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Pharmacological Activities of Reishi (Ganoderma Lucidum): Potent Medicinal Mushroom

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ABSTRACT

Medicinal mushroom, Ganoderma lucidum is a white rot mushroom used in medicinal properties and economic importance. It contains a wide variety of bioactive molecules, which have been proved to have several therapeutically properties to control various diseases and it has toxic effects on humans. However, broad spectrum of its pharmacological actions have been established which include immunomodulation, anticancer, ant diabetic, antioxidant, anti-inflammatory, antimicrobial properties and estrogenic activity. Therefore, in this review particular focus on assess the components of biologically active compounds, pharmacological activity, economical importance, and toxicity of Ganoderma lucidum medicinal mushroom. G. lucidum biological active compounds might be a valuable constituent for the treatment of sex-hormone related aging ailments such as osteoporosis. Various animal studies have been carried out on G. lucidum water and ethanol extracts and protective effects toward acute hepatitis in rat and mice have been reported. Immunomodulatory and anti-inflammatory activities of G. lucidum recommend potential application in the treatment of autoimmune disorder like rheumatoid arthritis Ganoderma lucidum has a significant result on the cardiovascular system, such as reduce blood cholesterol, triglyceride level and blood pressure. Benign prostatic hyperplasia (BPH) is one of the common widespread disease, symptoms are seen usually in older men age group. Ganoderma lucidum has a significant result on the cardiovascular system, such as reduce blood cholesterol, triglyceride level and blood pressure.

Keyword: bioactive, diseases, *Ganoderma lucidum*, pharmacological

1. INTRODUCTION

Mushrooms are a group of macro-fungi with conspicuous epigenous or hypogenous fruiting bodies. It is expected that there are more than million mushroom species are distributed in the world among them 70,000 species are illustrated. Approximately 10,000 known species of mushrooms are distributed globally among them 2000 are safe for human health and about 300 of them have medicinal properties (Wasser and Weis, 1999). Medicinal mushrooms are affluent sources of pharmacological active compounds. The reishi medicinal mushroom, *Ganoderma lucidum* is a white rot mushroom used in Asia for its medicinal properties for over 2,000 years. *Ganoderma lucidum* exhibits a significant role in treatment and prevention of various diseases in several countries. *Ganoderma lucidum* (Curtis) also known as Ling Zhi, Reishi, Mannentake is a medicinal, wood-degrading Basidiomycetes with numerous pharmacological effects in addition to its key role in the environment as decomposer in nutrient cycle. *G. lucidum* is considered as "the king of herbs" which grows on the decaying and dead logs of deciduous trees like willow, oak, sweet gum, maple, elm and coniferous trees (larix, picea and pinus) (Khatian and Aslam, 2018; Sudheer *et al*., 2018). The most important pharmacologically active constituents of *G. lucidum* are triterpenoids and polysaccharides. Triterpenoids have been reported to possess hepatoprotective, anti-hypertensive, hypocholesterolemic and anti-histaminic effects, anti-tumor and anti-engiogenic activities, effects on platelet aggregation and complement inhibition. Polysaccharides, especially β-D-glucans, have been known to have anti-tumor effects through immunomodulation and anti-angiogenesis. In addition to that, polysaccharides have a protective effect against free radicals and reduce cell damage caused by mutagens. In general, *G. lucidum* triterpenes could directly suppress growth and invasive behavior of cancer cells, whereas *G. lucidum* polysaccharides could synergistically stimulate the immune functions, resulting in the activation of anticancer activities of immune cells and production of cytokines (Boh, 2013; Hapuarachchi *et al*., 2016; Sohretoglu and Huang, 2018; Zhao *et al*., 2019).

The bioactive components found in this mushroom have numerous health properties to treat different pathologies such as hepatopathy, nephritis, hypertension, hyperlipemia, arthritis, neurasthenia, insomnia, bronchitis, asthma, gastric ulcers, atherosclerosis, leukopenia, diabetes, anorexia, and cancer (Copot and Tanase, 2017). Triterpenoids are the major group of secondary metabolites in *G. lucidum*. Triterpenoids have been found in the fruiting bodies, spores, and mycelia of this mushroom and are responsible for many of its therapeutic properties. This group of mushrooms is an underutilize source of bioactive pharmaceutical compounds. From that time until nowadays, it could be demonstrated a series of interesting biological activities for *Ganoderma lucidum*, including antitumor and anti-inflammatory effects and cytotoxicity to hepatoma cells (Geng *et al*., 2017). *Ganoderma lucidum*, the most famous species in this group is a legendary mushroom in China, with a long fascinating history dating back over two thousand years. Not only a sparkling beautiful woody mushroom, but more importantly, *G. lucidum* is known as the mushroom of immortality and is the number one medicinal mushroom in China.

The mushroom is popular due to its pharmaceutical ansed in folk medicine to prevent, manage or cure many diseases such as hepatitis, gastric ulcer, hypertension, bronchitis and hypercholesterolemia. Antibacterial activity of *G. lucidum* extract from basidiocarp against Gram-positive bacteria has also been reported. DNA protection from breakage of strand triggered by UV irradiation or hydroxyl radicals is another protective role of *G. lucidum*. *G. lucidum* fungus is an important mushroom and majority of researches had been centered on its traditional benefits and role in folk medicine (Batra *et al*., 2014).

2. Major bioactive components in Ganoderma lucidum

Ganoderma lucidum contains a wide variety of bioactive molecules, such as terpenoids, steroids, phenols, nucleotides and their derivatives, glycoproteins, and polysaccharides (**Table 1**). Beneficial components extracted from *Ganoderma* are Phosphorus, sulfur; potassium, calcium, and magnesium are their main mineral components. *G. lucidum* includes polysaccharides, flavonoids, and alkaloids, amino acids, steroids, oligosaccharides, proteins, mannitol, vitamins B1, B2, B6, choline, and inositol (Cör *et al*., 2018). The water content of this medicinal mushroom has been reported as 90% and its dry matter consists of 10-40% protein, 2-8% fat, 3-28% carbohydrate, 3-32% fiber, 8-10% ash, minerals (Ca, P, K, Mg, Cu, Fe, Zn and Se) and some vitamins.

2.1. Biological activities and pharmacological properties

2.2.1. Anticancer

Present pharmacological and clinical investigations have confirmed that G. lucidum exhibits a significant role as an antitumor effect; its antitumor activity is generally achieved by boosting host immune function (Lin *et al*., 2004). The immune function potentiation mediated by G. lucidum polysaccharide is considered to be a core mechanism of antitumor action. Among multiple polysaccharides, polysaccharides β-D-glucans produce major antitumor effects. Through binding with serum-specific proteins or leukocyte surfaces they activate the macrophages, natural killer (NK), T-helper and other effector cells. Not only the host defense potentiation but additional mechanisms are also occurred to produce antitumor result. The cytokine production, dendritic cell maturation and function, cytotoxic T lymphocyte and cytokine-induced killer cell (CIK) function were encouraged by *G. lucidum* polysaccharides (Cao and Lin, 2003). Presently accessible data illustrate that G. lucidum prevents cancer through diverse modalities, such as immune response activation host cells, Phase II metabolizing enzymes induction, cell differentiation induction, inhibition of the expression of urokinase-type plasminogen activator (uPA) and urokinase-type plasminogen activator receptor (uPAR) in cancer cells, direct cytotoxicity and angiogenesis inhibition (Lin *et al*., 2004).

2.2.2 Immunomodulatory effects

2.2.2.1 Effect on the T lymphocytes

G. lucidum extracts are efficient T cells activators, inducing the production of numerous cytokines. The crude water extract of G. lucidum induces the expression of cytokines including Interleukin-10 (IL- 10), Interleukin-1b, Interleukin-6 (IL-6), tumor necrosis factor (TNF)-a and

Interleukin-2 (IL-2) in peripheral blood mononuclear (PBM) cells of human (primarily T cells) in an in vitro study (Ishimoto *et al.,* 2017*).* It has been clarified that G. lucidum promotes the mixed lymphocyte culture (MLC) as well as increases consequence on delayed hypersensitivity induction to protein antigen. Advance study showed that through help of enhancement of DNA polymerase induction in the young and aged mice with polysaccharides of G. lucidum increase the synthesis of DNA in mixed lymphocyte culture of spleen cells (Patra, *et al.,* 2011). In addition, G. lucidum considerably enhances IFN-γ mRNA expression and improves the production of IFN-γ and in the T-lymphocytes. It is an efficient source to repair damaged subset T-cells in the gamma-irradiated mice spleen (Cao and Lin, 2003).

2.2.2.2. Effect on the B lymphocytes

Pharmacologically active compounds from G. lucidum have been confirmed to augment the proliferation and maturation of T and B lymphocytes, dendritic cells, NK cells and splenic mononuclear cells (Zhu *et al*., 2007). A bioactive G. lucidum immunomodulating substance isolated from fruiting body that stimulates the proliferation, activation and differentiation of B lymphocyte. B lymphocytes express CD71 and CD25 on the cell surface and raise the immunoglobulin secretion. G. lucidum polysaccharides lead to change the activities of macrophages, T-helper cells, NK cells and other effector cells using lymphocyte surfaces through specific receptors or serum specific proteins (Sanodiya *et al*., 2009).

2.2.3 Antioxidant

Polysaccharides, polysaccharide-peptide complex, triterpenes and phenolic components of *G. lucidum* have long been exhibited antioxidant properties (Kan *et al*., 2015). It has been demonstrated that Ganoderma lucidum antioxidants were found to be absorbed quickly after the ingestion, consequentially raise the antioxidant action in human plasma. *G. lucidum* glucans perform in food as scavengers of free radical and restrain lipid peroxidation, concurrently inspiring interferon production in human blood cells. It was reported that *G. lucidum* has significant effect against mammary carcinoma most likely result is achieved by its antioxidant and enzymatic action by decreasing the reaction enzymatically and non-enzymatically such as catalase, superoxide dismutase, reduced glutathione, glutathione peroxidase, lipid peroxidation, vitamin E, Vitamin C decreased mitochondrial and glycolytic enzymes (Sun *et al*., 2002).

2.2.4 Antidiabetic

Pharmacological active compounds of *G. lucidum* have been reported to have hypoglycemic effect in human as well as in animals. Phosphoenol-pyruvate carboxykinase (PEPCK) levels were markedly reduced by extract, which are normally high in obese/diabetic mice. Expected mechanism of decreasing the levels of serum glucose are through suppression of gene expression of hepatic PEPCK. Several experiments have been proved that G. lucidum therapy acts as a modulator of blood glucose levels (Agius, 2007). Furthermore, in the study it was observed that hypoglycemic effects of *G. lucidum* polysaccharides in mice are produced by raising plasma insulin and declining levels of plasma sugar by enhancing the performance of hepatic glucokinase, glucose-6-phosphate dehydrogenase and phosphofructokinase

simultaneously reduce the production of hepatic glucose and prevent hyperglycemia (Cormack *et al.*, 2001).

2.2.5 Antimicrobial

Various studies have been reported that antibacterial constituents of *G. lucidum* are able to inhibit gram-positive as well as gram-negative bacteria. Polysaccharides components of G. lucidum play significant antibacterial properties (Gao *et al*., 2003). Methanol extract of G. lucidum exhibited antimicrobial action against Escherichia coli, Staphylococcus aureus, Bacillus cereus, Enterobacter aerogenes and Pseudomonas aeruginosa (Alves *et al*., 2013). The additive effect of *G. lucidum* extract has also been observed with four antibiotics like ampicillin, oxytetracyline, cefazolin and chloramphenicol. Candida albicans is the most widespread oral fungus associated with oral candidial infections. Different concentrations of *Ganoderma lucidum* toothpaste were tested in vitro for its antifungal properties and exhibited antifungal result against Candida albicans (Dzubak *et al*., 2006).

2.2.6. Antiosteoporotic

It was reported in a research of *G. lucidum* ethanol extract that prevent ovariectomy-induced bone loss and decreases the blood serum osteocalcin levels, same as the action of 17β-estradiol. *G. lucidum* biological active compounds might be a valuable constituent for the treatment of sex-hormone related aging ailments such as osteoporosis. *G. lucidum* antiosteoporotic activities could be stimulated by either bind with estrogen receptors which reveal responses at the cellular and molecular levels or its act by improving the serum minerals content related to the bone health such as calcium, iron and phosphorus (Elhassaneen *et al*., 2016)

2.2.7 Anti-inflammatory

Anti-inflammatory properties of G. lucidum triterpenes are examined in murine macrophage cell line facilitated by constituent of gram-negative bacterial cell wall lipopolysaccharide (LPS). It is able to enhance the activation of a number of transcription factors including AP-1 and NF-κB and then lead to expression of a number of inflammatory genes such as *TNF-α*, *iNOS*, *COX-2* and *IL-6* in presence of bacterial cell wall lipopolysaccharide acting through Toll-like receptor-4. GLT induced cell cycle arrests via inhibiting production of several inflammatory mediators. These results advocate that G. lucidum triterpenes can be applied as an anti-inflammatory and antiproliferative agent (Dudhgaonkar *et al*., 2009). β-glucan of *G. lucidum* is an immunomodulatory polysaccharide that able to potential interacts with pattern recognition receptors dectin-1. Dectin-1 is a c-type lectin, which can collaborate with *TLR2* to activate response of innate immunes in antigen-presenting cells (Cai *et al*., 2016).

2.2.8. Hepatoprotective

Numerous animal studies have been carried out on *G. lucidum* water and ethanol extracts and protective effects toward acute hepatitis in rat and mice have been reported. It has also been reported that triterpenoids obtained from G. lucidum possess defensive action against acute hepatitis by carbon tetrachloride (Chatterjee *et al*., 2016) G. lucidum fruiting bodies have been used a favored conventional treatment for liver disorders and illustrates broad hepatoprotective properties (Yang *et al*., 2006). It is expected that hepatoprotective activities are exhibited

through triterpenes ability to block platelet-derived growth factor beta receptor and restraining hepatic stellate cells activation and proliferation an important event in hepatic fibrosis (Wang *et al,* .2009).The 92.4% of patients were observed to have positive results among 355 cases of hepatitis B when treated with wulingdan pill in which *G. lucidum* was a chief component. It has been reported from in vitro and in vivo research that potent radical scavenging and antioxidative effects of *G. lucidum* contribute to hepatoprotection (Liu.*et al*., 2015).

2.2.9. Anti-arthritic

Immunomodulatory and anti-inflammatory activities of G. lucidum recommend potential application in the treatment of autoimmune disorder like rheumatoid arthritis (Pan, 2017and Lin, 2005). It has been reported by in vitro studies, peripheral mononuclear cell production of numerous cytokines can be modulated by G. lucidum such as tumor necrosis factor (TNF)-α and ILs (interleukins) such as IL-1β, IL-2, and IL-6 which are linked with the origination and development of rheumatoid arthritis (Lin, 2005). G. lucidum considerably inhibited the proliferation of rheumatoid arthritis synovial fibroblasts (RASF), IL-1β or lipopolysaccharides induced IL-8 and monocyte chemo attractant protein (MCP)-1 production. The inhibitory effects of G. lucidum on IL-1β induced IL-8 and MCP-1 productions by RASF are exhibited partially due to inhibition of the NF-kB transcription pathway (Ho *et al*., 2007).

2.2.10. Anti-benign prostatic hyperplasia

Benign prostatic hyperplasia (BPH) is one of the common widespread disease and symptoms are seen usually in older men age groups. Dihydro testosterone (DHT) is the major prostatic androgen synthesised in presence of 5α-reducase enzymes from its substrate testosterone (Kumar *et al*., 2015). It is essential to maintain sufficient amount of the DHT. Two isoforms of 5α-reductase were reported that exhibit dissimilar patterns of tissue expression, enzyme kinetic parameters and chromosomal localization (Jenkins *et al.,* 1991). It was found that G. lucidum ethanol extract illustrated inhibitory action on 5α-reducase both isozymes as well as ventral prostate enlargement induced by testosterone (Liu and Zhang, 2005). Ganoderol B suppress re-growth of the ventral prostate and restrain androgen-induced LNCap cell growth in rats induced testosterone due to its 5αreducase inhibitory action with propensity to bind androgen receptor (AR). Ganoderol B exhibits down-regulation of AR signaling by a significant mechanism for its anti-androgenic activity. The results of various researches on ganoderol B suggest that it might be valuable in benign prostatic hyperplasia and prostate cancer treatment (Shimizu *et al*., 2006)

2.2.11. Suppression of angiogenesis

Angiogenesis is a physiological process concerning the improvement of new blood vessels from preexisting vessels. It has been found that G. lucidum is an stimulating mediator of angiogenesis overexpressed in tumours and have anti-angiogenic property as well as restrain the production of nitric oxide (NO) (Song *et al*., 2004). G. lucidum polysaccharide peptide (Gl-PP) in a dose-dependent manner acts as inhibitor of the proliferation of human umbilical cord vascular rendothelial cells (HUVEC) (Cao and Lin, 2006). Amount of secreted vascular endothelial growth factor led to a reduce lung carcinoma cells in human when high amount of Gl-PP is given for the duration of 18h in hypoxic condition (Kao *et al*., 2013).

2.2.12. Antinociceptive

The antinociceptive activity of *G. lucidum* has been revealed by ethyl acetate and methanolic extracts using writhing test by intra peritonial injection of 0.2ml acetic acid (0.6%) in mice. Animals were treated with the extracts (500 and 1000mg/kg) orally one hour prior to acetic acid injection. It has been observed that ethyl acetate and methanolic extracts inhibited abdominal constriction response in mice induced by acetic acid and methanolic extract has higher activity than ethyl acetate extract in a dose dependent manner. The activity of the extract is more than the commercial strain available in international market (Sheena *et al*., 2003)

2.2.13. Cardioprotective

Ganoderma lucidum has a significant result on the cardiovascular system, such as reduce blood cholesterol, triglyceride level and blood pressure. Normal blood pressure was observed after 2 months of G. lucidum extract administration involving the clinical trials to the primary stage of hypertensive patients (Xie *et al*., 2016). In other studies it was reported extract from *G. lucidum* reduced blood lipid level and prevented the development of atherosclerosis in rats (Wang *et al.*, 2009). It was also shown that polysaccharide and peptide complexes of G. lucidum revealed a protective action in relation to endothelial cells of blood vessels in human (Yang *et al*., 2010). Polysaccharides of G. lucidum have revealed hypotensive, antithrombotic and hypo lipidemic result, while improvement in ECG, lowered chest pain and palpitation as well as relief in shortness of breath have been observed by Ganopoly preparation in a double-blind, randomized, multi centered study. The *G. lucidum* treatment also has a propensity to elevate glutathione (GSH) which is a cofactor for antioxidant enzymes such as glutathione peroxidase (GPx), glutathione Stransferase (GST), catalase (CAT) and superoxide dismutase (SOD) indicating antioxidant defense that is a major contributor in cardio protection (Wachtel *et al*., 2004). ACE-inhibitory action has also been reported triterpenoids compounds. In another study, it has been reported that *G. lucidum* extracts act significant role in experiment of an anticancer drug adriamycin induced cardio toxicity via reducing generation of free radical or free radicals scavenging by raising the level of glutathione content and different antioxidant enzymes (Rajasekaran *et al*., 2012). In a current study cardio protective properties of G. lucidum extract revealed in a research with global ischemia (45min) and reperfusion (30min) of perfused isolated rat heart. 400mg/kg extract dose for 15 days reduced cardiomyocytes necrotic death as well decreased reperfusion contracture (Lasukova *et al*., 2015).

Table 1: Common pharmacological effects of *G. lucidum* major bioactive compounds

No	Major bioactive compounds	Pharmacological effects	References
1	Polysaccharides	Anti-cancer, (anti-angiogenic, cytotoxic, anti-tumor, anti-metastatic)	(Ferreira *et al*., 2015)
2	Glycopeptides and peptidoglycans	Anti-cancer, (anti-angiogenic, cytotoxic, anti-tumor, anti-	(Cör *et al*., 2018; Hapuarachchi *et al*., 2018; Sudheer *et al*.,

		metastatic)	2018)
3	Triterpenoids (ganoderic, ganodermic, ganolucidic acids, ganoderals, etc.)	Anti-cancer, (anti-angiogenic, cytotoxic, anti-tumor, anti-metastatic)	(Duru and Tel Çayan, 2015)
4	Protein Ling Zhi-8 (LZ-8), lectin, ribosome inactivating proteins, antimicrobial proteins, glycoproteins, peptidoglycans, ganodermin A, ribonucleases,	Immunomodulatory, anti-cancer and anti-tumour	(Cao *et al*., 2018; Sudheer *et al*., 2018)
5	Polysaccharides, proteoglycans, and triterpenoids	Antidiabetic	(Ma *et al*., 2015)
6	Ganoderic acids T-Q and lucideinic acids A, D2, E2, and P	Anti-inflammatory	(Sliva *et al*., 2003)
7	Triterpenes, polysaccharide-peptide complex and phenolic component; Methanolic extracts; Phenolic and polysaccharide extracts	Antioxidant	(Kana *et al.,* 2015; Yıldız *et al*., 2015; Kumari *et al*., 2016)
8	Polysaccharides (Ganopoly)	Cardiovascular problems	(Gao et al., 2004)
9	Triterpenoids against Enterovirus 71; Ganoderic acid derivatives against H5N1 and H1N1 influenza; Ganoderiol F, ganodermanontriol against HIV-1	Antiviral	(Zhu et al., 2015; Bishop et al., 2015)
10	Polysaccharides; Triterpenoids	Antimicrobial	(Mehta, 2014; Cör *et al*., 2018; Hapuarachchi *et al*., 2018)
11	Aqueous and methanolic extracts; methanolic extracts; Triterpenes and ganomycein	Antimicrobial	(Sudheer *et al.,* 2018; Stojkovic *et al*., 2014; Bal, 2019)

3. Economic importance of Ganoderma lucidum mushroom

Cultivation of the Genoderma mushroom in the countries of Asia is of great importance to its health benefits as well as the huge economic return from it. For a new business opportunity in Egypt, there are many factors which will help this industry to success, including the appropriate climate, spread of Ganoderma in the governorates of the Nile Delta region, the availability of suitable areas for cultivation (no need of special difficult preparations), the low cost and the most important factor are the studies and researchers who are able to develop this project and provide sufficient information to help the workers in it (Copot and Tanase, 2017). The

Ganoderma project can provide employment opportunities for young people, elder and women for ease of operation, providing foreign currency where the kilogram sold for about 36 dollars, also opening a new market in the field of pharmaceutical industries. In addition, strengthening the market with a natural product has 52 enormous benefits as reishi coffee and tea both for prevention and treatment of diseases (Mansour *et al.* 1998).

2.4. Toxicity of *Ganoderma lucidum*

Most papers on *Ganoderma lucidum* focused on its miraculous healing quantities but few have shown that it can have toxic effects on humans. Studies on the toxicity and adverse effects of *G. lucidum* are much less common; however, *in vitro* study revealed that *G. lucidum* extracts can have the potential to cause toxicity. When *G. lucidum* extracts exposed to cells at higher levels of concentrations than which required for stimulatory effects, it causes significant reduction in cell viability observed in some cell lines (Gill and Kumar, 2015). Further, patients with gastric ulcers and active gastrointestinal bleeding should be vigilant because of apparent anticoagulant effect of *G. lucidum.* Patients with tendency for bleeding should be cautious since *G. lucidum* has additive effects on clotting factors and prolongation of Prothrombin time (Ulbricht *et al*., 2010).

3. Conclusion and recommendation

3.1 Conclusion

Ganoderma lucidum has long been reputed to extend the life span and to increase youthful vigor and vitality. *Ganoderma lucidum* has been widely researched and it has been a part of many publications. The specific reported attributes of *G. lucidum* include lowering the risk of cancer, heart disease, and infections. These health-promoting effects are believed to be mediated via the antioxidant, hypotensive, anti-inflammatory, and Immunomodulatory properties of the mushroom. The data obtained from the research studies demonstrate the effect of *G. lucidum* only on the molecular level. On the basis of many such evidences, there are many products in the market which are sold primarily as neutraceuticals. Some of them are marketed as dietary supplements and very widely used by consumers in combination with coffee and tea. Hence further research on Ganoderma for validating its usage is a demand of the present day. It has been widely used through the centuries for numerous pharmacological benefits, including immuno-modulating, anti-inflammatory, anti-cancer, anti-diabetic, antioxidative properties. In addition to this, *Ganoderma lucidum* has a great importance to its health benefits as well as the huge economic return from it and new business opportunity. Global consumption of *G. lucidum* is high, and increasing series of patented and commercially available products that incorporate *G. lucidum* as an active ingredient are available as food supplements. On the basis of many such evidences, there are many products in the market which are sold primarily as neutraceuticals.

3.2 Recommendation

I recommend that *Ganoderma lucidum* medicinal mushroom has a greatest pharmacological and economic importance in the world. Cultivation of *Ganoderma lucidum* is the best way to increase the efficiency and conduct research for their pharmacological properties to overcome different diseases.

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