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Review Article

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"*Ganoderma lucidum sensu lato*" – a sacred mushroom for immortality

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Abstract

Ganoderma lucidum sensu lato, is an ancient Chinese mushroom commonly known as "Reishi" or "Linghzi" which has been used for nutritional and therapeutic purposes. Reishi is a basidiomycete widely distributed in temperate and tropical regions. Among 2000 classes of Reishi, only 6 types are commonly presented to be effective for therapeutic purpose. These 6 types were known as black, red, blue, yellow, white and purple, respectively. Main constituents of Reishi are Polysaccharides, Triterpenoids, Sterols and Proteins. Reishi has been clinically used as immune system modulator, antiviral, cytotoxic agent, antibacterial, hepatoprotective, anti-inflammatory and also in the treatment of neurological disorders. The wide clinical scope of Reishi has influenced to name it in English with the nickname of "the mushroom of immortality".

Keywords – Linghzi – Medicinal Mushroom – Reishi – Therapeutic value

Introduction

From ancient times, plants and mushrooms were used for both therapeutic and culinary purposes, due to the fact that they contain bioactive compounds which enhance human health and thus reduce illness (Wachtel-Galor et al. 2014). *Ganoderma lucidum* (*G. lucidum*), an immense dark color mushroom belonging to family Ganodermataceae, with gleaming exterior and woody texture. It is a widely cultivated mushroom due to its medicinal and clinical value (Chang & Buswell 1999). It originated as Chinese mushroom and known as 'linghzi' also famous in Korea known as 'Youngzhi' and in Japan where is known as 'Reishi'. It has been used to enhance strength, stamina and energy (Chang & Buswell 1999).

It is a basidiomycete and usually grows on wood in humid condition and dim light (Willard 1990). It usually grows on either living or dead wood of deciduous plants (Stamets 2000). It's widely distributed in temperate and tropical regions. In forests of USA, Europe and South America it grows in subtropical zone while in North America it is found on East Coast (Stamets 2000). Dead trees of Japanese plum *Prunus salicina* in Far East facilitate to grow on it. Different species of deciduous trees present in Europe allows this mushroom to grow on them in summer and autumn (Sokol 2000).

Many extractable compounds are present in *G. lucidum* with nutritional and medicinal values used in different ailments. The bioactive compounds include proteins, sterols, lectins, polysaccharides and group of triterpenes called Ganoderic acid. These compounds present a range

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of clinical effects i.e. anti-neoplastic, anti-inflammatory, anti-viral, anti-fungal, anti-diabetic, anti-oxidant and also boost the immune system. Among presented bioactive compounds, two of them are pharmacologically important i.e., polysaccharides and triterpenoids (Cör et al. 2018).

Classification

There are about 2000 classes of Ganoderma mushrooms out of which only 6 are known i.e., white, blue, black, purple, yellow and red (Table 1). Out of these 6, black Reishi (*G. sinensis*) and red Reishi (*G. lucidum*) have shown extensive health benefits (Babu & Subhasree 2008). The mature species measure up to six inches in diameter but black Reishi is irregular in shape and ten inches in diameter. Black Reishi isn't preferred for use because of low polysaccharide content. Purple Reishi is rare but shows similarity in content to red Reishi (Carlson 1996).

Table 1 Important classes of mushroom Lingzhi with therapeutic value (Komoda et al. 1989)

Color	Taste	Clinical Use
Black	Salty	Pulmonary diseases
Red	Bitter	Brain plasticity, Immune modulator
Blue	Sour	Eyesight improvement, Hepatic function modulator
Yellow	Sweet	Spleen function modulator
White	Hot	Kidney function modulator and act as protective agent
Purple	Sweet	Skin health modulator, Anti-infective for ears

Morphology

Physically Reishi consists of a stem, a cap which is more like a kidney and spores. Naturally, this mushroom grows on dried stem of dead plum trees while in Japan it is commercially cultivated onto aged Japanese oak. The stalk of this mushroom usually pulls nutrients and minerals from the trunk on which it is growing. So the nutrients present in Reishi majorly depend on its habitat (Mushrooms 1995). The cap is usually dark in color i.e., red, black, reddish black, brown and deep red. Its surface is shiny and is round, kidney shaped and sometimes flat. The diameter of the cap is usually ranges between 30-250 mm. Undeveloped fruit bodies of Reishi are yellow brown in color; they changed their color and gets darker with age. Spores Produced by Reishi are not properly round but elliptical or ovoid in shape. They consist of two layers i.e., external layer and internal layer. External layer has no color and is plane and smooth while internal layer is yellow brown in color and has lumps, and has size which usually fluctuate between 6-11 mm (Siwulski et al. 2015).

Bioactive components

General nutritional components

It usually consists of carbohydrates, proteins, minerals, fibers and fatty acids. Artificially cultivated mushrooms and wild mushrooms generally share identical nutritional components (Zhou et al. 2007). About 90% of the weight of this mushroom is due to the water content and remaining 10% consists of fat (28%), carbohydrate (3-28%), fiber (3-32%), protein (10-40%) and ash (8-10%) (Cör et al. 2018). Nutritive compounds generally include copper, zinc and selenium (Lee et al. 2009). Complex compounds include fatty acids and pro vitamins (Liu et al. 2011).

Major bioactive components

Hundreds of reports have been published about bioactive components of *G. lucidum* Spores, fruiting bodies and mycelia collectively contains many hundred compounds i.e. nucleotides, fatty acids, proteins, trace elements, peptides, polysaccharides, triterpenoids and nucleotides (Mizuno et al. 1995). Principally, *G. lucidum* is an important source of bioactive components (Grys et al. 2011).

Polysaccharides

Out of 279 active metabolites, polysaccharides are considered as an active group of compounds (Vickers 2017). A large number of polysaccharides are present in the cell wall of spores (Wu & Wang 2008). Hundreds of polysaccharides are also separated from fruit bodies, mycelium and from different liquid media of Linghzi (Wasser 2010) i.e., α-D-glucans, β-D-glucans and complex of proteins and polysaccharides. Different forms of these glucans, their branching; solubility in water and size determines their biological activity (Wasser 2011). Different polysaccharides obtained from fruit bodies are PL-1, PL-3, PL-4 and ganoderans A, B and C while which obtained from spores are SP and PSGL-1-1A (Huie & Di 2004). Free radicals scavenging effect of polysaccharides protects the cell from damage. As well as the glucans present in them have immunomodulatory effects (Sanodiya et al. 2009) and shows cytotoxic effect against cancer cells (Wiater et al. 2012). In diabetic patients, polysaccharides from Reishi are used in anticipation of cardiac complications (Meng et al. 2011). They also represent defensive action against destruction caused by gamma rays (Pillai et al. 2008). Low molecular weight polysaccharides obtained from aqueous extract of fruit bodies of reishi show their activity as immunity boosters (Zhu et al. 2013).

Triterpenoids

Another important group of compounds having complex structure, with carboxyl group present in them are triterpenoids, normally known as ganoderic acids. They are oxidative product of lanostane (Ma et al. 2003). They include derivatives (Table 2) with varying clinical efficacy are Ganoderic acid Mk, Ganoderic acid S, Ganoderic acid Mf, Ganoderic acid R, Ganoderic acid Mc (Li et al. 2013) and Ganoderic acid A, Ganoderic acid F, Ganoderic acid H (Jiang et al. 2008). Triterpenoids shows promising effect by boosting memory status (Zhang et al. 2011). Ganoderic acids have shown their cytotoxic effects on prostate and breast cancer cells (Liu et al. 2012). Other actions include hepatoprotective, anti-hypertensive, anti-cancer, anti-histamine, anti-HIV and cholesterol lowering effects (Sliva 2003).

Table 2 Triterpene compounds with their selective clinical action

Triterpene	Clinical Action	Reference
Ganoderic acid R, S, Mc, Mf	Cytotoxic	Li et al. 2013
Ganoderic acid A, H	Inhibits breast cancer cell growth	Jiang et al. 2008
Lucidenic acid C, N, A	Decrease cell growth by inhibiting cell cycle	Hsu et al. 2008
Ganoderic acid DM	Inhibit metastasis of prostate cancer cells.	Johnson et al. 2010
Ganoderic acid E	Cytotoxic	Wu et al. 2001
Ganoderic acid D	Inhibits proliferation of cancer cells	Yue et al. 2008
Ganoderic acid T	Inhibits growth of cancer cells	Xu et al. 2010

Proteins

Various proteins with medicinal effects are also present in reishi i.e., Ganodermin exhibits anti-fungal activity (Wang & Ng 2006) and LZ-8 protein which shows immunomodulatory activity (Lin et al. 1997). Protein is generally present in mycelium that is LZ-8, and has the molecular weight of about 12 kilo Dalton. This LZ-8 protein generally exhibits the mitogenic activity (Lin et al. 1997). Another protein Ganodermin which has molecular weight of 15 kilo Dalton separated from fruit bodies have anti-fungal activity (Wang & Ng 2006).

Sterols

Various sterols are also present in this mushroom complex species, in both fruit bodies and spores i.e., pro vitamin D2 also known as ergosterol and oxidative product of ergosterol. They usually act on breast cancer cells (Zheng et al. 2009).

Nucleosides & nucleotides

Some nucleosides i.e., guanosine, cystidine, inosine, thymidine and nucleotides i.e., uracil and thymine are also present in it (Gao et al. 2007). They are effective against the inhibition of platelet aggregation activity (Kawagishi et al. 1993).

Therapeutic effects

Immunomodulatory effect

Many substances present in reishi has immunomodulatory activities i.e., triterpenoids, various proteins and glucans. The mechanism of action behind this is the activation of various cells that belongs to immune system i.e. lymphocytes and macrophages. As well as the aqueous extract of reishi also promote the production of interleukins, various cytokines, tumor necrosis factor and interferon (Sanodiya et al. 2009). Extract obtained from spores of this mushroom exhibit anti-cancer activity and increase the production of macrophages (Song et al. 2010). Many substances obstruct allergic reactions by action on mast cells (Calder 2003). The high concentration of Polysaccharides, Germanium and Triterpenoids are proved to have effects on immune system and as well as strengthen immune system (El-Mekkawy et al. 1998).

Antimicrobial effect

Many constituents of reishi show antibiotic activity. They act on both gram positive and gram negative bacteria and inhibit their growth (Gao et al. 2003a). *Helicobacter pylori*, a bacteria involved in stomach ulcers is inhibited by its extract (Suay et al. 2000). Some constituents also shows anti-fungal activities (Sanodiya et al. 2009). A protein known as Ganodermin which is obtain from mycelium of this mushroom inhibit the mycelial growth of various fungus i.e., *Fusarium oxysporum* and *Physalospora piricola* (Zhang et al. 2011). The extracts exhibit greater therapeutic effect against *Staphylococcus aureus* than streptomycin (Heleno et al. 2003). Methanol extracts present activity against various micro-organisms i.e., *Escherichia coli*, *Pseudomonas aeruginosa* and *Staphylococcus aureus* (Shah et al. 2014).

Antiviral effect

Fruitbodies of reishi mushroom contains Ganoderic acid, which shows anti-viral activity against HIV and Epstein Barr virus (Eo et al. 2000). Some substances which reserve the replication of Influenza virus obtained from aqueous and methanol extract of reishi. Polysaccharide also shows anti-hepatitis B viral activity. Ganodermadiol, which is a triterpene, shows inhibitory activity against herpes virus (Bisko & Mitropolskaya 2003).

Cytotoxic effect

Extracts of *G. lucidum* show positive effects against many cancer cells such as MCF-7 cancer cells of breast (Zheng et al. 2009) and cancer cells present in ovary (Qu et al. 2011). Experiments performed on animals and their studies shows that the reason behind the reduction of tumor cells is related to the production of TNF and lymphocytes which induce necrosis and sometimes decreased blood supply to tumor cells by blockage or destruction of blood vessels. Immunity against cancer cells was shown by the mice after the administration of oil from *G. lucidum* (Nie et al. 2010). Apoptosis of leukemia cells was found to be inhibited by LZ-8 protein present in reishi (Guo et al. 2010). Many studies proved that the anti-tumor effect is due to the β-D-glucan present in reishi. β-D-glucan is a polymer, which is made by linking many small sugar molecules. These sugar molecules activate immune system or sometimes modulate it by stimulating T-cells and macrophages (Gao et al. 2003b).

Antidiabetic effect

Polysaccharide portion of reishi shows hypoglycemic effects. Extract of this mushroom is more operative as compared to anti-diabetic drugs for lowering glucose level in blood (Gao et al.

2004). Diabetic nephropathy is also inhibited by this mushroom showed by pre-clinical studies (Mao et al. 2009).

Hepatoprotective effect

G. lucidum have significant protective action on liver cells. A study performed on mice showed that the triterpenes present in reishi shows positive effects towards liver cells by removing free radicals from liver (Lin et al. 2002) (Lin et al. 2002). Polysaccharides present in reishi stabilize aminotransferases level in the patients suffering from Hepatitis (Gao et al. 2002). Chronic hepatitis can also be treated with reishi. Extract of reishi is found to be effective in the patients suffering from liver failure. An experiment on a mice having hepatitis due to carbon tetra chloride, showed positive results and regeneration of liver cells because of continuous dosing of tincture of reishi (Lin et al. 1993).

Cardio protective effect

The cardiovascular effect by lowering the cholesterol level and triglyceride level has been also reported, along with positive effects on heart and normalization of blood pressure. Two-month continuous administration of *G. lucidum* extract in patients in primary stage of hypertension has shown beneficial effects (Jin et al. 1996). Its extracts also inhibit atherosclerosis in rats by reducing lipid level (Wang et al. 2009). Defensive action shown by the complex formed by combination of polysaccharide and peptide on endothelial cells of vessels (Yang et al. 2010).

Anti-inflammatory effect

Reishi extract also exhibits anti-inflammatory activity and protective effects against colitis (Hasnat et al. 2015). Wound healing activity of aqueous extract of reishi was also found (Gupta et al. 2014). Many studies showed that extract of reishi inhibit many kinds of allergic reactions (Chen & Zhang 1987) such as asthma, dermatitis, conjunctivitis, bronchitis and rheumatism (Stavinoha et al. 1990).

Neurological effect

Many therapists in China and Japan have suggested that Reishi mushroom might be useful against insomnia (Jones 1990), many psychiatric disorders and neurological diseases (Chen & Li 1993). Patients with Alzheimer's disease, taking *G. lucidum* have showed noteworthy improvements (Yoon et al. 1994).

Conclusion

G. lucidum sensu lato has extensive medicinal value against chronic and infectious diseases; additionally, it is an excellent candidate in order to conduct extensive future research. A number of bioactive compounds with medicinal or nutraceutical properties still need to be extracted and thoroughly studied in clinical trials in order to increase our knowledge and ensure the therapeutic use this mushroom species complex.

Conflict of interest

No conflict of interest associated with this work.

Contribution of authors

Ayesha P and Ariza A conceptualize the protocol and content for current study. Maham A and Husnain H did literature review. All authors equally contributed in draft preparation and critical reviewing of manuscript. Husnain H is the guarantor for all authors' contribution.

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