

Healthy Benefits of *Ganoderma lucidum* as Herb Medicinal Mushroom

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Abstract

Ganoderma lucidum (Lingzhi/Reishi) has been utilized for centuries in East Asia to prevent or treat various diseases as herb medicinal mushroom. The primary bioactive components in *G.lucidum* are commonly considered to be polysaccharides and triterpenoids, which have intriguing healthy benefits due to its roles for immune modulator, anti-cancer/tumor, cardiovascular health, hepatoprotective activity, protection to kidney, neuroprotective effects, anti-obesity and anti-inflammation, *et al.* To explore the values of *G.lucidum* as the potential medicines in pharmaceutical industry and one of important resources of nutrition supplements in food industry, here, healthy benefits of *G.lucidum* were summarized according to numerous research reports and clinical trails.

Introduction

Ganoderma lucidum (Lingzhi), is also known as Reishi mushroom, which plays important roles for medical health as a very rare and precious traditional Chinese herb medicine. In Asian, especially in China and Japan, *G.lucidum* has been used for the promotion of health and longevity and treatment of various diseases for more than 2000 years. *G.lucidum* contain a wide range of immuno-modulatory and bioactive compounds, such polysaccharides, triterpenes, organic magnesium, and peptidoglycans, *et al.*, these compounds play main roles in the anti-diseases and promotion of health.

Immune Function Modulator

G.lucidum mushroom is considered an immune booster or modulator as it boosts and regulates the immune system. Numerous researches show *G.lucidum* produces stimulatory effects on immune cells. Yoshida H, *et al.* [1] show *G.lucidum* activate dendritic cells to produce large amount of IL-23, which induces Th17 differentiation both in vitro and in vivo. Water extracts of cultured mycelium from various species (*Agaricus blazei* Murrill, *Antrodia cinnamomea*, *G.lucidum* and *Hirsutella sinensis*) enhances NK cell cytotoxic activity against cancer cells [2]. Polysaccharides from *G.lucidum* increased the metabolic activity of macrophages and induced cell differentiation to dendritic like cells, also polysaccharides from *G.lucidum* are crucial for macrophages to acquire phagocytic ability by induced NO productions [3]. Furthermore, Lin YL, *et al.* [4] show treatment of human monocyte-derived dendritic cells with polysaccharide from *G.lucidum* increased cell-surface expression of CD80, CD86, CD83, CD40, CD54 and human leukocyte antigen (HLA)-DR, and enhanced production of interleukin (IL)-12p70, p40, IL-12p35, p40, and IL-10 expression. Also, treatment of dendritic cells with polysaccharide enhanced T cell-stimulatory capacity and increased T cells secretion of interferon-gamma and IL-10. However, previous studies have reported that *G.lucidum* may produce both stimulatory and inhibitory effects on immune cells, depending on conditions [2]. Based on our knowledge, *G.lucidum* contain many bioactive compounds, such as triterpenoids, steroids, phenols, nucleotides and their derivatives, glycoproteins, polysaccharides, organic germanium, Selenium and other rare elements, *et al.* [5], these bioactive compounds play different roles in immuno-regulatory effects, therefore, more researches on immunomodulator of *G.lucidum* need to be elucidated.

Anti-Cancer/Tumor Activity of *G.lucidum*

G.lucidum is believed to play a role in preventing and treating cancers. The numerous researches had shown the *G.lucidum* have capacity of anti-cancer/tumor in a dose- and time-dependent manner based on studies with cancer and immune cells, as well as animal models both in vitro and in vivo, also clinical studies disclosed the chemopreventive effects on cancer invasion and metastasis. Currently, researches and clinical investigations of *G.lucidum* on anti-cancer/tumor are mainly focused on prostate cancer, breast cancer, colorectal cancer, lung cancer, *et al.* Sliva D, *et al* [6,7] show *G. lucidum* inhibit constitutively active transcription factors AP-1 and NF-kappaB in breast MDA-MB-231 and prostate PC-3 cancer cells. And another research [8] showed that *G. lucidum* inhibit the early event in angiogenesis, capillary morphogenesis of the human aortic endothelial cells. These effects are caused by the inhibition of constitutively active AP-1 in prostate cancer cells, resulting in the down-regulation of secretion of VEGF and TGF-beta1 from PC-3 cells. In DU-145 human prostate cancer cells, triterpenes from *G. lucidum* inhibit cancer cell viability, migration and invasion while enhance apoptosis [9]. Research results from breast cancer MDA-MB-231 cells demonstrated that *G.lucidum* inhibits cancer cells proliferation (cell cycle arrest at G0/G1) by suppressing phosphorylation of Akt on Ser473 and downregulates the expression of Akt [10,11], furthermore, ganoderic acid A and F (GA-A, GA-F), and ganodermanontriol (GDNT), a Ganoderma alcohol, suppress growth (cell proliferation and colony formation) and invasive behaviors (adhesion, migration and invasion) of MDA-MB-231 cells [12]. Another research with human colon cancer cells HT-29 demonstrated that *G. lucidum* triterpene extract (GLT) suppresses proliferation of HT-29 cells and inhibits tumor growth in a xenograft model of colon cancer [13,14]. Sporoderm-broken spores of *G. lucidum* water extract also significantly inhibited colorectal cancer HCT116 cell viability in a time- and dose-dependent manner [15].

Lin TY, *et al.* [16,17] demonstrated that one of small weight recombinant polysaccharides (rLZ-8) suppressed tumor metastasis and increased the survival rate in Lewis lung carcinoma cell-bearing mice via induced cell cycle arrest and apoptosis.

In summary, these researches indicated polysaccharides and triterpenes from *G. lucidum* are main bioactive components to inhibit cancer development via suppressing cancer cells proliferation, invasion and metastasis, as well as promoting cancer cells apoptosis, although they work by different molecular mechanisms and signaling pathways in different cancers.

Cardiovascular Health

Recent Researches show *G. lucidum* have a potential cardioprotective role. *G. lucidum* extract exhibit antioxidant properties with global ischemia (45 min) and reperfusion (30 min) of isolated and perfused rat heart, which diminish necrotic death of cardiomyocytes and reduce reperfusion contracture with administration of the *G. lucidum* extract in a dose of 400 mg/kg for 15 days [18]. With pressure overload-induced cardiomyopathy mouse model, spore oil extracted from Ganoderma can reduce left ventricular hypertrophy [19], also genes expression associated with heart failure reduce in Ganoderma treated mouse. Moreover, the alcoholic extract of *G. lucidum* was found to minimize oxidative stress, restore cellular viability and aid in maintaining cellular redox balance under hypoxia [20].

Hepatoprotective Activity of *G. lucidum*

Nonalcoholic Steatohepatitis (NASH) is a common health problem worldwide due to altered food habits and life styles, these patients with NASH have obesity, type 2 diabetes mellitus, dyslipidemia, and/or metabolic syndrome. *G. lucidum* has a potential to ameliorate non-alcoholic steatosis and the associated complicated disorders via the induction of energy metabolizing enzymes in administered high fat diet mouse [21]. Also *G. lucidum* attenuate lipid accumulation induced by free fatty acid in HepG2 cells. *G. lucidum* polysaccharides were reported to have an ability to exert hypolipidemic, antioxidant, and antiapoptotic effects in high-fat diet induced obese mice [22]. Also researches showed triterpenoids from *G. lucidum* have hepatoprotective effects on α -AMA-induced liver injury via antioxidative, radical scavenging activities and antiapoptosis [23]. There are still many scientific reports on hepatoprotective effects of *G. lucidum*, most of these reports showed liver-protective effects of *G. lucidum* may be due to its antioxidative and antiapoptosis, although the mechanisms of hepatoprotective effects are various in different models. To our knowledge, it is possible that the different bioactive components, such as polysaccharides and triterpenoids are used or dominant in the different extract methods.

Protection to Kidney

Recently Researches showed *G. lucidum* also provide protection and promote kidney function. Research reports showed a novel proteoglycan from *G. lucidum* fruiting bodies provides protection against the renal functional and morphologic injuries by enhancing antioxidants and inhibiting accumulation of oxidation in diabetic nephropathy mouse [24]. With an in vivo mouse renal ischemia reperfusion injury model and an in vitro hypoxia/reoxygenation model, Zhong D, *et al.* [25] showed that renal dysfunction and

morphological damage were reduced in *G.lucidum* polysaccharide peptide treated groups due to reducing oxidative stress, alleviating the mitochondrial and ER stress-dependent apoptosis caused by excessive ROS. Furthermore, Beuy Joob and Viroj Wiwanitkit [26] summarized a few reports on renal protection roles of *G.lucidum* in human clinical trails, it showed *G.lucidum* improve renal function and relieve the injury of kidney.

Neuroprotective Effects of *G.lucidum*

According to lots of research investigations, *G.lucidum* can be considered as useful therapeutic agents to treat neurodegeneration diseases. Wang SQ, *et al.* [27] investigated anti-epileptic effect of *G.lucidum* polysaccharides (GLP), it showed GLP can protect epileptic neurons by inhibiting calcium overload and promoting CaMK II α expression. Also *G.lucidum* polysaccharides have significant neuroprotective effects by regulating expression of apoptosis-associated proteins and inhibiting oxidative stress-induced neuronal apoptosis [28]. Moreover, Other researches [29-32] showed bio-active components from *G.lucidum* are able to reducing beta amyloid-induced neurotoxicity, anti-acetylcholinesterase, stimulating neurite outgrowth, promoting nerve growth factor (NGF) synthesis, antioxidant, and anti-(neuro)inflammatory effects.

Other Effects of *G.lucidum*

Researchers [33, 34] observed that *G.lucidum* extract successfully inhibited the production of inflammatory cytokines and cell proliferation in rheumatoid arthritis synovial fibroblasts which are specialized cells that contribute to the progression of rheumatoid arthritis and may be responsible for starting the disease. Chih-Jung Chang, *et al.* [35] show water extract of *G.lucidum* fruit reduces body weight, inflammation and insulin resistance, reverses gut dysbiosis. It suggested *G.lucidum* may be used as prebiotic agents to prevent gut dysbiosis and obesity-related metabolic disorders in obese individuals. Moreover, traditional Chinese medicine practitioners also used *G.lucidum* to treat hay fever, insomnia, fatigue, viral infections, stomach ulcers, depression, *et al.*, however, it is still unclear the mechanisms that *G.lucidum* can treat and cure these diseases due to its complicated bioactive components.

Conclusion

The numerous research reports summarized in this article have highlighted the potential medicinal values of *G.lucidum*, and its benefits for promoting health and preventing chronic diseases. However, to elucidate anti-diseases mechanisms of *G.lucidum*, the extract and purified methods of *G.lucidum* must be further optimized in order to obtain the pure and single substances of different bioactive compounds. Also, toxicological information need be explored with the solid scientific experiments and clinical trails. Moreover, more clinical studies are needed to be set up according to the research reports.

Acknowledgments

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