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ISNI: 0000 0004 8495 2390

Dolna 17, Warsaw,
Poland 00-773
+48 226 0 227 03
editorial_office@rsglobal.pl

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EXPLORING THE THERAPEUTIC POTENTIAL OF THE MEDICINAL MUSHROOM GANODERMA LUCIDUM (REISHI) - A LITERATURE REVIEW

Barbara Ponitka *(Corresponding Author, Email: basiaponitka@gmail.com)*
Lower Silesian Oncology Center, Wroclaw, Poland
ORCID ID: 0009-0000-9077-9123

Marta Danuta Cendrowska
National Medical Institute of the Ministry of the Interior and Administration, Warsaw, Poland
ORCID ID: 0009-0008-0534-5995

Justyna Berent
District Hospital in Garwolin, Garwolin, Poland
ORCID ID: 0009-0009-7378-556X

Łukasz Brzost
District Hospital in Garwolin, Garwolin, Poland
ORCID ID: 0009-0003-4119-6679

Karolina Stępień
Private Practice, Warsaw, Poland
ORCID ID: 0009-0002-6812-5662

Beata Choromańska
Mazovian Brodnowski Hospital, Warsaw, Poland
ORCID ID: 0009-0009-1771-4265

Paulina Rzepa
Provincial Integrated Hospital in Elbląg, Elbląg, Poland
ORCID ID: 0009-0005-4497-0230

Julia Procyk
University Clinical Hospital in Wrocław, Wroclaw, Poland
ORCID ID: 0009-0009-7271-7047

Aleksandra Klukowska
Military Institute of Medicine, Warsaw, Poland
ORCID ID: 0009-0001-0064-3829

Julia Maszewska
Lower Silesian Oncology Center, Wroclaw, Poland
ORCID ID: 0009-0007-0788-9470

Wiktoria Szumlińska
National Medical Institute of the Ministry of the Interior and Administration, Warsaw, Poland
ORCID ID: 0009-0001-5286-4228

Szymon Milnerowicz
Lower Silesian Oncology Center, Wroclaw, Poland
ORCID ID: 0009-0004-5718-2367

ABSTRACT

Introduction: Ganoderma lucidum, also known as Reishi, is a medicinal mushroom that has been used for centuries in traditional Asian medicine for its diverse health-promoting properties. Rich in bioactive compounds such as polysaccharides and triterpenoids, G.lucidum exerts various effects such as modulating oxidative stress, inflammation and immune response.
Materials and methods: A systematic search of PubMed and Google Scholar was conducted, using key words and phrases such as "Ganoderma lucidum", "Reishi", "properties", "anticancer", and "metabolic health". A total of 22 high-quality, recent studies relevant to this review were selected for inclusion.
Results: This review summarizes evidence on the mushroom's hepatoprotective, neuroprotective, antitumor, cardioprotective, and metabolic effects. Findings from both in vitro and in vivo studies point to its promising role in battling hepatopathies, neurodegenerative disorders, various types of cancer, and metabolic disorders such as dyslipidemia and hypoglycemia.
Conclusion: While favorable data from preclinical studies exists, there remains limited data from clinical trials. This review highlights the need for large-scale well-controlled clinical trials to be conducted in order to establish G. lucidum's efficacy, safety, dosing standards, and potential drug interactions.

KEYWORDS

Ganoderma Lucidum, Reishi, Neuroprotective, Metabolic Health, Anticancer, Cardiovascular Disease, Hepatoprotective

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1. Introduction

Ganoderma lucidum is a species of mushroom that has been used for its health-promoting properties in traditional Chinese medicine for centuries (Seweryn et al., 2021). It is known by different names across various countries and cultures: in Japan it is being referred to as "Reishi" which means "spiritual potency", in China its name is "Lingzhi" which translates to "divine mushroom", while in Korea it is called "Youngzhi" meaning "mushroom of mortality" (Ekiz et al., 2023). In nature, it can be found in the subtropical and temperate climate zones, growing mainly in the forests of Asia, Europe, and North and South America (Cör et al., 2018).

Around 400 bioactive compounds have been found in different parts (fruting body, mycelia and spores) of *G. lucidum*, including polyphenols, polysaccharides, steroids, triterpenoids, nucleotides, amino acids, minerals and vitamins. Yet, the principal bioactive constituents responsible for the mushroom's beneficial effects are polysaccharides and triterpenoids (Ahmad et al., 2021).

To date, numerous in vitro and in vivo studies have examined Reishi's medicinal properties, pointing to its anti-tumor, anti-microbial, anti-atherosclerotic, anti-inflammatory, antioxidant and neuroprotective properties (Cör et al., 2018; Cör Andrejč et al., 2022).

This paper aims to synthesize the current evidence surrounding the multifaceted effects of Resihi, with a focus on its neuroprotective, hepatoprotective, anti-cancer, pro-metabolic and cardioprotective effects. The study also underscores the gaps of knowledge concerning Reishi's possible interactions with other drugs and the sparsity of large-scale double-blind clinical trials on its potential use among patients with various diseases.

2. Methodology

This comprehensive review assessed the broad therapeutic properties of the medicinal mushroom *Ganoderma lucidum*, focusing on its effects on neurological, cardiovascular, and metabolic health and its possible application in treating hepatopathies and various types of cancer. A systemic research was conducted across PubMed and Google Scholar databases, including relevant papers published after the year 2020. Following the application of the criteria, 22 recent studies have been selected for inclusion.

3. Results

3.1 Hepatoprotective properties of *Ganoderma lucidum*

The bioactive constituents of *Ganoderma lucidum* such as triterpenoids and polyglucans exhibit a plethora of hepatoprotective effects. It has been shown that they impact various chronic hepatopathies, including alcohol liver disease, NAFLD, fibrosis, viral hepatitis and hepatic cancer (Ahmad et al., 2023).

The mechanisms of *G. lucidum*'s hepatoprotective influence remain yet to be fully defined, yet studies show a variety of potential beneficial effects.

Studies show that GLE (*G. lucidum* extract) proves to have preventive and therapeutic properties in rats with formaldehyde-induced fibrosis. The mushroom's effectiveness was measured by assessing the levels of AST, ALP and ALT, whose high levels contribute to liver fibrosis. After treatment with *G.lucidum*, the levels of these hepatic enzymes in rats with FA-induced liver fibrosis were significantly lower.

The pathogenesis of liver fibrosis also shows a crucial role of pro-inflammatory cytokines such as IL-1, IL-6 and TNF. Among rats with FA-induced fibrosis, levels of these cytokines in the animals' livers rose significantly. However, the group that received 100mg/kg of *G.lucidum* had lower cytokine levels compared to the control group. These findings collectively suggest that *G.lucidum* may prove to be a potent anifibrotic agent, helping prevent and treat liver fibrosis.

Further evidence shows that *G.lucidum* prevents one of primary causes of ethanol-induced liver fibrosis - free radical-induced lipid peroxidation. In a study on ICR mice *G. lucidum* averted ethanol-induced lipid peroxidation by 95% in a dose-dependent way (Pen et al., 2023).

Finally, it has been established that ganoderic acids (GAs) from *G. lucidum* may play a role in suppressing the replication of HBV virus, a dangerous agent causing liver inflammation and dysfunction. Administration of GA from *G.lucidum* at a concentration of 8mcg/mL inhibited the replication of HBV in HepG2215 cells for eight days (Ahmad et al., 2023).

3.2 G. lucidum and neurodegenerative diseases

Neurodegenerative diseases (NDDs) are a group of neurological disorders characterized by progressive irreversible damage to neurons in the central or peripheral nervous system. Among the various mechanisms leading to the onset of NDDs lie neuroinflammation, oxidative stress, accumulation of pathogenic proteins, abnormal mitochondrial function and many others. Potent bioactive compounds found in *G. lucidum* including triterpenoids, polysaccharides, proteins, amino acids, and enzymes, have been shown to act on many of these pathological processes, thus becoming a possible alternative to existing treatment methods.

Studies show that G. lucidum may neutralize the neurotoxicity of AB amyloid in Alzheimer disease by maintaining synaptophysin levels. It also significantly inhibits neuronal apoptosis, which was signified primarily by the lowered amount of apoptotic bodies and decreased caspase3-like activity in neurons treated with AB.

Moreover, *Ganoderma lucidum* proves to be a promising preventive agent against neurodegeneration by altering the harmful inflammatory pathways and exerting antioxidant effects on neural systems. Zhang et al (Lian et al., 2024) underscored the mushroom' anti-inflammatory and antioxidant properties in a study focusing on cerebral ischemia/ reperfusion injury in rats.

Substantial animal and cell culture studies on the possible therapeutic effects of G.lucidum on NDDs have been completed. Yet, evidence based on human trials remains sparse, with available evidence being equivocal (Chen et al., 2024). Therefore, more clinical research needs to be conducted in order to determine Reishi's efficacy, safety and possible interactions with other substances.

Finally, it has been suggested that Reishi may be used as a form of adjunctive treatment for major depressive disorder (MDD). Alongside other potent medicinal mushrooms such as lion's mane (*Hericium erinaceus*) and caterpillar mushroom (*Cordyceps militaris*), *G.lucidum* was subjected to various experiments. Preclinical in vivo studies support the notion that it may modulate mechanisms involved in the pathogenesis of depression. However, large scale double-blind clinical trials need to be conducted in order to determine its safety and efficacy in treating MDDs (Fijałkowska et al., 2022).

3.3 *G. lucidum* and metabolic health

The active compounds of *Ganoderma lucidum*, such as triterpenoids, polysaccharides and proteoglycans, exhibited potent hypoglycemic properties in several in vitro and in vivo studies.

It has been suggested that the mechanisms underlying the substances' hypoglycemic activity include inhibiting the human aldolase reductase, enhancing glycogen synthesis, improving insulin resistance, preventing pancreatic B-cells apoptosis and enhancing B-cells regeneration (Chan et al., 2021).

Furthermore, several studies have pointed to the beneficial effects of *Ganoderma lucidum* on lowering the levels of cholesterol. It has been shown that some types of ganoderic acid might act similar to statin drugs, inhibiting HMG-CoA reductase (Chan et al., 2021). Aref and et al. performed a systematic review and meta-analysis on animal studies, investigating the effects of *G. lucidum* on serum lipid profiles. According to their findings, Reishi exerts lowering effects on TG, TC, LdL-C, HDL-C and VLDL levels. These properties were attributed to its ability to inhibit cholesterol synthesis in hepatocytes, and decrease cholesterol levels by targeting the HMG-CoA reductase (Aref et al., 2023).

In a randomized, double-blind, placebo-controlled trial Wang and et al. examined the efficacy of *Ganoderma lucidum* spore oil (GLSO) extract on reducing dyslipidemia among individuals with borderline high dyslipidemia, defined as TG concentration of 1.69–2.25 mmol/L (Wang et al., 2025). Participants belonging to the intervention group were administered softgel capsules containing GLSO extract with daily intake of 3g, corresponding to an intake of approximately 1.011g of triterpens. Participants in the placebo group received identical placebo capsules which were indistinguishable from the capsules containing GLSO. After the completion of 12 weeks of treatment, the intervention group showed improvement in lipid profiles: levels of TG, LDL-C and TC were significantly lowered, while HDL-C levels were markedly higher than in the placebo group. Moreover, aside from its vital role in regulation of lipid levels, GLSO extract also lowered AST and ALT levels, pointing to its potential hepatoprotective effect.

The study demonstrates that GLSO may be effectively used as a lipid lowering drug in individuals with borderline high dyslipidemia. However, more large-scale clinical trials need to be conducted in order to specify GLSO's safety and efficacy among patients with lower plasma lipid levels.

In another study, Pazzi et al. examined the effects of *Ganoderma lucidum* (GL) and *Ceratonia siliqua* (CS) on blood glucose, lipid profile and body composition in women with fibromyalgia. (Pazzi et al., 2021). In this randomized, double-blind pilot trial participants diagnosed with fibromyalgia were randomly allocated to either the group receiving 6g of GL carpophores dissolved in water or 6g of CS flour daily. The trial lasted for 6 weeks, after which such parameters as blood glucose, triglycerides and total cholesterol levels, as well as blood pressure, heart rate and body composition were assessed among the participants. The results of the study did not show GL or CS to exert any statistically significant effect on either blood parameters or body composition in women diagnosed with FM. This study highlights the need to conduct clinical trials on GL's efficacy on groups of participants suffering from chronic, systemic diseases in order to broaden the knowledge about its possible applications.

3.4 Antitumor properties of *Ganoderma lucidum*

Cancer is among the leading causes of deaths worldwide, which makes it crucial to look for and study new chemicals that could help treat and alleviate symptoms of the disease. In recent years there has been a rise in studies on substances coming from natural sources, such as those extracted from mushrooms. The bioactive compounds extracted from mushrooms such as *C. sinensis, C. versicolor, G. lucidum, G. frondos* have been coined as mycomedicine and are being subjected to more and more in vitro and in vivo trials. (Dai et al., 2021).

Studies document various active compounds of the Reishi mushroom exerting anticancer properties, including polysaccharides, triterpenoids, sterols, proteins, nucleotides, fatty acids, vitamins, and minerals. Out of these, polysaccharides and triterpenoids are the main groups of chemicals proven to be effective in various types of cancer. (Cadar et al, 2023; Ahmad et al., 2020).

Ganoderma lucidum's active constituents exhibit anticancer properties through various mechanisms. Among these are the activation of immune host response, inhibition of angiogenesis, induction of apoptosis, induction of cytoprotective autophagy, reversal of multidrug resistance and increasing sensitivity to chemotherapy (Cancemi et al, 2024; Xu et al., 2022).

Breast cancer

Evidence shows that active compounds extracted from *Ganoderma lucidum* may be used in different types of cancer. Gariboldi et al. and Wong et al. conducted studies on the anti-breast cancer activity of various mushrooms. These studies underscore *Ganoderma's* cytotoxic, antiproliferative and proapoptotic properties all contributing to its anti-breast cancer activity which has been studied both on human breast cancer cells and tumor-bearing mice. (Gariboldi et al., 2023; Wong et al., 2020). Nevertheless, clinical trials need to be undertaken to further study and determine *Ganoderma*'s role and safety in treating breast cancer.

Gastrointestinal cancer

Studies show that Reishi exhibits potent anti-tumor activity in gastrointestinal cancer which refers to any kind of benign or malignant tumor originating from the human digestive tract, such as gastric cancer, esophageal cancer, colorectal cancer, liver cancer and pancreatic cancer. The main active constituents of the mushroom responsible for these properties are triterpenoids (e.g. ganoderic acids) and polysaccharides. Various types of ganoderic acid exert anti-cancer mechanisms including inhibiting cancer cell proliferation, inducing apoptosis, inhibiting metastasis and regulating autophagy (Ye et al., 2023).

Moreover, Ye et al. have shown that *G. lucidum* may be an effective agent in reversing multi drug resistance which poses a big issue when treating patients with gastrointestinal cancer. Several studies demonstrate that Reishi may also be effectively used in combination with other drugs, helping reduce side effects of already used anticancer medication.

However, as research is primarily based on in vitro and in vivo studies, there is a pressing need for large scale clinical trials to be conducted in order to determine *Ganoderma's* efficacy, safety, appropriate dosage and possible interactions with other substances.

Cervical cancer

Another type of cancer that has been shown to be susceptible to *Ganoderma lucidum's* active compounds is cervical cancer. According to the study conducted by Rokos et al., *G. lucidum* extract shows antitumor activity in cervical cancer cells, specifically by inducing apoptosis and inhibiting proliferation of the abnormal cells. In cells treated with *G. lucidum,* Western blot assay analysis showed a higher expression of pro-apoptotic proteins like Bax and caspase-3 and lower expression of anti-apoptotic protein Bcl-2. What is more, polysaccharides from the mushroom reduced cervical cancer cells' invasion and migration abilities (Rokos et al., 2023). Yet, given the limited scope of studies on the topic, Reishi's possible role in treating cervical cancer needs to be examined further and clinical trials on its efficacy and safety are essential.

4. Discussion

This literature review shows the broad therapeutic potential of Ganoderma lucidum, which can be attributed mainly to its triterpenoid and polysaccharide components. The mushroom appears to exert a range of antioxidant, immunomodulatory, hepatoprotective, neuroprotective, and anticancer effects.

Despite its promising properties, research on Ganoderma lucidum also reveals notable weaknesses, particularly the reliance on preclinical data. Much of the research supporting cinnamon's therapeutic effects comes from animal models and in vitro studies, which, while informative, may not always translate to human clinical outcomes.

Research to date has been confined primarily to preclinical evaluations and has lacked well-controlled, large-scale clinical trials, with a notable gap in high-quality evidence. Many human studies suffer from limitations including small sample sizes, short duration of attending to health outcomes, and contrasting results. Furthermore, there is a lack of information about *G. lucidum's* drug interactions and pharmacokinetics, an important consideration due to the large number of individuals taking *G. lucidum* products as a dietary supplement. Moreover, while some clinical trials show improvements in lipid profiles and liver function confirmed via liver function tests, others have not shown significant changes, suggesting that the outcome is dependent on study population, dose of *G. lucidum*, and method of extract preparation. To see replicable results from clinical studies, the extracts of *G. lucidum* must be standardized.

To address the existing gaps in evidence, future research should examine a number of other key areas. Large-scale randomized double-blind trials are needed to establish efficacy and safety of interventions. Second, the long-term safety and effectiveness of interventions should be scrutinized, in order to assess ongoing effects and unexpected side effects. Third, interactions between herbal remedies and conventional pharmaceuticals should be studied as it may lead to important clinical consequences. Lastly, investigations should work towards standardizing all herbal extraction methods and implementing robust quality control processes to assure the herbal products being used in research laboratories and clinical practice are both reliable and consistent. Filling the gaps in knowledge would clarify the therapeutic implications of *G. lucidum* and assist with developing evidence-based practice for its use.

5. Conclusions

This study underscores *Ganoderma lucidum's* broad therapeutic potential across various domains, especially its hepato- and neuroprotective and anticancer properties. The cumulative evidence shows Reishi's effects extend to cardiovascular and metabolic health.

Several bioactive constituents extracted from the mushroom, mainly triterpenoids and polysaccharides, were effective in hepatopathies of various origin, neurodegenerative diseases and major depressive disorder. *Ganoderma* also exerted hypoglycemic and lipid-lowering properties, along with acei-inhibitor like activity, which ultimately positions the mushroom as a promising agent with multifaceted medicinal properties.

Moreover, Reishi's ability to inhibit cancer cells' growth through different molecular mechanisms may pave the way for its potential future application in antitumor therapy.

Notably, as existing evidence is based mainly on in vitro and in vivo studies, more large scale, well-controlled clinical studies are crucial in order to determine *Ganoderma's* long term safety and appropriate dosage. Additionally, further research into *Ganoderma's* possible interactions with other substances would provide comprehensive understanding of its scope of application.

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Author's contribution:

Research concept and design: *Barbara Ponitka, Marta Danuta Cendrowska, Beata Chromańska, Szymon Milnerowicz*

Data collection and/or compilation: *Julia Maszewska, Justyna Berent, Aleksandra Klukowska, Szymon Milnerowicz*

Data analysis and interpretation: *Barbara Ponitka, Łukasz Brzost, Karolina Stępień, Julia Maszewska*

Writing: *Barbara Ponitka, Julia Procyk, Paulina Rzepa, Justyna Berent*

Critical review of the article: *Barbara Ponitka, Wiktoria Szumlińska*

Supervision, project administration: *Barbara Ponitka*

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