

## A Comprehensive Review on the Pharmacological Mechanisms and Applications of *Ganoderma lucidum* Active Components in Modern Medicine

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The authors declare that no funding was received for this work.



Received: 15-April-2026

Accepted: 04-May-2026

Published: 07-May-2026

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This article is published in the **MSI Journal of Medicine and Medical Research (MSIJMMR)**  
ISSN 3049-1401 (Online)

The journal is managed and published by MSI Publishers.

Volume 3, Issue 2 (May-Aug), 2026

**ABSTRACT:** *Ganoderma lucidum* (Lingzhi) has been utilized as a traditional medicinal fungus in East Asia for thousands of years. Modern scientific investigations have confirmed that *G. lucidum* contains a wealth of bioactive components, primarily polysaccharides, triterpenoids, and sterols. These constituents exhibit significant pharmacological activities, including anti-tumor, anti-inflammatory, immunomodulatory, and antiviral effects, particularly against COVID-19. This paper provides a comprehensive review of the chemical properties, extraction technologies (such as ultrasound-assisted extraction), and molecular mechanisms, focusing on the STAT3 and NF-κB signaling pathways. Furthermore, its applications in neuroprotection (e.g., Alzheimer's disease) and metabolic regulation are discussed. Finally, artificial cultivation techniques are summarized to provide a reference for the industrial development and medical application of *G. lucidum*. (152 words)

**Keywords:** *Ganoderma lucidum*, Polysaccharides, Triterpenoids, Immunomodulation, COVID-19

## I、 Introduction

*Ganoderma lucidum* belongs to the phylum Basidiomycota, order Polyporaceae, and family Ganodermataceae. Since ancient times, *Ganoderma lucidum* has been listed as a "superior medicine" in both the \*Shennong Bencao Jing\* and the \*Compendium of Materia Medica\*, possessing nourishing, strengthening, and longevity-promoting effects (Liu, 2015; Li et al., 2017; Liu Zhijun, 2015). Modern research shows that *Ganoderma lucidum* is a complex species complex, and its taxonomic name remains controversial internationally. For example, the Asian cultivated *Ganoderma lucidum* is genetically closer to \**G. lingzhi*\* or \**G. multipileum*\* than the European \**G. lucidum*\* (Wasser, 2011; Fan et al., 2022; Li et al., 2017). *Ganoderma lucidum* contains over 400 bioactive substances, and its pharmacological value has been widely confirmed in modern molecular biology and clinical medicine.

## II、 Main active ingredients and extraction technology

### (I) *Ganoderma lucidum* polysaccharides and peptide polysaccharides

*Ganoderma lucidum* polysaccharides are major immunomodulatory components. Structurally, they are based on  $\beta$ - (1→3) glucan with  $\beta$ - (1→6) side chains. Studies have found that high molecular weight polysaccharides have stronger antitumor activity (Wasser, 2011; Zhao et al., 2010). In terms of extraction techniques, \*\*ultrasound-assisted extraction (UAE)\*\* and reactive surface methodology (RSM) can significantly improve the extraction efficiency and purity of polysaccharides (Chen et al., 2010; Zhao et al., 2010).

### (II) Triterpenoids

*Ganoderma* triterpenes (such as ganoderic acids) are the source of the bitterness in *Ganoderma lucidum*. More than 300 triterpenoids have been identified, which can be classified into five basic skeletons based on their structure (Zou et al., 2015; Cheng et al., 2010). Their biosynthetic pathway mainly involves the mevalonate pathway (MVA pathway), and they undergo oxidative modification by cytochrome P450 enzymes (Zou et al., 2015; Xu, Zhao & Zhong, 2010).

### (III) Ganoderma sterols

Ganoderma lucidum contains more than 40 sterols, with ergosterol being the main component. Recent studies have shown that ganoderic acid (GLS) has significant anti-inflammatory activity (Xu et al., 2021).

## III. Pharmacological activity and molecular mechanism

### (I) Anti-tumor and anti-metastasis mechanisms

Ganoderma lucidum components can inhibit the proliferation of various cancer cells (such as HeLa, CaSki, and 95-D) (Chen et al., 2010; Cheng et al., 2010; Xu et al., 2010). The mechanisms include:

1. **Induction of apoptosis:** through activation of Caspase-3, regulation of Bax/Bcl-2 ratio and p53 protein (Calviño et al., 2011; Xu et al., 2010).
2. **Inhibition of metastasis:** Ganoderma triterpenes (such as ganoderic acid T) can inhibit the **NF- $\kappa$ B signaling pathway** and reduce the expression of matrix metalloproteinases (MMP-2, MMP-9), thereby preventing cancer cell invasion and angiogenesis (Weng & Yen, 2010; Xu et al., 2010).
3. **Blocking the STAT3 pathway:** STAT3 is a core transcription factor in tumor formation. Ganoderma lucidum components are considered potential STAT3 inhibitors that can prevent tumor immune escape (Wang et al., 2022).

### (II) Immunomodulatory effects

Ganoderma lucidum can activate macrophages (converting them to M1 type), natural killer cells (NK cells), T cells, and B cells (Fan et al., 2022; Xu et al., 2011). Its polysaccharide components can bind to TLR4 or Dectin-1 receptors, triggering downstream MAPK pathways and promoting the secretion of cytokines (TNF- $\alpha$ , IL-2, IFN- $\gamma$ ) (Ahmad et al., 2021; Xu et al., 2011; Liu and Zhang, 2015).

## IV. Applications in modern disease prevention and treatment

### 4.1 Research on Combating COVID-19

During the SARS-CoV-2 pandemic, *Ganoderma lucidum* demonstrated its antiviral potential. **Ganoderma triterpenes were shown to inhibit viral protease activity and help maintain the ACE/ACE2 ratio balance, reducing lung damage caused by cytokine storms** (Rahman et al., 2021; Ahmad et al., 2021; AL- jumaili et al., 2020; Lin, 2020). Clinical observations showed that *Ganoderma lucidum* intake improved hematological parameters and enhanced immune responses in COVID-19 patients (AL- jumaili et al., 2020; Sevindik, 2021).

#### 4.2 Neuroprotection and metabolic regulation

Reishi mushroom has also shown efficacy in improving Alzheimer's disease (AD) and hypercholesterolemia. Animal experiments have shown that water extracts of reishi mushroom can enhance spatial learning and memory abilities, and increase the expression of brain neurotrophic factor (BDNF) and synaptic-associated protein (SNAP 25) (Rahman et al., 2020; Liu, 2015).

### V、 Cultivation techniques and industrial development

Artificial cultivation of *Ganoderma lucidum* has evolved from log cultivation to **bag cultivation** (Li et al., 2017). During cultivation, the carbon dioxide concentration in the environment must be strictly controlled below 1,000 ppm to avoid the formation of antler-shaped deformed fruiting bodies (Li et al., 2017). Meanwhile, electron microscopy (EM) plays a crucial role in identifying the morphology and structure of *Ganoderma lucidum* and its pathogenic microorganisms (such as viruses, bacteria, and fungi) (Centers for Disease Control, Department of Health, Executive Yuan, 2009; Yang Wen-Jen, nd).

### VI、 Conclusion

Reishi mushroom serves as a bridge between traditional and modern medicine, and its active ingredients exhibit multi-target pharmacological effects. Future research should combine genomics and proteomics to further clarify the precise biosynthetic mechanism of *Ganoderma triterpenes* and verify its efficacy as a biological response modifier (BRM) in cancer and emerging viral diseases through high-quality double-blind clinical trials.

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