

## *Ganoderma lucidum* (Reishi): source of pharmacologically active compounds

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Traditional medicine has been gradually gaining attention amongst medical practitioners<sup>1</sup>. Plants have been a source of chemicals which act as drugs. Mushrooms have been considered as medicinal agents since long in Asian countries, but their use in the Western world has been slightly increasing only since the last few years<sup>2</sup>. *Ganoderma lucidum* (a wood-decomposing fungi), belonging to the family Ganodermaceae, is also a traditional Chinese medicine which has been used for centuries in East Asia to treat various diseases, such as immunological disorders, inflammatory conditions and cancer<sup>3,4</sup>. Commonly known as reishi mushroom (herb of commerce), it is also known as the herb of immortality, lingzhi, ganoderma, young ji, etc.<sup>5</sup>.

Reishi mushroom contains a number of bioactive compounds<sup>6</sup>. These include specific polysaccharides like triterpenes (ganoderic acids), glycoproteins, sterols, coumarin, phenols, nucleotides, peptides, fatty acids, trace elements and mannitol<sup>7</sup>. They also contain volatile oils, tocopherols, phenolics compounds, carotenoids, folates, ascorbic acids, enzymes and organic acids. Triterpenes and polysaccharides are the major physiologically active components of *G. lucidum*<sup>8</sup>.

*G. lucidum* is considered as the most beneficial herb among 120 superior tonics mentioned in China<sup>5</sup>. It is frequently consumed throughout the world as tea, powder and dietary supplement. Fruiting body or cap is generally used to prepare these products<sup>9</sup>.

### Pharmacological properties based on active compounds

#### Triterpenes

Triterpene being a subtype of terpenes, is a potential active compound of reishi mushroom. It has potent anti-inflammatory, anti-tumorigenic and hypolipidemic properties<sup>10</sup>. Triterpenes from reishi may cause apoptosis of multiple human cancer cell lines. Ganoderic acid is an important triterpene which has shown inhibitory properties on cancer

cells both *in vitro* and *in vivo*<sup>11</sup>. Triterpenes are known for antioxidative properties. Smina *et al.*<sup>12</sup> showed that triterpenes extracted from *G. lucidum* have antioxidative properties *in vitro* and can reduce oxidative damage by directly scavenging free radicals generated in the cell. It has been shown that administration of triterpenes in mice increased the activity of antioxidant enzymes, and reduced radiation-induced oxidative DNA damage in mice splenocytes. According to Ko *et al.*<sup>13</sup>, triterpenes from *G. lucidum* showed potent anti-inflammatory properties in human keratinocytes. It was found that reishi extract inhibited the inflammatory damage in carrageenan-induced inflammation in experimental animals<sup>14</sup>. This suggests that it can be used against arthritis also.

#### Polysaccharides

Various polysaccharides with molecular weights ranging from  $4 \times 10^5$  to  $1 \times 10^6$  Da have been identified from

reishi<sup>15</sup>. Glucose, xylose, mannose, galactose and fructose are the chief constituents among the polysaccharides. These show antitumour properties by improving host immune response and inducing cytotoxic pathways<sup>16,17</sup>. Polysaccharides can also act as antioxidants by oxidative damage induced by ROS and preventing DNA strand breaks.

Ganopoly (a polysaccharide from *G. lucidum*) enhanced the immune responses in patients with advanced stage cancer<sup>18</sup>. Polysaccharides of *G. lucidum* (M.A. Curtis: Fr.) P. Karst accelerated wound healing in streptozotocin-induced diabetic rats<sup>19</sup>.

#### Phenolic compounds

Phenolic compounds possess established antioxidative ability and their antiradical mechanism has almost been completely revealed. These possess strong antioxidant properties that enable them to scavenge free radicals, donate hydrogen, chelate metal ions, break radical chain



**Figure 1.** *Ganoderma lucidum* growing horizontally on wood log.

reactions, and quench singlet oxygen *in vitro* and *in vivo*<sup>20</sup>. According to Hasnat *et al.*<sup>21</sup>, *G. lucidum* grown on brown rice displayed potential antioxidant activity. Polysaccharides are the best recognized and most effective mushroom-derived substances with anti-cancerous and immunostimulatory properties.  $\beta$ -Glucan (polysaccharide) is the most versatile metabolite because of its broad-spectrum biotherapeutic activities. It contains a backbone of glucose residues linked by  $\beta$ -(1  $\rightarrow$  3)-glycosidic bonds, often with attached side-chain glucose residues joined by  $\beta$ -(1  $\rightarrow$  6) linkages<sup>22</sup>.

The scavenging of free radicals is the principle mechanism involved in controlling many pathological conditions like ageing, cancer, Alzheimer's disease, heart diseases, neurodegenerative disorders, atherosclerosis, cataracts and inflammation<sup>23</sup>. Phenolic compounds showed antimicrobial properties when used against *Escherichia coli*, *Pseudomonas aeruginosa*, *Staphylococcus aureus* and *Klebsiella pneumoniae*<sup>24</sup>.

### Sterols

Sterols are useful for maintaining the proper structure and function of all the eukaryotic cells. Ergosterol is usually found in fungi. Six sterols obtained from the fruiting body of *G. lucidum* possessed antiviral property against Epstein bar virus early antigen<sup>25</sup>. Ergosterol and its analogues contained in *Ganoderma* had multiple pharmacological effects such as anti-HIV-1 (ref. 26), anti-complement<sup>27</sup>, anti-ageing activities<sup>28</sup>, and protecting cerebral cortical neurons from hypoxia/re-oxygenation injury. Ganoderterone has been isolated as a steroid which plays a role as antihepatotoxic. A sterol derivative of *Ganoderma* may help inhibit cholesterol synthesis.

### Proteins, peptides and amino acids

Proteins are known to possess strong antioxidant properties. Animal and plant proteins can be used to prepare biologically active peptides to act as an antioxidant. Protein can inhibit the oxidative reaction by changing the physical location of transition metals forming insoluble metal complexes. Similarly, peptides have potential antioxidative properties. Bioactive proteins have been isolated

from *G. lucidum*. Ling Zhi-8 (LZ-8) was isolated from the mycelia of *G. lucidum*<sup>29</sup>. This protein has potent mitogenic properties. A variety of amino acids have been isolated from *G. lucidum*. Sun *et al.*<sup>30</sup> reported antioxidative nature of peptides which can be used against cancer, ageing and atherosclerosis. Polysaccharide-peptide complex from *G. lucidum* is effective as an antioxidant<sup>31</sup>. A 15 kDa protein, Ganodermin was isolated from *G. lucidum*. It has antifungal properties against *Botrytis cinerea*, *Fusarium oxysporum* and *Physalospora piricola*<sup>32</sup>.

### Other bioactive compounds

Alkaloids, vitamins, essential minerals, flavours and fatty acids are also found in *G. lucidum*<sup>32</sup>. Fatty acids isolated from *G. lucidum* are shown to inhibit histamine. These can be used in inflammatory diseases, allergies and anaphylactic shocks<sup>33</sup>. Zhang *et al.*<sup>34</sup> analysed the vitamin content in the spores of *Ganoderma* using high performance liquid chromatography. The result indicated the presence of vitamins C and E as well as  $\beta$ -carotene. Alkaloids, choline and betaine were isolated from the spores of *G. lucidum*. Alkaloids stimulate the central nervous system, act as antimicrobial, sympathomimetic, vasodilator, antihypertensive, antipyretic and anti-malarials. In a recent study, Islam *et al.*<sup>35</sup> isolated 11 bioactive chemicals from *G. lucidum*. Among these, polyphenols, flavonoids, tannins, coumarins, vitamin-C, and anthocyanin were found in highest concentration. Ash of *G. lucidum* contains calcium, potassium, sodium, iron, manganese, zinc, phosphorus, magnesium and copper. Presence of these elements in *G. lucidum* suggests that it can be used as feed supplement<sup>36</sup>.

*G. lucidum* has been widely used in many pharmacological studies. Its use in combination with other nutraceuticals may be a new area of research. It is considered to be a natural medicine that promotes longevity and maintains vitality in human beings. Its beneficial clinical effects in patients with hepatitis, hyperglycemia, chronic bronchitis, cancer, muscular dystrophy, arteriosclerosis, hypertension, hypercholesterolemia and leukopenia have been documented by many researchers. *G. lucidum* represents a growing segment of today's pharmaceutical industry. More pharmacological

studies are warranted to explore the unknown bioactive compounds and associated pharmacological properties of *G. lucidum*.

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