Comprehensive Review on *Ganoderma lucidum karst*- Pharmacognostic Perspective

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ABSTRACT

Ganoderma lucidum is a medicinal mushroom traditionally used in Asian medicine for its health benefits. It contains bioactive compounds like polysaccharides and triterpenoids, which contribute to its therapeutic effects. Polysaccharides, especially β-glucans, enhance immune function and reduce inflammation, while triterpenoids show anticancer, liver-protective, and antiviral properties. Studies have confirmed its antioxidant, anti-inflammatory, and antitumor activities in lab settings. These effects are linked to the activation of immune cells such as macrophages and lymphocytes. Triterpenoids also help inhibit tumor growth and reduce inflammation. Experimental research supports its role in boosting immunity and controlling chronic diseases. However, clinical trials in humans are still limited. More research is needed to confirm its safety, dosage, and effectiveness. Overall, *Ganoderma lucidum* shows promise as a natural therapeutic agent, but further clinical validation is required.

Keywords: - anti-bacterial, anti-oxidant, anti-viral, anti-inflammatory, anti-fungal, Immunomodulatory effects

INTRODUCTION

Ganoderma lucidum is a medicinal fungus that has been a part of traditional Chinese medicine for more than two millennia. It is recognized by its hard, woody texture, shiny surface, and reddish-brown color. Commonly referred to as the "Mushroom of Immortality," it earned this title from ancient legends suggesting it grew only in the dwellings of immortals, symbolizing health and longevity. In nature, *Ganoderma lucidum* is now mostly found growing on decaying hardwood, though it has become increasingly rare in the wild. To meet the growing demand driven by its medicinal value, large-scale cultivation has become the main source of supply. It is believed to help prevent and manage a wide range of health conditions and is also noted for its potential anticancer properties. Despite these claims, most supporting evidence comes from laboratory and experimental studies, and further clinical research is required to confirm its therapeutic benefits (Unlu et al., 2016). *Ganoderma lucidum*, commonly known as Reishi or Lingzhi, is a well-known medicinal mushroom that has been extensively studied for both its mycological characteristics and pharmacological properties. Mycologically, *Ganoderma lucidum* belongs to the division: Basidiomycota, order: Polyporales, and family: Ganodermataceae. It is characterized by a large, woody, shelf-like fruiting body with a distinctive red-varnished appearance. This fungus primarily grows on decaying hardwood trees and plays a critical ecological role in lignin degradation and nutrient cycling in forest ecosystems (Wasser, 2005). *Ganoderma lucidum* is revered in traditional Asian medicine for its broad spectrum of therapeutic properties. Its bioactive compounds include polysaccharides, triterpenoids, sterols, and peptides, which have demonstrated significant immunomodulatory, anti-inflammatory, antioxidant, and antitumor activities in both in vitro and in vivo studies (Boh et al., 2007). Notably, the polysaccharides are associated with immunostimulatory effects, while triterpenoids contribute to hepatoprotective and anticancer activities (Zhou et al., 2007). Due to these diverse pharmacological effects, G*anoderma lucidum* is widely used as a complementary therapeutic agent and is the subject of ongoing pharmacological research and clinical evaluation.

Taxonomic history and controversies

Ganoderma species identification and circumscriptions have often been unclear and taxonomic segregation of the genus has been controversial (Moncalvo et al. 1995). Numerous *Ganoderma* specimens and species have been misidentified, largely due to the presence of heterogeneous forms, taxonomic challenges, and inconsistencies in the subdivision of the genus (Mueller et al. 2007). Due to the genetic heterogeneity of *Ganoderma* species, considerable genetic variation has been observed, which is primarily attributed to out crossing over successive generations and differing geographical origins (Miller et al., 1999; Pilotti et al., 2003). As a result, significant morphological variability has been documented, even among individuals classified within the same species.

Traditional Chinese texts categorize *Ganoderma* into six types based on the color of their fruiting bodies: Sekishi (red), Shishi (purple), Kokushi (black), Oushi (yellow), Hakushi (white), and Seishi (blue). These classifications are linked to distinct triterpenoid profiles found in each variety. Szedlay (2002), Liu (1974) authored a comprehensive monograph on traditional Chinese medicinal fungi, in which he identified *Ganoderma lucidum* as "Lingzhi."

The scientific name *G. lucidum* became widely accepted as the binomial designation for "Lingzhi" in numerous studies concerning Chinese edible and medicinal mushrooms (Ying, 1987; Mao, 1998; Dai et al., 2009;Cao et al., 2012).The taxonomy of the *Ganoderma* genus remains ambiguous due to ongoing confusion surrounding both species and genus classifications (Hapuarachchi et al., 2018). This complexity arises in part because morphologically similar fungi are also found in related genera such as *Fomes*, *Polyporus*, and *Tomophagus* (Paterson, 2006).The traditional classification of the Ganodermataceae family has relied primarily on morphological characteristics. However, species identification within the group remains uncertain, and the delimitation of genera has been a subject of ongoing debate due to fundamentally differing perspectives among mycologists (Moncalvo et al., 1995; Moncalvo and Ryvarden, 1997).

Figure: Fruiting bodies of *Ganoderma lucidum*

Taxonomic position

Belonging to the Ganodermataceae family, *Ganoderma lucidum* is a polypore fungus that primarily grows on hardwood trees, particularly in humid and tropical climates (Boh et al., 2007). Its characteristic glossy, reddish-brown fruiting body contains bioactive compounds such as polysaccharides, triterpenoids, sterols, and phenolic compounds, which contribute to its medicinal properties (Paterson, 2006).

The systematic position of *Ganoderma lucidum* is:

- **Kingdom**: Fungi
- **Phylum**: Basidiomycota
- **Class**: Agaricomycetes
- **Order**: Polyporales
- **Family**: Polyporaceae
- **Genus**: *Ganoderma*
- **Species**: *Ganoderma lucidum*

Pharmacological properties

Ganoderma lucidum is considered a rich source of bioactive compounds with significant therapeutic potential. (Grys et al., 2011) As reported in the most recent study (Grienke et al., 2015) a total of 279 bioactive secondary metabolites have been extracted from Reishi. Among these, polysaccharides specifically *Ganoderma lucidum* polysaccharides (GLP) are recognized as the primary active components responsible for its beneficial health effects. Polysaccharides make up approximately 10–50% of the dry weight of *Ganoderma lucidum* fruiting bodies (Skalicka-Wozniak et al., 2012).These compounds are known for their immune-enhancing and anticancer properties (Xu et al., 2011; Kao wt al., 2013). So far, researchers have identified over 200 distinct polysaccharides derived from Reishi's fruiting bodies, spores, mycelium, and liquid cultures (Wasser,2010). These include, among others, β-D-glucans, α-D-glucans, α-D-mannans, and polysaccharide-protein complexes. The study (Chen XiaoPing et al., 2009) demonstrated that polysaccharides extracted from Reishi fruiting bodies possess antioxidant properties. Furthermore, studies have shown that H-GLP, a structurally modified form of the slightly water-soluble *Ganoderma lucidum* polysaccharides (GLP), exhibits enhanced antioxidant activity compared to the unmodified version (Liu et al., 2010). Triterpenoids present in *Ganoderma* that contain a carboxyl group are commonly referred to as ganoderic acids. These compounds are known for their complex structures, high lipophilicity, and molecular weights ranging from 450 to 650 kDa. Chemically, they are highly oxidized derivatives of lanostane (Ma Lin et al., 2003). These triterpenoids can contain 30, 27, or 24 carbon atoms per molecule. So far, more than 150 ganoderic acid derivatives and other triterpenoids have been identified in *Ganoderma lucidum* and related species within the *Ganoderma* genus (Paterson, 2006). *Ganoderma lucidum* has also been found to contain proteins with therapeutic properties. One such protein, LZ-8, is a 12 kDa polypeptide composed of 110 amino acids, found in the mycelium. It demonstrates immunomodulatory and mitogenic activities (Lin et al., 1997). Another protein, ganodermin, with a molecular weight of 15 kDa, was isolated from the fruiting bodies and is known for its antifungal properties (Wang, H., & Ng, T. B. (2006). Reishi also contains various nucleosides such as adenosine, cytidine, guanosine, inosine, thymidine, and uridine as well as nucleotides, including adenine, guanine, hypoxanthine, thymine, and uracil (Gao et al., 2007).

Anti-inflammatory activity

Animal studies have demonstrated that *Ganoderma* extract exhibits anti-inflammatory properties and provides protective effects against colitis (Hasnat et al, 2015). Additionally, this study (Gupta et al. 2014) confirmed that an aqueous lyophilized extract of *Ganoderma lucidum* has notable wound-healing potential. The anti-inflammatory effects of GLPs (Glucagon-like peptides) were evaluated using carrageenan-induced and formalin-induced edema models. The findings indicated that the polysaccharide effectively suppressed both acute inflammations caused by carrageenan and chronic inflammation triggered by formalin (Joseph et al., 2011) *Ganoderma lucidum* extracts demonstrate strong anti-inflammatory effects by significantly reducing the expression of cytokines such as IL-6 (Interleukin 6) and IL-23p19 (Interlukin 23 subunit p19), immunomodulatory proteins like S100A7 (S 100 Calcium-binding protein A7), S100A8 (S 100 Calcium-binding protein A8), and S100A9 (S 100 Calcium-binding protein A9), as well as chemokines including CXCL8 (C-X-C motif chemokine ligand 8), CCL5 (C-X-C motif chemokine ligand 5), and CCL20 (C-X-C motif chemokine ligand 20) (Dudhgaonkar et al., 2009). In a separate study, Zhang et al. (2018) explored the anti-inflammatory potential of chemically sulfated polysaccharides and found that these compounds not only suppressed L-selectin-mediated inflammation but also had a broader inhibitory effect on the overall inflammatory response."

Antibacterial activity

Terpenes, lectins, polysaccharides, etc., are considered antimicrobial compounds, and act on the bacterial cytoplasmic membrane (Quereshi et al., 2010). The bioactive compounds present in *G. lucidum* are capable of inhibiting both gram-positive and gram-negative bacteria. For example, its aqueous extract has been shown to suppress the growth of 15 different bacterial species from both groups (Gao et al., 2003). Some compounds, such as ganomycin and triterpenoids, have been reported to exhibit broad-spectrum antibacterial activity (Shah et al., 2014). Several studies have examined different extracts of *Ganoderma lucidum*, including methanolic, chloroform, acetone, and aqueous forms, and have reported antibacterial effects against a range of bacterial strains such as *Bacillus subtilis*, *Staphylococcus aureus*, *Enterobacter aerogenes*, *Corynebacterium diphtheriae*, *Escherichia coli*, *Salmonella* species, and *Pseudomonas aeruginosa* (Quereshiet al., 2010; Goud et al., 2019;). Additionally, research by Heleno et al. (2013) revealed that certain *Ganoderma lucidum* extracts possess stronger antimicrobial activity than conventional antibiotics like streptomycin and penicillin. Collectively, these findings indicate that *G. lucidum* has the potential to suppress the growth of various bacterial pathogens.

Antiviral activity

Findings from multiple studies indicate that *Ganoderma lucidum* holds promise as a source for developing antiviral agents (Eo et al., 1999). Genomic analyses suggest that *G. lucidum* may be effective against a variety of viruses, including herpes, influenza, Epstein-Barr, and hepatitis viruses, as well as the highly virulent H1N1 influenza strain.

Ganoderic acids extracted from the fruiting bodies of *Ganoderma lucidum* have demonstrated antiviral properties, including activity against HIV and the Epstein-Barr virus (Eo et al., 2000). Water-soluble compounds such as GLhw and GLlw, along with methanol-soluble fractions GLMe-1 to GLMe-8, have been found to inhibit the replication of the influenza A virus. Additionally, polysaccharides from *Ganoderma lucidum* exhibit antiviral effects against hepatitis B virus (HBV) by suppressing DNA polymerase activity. Ganodermadiol has shown efficacy against herpes simplex virus type 1 (Bisko et al., 2003), while water extracts of *Ganoderma lucidum* have been reported to inhibit the proliferation of VPH-transformed cells (Hernandez-Marquez et al., 2014).

The recent emergence of the novel corona virus (SARS-CoV-2) poses a significant global public health challenge. Although clinical evidence is still limited, existing literature strongly suggests that various bioactive compounds found in *Ganoderma lucidum*—such as triterpenoids, polysaccharides, nucleotides, sterols, steroids, fatty acids, and proteins/peptides—may have therapeutic potential against COVID-19 (Hetland et al., 2021). Findings from Al-Jumaili et al. (2020) report an increase in lymphocyte counts among COVID-19 patients supplemented with *Ganoderma lucidum*. β-glucans derived from the fungus are known to enhance pattern recognition receptor (PRR) signaling, thereby promoting protective inflammatory responses that help prevent infections, including those caused by corona viruses.

Furthermore, triterpene glycosides present in several plants including *Ganoderma lucidum*—have been shown to significantly inhibit early-stage infection of human corona virus 229E by disrupting viral replication, attachment, and entry into host cells (Cheng et al., 2006). *G. lucidum* also demonstrates antiviral efficacy against dengue virus (DENV) and enter virus 71 (EV71), as well as inhibitory effects on HIV-1 protease activity. These findings highlight *Ganoderma lucidum* as a promising antiviral agent, particularly in the context of COVID-19.

Anti-oxidant activity

Multiple in vitro assays have validated the antioxidant properties of polysaccharides and their complexes derived from *Ganoderma lucidum* (Bukhman et al., 2007). Excessive free radicals in the body disrupt redox balance, resulting in oxidative damage to tissues. This oxidative stress contributes significantly to the onset and progression of various diseases by damaging proteins, lipids, and DNA. Polysaccharides extracted from *Ganoderma lucidum* possess antioxidant properties that protect tissues from the harmful effects of reactive oxygen species. Additionally, they help maintain the body's oxidative balance (Jeong and Park, 2020). Chloroform extracts of *Ganoderma lucidum* demonstrated significant antioxidant and lipid peroxidation inhibitory activities, as reported by (Joseph et al., 2009). Similarly, methanolic extracts were shown to prevent kidney damage by reestablishing the kidneys' antioxidant defense mechanisms (Sheena et al., 2003b). Collectively, these findings indicate that the antioxidant properties of *Ganoderma lucidum* may play a crucial role in preventing lipid peroxidation within biological systems.

Antifungal activity

The antifungal activity of *Ganoderma lucidum* has been the subject of very few publications. Wang and Ng (2006) effectively extracted the so-called ganodermin antifungal protein, which prevents the mycelial growth of Physalosporapiricola, Fusariumoxysporum, and Botrytis cinerea.

In terms of antifungal properties, triterpenoids derived from *Ganoderma gibbosum* have demonstrated the most potent activity, with MIC_{50} values against *Candida albicans* ranging from 3.8 to 129.1 µg/ml (Pu et al., 2019). Benzolactones isolated from *Ganoderma lucidum* have also shown strong antifungal effects, with MIC_{90} values against *Microsporum gypseum* ranging from 18.5 to over 128 µg/ml (Lu et al., 2020). However, research on the antifungal potential of various *Ganoderma* species remains limited. For instance, farnesyl hydroquinone's from *Ganoderma pfeifferi* did not exhibit detectable antifungal activity in one study, but the MIC values were only tested up to 100 µg/ml (Mothana et al., 2000). This suggests that hydroquinones should be evaluated at higher concentrations to definitively assess their antifungal potential.

Antitumor activity

For survival, a tumor requires a continuous supply of nutrients, which it receives through blood and lymphatic vessels. These same vessels also serve as pathways for the spread of invasive cancer cells. Therefore, inhibiting angiogenesis the formation of new blood vessels is a critical therapeutic strategy. Angiogenesis-inhibiting drugs can limit tumor growth by reducing its access to nutrients. Additionally, targeting cellular mechanisms involved in adhesion, invasion, and migration can help control metastasis. Chemotherapy contributes to this effort by preventing angiogenesis, thereby decreasing the number of blood vessels that feed the tumor and effectively starving it (Sharma et al., 2019). Furthermore, compounds derived from *Ganoderma lucidum*, particularly polysaccharides and triterpenes, have demonstrated both anticancer and chemo preventive properties.

Research has shown that various extracts and isolated compounds from *Ganoderma lucidum* exhibit carcinostatic effects on a range of cancer cell lines, including those from the lung (Li et al., 2013), colon (Li P. et al., 2020), pancreas (Chen et al., 2022), liver (Li et al., 2005), breast (Barbieri et al., 2017; Jiao et al., 2020), skin (Shahid et al., 2022), and prostate (Wang et al., 2020). Specific ganoderic acids such as GA-Mk, GA-S, GA-Mf, GA-R, GA-Mc, and GA-T have demonstrated effectiveness against metastatic lung cancer cells (95-D) and human cervical cancer cells (HeLa) (Li et al., 2013). Additionally, GA-H and GA-A have been found to inhibit the proliferation and invasive characteristics of breast cancer cells by influencing the AP-1 and NF-κB signaling pathways (Jiang et al., 2008). These findings highlight ganoderic acids as the principal bioactive components among triterpenes. Certain ganoderic and lucidenic acids have also shown promising antitumor effects.

Immunomodulatory activity

Ganoderma lucidum is known to contain several key bioactive compounds with strong immunomodulatory properties. These include polysaccharides (notably β-D-glucan), proteins such as Ling Zhi-8, and triterpenoids. The primary immunomodulatory actions of these compounds involve stimulating immune effector cells—such as T cells, macrophages, and natural killer (NK) cells. This stimulation promotes mitogenic activity and leads to the secretion of various cytokines, including interleukins, tumor necrosis factor-alpha (TNF-α), and interferon's (Sanodiya et al., 2009).

According to Smina et al. (2017), total triterpenes extracted from *Ganoderma lucidum* trigger apoptosis in human breast adenocarcinoma cells by modulating the expression of cyclin D1 and B-cell lymphoma proteins, as well as by increasing the levels of pro-apoptotic markers such as Bax and caspase-9. Additionally, Zheng et al. (2018) suggested that *Ganoderma*'s antitumor activity may involve its function as a dehydroergosterol peroxide enzyme, which contributes to reduced expression of the myeloid leukemia cell differentiation protein, cytochrome-c release, and mitochondrial membrane damage.

CONCLUSION

Pharmacognostic methods offer a structured approach for the detailed examination and standardization of *Ganoderma lucidum*, a fungus highly valued for its medicinal benefits. Through extensive macro- and microscopic studies, scientists can accurately identify *Ganoderma lucidum* and distinguish it from similar species, which is essential for ensuring quality in herbal products (Paterson, 2006). Physicochemical testing helps verify the purity and uniformity of the raw materials, which is crucial for consistent therapeutic effects. Phytochemicals analyses have revealed that *Ganoderma lucidum* contains numerous bioactive compounds, including triterpenoids, polysaccharides, and sterols, which are responsible for its diverse pharmacological actions such as antioxidant, antiviral, and immune-enhancing properties (Wachtel-Galor et al., 2011).

The use of advanced molecular tools like DNA bar-coding and genome sequencing has improved the accuracy of species identification, minimizing adulteration and enhancing product reliability (Li et al., 2023). Furthermore, bioactivity assays link these chemical constituents to their health benefits, supporting both traditional uses and modern clinical applications of *Ganoderma lucidum*. Collectively, pharmacognostic approaches enable the creation of standardized and efficacious *Ganoderma lucidum* products while providing a scientific foundation for their integration into contemporary medicine. Ongoing research employing these methods will be essential to fully harness the therapeutic potential of *Ganoderma lucidum* as a natural bioactive compound.

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