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Ganoderma lucidum (Reishi): Biological and Pharmacological Perspectives

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ABSTRACT

Ganoderma lucidum is a traditional mushroom with a long history of usage in East Asian medicine and rising recognition worldwide as a functional and nutritional food. This review highlights the pharmacological properties, bioactive components, and therapeutic effects of *G. lucidum*. Triterpenoids, polysaccharides, proteins, and phenolic compounds are among its primary components, exhibiting various medicinal effects, including immunomodulatory, anticancer, anti-inflammatory, antiviral, antimicrobial, antioxidant, and antidiabetic properties. These compounds modulate immune responses, suppress oxidative stress, and enhance the ability of cancer cells to undergo apoptosis, and regulate metabolic processes. Preclinical and clinical studies suggest promising applications of *G. lucidum* in cancer therapy, metabolic disorders, infectious diseases, and as an adjuvant to conventional treatments. However, concerns still exist regarding potential toxicity at high concentrations, drug interactions, and the need for standardized extracts. Overall, *G. lucidum* represents a valuable natural source for treatment, warranting further well- designed clinical trials and molecular studies to understand its traditional uses in evidence-based medicine.

1. Introduction

Herbal therapy, one of the oldest forms of medicine known to humanity, involves using whole plants or their parts to treat various conditions. Approximately 80% of individuals globally utilize medicinal products as their primary healthcare system, a trend that is growing rapidly daily due to the toxicity and adverse reactions linked to modern allopathic medications, resulting in a rapid rise in herbal drug manufacturers [1].

G. *lucidum* is an herbal mushroom, belongs to Kingdom *Fungi*, family *Ganodermataceae* and it has been utilized for several thousand years for its enhancing and health-promoting [2], medicinal, edible properties interest [3]. These fungi are either parasitic or saprophytic [4], and grows

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on dead or dying trees, particularly hardwoods like oak, maple, and elm etc. [5]. It contains various active compounds and pharmacological effects, garnering significant public interest [3].

G. lucidum has been revered in classical treatment for over two thousand years, particularly within East Asian cultures. Its historical significance is underscored by its classification as a symbol of health and longevity. When *Ganoderma* was first discovered, it was highly valuable and inaccessible to ordinary people—reserved only for royalty and nobility due to its perceived miraculous properties. However, thanks to advancements in 21st-century American biotechnology, G. *lucidum* can now be cultivated in laboratories under controlled conditions [6].

Species of *Ganoderma* are located in subtropical and tropical areas, where warm and humid climate enhance their growth [7]. G. *lucidum* is primarily found to grow in Japan, China, and Korea in Asia, and it is also available in Denmark, Poland, and Sweden in Europe. In Africa, G. *lucidum* is found in Kenya, Ghana, and Tanzania. G. *lucidum* grows near China's Yangtze and Yellow rivers [8]. *G. lucidum* extracts are produced in various forms, including powder, nutritional supplements, and tea, which treat various diseases [9].

The mushroom's therapeutic potential is attributed to numerous effective compounds, including triterpenoids and polysaccharides, specific proteins, vitamins, minerals, and phenolic compounds, which exhibit various health benefits [10]. These health benefits are due to the interaction of all bioactive constituents of mushrooms. *G. lucidum* has traditionally been utilized to manage asthma, insomnia, liver dysfunction, bronchitis, chronic hepatitis, high blood pressure, arthritis, and stomach ulcers. In recent years, it has also been recognized for its potential in addressing advanced and emerging health conditions such as diabetes, Cancer, seizures, high cholesterol, and immune-related disorders [9]. So, *G. lucidum* has become a prominent focus within medical research and the production of natural drugs [11].

The documented therapeutic properties of the genus have facilitated its extensive commercialization, with *Ganoderma*-based formulations being widely marketed and consumed in diverse forms, including dietary supplements, herbal teas, and incorporation into various functional products [12].

This review aims to provide a literature review concerning the taxonomy, nutraceutical and nutritional value, pharmacological effects, therapeutic potential, anticancer, antiviral, immunomodulatory, antibacterial, antidiabetic, antioxidant, anti-aging, toxicity, and anti-inflammatory properties of *G. lucidum*.

2. Taxonomic implications of Ganoderma lucidum

In England, *G. lucidum* was first described by Curtis and subsequently formalized by Fries [13]. Cao *et al*. (2012) later noted that this fungus had long been recognized in China as "Lingzhi," a medicinal mushroom utilized for over 2,000 years. Later on, a molecular study on *G. lucidum* indicated that the East Asian "Lingzhi" was different from the European *G. lucidum* [14]. Through combined molecular and morphological analyses, Wang *et al.* (2012) discovered that the Chinese "Lingzhi" has a close relationship with *G. lucidum* from the United Kingdom and other species of *Ganoderma* [15].

Additionally, taxonomic studies by Kwon *et al*. (2016) identified 62 distinct strains within the *Ganoderma* genus [16]. According to the taxonomic framework outlined by Nahata (2013), *Ganoderma lucidum* is classified as follows: Kingdom *Fungi*, Phylum *Basidiomycota*, Class *Agaricomycetes*, Order *Polyporales*, Family *Ganodermataceae*, Genus *Ganoderma*, and Species *lucidum* [17,18].

Ganoderma species display significant morphological diversity, encompassing variations in fruiting body shape, coloration, host specificity, and geographical range (Figure 1), all of which contribute to species delimitation [18]. However, *G. lucidum* poses notable taxonomic difficulties due to pronounced morphological plasticity of the genus under different environmental conditions, while maintaining stable microscopic features [19]. *Ganoderma* is distinguished by either non-laccate or laccate basidiocarps, which range from sessile to stipitate forms, typically exhibiting red-brown, truncate, white to pale-yellow margins, double-walled basidiospores [20]. These spores possess a distinctive apical germinal pore, exosporium (a hyaline and thin outer wall), and endosporium (brown to dark interwall pillars). The presence of basidiospores with pillars constitutes a primary diagnostic trait for the genus [21]. In addition to their ecological role as agents of white rot in woody plants, *Ganoderma* species are widely recognized for their pharmacological value [22].

The species concept within the genus *Ganoderma* remains both contentious and insufficiently defined, mainly due to morphological variation in the same species [23]. Environmental influences, interspecific hybridization, and observer-related morphological biases further complicate accurate taxonomic identification [24]. *G. lucidum* poses substantial taxonomic difficulties, as its shape changes with changes in the surrounding environments, but microscopic characteristics remain unchanged [19]. Moreover, about 50% of recorded species names have been recognized as synonyms, highlighting Ganoderma taxonomy's complexity and historical inconsistencies [25]. Despite these difficulties, advanced phylogenetic and molecular approaches have verified the presence of 191 legitimate *Ganoderma* taxa [26]. Another method for recognizing *Ganoderma* species, is the content of triterpenoids and Polysaccharide in *Ganoderma* [27].

Figure 1. Typical forms of *G. lucidum* [28].

3. Cultivation of G. lucidum

G. lucidum exhibits a broad ecological amplitude and is commonly found in temperate and tropical regions worldwide [7]. It typically grows as a saprophytic fungus on decaying hardwoods, including oak, elm, and maple, and occasionally on conifers. The species prefers moist, shaded environments with well-aerated soils rich in organic matter [5]. In Egypt, *G. lucidum* has been recorded on date palm trunks and various hardwood substrates in several governorates, indicating its adaptability to local climatic conditions [29].

Temperature is a critical factor influencing mycelial growth and is carefully regulated during cultivation. While the fungus can grow within a temperature range of 30–34 °C, optimal growth occurs at 37 °C, where *G. lucidum* exhibits a rapid growth rate of approximately 7–8 mm per day [5].

The cultivation of mushrooms has become a primary source of mushrooms because of the highly variable natural quality of G. *lucidum* worldwide and the increasing requirements for it across cosmetics, health products, and pharmaceutical industries [30]. However, the artificial cultivation process of *G. lucidum* is time-consuming, and its yield is sensitive to the surrounding conditions. To overcome these limitations, solid- and liquid-state fermentation are widely applied for large-scale cultivation of the secondary metabolites and mycelia of G. *lucidum* [8].

The cultivation stargates for production of mycelia and fruiting bodies of *G. lucidum* are categorized into two main approaches: fruiting body cultivation and mycelial cultivation in bioreactors. Fruiting body production can be carried out using several substrate types and conditions, including unsterilized long wood in outdoor environments, sterilized long wood under indoor conditions, or sawdust-based systems prepared in bags, bottles, or beds/trays. In contrast, mycelial cultivation employs controlled biotechnological methods, most notably submerged cultivation in liquid media and solid-state cultivation, which facilitate large-scale production and efficient harvesting of bioactive compounds. This structured overview highlights the diversity of cultivation techniques, accommodating both traditional methods and modern industrial-scale processes to meet the growing demand for *G. lucidum* in various commercial sectors [13].

4. Morphology of G. lucidum

G. lucidum is characterized by laccate (glossy) basidiocarps bearing thick-walled pilocystidia embedded within an extracellular melanin matrix [5]. Its fruiting body commonly appears in kidney-shaped, fan-shaped, or semicircular forms, displaying colors that range from dark red and reddish-brown to reddish-black, with yellow or ochre tones often accentuating the margins. Its flesh varies from yellowish-brown to dark brown [10]. The species name "*lucidum*" originated from the Latin word meaning "bright," which refers to the mushroom's characteristic glossy surface [31].

5. Ganoderma as a plant pathogen

Ganoderma lucidum has been identified as a pathogenic agent causing butt rot in mangrove tree species across various mangrove habitats in southern Thailand. It has also been associated with both foot rot and butt rot in black pepper (*Piper nigrum*), resulting in considerable damage to the host plant [32]. Cultivation studies have demonstrated that sugarcane bagasse and rubber tree sawdust are highly efficient substrates, achieving approximately 60% biological efficiency. Furthermore, sawdust-based substrates have enhanced biological efficiency relative to the traditional log method. Moreover, contamination occurs less frequently in bag cultures (13 cases) than in log cultures (22 cases) [33]. These findings distinguish the dual significance of *G. lucidum*, both as a pathogenic species causing considerable agricultural and ecological damage, and as an economically important fungus whose optimized cultivation can yield high productivity with minimal contamination.

6. Biochemical composition of G. lucidum

Numerous studies on *Ganoderma lucidum* have revealed that approximately 90% of its total weight consists of water, while the remaining 10% contains a variety of valuable constituents. These include proteins (10–40%), fats (0.4–0.7%), carbohydrates (3–20%), fiber (3–32%), and ash (8–10%). This dry fraction has essential elements and minerals such as selenium, potassium, zinc, copper, calcium, iron, phosphorus, and magnesium [34]. Together with these components, *G. lucidum* contains a variety of effective molecules, including terpenoids, steroids, nucleotides, phenols, polysaccharides, and glycoproteins. It provides all essential amino acids, with proteins particularly abundant in leucine and lysine. Among its constituents, polysaccharides, peptidoglycans, and triterpenes are considered the most significant bioactive compounds due to their diverse therapeutic properties [10].

Research has shown that *G. lucidum* contains more than 432 secondary metabolites and over 200 distinct polysaccharide types. These secondary metabolites include more than 380 terpenoids and upwards of 30 steroidal compounds [35]. The polysaccharides and triterpenoids of *G. lucidum* have garnered substantial scientific interest due to their structural diversity, abundance, and broad spectrum of bioactivities [36]. The composition and concentration of

these bioactive constituents can vary considerably, and they are affected by various factors such as geographic origin, cultivation strategies, specific strain used, and extraction techniques [37].

6.1 Triterpenes

Terpenoids, the derivatives of terpenes, can be classified into several subtypes, including essential oils, carotenoids, sterols, volatile triterpenoids, and less volatile diterpenes [10]. The distinct bitterness of fruiting bodies of *G. lucidum* is attributed to their triterpene and triterpenoid secondary metabolites, with higher bitterness levels correlating with increased triterpene content [38]. *G. lucidum* contains a variety of triterpenoids, most notably C30 lanostans such as aldehydes, esters, lactones, ketones, alcohols, glycosides, and ganoderic acids. In addition, other groups include C24 lanostans, C25 lanostans, C30 pentacyclic triterpenes, and also C27 lanostans (such as alcohols, lactones, esters, and lucidenic acids) [39, 40]. The species also produces ergosterol and its derivatives, along with numerous lanostane derivatives, such as ganoderenic acids (A, B, D), ganoderic acids (A, B, C1, C2, D, F, G, H, K, S, T, Y AM1, DM, Me, Mk, TR), ganoderate G, ganoderols (A, B), *ganoderma*triol, ganoderiol F, Me ganoderate D, ganoderal A, and lucideric acid A (Siwulski *et al*., 2015). Among these, compounds such as ganoderic acids A, C, DM, T, X, H, F, and Y have demonstrated the highest bioactivity Figure (2) [41]. Triterpenoids can be obtained from fruiting bodies, basidiospores, and mycelia of *Ganoderma* [42].

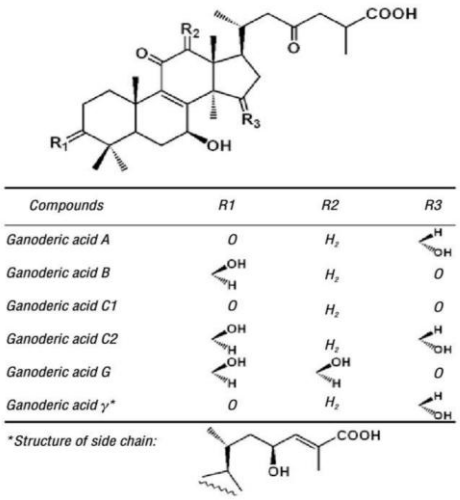

Figure 2. Chemical structure of ganoderic acids isolated from Ganoderma lucidum. Variations in side chains (R_1–R_3) define different derivatives such as ganoderic acids A, B, C_1, C_2, G, and γ [19].

The extraction of triterpenoids from *Ganoderma* species is achieved through a range of solvent-based and non-solvent-based techniques. Solvent extraction methods, including acid, alkali, chloroform, and organic solvent extraction, are widely utilized for isolating these bioactive compounds due to their efficiency in breaking down cellular structures and facilitating compound solubilization. Additionally, specific non-solvent-based techniques, such as microwave- and ultrasound-assisted methods, have enhanced yield and reduced processing time [10, 43-44].

Triterpenoids, particularly ganoderic acids, exhibit a broad spectrum of pharmacological and biological effects. They have been shown to exert inhibitory activity against various fungi and microorganisms, such as both Gram-negative and Gram-positive bacteria [45]. Many compounds can suppress the HIV-1 virus and protease activity while also affecting mitochondrial function in cancer cells, thereby inducing apoptosis [46]. Additionally, they reduce hepatocyte degeneration, so they protect the liver and display more potent antioxidant activity compared to polysaccharides. Triterpenoids enhance immune function by regulating tumor necrosis factor and interleukin-6 expression [47]. In addition, they exhibit pro-apoptotic activities against lung cancer, possess notable anti-inflammatory properties, and contribute to reducing glucose levels and blood lipids [48].

6.2 Polysaccharides

Polysaccharides in *Ganoderma* are synthesized from various monosaccharides, including fructose, glucose, xylose, galactose, and mannose. The diversity of glycosidic linkages between these monosaccharides gives rise to structurally diverse polysaccharides, each characterized by significant health-promoting potential and distinct properties [49]. *G. lucidum* is especially enriched with bioactive components, such as (1→6)-α/β-glucans, (1→3)-α/β-glucans, α-D-mannans, heteropolysaccharides, and glycoproteins, all of which are water-soluble polysaccharides [50]. Among these polysaccharides, β-1,6-D- and β-1,3-glucans are recognized as the most biologically effective consistent Figure (3) [51]. The activity of glucans is primarily determined by their physicochemical properties, including molecular weight, structural conformation, water solubility, and degree of branching (Siwulski *et al*., 2015). The spore cell walls of G. *lucidum* are rich in polysaccharides , particularly α-D-glucans, which exhibit a cytotoxic effect against HeLa cancer cells [52]. The principal monosaccharides that compose these polysaccharides are rhamnose, mannose, galactose, and glucose [8].

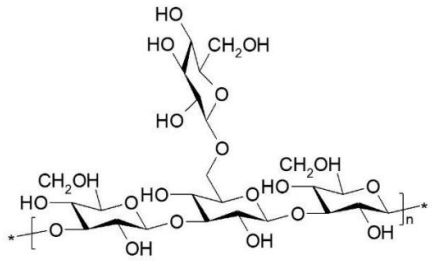

Figure 3. Chemical structure of *Ganoderma lucidum* polysaccharide (GLP). The structure represents β-(1→3)-glucan with β-(1→6)-branching [53].

The extraction strategies of polysaccharides from *G. lucidum* involve a diverse range of techniques broadly categorized into solvent-based methods and alternative extraction strategies. Solvent extraction, particularly through water, acid, alkali, and salt treatments, represents the most conventional approach, enabling the efficient solubilization and isolation of bioactive polysaccharide fractions. In addition to solvent-based methods, modern extraction technologies—including ultrasonic, microwave-assisted, enzymatic hydrolysis, superfine grinding, and steam explosion—offer notable advantages in improving yield and structural integrity of polysaccharides [10, 43-44].

G. lucidum polysaccharides exert various effects, such as anticancer, antimicrobial, antioxidant, anti-inflammatory activities, hypoglycemic, and immunomodulatory. Furthermore, they contribute significantly to maintaining and protecting the intestinal mucosal barrier [54].

6.3 Steroids

Sterols ($C_{17}H_{28}O$) are cyclic secondary monohydric alcohols belonging to the steroid family [55]. In *G. lucidum*, over 20 different sterols have been identified, which are structurally categorized into two main groups: cholesterols and ergosterols [38]. Among these sterols, ergosterol is predominant, accounting for approximately 3‰ % of total sterols. The spores and fruiting bodies of *G. lucidum* contain sterols such as ergosterol peroxide and ergosterol (provitamin D2), and, with ergosterol peroxide, have been shown to suppress the proliferation of breast cancer cells [56]. Sterols derived from *Ganoderma lucidum* exhibit diverse pharmacological properties, particularly in cancer prevention by hidden antitumor promoters [57]. Ergosterol peroxide has been shown to regulate lipid metabolism by suppressing triglyceride synthesis and adipocyte differentiation, mediating anti-inflammatory activity [57].

6.4 Alkaloids

Alkaloids, a structurally diverse class of nitrogen-containing heterocyclic metabolites, constitute a minor but functionally important component of *G. lucidum* [58]. Although their relatively low abundance compared to other bioactive constituents of *G. lucidum*, they exhibit notable pharmacological properties, including hepatoprotective, cardioprotective, hypolipidemic, and antioxidant effects. Major alkaloids identified include ganoderine B, betaine, choline, ganoderine A, and nicotinic acid [57]. Several studies have highlighted their therapeutic effects: lucidimine B demonstrated superior antiproliferative and antioxidant effects against MCF-7 breast cancer cells [59], while *lucidum*ins A–E showed neuroprotective and anti-inflammatory activities [60].

6.5 Amino acids and Proteins, polypeptide

G. lucidum contains many amino acids, including proline, aspartic acid, glutamic acid, etc., which are necessary for the body's physiology, and collectively account for approximately 2.94% of its total mass [61]. Eighteen kinds of amino acids have been recognized in G. *lucidum* [62]. Identified amino acids contribute to the activation of cell regeneration and supply sufficient energy to support protein and nucleic acid synthesis in the hypha. Different types of amino acids are found in different *G. lucidum*, such as glutamic acid; its concentration in *G. lucidum* is nearly twice that of standard varieties. In addition, polypeptides derived from *G. lucidum* exhibit strong antioxidant effects [57]. Meanwhile, leucine has been reported to possess significant antioxidant and hypoglycemic effects [62]. Furthermore, oligopeptides exert significant anticancer effects [63]. Proteins of *G. lucidum* demonstrate various medicinal effects, including antitumor, blood coagulation, and anti-allergy activities [64].

6.6 vitamins

G. *lucidum* has various water-soluble vitamins, including vitamins from the B and C families (B1, β-carotene, B2, B6, C, D, and E.). Among these vitamins, vitamin C plays a crucial role as a potent antioxidant by removing oxygen-derived free radicals and contributes to the prevention of tooth bleeding, whereas vitamins B-complex help to protect against pernicious anemia and act as a coenzyme in numerous biochemical processes [57,61].

6.7 Minerals

G. *lucidum* includes a variety of minerals, including magnesium, potassium, manganese, calcium, iron, selenium, chromium, nickel, vanadium, germanium, and zinc. The body can easily absorb these elements [57].

6.8 Enzymes

Several enzymes have been identified in *Ganoderma lucidum*, including α-1,2-mannosidase, glutamic protease, endo-β-1,3-glucanase, β-N-acetyl hexosaminidase, and β-1,3-glucanase. Glutamic protease constitutes the main protein component in *G. lucidum* extract [65].

6.9 Nucleosides

G. lucidum is a source of nucleosides, including guanosine, thymidine, cytidine, uridine, inosine, and adenosine. In addition, nucleotides like thymine, hypoxanthine, uracil, adenine, and guanine [66].

7. Health-Promoting properties of G. lucidum

Over the past several decades, experimental research has confirmed the diverse health-enhancing effects of G. *lucidum*. The pharmacological activities of *G. lucidum* include anti-ageing, anticancer, antioxidant, anti-inflammatory, immunomodulatory, antidiabetic, antiviral, and antibacterial [9, 67].

7.1 Tumor suppression and anticancer activity

The American Cancer Society (2022) describes Cancer as the uncontrolled growth of abnormal cells that can invade healthy tissues and metastasize to distant organs through lymphatic and blood circulation, making it a significant cause of mortality worldwide. Its progression is affected by many factors, including smoking, alcohol consumption, environmental toxins, nutrition, radiation, and chemical

exposure [68].

Clinical findings indicate that extracts of *G. lucidum* may extend patient survival by approximately 3–6 months, reducing adverse effects of chemotherapy [67]. Evidence of anticancer potential has also been reported in traditional Thai medicinal teas incorporating *G. lucidum* [67], and mycelial extracts have been shown to inhibit breast cancer cell viability [69]. The tumor-suppressive and anticancer properties of *G. lucidum* are among its important therapeutic effects. In vivo studies demonstrated that tumor reduction was primarily caused by vascular destruction, which limited the blood supply to the tumor and necrosis induced by T lymphocytes and the localized release of TNF-α. Additionally, the anticancer activity was associated with the inhibition of DNA polymerase [70]. Polysaccharides, phenolic compounds, triterpenoids, and flavonoids extracted from *G. lucidum* have been reported to exert anticancer effects through multiple molecular and cellular mechanisms.

The polysaccharides of *G. lucidum* exert their anticancer effects mainly by enhancing immune response as they stimulate B and T cells and macrophages to activate the cytotoxic functions of immune cells and produce cytokines [71]. Its anticancer effects are mediated by several pathways, including the induction of cytotoxic responses, stimulation of apoptosis in malignant cells, downregulation of integrin expression to inhibit tumor adhesion, and inhibition of angiogenesis [35,63]. Its polysaccharides with higher molecular weights and extended glycosidic linkage are particularly active [71]. Among them, β-1-6-D-β- and 1-3-glucans mediate their effects through complement type 3 receptor, which recognizes explicitly β-glucan structures, thereby contributing to the modulation of immune responses against cancer cells [35,72].

Triterpenoids exert anticancer effects via many mechanisms, such as downregulating protein kinase C and β-catenin signaling pathways, inhibiting metastatic cell growth, and suppressing tumor cell invasion [73]. Among them, ganoderic acids have shown significant cytotoxicity against various cancer cell types [72]. Specifically, ganoderiol F, ganoderic acid T, and D have been known as potent anticancer agents [61]. Moreover, other ganoderic acids, such as X, U, Y, W, and V, have demonstrated marked cytotoxic activity against hepatoma cells [72].

Phenolic compounds suppress metastasis and the invasion of cancer cells. At the same time, flavonoids contribute to anticancer effects by inducing DNA fragmentation, inhibiting angiogenesis, enhancing phosphorylation of the epidermal growth factor receptor (EGFR), and blocking enzymes' signal transduction [74].

7.2 Anti-inflammatory activity

Inflammation, an essential component of wound repair and host defense, is defined as a natural physiological response to injury or infection of tissue [75]. *G. lucidum* has various effective compounds consistent with anti-inflammatory properties, such as Zhi-8 proteins, β-D-glucans, and triterpenoids. These constituents modulate immune responses primarily through enhancing the functional responses of key immune system cells such as macrophages, T cells, and NK cells. Moreover, spore extracts of *G. lucidum* have been shown to increase macrophage and NK cell production in murine models while suppressing tumor development [70]. Elevated IL-4, IFN-γ, and TNF-α levels within inflamed tissues impair epidermal barrier integrity and increase dermal inflammation [67]. Notably, *G. lucidum* polysaccharides (GLPs) demonstrate marked anti-inflammatory effects by regulating the intestinal immune barrier and sustaining intestinal homeostasis. In murine studies, GLPs have been shown to significantly suppress the secretion of critical pro-inflammatory cytokines, such as IL-6, IL-4, TNF-α, and IL-1β [77]. These immunomodulatory effects underscore the clinical relevance of GLPs, particularly in therapeutic applications for sensitive skin, where inflammation is a key pathological feature [62].

7.3 Immunomodulatory effect

G. *lucidum* exerts Immunomodulating effects by enhancing the mononuclear phagocyte system and boosting both antibody-mediated (humoral) and cell-mediated immunity, as well as the activity of antigen-presenting cells [57]. Additionally, *G. lucidum*-derived substances exert anti-allergic effects by modulating mast cell and B lymphocyte activity. Beyond allergy modulation, *G. lucidum* has been reported to influence immunocirculatory balance, thereby showing therapeutic promise in conditions such as nephrotic syndrome and other immune-mediated disorders [67]. Extracts of *G. lucidum* have been associated with improving the quality of life for chronic fatigue syndrome (CFS) and reducing fatigue [78].

7.4 Antibacterial and Antifungal activity

The methanolic extract of G. *lucidum* demonstrated marked antibacterial effects against a wide range of foodborne pathogens such as Gram-positive and Gram-negative bacteria [79]. Furthermore, *G. lucidum* extracts have been reported to inhibit the growth of the bacterium found in gastric Cancer, gastric ulcers, and *Helicobacter pylori* [80]. Specific metabolites, such as ganosinoside A, demonstrated antibacterial efficacy against *Staphylococcus aureus* by exhibiting high binding efficacy for clumping factor A [67]. In addition, Ganodermin obtained from mycelium displayed antifungal activity by suppressing the mycelial development of phytopathogens, including *Botrytis cinerea*, *Fusarium oxysporum*, and *Physalospora piricola* [81].

7.5 Antiviral properties

Ganoderic acids isolated from the fruiting bodies of *G. lucidum* have demonstrated antiviral properties. Several bioactive constituents from *G. lucidum* show inhibitory efficacy on the development of HIV. Specially, triterpenoids such as ganolucidic acid A, ganodermanontriol, ganodermanondiol, ganoderic acid β, and lucidumol B, exhibit marked inhibitory activity against HIV by targeting HIV-1 protease, with IC_{50} values ranging between 20 and 90

μM [82,83]. In addition to triterpenoids, Polysaccharides suppress hepatitis B virus (HBV) replication by inhibiting DNA polymerase activity. At the same time, ganodermadiol has been reported to suppress the replication of herpes simplex virus type 1 [84]. Additionally, aqueous extracts of *G. lucidum* were found to suppress the growth of cells transformed by human papillomavirus (HPV) [85].

7.6 Antidiabetic activity

Recently, considerable interest has focused on hypoglycemic mechanisms and the antidiabetic efficacy of *G. lucidum*. One promising target in diabetes therapy is protein tyrosine phosphatase 1B (PTP1B) [62].

Animal studies have demonstrated that the polysaccharides such as ganoderans D and B, exert a significant hypoglycemic effect [70]. Fudan-Yueyang-*G. Lucidum* (FYGL), A novel proteoglycan, has also been identified as a potent bioactive compound with dose-dependent hypolipidemic and hypoglycemic activities. Mechanistically, FYGL lowers blood glucose levels in insulin-resistant mice, enhances insulin secretion, suppresses PTP1B overexpression, and promotes insulin-mediated glycogen synthesis [62]. Moreover, FYGL has demonstrated the ability to ameliorate type 2 diabetes mellitus linked to mitochondrial dysfunction by decreasing reactive oxygen species (ROS) levels [62].

7.7 Antioxidant properties

In the human body, the generation of free radicals occurs as a natural byproduct of metabolic processes, with reactive oxygen species (ROS) being the most prominent. These highly reactive molecules can disrupt cellular integrity and impair normal physiological functions of the body. Like lipid peroxidation products, excessive ROS have been strongly associated with the pathogenesis of multiple disorders, including diabetes, Cancer, immune system disorders, neurodegenerative diseases, aging, inflammatory diseases, and cardiovascular diseases [86]. Oxidation contributes to the deterioration of food quality by reducing its nutritional value, generating harmful compounds, and ultimately shortening shelf life while diminishing consumers' acceptability. Antioxidants exert these effects through several mechanisms, including extinguishing singlet oxygen, inactivating lipoxygenase, chelating pro-oxidative metals, and scavenging free radicals and photosensitive substances. Collectively, these actions slow the progression of food oxidation and preserve both the safety and quality of food products [87].

Antioxidant properties are related to several bioactive constituents of *G. lucidum*, such as amino acids, triterpenes, phenolic compounds, glycoproteins, and polysaccharides. Polysaccharides, especially, exert antioxidant effects through several mechanisms, such as preventing or terminating chain reactions by neutralizing free radicals through hydrogen–electron combinations or donating hydrogen. These polysaccharides also play a role in inhibiting lipid peroxidation and malondialdehyde, while enhancing the effect of glutathione peroxidase, a key enzyme in cellular antioxidant defense. This protective effect occurs by promoting the synthesis of superoxide dismutase and catalase through redox cycling [40,50].

Antioxidant effect of triterpenes, leucine-derived amino acids, and glycoproteins, formed by covalent bonding between polysaccharides and peptides or proteins. Phenolic compounds of *G. lucidum*, such as p-hydroxybenzoic acid, Quercetin, protocatechuic acid, myricetin, gallic acid, chlorogenic acid, cinnamic acid, and p-coumaric acid, contribute to the antioxidant capacity of *G. lucidum* [31,50].

7.8 Anti-ageing

Aging is closely associated with the accumulation of free radicals generated within tissue, arising when the extent of oxidative injury surpasses the body's intrinsic repair capacity. G. *lucidum* possesses various natural antioxidant compounds capable of reducing oxidative stress, thereby contributing to the delay of aging processes and promoting healthy longevity. [88]. G. *lucidum* spore oil (GLSO) has been reported to extend the mean survival time of organisms exposed to oxidative stress. Such an effect arises from its potent free radical scavenging activity. It markedly enhances mRNA levels of major antioxidant enzymes, such as manganese superoxide dismutase (Mn-SOD), copper-zinc superoxide dismutase (Cu, Zn-SOD), and catalase (CAT). Furthermore, GLSO decreases the malondialdehyde levels, a biomarker of lipid peroxidation, while stimulating the enzymatic activities of CAT and SOD [39]. Experimental studies have shown that these polysaccharides decrease lipid peroxidation in the liver of mice and enhance the effect of key antioxidant enzymes, including liver peroxidase and superoxide dismutase (SOD). Such findings highlight the potent antioxidant capacity of *G. lucidum*, underscoring its protective role against oxidative damage and its potential in delaying the aging process [89].

8. Side effects and toxicity

Although *G. lucidum* has many health functions, its side effects and toxicity should not be neglected. When using *G. lucidum* in treatment, careful consideration is necessary due to its interactions with components of other drugs. Patients with diabetes or those receiving anticoagulant or antiplatelet therapy should follow particular caution, as *G. lucidum* may modify the expected therapeutic effects [90]. Although it has anticancer properties, its concurrent use with chemotherapy demands vigilance because of possible toxicity; the systemic levels of *G. lucidum* should be controlled to avoid reaching harmful concentrations in plasma [91]. In vitro experiments demonstrated that *G. lucidum* extracts exerted cytotoxic effects at doses exceeding their stimulatory range, significantly decreasing cell viability across various cell lines [92]. Moreover, *G. lucidum* possesses antihypertensive

properties that may stimulate the effects of antihypertensive medications [93]. Additionally, *G. lucidum* polysaccharides (GL-Ps) show antibacterial potential and can potentiate the efficacy of certain antibiotics, including tetracycline and cefazolin [94]. Studies showed that *Ganoderma* spores lead to diarrhea [95].

9. Conclusion

The accumulated evidence underscores *G. lucidum* as a multifunctional medicinal mushroom with significant potential in modern healthcare. Its polysaccharides and triterpenoid components contribute to several pharmacological effects, ranging from immune regulation to anticancer, antioxidant, antimicrobial, and antidiabetic properties. While centuries of traditional use support its safety, recent findings highlight caution in cases of drug interactions, particularly with anticoagulants, antihypertensives, and chemotherapeutic agents. The therapeutic promise of *G. lucidum* depends on direct disease management and its role as an adjunct therapy, stimulating the efficacy of standard treatments while minimizing side effects. With such efforts, *G. lucidum* may link the gap between traditional medicine and modern pharmacology, establishing itself as an evidence-based functional food and therapeutic agent.

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