

Advances in the pharmacological research of *Ganoderma lucidum*: from traditional Chinese medicine to modern clinical applications

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Author contributions

Zhang YK was responsible for writing the manuscript, reviewing and editing. Yao Y, Liu ZJ and Wang XJ participated in the manuscript revision. Zhang YK and Yang BX were responsible for overseeing and writing comments. Yang BX was involved in the conceptualization, supervision and review. All authors contributed to the article and approved the final submitted version.

Competing interests

The authors declare no conflicts of interest.

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Abbreviations

G. lucidum, *Ganoderma lucidum*; TCM, Traditional Chinese Medicine; GLPs, *Ganoderma lucidum* polysaccharides; GA, Ganoderic acid; GTs, *Ganoderma* triterpenes; MAPK, Mitogen-activated protein kinase; TLR, Toll-like receptor; MyD88, Myeloid differentiation primary response 88; NF- κ B, Nuclear factor- κ B; TNF- α , Tumor necrosis factor- α ; IL-1 β , Interleukin-1 β ; NK, Natural killer; Th1/Th2/Th17/Treg, T helper 1/T helper 2/T helper 17/Regulatory T; AD, Alzheimer's disease; PD, Parkinson's disease; A β , Amyloid-beta; I/R, Ischemia/reperfusion; AKI, Acute kidney injury; CKD, Chronic kidney disease; Scr, Serum creatinine; BUN, Blood urea nitrogen; GFR, Glomerular filtration rate; LPS, Lipopolysaccharide; DN, Diabetic nephropathy; ADPKD, Autosomal dominant polycystic kidney disease; FAK, Focal Adhesion Kinase; IBS, Irritable Bowel Syndrome; DSS, Dextran sulfate sodium; ALT, Alanine transaminase; AST, Aspartate transaminase; HFD, High-fat diet; PTP1B, Protein tyrosine phosphatase 1B; hIAPP, Human islet amyloid polypeptide; CP, Cisplatin; GLSP, *G. lucidum* sporoderm-broken spore polysaccharide.

Citation

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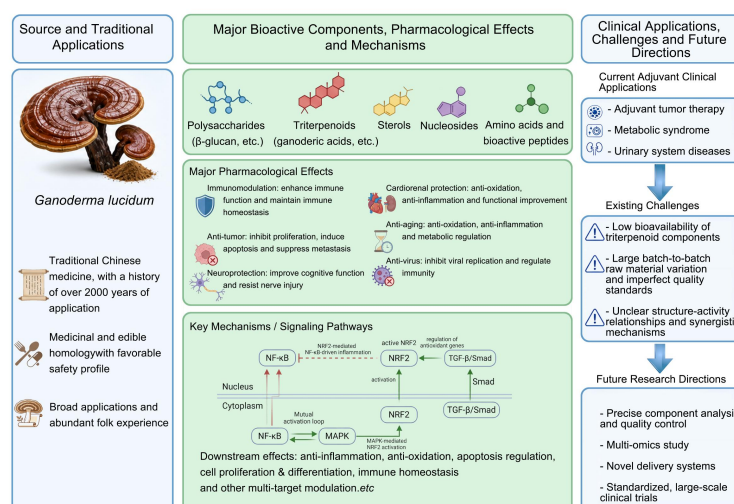
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Abstract

Ganoderma lucidum, a classical top-grade herbal medicine with over 2000 years of application history, is officially listed as a food-medicine homologous material. Its core bioactive substances include polysaccharides and triterpenoids (including ganoderic acids), alongside sterols, nucleosides and amino acids, which endow multi-target pharmacological properties. This review systematically summarizes extraction, structural characteristics and quality control bottlenecks of its key components, and elaborates comprehensive preclinical pharmacological effects covering immunoregulation, neuroprotection, cardiovascular and renal protection, gastrointestinal homeostasis, anti-tumor, anti-aging, radioprotection and antiviral activities, with underlying signaling pathways such as NF- κ B, MAPK, Nrf2 and TGF- β /Smad clarified. Current clinical trials suggest its auxiliary therapeutic value in tumors, metabolic syndromes and urinary tract disorders, yet high-quality multi-center clinical evidence remains insufficient. Critical challenges include unclear structure-activity relationships, low bioavailability of lipophilic triterpenoids, severe raw material batch variation and incomplete component synergism mechanisms. Future research directions involve precise component characterization, multi-omic mechanistic dissection, novel delivery system development and standardized large-scale clinical verification to facilitate translational application of *G. lucidum* in modern biomedicine.

Keywords: *Ganoderma lucidum*; Ganoderic acid; pharmacologic effect; bioactive compounds; clinical applications



Highlights

1. This review systematically interprets multi-target pharmacological profiles of *Ganoderma* polysaccharides and triterpenoids across multiple organ-related disease models.
2. It summarizes critical bottlenecks, including raw-material batch variation, ambiguous structure-activity relationships and insufficient high-quality clinical evidence for *Ganoderma* research.
3. Multi-omic strategies, novel drug delivery systems and large-scale clinical trials are proposed to advance translational applications of *Ganoderma* bioactive constituents.

Medical history of objective

Ganoderma lucidum (Lingzhi), a renowned traditional Chinese medicinal fungus, boasts a medicinal application history of over 2,000 years, rooted in the core TCM theories of “tonifying primordial qi”, “regulating zang-fu organs” and “calming mind and soothing nerves”. The earliest textual record of lingzhi dates back to the pre-Qin classics. Its medication logic adheres to the holistic concept of traditional Chinese medicine, focusing on overall bodily conditioning rather than single-symptom relief, forming a complete theoretical and practical system for health preservation and treatment. *Ben Cao Gang Mu* (Compendium of Materia Medica), written by Li Shizhen in the Ming Dynasty (1578 AD), refined the properties and indications of Lingzhi, confirming its mild nature, non-toxicity, and long-term edible safety, and summarized its core effects of tonifying qi (qi, vital energy), calming the mind, relieving cough and asthma.

Introduction

Ganoderma, referred to as “Lingzhi” within traditional Chinese medicine (TCM), was categorized as a “superior medicinal herb” in Shen Nong Ben Cao Jing. Boasting a medicinal heritage of more than 2,000 years, it is widely recognized for its functions of tonifying qi, tranquilizing the mind, and alleviating cough and asthma. As a typical representative of the integration of TCM and modern biomedicine, *Ganoderma* has been officially included in the list of “food and medicinal homologous substances” and “health food raw materials” in recent years, with its application expanding from TCM formulations to modern health products, pharmaceutical preparations and clinical adjuvant therapy, showing broad application prospects.

The *Chinese Pharmacopoeia* (2025 edition) defines *Ganoderma* as the dried fruiting bodies of two species of fungi from the *Ganoderma* taceae family: *Ganoderma lucidum* (Leyss. ex Fr.) Karst. (Chizhi) and *Ganoderma sinense* Zhao, Xu et Zhang (Zizhi); *Ganoderma lucidum* (*G. lucidum*) is characterized by an umbrella-shaped, reddish-brown to yellowish-brown pileus with a glossy surface and annular ridges, while *Ganoderma sinense* features a purplish-black pileus with a lacquer-like luster and rust-brown context, and cultivated products are generally stouter and thicker with powdery spores on the surface (Figure 1).

The bioactive components of *Ganoderma* are diverse and complex, mainly including triterpenoids, polysaccharides, sterols, amino acids and nucleosides, among which polysaccharides (mainly glucans with diverse glycosidic linkages), triterpenoids (over 300 types, mainly tetracyclic lanostane-type and pentacyclic triterpenoids such as ganoderic acids) and sterols (mainly ergosterol and its derivatives) are the core active fractions, serving as the material basis for its pharmacological activities (Figure 2).

Over the past decades, a wealth of *in vitro* and *in vivo* studies has demonstrated that *Ganoderma* possesses a range of potent pharmacological properties, including immunomodulation, antitumor activity, hepatoprotection, antioxidant activity, anti-inflammatory activity, and neuroprotection. Substantial advances have also been

achieved in deciphering its molecular mechanisms and advancing its clinical translation. However, there are still obvious gaps in the current research, such as unclear structure-activity relationships of partial active components, insufficient clinical evidence for some pharmacological effects and bottlenecks in clinical translation. Therefore, this review intends to systematically summarize the research progress on the active components of *Ganoderma*, the current status of its main pharmacological effects, the advances in clinical transformation and the existing problems, aiming to clarify the core direction of *Ganoderma* pharmacological research, highlight its application potential, and provide a comprehensive theoretical basis and reference for the in-depth research, development and utilization of *Ganoderma* resources in the future.

Core bioactive components of *G. lucidum* and their basic research**Polysaccharides from *G. lucidum***

Polysaccharides are the representative bioactive macromolecules in *G. lucidum*. Their varied structural features are strongly associated with pharmacological functions. These polysaccharides mainly consist of monosaccharide units including glucose, galactose and mannose connected by diverse glycosidic linkages, and are categorized as β -glucans, heteropolysaccharides and proteoglycans. Among them, the specific structure built by the β -(1 $\rightarrow$ 3)-D-glucan main chain and β -(1 $\rightarrow$ 6)-D-glucan side chains are considered key sites for their immunomodulatory activity [1].

In terms of extraction and purification, traditional methods include hot water extraction [2], acid/alkali extraction [3] and enzyme-assisted extraction [4]. Modern techniques such as ultrasound-assisted extraction, microwave-assisted extraction and supercritical fluid extraction can significantly improve extraction efficiency while preserving the bioactivity of polysaccharides. Purification steps typically involve ethanol precipitation, ion exchange chromatography and gel filtration chromatography to obtain homogeneous polysaccharide fractions. Studies have shown that the molecular weight, degree of branching and spatial conformation of polysaccharides are important factors affecting their biological activity. For example, high-molecular-weight β -glucans exhibit stronger activity in activating macrophages and promoting cytokine release. However, due to its large molecular weight, complex structure and poor stability, current research is primarily focused on its pharmacological efficacy. There are still certain difficulties in studying its targets, mechanisms and structure-activity relationships.

Triterpenoids from *G. lucidum*

Triterpenoids are another important class of active components in *G. lucidum*, belonging to the tetracyclic and pentacyclic triterpenoid compounds. To date, 540 triterpenoid components with 114 kinds parent nucleus have been isolated and identified [5]. According to the structure of *Ganoderma* triterpenoids (GTs), they can be classified into Ganoderic acid and neutral GTs. In Ganoderic acid, there are 8, 9-ene-ganoderic acid, 7,9 (11)-diene-ganoderic acid, other Ganoderic acids and ganoderic acid esters. Neutral triterpenoids are classified into 8, 9-ene-neutral triterpenoids, 7,9 (11)-diene-neutral triterpenoids and other neutral triterpenoids. Most of these triterpenoids have relatively complex isolation conditions, and it is impossible to obtain sufficient quantities for cell and animal experiments. Therefore, the research on the structure-activity relationship of triterpenoids in *G. lucidum* is still very lacking [6]. Among these, Ganoderic acid (GA-A, GA-B, GA-C, GA-D) and ganodermanediol are the most widely studied representative components. The typical triterpene skeleton structure of *G. lucidum* and its pharmacological activities are shown in Figure 3.

Structure-activity relationship studies showed that the pharmacological activities of triterpenoids are closely related to the functional groups in their molecules. For example, structural features such as the hydroxyl group at the C-3 position, the carbonyl group at

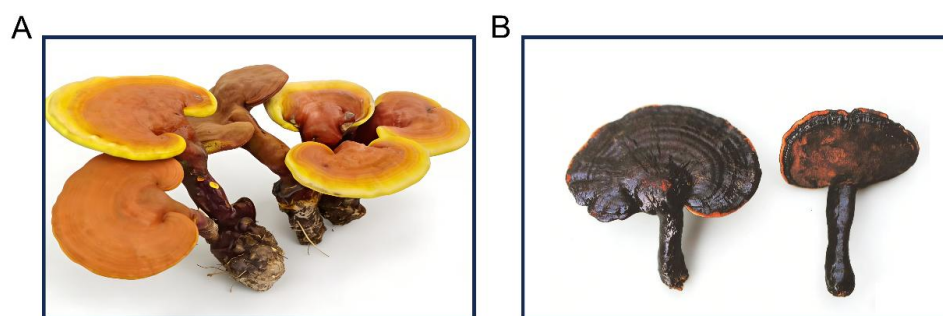


Figure 1 Representative pictures of *Ganoderma lucidum* (Leyss. ex Fr.) Karst. (Chizhi) and *Ganoderma sinense* Zhao, Xu et Zhang (Zizhi). (A) *Ganoderma lucidum* (Leyss. ex Fr.) Karst. (Chizhi). (B) *Ganoderma sinense* Zhao, Xu et Zhang (Zizhi).

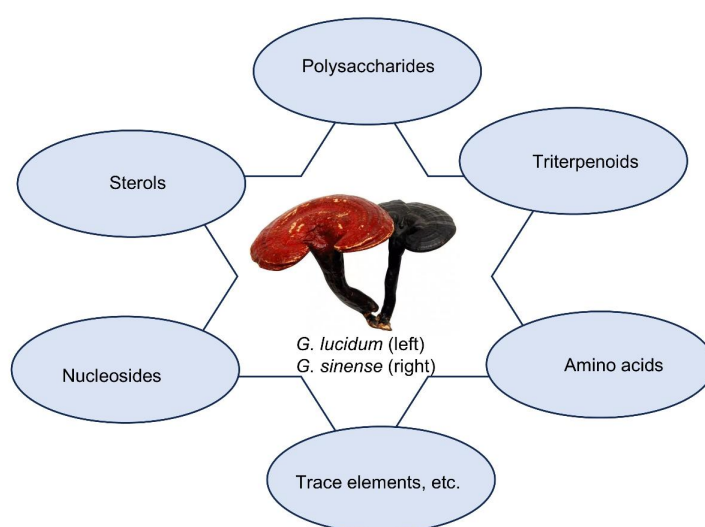


Figure 2 Bioactive components of *Ganoderma lucidum* (*G. Lucidum*) and *Ganoderma sinense*.

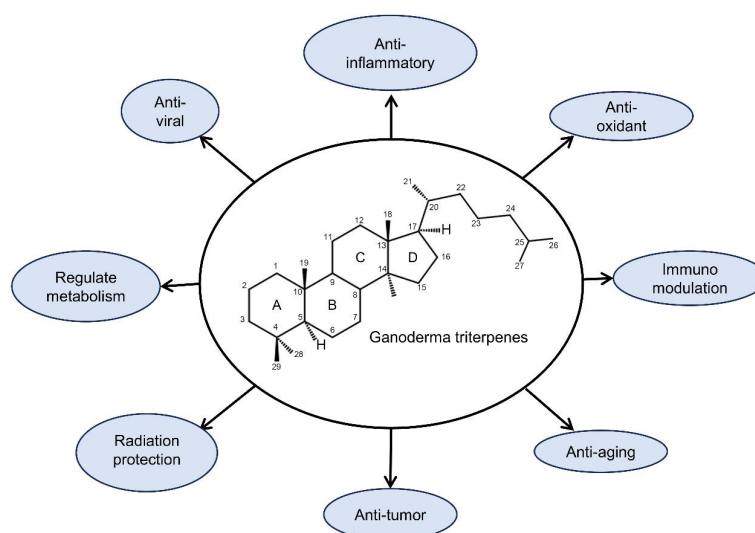


Figure 3 The typical triterpene skeleton structure of *G. lucidum* and its pharmacological activities.

the C-7 position and the carboxyl group on the side chain have important effects on their anti-tumor, anti-inflammatory and hepatoprotective activities. Specifically, Ganoderic acid (GA)-A, which contains multiple hydroxyl and carboxyl groups, shows a strong ability to inhibit tumor cell proliferation [7] and induce apoptosis [8]. Some of the structure-activity studies have shown that conjugated double bonds in GTs, including side-chain Δ^{20} , Δ^{22} , Δ^{24} , Δ^{25} , and core Δ^7 , $^8/\Delta^9$, are usually beneficial for almost all biological activities. The C15

site is a multifunctional active site: hydroxyl or acetoxy substitution significantly enhances anti-tumor, anti-inflammatory and hypoglycemic capabilities, while C15 ketone substitution leads to the loss of activity. Free side-chain carboxyl groups (-COOH) are crucial for hypoglycemic activity (inhibition of aldose reductase and α -glucosidase) and hepatoprotective activity, while methyl esterification significantly reduces the corresponding biological activity. It is worth noting that methyl ester modification, as an exception, selectively

enhanced the promoting activity of type I microtubules. Carbonyl groups exhibit bidirectional regulatory effects: the C3 carbonyl group on the type II skeleton enhances microtubule regulatory activity, while the C11 or C23 ketone components inhibit hypoglycemic and anti-inflammatory efficacy. In addition, the stereochemical configuration also dominates biological activity [9, 10]. Specifically, the substitution of C3 β has better therapeutic effects compared to its α epimer [11], while the substitution of C15 α shows superior efficacy relative to its β epimer [12]. Research on structure-activity relationships based on different animal or cell models still needs to be further deepened.

Sterols and other bioactive components from *G. lucidum*

Beyond polysaccharides and triterpenoids, *G. lucidum* possesses numerous additional bioactive constituents, such as sterols, nucleosides, amino acids, and peptides. Sterol components such as ergosterol and its derivatives are precursors of vitamin D and have roles in regulating calcium and phosphorus metabolism and immune modulation [13, 14]. Nucleoside components such as adenosine and uridine have effects on improving microcirculation, inhibiting platelet aggregation and sedation [15]. Furthermore, various amino acids (e.g., lysine, glutamic acid) and small-molecule peptides in *G. lucidum* are also involved in regulating the body's metabolism and immune responses. However, these components are not unique to *G. lucidum* and thus will not be discussed in detail in this review.

Batch variability of core components and modern quality control strategies

Ganoderma lucidum polysaccharides (GLPs) and triterpenoids show drastic batch fluctuations with multiple-fold content differences. Geographical origin causes GLP levels ranging 0.22%–3.31% (15-fold) and total triterpenoids 0.21%–10.56% (over 50-fold). Linden log cultivation yields 2–3 times more triterpenoids than bag cultivation, while hot water extraction recovers > 85% GLPs yet only 3%–8% triterpenoids; ethanol extraction captures over 90% triterpenoids but $\leq$ 5% GLPs, and extraction parameters alter component recoveries by 2–4 folds. To address such inconsistency, integrated quality control systems are essential. High-Performance Liquid Chromatography / Ultra Performance Liquid Chromatography triterpenoid fingerprints and High-Performance Gel Permeation Chromatography

polysaccharide molecular weight profiles serve as core identification tools, with a similarity threshold ≥ 0.90 . Multi-parameter evaluation covers ITS2 species authentication, dual limits of $\geq 0.9\%$ GLPs and $\geq 0.5\%$ total triterpenoids, fingerprint matching, and safety detection. Uncontrolled batch variation hinders industrial translation and clinical reproducibility. Full-chain traceability combining standardized cultivation, unified extraction, and mandatory multi-marker fingerprint testing is required to stabilize raw material quality and support consistent clinical and industrial applications of *G. lucidum*.

Major pharmacological effects and mechanisms of *G. lucidum*

Similar to other TCMs, *G. lucidum* possesses characteristics such as "multi-component, multi-target". Most importantly, through the coordinated and combined effects of its anti-inflammatory, antioxidant and immune-regulating properties, it can "strengthen the body's vital energy and consolidate the foundation", thereby improving diseases. Organ-specific pharmacological effects of GLPs and GTs were shown in Figure 4.

Effect of *G. lucidum* on immunomodulation and immune-related diseases

The active and effective components in *G. lucidum*, such as GLPs and GTs, have been proven to exhibit immunomodulatory activities in *in vivo* studies. *Ganoderma* exerts a profound regulatory effect on both innate and adaptive immune systems. Polysaccharides and triterpenoids serve as the major bioactive substances that mediate the above biological functions. In terms of innate immune regulation, GLPs can trigger macrophage activation, which potentiates phagocytic capacity and stimulates the release of pro-inflammatory cytokines, including tumor necrosis factor- α (TNF- α) and interleukin-1 β (IL-1 β). Furthermore, GLPs strengthen the cytotoxicity of natural killer (NK) cells [12, 16], which act as a pivotal innate immune barrier to eliminate virus-infected and mutated cells. The immunomodulatory mechanisms of GLPs are speculated to involve the modulation of macrophage polarization, dendritic cell maturation, as well as T and B lymphocyte activation. These biological processes ultimately activate key signaling cascades, such as the Toll-like receptor (TLR) 4/myeloid

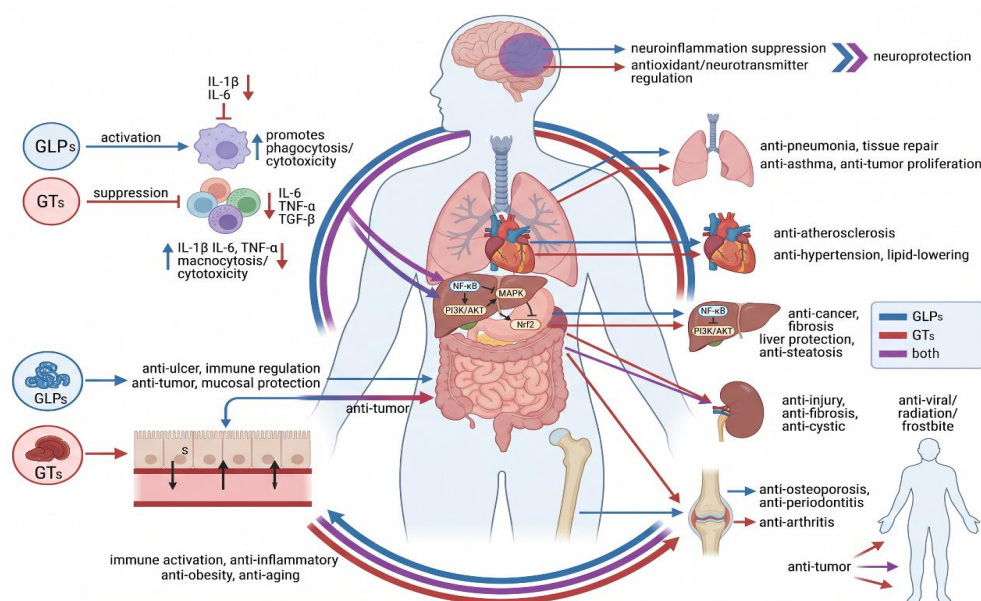


Figure 4 Organ-specific pharmacological effects of GLPs and GTs.

GLPs, *Ganoderma lucidum* polysaccharides; GTs, *Ganoderma* triterpenoids; IL, Interleukin; TNF- α , tumor necrosis factor- α ; TGF- β , Transforming growth factor- β .

differentiation primary response 88 (MyD88)/nuclear factor- κ B (NF-

κ B) axis [12], NOD-like receptor thermal protein domain associated

protein 3 (NLRP3) inflammasome [3], and mitogen-activated protein kinase (MAPK) signaling pathway [17]. Collectively, these pathways synergistically boost both innate and adaptive immune responses. Recent research further indicates that polysaccharides can also reshape the gut microbiota-immune metabolism axis by promoting the production of short-chain fatty acids and activating receptors (such as G protein-coupled receptor 43), indirectly regulating systemic immune responses [18]. In adaptive immunity, *Ganoderma* extracts modulate the proliferation and differentiation of T and B lymphocytes. Specifically, they promote the differentiation of CD4⁺ helper T cells (Ths), particularly the Th1 subset, which is crucial for cell-mediated immunity, and stimulate B-cell maturation and antibody production, thereby enhancing humoral immunity [19].

The immunomodulatory effects of *Ganoderma* are mediated through the modulation of key signaling pathways. A primary target is the NF- κ B pathway, a central regulator of inflammation and immune responses. *Ganoderma* components, such as polysaccharides, can activate NF- κ B in immune cells, leading to the transcription of genes encoding pro-inflammatory cytokines and co-stimulatory molecules in *in vitro* and *in vivo* study [18, 20]. Conversely, in pathological conditions characterized by excessive inflammation, certain triterpenoids, including GA-A [21], lucidumol A, ganoderiol J, ganoderterpene A, ganodermanontriol and lucidone D [22], have been shown to inhibit NF- κ B activation, thereby exerting anti-inflammatory effects in *in vitro* and *in vivo* studies. Additionally, GLPs are believed to activate pattern recognition receptors [23, 24], particularly TLRs, such as TLR-4.

Based on the above immune modulatory effects, *Ganoderma* extracts show promise in various disease contexts. In models of immunodeficiency, particularly in patients with advanced cancer [25, 26], *Ganoderma* extracts have been shown to restore immune cell counts and function, thereby improving host resistance to infections. For autoimmune diseases such as rheumatoid arthritis [27–29] and systemic lupus erythematosus [30], *Ganoderma*'s ability to regulate the balance between pro- and anti-inflammatory cytokines and to suppress overactive immune responses presents a potential therapeutic strategy.

Asthma is a heterogeneous airway inflammatory disease. GA-A can alleviate asthma by regulating and inhibiting the TLR/NF- κ B signaling pathway in ovalbumin-induced mice [31]. In addition, GA-C1 alleviates asthma by inhibiting the NF- κ B signaling pathway and partially inhibiting the MAPK and Activator Protein-1 signaling pathways in an *in vitro* study, thereby reducing TNF- α level produced by macrophages and neutrophils [32]. Besides, *G. lucidum* has also been found to regulate allergic asthma in a mouse model through its anti-inflammatory effects [33].

A water-soluble β -glucan extracted from *G. lucidum* significantly promotes delayed-type ear swelling induced by dinitrochlorobenzene in mice [34]. *In vivo* murine research has demonstrated that GLP-2, a polysaccharide fraction isolated from *G. lucidum* originating from Mount Taishan, is capable of modulating immune cell differentiation by driving the transformation of Th0 cells into Th1 cells. This bioactive component also suppresses mast cell infiltration, modulates serum levels of IgE and the inflammatory mediator IL-4, and ameliorates inflammatory responses via the MAPK/NF- κ B signaling cascade. Through the above regulatory effects, GLP-2 facilitates the restoration of impaired skin barrier function and effectively relieves atopic dermatitis symptoms in murine models [35]. The polysaccharide component extracted from *G. lucidum* spore powder can alleviate colonic inflammation induced by dextran sulfate sodium (DSS) in mice by regulating the Th17/Treg balance, restoring the balance of gut microbiota [36]. In DSS-induced colitis in mice, the ethanol extract of *G. lucidum* has also been shown to have similar effects [37]. *G. lucidum* spore powder can alleviate pain and hypersensitivity associated with rheumatoid arthritis by inhibiting the accumulation and N1 polarization of neutrophils in mice [38]. Research indicates that *Ganoderma* can reduce autoantibody production and alleviate disease symptoms in animal models, suggesting its potential as an adjunctive therapy for autoimmune conditions.

In all, the immune-regulating effect of *Ganoderma lucidum* extract and its improvement effect on immune-related diseases are summarized in Figure 5.

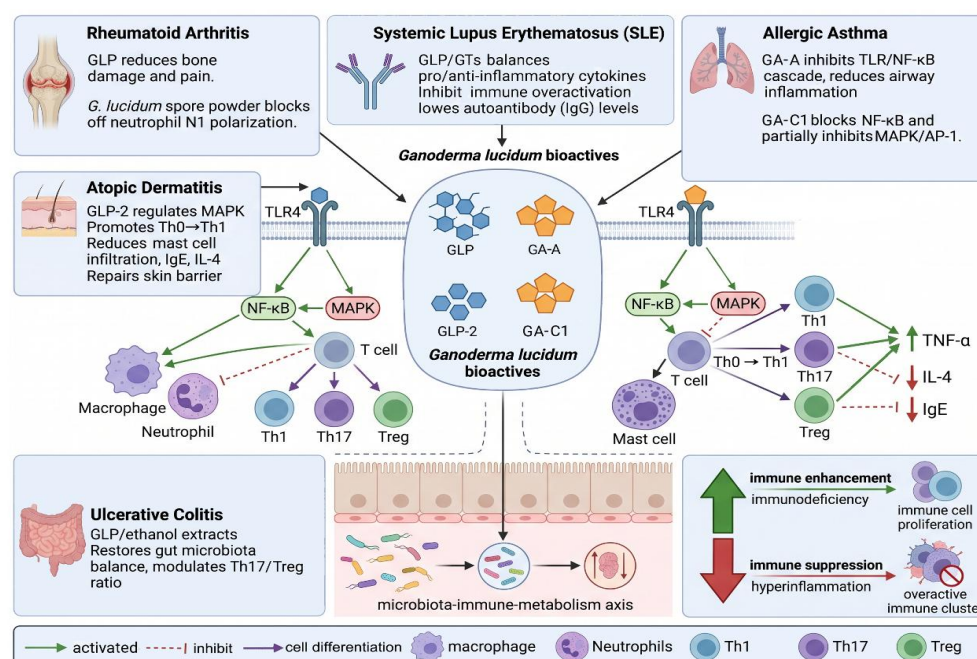


Figure 5 *Ganoderma lucidum* extract alleviates immune-related diseases and the underlying mechanisms.

GLP, *Ganoderma lucidum* polysaccharide; GTs, Ganoderma triterpenoids; GA-A, Ganoderic acid A; GA-C1, Ganoderic acid C1; TLR4, Toll-like receptor 4; NF- κ B, Nuclear factor- κ B; MAPK, Mitogen-activated protein kinase; Th1, T helper 1 cell; Th 17, T helper 17 cell; IL, Interleukin; TNF- α , tumor necrosis factor- α ; IgE, Immunoglobulin E; RA, Rheumatoid Arthritis; SLE, Systemic Lupus Erythematosus.

Effect of *G. lucidum* on the nervous system

Previous studies have indicated that *G. lucidum* extract may improve

central and peripheral nervous system diseases by nourishing nerves [39], inhibiting neuroinflammation [40] and reducing oxidative stress.

G. lucidum is mostly consumed orally, can regulate gut microbiota homeostasis and short-chain fatty acid levels through the brain-gut axis [41]. Irritable bowel syndrome (IBS) is a prevalent functional gastrointestinal illness predominantly manifested as visceral hypersensitivity and abnormal intestinal peristalsis. A previous animal study conducted by Kou *et al.* revealed that GA-A exerts regulatory effects on enteric neurons and intestinal microecological homeostasis [42]. Mechanistically, GA-A remodels the composition of intestinal flora, alters the abundance of pivotal bacterial taxa involved in tryptophan metabolism, and elevates the generation of indole-3-aldehyde. These metabolic alterations ultimately trigger the activation of the aryl hydrocarbon receptor signaling pathway in mice [42]. In HT22 cells and the zebrafish model, compounds extracted from *Ganoderma calidophilum*, such as gacalitone F, may exert neuroprotective effects through the brain-gut axis [43]. A study based on a dynamic simulator of the human gut microbiota ecosystem suggests that *G. lucidum* may potentially play a role in regulating mood disorders through gut microbiota [44].

Some literature also indicates that small molecular polysaccharides from *G. lucidum* and some triterpenoids from *G. lucidum* can protect the blood-brain barrier and exert their effects in the central nervous system in mouse models [45]. Emerging evidence suggests that *Ganoderma* exerts neuroprotective effects in various neurodegenerative diseases, such as Alzheimer's disease (AD) and Parkinson's disease (PD) [46–48]. In AD models, it inhibits the aggregation of amyloid-beta (A β) peptides and tau protein hyperphosphorylation, key pathological hallmarks of AD [49, 50]. In formaldehyde-exposed mice with cognitive dysfunction, *Ganoderma* ameliorates abnormal brain metabolism, reduces neuroinflammation and oxidative stress in the brain, protects neurons, and improves cognitive performance [51]. In addition, *G. lucidum* extract also has an improving effect on other age-related neurodegenerative diseases [52]. Combined supplementation with fermented *Moringa oleifera* leaves and *G. lucidum* has been proven to alleviate cognitive impairment in scopolamine-challenged dementia rat models. This protective effect is achieved by boosting cerebral antioxidant capacity and improving cholinergic system function [53]. Epilepsy can cause transient cerebral dysfunctions. Based on a series

of *in vitro* studies, various components in *G. lucidum* are effective against epilepsy. Moreover, GLPs may inhibit calcium overload and promote CaMKII α expression to protect epileptic neurons [54]. *G. lucidum* spores may protect hippocampal neurons by promoting neurotrophin-4 expression and inhibiting N-Cadherin expression [55]. In addition, in the *in vitro* and *in vivo* studies, *G. lucidum* has been proven to enhance memory [56] and improve age-related cognitive impairment [57, 58]. In conclusion, the effects of *G. lucidum* extracts on the nervous system were summarized in Figure 6.

Effects of *G. lucidum* on cardiovascular and cerebrovascular diseases

G. lucidum and its main active components (triterpenoids, polysaccharides, sterols, etc.) exhibit a wide range of pharmacological effects and potential applications in cardiovascular and cerebrovascular diseases such as hypertension, coronary heart disease, heart failure, arrhythmia and dyslipidemia, via various mechanisms including lowering blood pressure, lipid regulation, anti-atherosclerosis, anti-myocardial ischemia, cardiac function improvement, anti-arrhythmia, antioxidant, anti-inflammatory properties and vascular endothelium protection.

As early as 1988, scholars reported that *G. lucidum* could reduce blood pressure and serum and liver cholesterol levels in spontaneously hypertensive rats [59]. In 2018, Kumakura *et al.* proposed that protein components extracted from the fruiting body of *G. lucidum* contribute to the production of antihypertensive functional molecules in an *in vitro* study [60, 61]. Wu *et al.* identified three peptides with antihypertensive activity, namely Gln-Leu-Val-Pro (QLVP), Gln-Asp-Val-Leu (QDVL) and Gln-Leu-Asp-Leu (QLDL), from *G. lucidum* using mature ACE as a target in an *in vitro* study [62]. Rho kinase inhibitors represent promising therapeutic candidates for hypertension management. *In vitro* experimental evidence has verified that triterpenoids purified from the total ethanol extract of *G. lucidum* possess potent Rho kinase suppressive activity. This finding offers a novel mechanistic explanation for the antihypertensive properties of *G. lucidum*-derived triterpenoids [63].

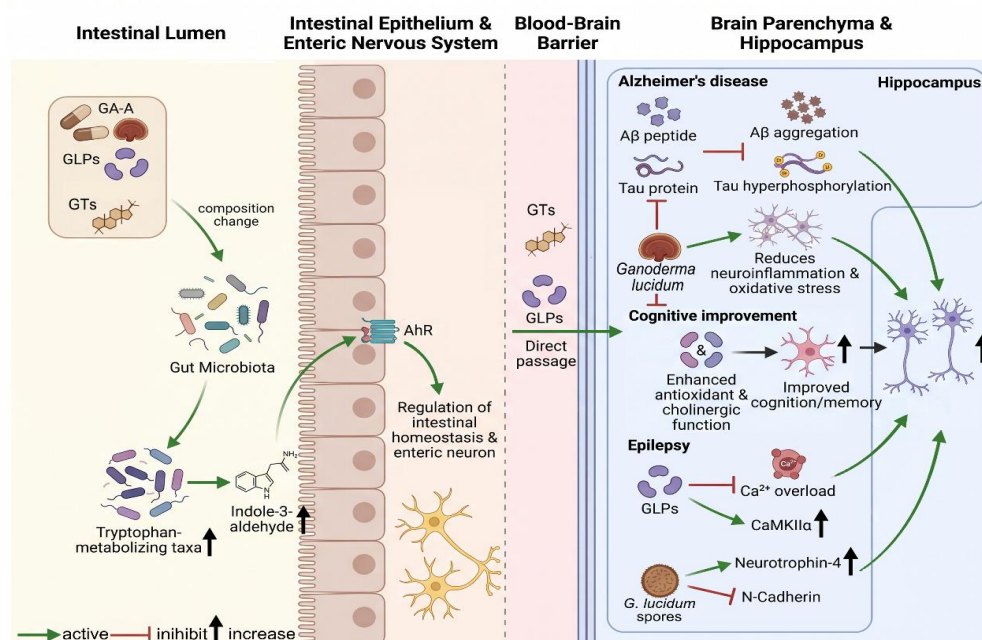


Figure 6 The effects of *G. lucidum* extracts on the nervous system.

GLP, *Ganoderma lucidum* polysaccharide; GTs, *Ganoderma* triterpenoids; GA-A, Ganoderic acid A; AhR, Aryl hydrocarbon receptor; A β , Amyloid β ; CaMKII α , Calcium/calmodulin-dependent protein kinase II α .

Heart diseases are considered a significant cause of global mortality. Myocardial ischemia is an important factor in atherosclerosis, angina pectoris, etc. Polysaccharide peptides extracted from *G. lucidum*

contain the active substance β -glucan, which has been proven to improve endothelial dysfunction and alleviate ischemia in a clinical trial by its antioxidant effect [64]. In a rat myocardial ischemia-

reperfusion (I/R) model, prophylactic administration of *G. lucidum* extract reduced myocardial cell necrosis and reperfusion contracture [65]. GLPs also have a protective effect on hypoxic injury of neonatal rat cardiomyocytes [66]. Accumulating evidence has indicated that *G. lucidum* can mitigate myocardial mitochondrial injury in rats with myocardial infarction. This protective effect is closely associated with the improved activity of key enzymes involved in the tricarboxylic acid cycle and elevated function of mitochondrial respiratory chain complexes [67]. Thus, the alleviating effect of *G. lucidum* on myocardial ischemia is closely related to its antioxidant activity. Moreover, Z16b, a natural compound from *Ganoderma cochlear*, can act as an RyR2 stabilizer to prevent catecholaminergic polymorphic ventricular tachycardia in a mouse model [68].

Abnormal blood lipids are the main risk factor for cardiovascular and cerebrovascular diseases. GLPs and GTs have been proven to correct blood lipids in animal models. Mechanistically, the role of GLPs in balancing blood lipids may be related to improving fat metabolism [69], increasing insulin sensitivity and improving glucose metabolism [70, 71], as well as regulating microbiota and fecal metabolism [72, 73]. The polysaccharide extract of applanatum can significantly lower the levels of total cholesterol, triglycerides, low-density lipoprotein cholesterol and atherosclerosis index of MACAPOS-2-induced obese rats [74]. However, ethanol extracts of *Ganoderma* spores have been shown to improve blood lipids by upregulating liver X receptor α [75].

Stroke is considered one of the leading causes of disability and death globally, posing significant challenges, especially in developing countries. The mechanism by which it alleviates ischemic stroke is related to the inhibition of oxidative stress and inflammation [76]. In depth, Ma *et al.* confirmed that multiple acidic triterpenoids in *G. lucidum* can directly interact with Myeloid Differentiation protein 2 (MD2), which is verified by a variety of combination experiments, including surface plasmon resonance, inhibiting neuroinflammation

and alleviating stroke in a mouse transient middle cerebral artery occlusion model [77]. In summary, the effects and potential mechanisms of *G. lucidum* extract on the cardiovascular and cerebrovascular systems are shown in Figure 7.

Effects of *G. lucidum* on the urinary system

G. lucidum exerts multi-targeted protective effects on the urinary system by its bioactive components (e.g., polysaccharides, triterpenoids and methyl terpenes). Its pharmacological actions against common urinary system disorders are systematically summarized as follows:

The main causes of urinary bladder dysfunction are oxidative stress caused by I/R, secondary to benign prostatic hyperplasia, which is a major affliction of aging men. In a rabbit I/R model, *G. lucidum* shell-broken spore pretreatment completely suppressed the negative effects of I/R on compliance and contraction response [78]. A recent review identified *G. lucidum* as a natural product with potential benefits for bladder and lower urinary tract dysfunction [79]. Additionally, a randomized, double-blind, placebo-controlled dose-ranging clinical trial has validated the safety and efficacy of *G. lucidum* extract. The results confirmed that this herbal formulation is well tolerated and capable of improving the International Prostate Symptom Score. For adult males suffering from lower urinary tract symptoms, the optimal administration dosage of *G. lucidum* extract is determined to be 6 mg [80]. Renal diseases are generally grouped into acute kidney injury (AKI) and chronic kidney disease (CKD) based on their clinical progression. Numerous investigations have explored the renoprotective impacts of *G. lucidum* in renal disorders. *G. lucidum* effectively ameliorates renal function by reducing serum creatinine (Scr), blood urea nitrogen (BUN) and uric acid levels, while improving the glomerular filtration rate (GFR) in *in vitro* and *in vivo* experimental models.

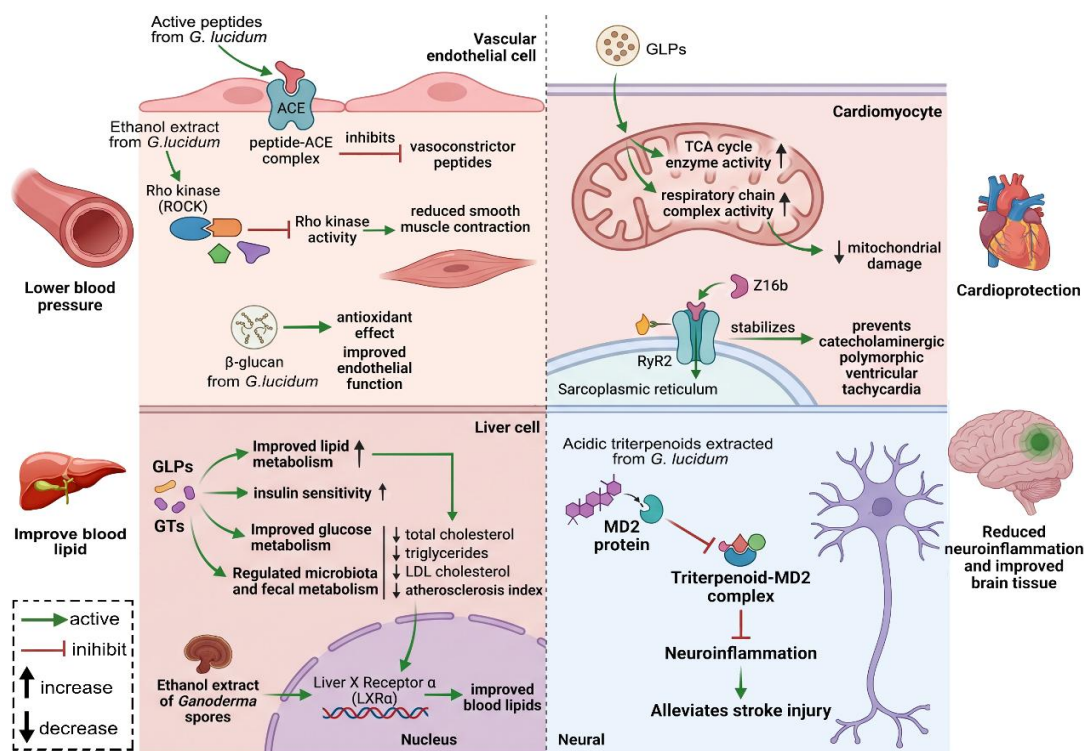


Figure 7 The effects and potential mechanisms of *G. lucidum* extract on the cardiovascular and cerebrovascular systems.

GLP, *Ganoderma lucidum* polysaccharide; GTs, *Ganoderma* triterpenoids; ACE, Angiotensin-converting enzyme; ROCK, Rho-associated protein kinase; TCA cycle, Tricarboxylic acid cycle; RyR2, Ryanodine receptor 2; LXR α , Liver X receptor α ; MD2, Myeloid differentiation protein 2; Z16b, Zinc finger protein 16b; LDL, Low-density lipoprotein.

It exhibits a significant protective effect against AKI induced by I/R [81, 82], nephrotoxic drugs [83, 84], lipopolysaccharide (LPS), as well as environmental toxins [85]. Furthermore, *G. lucidum* and its extracts mitigate tubular epithelial cell damage and delay the progression of

CKD, thereby maintaining the structural and functional integrity of the kidneys. In diabetic nephropathy (DN), the most prevalent cause of end-stage renal disease, *G. lucidum* alleviates renal hyperfiltration and hyperperfusion, the early pathological hallmarks of DN in mice.

Extracts from *G. lucidum* reduce urinary microalbuminuria and proteinuria by stabilizing the glomerular filtration barrier and protecting podocytes from damage. Mechanistically, it suppresses oxidative stress and inflammatory responses in the renal cortex, which are critical for inhibiting the progression of DN to renal failure in rats [86].

Renal interstitial fibrosis is the common pathological endpoint of all progressive CKD. GTs inhibit the transforming growth factor- β (TGF- β)/Smad signaling pathway, a key regulator of fibrosis [87, 88]. It reduces the deposition of extracellular matrix components (e.g. collagen and fibronectin) and suppresses the epithelial-mesenchymal transition of tubular epithelial cells, thereby effectively delaying renal interstitial fibrosis and renal sclerosis. Moreover, Liu *et al.* propose that *G. lucidum* sporoderm-broken spore powder alleviates kidney aging by modulating gut microbiota [89]. In conclusion, the protective effects of *G. lucidum* extract on both acute and chronic kidney injury are based on its direct or indirect anti-inflammatory effects.

Autosomal dominant polycystic kidney disease (ADPKD) ranks among the most prevalent hereditary disorders. It is distinguished by progressive formation of fluid-containing renal cysts originating from renal tubular epithelial cells. GTs [90], especially GA-A [91], inhibited cyst growth in the Madin-Darby Canine Kidney cyst model and the embryonic kidney cyst model *in vitro*, as well as in kidney-specific Pkd1 knockout mice *in vivo* (Figure 8). Its core mechanism suppresses Ras/MAPK signaling cascades and facilitates cellular differentiation. The effects of *G. lucidum* extract on the kidneys are summarized in Table 1 [81–86, 90–111].

Furthermore, we summarized potential mechanisms by which GLPs and GTs alleviate acute and chronic kidney injury (Figure 9, Figure 10).

Effects of *G. lucidum* on the digestive system

The digestive system is composed of the digestive tract and digestive glands, responsible for food intake, digestion and decomposition,

nutrient absorption and residue excretion, providing the body with important physiological systems for energy and nutrition. From an anatomical perspective, the digestive system begins in the oral cavity.

Research reports that freeze-dried powder from *G. lucidum* mycelia may alleviate recurrent oral ulcers by promoting CD4⁺ CD25⁺ Foxp3⁺ Treg cells and inhibiting T helper 17 cell differentiation in a rat model [112]. Oral submucous fibrosis has been identified as one of the potentially malignant disorders of the oral cavity. Epidemiological studies attribute this pathological fibrosis to the habit of chewing betel nut, which leads to chronic inflammation in the oral cavity and persistent activation of myofibroblasts in both *in vitro* and *in vivo* studies [113]. In an *in vitro* study, Lee *et al.* [114] found that after myofibroblasts were exposed to *Ganoderma* microsporium immunomodulatory protein, it suppressed pro-inflammatory cytokines and myofibroblast characteristics in fibrotic buccal mucosal fibroblasts and may serve as a promising natural anti-fibrotic agent.

Gastric ulcer is an ulcerative lesion of the gastric wall formed by the erosion of gastric acid and pepsin due to the imbalance of damage and defense of the gastric mucosa. The lifetime prevalence rate of gastric ulcer is about 10%. A novel galactoglucan derived from *G. lucidum* has been shown to ameliorate ethanol-induced gastric ulcers through the modulation of the Focal Adhesion Kinase (FAK)-MAPK signaling pathway in mice [115]. In addition, *G. lucidum* pharmacopuncture has been demonstrated to exert therapeutic effects on ethanol-induced chronic gastric ulcers [116] and acute gastric ulcers [117] in rat models. Moreover, polysaccharide fractions isolated from *G. lucidum* can accelerate the healing process of acetic acid-induced gastric ulcers in rats [118]. The antiulcerogenic mechanism of GLPs on indomethacin-induced gastric lesions in rats has also been explored [119]. Furthermore, mycelial polysaccharides from *Ganoderma lucidum* alleviate indomethacin-triggered small intestinal damage by stimulating macrophage-derived granulocyte-macrophage colony-stimulating factor in a murine model [120].

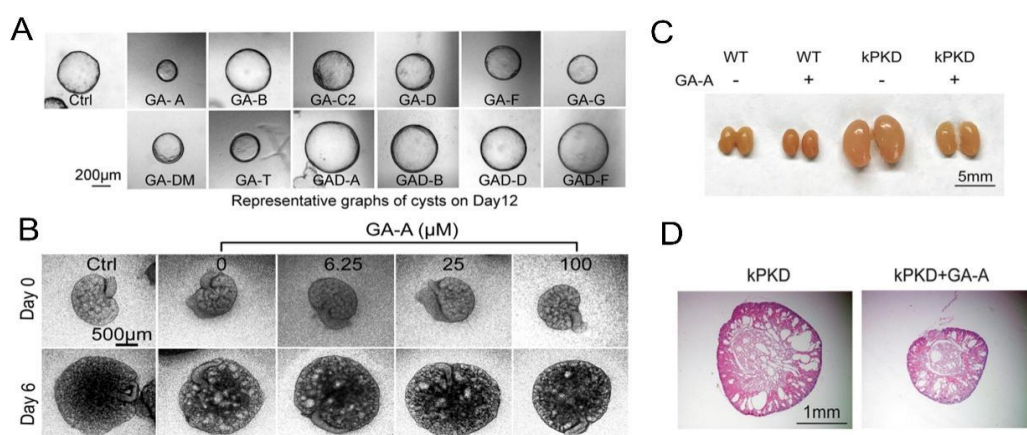


Figure 8 GA-A was identified as the active GT monomer in restorative renal cyst development.

A. Representative light micrographs of MDCK cysts in collagen gel on day 12, treated with the 12 GA monomers for the initial screening. GA-A, GA-B, GA-C2, GA-D, GA-F, GA-G, GA-DM and GA-T are the abbreviations for Ganoderic acid A, Ganoderic acid B, Ganoderic acid C2, Ganoderic acid D, Ganoderic acid F, Ganoderic acid G, Ganoderic acid DM and Ganoderic acid T, respectively. GAD-A, GAD-B, GAD-D and GAD-F are the abbreviations for Ganoderenic acid A, Ganoderenic acid B, Ganoderenic acid D and Ganoderenic acid F, respectively. Scale bars, 200 μ m. B. Representative light micrographs of embryonic kidneys cultivated as the negative Ctrl (left) without 100 μ M 8-Br-cAMP or exposed to different GA-A concentrations (0, 6.25, 25 and 100 μ M) in the presence of 100 μ M 8-Br-cAMP on day 0 and day 6. Scale bar = 500 μ m. C. Mouse kidneys from wild-type (WT) mice and kPKD mice on postnatal day 4 were treated with vehicle or 50 mg/kg/d GA-A for 4 days. Scale bar, 5 mm. D. Hematoxylin and eosin staining of kidneys in vehicle- or GA-A-treated kPKD mice. Scale bar, 1 mm. Reproduced with permission. Meng J, Sai-Zhen Wang, He JZ, et al. Ganoderic acid A is the effective ingredient of *Ganoderma* triterpenes in retarding renal cyst development in polycystic kidney disease. *Acta Pharmacol Sin.* 2020;41(6):782–790. Copyright 2019, Chinese Pharmacological Society and Shanghai Institute of Materia Medica, Chinese Academy of Sciences.

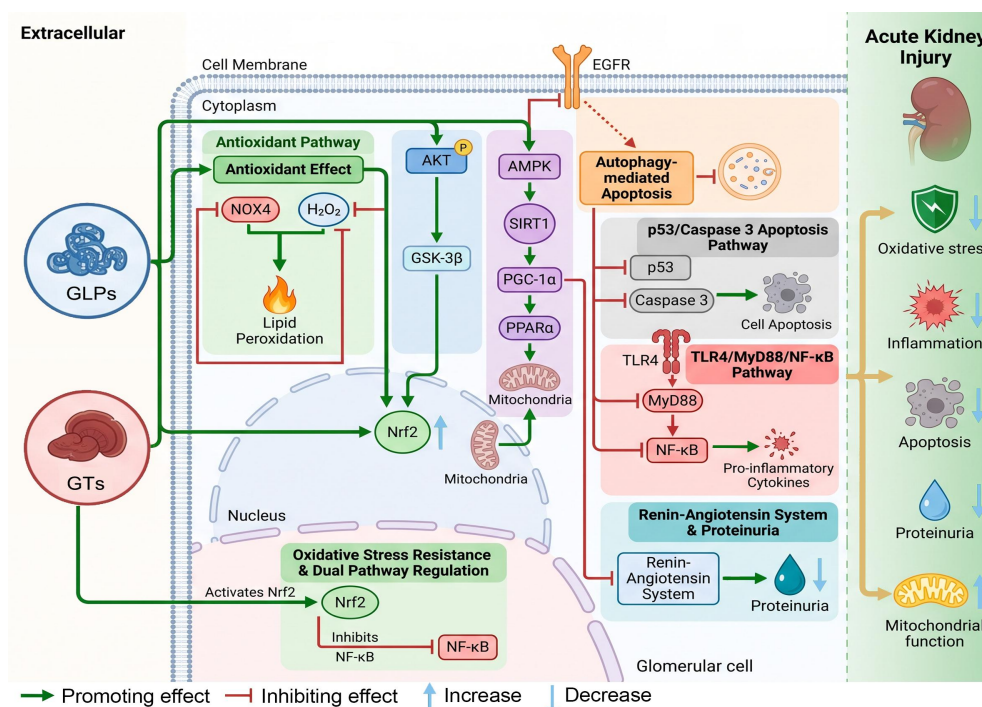


Figure 9 Potential mechanisms of GLPs and GTs in alleviating AKI.

GLPs, *Ganoderma lucidum* polysaccharides; GTs, *Ganoderma* triterpenoids; EGFR, Epidermal growth factor receptor; AKT, Protein kinase B; AMPK, Adenosine 5'-monophosphate-activated protein kinase; SIRT1, Silent information regulator 1; GSK-3β, Glycogen synthase kinase-3β; PGC-1α, Peroxisome proliferator-activated receptor γ coactivator-1α; PPARα, Peroxisome proliferator-activated receptor α; NOX4, NADPH oxidase 4; Nrf2, Nuclear factor erythroid 2-related factor 2; TLR4, Toll-like receptor 4; MyD88, Myeloid differentiation primary response protein 88; NF-κB, Nuclear factor-kappa B.

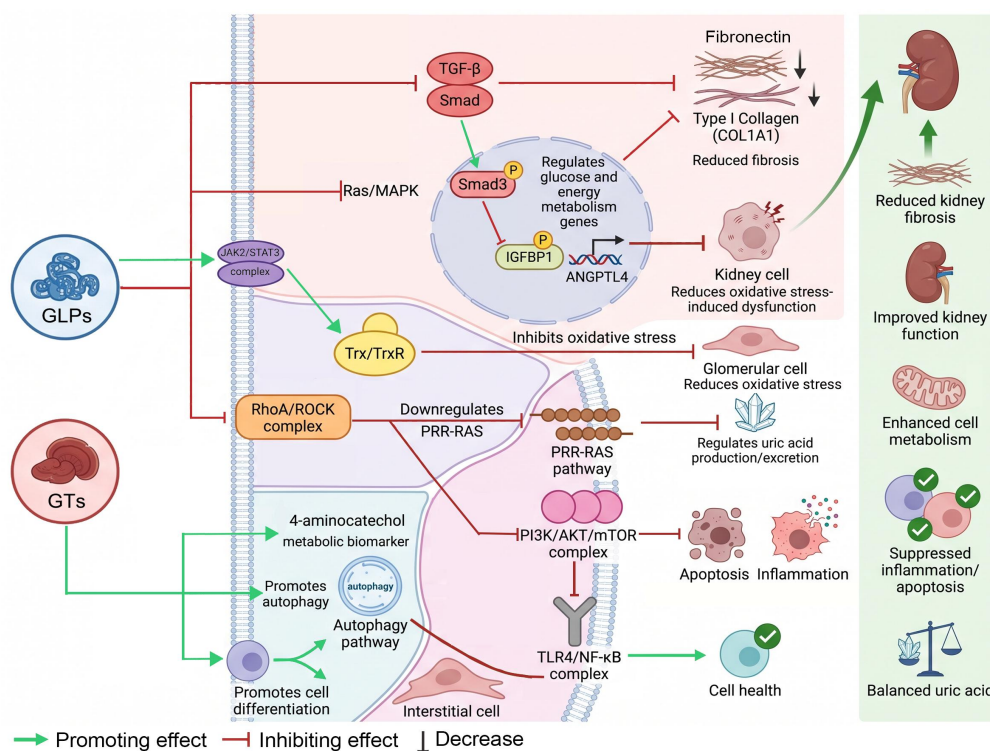


Figure 10 Potential mechanisms of GLPs and GTs in alleviating CKD.

GLPs, *Ganoderma lucidum* polysaccharides; GTs, *Ganoderma* triterpenoids; TGF-β, Transforming growth factor-β; MAPK, Mitogen-activated protein kinase; JAK2, Janus kinase 2; STAT3, Signal transducer and activator of transcription 3; Trx, Thioredoxin; TrxR, Thioredoxin reductase; ROCK, Rho-associated protein kinase; PRR-RAS, (Pro)renin receptor-renin-angiotensin system; PI3K, Phosphoinositide 3-kinase; AKT, Protein kinase B; mTOR, Mammalian target of rapamycin; TLR4, Toll-like receptor 4; NF-κB, Nuclear factor-kappa B; IGFBP1, Insulin-like growth factor binding protein 1; ANGPTL4, Angiotensin-like protein 4; COL1A1, Collagen type 1 alpha 1 chain.

Table 1 The effect of *G. lucidum* extract on the kidneys

Active ingredient	Animal model	Cellular model	Mechanisms	References
Acute kidney injury (AKI)				
<i>G. lucidum</i>	Cisplatin-induced nephrotoxicity in ICR mice, Cisplatin-induced nephrotoxicity in rats	Cisplatin-treated RAW264.7 cells,	Antioxidant effect, Inhibition of epidermal growth factor receptor signaling and autophagy-mediated apoptosis	[83, 84]
<i>G. lucidum</i> polysaccharide peptides	Cisplatin-induced nephrotoxicity in C57BL/6 mice	Cisplatin-treated NRK52E cells	Activating the protein kinase B/glycogen synthase kinase-3 beta/nuclear factor erythroid 2-related factor 2 signaling pathway	[92]
The methanolic extracts of <i>Ganoderma tuberculosum</i> Murill., <i>Ganoderma parvigibbosum</i> Welte & Courtec.	/	Human proximal tubular cells (HK-2) intoxicated by cisplatin	Prevented a loss of viability, apoptosis Prevented ROS overproduction and exhibited scavenger activity	[93]
Terpenes isolated from <i>G. lucidum</i>	Cisplatin-induced nephrotoxicity in mice	/	Inhibits renal tissue lipid peroxidation	[94]
<i>G. lucidum</i> polysaccharide peptide	Doxorubicin-induced nephropathy in BALB/c mice	/	Modulation of the renin-angiotensin system and proteinuria, and inhibits the upregulation of NOX4 and H ₂ O ₂	[95]
<i>G. lucidum</i> (Leyss. ex Fr.) Karst spore	Gentamicin-induced rat AKI model	/	Reducing apoptosis via p53/Caspase 3 signaling pathway	[96]
Ganoderic Acids	Renal I/R injury in C57 mice	Hypoxia/reoxygenation model in NRK52E cells	Inhibiting TLR4/MyD88/NF- κ B signaling pathway	[81]
<i>G. lucidum</i> polysaccharide peptide	Renal I/R injury in C57 mice	Hypoxia/reoxygenation model, and tunicamycin-stimulated NRK-52E cells	Counteracting oxidative stress	[82]
<i>G. lucidum</i> polysaccharide peptide (GL-PP2)	Sepsis-induced organ injury	/	Activating the Nrf2/NF- κ B pathways	[97]
Chronic kidney disease (CKD)				
Meroterpenoids from <i>G. lucidum</i>	/	TGF- β -treated NRK52E cells	Inhibit the expression of cellulose and collagen I	[98]
Ganoderic acid A	CCl ₄ -induced kidney inflammation, fibrosis, and oxidative stress in mice	/	Regulating the Trx/TrxR, JAK2/STAT3 and RhoA/ROCK pathways	[99]
Ganoderic acids	Unilateral ureteral obstruction mouse model	TGF- β -treated HK2 cells	Suppressing the TGF- β /Smad and MAPK signaling pathways	[100]
<i>G. lucidum</i>	/	TGF- β 1reated MDCK and CRFK cells	/	[101]
<i>G. lucidum</i> and <i>Robinia pseudoacacia</i> Flower Extract	0.25% adenine diet (AD) induces the mouse kidney fibrosis	LPS and H ₂ O ₂ -treated NRK52E cells	Inhibiting oxidative stress	[85]
Lingzhi lactones from <i>Ganoderma lingzhi</i>	Adriamycin-induced mice nephropathy	Rat tubular epithelial cells	Inhibition of Smad3 phosphorylation	[102]

Table 1 The effect of *G. lucidum* extract on the kidneys (Continued)

Active ingredient	Animal model	Cellular model	Mechanisms	References
Sporoderm-broken spores of <i>G. lucidum</i>	Diabetes mellitus induced by streptozotocin and a high-fat diet in Sprague-Dawley rats	/	Affecting the expression of glucose and energy metabolism-related genes (Igfbp1 and Angptl4) and enhancing the metabolic biomarkers of 4-aminocatechol	[86]
FYGL (a proteoglycan isolated from <i>G. lucidum</i>)	Diabetic db/db mice	Rat glomerular mesangial cells induced by high glucose with palmitate	Reduce oxidative stress-induced dysfunction	[103]
Meroterpenoids from <i>G. lucidum</i>		TGF- β 1-induced rat Kidney proximal tubular cells	Inhibit the expression of collagen I	[104]
<i>G. lucidum</i> polysaccharide peptides	Unilateral nephrectomy and inject BSA 5g/kg/day for 7 consecutive days	BSA-induced HK-2 cell injury model	Inhibiting the intrarenal PRR-RAS pathway	[105]
Ganoderic acid A	Kidney-specific Pkd1 knockout mice	MDCK cystogenesis model	Downregulated the Ras/MAPK signaling pathway	[91]
<i>Ganoderma</i> triterpenes	Kidney-specific Pkd1 knockout mice	MDCK cystogenesis model	Downregulating Ras/MAPK signaling and promoting cell differentiation	[90]
<i>G. lucidum</i> polysaccharide peptide	Potassium oxonate-induced mouse model	Adenosine-induced cell model	Regulating the uric acid production and excretion	[106]
<i>G. lucidum</i> Polysaccharides	Streptozotocin-Induced Diabetic Rats	/	Via the PI3k/Akt/mTOR signaling pathway, by inhibition of apoptosis and inflammation, and activation of the autophagy process	[107]
<i>G. lucidum</i>	Streptozotocin-Induced Diabetic Rats	/	Blocking the TLR4/NF- κ B signaling pathway	[108]
Other kidney diseases				
<i>G. lucidum</i>	Prenatal Chlorpyrifos-Induced Developmental Nephrotoxicity in rats (pregnant rats received chlorpyrifos 5 mg/kg)	/	Restoring antioxidant defense systems, modulating the Bax/Bcl-2 apoptotic balance, suppressing pro-inflammatory cytokine production, reducing tubular injury markers, and normalizing stereologically detected renal structural changes	[109]
Petchiether A (a novel small-molecule meroterpenoid from <i>G. lucidum</i>)	Unilateral ureteral obstruction in mice	/	Inhibiting TGF- β /Smad3 signaling	[110]
FYGL	Diabetic nephropathy in db/db mice	/	Antioxidant and inhibition of oxidative accumulation	[111]

Oral *G. lucidum* is mostly absorbed in the intestine, and its role in the intestine cannot be ignored. Based on its immunomodulatory, anti-inflammatory and antioxidant activities, *Ganoderma* exerts multiple protective effects against intestinal inflammation. It exhibits a repairing effect on the intestinal mechanical barrier. Specifically, FYGL has been shown to exert a protective effect on intestinal epithelium in mice with type 2 diabetes [121]. GA-A can improve IBS by regulating the enteric nervous system and intestinal homeostasis [42]. Meanwhile, *G. lucidum* dietary fiber can alleviate constipation [122]. Sporoderm-broken *G. lucidum* spore polysaccharides have been demonstrated to alleviate DSS-induced colonic inflammation [37]. Both GA [123] and GA-A [124] can ameliorate DSS-induced ulcerative colitis in mice, and the underlying mechanism may be associated with the regulation of microbial tryptophan metabolism.

In addition, a variety of other *Ganoderma*-derived components also exert beneficial effects on DSS-induced mouse colitis, including *G. lucidum* (Agaricomycetes) spore powder [125], *G. lucidum* spore shells modified into probiotic carriers [126], *G. lucidum* β -d-glucans [127] and *G. lucidum* ethanol extraction [37]. Previous work also demonstrated that MAK, a water-soluble extract obtained from *Ganoderma lucidum* (Reishi) mycelial culture medium, relieves trinitrobenzene sulphonic acid-provoked colitis in mice [128]. Beyond the protective effects on chronic intestinal inflammation, *Ganoderma* extracts are also effective against acute intestinal infections. For instance, combined therapy with GLPs and ciprofloxacin can alleviate *Salmonella enterica* infection. Reishi Protein LZ8 promotes the expansion of FOXP3(+) Tregs via a CD45-dependent signaling cascade, which ameliorates acute intestinal inflammation in mice [129]. GLPs can reduce methotrexate-induced small intestinal damage in mice [130].

The microbial barrier plays an important role in maintaining intestinal microbiota balance, stimulating barrier development and immune maturation. The gut microbiota regulates metabolism, inflammation and immune homeostasis through the gut-liver axis, and its structural imbalance is closely related to the occurrence and development of various liver diseases. GLPs have been proven to improve dyslipidemia in mice [73, 131]. Polysaccharides in broken *G. lucidum* spore powder can alleviate high-fat diet-induced obesity in mice [72]. Similarly, GLPs can inhibit inflammation via the *Lactobacillus*-butyrate axis, exerting a similar effect [69]. GLPs [132] have also been confirmed to alleviate acute liver injury in mice. A series of studies at the animal level have shown that *G. lucidum* fruiting bodies [133], ethanol extract of *G. lucidum* [134], alcoholic extracts from the *G. lucidum* fermentation product [135] and GA-A [136] improve alcoholic liver injury by regulating intestinal flora. In addition, GLPs can alleviate non-alcoholic fatty liver disease by regulating intestinal flora, inhibiting the TLR4/NF- κ B/MAPK signaling pathway, and activating the AMPK signaling pathway [23]. In addition, GLPs [137] and resistant starch-encapsulated *G. lucidum* spores [138] can also improve diabetes by regulating the flora.

Besides the above-mentioned liver-related diseases, *G. lucidum* and its extracts can also ameliorate other diseases by regulating intestinal flora. For instance, heteropolysaccharide from *G. lucidum* can ameliorate AD in rats [139]; *G. lucidum* sporoderm-broken spores mitigate renal senescence in both naturally aged mice and a murine model of radiation-triggered premature aging [89]. *G. lucidum* can prevent osteoporosis [140]; GLPs can improve D-galactose-induced learning and memory impairment [58]. Moreover, the alcohol extract of *G. lucidum* mycelia was reported to promote sleep [141] in murine models, etc.

Additionally, the effects of *G. lucidum* on digestive system tumors and metabolic diseases will be separately reviewed in detail in the following sections.

Effects of *G. lucidum* on the respiratory system

The protective effects of *G. lucidum* extract on the respiratory system primarily focus on treating asthma [142], reducing lung inflammation [143] and improving pulmonary nodules [144], pulmonary fibrosis [145] and lung cancer [146], which mainly rely on the anti-

inflammatory and immune-regulating effects [147].

Asthma represents a complex heterogeneous disorder driven by interactive genetic and environmental stimuli that initiate persistent airway inflammation. This pathological process promotes airway hyperresponsiveness, smooth muscle contraction, excessive mucus production and airway remodeling, ultimately resulting in recurrent wheeze, dyspnea and reversible airflow restriction. The Guominkang formula containing *G. lucidum* has been shown to alleviate airway inflammation induced by house dust mite in asthma by regulating the Wnt/ β -Catenin signaling pathway in mice [142]. GA-B exerts time-dependent bidirectional regulation of IFN- γ , IL-5, and Treg-associated cytokines in peripheral blood mononuclear cells isolated from asthmatic patients, suggesting its distinctive regulatory capacity on cytokine profiles [148]. Triterpenoid-rich extracts of *Ganoderma tsugae* were reported to exert anti-inflammatory effects on airway responses and attenuate Th2 responses without the overall immunosuppressive effects in allergic murine models of asthma [149].

G. lucidum extract also has a significant inhibitory effect on lung inflammation. In the LPS-induced rat pneumonia model, *Ganodermanontriol* inhibits phosphorylation and activation of the TNF/NF- κ B/MAPK signaling pathway [143]. A recombinant protein LZ-8, originally extracted from *G. lucidum*, ameliorates ovalbumen-induced lung inflammation by regulating Th17/Treg balance in mice [150]. It has also been reported in murine models that GLPs ameliorate LPS-induced acute pneumonia via inhibiting NRP1-mediated inflammation [151] and alleviate intestinal I/R induced lung injury via inhibiting cytotoxic neutrophil extracellular traps [152]. In lung injury induced by cadmium poisoning, *G. lucidum* active peptide GLP4 reduces cadmium-induced lung injury in mice by inhibiting the activation of the NLRP3 inflammasome [153]. GA-A was reported to alleviate mice lipopolysaccharide-induced acute lung injury by inhibiting the Rho/ROCK/NF- κ B signaling pathway [154].

Acute lung injury can lead to pulmonary fibrosis. GA-A exerts a protective effect against bleomycin-induced pulmonary fibrosis in mice, and the TGF- β /Smad-3/NF- κ B signaling pathway plays an important role in this process [155]. GLPs also show protective effects on bleomycin-induced pulmonary fibrosis in rats [145]. The beneficial effects of *G. lucidum* extract on lung cancer have also been extensively studied, and we will elaborate in detail on its anti-tumor effects.

Effects of *G. lucidum* on the reproductive system

Accumulating evidence has validated the protective efficacy of GTs against cadmium-triggered testicular damage in chickens [156]. Mechanistically, GTs diminish cadmium deposition in testicular tissues, lower the expression levels of pro-inflammatory cytokines (IL-1 β , IL-6 and TNF- α) in cadmium-injured testes, and enhance the enzymatic activities of superoxide dismutase and GSH-Px while reducing malondialdehyde accumulation. Additionally, GTs modulate the expression of apoptosis-related proteins (Bax, caspase-3 and Bcl-2), thereby effectively mitigating testicular tissue lesions caused by cadmium toxicity [156]. Recent clinical investigations have confirmed that chemotherapy severely impairs sperm quality in male patients, typically inducing oligospermia and ultimately resulting in male infertility [157, 158]. Furthermore, GLPs have been verified to alleviate cyclophosphamide-caused male reproductive dysfunction in mice and protect spermatogenic cells at various developmental stages [159]. This protective effect is achieved via the regulation of two core signaling pathways: the Keap1/Nrf2/HO-1-dependent oxidative stress pathway and the Bax/Bcl-2-mediated apoptotic pathway.

Effects of *G. lucidum* on metabolic diseases

G. lucidum extract exhibits potent anti-metabolic disorder effects. The liver is the core metabolic center of the human body, comprehensively regulating the synthesis, breakdown and transformation of substances such as sugars, lipids, proteins, vitamins and hormones, and maintaining the body's metabolic homeostasis. *G. lucidum* demonstrated significant hepatoprotective effects against various forms of liver injury. In the context of drug-induced or chemical hepatotoxicity (e.g., from acetaminophen or carbon tetrachloride),

pretreatment with *Ganoderma* extracts significantly reduces serum levels of liver function markers, such as alanine transaminase and aspartate transaminase, and mitigates histological liver damage in mice. For non-alcoholic fatty liver disease, *Ganoderma* was shown to reduce hepatic lipid accumulation, improve insulin sensitivity and alleviate hepatic steatosis. In mice models of liver fibrosis, *Ganoderma* inhibits the activation of hepatic stellate cells, the key effectors in fibrogenesis, thereby reducing the deposition of extracellular matrix proteins and slowing the progression of fibrosis.

The liver is the largest metabolic organ in the body, and its damage may induce a series of metabolic diseases. *G. lucidum* exhibits extensive hepatoprotective effects in various liver diseases, including liver cancer, nonalcoholic fatty liver disease, alcoholic liver disease, hepatitis B, liver fibrosis as well as liver injury induced by CCl₄ and α -amanitin in mice [160]. The detailed effects of *G. lucidum* on the liver was reviewed as follows:

GTs help prevent and improve hyperlipidemia. Tong and colleagues studied the effects of GTs on hyperlipidemia and gut microbiota changes induced by a high-fat diet (HFD) in rats. GTs can improve lipid levels in hyperlipidemic rats and reverse HFD-induced gut microbiota dysbiosis, including a significant increase in the proportion of *Alloprevotella* and a decrease in the proportion of *Blautia* [161]. GA-A can also improve weight gain and hepatic steatosis, liver injury, lipid metabolic disorders and hepatocyte apoptosis via inhibiting ACC activity [162]. Guo *et al.* [163] reported that GA-A regulates gut microbiota composition and lipid metabolism in HFD mice. GA-A significantly reduced abnormal weight gain and epididymal white adipose tissue enlargement in HFD mice, improved biochemical indicators related to lipid metabolism in the liver and serum and significantly alleviated hepatic lipid droplet accumulation.

Atherosclerosis is a common cardiovascular disease characterized by lipid deposition, oxidative stress and inflammation in the vascular endothelium. The anti-inflammatory, antioxidant and glucose-lipid regulation effects of GLPs to improve obesity all suggest that they have certain effects on atherosclerosis. Literature reports that GLPs can significantly reduce the aortic plaque area in rabbit atherosclerosis models via alleviating endothelial dysfunction and inflammatory polarization in macrophages, thereby promoting the apoptosis of foam cells [164]. In a high-cholesterol diet-fed Wistar rat hyperlipidemia model, GLPs can reduce hydrogen peroxide, IL-10 levels and the number of endothelial progenitor cells in serum, and decrease aortic intima-media thickness, showing potential anti-atherosclerotic effects [165].

Obesity and its major complication, type 2 diabetes, pose serious threats to human health, but currently there is no effective treatment. GA-A inhibits the expression of SREBPs *in vitro*, reducing cholesterol and fatty acid levels. GA-A regulates SREBP target genes and metabolism-related genes in the liver or adipose tissue in mice, which may directly help reduce lipid levels and improve insulin resistance [166].

In studies on the anti-diabetic effects of GLPs, researchers investigated the mechanisms of FYGL and GLP F31. The anti-diabetic effects of FYGL, in addition to being related to the regulation of lipid metabolism and insulin resistance, can improve muscle atrophy in diabetic mouse models through antioxidant activity [167] and can also improve insulin resistance by upregulating PGC-1 α [168]. The protein part of FYGL plays an important role in inhibiting the amyloid aggregation of human islet amyloid polypeptide (hIAPP). Mechanistically, the strong, specific and enthalpy-driven interactions between hIAPP and FYGL through π - π stacking and electrostatic forces significantly inhibit hIAPP amyloid aggregation. The antidiabetic effect of FYGL may also be related to preventing the misfolding of hIAPP [169]. Protein tyrosine phosphatase 1B (PTP1B) is a key negative regulator of insulin and is also an effective target for the treatment of type 2 diabetes in mice. FYGL can also reduce blood glucose by inhibiting PTP1B. This study demonstrated that there is a strong, enthalpy-driven and multi-target electrostatic interaction between PTP1B and FYGL, which greatly inhibits the catalytic activity of PTP1B [170, 171]. The anti-hyperglycemic capacity of GLP F31 is

attributed to multiple regulatory mechanisms, including the restoration of pancreatic islet cell function and elevated insulin secretion. It also facilitates hepatic glycogen synthesis and storage, and simultaneously enhances antioxidant enzyme activity while ameliorating insulin resistance [137]. 16S rRNA gene sequencing results showed that F31 can reduce the number of Firmicutes and increase the number of Bacteroidetes in mice, thereby decreasing the release of endotoxins from the gut into the bloodstream, promoting carbohydrate fermentation in the gut and activation of the gut-brain axis to lower blood sugar and reduce insulin resistance and inflammation. In addition, F31 can also alleviate hyperglycemia through renal protection and promote adipocyte apoptosis in db/db mice [172].

Effects of *G. lucidum* on its antitumor effect

The anti-tumor research of *G. lucidum* is also very extensive, mostly based on its killing effect on tumor cells. Among them, GTs have better effects, manifested as inhibiting tumor cell proliferation, promoting tumor cell apoptosis, regulating autophagy and other effects. The polysaccharides in *G. lucidum* mainly enhance the sensitivity of chemotherapy drugs and reduce adverse reactions through their immune regulatory activity, playing an indirect anti-tumor role.

Direct antitumor effects. It has been reported that *G. lucidum* has inhibitory effects on lung cancer, liver cancer [7, 173, 174], breast cancer [175–177], papillary thyroid cancer [178], endometrial cancer [179], colon and rectal cancer [180, 181], prostate cancer [182], *etc.*

Ganoderma exhibits direct cytotoxic effects on a variety of tumor cell lines *in vitro* and *in vivo*. Triterpenoids, particularly GAs, are the main contributors to these effects. They trigger apoptotic cell death in tumor cells via diverse routes, such as caspase cascade activation, elevated expression of pro-apoptotic mediators (e.g., Bax), and suppressed levels of anti-apoptotic counterparts (e.g., Bcl-2). Furthermore, *Ganoderma* components inhibit tumor cell proliferation by arresting the cell cycle at the G0/G1 or G2/M phases *in vitro*. They also suppress tumor invasion and metastasis by downregulating matrix metalloproteinase expression, which degrades the extracellular matrix, and by inhibiting angiogenesis, a critical process in tumor growth and metastasis.

Due to its low bioavailability, different formulations have also been attempted for anti-tumor research of *G. lucidum*. A novel Pt(IV)-GA-A conjugate was proven to have anti-glioblastoma activity *in vitro* [183]. WSG is a polysaccharide from *G. lucidum*. WSG-based dissolvable microneedle patch provided a new effective method in treating cutaneous melanoma *in vitro* [184]. A nano-bioconjugate formed by conjugating GLPs with low-pH culture medium reprogrammed CT26 tumor cell-derived extracellular vesicles showed tumor-targeting delivery and potent immunomodulatory effects via repolarizing M2-like macrophages towards the M1 phenotype, promoting dendritic cell maturation, activating cytotoxic T lymphocytes and inhibiting immunosuppressive regulatory T cells [185]. A *G. lucidum* spore-based solid self-nanoemulsifying delivery system for paclitaxel enhances lymphatic absorption and exerts synergistic immunotherapeutic and antitumor effects. This novel formulation serves as a robust oral platform that integrates chemotherapy and immunotherapy, with validated efficacy in both *in vitro* and *in vivo* models [186]. In the positive, recurrent and metastatic 4T1 breast cancer models, DC-targeted full-cell nanovaccine based on chitosan oligosaccharide self-assembled with GLP showed strong anti-tumor effects, significantly inhibiting the growth of primary tumors and inhibiting distant lung metastasis [146]. GLP-based multifunctional tellurium nanorods exhibit potential to initiate anti-tumor immune responses, which is suitable for cases when single-agent therapy is suboptimal [187]. The new formulation of *G. lucidum* extract has become a new trend in anti-tumor treatment.

Indirect antitumor effects. In addition to direct cytotoxicity, *Ganoderma* acts as an effective adjuvant in cancer therapy. It enhances the sensitivity of tumor cells to conventional chemotherapeutic agents and radiation, thereby improving treatment efficacy [188]. This chemosensitization effect is often mediated by the inhibition of drug

efflux pumps, such as P-glycoprotein, which are responsible for multidrug resistance [189]. Equally important, *Ganoderma* mitigates the severe side effects associated with chemoradiotherapy, such as myelosuppression, gastrointestinal toxicity and immunosuppression [190]. In addition, GA-A was reported to enhance the cytotoxicity of cisplatin against gallbladder cancer cells by promoting DNA damage and inhibiting cell stemness [191]. GA-T, a triterpenoid of *G. lucidum*, regulates the tumor microenvironment and enhances chemotherapy and immunotherapy efficacy in the *in vivo* study by downregulating the level of galectin-1 [192]. This suggests that *G. lucidum* extract also has outstanding contributions in assisting the treatment of cancer, as it improves the quality of life and treatment tolerance of cancer patients.

Antitumor-related signaling pathway mechanisms. The antitumor effects of *Ganoderma* are mediated through the modulation of several key signaling pathways involved in immune regulation [173, 193], cellular energy metabolism [194, 195], apoptosis [196], autophagy [197], aging [181], etc.

Ganoderma extracts exert antitumor effects mainly in multiple aspects, including regulating immunity, modulating autophagy, modulating energy metabolism and inducing senescence. Sporoderm-removed *G. lucidum* spore powder was shown to enhance the antitumor efficacy of anti-PD-L1 antibody in a lung cancer mouse model [198]. A water extract of *G. lucidum* mycelium has also been confirmed to exert similar effects, which may be attributed to the stimulation of NK cell cytotoxicity by inducing NKG2D/NCR activation and the secretion of perforin and granulysin *in vitro* [199]. Additionally, some studies proposed that the antitumor effect of *G. lucidum* is associated with regulating macrophage polarization [200–202] and increasing the phagocytic function of macrophages [193], both in *in vitro* and *in vivo* studies. Modulating the autophagic level of tumor cells is also one of the important measures to inhibit tumor progression [203]. Existing research has demonstrated that GA-D is capable of triggering synergistic autophagic cell death in tumor cells [204]. *In vitro* experiments have further validated that GA-A exerts cytotoxic effects against human glioblastoma by targeting the PI3K/Akt signaling cascade [205]. GLPs, on the other hand, can inhibit autophagy and promote apoptosis of human colon cancer cells by activating the MAPK/ERK signaling pathway *in vitro* [206]. In human gastric cancer SGC-7901 cells, LZ-8 can regulate autophagic cell death through endoplasmic reticulum stress [207]. The above literature indicated that *G. lucidum* and its extracts exert anti-tumor effects through multiple pathways.

Multi-omics analysis has revealed that sporoderm-removed *G. lucidum* spores inhibit osteosarcoma progression *in vitro* and *in vivo* by targeting glycerophospholipid and fatty acid metabolism [194]. GA-A possesses dual inhibitory potential on GLUT1/3, which targets glucose metabolism in human lung cancer in the *in vitro* study [195]. GA-D attenuates gemcitabine resistance in triple-negative breast cancer cells by inhibiting glycolysis through HIF-1 α destabilization both *in vitro* and *in vivo* [208]. Moreover, GLPs can alleviate colorectal cancer by regulating gut microbial metabolism [209]. By targeting these oncogenic pathways, *Ganoderma* effectively inhibits tumor growth and metastasis.

Anti-aging effect of *G. lucidum*

Excessive oxidative stress response in the body can continuously damage cells, proteins, and DNA, leading to the accumulation of oxidative damage and accelerating cell aging and tissue function decline, which is one of the core mechanisms driving natural aging of the body. The various components in *G. lucidum*, including GLPs, GTs, etc., have antioxidant capacity. In recent years, with the intensification of aging, the role of *G. lucidum* in elderly patients has been further emphasized.

G. lucidum exhibits more potent therapeutic effects in aged mice compared with young mice. This superior efficacy is potentially attributed to the activation of Treg cells through the modulation of arginine metabolism [210]. Moreover, nanovesicles derived from *G. lucidum* can markedly alleviate multi-organ senescence in a mouse

model of doxorubicin-triggered acute aging [211]. *G. lucidum* spore polysaccharide (GLSP) alleviates vascular aging by promoting SIRT7-mediated deacetylation of Keap1 and dissociation of Keap1-NRF2, which is investigated both *in vitro* and *in vivo* [212].

GA-A can effectively inhibit senescent cell buildup and ameliorate multi-organ physiological deterioration in three types of mouse models, including irradiation-induced premature aging, natural aging, and Western diet-triggered obesity. Intriguingly, GA-A is capable of improving physical performance and enabling metabolic adaptation to physiological alterations during aging. Mechanistically, GA-A directly interacts with TCOF1 to sustain ribosome homeostasis, which serves as a core mechanism to suppress cellular senescence [213]. Moreover, *G. lucidum* sporoderm-broken spore powder also enhances klotho expression, highlighting its potential as an anti-aging intervention *in vivo* [214]. *In vitro*, GA-D prevents oxidative stress-induced senescence [215] by targeting 14-3-3 ϵ to activate the CaM/CaMKII/NRF2 signaling pathway in mesenchymal stem cells [216].

Some studies based on mice indicated that regulation of gut microbiota was considered to be one of the most important mechanisms to alleviate aging. GLPs were reported to target the gut-brain axis, alleviating cognitive impairment caused by aging by regulating gut microbiota homeostasis and short-chain fatty acid levels [41]. A similar effect induced by GTs may be via regulating *Eubacterium lentum*-mediated serine metabolism [57]. *G. lucidum* sporoderm-broken powder alleviates kidney aging [89], and GLPs improve learning and memory impairment [58], which can also be affected by intestinal flora. Mitochondrial dysfunction is an important sign of cellular and even individual aging. Wang *et al.* reported that *G. lucidum* extracts reduce skin aging by reducing mitochondrial stress and controlling mitochondrial numbers [217].

In all, *Ganoderma* has been found to extend the lifespan or healthspan of model organisms, such as *Caenorhabditis elegans* [218] and *Drosophila* [219], by modulating insulin/IGF-1 signaling and sirtuin pathways, which are key regulators of longevity.

Radiation protection effect of *G. lucidum*

Ionizing radiation can cause severe damage to the body. The anti-radiation effect of *G. lucidum* is closely related to its expected properties on reducing lipid peroxidation, ameliorating cell apoptosis, restoring DNA damage and regulating the immune system [220, 221].

GTs can effectively lower the levels of lipid peroxidation and protein oxidation in the liver and brain tissue induced by γ -ray radiation, and successfully restore the antioxidant enzyme activities and GSH levels in the liver and brain of irradiated mice [222]. UVB radiation can induce cataract. Moreover, topical and oral *G. lucidum* alleviates oxidative stress and inflammatory response in rat caused by UVB damage [223]. Commercial products with a 30:8 ratio of *Ganoderma* spores to fruiting bodies (named GLSF) were shown to attenuate immune suppression caused by UV-induced skin cancer *in vivo* [224]. GA-A can increase the cell viability, Bcl2/Bax ratio and superoxide dismutase activity of irradiated lens epithelial cells and reduce malondialdehyde content and cleaved Caspase-3 level, thereby delaying lens opacity caused by UVB radiation in lens epithelial cells [225]. The mechanism by which GLPs inhibit UVB-induced melanin production and aging *in vitro* may be related to antagonizing the cAMP/PKA and ROS/MAPK signaling pathways [226, 227]. GA-T has been found to improve the radiosensitivity of HeLa cells via converting apoptosis to necroptosis [228]. Serum metabolomics based on Ultra Performance Liquid Chromatography-Tandem Mass Spectrometry showed that the water-soluble components, GLPs, can play a role in radiation protection by regulating taurine metabolism and glycerophospholipid metabolism in mice [229].

Antiviral effect of *G. lucidum* and other functions

In addition, *G. lucidum* extracts have resistance to various viruses. GLPs have been reported to inhibit viral invasion, replication and destruction in the body and exert antiviral effects by enhancing the body's nonspecific and specific immune functions. A protein-bound polysaccharide GLhw-02, isolated from the water-soluble substances of

G. lucidum through activity-guided separation, exhibits antiviral activity against herpes simplex virus type 1 (HSV-1) and type 2 (HSV-2) *in vitro* [230, 231]. Reviews have summarized that GLPs may exert inhibitory effects against coronavirus infection, which remains to be validated by direct *in vitro* experimental evidence [232]. Other studies have found that GLPs, as immune adjuvants, can promote the production of specific antibodies IgG and IgA in mice vaccinated with the inactivated enterovirus EV-A71 vaccine (nasal drop), alleviate the symptoms of EV-A71-infected mice, and reduce mortality, thereby providing immune protection in mice [232]. Research on the antiviral effects of GLPs provides a theoretical basis for the clinical prevention and treatment of viral diseases, and also offers potential candidate drugs for the prevention and control of the COVID-19 pandemic.

A study based on the virtual screening approach predicts that four functional triterpenoids, including Ganodermanontriol (−6.291 kcal/mol), lucidumol A (−5.993 kcal/mol), Ganoderic acid C2 (−5.948 kcal/mol) and Ganosporic acid A (−5.983 kcal/mol) from *G. lucidum*, are potential inhibitors of DENV NS2B-NS3 protease, a primary target for anti-dengue drug discovery. A subsequent *in vitro* study that indicated that ganodermanontriol is a potent bioactive triterpenoid [233]. In addition, some *G. lucidum* extracts alleviate the infection of SARS-CoV-2 in an *in vitro* experiment [234]. For example, *G. lucidum* spore powder enhances the IFN- α -mediated antiviral capacity of the COVID-19 vaccine [235, 236]. Jiang *et al.* propose that GA-T has the potential to prevent Sendai virus infection via transcriptome profiling and bioinformatic analysis [237].

Clinical trials of *G. lucidum* and its bioactive compounds

Overall, although several clinical trials have confirmed some beneficial effects of *G. lucidum* and its extracts in humans, relevant clinical research remains insufficient. Moreover, most studies have focused on its adjuvant therapeutic effects in cancer patients and its benefits in improving chronic diseases.

A prospective evaluation of 120 patients with breast cancer and lung cancer, in which T lymphocyte subsets and related cytokines were measured by flow cytometry and polymerase chain reaction and assessed by Spearman correlation analysis, showed that Ganoderma spore powder could improve immune function in patients postoperatively [238]. Likewise, a study based on 34 patients reported that oral administration of GLPs (5400 mg/day) before meals significantly increased natural killer cell activity in patients with advanced cancer [25].

In addition, the antioxidant effects of *G. lucidum* have received considerable attention and have been linked to improvements in several chronic diseases. Chiu *et al.* demonstrated in healthy volunteers that *G. lucidum* exerted antioxidant, anti-aging and hepatoprotective effects and effectively inhibited oxidative stress [239]. In another double-blind, placebo-controlled and crossover intervention study, blood and urine samples were collected from 10 healthy volunteers after a single dose of *G. lucidum*. The results indicated that ingestion of *G. lucidum* acutely increased plasma antioxidant capacity, and this antioxidant status may be beneficial in reducing the risk of coronary heart disease [240]. However, in healthy adult volunteers (aged 22–52 years, 18 subjects) who received oral administration of a commercially available *G. lucidum* capsule for 4 weeks, no significant change in any variables was observed in acute tests of fasting blood and urine compared with the placebo group, although there was a slight decreasing trend in blood lipids and an increase in urinary antioxidant capacity [241]. We speculate that the inconsistencies between these two studies may be attributed to differences in dosage and duration of administration. It could also be that the sample size of the experiment was too small to eliminate individual differences, thereby causing deviations. Nevertheless, some studies suggested that *G. lucidum* may exert mild antidiabetic effects and improve diabetic dyslipidemia, as shown in several previous animal studies [242].

GLP peptide is a potent antioxidant that can effectively inhibit the pathogenesis of stable angina pectoris and atherosclerosis in high-risk patients [64]. In a prospective, double-blind, randomized, placebo-controlled trial conducted in 2016, after 84 participants with type 2 diabetes and metabolic syndrome were randomized to receive *G. lucidum*, *G. lucidum* plus Cordyceps sinensis, or placebo for 16 weeks. Measurements of glycated hemoglobin, fasting glucose, and other secondary outcomes did not support the use of *G. lucidum* for the treatment of cardiovascular risk factors in patients with diabetes or metabolic syndrome [243].

In terms of mental health, oral administration of *G. lucidum* can improve the clinical symptoms of neurasthenia to some extent [244]. In a study on the treatment of AD with *G. lucidum* spore powder, it was noted that after 6 weeks of treatment, no improvement in the effect of *G. lucidum* on AD was observed, which was inconsistent with the results in animal studies [245]. We propose that the observed result may be attributed to the small sample size, which is inadequate to mitigate data fluctuations arising from individual differences. This limitation is further exacerbated by a short treatment duration. Additionally, comparing the conversion of dosage from animal studies, a relatively low dosage caused insufficient bioavailability, which could also significantly contribute to the inconsistencies in the results.

In clinical trials related to the urinary system, a randomized double-blind experiment evaluated the safety and efficacy of *G. lucidum* extract in men with lower urinary tract symptoms. This study showed that the *G. lucidum* extract was well tolerated and improved the International Prostate Symptom Score. It also indicated that the recommended dosage for men with lower urinary tract symptoms is 6 mg [80, 246].

Some clinical trials have also indicated that *G. lucidum* may exacerbate symptoms in some patients with Gulf War illness, which may be related to its potent immunomodulatory effects [247]. Although *in vitro* reports suggested that *G. lucidum*-derived components may inhibit platelets [248] and exert other antithrombotic and fibrinolytic activities, ingestion of *G. lucidum* did not impair hemostatic function in healthy volunteers [249]. In a study of women with fibromyalgia, administration of *G. lucidum* for 6 weeks significantly improved aerobic endurance, body flexibility and velocity [250]. An herbal formula containing *G. lucidum* alleviated pain in five Japanese patients with herpes zoster [251]. Similar studies have reported that a herbal mixture containing *G. lucidum* shortened recovery time in patients with genital herpes and cold sores [252]. In a randomized pilot trial involving patients with active rheumatoid arthritis, *G. lucidum* and San Miao San appeared to exert an analgesic effect and were generally safe and well-tolerated. However, no significant antioxidant, anti-inflammatory, or immunomodulatory effect was observed at present [253].

In conclusion, to better understand the current status of clinical research on *G. lucidum*, the quality of all included clinical studies in this narrative review was independently graded using the Oxford Centre for Evidence-Based Medicine (OCEBM) 2009 evidence rating system. Two authors completed the evidence grading independently, and any discrepancies were resolved by consensus discussion to ensure accuracy. The detailed evidence grading results of all included studies are presented in Table 2 [25, 64, 238–247, 249–253].

G. lucidum has a long history of medicinal and edible use in China. The translation of Ganoderma's promising preclinical findings into clinical practice is hampered by significant shortcomings in clinical research. Most human studies are characterized by small sample sizes, a lack of rigorous, double-blind, placebo-controlled designs and insufficient follow-up periods. Consequently, the evidence supporting the efficacy of Ganoderma for specific clinical indications remains weak and inconclusive. The absence of large-scale, multi-center clinical trials makes it difficult to draw definitive conclusions about its therapeutic benefits, safety profiles and optimal dosing regimens in diverse patient populations. This lack of high-quality clinical evidence impedes its acceptance and integration into mainstream modern medical practice.

Table 2 Summary and evidence-based medicine grading of clinical studies related to *G. lucidum*

Literature	Types of extracts	Research types	Sample sizes	Intervention measures	Control groups	Core conclusions	Level of Evidence	Reason for downgrade
Deng, [238]	2021 Ganoderma spore powder	RCT	120	<i>G. lucidum</i>	Without <i>G. lucidum</i>	T lymphocyte subsets, along with relevant cytokines and AGR/NLR inflammatory predictors, may help identify patients most likely to benefit from the immunologic enhancements conferred by <i>G. lucidum</i> treatment.	1b	
Gao, 2003 [25]	Ganopoly (a <i>G. lucidum</i> polysaccharide extract)	One-group pre-post study	34	1800 mg Ganopoly, three times daily orally before meals for 12 weeks	/	Ganopoly enhanced the immune responses in patients with advanced-stage cancer.	4	Self-comparison before and after cannot exclude confounding factors such as self-healing, time effects, placebo effects, and lifestyle interventions.
Chiu, [239]	2017 <i>G. lucidum</i>	RCT	42	<i>G. lucidum</i> (225 mg; after lunch or dinner) for 6 months	Placebo(225 mg; after lunch or dinner) for 6 months	<i>G. lucidum</i> has antioxidant, anti-aging and liver-protective effects.	1b	
Wachtel-Galor, 2004 [240]	<i>G. lucidum</i>	RCT	10	Oral <i>G. lucidum</i> 0.72 g, 1.1 g, 3.3 g per day for 4 weeks	Placebo for 4 weeks	<i>G. lucidum</i> intake causes an acute increase in plasma antioxidant capacity. No deleterious effects on measured variables were seen.	2b	Insufficient sample size
Wachtel-Galor, 2004 [241]	<i>G. lucidum</i>	RCT	18	1.44 g Lingzhi/d; equivalent to 13.2 g fresh mushroom/d for 4 weeks	Placebo for 4 weeks	A slight decrease in blood lipids and an improvement in urine antioxidant capacity, with no evidence of liver, kidney, or DNA toxicity.	2b	Insufficient sample size
Chu, [242]	2012 <i>G. lucidum</i>	RCT	26	1.44 g <i>G. lucidum</i> for 12 weeks	Placebo for 12 weeks	<i>G. lucidum</i> may exert mild anti-diabetic effects and improve diabetic dyslipidemia	1b	

Table 2 Summary and evidence-based medicine grading of clinical studies related to *G. lucidum* (Continued)

Literature	Types of extracts	Research types	Sample sizes	Intervention measures	Control groups	Core conclusions	Level of Evidence	Reason for downgrade
Sargowo, 2018 [64]	Polysaccharide peptide of <i>G. lucidum</i>	One-group pre-post study	37 high-risk and 34 stable angina patients	Polysaccharide peptide of <i>G. lucidum</i> 750mg/day for 90 days	/	Polysaccharide of <i>G. lucidum</i> is a potent antioxidant against the pathogenesis of atherosclerosis in stable angina and high-risk patients.	4	Self-comparison before and after cannot exclude confounding factors such as self-healing, time effects, placebo effects, and lifestyle interventions.
Klupp, 2016 [243]	<i>G. lucidum</i>	RCT	84 participants with type 2 diabetes and metabolic syndrome	3 g of <i>G. lucidum</i> orally per day for 16 weeks	Placebo for 16 weeks	Does not support the use of <i>G. lucidum</i> for treatment of cardiovascular risk factors in people with diabetes mellitus or metabolic syndrome.	1b	
Tang, 2005 [244]	Ganopoly	RCT	132 patients with neurasthenia	Ganopoly 5400 mg/day for 8 weeks	Placebo 5400 mg/day for 8 weeks	Ganopoly showed significant improvement in clinical symptoms of neurasthenia compared to placebo.	1b	
Wang, 2018 [245]	<i>G. lucidum</i> spore powder	RCT	42 AD patients	<i>G. lucidum</i> spore powder for 6 weeks	Placebo for 6 weeks	Did not find promising efficacy of <i>G. lucidum</i> spore powder for the treatment of AD after a 6-week treatment.	1b	
Noguchi, 2008 [246]	<i>G. lucidum</i> extract	RCT	88 men over the age of 49 years who had slight-to-moderate lower urinary tract symptoms for 12 weeks of treatment	<i>G. lucidum</i> extract (6 mg once a day)	Placebo	<i>G. lucidum</i> extract was well tolerated and improved the International Prostate Symptom Score. It also indicated that the recommended dosage for men with lower urinary tract symptoms is 6 mg	1b	
Younger, 2021 [247]	<i>G. lucidum</i>	Placebo-controlled, pseudo-randomized crossover trial	29 Gulf War Illness patients	<i>G. lucidum</i>	/	<i>G. lucidum</i> may exaggerate symptoms in some Gulf War Illness sufferers	4	

Table 2 Summary and evidence-based medicine grading of clinical studies related to *G. lucidum* (Continued)

Literature	Types of extracts	Research types	Sample sizes	Intervention measures	Control groups	Core conclusions	Level of Evidence	Reason for downgrade
Kwok, 2005 [249]	<i>G. lucidum</i>	RCT	40 healthy volunteers	<i>G. lucidum</i> 1.5 g for 4 weeks	Placebo for 4 weeks	Ingestion of <i>G. lucidum</i> does not cause impairment of hemostatic function in healthy volunteers. The use of Ganoderma lucidum preoperatively is unlikely to increase the risk of surgical bleeding in otherwise healthy patients.	1b	
Mateo, 2015 [250]	<i>G. lucidum</i>	RCT	64 women with fibromyalgia	<i>G. lucidum</i> 6 g for 6 weeks	Ceratoniasilqua per day for 6 weeks	<i>G. lucidum</i> may improve physical fitness in women with fibromyalgia, whereas Ceratoniasilqua seemed to be ineffective at increasing physical fitness.	1b	
Hijikata, 2005 [251]	An herbal formula containing <i>G. lucidum</i>	Case Series	5 Japanese patients with herpes zoster	An herbal formula containing <i>G. lucidum</i>	/	Pain relief started within a few days of intake and was almost complete within 10 days.	4	
Hijikata, 2007 [252]	Herbal mixtures containing the mushroom <i>G. lucidum</i>	Case Series	15 patients with herpes genitalis and 13 patients with herpes labialis	Herbal mixtures containing the mushroom <i>G. lucidum</i>	/	Administration of herbal mixtures containing the mushroom <i>G. lucidum</i> to patients suffering from herpes genitalis and labialis appears to shorten the time required to obtain symptom relief.	4	
Li, 2007 [253]	<i>G. lucidum</i> and San Miao San	RCT	65 patients with active rheumatoid arthritis	<i>G. lucidum</i> 4 g and San Miao San 2.4 g daily for 24 weeks	Placebo for 24 weeks	<i>G. lucidum</i> appeared to exert an analgesic effect and was generally safe and well-tolerated. However, no significant antioxidant, anti-inflammatory, or immunomodulatory effect was observed at present	1b	

Classification criteria for evidence levels. 1a: Systematic review/meta-analysis of homogeneous randomized controlled trials (RCTs); 1b: Individual high-quality randomized controlled trial; 2a: Systematic review of homogeneous cohort studies; 2b: Individual cohort study or low-quality RCT; 3a: Systematic review of homogeneous case-control studies; 3b: Individual case-control study; 4: Case series, cross-sectional study, low-quality observational study; 5: Case report, expert opinion, narrative review without original data.

Deficiencies in existing research

Despite the identification of numerous bioactive components from *G. lucidum*, several critical limitations remain. The purity and structural homogeneity of isolated components are often suboptimal, which hinders the establishment of definitive structure-activity relationships. Many studies rely on crude extracts or partially purified fractions, making it difficult to attribute specific pharmacological effects to a single, well-defined molecule, especially in research on GLPs. Many studies have identified correlations between *Ganoderma* treatment and the modulation of specific signaling pathways (e.g., NF- κ B, PI3K/Akt), but the direct molecular targets of its active components are frequently unknown. This lack of mechanistic clarity creates a significant translational gap between basic research findings and clinical applications. Without a precise understanding of how *Ganoderma* components interact with biological systems, the rational design of novel therapeutic agents or optimized treatment protocols is severely limited.

Furthermore, the synergistic interactions among components, such as polysaccharides and triterpenoids, remain poorly understood. The molecular mechanisms underlying these synergistic effects, and how they contribute to the overall therapeutic efficacy of *Ganoderma*, remain largely uncharacterized. Although we speculate that there may be similar mechanisms, such as water-soluble GLPs acting as prebiotics, which can reshape the intestinal microbiota, promote the secretion of short-chain fatty acids, activate CD8⁺ T cells and natural killer cells, and reverse the accumulation of immunosuppressive regulatory T cells, thereby restoring systemic anti-tumor immunity. Lipophilic GTs (such as GA-A) directly block the proliferation of tumor cells, induce apoptosis of cancer cells, and inhibit the signaling of pro-tumor inflammatory NF- κ B. Their combined treatment has produced dual anti-cancer benefits: GLPs enhance immune surveillance, while GTs directly eliminate malignant cells; They jointly stabilize the homeostasis of the intestinal barrier and restore the host's metabolic characteristics to normal. However, this requires more scientific experimental data for verification.

Besides, the industrial development and clinical application of *Ganoderma*-based products face several practical challenges. Current pharmaceutical formulations are often limited to traditional forms such as powders, extracts and capsules, which suffer from low bioavailability (< 5%) and inconsistent pharmacokinetic profiles. The poor water solubility and stability of key components like triterpenoids further complicate their delivery. Moreover, a novel type of nanoparticle, which encapsulates GA-A with heat-sensitive liposomes, has been proven to significantly improve the polarity and water solubility of GA-A. Moreover, it has demonstrated superior antibacterial and anti-tumor activities compared to GA-A and better safety in mice in both *in vitro* and *in vivo* experiments [254]. For a more detailed safety evaluation of *Ganoderma lucidum* extract, such as its interaction with anticoagulants and immunosuppressants, its inhibitory effect on CYP450, and its influence on platelet aggregation, a more scientific assessment is still needed. In addition, its application in specific groups such as pregnant women and patients with autoimmune diseases should be more cautious. Additionally, the lack of standardized quality control measures for *Ganoderma* raw materials and finished products leads to significant batch-to-batch variability, which undermines the reproducibility of therapeutic effects and hinders regulatory approval for broader clinical use.

Future perspectives and outlook

Based on the above review, we hold the idea that future investigations into *G. lucidum* will prioritize the precision characterization and targeted development of its bioactive components. Advanced techniques such as high-throughput screening, affinity chromatography and CRISPR-based functional screening will enable

the targeted isolation of novel and structurally defined compounds. Structure-activity relationship studies will be deepened through rational structural modification and semi-synthesis, aiming to enhance potency, selectivity and pharmacokinetic properties. Furthermore, the development of novel delivery systems, including liposomes, polymeric nanoparticles and nanocrystals, will address the poor solubility and bioavailability of key components, such as triterpenoids, thereby improving their therapeutic efficacy and enabling targeted tissue distribution.

The next frontier in *Ganoderma* research lies in the systematic and multi-omic dissection of its pharmacological mechanisms. The integration of transcriptomics, proteomics, metabolomics and microbiomics will provide a holistic understanding of the complex biological networks modulated by *Ganoderma* extracts. This multi-layered approach will facilitate the identification of direct molecular targets and key signaling nodes, moving beyond correlative observations to causal mechanistic insights. Advanced technologies such as CRISPR-Cas9 gene editing, single-cell RNA sequencing, and spatial transcriptomics will be instrumental in validating these targets and elucidating the cell-type-specific and context-dependent actions of *Ganoderma* components in physiological and pathological settings.

Large-scale, multi-center, randomized controlled clinical trials with standardized protocols and rigorous endpoints to generate high-level evidence for *Ganoderma*'s efficacy and safety are needed. Recently, industrial upgrading needs to focus on the development of innovative pharmaceutical formulations, such as sustained-release tablets, transdermal patches and targeted drug delivery systems, to improve patient compliance and therapeutic outcomes. Finally, the expansion of clinical indications beyond traditional uses, leveraging insights from mechanistic studies, will unlock new therapeutic potentials for *Ganoderma*-based interventions in areas such as metabolic syndrome, neurodegenerative diseases, and cancer immunotherapy.

References

1. Wu ZW, Liu XC, Zhao XF, et al. Ultrasound-assisted extraction optimization of *Ganoderma sinense* polysaccharides and comparative structural analysis across six *Ganoderma* species. *Int J Biol Macromol.* 2025;330(Pt 1):147899. Available at: <https://doi.org/10.1016/j.ijbiomac.2025.147899>
2. Cai ZX, Lv HX, Yang Y, et al. Effects of hot water extract of *Juncao*-substrate *Ganoderma lucidum* residue on meat quality and antioxidant capacity of Liancheng white ducks. *Poult Sci.* 2026;105(7):106822. Available at: <https://doi.org/10.1016/j.psj.2026.106822>
3. Jiang YD, Wang Z, Wang WS, et al. *Ganoderma lucidum* polysaccharide alleviates cognitive dysfunction by inhibiting neuroinflammation via NLRP3/NF- κ B signaling pathway. *J Ethnopharmacol.* 2025;338(Pt 2):119065. Available at: <https://doi.org/10.1016/j.jep.2024.119065>
4. Yang MH, Qin XM, Liu XJ. A review of polysaccharides from *Ganoderma lucidum*: Preparation methods, structural characteristics, bioactivities, structure-activity relationships and potential applications. *Int J Biol Macromol.* 2025;303:140645. Available at: <https://doi.org/10.1016/j.ijbiomac.2025.140645>
5. Lin Z, ed. *Modern Research on Ganoderma lucidum*. 5th ed. Beijing, China: Peking University Medical Press; 2026. ISBN: 9787565935862
6. Hong J et al. Research progress on the chemical composition and pharmacological activities of *Ganoderma lucidum* triterpenoids. *Fungal Research.* 2024;22(1):39–59. Available at: <https://doi.org/10.13341/j.jfr.2023.1671>
7. Song H, Chen FC, Lin SY, et al. Targeting HSP90 destabilization with ganoderic acid a as a novel therapeutic strategy for hepatoblastoma. *Int J Biol Macromol.* 2026;354:151302. Available at: <https://doi.org/10.1016/j.ijbiomac.2026.151302>

8. Wang MC, Han Q, Zhang XL, et al. Ganoderic acid a derivative induces apoptosis of cervical cancer cells by inhibiting JNK pathway. *Chin Herb Med*. 2024;17(4):756–767. Available at: <https://doi.org/10.1016/j.chmed.2024.07.002>
9. Teng LM, Wang C, Cui BK, et al. Lanostane triterpenoids from mycelia-associated *Ganoderma sinense* and their anti-inflammatory activity. *Phytochemistry*. 2023;215:113870. Available at: <https://doi.org/10.1016/j.phytochem.2023.113870>
10. Grienke U, Mihály-Bison J, Schuster D, et al. Pharmacophore-based discovery of FXR-agonists. Part II: identification of bioactive triterpenes from *Ganoderma lucidum*. *Bioorg Med Chem*. 2011;19(22):6779–6791. Available at: <https://doi.org/10.1016/j.bmc.2011.09.039>
11. Zhang XQ, Gao XX, Long GQ, et al. Lanostane-type triterpenoids from the mycelial mat of *Ganoderma lucidum* and their hepatoprotective activities. *Phytochemistry*. 2022;198:113131. Available at: <https://doi.org/10.1016/j.phytochem.2022.113131>
12. Wu X, Cao JL, Li MX, et al. An integrated microbiome and metabolomic analysis identifies immunoenhancing features of *Ganoderma lucidum* spores oil in mice. *Pharmacol Res*. 2020;158:104937. Available at: <https://doi.org/10.1016/j.phrs.2020.104937>
13. Deen KR, Rithick S, Muthumari M, et al. Hepatoprotective Ergostane and Lanostane Derivatives from Mushrooms for the Management of Metabolic Dysfunction-Associated Fatty Liver Disease: A Review. *Int J Med Mushrooms*. 2026;28(2):1–16. Available at: <https://doi.org/10.1615/intjmedmushrooms.2025061742>
14. Wang CY, Li ZY. A Review on the Botany, Phytochemical Constituents, Pharmacological Activities, Toxicology, and Quality Control of the Medicinal Fungus *Lasiosphaera calvatia*. *Molecules*. 2026;31(6):948. Available at: <https://doi.org/10.3390/molecules31060948>
15. Arı M, Sağdılek E, Kılınc E, Cansev M, Özlük K. Effects of uridine and nucleotides on hemostasis parameters. *J Thromb Thrombolysis*. 2023;55(4):626–633. Available at: <https://doi.org/10.1007/s11239-023-02793-y>
16. Zhao LT, Geng ZJ, Wang Y, Wen JW, Liu D. Immunomodulatory Effects of *Ganoderma lucidum* Bioactive Compounds on Gut-Brain and Gut-Liver Axis Disorders. *Curr Issues Mol Biol*. 2025;47(10):842. Available at: <https://doi.org/10.3390/cimb47100842>
17. Gao YC, Wang H, Sheng RW, et al. ROS-responsive *Ganoderma lucidum* polysaccharide nanocomposite targeting prosenescence oxidative stress niche for structural and functional diabetic tendon regeneration. *J Nanobiotechnology*. 2026;24(1):291. Available at: <https://doi.org/10.1186/s12951-026-04156-0>
18. Gao ZL, Liu XJ, Yu JX, et al. Structural basis of immunomodulation by edible fungal polysaccharides: From molecular characteristics to action mechanisms. *Carbohydr Res*. 2025;555:109591. Available at: <https://doi.org/10.1016/j.carres.2025.109591>
19. Ren L, Zhang J, Zhang TH. Immunomodulatory activities of polysaccharides from *Ganoderma* on immune effector cells. *Food Chem*. 2021;340:127933. Available at: <https://doi.org/10.1016/j.foodchem.2020.127933>
20. Xing YQ, Jiang YH, He L, et al. Structural characterization and biological activity of polysaccharides from *Ganoderma lucidum* cultivated under forest conditions. *Int J Biol Macromol*. 2026;379:152849. Available at: <https://doi.org/10.1016/j.ijbiomac.2026.152849>
21. Hu H, Chen ZK, Han JL, et al. Multi-omics integration identifies ganoderic acid A as a TNF α inhibitor for treating sepsis-related liver injury. *Front Pharmacol*. 2026;17:1754172. Available at: <https://doi.org/10.3389/fphar.2026.1754172>
22. Pozzobon RG, Rutckevskis R, de Lima LS, Oliveira CS, Smiderle FR. Anti-Inflammatory Potential of *Ganoderma lucidum* Triterpenes: A Systematic Review and Meta-Analysis of Preclinical Evidence. *Pharmaceuticals (Basel)*. 2026;19(1):188. Available at: <https://doi.org/10.3390/ph19010188>
23. Zhao HJ, Li Y, Liu NN, et al. *Ganoderma lucidum* polysaccharides alleviate non-alcoholic fatty liver disease by modulating gut microbiota against TLR4/NF- κ B/MAPK pathway and activating AMPK pathway. *J Ethnopharmacol*. 2026;355(Pt B):120723. Available at: <https://doi.org/10.1016/j.jep.2025.120723>
24. Hua KF, Hsu HY, Chao LK, et al. *Ganoderma lucidum* polysaccharides enhance CD14 endocytosis of LPS and promote TLR4 signal transduction of cytokine expression. *J Cell Physiol*. 2007;212(2):537–550. Available at: <https://doi.org/10.1002/jcp.21050>
25. Gao YH, Zhou SF, Jiang WQ, Huang M, Dai XH. Effects of ganopoly (a *Ganoderma lucidum* polysaccharide extract) on the immune functions in advanced-stage cancer patients. *Immunol Invest*. 2003;32(3):201–215. Available at: <https://doi.org/10.1081/imm-120022979>
26. Chen X, Hu ZP, Yang XX, et al. Monitoring of immune responses to a herbal immuno-modulator in patients with advanced colorectal cancer. *Int Immunopharmacol*. 2006;6(3):499–508. Available at: <https://doi.org/10.1016/j.intimp.2005.08.026>
27. Meng M, Yao JL, Zhang YK, Sun HJ, Liu MZ. Potential Anti-Rheumatoid Arthritis Activities and Mechanisms of *Ganoderma lucidum* Polysaccharides. *Molecules*. 2023;28(6):2483. Available at: <https://doi.org/10.3390/molecules28062483>
28. Heo Y, Kim M, Suminda GGD, et al. Inhibitory effects of *Ganoderma lucidum* spore oil on rheumatoid arthritis in a collagen-induced arthritis mouse model. *Biomed Pharmacother*. 2023;157:114067. Available at: <https://doi.org/10.1016/j.biopha.2022.114067>
29. Guzel Erdogan D, Demir A, Baylan H, Budak Ö, Cokluk E, Tanyeri P. Effects of different doses of Ganoderic Acid A on nociceptive behaviour and inflammatory parameters in polyarthritic mice rheumatoid arthritis model. *Sci Rep*. 2025;15(1):15759. Available at: <https://doi.org/10.1038/s41598-025-99917-6>
30. Cai Z, Wong CK, Dong J, et al. Anti-inflammatory activities of *Ganoderma lucidum* (Lingzhi) and San-Miao-San supplements in MRL/lpr mice for the treatment of systemic lupus erythematosus. *Chin Med*. 2016;11:23. Available at: <https://doi.org/10.1186/s13020-016-0093-x>
31. Lu XH, Xu CY, Yang R, Zhang GJ. Ganoderic Acid A Alleviates OVA-Induced Asthma in Mice. *Inflammation*. 2021;44(5):1908–1915. Available at: <https://doi.org/10.1007/s10753-021-01468-1>
32. Liu CD, Yang N, Song Y, et al. Ganoderic acid C1 isolated from the anti-asthma formula, ASHMI™ suppresses TNF- α production by mouse macrophages and peripheral blood mononuclear cells from asthma patients. *Int Immunopharmacol*. 2015;27(2):224–231. Available at: <https://doi.org/10.1016/j.intimp.2015.05.018>
33. Li YF, Li MM, Wang R, Wang BY, Athari SS, Wang JL. *Ganoderma* modulates allergic asthma pathologic features via anti-inflammatory effects. *Respir Physiol Neurobiol*. 2022;299:103843. Available at: <https://doi.org/10.1016/j.resp.2022.103843>
34. Wang Y, Liu YF, Yu HZ, et al. Structural characterization and immuno-enhancing activity of a highly branched water-soluble β -glucan from the spores of *Ganoderma lucidum*. *Carbohydr Polym*. 2017;167:337–344. Available at: <https://doi.org/10.1016/j.carbpol.2017.03.016>
35. Zhang D, Wei YW, Zhu XY, et al. Study on the intervention mechanism of *Ganoderma lucidum* polysaccharides in mice with

- atopic dermatitis. *Food Res Int*. 2025;221(Pt 1):117212. Available at: <https://doi.org/10.1016/j.foodres.2025.117212>
36. Qiao HY, He J, Chen YW, et al. Sporoderm-broken of Ganoderma lucidum spore polysaccharides alleviate dextran sulfate sodium-induced colon inflammation in mice by regulating Th17/Treg homeostasis and restore gut microbiota balance. *Int J Biol Macromol*. 2025;323(Pt 1):147015. Available at: <https://doi.org/10.1016/j.ijbiomac.2025.147015>
 37. Li MY, Yu LL, Zhai QX, et al. Ganoderma lucidum Ethanol Extraction Promotes Dextran Sulphate Sodium Induced Colitis Recovery and Modulation in Microbiota. *Foods*. 2022;11(24):4023. Available at: <https://doi.org/10.3390/foods11244023>
 38. Huang S, Zhan ZC, Xu F, et al. Ganoderma lucidum spore powder alleviates rheumatoid arthritis-associated pain hypersensitivity through inhibiting accumulation, N1 polarization, and ROS production of neutrophils in mice. *Front Immunol*. 2025;16:1569295. Available at: <https://doi.org/10.3389/fimmu.2025.1569295>
 39. Zhang XQ, Ip FC, Zhang DM, et al. Triterpenoids with neurotrophic activity from Ganoderma lucidum. *Nat Prod Res*. 2011;25(17):1607–1613. Available at: <https://doi.org/10.1080/14786419.2010.496367>
 40. Sheng FY, Zhang LL, Wang SS, Yang LL, Li P. Deacetyl Ganoderic Acid F Inhibits LPS-Induced Neural Inflammation via NF- κ B Pathway Both In Vitro and In Vivo. *Nutrients*. 2019;12(1):85. Available at: <https://doi.org/10.3390/nu12010085>
 41. Chen YC, Zeng XX, Gong XR, Chen YL, Zhang X, Luo SM. Ganoderma lucidum polysaccharides target the gut-brain axis: Unveiling a novel mechanism for ameliorating aging-induced cognitive impairment and oxidative stress. *Int J Biol Macromol*. 2026;337(Pt 1):149519. Available at: <https://doi.org/10.1016/j.ijbiomac.2025.149519>
 42. Kou RW, Zhang RJ, Xia B, et al. Ganoderic Acid A Modulates Enteric Neurons and Intestinal Homeostasis in Irritable Bowel Syndrome by Microbiota Sensing. *J Agric Food Chem*. 2026;74(5):4566–4581. Available at: <https://doi.org/10.1021/acs.jafc.5c15628>
 43. Guo YF, Feng YZ, Xu JY, et al. Ganoderma calidophilum-derived highly oxygenated lanostane triterpenoids: Multitarget neuroprotection through AMPK/mTOR/SIRT1 axis modulation and gut-brain axis crosstalk. *Bioorg Chem*. 2025;163:108757. Available at: <https://doi.org/10.1016/j.bioorg.2025.108757>
 44. Koszła O, Kukula-Koch W, Józwiak K, et al. Biotransformation of Ganoderma lucidum and Hericium erinaceus for ex vivo gut-brain axis modulation and mood-related outcomes in humans: CREB/BDNF signaling and microbiota-driven synergies. *J Ethnopharmacol*. 2025;342:119393. Available at: <https://doi.org/10.1016/j.jep.2025.119393>
 45. Wu JF, Tang YD, Wang YJ, et al. Ganoderic Acid a Promotes Functional Recovery After Traumatic Brain Injury By Protecting Blood-brain Barrier Integrity and Modulating Microglial Polarization. *J Neuroimmune Pharmacol*. 2026;21(1):20. Available at: <https://doi.org/10.1007/s11481-026-10289-8>
 46. Chen L, Ling YJ, Sun JX, et al. A glucan from Ganoderma lucidum: Structural characterization and the anti-inflammatory effect on Parkinson's disease via regulating dysfunctions of intestinal microecology and inhibiting TLR4/MyD88/NF- κ B signaling pathway. *J Ethnopharmacol*. 2025;343:119446. Available at: <https://doi.org/10.1016/j.jep.2025.119446>
 47. Ren ZL, Ding H, Zhou M, Chan P. Ganoderma lucidum Modulates Inflammatory Responses following 1-Methyl-4-Phenyl-1,2,3,6-Tetrahydropyridine (MPTP) Administration in Mice. *Nutrients*. 2022;14(18):3872. Available at: <https://doi.org/10.3390/nu14183872>
 48. Ren ZL, Wang CD, Wang T, et al. Ganoderma lucidum extract ameliorates MPTP-induced parkinsonism and protects dopaminergic neurons from oxidative stress via regulating mitochondrial function, autophagy, and apoptosis. *Acta Pharmacol Sin*. 2019;40(4):441–450. Available at: <https://doi.org/10.1038/s41401-018-0077-8>
 49. Mia M, Dutta A, Hossain MM, Adhikari J, Rahman MM, Shibly AZ. Exploring the neuroprotective, antioxidant, and anti-amyloid effects of Ganoderma lucidum compounds in Alzheimer's disease: insights from experimental and computational approaches. *J Genet Eng Biotechnol*. 2026;24(2):100706. Available at: <https://doi.org/10.1016/j.jgeb.2026.100706>
 50. Ali A, Ganeshpurkar A, Ganeshpurkar A, Dubey N. In Silico Investigation of Ganoderic Acid A Targeting Amyloid-Beta and Tau Protein Aggregation in Alzheimer's Disease. *Int J Med Mushrooms*. 2025;27(9):85–92. Available at: <https://doi.org/10.1615/IntJMedMushrooms.2025059137>
 51. Wang W, Sun YY, Cao RT, et al. Illustrate the metabolic regulatory effects of Ganoderma lucidum polysaccharides on cognitive dysfunction in formaldehyde-exposed mouse brain by mass spectrometry imaging. *Ecotoxicol Environ Saf*. 2025;294:118060. Available at: <https://doi.org/10.1016/j.ecoenv.2025.118060>
 52. Lian WH, Yang X, Duan QD, et al. The Biological Activity of Ganoderma lucidum on Neurodegenerative Diseases: The Interplay between Different Active Compounds and the Pathological Hallmarks. *Molecules*. 2024;29(11):2516. Available at: <https://doi.org/10.3390/molecules29112516>
 53. Aprizal YM, Mohamad Yusof MI, Mohamad Jamil N, et al. Fermented Moringa oleifera leaves and Ganoderma lucidum mixtures ameliorate cognitive deficits in scopolamine-induced dementia rats by enhancing brain antioxidant and cholinergic functions. *Pharm Biol*. 2026;64(1):234–255. Available at: <https://doi.org/10.1080/13880209.2026.2613838>
 54. Wang SQ, Li XJ, Qiu HB, et al. Anti-epileptic effect of Ganoderma lucidum polysaccharides by inhibition of intracellular calcium accumulation and stimulation of expression of CaMKII α in epileptic hippocampal neurons. *PLoS One*. 2014;9(7):e102161. Available at: <https://doi.org/10.1371/journal.pone.0102161>
 55. Wang SQ, Li XJ, Zhou S, et al. Intervention effects of ganoderma lucidum spores on epileptiform discharge hippocampal neurons and expression of neurotrophin-4 and N-cadherin. *PLoS One*. 2013;8(4):e61687. Available at: <https://doi.org/10.1371/journal.pone.0061687>
 56. Xie YC, Gao FS, Geng Y, et al. Lucidenic acid A drives PI3K/AKT/BDNF signaling to improve memory impairment in mice and alleviate cellular nerve damage. *J Ethnopharmacol*. 2026;359:121099. Available at: <https://doi.org/10.1016/j.jep.2025.121099>
 57. Zhou ZH, Yu TJ, Wang ZB, et al. Ganoderma lucidum triterpenes ameliorate age-related cognitive impairment via regulating Eubacterium lentum-mediated serine metabolism. *Phytomedicine*. 2025;149:157557. Available at: <https://doi.org/10.1016/j.phymed.2025.157557>
 58. Chen YY, Li JH, Zhang S, Zhao YH, Gao DM, Xu GY. Effects of Ganoderma lucidum polysaccharide on learning and memory impairment and intestinal flora in mice with D-galactose-induced aging. *Naturwissenschaften*. 2025;112(3):46. Available at: <https://doi.org/10.1007/s00114-025-01997-x>
 59. Kabir Y, Kimura S, Tamura T. Dietary effect of Ganoderma lucidum mushroom on blood pressure and lipid levels in spontaneously hypertensive rats (SHR). *J Nutr Sci Vitaminol (Tokyo)*. 1988;34(4):433–438. Available at: <https://doi.org/10.3177/jnsv.34.433>

60. Kumakura K, Hori C, Matsuoka H, Igarashi K, Samejima M. Protein components of water extracts from fruiting bodies of the reishi mushroom *Ganoderma lucidum* contribute to the production of functional molecules. *J Sci Food Agric*. 2019;99(2):529–535. Available at: <https://doi.org/10.1002/jsfa.9211>
61. Abdullah N, Ismail SM, Aminudin N, Shuib AS, Lau BF. Evaluation of Selected Culinary-Medicinal Mushrooms for Antioxidant and ACE Inhibitory Activities. *Evid Based Complement Alternat Med*. 2012;2012:464238. Available at: <https://doi.org/10.1155/2012/464238>
62. Wu Q, Li Y, Peng K, et al. Isolation and Characterization of Three Antihypertension Peptides from the Mycelia of *Ganoderma lucidum* (Agaricomycetes). *J Agric Food Chem*. 2019;67(29):8149–8159. Available at: <https://doi.org/10.1021/acs.jafc.9b02276>
63. Amen Y, Zhu Q, Tran HB, et al. Partial contribution of Rho-kinase inhibition to the bioactivity of *Ganoderma lingzhi* and its isolated compounds: insights on discovery of natural Rho-kinase inhibitors. *J Nat Med*. 2017;71(2):380–388. Available at: <https://doi.org/10.1007/s11418-016-1069-y>
64. Sargowo D, Oviati N, Susilowati E, et al. The role of polysaccharide peptide of *Ganoderma lucidum* as a potent antioxidant against atherosclerosis in high risk and stable angina patients. *Indian Heart J*. 2018;70(5):608–614. Available at: <https://doi.org/10.1016/j.ihj.2017.12.007>
65. Lasukova TV, Maslov LN, Arbuzov AG, Burkova VN, Inisheva LI. Cardioprotective Activity of *Ganoderma lucidum* Extract during Total Ischemia and Reperfusion of Isolated Heart. *Bull Exp Biol Med*. 2015;158(6):739–741. Available at: <https://doi.org/10.1007/s10517-015-2851-7>
66. Li WJ, Nie SP, Chen Y, et al. *Ganoderma atrum* polysaccharide protects cardiomyocytes against anoxia/reoxygenation-induced oxidative stress by mitochondrial pathway. *J Cell Biochem*. 2010;110(1):191–200. Available at: <https://doi.org/10.1002/jcb.22526>
67. Sudheesh NP, Ajith TA, Janardhanan KK. *Ganoderma lucidum* ameliorate mitochondrial damage in isoproterenol-induced myocardial infarction in rats by enhancing the activities of TCA cycle enzymes and respiratory chain complexes. *Int J Cardiol*. 2013;165(1):117–125. Available at: <https://doi.org/10.1016/j.ijcard.2011.07.103>
68. Wan JF, Wang G, Qin FY, et al. Z16b, a natural compound from *Ganoderma cochlear* is a novel RyR2 stabilizer preventing catecholaminergic polymorphic ventricular tachycardia. *Acta Pharmacol Sin*. 2022;43(9):2340–2350. Available at: <https://doi.org/10.1038/s41401-022-00870-1>
69. Sang TT, Xu T, Chen C, et al. *Ganoderma lucidum* Polysaccharides Alleviate High-Fat Diet-Induced Obesity by Promoting Lipolysis and Inhibiting Inflammation through *Lactobacillus johnsonii*-Butyrate Axis. *J Agric Food Chem*. 2026;74(1):834–850. Available at: <https://doi.org/10.1021/acs.jafc.5c12282>
70. Lee HA, Cho JH, Afinanisa Q, et al. *Ganoderma lucidum* Extract Reduces Insulin Resistance by Enhancing AMPK Activation in High-Fat Diet-Induced Obese Mice. *Nutrients*. 2020;12(11):3338. Available at: <https://doi.org/10.3390/nu12113338>
71. Huang CH, Lin WK, Chang SH, Tsai GJ. *Ganoderma lucidum* culture supplement ameliorates dyslipidemia and reduces visceral fat accumulation in type 2 diabetic rats. *Mycology*. 2020;12(2):94–104. Available at: <https://doi.org/10.1080/21501203.2020.1740409>
72. Sang TT, Guo CJ, Guo DD, et al. Suppression of obesity and inflammation by polysaccharide from sporoderm-broken spore of *Ganoderma lucidum* via gut microbiota regulation. *Carbohydr Polym*. 2021;256:117594. Available at: <https://doi.org/10.1016/j.carbpol.2020.117594>
73. Wang WS, Sun R, Zhang JJ, Jia L, Dong YJ. Study on the Mechanism of *Ganoderma lucidum* Polysaccharides for Ameliorating Dyslipidemia via Regulating Gut Microbiota and Fecal Metabolites. *Biomolecules*. 2026;16(1):153. Available at: <https://doi.org/10.3390/biom16010153>
74. Mfopa A, Mediesse FK, Mvongo C, et al. Antidyslipidemic Potential of Water-Soluble Polysaccharides of *Ganoderma applanatum* in MACAPOS-2-Induced Obese Rats. *Evid Based Complement Alternat Med*. 2021;2021:2452057. Available at: <https://doi.org/10.1155/2021/2452057>
75. Lai P, Cao X, Xu Q, et al. *Ganoderma lucidum* spore ethanol extract attenuates atherosclerosis by regulating lipid metabolism via upregulation of liver X receptor alpha. *Pharm Biol*. 2020;58(1):760–770. Available at: <https://doi.org/10.1080/13880209.2020.1798471>
76. Liu Y, Feng XM, Wang JA, Li MF. Neuroprotective Effect of *Ganoderic Acid* against Focal Ischemic Stroke Induced by Middle Cerebral Artery Occlusion in the Rats via Suppression of Oxidative Stress and Inflammation. *Dokl Biochem Biophys*. 2024;518(1):361–371. Available at: <https://doi.org/10.1134/s1607672924600313>
77. Ma A, Zhu YH, Ying Y, et al. *Ganoderic Acids* Alleviate Neuroinflammation by Targeting Myeloid Differentiation Factor 2 for Ischemic Stroke Therapy. *Exploration (Beijing)*. 2026;6(1):20240147. Available at: <https://doi.org/10.1002/exp.20240147>
78. Levin RM, Xia L, Wei W, Schuler C, Leggett RE, Lin AD. Effects of *Ganoderma lucidum* shell-broken spore on oxidative stress of the rabbit urinary bladder using an in vivo model of ischemia/reperfusion. *Mol Cell Biochem*. 2017;435(1–2):25–35. Available at: <https://doi.org/10.1007/s11010-017-3053-6>
79. Chen H, Hoi MPM, Lee SMY. Medicinal plants and natural products for treating overactive bladder. *Chin Med*. 2024;19(1):56. Available at: <https://doi.org/10.1186/s13020-024-00884-3>
80. Noguchi M, Kakuma T, Tomiyasu K, et al. Effect of an extract of *Ganoderma lucidum* in men with lower urinary tract symptoms: a double-blind, placebo-controlled randomized and dose-ranging study. *Asian J Androl*. 2008;10(4):651–658. Available at: <https://doi.org/10.1111/j.1745-7262.2008.00336.x>
81. Shao GY, He JZ, Meng J, et al. *Ganoderic Acids* Prevent Renal Ischemia Reperfusion Injury by Inhibiting Inflammation and Apoptosis. *Int J Mol Sci*. 2021;22(19):10229. Available at: <https://doi.org/10.3390/ijms221910229>
82. Zhong DD, Wang HK, Liu M, et al. *Ganoderma lucidum* polysaccharide peptide prevents renal ischemia reperfusion injury via counteracting oxidative stress. *Sci Rep*. 2015;5:16910. Available at: <https://doi.org/10.1038/srep16910>
83. Mahran YF, Hassan HM. *Ganoderma lucidum* Prevents Cisplatin-Induced Nephrotoxicity through Inhibition of Epidermal Growth Factor Receptor Signaling and Autophagy-Mediated Apoptosis. *Oxid Med Cell Longev*. 2020;2020:4932587. Available at: <https://doi.org/10.1155/2020/4932587>
84. Ota N, Endo S, Tatsunami R, et al. Effect of *Ganoderma lucidum* on Cisplatin-induced Nephrotoxicity and Gastrointestinal Toxicity. *Anticancer Res*. 2024;44(8):3605–3613. Available at: <https://doi.org/10.21873/anticancer.17183>
85. Kim S, Kim J, Kim JL, Park MR, Park KW, Chung KW. *Ganoderma lucidum* and Robinia pseudoacacia Flower Extract Complex Alleviates Kidney Inflammation and Fibrosis by Modulating Oxidative Stress. *Antioxidants (Basel)*. 2025;14(4):409. Available at: <https://doi.org/10.3390/antiox14040409>
86. Hu LD, Yu LL, Cao ZK, et al. Integrating transcriptomics, metabolomics, and network pharmacology to investigate multi-target effects of sporoderm-broken spores of *Ganoderma lucidum* on improving HFD-induced diabetic nephropathy rats. *J Pharm Anal*. 2024;14(12):101105. Available at:

- <https://doi.org/10.1016/j.jpha.2024.101105>
87. Yu H, Yang Y, Jiang TY, et al. Effective Radiotherapy in Tumor Assisted by Ganoderma lucidum Polysaccharide-Conjugated Bismuth Sulfide Nanoparticles through Radiosensitization and Dendritic Cell Activation. *ACS Appl Mater Interfaces*. 2019;11(31):27536–27547. Available at: <https://doi.org/10.1021/acsami.9b07804>
 88. Liu YY, Cai D, Tang XP, Cheng YX. Baoslingzhines Q-X: Structurally previously undescribed trace phenolic meroterpenoids from Ganoderma lucidum and their biological activities toward renal fibrosis and cytotoxicity. *Phytochemistry*. 2025;235:114448. Available at: <https://doi.org/10.1016/j.phytochem.2025.114448>
 89. Liu XJ, Zhao JM, Liu J, et al. Ganoderma lucidum sporoderm-broken spore powder alleviates kidney aging by modulating gut microbiota. *J Ethnopharmacol*. 2025;353(Pt A):120344. Available at: <https://doi.org/10.1016/j.jep.2025.120344>
 90. Su LM, Liu LY, Jia YL, et al. Ganoderma triterpenes retard renal cyst development by downregulating Ras/MAPK signaling and promoting cell differentiation. *Kidney Int*. 2017;92(6):1404–1418. Available at: <https://doi.org/10.1016/j.kint.2017.04.013>
 91. Meng J, Sai-Zhen Wang, He JZ, et al. Ganoderic acid A is the effective ingredient of Ganoderma triterpenes in retarding renal cyst development in polycystic kidney disease. *Acta Pharmacol Sin*. 2020;41(6):782–790. Available at: <https://doi.org/10.1038/s41401-019-0329-2>
 92. Hou ZM, Ji WL, Yang SP, et al. Protective effects of Ganoderma lucidum polysaccharide peptides against cisplatin-induced toxicity. *J Ethnopharmacol*. 2026;360:121210. Available at: <https://doi.org/10.1016/j.jep.2026.121210>
 93. Sinaeve S, Husson C, Antoine MH, Welti S, Stéveny C, Nortier J. Nephroprotective Effects of Two Ganoderma Species Methanolic Extracts in an In Vitro Model of Cisplatin Induced Tubulotoxicity. *J Fungi (Basel)*. 2022;8(10):1002. Available at: <https://doi.org/10.3390/jof8101002>
 94. Pillai TG, John M, Sara Thomas G. Prevention of cisplatin induced nephrotoxicity by terpenes isolated from Ganoderma lucidum occurring in Southern Parts of India. *Exp Toxicol Pathol*. 2011;63(1–2):157–160. Available at: <https://doi.org/10.1016/j.etp.2009.11.003>
 95. Fang H, Lin DM, Li XX, Wang LF, Yang T. Therapeutic potential of Ganoderma lucidum polysaccharide peptide in Doxorubicin-induced nephropathy: modulation of renin-angiotensin system and proteinuria. *Front Pharmacol*. 2023;14:1287908. Available at: <https://doi.org/10.3389/fphar.2023.1287908>
 96. Zhou Y, Zhang BW, Wang XD, et al. A network pharmacology approach and experimental validation to investigate the protection mechanism of Ganoderma lucidum (Leyss. ex Fr.) Karst spore for acute kidney injury through induction of apoptosis via p53/Caspase 3 signaling pathway. *J Ethnopharmacol*. 2025;351:120075. Available at: <https://doi.org/10.1016/j.jep.2025.120075>
 97. Yang T, Fang H, Lin DM, et al. Ganoderma Lucidum polysaccharide peptide (GL-PP2): A potential therapeutic agent against sepsis-induced organ injury by modulating Nrf2/NF-κB pathways. *Int J Biol Macromol*. 2025;285:138378. Available at: <https://doi.org/10.1016/j.ijbiomac.2024.138378>
 98. Wang YX, Peng YL, Qiu B, Lv Q, Huang LS, Cheng YX. Meroterpenoids with a large conjugated system from Ganoderma lucidum and their inhibitory activities against renal fibrosis. *Fitoterapia*. 2022;161:105257. Available at: <https://doi.org/10.1016/j.fitote.2022.105257>
 99. Ma JQ, Zhang YJ, Tian ZK. Anti-oxidant, anti-inflammatory and anti-fibrosis effects of ganoderic acid A on carbon tetrachloride induced nephrotoxicity by regulating the Trx/TrxR and JAK/ROCK pathway. *Chem Biol Interact*. 2021;344:109529. Available at: <https://doi.org/10.1016/j.cbi.2021.109529>
 100. Geng XQ, Ma A, He JZ, et al. Ganoderic acid hinders renal fibrosis via suppressing the TGF-β/Smad and MAPK signaling pathways. *Acta Pharmacol Sin*. 2020;41(5):670–677. Available at: <https://doi.org/10.1038/s41401-019-0324-7>
 101. Gogulski M, Leciejewska N, Nowak M, et al. Antifibrotic action of medicinal mushrooms Ganoderma lucidum and Polyporus umbellatus in MDCK and CRFK cells. *Vet Res Commun*. 2026;50(3):222. Available at: <https://doi.org/10.1007/s11259-026-11155-x>
 102. Yan YM, Wang XL, Zhou LL, et al. Lingzhilactones from Ganoderma lingzhi ameliorate adriamycin-induced nephropathy in mice. *J Ethnopharmacol*. 2015;176:385–393. Available at: <https://doi.org/10.1016/j.jep.2015.11.024>
 103. Pan YN, Zhang Y, Li JQ, et al. A proteoglycan isolated from Ganoderma lucidum attenuates diabetic kidney disease by inhibiting oxidative stress-induced renal fibrosis both in vitro and in vivo. *J Ethnopharmacol*. 2023;310:116405. Available at: <https://doi.org/10.1016/j.jep.2023.116405>
 104. Li D, Gao Q, Cheng YX, Luo Q. Five undescribed meroterpenoids from Ganoderma lucidum and their inhibitory activities against renal fibrosis. *Fitoterapia*. 2024;176:106031. Available at: <https://doi.org/10.1016/j.fitote.2024.106031>
 105. Fang H, Li XX, Lin DM, Wang LF, Yang T, Yang BX. Inhibition of intrarenal PRR-RAS pathway by Ganoderma lucidum polysaccharide peptides in proteinuric nephropathy. *Int J Biol Macromol*. 2023;253(Pt 7):127336. Available at: <https://doi.org/10.1016/j.ijbiomac.2023.127336>
 106. Lin SM, Meng J, Li F, et al. Ganoderma lucidum polysaccharide peptide alleviates hyperuricemia by regulating adenosine deaminase and urate transporters. *Food Funct*. 2022;13(24):12619–12631. Available at: <https://doi.org/10.1039/d2fo02431d>
 107. Hu Y, Wang SX, Wu FY, et al. Effects and Mechanism of Ganoderma lucidum Polysaccharides in the Treatment of Diabetic Nephropathy in Streptozotocin-Induced Diabetic Rats. *Biomed Res Int*. 2022;2022:4314415. Available at: <https://doi.org/10.1155/2022/4314415>
 108. Hassan HM, Mahran YF, Ghanim AMH. Ganoderma lucidum ameliorates the diabetic nephropathy via down-regulatory effect on TGFβ-1 and TLR-4/NFκB signalling pathways. *J Pharm Pharmacol*. 2021;73(9):1250–1261. Available at: <https://doi.org/10.1093/jpp/rgab058>
 109. Kara ŞŞ, Sağır D. Protective Antioxidant Effects of Ganoderma lucidum Against Prenatal Chlorpyrifos-Induced Developmental Nephrotoxicity in Rats. *Biomedicines*. 2026;14(3):658. Available at: <https://doi.org/10.3390/biomedicines14030658>
 110. You YK, Luo Q, Wu WF, et al. Petchiether A attenuates obstructive nephropathy by suppressing TGF-β/Smad3 and NF-κB signalling. *J Cell Mol Med*. 2019;23(8):5576–5587. Available at: <https://doi.org/10.1111/jcmm.14454>
 111. Pan D, Zhang D, Wu JS, et al. A novel proteoglycan from Ganoderma lucidum fruiting bodies protects kidney function and ameliorates diabetic nephropathy via its antioxidant activity in C57BL/6 db/db mice. *Food Chem Toxicol*. 2014;63:111–118. Available at: <https://doi.org/10.1016/j.fct.2013.10.046>
 112. Xie L, Zhong XH, Liu DB, Liu L, Xia ZL. The effects of freeze-dried Ganoderma lucidum mycelia on a recurrent oral ulceration rat model. *BMC Complement Altern Med*. 2017;17(1):511. Available at: <https://doi.org/10.1186/s12906-017-2021-8>
 113. Wang SY, Zhang SJ, Meng HF, et al. DPSCs regulate epithelial-T cell interactions in oral submucous fibrosis. *Stem Cell Res Ther*. Available at: <https://doi.org/10.1186/s12906-017-2021-8>

- 2024;15(1):113. Available at: <https://doi.org/10.1186/s13287-024-03720-5>
114. Lee PH, Hsieh PL, Liao YW, Yu CC. Inhibitory effect of GMI, an immunomodulatory protein from *Ganoderma microsporum*, on myofibroblast activity and proinflammatory cytokines in human fibrotic buccal mucosal fibroblasts. *Environ Toxicol*. 2018;33(1):32–40. Available at: <https://doi.org/10.1002/tox.22489>
 115. Luo HJ, Zhang YK, Yao Y, et al. A novel galactoglucan from *Ganoderma lucidum* ameliorates ethanol-induced gastric ulcers by modulating FAK-MAPK signaling pathway. *Carbohydr Polym*. 2025;360:123594. Available at: <https://doi.org/10.1016/j.carbpol.2025.123594>
 116. Park JH, Jang KJ, Kim CH, Kim JH, Kim YK, Yoon HM. *Ganoderma lucidum* Pharmacopuncture for Treating Ethanol-induced Chronic Gastric Ulcers in Rats. *J Pharmacopuncture*. 2015;18(1):72–78. Available at: <https://doi.org/10.3831/KPI.2015.18.008>
 117. Park JH, Jang KJ, Kim CH, et al. *Ganoderma lucidum* Pharmacopuncture for the Treatment of Acute Gastric Ulcers in Rats. *J Pharmacopuncture*. 2014;17(3):40–49. Available at: <https://doi.org/10.3831/kpi.2014.17.025>
 118. Gao YH, Tang WB, Gao H, Chan E, Lan J, Zhou SF. *Ganoderma lucidum* polysaccharide fractions accelerate healing of acetic acid-induced ulcers in rats. *J Med Food*. 2004;7(4):417–421. Available at: <https://doi.org/10.1089/jmf.2004.7.417>
 119. Gao YH, Zhou SF, Wen JB, Huang M, Xu AL. Mechanism of the antitumor effect of *Ganoderma lucidum* polysaccharides on indomethacin-induced lesions in the rat. *Life Sci*. 2002;72(6):731–745. Available at: [https://doi.org/10.1016/s0024-3205\(02\)02301-9](https://doi.org/10.1016/s0024-3205(02)02301-9)
 120. Nagai K, Ueno Y, Tanaka S, Hayashi R, Shinagawa K, Chayama K. Polysaccharides derived from *Ganoderma lucidum* fungus mycelia ameliorate indomethacin-induced small intestinal injury via induction of GM-CSF from macrophages. *Cell Immunol*. 2017;320:20–28. Available at: <https://doi.org/10.1016/j.cellimm.2017.08.001>
 121. Zhang QQ, Chen JY, Zhang Y, et al. Intestinal epithelial protection and gut microbiota modulation by *Ganoderma lucidum* proteoglycan are associated with its hypoglycemic potential in type 2 diabetes. *Int J Biol Macromol*. 2026;354:151441. Available at: <https://doi.org/10.1016/j.ijbiomac.2026.151441>
 122. Wang CH, Zhang QY, Wei CZ, Jin YX. *Ganoderma lucidum* dietary fiber and lactobacillus fermentum CECT5716 alleviate constipation via regulation of gut barrier and microbiota. *Int J Biol Macromol*. 2025;333(Pt 2):149010. Available at: <https://doi.org/10.1016/j.ijbiomac.2025.149010>
 123. Ye Y, Abulizi A, Zhang Y, et al. *Ganoderic Acid* Ameliorates Ulcerative Colitis by Improving Intestinal Barrier Function via Gut Microbiota Modulation. *Int J Mol Sci*. 2025;26(6):2466. Available at: <https://doi.org/10.3390/ijms26062466>
 124. Kou RW, Li ZQ, Wang JL, et al. *Ganoderic Acid A* Mitigates Inflammatory Bowel Disease through Modulation of AhR Activity by Microbial Tryptophan Metabolism. *J Agric Food Chem*. 2024;72(32):17912–17923. Available at: <https://doi.org/10.1021/acs.jafc.4c01166>
 125. Zhao Y, Zhu L. Oral Lingzhi or Reishi Medicinal Mushroom *Ganoderma lucidum* (Agaricomycetes) Spore Powder Ameliorates Murine Colitis by Inhibiting Key Kinases Phosphorylation in MAPK Pathway. *Int J Med Mushrooms*. 2023;25(10):39–48. Available at: <https://doi.org/10.1615/intjmedmushrooms.2023049699>
 126. Liao N, Wang J, Liu GW, et al. Modification of *Ganoderma lucidum* spore shells into probiotic carriers: selective loading and colonic delivery of *Lactobacillus rhamnosus* and effective therapy of inflammatory bowel disease. *Food Funct*. 2025;16(3):908–927. Available at: <https://doi.org/10.1039/d4fo04523h>
 127. Liu LP, Feng J, Jiang SQ, et al. Anti-inflammatory and intestinal microbiota modulation properties of *Ganoderma lucidum* β -D-glucans with different molecular weight in an ulcerative colitis model. *Int J Biol Macromol*. 2023;251:126351. Available at: <https://doi.org/10.1016/j.ijbiomac.2023.126351>
 128. Hanaoka R, Ueno Y, Tanaka S, et al. The water-soluble extract from cultured medium of *Ganoderma lucidum* (Reishi) mycelia (Designated as MAK) ameliorates murine colitis induced by trinitrobenzene sulphonic acid. *Scand J Immunol*. 2011;74(5):454–462. Available at: <https://doi.org/10.1111/j.1365-3083.2011.02601.x>
 129. Hsu HY, Kuan YC, Lin TY, et al. Reishi Protein LZ-8 Induces FOXP3(+) Treg Expansion via a CD45-Dependent Signaling Pathway and Alleviates Acute Intestinal Inflammation in Mice. *Evid Based Complement Alternat Med*. 2013;2013:513542. Available at: <https://doi.org/10.1155/2013/513542>
 130. Chen LH, Lin ZB, Li WD. *Ganoderma lucidum* polysaccharides reduce methotrexate-induced small intestinal damage in mice via induction of epithelial cell proliferation and migration. *Acta Pharmacol Sin*. 2011;32(12):1505–1512. Available at: <https://doi.org/10.1038/aps.2011.126>
 131. Wang WS, Zhang YH, Wang ZY, Zhang JJ, Jia L. *Ganoderma lucidum* polysaccharides improve lipid metabolism against high-fat diet-induced dyslipidemia. *J Ethnopharmacol*. 2023;309:116321. Available at: <https://doi.org/10.1016/j.jep.2023.116321>
 132. Zhang XT, Yang Y, Ji CL, Fu YJ, Pu XY, Xu GY. *Ganoderma lucidum* polysaccharides reduce the severity of acute liver injury by improving the diversity and function of the gut microbiota. *Heliyon*. 2024;10(15):e35559. Available at: <https://doi.org/10.1016/j.heliyon.2024.e35559>
 133. Cao YJ, Huang ZR, You SZ, et al. The Protective Effects of *Ganoderic Acids* from *Ganoderma lucidum* Fruiting Body on Alcoholic Liver Injury and Intestinal Microflora Disturbance in Mice with Excessive Alcohol Intake. *Foods*. 2022;11(7):949. Available at: <https://doi.org/10.3390/foods11070949>
 134. Guo WL, Cao YJ, You SZ, et al. *Ganoderic acids*-rich ethanol extract from *Ganoderma lucidum* protects against alcoholic liver injury and modulates intestinal microbiota in mice with excessive alcohol intake. *Curr Res Food Sci*. 2022;5:515–530. Available at: <https://doi.org/10.1016/j.crfs.2022.02.013>
 135. Zhao ZK, Ma XX, Li MY, et al. Alcoholic Extracts from the *Ganoderma lucidum* Fermentation Product Alleviated Ethanol-Induced Liver Injury, Gut Leakiness, and Gut Dysbiosis in Mice. *Plant Foods Hum Nutr*. 2024;80(1):2. Available at: <https://doi.org/10.1007/s11130-024-01271-x>
 136. Lv XC, Wu Q, Cao YJ, et al. *Ganoderic acid A* from *Ganoderma lucidum* protects against alcoholic liver injury through ameliorating the lipid metabolism and modulating the intestinal microbial composition. *Food Funct*. 2022;13(10):5820–5837. Available at: <https://doi.org/10.1039/d1fo03219d>
 137. Shao WM, Xiao C, Yong TQ, et al. A polysaccharide isolated from *Ganoderma lucidum* ameliorates hyperglycemia through modulating gut microbiota in type 2 diabetic mice. *Int J Biol Macromol*. 2022;197:23–38. Available at: <https://doi.org/10.1016/j.ijbiomac.2021.12.034>
 138. Jiang YM, Zhang N, Zhou YW, et al. Manipulations of glucose/lipid metabolism and gut microbiota of resistant starch encapsulated *Ganoderma lucidum* spores in T2DM rats. *Food Sci Biotechnol*. 2021;30(5):755–764. Available at: <https://doi.org/10.1007/s10068-021-00908-w>
 139. Chen L, Wang XY, Sun JX, Xue JF, Yang XD, Zhang Y. Structural characteristics of a heteropolysaccharide from *Ganoderma*

- lucidum and its protective effect against Alzheimer's disease via modulating the microbiota-gut-metabolomics. *Int J Biol Macromol.* 2025;297:139863. Available at: <https://doi.org/10.1016/j.ijbiomac.2025.139863>
140. Li K, Jiang YP, Wang NN, et al. Traditional Chinese Medicine in Osteoporosis Intervention and the Related Regulatory Mechanism of Gut Microbiome. *Am J Chin Med.* 2023;51(8):1957–1981. Available at: <https://doi.org/10.1142/s0192415x23500866>
 141. Yao CY, Wang ZY, Jiang HY, et al. Ganoderma lucidum promotes sleep through a gut microbiota-dependent and serotonin-involved pathway in mice. *Sci Rep.* 2021;11(1):13660. Available at: <https://doi.org/10.1038/s41598-021-92913-6>
 142. Zong YH, Kong JW, Yang F, Wang MT, Wang J, Wang Q. Guominkang formula alleviates airway inflammation in HDM-induced asthma mice by regulating Wnt/ β -Catenin pathway. *Chin Med.* 2026;21(1):90. Available at: <https://doi.org/10.1186/s13020-025-01244-5>
 143. Deng SZ, Zhong DQ, Dong YG, et al. Network Pharmacology and Experimental Validation Reveal Ganodermanontriol Modulates Pneumonia via TNF/NF- κ B/MAPKs Signaling Pathway. *Food Sci Nutr.* 2025;13(4):e70123. Available at: <https://doi.org/10.1002/fsn3.70123>
 144. Liu Y, Xu WD, Wang KX, et al. Integrated metabolomic, transcriptomic and network analysis elucidates therapeutic mechanisms of Ganoderma lucidum spore oil against granulomatous pulmonary nodules. *Front Pharmacol.* 2025;16:1612043. Available at: <https://doi.org/10.3389/fphar.2025.1612043>
 145. Chen JH, Shi YY, He L, et al. Protective roles of polysaccharides from Ganoderma lucidum on bleomycin-induced pulmonary fibrosis in rats. *Int J Biol Macromol.* 2016;92:278–281. Available at: <https://doi.org/10.1016/j.ijbiomac.2016.07.005>
 146. Hu WJ, Ma Y, Zhang Q, et al. DCs-targeted full-cell nanovaccine based on chitosan oligosaccharide self-assembled with ganoderma lucidum polysaccharide for enhancing tumor immunotherapy. *Int J Biol Macromol.* 2025;334(Pt 1):148934. Available at: <https://doi.org/10.1016/j.ijbiomac.2025.148934>
 147. Xia Q, Zhang HZ, Sun XF, et al. A comprehensive review of the structure elucidation and biological activity of triterpenoids from Ganoderma spp. *Molecules.* 2014;19(11):17478–17535. Available at: <https://doi.org/10.3390/molecules191117478>
 148. Liu CD, Cao MZ, Yang N, et al. Time-dependent dual beneficial modulation of interferon- γ , interleukin 5, and Treg cytokines in asthma patient peripheral blood mononuclear cells by ganoderic acid B. *Phytother Res.* 2022;36(3):1231–1240. Available at: <https://doi.org/10.1002/ptr.7266>
 149. Chen ML, Lin BF. Effects of triterpenoid-rich extracts of Ganoderma tsugae on airway hyperreactivity and Th2 responses in vivo. *Int Arch Allergy Immunol.* 2007;143(1):21–30. Available at: <https://doi.org/10.1159/000098222>
 150. Liu HZ, Qiu FF, Wang YY, et al. A recombinant protein rLZ-8, originally extracted from Ganoderma lucidum, ameliorates OVA-induced lung inflammation by regulating Th17/Treg balance. *J Leukoc Biol.* 2020;108(2):531–545. Available at: <https://doi.org/10.1002/jlb.5ma0420-453r>
 151. Zhang XL, Wu DS, Tian Y, et al. Ganoderma lucidum polysaccharides ameliorate lipopolysaccharide-induced acute pneumonia via inhibiting NLRP1-mediated inflammation. *Pharm Biol.* 2022;60(1):2201–2209. Available at: <https://doi.org/10.1080/13880209.2022.2142615>
 152. Lin DM, Zhang YK, Wang SZ, et al. Ganoderma lucidum polysaccharide peptides GL-PPSQ2 alleviate intestinal ischemia-reperfusion injury via inhibiting cytotoxic neutrophil extracellular traps. *Int J Biol Macromol.* 2023;244:125370. Available at: <https://doi.org/10.1016/j.ijbiomac.2023.125370>
 153. Zhu SR, Wang XL, Liu GQ. The Protective Effects of Ganoderma lucidum Active Peptide GLP4 on Lung Injury Induced by Cadmium Poisoning in Mice. *Toxics.* 2024;12(6):378. Available at: <https://doi.org/10.3390/toxics12060378>
 154. Wan B, Li Y, Sun SS, et al. Ganoderic acid A attenuates lipopolysaccharide-induced lung injury in mice. *Biosci Rep.* 2019;39(5):BSR20190301. Available at: <https://doi.org/10.1042/bsr20190301>
 155. Wen GY, Li T, He H, Zhou XM, Zhu J. Ganoderic Acid A Inhibits Bleomycin-Induced Lung Fibrosis in Mice. *Pharmacology.* 2020;105(9–10):568–575. Available at: <https://doi.org/10.1159/000505297>
 156. Wang HM, Zhang RL, Song YY, Li TQ, Ge M. Protective Effect of Ganoderma Triterpenoids on Cadmium-Induced Testicular Toxicity in Chickens. *Biol Trace Elem Res.* 2019;187(1):281–290. Available at: <https://doi.org/10.1007/s12011-018-1364-4>
 157. Zhang YS, Liu YN, Teng Z, et al. Human umbilical cord mesenchymal stem cells (hUC-MSCs) alleviate paclitaxel-induced spermatogenesis defects and maintain male fertility. *Biol Res.* 2023;56(1):47. Available at: <https://doi.org/10.1186/s40659-023-00459-w>
 158. Feraille A, Liard A, Rives N, et al. Impact of low- or moderate-risk gonadotoxic chemotherapy prior to testicular tissue freezing on spermatogonia quantity in human (pre)pubertal testicular tissue. *Hum Reprod.* 2023;38(11):2105–2118. Available at: <https://doi.org/10.1093/humrep/dead161>
 159. Zhang H, Li NN, Zhang YK, et al. Ganoderma lucidum Polysaccharide Peptide Alleviates Cyclophosphamide-Induced Male Reproductive Injury by Reducing Oxidative Stress and Apoptosis. *Biomedicines.* 2024;12(8):1632. Available at: <https://doi.org/10.3390/biomedicines12081632>
 160. Ahmad MF, Ahmad FA, Zeyaulah M, et al. Ganoderma lucidum: Novel Insight into Hepatoprotective Potential with Mechanisms of Action. *Nutrients.* 2023;15(8):1874. Available at: <https://doi.org/10.3390/nu15081874>
 161. Tong AJ, Wu WH, Chen ZX, et al. Modulation of gut microbiota and lipid metabolism in rats fed high-fat diets by Ganoderma lucidum triterpenoids. *Curr Res Food Sci.* 2023;6:100427. Available at: <https://doi.org/10.1016/j.crf.2022.100427>
 162. Yao Y, Liu ZJ, Wang XJ, et al. Ganoderic acid A alleviates metabolic dysfunction-associated fatty liver disease through attenuating steatosis and cellular apoptosis by targeting acetyl-CoA carboxylase. *Int Immunopharmacol.* 2026;186:117108. Available at: <https://doi.org/10.1016/j.intimp.2026.117108>
 163. Guo WL, Guo JB, Liu BY, et al. Ganoderic acid A from Ganoderma lucidum ameliorates lipid metabolism and alters gut microbiota composition in hyperlipidemic mice fed a high-fat diet. *Food Funct.* 2020;11(8):6818–6833. Available at: <https://doi.org/10.1039/d0fo00436g>
 164. Li YH, Tang J, Gao HL, et al. Ganoderma lucidum triterpenoids and polysaccharides attenuate atherosclerotic plaque in high-fat diet rabbits. *Nutr Metab Cardiovasc Dis.* 2021;31(6):1929–1938. Available at: <https://doi.org/10.1016/j.numecd.2021.03.023>
 165. Wihastuti TA, Heriansyah T. The inhibitory effects of polysaccharide peptides (PsP) of Ganoderma lucidum against atherosclerosis in rats with dyslipidemia. *Heart Int.* 2017;12(1):e1–e7. Available at: <https://doi.org/10.5301/heartint.5000234>
 166. Zhu J, Jin J, Ding JX, et al. Ganoderic Acid A improves high fat diet-induced obesity, lipid accumulation and insulin sensitivity through regulating SREBP pathway. *Chem Biol Interact.*

- 2018;290:77–87. Available at: <https://doi.org/10.1016/j.cbi.2018.05.014>
167. Li JQ, Zhang Y, Yu FZ, et al. Proteoglycan Extracted from *Ganoderma lucidum* Ameliorated Diabetes-Induced Muscle Atrophy via the AMPK/SIRT1 Pathway In Vivo and In Vitro. *ACS Omega*. 2023;8(33):30359–30373. Available at: <https://doi.org/10.1021/acsomega.3c03513>
 168. Yang Z, Zhang Z, Zhao J, He YM, Yang HJ, Zhou P. Modulation of energy metabolism and mitochondrial biogenesis by a novel proteoglycan from *Ganoderma lucidum*. *RSC Adv*. 2019;9(5):2591–2598. Available at: <https://doi.org/10.1039/c8ra09482a>
 169. Yu FZ, Teng YL, Yang ST, et al. The thermodynamic and kinetic mechanisms of a *Ganoderma lucidum* proteoglycan inhibiting hIAPP amyloidosis. *Biophys Chem*. 2022;280:106702. Available at: <https://doi.org/10.1016/j.bpc.2021.106702>
 170. Yu FZ, Wang YX, Teng YL, et al. Interaction and Inhibition of a *Ganoderma lucidum* Proteoglycan on PTP1B Activity for Anti-diabetes. *ACS Omega*. 2021;6(44):29804–29813. Available at: <https://doi.org/10.1021/acsomega.1c04244>
 171. Teng BS, Wang CD, Yang HJ, et al. A protein tyrosine phosphatase 1B activity inhibitor from the fruiting bodies of *Ganoderma lucidum* (Fr.) Karst and its hypoglycemic potency on streptozotocin-induced type 2 diabetic mice. *J Agric Food Chem*. 2011;59(12):6492–6500. Available at: <https://doi.org/10.1021/jf200527y>
 172. Jiao JQ, Yong TQ, Huang LH, et al. A *Ganoderma lucidum* polysaccharide F31 alleviates hyperglycemia through kidney protection and adipocyte apoptosis. *Int J Biol Macromol*. 2023;226:1178–1191. Available at: <https://doi.org/10.1016/j.ijbiomac.2022.11.231>
 173. Lu JH, Zhang TH, Jiang CY, et al. Ganoderic acid A regulates CSF1R to reprogram tumor-associated macrophages for immune therapy of hepatocellular carcinoma. *Int Immunopharmacol*. 2025;161:114989. Available at: <https://doi.org/10.1016/j.intimp.2025.114989>
 174. Ye T, Ge Y, Zhang J, et al. Inhibition of Hepatoblastoma by *Ganoderma lucidum* Polysaccharide via the Induction of HDAC4-p16-RB Axis-Mediated Cellular Senescence. *Phytother Res*. 2025;39(6):2625–2640. Available at: <https://doi.org/10.1002/ptr.8493>
 175. Güllüm L, Güler E, Çapkınoğlu E, Çelik AB, Tutar Y. Evaluation of Anticancer Potential of *Ganoderma lucidum* on MCF-7 Breast Cancer Cells Through Genetic Transcription of Energy Metabolism. *Antioxidants (Basel)*. 2025;14(12):1471. Available at: <https://doi.org/10.3390/antiox14121471>
 176. Swallah MS, Bondzie-Quaye P, Yu X, Fetisoa MR, Shao CS, Huang Q. Elucidating the protective mechanism of ganoderic acid DM on breast cancer based on network pharmacology and in vitro experimental validation. *Biotechnol Appl Biochem*. 2025;72(2):415–436. Available at: <https://doi.org/10.1002/bab.2673>
 177. Arroyo-Cruz LV, Sagardía-González S, Miller K, Ling T, Rivas F, Martínez-Montemayor MM. Selective Antineoplastic Potential of Fractionated Caribbean Native *Ganoderma* Species Extracts on Triple-Negative Breast Cancer Cells. *Pharmaceuticals (Basel)*. 2024;17(7):864. Available at: <https://doi.org/10.3390/ph17070864>
 178. Shi LH, Xie L, Yu JG, et al. Study on the anti-tumor effect of Wall-broken *ganoderma lucidum* spore powder on papillary thyroid cancer. *Sci Rep*. 2025;15(1):43798. Available at: <https://doi.org/10.1038/s41598-025-27791-3>
 179. Qin W, Qi YZ, Li QW, et al. Molecular Pharmacological Interventions for Endometrial Cancer: A Comprehensive Review. *Drug Des Devel Ther*. 2025;19:7381–7392. Available at: <https://doi.org/10.2147/dddt.s524181>
 180. Benthavithana J, Islam T, Xu BJ. Medicinal Mushrooms in Colon Cancer Therapy: Mechanisms of Action of Bioactive Compounds and Therapeutic Potential. *Int J Mol Sci*. 2025;26(11):5304. Available at: <https://doi.org/10.3390/ijms26115304>
 181. Huo J, Nie K, Yang TF, et al. Network pharmacology combined with transcriptomics reveals that *Ganoderma lucidum* spore and *Sanghuangporus vaninii* compound extract exerts anti-colorectal cancer effects via CYP24A1-mediated VDR pathway and TERT-mediated Wnt signaling pathway. *J Ethnopharmacol*. 2025;348:119820. Available at: <https://doi.org/10.1016/j.jep.2025.119820>
 182. Wang XM, Wang B, Zhou LQ, et al. *Ganoderma lucidum* put forth anti-tumor activity against PC-3 prostate cancer cells via inhibition of Jak-1/STAT-3 activity. *Saudi J Biol Sci*. 2020;27(10):2632–2637. Available at: <https://doi.org/10.1016/j.sjbs.2020.05.044>
 183. Gaiaochi L, De Luca F, Serapian SA, et al. In Vitro Anti-Glioblastoma Activity of a Novel Pt(IV)-Ganoderic Acid A Conjugate. *Int J Mol Sci*. 2026;27(6):2760. Available at: <https://doi.org/10.3390/ijms27062760>
 184. Lo HC, Lin TE, Lin CY, et al. Targeting TGFβ receptor-mediated snail and twist: WSG, a polysaccharide from *Ganoderma lucidum*, and it-based dissolvable microneedle patch suppress melanoma cells. *Carbohydr Polym*. 2024;341:122298. Available at: <https://doi.org/10.1016/j.carbpol.2024.122298>
 185. Ouyang ZR, Li SY, Zhang A, et al. *Ganoderma lucidum* polysaccharide-decorated extracellular vesicle enables synergistic antitumor immunotherapy. *Mater Today Bio*. 2026;37:102832. Available at: <https://doi.org/10.1016/j.mtbio.2026.102832>
 186. Fang WY, Xu MC, Li HR, et al. Multicomponent *Ganoderma lucidum* spore-based solid self-nanoemulsifying system of paclitaxel for improved lymphatic absorption and immune synergistic antitumor strategy. *J Nanobiotechnology*. 2026;24(1):293. Available at: <https://doi.org/10.1186/s12951-026-04177-9>
 187. Liu WH, Jiang HJ, Xu J, Guo YQ. Preparation and characterization of *Ganoderma lucidum* polysaccharide-based multifunctional tellurium nanorods to realize combination cancer therapy. *Int J Biol Macromol*. 2025;322(Pt 3):146529. Available at: <https://doi.org/10.1016/j.ijbiomac.2025.146529>
 188. Yu Y, Qian LQ, Du N, Liu YX, Zhao X, Zhang X. *Ganoderma lucidum* polysaccharide enhances radiosensitivity of hepatocellular carcinoma cell line HepG2 through Akt signaling pathway. *Exp Ther Med*. 2017;14(6):5903–5907. Available at: <https://doi.org/10.3892/etm.2017.5340>
 189. Jiao CW, Qiu JS, Gong CC, et al. *Ganoderma lucidum* extract reverses multidrug resistance in breast cancer cells through inhibiting ATPase activity of the P-glycoprotein via MAPK/ERK signaling pathway. *Exp Cell Res*. 2025;444(2):114355. Available at: <https://doi.org/10.1016/j.yexcr.2024.114355>
 190. Jin XZ, Ruiz Beguerie J, Sze DM, Chan GC. *Ganoderma lucidum* (Reishi mushroom) for cancer treatment. *Cochrane Database Syst Rev*. 2012;(6):CD007731. Available at: <https://doi.org/10.1002/14651858.CD007731.pub2>
 191. Zhang G, Lan HM, Wu J, et al. Ganoderic acid a potentiates cisplatin's cytotoxicity on gallbladder cancer cells by promoting DNA damage and inhibiting cell stemness. *World J Surg Oncol*. 2025;23(1):148. Available at: <https://doi.org/10.1186/s12957-025-03799-x>
 192. Chen SY, Chen K, Lin Y, et al. Ganoderic acid T, a *Ganoderma* triterpenoid, modulates the tumor microenvironment and enhances the chemotherapy and immunotherapy efficacy through downregulating galectin-1 levels. *Toxicol Appl Pharmacol*. 2024;491:117069. Available at: <https://doi.org/10.1016/j.taap.2024.117069>

193. Phan SN, Hua WJ, Liao LL, et al. The dual role of Ganoderma lucidum polysaccharides in cancer treatment: Meridian tropism-based direct inhibition and immune-mediated modulation. *J Chin Med Assoc.* 2026;89(8):562–577. Available at: <https://doi.org/10.1097/JCMA.0000000000001403>
194. Pan HT, Li CS, Wang MY, et al. Multi-omics analysis reveals inhibition of osteosarcoma progression by sporoderm-removed Ganoderma lucidum spores via targeting glycerophospholipid and fatty acid metabolism. *Sci Rep.* 2025;15(1):22111. Available at: <https://doi.org/10.1038/s41598-025-05890-5>
195. Bashir MA, Abdalla M, Shao CS, et al. Dual inhibitory potential of ganoderic acid A on GLUT1/3: computational and in vitro insights into targeting glucose metabolism in human lung cancer. *RSC Adv.* 2024;14(39):28569–28584. Available at: <https://doi.org/10.1039/d4ra04454a>
196. Jiao CW, Chen W, Tan XP, et al. Ganoderma lucidum spore oil induces apoptosis of breast cancer cells in vitro and in vivo by activating caspase-3 and caspase-9. *J Ethnopharmacol.* 2020;247:112256. Available at: <https://doi.org/10.1016/j.jep.2019.112256>
197. Hasan MM, Azme E, Alam R, et al. Mushrooms as potent autophagy modulators in cancer therapy: Current evidence and therapeutic prospects. *Cancer Pathog Ther.* 2025;4(4):261–288. Available at: <https://doi.org/10.1016/j.cpt.2025.08.001>
198. Wang Q, Zheng XR, Zhang Z, et al. Additive anti-tumor and immunomodulatory effects of Sporoderm-removed Ganoderma lucidum spore powder and anti-PD-L1 antibody in lung cancer mice. *Discov Oncol.* 2026;17(1):654. Available at: <https://doi.org/10.1007/s12672-026-04854-z>
199. Chang CJ, Chen YY, Lu CC, et al. Ganoderma lucidum stimulates NK cell cytotoxicity by inducing NKG2D/NCR activation and secretion of perforin and granulysin. *Innate Immun.* 2014;20(3):301–311. Available at: <https://doi.org/10.1177/1753425913491789>
200. Qi YF, Yan JN, Huang XX, et al. Targeting tumor-associated macrophage polarization with traditional Chinese medicine active ingredients: Dual reversal of chemoresistance and immunosuppression in tumor microenvironment. *Pharmacol Res.* 2025;216:107788. Available at: <https://doi.org/10.1016/j.phrs.2025.107788>
201. Li GL, Tang JF, Tan WL, et al. The anti-hepatocellular carcinoma effects of polysaccharides from Ganoderma lucidum by regulating macrophage polarization via the MAPK/NF- κ B signaling pathway. *Food Funct.* 2023;14(7):3155–3168. Available at: <https://doi.org/10.1039/d2fo02191a>
202. Song M, Li ZH, Gu HS, et al. Ganoderma lucidum Spore Polysaccharide Inhibits the Growth of Hepatocellular Carcinoma Cells by Altering Macrophage Polarity and Induction of Apoptosis. *J Immunol Res.* 2021;2021:6696606. Available at: <https://doi.org/10.1155/2021/6696606>
203. Wang WB, Hu XG. DH-AUTAC induces ferroptosis in colorectal cancer by targeting DHODH for autophagic degradation through KCTD10-SQSTM1 signaling. *J Gastroenterol.* 2026. Available at: <https://doi.org/10.1007/s00535-026-02492-4>
204. Shao CS, Zhou XH, Zheng XX, Huang Q. Ganoderic acid D induces synergistic autophagic cell death except for apoptosis in ESCC cells. *J Ethnopharmacol.* 2020;262:113213. Available at: <https://doi.org/10.1016/j.jep.2020.113213>
205. Cheng Y, Xie P. Ganoderic acid A holds promising cytotoxicity on human glioblastoma mediated by incurring apoptosis and autophagy and inactivating PI3K/AKT signaling pathway. *J Biochem Mol Toxicol.* 2019;33(11):e22392. Available at: <https://doi.org/10.1002/jbt.22392>
206. Pan HT, Wang YJ, Na K, et al. Autophagic flux disruption contributes to Ganoderma lucidum polysaccharide-induced apoptosis in human colorectal cancer cells via MAPK/ERK activation. *Cell Death Dis.* 2019;10(6):456. Available at: <https://doi.org/10.1038/s41419-019-1653-7>
207. Liang CY, Li HR, Zhou H, et al. Recombinant Lz-8 from Ganoderma lucidum induces endoplasmic reticulum stress-mediated autophagic cell death in SGC-7901 human gastric cancer cells. *Oncol Rep.* 2012;27(4):1079–1089. Available at: <https://doi.org/10.3892/or.2011.1593>
208. Luo BB, Song LY, Chen LM, Cai Y, Zhang MW, Wang SY. Ganoderic acid D attenuates gemcitabine resistance of triple-negative breast cancer cells by inhibiting glycolysis via HIF-1 α destabilization. *Phytomedicine.* 2024;129:155675. Available at: <https://doi.org/10.1016/j.phymed.2024.155675>
209. Luo JM, Li TX, Xie JL, et al. Guar gum different from Ganoderma lucidum polysaccharide in alleviating colorectal cancer based on omics analysis. *Food Funct.* 2020;11(1):572–584. Available at: <https://doi.org/10.1039/c9fo02786f>
210. Deng CM, Chen YF, Xu JJ, et al. Ganoderma lucidum polysaccharide ameliorates cancer cachexia with enhanced efficacy in aged group by reprogramming arginine metabolism to modulate Treg formation. *Cancer Lett.* 2026;642:218247. Available at: <https://doi.org/10.1016/j.canlet.2026.218247>
211. Qi F, Zhang Y, Xie HJ, Guo X, Zhang Y. Ganoderma lucidum-Derived Nanovesicles Attenuate Multiorgan Senescence via Modulation of Oxidative Stress and Inflammation. *Mol Pharm.* 2026;23(1):239–251. Available at: <https://doi.org/10.1021/acs.molpharmaceut.5c00862>
212. Cheng YF, Zheng GB, Huang HM. GLSP mitigates vascular aging by promoting Sirt7-mediated Keap1 deacetylation and Keap1-Nrf2 dissociation. *Theranostics.* 2025;15(10):4345–4367. Available at: <https://doi.org/10.7150/thno.110324>
213. Chen L, Wu BF, Mo L, et al. High-content screening identifies ganoderic acid A as a senotherapeutic to prevent cellular senescence and extend healthspan in preclinical models. *Nat Commun.* 2025;16(1):2878. Available at: <https://doi.org/10.1038/s41467-025-58188-5>
214. Liu XJ, Zhao JM, Liu J, et al. Association of α -Klotho with anti-aging effects of Ganoderma lucidum in animal models. *J Ethnopharmacol.* 2025;345:119597. Available at: <https://doi.org/10.1016/j.jep.2025.119597>
215. Xu Y, Yuan H, Luo Y, Zhao YJ, Xiao JH. Ganoderic Acid D Protects Human Amniotic Mesenchymal Stem Cells against Oxidative Stress-Induced Senescence through the PERK/NRF2 Signaling Pathway. *Oxid Med Cell Longev.* 2020;2020:8291413. Available at: <https://doi.org/10.1155/2020/8291413>
216. Yuan H, Xu Y, Luo Y, Zhang JR, Zhu XX, Xiao JH. Ganoderic acid D prevents oxidative stress-induced senescence by targeting 14-3-3 ϵ to activate CaM/CaMKII/NRF2 signaling pathway in mesenchymal stem cells. *Aging Cell.* 2022;21(9):e13686. Available at: <https://doi.org/10.1111/acer.13686>
217. Wang H, Tai ML, Li WZ, et al. Ganoderma lucidum extract reduces skin aging by reducing mitochondrial stress and controlling mitochondrial numbers. *Fitoterapia.* 2025;184:106627. Available at: <https://doi.org/10.1016/j.fitote.2025.106627>
218. Cuong VT, Chen WD, Shi JH, et al. The anti-oxidation and anti-aging effects of Ganoderma lucidum in Caenorhabditis elegans. *Exp Gerontol.* 2019;117:99–105. Available at: <https://doi.org/10.1016/j.exger.2018.11.016>
219. Teseo S, Houot B, Yang KY, Monnier V, Liu GR, Tricoire H. *G. sinense* and *P. notoginseng* Extracts Improve Healthspan of Aging Flies and Provide Protection in A Huntington Disease Model. *Aging Dis.* 2021;12(2):425–440. Available at: <https://doi.org/10.14336/AD.2020.0714-1>
220. Zou XG, Shen MJ, Hamed YS, et al. Radioprotective effect of edible and medicinal mushrooms against ionizing radiation:

- Components, potential mechanisms, and applications. *Food Res Int.* 2025;221(Pt 2):117358. Available at: <https://doi.org/10.1016/j.foodres.2025.117358>
221. González A, Atienza V, Montoro A, Soriano JM. Use of Ganoderma lucidum (Ganodermataceae, Basidiomycota) as Radioprotector. *Nutrients.* 2020;12(4):1143. Available at: <https://doi.org/10.3390/nu12041143>
 222. Smina TP, Joseph J, Janardhanan KK. Ganoderma lucidum total triterpenes prevent γ -radiation induced oxidative stress in Swiss albino mice in vivo. *Redox Rep.* 2016;21(6):254–261. Available at: <https://doi.org/10.1080/13510002.2015.1126098>.
 223. Güvenç U, Akkaya S, Telek HH, Yumuşak N, Kaya HB, Burcu A. Protective effects of topical and oral Ganoderma lucidum extracts against ultraviolet B-induced cataract development and chemical ocular surface injury in a rat model. *Exp Eye Res.* 2026;268:111029. Available at: <https://doi.org/10.1016/j.exer.2026.111029>
 224. Shahid A, Huang M, Liu M, et al. The medicinal mushroom Ganoderma lucidum attenuates UV-induced skin carcinogenesis and immunosuppression. *PLoS One.* 2022;17(3):e0265615. Available at: <https://doi.org/10.1371/journal.pone.0265615>
 225. Kang LH, Zhang GW, Zhang JF, Qin B, Guan HJ. Ganoderic acid A protects lens epithelial cells from UVB irradiation and delays lens opacity. *Chin J Nat Med.* 2020;18(12):934–940. Available at: [https://doi.org/10.1016/s1875-5364\(20\)60037-1](https://doi.org/10.1016/s1875-5364(20)60037-1)
 226. Hu SH, Huang JH, Pei SY, et al. Ganoderma lucidum polysaccharide inhibits UVB-induced melanogenesis by antagonizing cAMP/PKA and ROS/MAPK signaling pathways. *J Cell Physiol.* 2019;234(5):7330–7340. Available at: <https://doi.org/10.1002/jcp.27492>
 227. Zeng QH, Zhou F, Lei L, et al. Ganoderma lucidum polysaccharides protect fibroblasts against UVB-induced photoaging. *Mol Med Rep.* 2017;15(1):111–116. Available at: <https://doi.org/10.3892/mmr.2016.6026>
 228. Shao CS, Feng N, Zhou S, et al. Ganoderic acid T improves the radiosensitivity of HeLa cells via converting apoptosis to necroptosis. *Toxicol Res (Camb).* 2021;10(3):531–541. Available at: <https://doi.org/10.1093/toxres/tfab030>
 229. Yu CM, Fu JQ, Guo LD, Lian L, Yu DH. UPLC-MS-based serum metabolomics reveals protective effect of Ganoderma lucidum polysaccharide on ionizing radiation injury. *J Ethnopharmacol.* 2020;258:112814. Available at: <https://doi.org/10.1016/j.jep.2020.112814>
 230. Eo SK, Kim YS, Lee CK, Han SS. Antiherpetic activities of various protein bound polysaccharides isolated from Ganoderma lucidum. *J Ethnopharmacol.* 1999;68(1–3):175–181. Available at: [https://doi.org/10.1016/s0378-8741\(99\)00086-0](https://doi.org/10.1016/s0378-8741(99)00086-0)
 231. Eo SK, Kim YS, Lee CK, Han SS. Possible mode of antiviral activity of acidic protein bound polysaccharide isolated from Ganoderma lucidum on herpes simplex viruses. *J Ethnopharmacol.* 2000;72(3):475–481. Available at: [https://doi.org/10.1016/s0378-8741\(00\)00266-x](https://doi.org/10.1016/s0378-8741(00)00266-x)
 232. Ekiz E, Oz E, Abd El-Aty AM, et al. Exploring the Potential Medicinal Benefits of Ganoderma lucidum: From Metabolic Disorders to Coronavirus Infections. *Foods.* 2023;12(7):1512. Available at: <https://doi.org/10.3390/foods12071512>
 233. Bharadwaj S, Lee KE, Dwivedi VD, et al. Discovery of Ganoderma lucidum triterpenoids as potential inhibitors against Dengue virus NS2B-NS3 protease. *Sci Rep.* 2019;9(1):19059. Available at: <https://doi.org/10.1038/s41598-019-55723-5>
 234. Jan JT, Cheng TR, Juang YP, et al. Identification of existing pharmaceuticals and herbal medicines as inhibitors of SARS-CoV-2 infection. *Proc Natl Acad Sci USA.* 2021;118(5):e2021579118. Available at: <https://doi.org/10.1073/pnas.2021579118>
 235. Li AY, Lu XY, Guo RF, et al. Ganoderma lucidum spore powder enhances IFN- α -mediated antiviral capacity of COVID-19 vaccine boosters revealed by single-cell multi-omics sequencing. *J Adv Res.* 2026;85:737–759. Available at: <https://doi.org/10.1016/j.jare.2025.10.014>
 236. Rowaiye AB, Ogugua AJ, Bur D, et al. The Lingzhi or Reishi Medicinal Mushroom Ganoderma lucidum (Agaricomycetes) Can Combat Cytokine Storm and Other COVID-19 Related Pathologies: A Review. *Int J Med Mushrooms.* 2023;25(5):1–15. Available at: <https://doi.org/10.1615/intjmedmushrooms.2023048109>
 237. Jiang L, Zhang W, Zhai DD, et al. Transcriptome profiling and bioinformatic analysis of the effect of ganoderic acid T prevents Sendai virus infection. *Gene.* 2023;862:147252. Available at: <https://doi.org/10.1016/j.gene.2023.147252>
 238. Deng Y, Ma J, Tang D, Zhang Q. Dynamic biomarkers indicate the immunological benefits provided by Ganoderma spore powder in post-operative breast and lung cancer patients. *Clin Transl Oncol.* 2021;23(7):1481–1490. Available at: <https://doi.org/10.1007/s12094-020-02547-9>
 239. Chiu HF, Fu HY, Lu YY, et al. Triterpenoids and polysaccharide peptides-enriched Ganoderma lucidum: a randomized, double-blind placebo-controlled crossover study of its antioxidation and hepatoprotective efficacy in healthy volunteers. *Pharm Biol.* 2017;55(1):1041–1046. Available at: <https://doi.org/10.1080/13880209.2017.1288750>
 240. Wachtel-Galor S, Szeto YT, Tomlinson B, Benzie IF. Ganoderma lucidum ('Lingzhi'); acute and short-term biomarker response to supplementation. *Int J Food Sci Nutr.* 2004;55(1):75–83. Available at: <https://doi.org/10.1080/09637480310001642510>
 241. Wachtel-Galor S, Tomlinson B, Benzie IF. Ganoderma lucidum ('Lingzhi'), a Chinese medicinal mushroom: biomarker responses in a controlled human supplementation study. *Br J Nutr.* 2004;91(2):263–269. Available at: <https://doi.org/10.1079/bjn20041039>
 242. Chu TT, Benzie IF, Lam CW, Fok BS, Lee KK, Tomlinson B. Study of potential cardioprotective effects of Ganoderma lucidum (Lingzhi): results of a controlled human intervention trial. *Br J Nutr.* 2012;107(7):1017–1027. Available at: <https://doi.org/10.1017/s0007114511003795>
 243. Klupp NL, Kiat H, Bensoussan A, Steiner GZ, Chang DH. A double-blind, randomised, placebo-controlled trial of Ganoderma lucidum for the treatment of cardiovascular risk factors of metabolic syndrome. *Sci Rep.* 2016;6:29540. Available at: <https://doi.org/10.1038/srep29540>
 244. Tang WB, Gao YH, Chen GL, et al. A randomized, double-blind and placebo-controlled study of a Ganoderma lucidum polysaccharide extract in neurasthenia. *J Med Food.* 2005;8(1):53–58. Available at: <https://doi.org/10.1089/jmf.2005.8.53>
 245. Wang GH, Wang LH, Wang C, Qin LH. Spore powder of Ganoderma lucidum for the treatment of Alzheimer disease: A pilot study. *Medicine (Baltimore).* 2018;97(19):e0636. Available at: <https://doi.org/10.1097/md.00000000000010636>
 246. Noguchi M, Kakuma T, Tomiyasu K, et al. Randomized clinical trial of an ethanol extract of Ganoderma lucidum in men with lower urinary tract symptoms. *Asian J Androl.* 2008;10(5):777–785. Available at: <https://doi.org/10.1111/j.1745-7262.2008.00361.x>
 247. Younger J, Donovan EK, Hodgins KS, Ness TJ. A Placebo-Controlled, Pseudo-Randomized, Crossover Trial of Botanical Agents for Gulf War Illness: Reishi Mushroom (Ganoderma lucidum), Stinging Nettle (Urtica dioica), and Epimedium (Epimedium sagittatum). *Int J Environ Res Public Health.*

- 2021;18(7):3671. Available at:
<https://doi.org/10.3390/ijerph18073671>
248. Kumaran S, Palani P, Nishanthi R, Kaviyarsan V. Studies on screening, isolation and purification of a fibrinolytic protease from an isolate (VK12) of *Ganoderma lucidum* and evaluation of its antithrombotic activity. *Med Mycol J*. 2011;52(2):153–162. Available at:
<https://doi.org/10.3314/jjmm.52.153>
 249. Kwok Y, Ng KFJ, Li CCF, Lam CCK, Man RYK. A prospective, randomized, double-blind, placebo-controlled study of the platelet and global hemostatic effects of *Ganoderma lucidum* (Ling-Zhi) in healthy volunteers. *Anesth Analg*. 2005;101(2):423–426. Available at:
<https://doi.org/10.1213/01.ane.0000155286.20467.28>
 250. Collado Mateo D, Pazzi F, Domínguez Muñoz FJ, et al. GANODERMA LUCIDUM IMPROVES PHYSICAL FITNESS IN WOMEN WITH FIBROMYALGIA. *Nutr Hosp*. 2015;32(5):2126–2135. Available at:
<https://doi.org/10.3305/nh.2015.32.5.9601>
 251. Hijikata Y, Yasuhara A, Sahashi Y. Effect of an herbal formula containing *Ganoderma lucidum* on reduction of herpes zoster pain: a pilot clinical trial. *Am J Chin Med*. 2005;33(4):517–523. Available at:
<https://doi.org/10.1142/s0192415x05003120>
 252. Hijikata Y, Yamada S, Yasuhara A. Herbal mixtures containing the mushroom *Ganoderma lucidum* improve recovery time in patients with herpes genitalis and labialis. *J Altern Complement Med*. 2007;13(9):985–987. Available at:
<https://doi.org/10.1089/acm.2006.6297>
 253. Li EK, Tam LS, Wong CK, et al. Safety and efficacy of *Ganoderma lucidum* (lingzhi) and San Miao San supplementation in patients with rheumatoid arthritis: a double-blind, randomized, placebo-controlled pilot trial. *Arthritis Rheum*. 2007;57(7):1143–1150. Available at:
<https://doi.org/10.1002/art.22994>
 254. Zhang WW, Yu WW, Ding XY, et al. Self-assembled thermal gold nanorod-loaded thermosensitive liposome-encapsulated ganoderic acid for antibacterial and cancer photochemotherapy. *Artif Cells Nanomed Biotechnol*. 2019;47(1):406–419. Available at:
<https://doi.org/10.1080/21691401.2018.1559177>