation on the results. Most current evidence base clinical practice does not encompass this important follow-up period because it is

not based on evidence. A more conclusive study must be performed that evaluates the long-term effects of *G. lucidum* to support the use or otherwise of *G. lucidum* treatments. More studies on the bioactive compounds of *G. lucidum* are needed to identify the active compounds and the precise amount thereof for clinical trials. In spite of such promising results, further research is needed with regard to active drugs for better more clinical indications for the use of the components of *G. lucidum*. There is a need for more in-depth studies on the safety and efficacy of the preparation of *G. lucidum* in human patients as data available today are inadequate. More studies are needed to evaluate the safety of *G. lucidum* preparations in human subjects to achieve biological action in achieving successful clinical results. More extensive studies are required to assess the safety and potential toxicity of *G. lucidum* in humans, as current data is insufficient. These areas highlight the need for further research to validate the therapeutic potential and safety profile of *G. lucidum.*

## 3. Conclusions

*Ganoderma lucidum*, rich in a plethora of bioactive agents, has great prospects of being used as complementary therapy alongside cancer treatment. These compounds such as triterpenes, polysaccharides and proteins offer various benefits such as enhancing immunity, inducing apoptosis and inhibiting cancer cell proliferation. However, the available evidence from clinical studies can certainly be considered preliminary, as investigation into this area is usually plagued by small population size and other restrictive elements. Even if these conclusions were to be proved although authors of the review stress the need for more extensive and controlled clinical studies in order to test such claims in reality, *G. lucidum* cannot be relieved from the supplementary role in cancer treatment without adequate proof. Additional studies would be necessary in order to change that perception and to find how it could best be integrated in the management of cancer.

## Compliance with ethical standards

### *Acknowledgment*

The author thanks Indian Council of Medical Research Regional Medical Research Centre Northeast, Dibrugarh, Assam, for the provision of resources and material that played a vital role in the development of this study.

### *Disclosure of conflict of interest*

The author declares that there is no conflict of interest in this study. The author has no financial and/or personal relationship that may cause direct conflict of interest with the following outcome of this research.

## References

[1] Dinesh Babu PD, Subhasree RS. The sacred mushroom "Reishi"—a review. Am Eurasian J Bot. 2008, 1:107-10.

[2] Beulah H, Margret AA, Nelson J. Marvelous medicinal mushrooms. Int J Pharma Bio Sci. 2013, 3:611-15.

[3] Wasser SP. Medicinal mushroom science: current perspectives, advances, evidences, and challenges. Biomed J. 2014, 37:345-56. doi: 10.4103/2319-4170.138318.

[4] Integrative P. Medicinal mushrooms (PDQ®): health professional version. 2002. Available online: https://pubmed.ncbi.nlm.nih.gov/27929633/

[5] Swallah M, Bondzie-Quaye P, Wu Y, Acheampong A, Sossah F, Elsherbiny S, Huang Q. Therapeutic potential and nutritional significance of Ganoderma lucidum: a comprehensive review from 2010 to 2022. Food Funct. 2023. https://doi.org/10.1039/d2fo01683d

[6] Łysakowska P, Sobota A, Wirkijowska A. Medicinal mushrooms: their bioactive components, nutritional value and application in functional food production—a review. Molecules. 2023. https://doi.org/10.3390/molecules28145393

[7] Sanodiya BS, Thakur GS, Baghel RK, Prasad GBKS, Bisen PS. Ganoderma lucidum: a potent pharmacological macrofungus. Curr Pharm Biotechnol. 2009, 10:717-42.

[8] Batra P, Sharma AK, Khajuria R. Probing Lingzhi or Reishi medicinal mushroom *Ganoderma lucidum* (Higher Basidiomycetes): a bitter mushroom with amazing health benefits. Int J Med Mushrooms. 2013, 15:127-43.

[9] 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.

[10] Karwa AS, Rai MK. Naturally occurring medicinal mushroom-derived antimicrobials: a case study using Lingzhi or Reishi *Ganoderma lucidum* (W. Curt.) P. Karst. (Higher Basidiomycetes). Int J Med Mushrooms. 2012, 14:481-90.

[11] Srivastav AK, Das P. Phytochemical extraction and characterization of *Acorus calamus, Moringa oleifera, Cucurbita maxima, Hibiscus rosa-sinensis,* and *Chrysanthemum leucanthemum* for their antibacterial and antioxidant activity. Int J Pharmaceut Res Bio-Sci. 2015, 4(3):356-77.

[12] Yue QX, Song XY, Ma C, Feng LX, Guan SH, Wu WY, et al. Effects of triterpenes from *Ganoderma lucidum* on protein expression profile of HeLa cells. Phytomedicine. 2010, 17:606-13.

[13] Liu J, Kurashiki K, Shimizu K, Kondo R. 5α-Reductase inhibitory effect of triterpenoids isolated from *Ganoderma lucidum*. Biol Pharm Bull. 2006, 29:392-5.

[14] Chen NH, Liu JW, Zhong JJ. Ganoderic acid T inhibits tumor invasion in vitro and in vivo through inhibition of MMP expression. Pharmacol Rep. 2010, 62:150-63.

[15] Li F, Wang Y, Wang X, Li J, Cui H, Niu M. Ganoderic acids suppress growth and angiogenesis by modulating the NF-κB signaling pathway in breast cancer cells. Int J Clin Pharmacol Ther. 2012, 50:712-21.

[16] Zhu M, Chang Q, Wong LK, Chong FS, Li RC. Triterpene antioxidants from *Ganoderma lucidum.* Phytother Res. 1999, 13:529-31.

[17] 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.

[18] Kumar A. *Ganoderma lucidum*: a traditional Chinese medicine used for curing tumors. Int J Pharm Pharm Sci. 2021, 1–13. doi: 10.22159/ijpps.2021v13i3.40614.

[19] Cör D, Knez Ž, Hrnčič MK. Antitumour, antimicrobial, antioxidant and antiacetylcholinesterase effect of *Ganoderma lucidum* terpenoids and polysaccharides: a review. Molecules. 2018, 23(3):649. doi: 10.3390/molecules23030649.

[20] Cherian E, Sudheesh NP, Janardhanan KK, Patani G. Free radical scavenging and mitochondrial antioxidant activities of Reishi—*Ganoderma lucidum*. J Basic Clin Physiol Pharmacol. 2011, 20:289-308.

[21] Ahmad MF, Alsayegh AA, Ahmad FA, Akhtar MS, Alavudeen SS, Bantun F, et al. *Ganoderma lucidum*: insight into antimicrobial and antioxidant properties with development of secondary metabolites. Heliyon. 2024, 10(3) . doi: 10.1016/j.heliyon.2024.e25607.

[22] Chaturvedi VK, Agarwal S, Gupta KK, Ramteke PW, Singh MP. Medicinal mushroom: boon for therapeutic applications. 3 Biotech. 2018, 8:334.

[23] Venturella G, Ferraro V, Cirlincione F, Gargano ML. Medicinal mushrooms: bioactive compounds, use, and clinical trials. Int J Mol Sci. 2021, 22(2):634. doi: 10.3390/ijms22020634.

[24] El-Maradny YA, El-Fakharany EM, Abu-Serie MM, Hashish MH, Selim HS. Lectins purified from medicinal and edible mushrooms: insights into their antiviral activity against pathogenic viruses. Int J Biol Macromol. 2021, 179:239-58.

[25] Singh RS, Kaur Preet H, Kanwar JR. Mushroom lectins as promising anticancer substances. Curr Protein Pept Sci. 2016, 17:797-807.

[26] Sirisidthi K, Kosai P, Jiraungkoorskul W. Antidiabetic activity of the lingzhi or reishi medicinal mushroom Ganoderma lucidum. SA Pharm J. 2016, 83:45-7. Available from: https://hdl.handle.net/10520/EJC196849.

[27] World Health Organization (WHO). Diabetes. 2020. Available from: https://www.who.int/healthtopics/diabetes#tab=tab_1. Accessed 2022 Oct 12.

[28] Urbain P, Singler F, Ihorst G, Biesalski HK, Bertz H. Bioavailability of vitamin D2 from UV-B-irradiated button mushrooms in healthy adults deficient in serum 25-hydroxyvitamin D: a randomized controlled trial. Eur J Clin Nutr. 2011, 65:965-71.

[29] Zheng J, Wang Y, Wang J, Liu P, Li J, Zhu W. Antimicrobial ergosteroids and pyrrole derivatives from halotolerant Aspergillus flocculosus PT05-1 cultured in a hypersaline medium. Extremophiles. 2013, 17:963-71.

[30] Yang Y, Zhang H, Zuo J. Advances in research on the active constituents and physiological effects of Ganoderma lucidum. Biomed Dermatol. 2019, 3:6.

[31] Wang J, Cao B, Zhao H, Feng J. Emerging roles of Ganoderma lucidum in anti-aging. Aging Dis. 2017, 8:691-707.

[32] Sun Y, Hu X, Li W. Antioxidant, antitumor, and immunostimulatory activities of the polypeptide from Pleurotus eryngii mycelium. Int J Biol Macromol. 2017, 97:323-30.

[33] Das AK, Nanda PK, Dandapat P, Bandyopadhyay S, Gullón P, Sivaraman GK, et al. Edible mushrooms as functional ingredients for development of healthier and more sustainable muscle foods: a flexitarian approach. Molecules. 2021, 26:2463.

[34] Podkowa A, Kryczyk-Poprawa A, Opoka W, Kozarski M, Wróbel MS. Culinary medicinal mushrooms: a review of organic compounds and bioelements with antioxidant activity. Eur Food Res Technol. 2021, 247:513-33.

[35] Ma G, Yang W, Zhao L, Pei F, Fang D, Hu Q. A critical review on the health promoting effects of mushroom nutraceuticals. Food Sci Hum Wellness. 2018, 7:125-33.

[36] Taşkin H, Süfer Ö, Attar SH, Kılıç Ö, Güzel M, Atakol O. Total phenolics, antioxidant activities, and fatty acid profiles of six Morchella species. J Food Sci Technol. 2021, 58:692-700.

[37] Sharpe E, et al. Comparison of antioxidant activity and extraction techniques for commercially and laboratory prepared extracts from six mushroom species. J Agric Food Res. 2021, 4:100130.

[38] Masjedi M, Nateghi L, Berenjy S, Eshaghi M. Chemical methodologies determination of antioxidant and antimicrobial compounds of Ganoderma lucidum extract in laboratory different conditions. [Internet]. 2022. Available from: https://doi.org/10.22034/chemm.2022.316157.1398.

[39] Chen S. The pharmacological effects of triterpenoids from Ganoderma lucidum and the regulation of its biosynthesis. Adv Biol Chem. 2020, 10(02):55-65. doi: 10.4236/abc.2020.102005.

[40] Kimura Y, et al. Anti-angiogenic and anti-metastatic effects of Ganoderic acid T. Biol Pharm Bull. 2002.

[41] Su CH, et al. Ganoderma lucidum triterpenoids reduce invasiveness of breast cancer cells by inhibiting MMP expression and activity. Integr Cancer Ther. 2011.

[42] Ooi VEC, Liu F. Immunomodulation and anticancer activity of polysaccharide-protein complexes. Curr Med Chem. 2000.

[43] Wasser SP. Reishi or Ling Zhi (*Ganoderma lucidum*): biomolecular and clinical aspects. Adv Food Nutr Res. 2005.

[44] Zhang HN, et al. Ling Zhi-8: a novel immunomodulatory protein from *Ganoderma lucidum.* J Biol Chem. 1999.

[45] Hsu HY, et al. *Ganoderma lucidum:* promising anti-cancer agent with multiple mechanisms. Anti-Cancer Agents Med Chem. 2011.

[46] Yuen JW, Gohel MD. Anti-cancer effects of *Ganoderma lucidum*: a review. Int J Med Mushrooms. 2005.

[47] Zhang W, et al. Ergosterol peroxide from medicinal fungus: anti-inflammatory and anticancer activity. Bioorg Med Chem Lett. 2006.

[48] Cheng CR, Leung AY. Ganodermin, a novel antifungal protein from *Ganoderma lucidum.* Int J Med Mushrooms. 2008.

[49] Zaidman BZ, et al. Medicinal properties of the mushroom *Ganoderma lucidum*. Food Rev Int. 2005.

[50] Xu Z, et al. Lectins from medicinal fungi and their therapeutic potentials. Evid Based Complement Alternat Med. 2011.

[51] Chien CM, Cheng JL, Chang WT, Tien MH, Tsao CM, Chang YH, et al. Polysaccharides of *Ganoderma lucidum* alter cell immunophenotypic expression and enhance CD56+ NK-cell cytotoxicity in cord blood. Bioorg Med Chem. 04, 12:5603-9.

[52] Reishi/Ling Zhi—The mushroom of immortality. Available from: https://www.chinesemedicineliving.com/eastern-philosophy/reishi-ling-zhi-the-mushroom-of-immortality/. Accessed 2017 Sep 25.

[53] Hsu CL, Yu YS, Yen GC. Lucidenic acid B induces apoptosis in human leukemia cells via a mitochondria-mediated pathway. J Agric Food Chem. 2008, 56:3973-80.

[54] Jiang J, Jedinak A, Sliva D. Ganodermanontriol (GDNT) exerts its effect on growth and invasiveness of breast cancer cells through the down-regulation of CDC20 and uPA. Biochem Biophys Res Commun. 2011, 415:325-9.

[55] Xu K, Liang X, Gao F, Zhong J, Liu J. Antimetastatic effect of ganoderic acid T in vitro through inhibition of cancer cell invasion. Process Biochem. 2010, 45:1261-7.

[56] Chen NH, Liu JW, Zhong JJ. Ganoderic acid T inhibits tumor invasion in vitro and in vivo through inhibition of MMP expression. Pharmacol Rep. 2010, 62:150-63.

[57] Cör D, Knez E, Hrnčič MK. Antitumour, antimicrobial, antioxidant, and antiacetylcholinesterase effect of *Ganoderma lucidum* terpenoids and polysaccharides: a review. Molecules. 2018, 23(3):649. doi: 10.3390/molecules23030649.

[58] Pang X, Chen Z, Gao X, Liu W, Slavin M, Yao W, et al. Potential of a novel polysaccharide preparation (GLPP) from Anhui-grown *Ganoderma lucidum* in tumor treatment and immunostimulation. J Food Sci. 2007, 72 doi: 10.1111/j.1750-3841.2007.00431.x.

[59] Chen XP, Chen Y, Li SB, Chen YG, Lan JY, Liu LP. 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. doi: 10.1016/j.carbpol.2009.01.009.

[60] Wang PY, Zhu XL, Lin ZB. Antitumor and immunomodulatory effects of polysaccharides from broken-spore of *Ganoderma lucidum*. Front Pharmacol. 2012, 3:135. doi: 10.3389/fphar.2012.00135.

[61] Cao Y, Xu X, Liu S, Huang L, Gu J, Zhang R. *Ganoderma:* a cancer immunotherapy review. Front Pharmacol. 2018, 9:1217. doi: 10.3389/fphar.2018.01217.

[62] Kaushal S, Kumar SA, Priyanka D. Anti-cancer properties of *Ganoderma lucidum's* active constituents and pathways. Int J Zool Investig. 2023, 9(2):524-533. doi: 10.33745/ijzi.2023.v09i02.060.

[63] Wachtel-Galor S, Yuen J, Buswell JA, Benzie IFF. *Ganoderma lucidum* (Lingzhi or Reishi): a medicinal mushroom. In: Benzie IFF, Wachtel-Galor S, editors. Herbal Medicine. 2nd ed. Boca Raton (FL): CRC Press/Taylor & Francis, 2011. p. 53. ISBN 978-1-4398-0713-2.

[64] Hapuarachchi KK, Wen TC, Jeewon R, Wu XL, Kang JC. *Ganoderma lucidum*–are the beneficial medical properties substantiated? Mycosphere. 2016, 7(6):687-715.

[65] Bulam S, Üstün NU, Pekşen A. Health benefits of *Ganoderma lucidum* as a medicinal mushroom. Turk J Agric Food Sci Technol. 2019, 7:84-93. doi: 10.24925/turjaf.v7isp1.84-93.2728.

[66] Wanmuang H, Leopairut J, Kositchaiwat C, Wananukul W, Bunyaratvej S. Fatal fulminant hepatitis associated with *Ganoderma lucidum* (Lingzhi) mushroom powder. J Med Assoc Thai. 2007, 90:179.

[67] Ekiz E, Oz E, El-Aty AA, Proestos C, Brennan C, Zeng M, et al. Exploring the potential medicinal benefits of *Ganoderma lucidum*: from metabolic disorders to coronavirus infections. Foods. 2023;12(7):1512. doi: 10.3390/foods12071512.