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Ganoderma lucidum and Antimicrobial Activity

Mohammad Hadi Rezghi Jahromi* and Milad Mozafari

[1]*Department of Horticultural Sciences, Faculty of Agriculture and Natural Resources, University of Mohaghegh Ardabili, Ardabil, Iran*

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Abstract

Global interest in edible herbs for health care and health promotion has increased significantly in recent years. *Ganoderma lucidum* is a forest fungus with a woody texture that has been used since ancient times to enhance health and prevent and treat many diseases due to its wide range of secondary metabolites with abundant medicinal properties. So far, many cellular mechanisms have been proposed to explain how the active metabolites function and the health and hygienic properties of this valuable medicinal fungus, including anti-cancer, anti-viral, anti-bacterial, enhanced cellular immunity, antioxidant and many more. This article reviews the scientific findings of scientists on the antimicrobial properties of the medicinal fungus *G. lucidum*.

1. Introduction

There are approximately 10,000 known species of fungi in the world, of which about 300 species have medicinal properties (Wasser & Weis., 1999; Copot & Tanase., 2017). Fungi have long been known and used as therapeutic drugs in traditional medicine around the world (Sharma, 2019). Fungi are a rich source of biologically active factors (Lee *et al*., 2016). Modern advances in technology and modern science have improved human health to some extent, but there is still a need to consider superior natural and organic alternatives with fewer side effects. *Ganoderma lucidum* ("Lingzhi" in Chinese and "Reishi" in Japanese) is a basidiomycete fungus that is widely used in traditional medicine and as a medicinal fungus in China, Japan and many other countries, including Asian countries (Gil *et al*., 2016; Sanodia *et al*., 2009; Wachtel *et al*., 2004) Figure (1). This medicinal mushroom was first registered in the ancient encyclopedia "Shen Nong's Ben Cao Jing" and has been known as a medicinal mushroom for more than 2000 years (Batra *et al*., 2013; Chiu *et al*., 2017). Chinese medicine doctors know red Ganoderma as a fungus of immortality. In the wild, this medicinal fungus grows on decaying tree trunks. The body of young bean-shaped fungi is yellowish-brown, reddish-yellow in color, and darkens with age. *G. lucidum*-derived products are currently highly valued in the global mushroom industry and are available in a variety of forms, including powders, supplements, and teas derived from mycelium, spores, and fruits (Lindequist *et al*., 2005). *G. lucidum* belongs to the branch of basidiomycetes, which contains many biologically active compounds, including polysaccharides (β-glucan, mannitol), alkaloids, triterpenoids (ganodric acid), sterols, amino acids, proteins, and other compounds that give this fungus many medicinal properties (Paterson, 2006). To date, more than 140 triterpenoids have been identified in the medicinal fungus *G. lucidum*, and a number of new compounds are being identified (Sudheer *et al*., 2016; Weng *et al*., 2010, 2011). Modern pharmacological and clinical research has shown that G. lucidum has several medicinal properties. Among them, polysaccharides and triterpenoids, especially ganoderic acid, are among the most important compounds produced by *G. lucidum*, which have various and important medicinal activities such as antioxidants (Krishna *et al*., 2016; Gill *et al*, 2016), reatment of type 2 diabetes (Rezghi, 2018; Liang *et al*., 2010) immune system balancer (Ishimoto *et al*, 2017), liver protection (Ren *et al*. 2010; Lee *et al*., 2016), neuroprotection (Zhao *et al*., 2019), histamine inhibition (Yu *et al*., 2013), cardiac protection (Rajasekaran *et al*, 2012; Zeng *et al*, 2018), anti-inflammatory (Cai *et al*, 2017), anti-allergy (Ji *et al*, 2007), Anti-viral (Wang *et al*, 2004), anti-cancer (Zolj *et al*., 2018; Gurovic *et al*, 2018; Ahmad, 2020), Anti-arthritis, (Pan *et al*, 2017), anti-HIV (Akbar *et al*, 2011; Kang *et al*, 2015; Seo & Choi, 2021), antibacterial (Sarnthima *et al*, 2017; Quereshi *et al*, 2010), anti-

*Corresponding Author: Department of Horticultural Sciences, Faculty of Agriculture and Natural Resources, University of Mohaghegh Ardabili, Ardabil, Iran.
E-mail Address: rezghi@student.uma.ac.ir

fungal (Geng *et al*, 2017; Nayak et al, 2010), anti-osteoporotic (Elhassaneen *et al*, 2016), anti-androgenic (Fujita *et al*, 2005), antinociceptive (Sheena *et al*, 2005), and many other. Bacteria are a group of prokaryotes. These organisms, which are mostly several microns in size, are among the most diverse and important microorganisms.

Bacteria coexist to a large extent with living organisms, so that without their activity, life on earth would be disrupted. In general, a small percentage of bacteria are pathogenic and cause infectious diseases including cholera, tuberculosis, anthrax, leprosy, plague, etc. Today, antibiotics are used to prevent and treat bacterial infections. A virus is a small pathogen that multiplies only in the living cells of an organism. Viruses can infect all forms of life, from animals and plants to microorganisms, including bacteria. Viruses can enter the host body and multiply using its cells. Unlike bacteria, which can be killed by antibiotics, the immune system is the only defense we have against viruses. These conditions may seem worrisome, but some measures can help boost the immune system and help viral infections heal faster. The stronger the immune system is able to detect and fight viruses, the milder the symptoms of the disease.

1.1. Dealing with bacterial and viral infections

The goal of research into the treatment of viral and bacterial infections is to discover factors that specifically inhibit viral and bacterial activity without affecting normal cells. Due to the adverse side effects of antibiotics and the emergence of resistant and mutant species, researchers are looking for new antibacterial, antifungal and antiviral agents from medicinal plants. (Zhong and Xiao, 2009). In an experiment, oral injection of *G. lucidum* in laboratory mice did not show any toxicity to normal cells in the body (Kim *et al*. 1986). Several studies have reported that G. lucidum antibacterial compounds are able to inhibit gram-positive and gram-negative bacteria (Ferreira *et al*, 2015; Sakthivigneswari *et al*, 2013; Wasser, 1999). Components of *G. lucidum* polysaccharides have significant antibacterial properties (Smania *et al*, 2007). Some compounds such as ganomycin, triterpenoids, etc. have been shown to have a wide range of antibacterial activity (Gao *et al*., 2003; Suay *et al*., 2000; Shah *et al*., 2014). Extracts extracted from *G. lucidum* have been shown to show antibiotic properties by inhibiting the growth of gram-positive and gram-negative bacteria (Gao *et al*, 2003). Researchers have evaluated extracts of *G. lucidium* against various bacteria, including *Escherichia coli*, *Bacillus subtilis*. They observed different levels of antibiotic activity against (Staphylococcus aureus, Salmonella sp., Corynebacterium diphtheria, Enterobacter aerogenesis and Pseudomonas aeruginosa. Sheena *et al*., 2003; Shah *et al*., 2014; Kamble-*et al*., 2011; Singh *et al*., 2014). A study showed that the extract extracted from Ganoderma lucidam inhibits Helicobacter pylori, which is responsible for gastric ulcer formation and other gastric complications (Suay *et al*, 2000). In another study, various extracts extracted from *G. lucidem* were studied. Among them, methanolic extract extracted from *G. lucidum* had antimicrobial activity against Escherichia coli, Bacillus cereus, Staphylococcus aureus, Enterobacter aeruginosa and Pseudomonas aeruginosa. (Gaylan *et al*, 2018; Siwulski *et al*, 2015). (Heleno *et al*. 2013) in a study examined the effect of some antibiotics and extracts of *G. lucidum* against a number of bacteria.They found that *G. lucidum* extracts were more active against Staphylococcus aureus and B cereus than the antibiotics ampicillin and streptomycin. Further research has also shown an additive effect of *G. lucidum* extract with four antibiotics such as ampicillin, oxytetracycline, cefazolin and chloramphenicol. It has also been shown that different extracts of *G. lucidum* have equal value against bacteria compared to gentamicin sulfate (Dulger *et al*, 2004; Quereshi *et al*, 2010). Some species of *G. lucidum* have been shown to inhibit the growth of methicillin-resistant Staphylococcus aureus by producing ganomycin. (Mothana *et al*, 2000). *G. lucidum* has been shown to have antifungal activities and various substances with antifungal properties have been isolated from *G. lucidum* (Naveenkumar *et al*, 2018; Sanodiya *et al*, 2009). Ganodermin obtained from Ganoderma was shown to inhibit the growth of Fusarium oxysporum, Botrytis cinerea and Physalospora piricola. Candida albicans is one of the most common oral fungi that cause candidal infections of the mouth. In an in vitro study, different concentrations of *G. lucidum* against Candida albicans were tested and showed antifungal results against Candida albicans (Nayak *et al*, 2010).

Many studies are done to identify antiviral agents that specifically prevent the virus from replicating without affecting the body's natural cell division. In a study by (Eo *et al*., 1999), the antiviral activity of compounds isolated from extracts of the medicinal fungus *G. lucidum* was demonstrated. Five compounds isolated from *G. lucidem* were able to significantly inhibit the cytopathic effects of VSV (vesicular stomatitis virus) and HSV (herpes simplex). Laboratory studies have shown that polysaccharides and triterperoids have antimicrobial activity against hepatitis B virus, HIV virus and Epstein-Barr virus (EBV). In another study, ganoderic acid isolated from *G. lucidum* showed inhibitory effects on hepatitis B virus replication over 8 days (Li and Wang, 2006). Metabolites isolated from Ganoderma showed anti-herpes activity. Aqueous and methanolic extracts of *G. lucidem* confirmed the

prophylactic effect on vesicular stomatitis virus (VSV), herpes simplex virus type 1 (HSV-1) and herpes simplex virus type 2 (HSV-2). Herpes simplex is a viral disease caused by herpes viruses, herpes simplex virus one (HSV-1) and herpes simplex virus two (HSV-2). *G. lucidum* is a potent inhibitor of both herpes simplex virus 1 (HSV-1) and herpes simplex virus 2 (HSV-2) (Liu *et al*., 2004; Kim *et al*, 2000; Oh *et al*, 2000). In another study, proteoglycans obtained from the mycelium of *G. lucidem* showed inhibitory effects on HSV-1 and HSV-2 (Liu *et al*, 2004; Li *et al*, 2005; Wachtel-Galor *et al*, 2011). A study by (Zheng *et al*., 2017) Showed that five tert-terpenoids isolated from *G. lucidum*, including Ganoderic Acid A, Ganodric Acid B, Ganodrol B, Ganodermanontriol, and Ganodermanondiol, can inhibit Nasopharyngeal carcinoma (NPC)-associated Epstein-Barr virus (EBV) infection. Ganoderic acid B, a triterpene isolated from *G. lucidum*, has been shown to inhibit the activation of Epstein-Barr virus (EBV) antigens as a telomerase inhibitor. Various studies have also shown that ganoderic acid B is a relatively active inhibitor of HIV-1 protease (Zhou *et al*, 2018; Zheng *et al*, 2017) Figure (2).

1.2. Activities against Human Immunodeficiency Virus (HIV)

AIDS, or Acquired Immune Deficiency Syndrome, is a disease of the immune system caused by the human immunodeficiency virus (HIV). The disease is known as the global epidemic, which is currently very widespread and expanding. More than 3 million people die each year from AIDS-related diseases. Immune Deficiency Syndrome (AIDS) caused by HIV infection has become an important social and medical problem (Kartikian *et al*., 2007; Paydary *et al*., 2013). The HIV virus leads to AIDS by weakening the T lymphocytes, which are the body's defense cells, and weakens the immune system and infects. The presence of T cells is essential for an immune response, and without them, the body cannot fight infections or kill cancer cells. Current HIV treatment strategies include delaying the progression of AIDS. Primary treatment for HIV is typically a non-nucleoside reverse analog transcript (NNRTI) inhibitor plus two inverse Nucleoside analog transcriptase (NRTIs) inhibitors, which is an effective and major approach to the treatment of immunodeficiency syndrome (Choengpanya *et al*., 2021; Matsushita and Kimura, 2002). These agents include protease inhibitors (PIs) and potent inhibitors of reverse transcriptase (RT). However, the emergence of drug-resistant and toxic variants greatly limits the long-term effects of these drugs. Recent studies have shown that many natural products are active as anti-HIV agents (Kartikian *et al*., 2007).

Fig. 1 Images of the medicinal fungus *G. lucidum*.

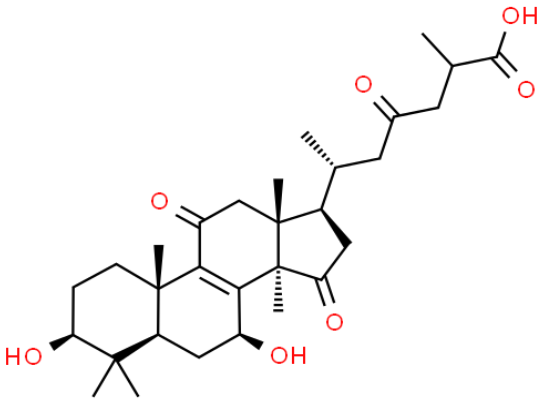

Fig. 2 Ganoderic acid B

These compounds belong to a wide range of different structural classes, for example coumarins, flavonoids, tannins, alkaloids, lignins, terpenes, and polysaccharides (Vermani and Garg, 2002). Various in vitro studies have shown that various triterperoids of *Ga. lucidum* have potent inhibitory activity against HIV. They exhibit anti-HIV-1 protease activity. In one study, the anti-HIV-1 activity of extracts produced by Ganoderma and Lentinus was evaluated in an in vitro cell culture model. The results showed that Ganoderma and Lentinus inhibited HIV-1 replication by 80 to 90% and reduced the production of primary and secondary virus transcripts by 55.5% -91.3% and 82.1% -93.6%, respectively (Flórez-Sampedro *et al*., 2016). Lucidenic acid O and lucidenic lactone isolated from the fruiting bodies of *G. lucidum* inhibit the activity of DNA polymerase-α and DNA polymerase-β as well as HIV-1 RT. Ganoderic acid B and ganoderiol B, as well as other tri-tetanopenoids including ganoderic acid α, ganoderic acid C1, ganoderiolA, ganoderic acid H, ganodermanondiol, lucidumol B, and many others showed anti-HIV-1 activity. (Sahar *et al*., 1997; McKennan *et al*., 2002; Gao *et al*., 2003). Another study showed that ganolosidic acid A, ganoderic acid-β, lucidomol B, ganodermanondiol, and ganodermanontriol also had significant anti-HIV-1 protease activity. (Min *et al*., 1998). In another study, (Kang *et al*., 2015) Showed that ganoderic acid B had the highest inhibitory activity for HIV-protease among the four triterpenoids tested. In an experiment, (Zhang *et al*., 2011) reported that extracts extracted from *G. lucidum* could inhibit HIV-1 reverse transcriptase, and that the triterpenoids in the fungus had great potential for treating HIV.

2. Conclusions

Today, the needs of society in every aspect are increasing rapidly. One of these aspects is increasing public health and medical needs. *G. lucidum* this valuable fungus has a wide range of therapeutic benefits that can be used as complementary and alternative methods to prevent and treat a wide range of diseases. *G. lucidum* has different types of chemical compounds that with the advancement of science, we are still witnessing the unveiling of more compounds. These chemical compounds can cure the disease in different ways. So far, Ganoderma has shown many therapeutic activities, including antibacterial, antiviral, antifungal, antioxidant, anti-cancer, immune-boosting, liver protection, treatment of autoimmune disorders, asthma and allergies. Protection against diabetes, obesity, neurological diseases such as parkinson's and alzheimer's and many more.

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