

Ganoderma lucidum: A Potent Medicinal Mushroom with Numerous Health Benefits

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Herbal medicines which formed the basis of health care throughout the world since the earliest days of mankind are still attracting more and more attention within the context of health care provision and health sector reform. Recording of their clinical, pharmaceutical and economic value is encouraging for international trading, through it varies widely between countries.

A number of plant based traditional system of medicines have been in use in India and also in many parts of the world for ages. Before the advent of modern medicine, the traditional systems of medicine were playing a central role in healthcare. According to an estimate, majority of the world population, especially in the developing countries, still depend on herbal products for their primary health care needs, possibly for the following reasons:

1. Lack of easy access to drugs of modern medicine.
2. Popular belief that herbal drugs are free of adverse effects.
3. Most economic as against prohibitive cost of most of the allopathic drugs.
4. Concern over the toxicity and side effects of modern drugs.
5. The holistic approach and belief towards the plant based medicines.

The traditional medicine has been steadily gaining interest and acceptance even amongst the practitioners of modern medicine also [1]. Plants have also been a source of chemical substances which serves as drugs in their own right or as key ingredients in synthetic drugs. Many plants derived drugs used in modern medicine are developed by ethno medical leads and subsequent ethno pharmacological studies. There are more than 100 drugs of known structure that are extracted from higher plants and included in modern medicine [2]. A proper ethno pharmacological search and follow up studies can lead to many more useful drugs. Synthetic studies available on a good number of plants indicate that promising phytochemicals (drugs) can be developed for many health problems. This phytochemical approach of plant discovery emphasizes the development of pure phytochemicals as drugs. The method is expensive and much time consuming [3]. In phytotherapeutic approach, a fraction of an active extract or mixture of such fractions may prove better therapeutically, less toxic and inexpensive compared to pure isolated compounds. However crude plant preparations require modern standards of safety and efficacy.

Ganoderma lucidum (Curtis) P. Karst

Family Ganodermataceae

Common Names

United States : Reishi mushroom (*Herbs of Commerce*), ganoderma.
China : Ling zhi, ling zhi cao, ling chih, hong ling zhi, chi zhi
Japan : Reishi, mannentake; rokkakureishi (antler form).
Korea : Young ji

Vietnam : Ling chi

Taxonomical Classification

Kingdom : Fungi

Phylum : Basidiomycota

Class : Agaricomycetes

Order : Polyporales

Family : Ganodermataceae

Genus : *Ganoderma*

Species : *G. lucidum*

Numerous legends surrounding reishi mushroom provide an historical record which spans 2000 years. Traditionally, it was used in China by Taoist monks to promote a centered calmness, improve meditative practices, and attain a long and healthy life. Reishi mushroom has also been revered in Japanese culture where it is considered to be the most important of all the Japanese medicinal polypores [sarunokoshikake] [4]. The characters making up the Chinese name for reishi mushroom [ling zhi] originally depicted a “shaman crying for rain”, represent the magical or divine properties which were associated with ling zhi. Reishi mushroom has also been commonly referred to as the “mushroom of immortality”, “ten-thousand-year mushroom”, “mushroom of spiritual potency”, and “spirit plant” [5, 6]. Reishi mushroom was listed among the superior tonics [Shang pin] in the most famous of all Chinese material medicas, the *Shen Nung Ben Cao Jing* (206 BC-AD 8) [4,7]. Superior herbs were among the most highly regarded of all medicines since they were considered to prolong life, prevent aging, boost qi, make the body light and limber, and corresponded to heavy heaven. Reishi mushroom was listed as the most respected out of the 120 superior tonics cited. Specifically, in this text, red reishi was reported to treat binding in the chest, tonify the heart, nourish the center, sharpen the wit, and improve memory. In addition to its physical properties, reishi was said to “cultivate virtue” [8,9].

Work Done on the Phytochemical Profile

Lalitha Kumari and Sirsi [10] partially purified the enzyme laccase from the culture fluid of *Ganoderma lucidum* by acetone precipitation,

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ammonium sulphate fractionation and adsorption on alumina Cy gel [10]. Kawagishi et al. [11] isolated a lectin (GLL-M) from mycelia of *G. lucidum* using affinity chromatography on BSM-Toy pearl [11]. Ko et al. [12] purified and characterized laccase isozymes from *G. lucidum* through anion exchange chromatography, preparative gel electrophoresis, and electroelution [12]. Bao et al. [13] studied the structural features of immunologically active polysaccharides from *G. lucidum* [13]. Guan et al. [14] carried out the structure elucidation and complete NMR spectral assignments of three new lanostanoid triterpenes with unprecedented $\delta 16$, 17 double bond from *G. lucidum* [14]. Di et al. [15] carried out the fingerprint profiling of acid hydrolyzates of polysaccharides extracted from the fruiting bodies and spores of Lingzhi by high-performance thin-layer chromatography [15]. Gao et al. [16] carried out the quantitative determination of bitter principles in specimens of *G. lucidum* using High-Performance Liquid Chromatography and discussed its application to the evaluation of Ganoderma products [16]. Lim et al. [17] isolated a new inhibitor for peptidylprolyl-cis-trans isomerase (PPIase) from *G. lucidum* and purified to homogeneous state by organic solvent extraction. They also purified and characterized a new Cyclophilin Inhibitor from *G. lucidum* [17]. Mdachi et al. [18] identified sixteen known amino acids in *G. lucidum* [18]. Yan et al. [19] used the hybrid organic-inorganic monolithic column to separate triterpenoids from *G. lucidum* by capillary electro-chromatography [19]. Chen et al. [20] isolated Reishi polysaccharides for the study of their effect on cytokine expression in mouse splenocytes [20]. The conditions of polysaccharide production by *G. lucidum* were optimized by Babitskaya et al. [21]. Tang et al. [22] established that Ganoderic acid T from *G. lucidum* mycelia induces mitochondria mediated apoptosis in lung cancer cells [22]. Liu et al. [23] studied the structure-activity relationship for inhibition of 5 α -reductase by triterpenoids isolated from *G. lucidum* [23]. Paterson (2006) [24] reviewed the phytochemical profile of Ganoderma and considered it to be a therapeutic fungal biofactory [24]. Wang and Ng (2006) [25] isolated Ganodermin, an antifungal protein from the fruiting bodies of *G. lucidum* [25]. Zhang et al. [26] developed a novel on-line system combining supercritical fluid extraction (SFE) and two dimensional high performance liquid chromatography (2D-HPLC) for the analysis of fruiting bodies of *G. lucidum*, and at least 73 components in the extract were resolved with calculated peak capacity of up to 1643 [26]. Wang et al. [27] developed a reversed-phase liquid chromatographic method for the quantitative determination of six triterpenoids, namely ganoderic acids C2, B, AM1, K, H and D in *G. lucidum* and its related species [27]. Tang et al. [28] carried out the separation of targeted ganoderic acids from *G. lucidum* by reversed phase liquid chromatography with ultraviolet and mass spectrometry detections [28]. Thakur et al. [29] purified and characterized a novel 114 kDa hexameric lectin from the fruiting bodies of *G. lucidum* [29]. Wang et al. [30] carried out the HPLC determination of four triterpenoids in rat urine after oral administration of total triterpenoids from *G. lucidum* [30]. Gao et al. [31] developed a high-performance liquid chromatography-diode array detector-mass spectrometry (HPLC-DAD-MS) analytical method for detection of the nucleosides and nucleobases in *G. lucidum* [31]. Ye et al. [32] carried out the structural elucidation of the polysaccharide moiety of a glycopeptides (GLPCW-II) from *G. lucidum* fruiting bodies [32].

Work Done on the Pharmacological Profile

Eo et al. [33] studied the antiherpetic activities of various protein bound polysaccharides isolated from *G. lucidum* [33]. Zhu et al. [34] studied the antioxidant activity of triterpenes from *G. lucidum* [34]. Gao et al. [35] studied the mechanism of the antiulcerogenic effect

of *G. lucidum* polysaccharides on indomethacin-induced lesions in the rat [35]. Song et al. [36] assessed anti-angiogenic activity of *G. lucidum* and its inhibitory activity on inducible nitric oxide production in RAW 264.7 macrophages [36]. Lu et al. [37] established the fact that *G. lucidum* extracts inhibit growth and induce actin polymerization in bladder cancer cells *in vitro* [37]. Chien et al. [38] found that polysaccharides of *G. lucidum* alter cell immunophenotypic expression and enhance CD56+ NK-cell cytotoxicity in cord blood [38]. Liu et al. [39] have proposed a possible mode of action of antiherpetic activities of a proteoglycan isolated from the mycelia of *G. lucidum* *in vitro* [39]. Liu et al. [40] studied the anti-androgen effect of ganoderol B isolated from the fruiting body of *G. lucidum* [40]. Fujita et al. [41] established the anti-androgenic activities of methanol extracts of *G. lucidum* by performing the 5 α -reductase inhibitory activity [41]. Johnston [42] established the mechanism of action of *G. lucidum* against prostate cancer cells and found out that mushroom cuts off the blood supply to the prostate cancer cells [42]. Muller et al. [43] found out that *G. lucidum* causes apoptosis in leukemia, lymphoma and multiple myeloma cells. In this study, *G. lucidum* extract was screened for its anti-proliferative activity using a panel of 26 human cancer cell lines [43]. Lakshmi et al. [44] studied the antimutagenic activity of methanolic extract of *G. lucidum* and its effect on hepatic damage caused by benzo [a] pyrene [44]. Silva [45] published a guest editorial in Leukemia research emphasizing the importance of *G. lucidum* in cancer research [45]. Cao and Lin [46] established that *G. lucidum* polysaccharides peptide inhibits the growth of vascular endothelial cell and the induction of VEGF in human lung cancer cell [46]. Zhu and Lin [47] showed that *G. lucidum* polysaccharides (GI-PS) have a variety of immune modulating effects. These polysaccharides can modulate of cytokine production, granzyme B and perforin in murine CIK cells [47]. Liu et al. [48] found out that the triterpenoids fraction of *G. lucidum* might be a useful ingredient in the treatment of benign prostatic hyperplasia [48]. Zhu et al. [49] found out that *G. lucidum* polysaccharides enhance the function of immunological effector cells in immunosuppressed mice [49]. Li et al. [50] indicated that *G. lucidum* polysaccharides have potent antioxidant properties *in vitro* in mitochondrial membranes of rat liver [50]. Ko et al. [51] explored the anti-inflammatory activity of triterpenoids and steroids from *G. lucidum* [51]. Ganoderma possesses the following pharmacological properties according to an overview of the American Herbal Pharmacopoeia (2006) [9].

Analgesic; anti-inflammatory; antitumor; antiviral; hepatoprotective; hypoglycemic; hypocholesterolemic; hypotensive (ACE inhibitor); immune-modulating; increases IL-1- β , IL-2, and IL-6, increases cytotoxicity of T lymphocytes, increases TNF- α in macrophage cultures; inhibits platelet aggregation [9].

Clinical Trials

Ganoderma lucidum is reported to inhibit platelet aggregation [52, 53]; in immunologically compromised subjects, increases T lymphocyte and T helper cells and decreases T suppressor cells; improves immunocompetency after chemo- and/or radiation therapies [54]. Clinical information about the hepatoprotective action of reishi was reported in one small uncontrolled trial. Four patients with hepatitis B and elevated bilirubin and SGPT/SGOT levels were given 6 g of a reishi extract (concentration undefined) for 3 months. After 1 month, bilirubin, SGPT, and SGOT levels were significantly reduced ($P < 0.01$); after 90 days all values returned to within normal ranges [55]. Noguchi et al. [56] conducted a phase I clinical trial to evaluate the safety and efficacy of the extract of *G. lucidum* in men with mild symptoms of bladder outlet obstruction (BOO) [56].

Work Undertaken by Our Group

We carried out phytochemical and pharmacological investigations on *G. lucidum* for testing its anti-androgenic activity. We demonstrated the basis for the future use of *Ganoderma* in therapy by measuring the weekly urine output, testosterone levels and prostatic specific antigen levels using testosterone induced hyperplasia model in rats. Petroleum ether extract which remained untouched in the previous studies was included in the study and it came out to be the best inhibitor of prostatic hyperplasia induced by testosterone. Histological studies on the prostate sections also confirmed our findings [57]. It was also found to be a potent 5 α -reductase inhibitor on the basis of our studies which is indicative of the mechanism of its action against benign prostatic hyperplasia [57, 58]. β -sitosterol was identified in the *Ganoderma* extracts using TLC and HPTLC studies [57]. As β -sitosterol is a well-known molecule established clinically for the treatment of benign prostatic hyperplasia [59], the presence of β -sitosterol as a major constituent in the extracts further support our observations [57]. Certain studies on the in vitro cytotoxicity activity were also performed using *G. lucidum* extracts in human cancer cell lines [60].

Pharmacological Activity and Uses

It is considered to be a natural medicine that promotes longevity and maintains the vitality of human beings. Its beneficial clinical effects in patients with hepatitis, hyperglycemia, chronic bronchitis, cancer, muscular dystrophy, arteriosclerosis, hypertension, hypercholesterolemia, and leukopenia have been confirmed in pharmacologic studies in recent years. The fruiting bodies, mycelia, and spores have recently received more and more attention not only as home remedies but also as new drug sources [61].

Conclusion

Ganoderma lucidum has been widely researched and hence it has been a part of many publications as it is already evident from the literature cited above. Actually this literature constituted a part of literature survey carried by me during my studies on *G. lucidum* and I still find the compilation of these data worth sharable with the readers and various researchers. On the basis of many such evidences, there are many products in the market which are sold primarily as nutraceuticals. 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.

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