

## REVIEW ARTICLE

### *Ganoderma lucidum* (Curt.: Fr.) Karst. – health-promoting properties.

#### A review

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#### Summary

This paper presents the characteristics of the species *Ganoderma lucidum* in terms of health-promoting properties. This species is rare in Poland, and is subject to strict protection. Reishi is classified as a medicinal mushroom which fruiting bodies are characterized by a content of active substances with diverse positive effects on human health. *G. lucidum* is particularly rich source of bioactive compounds, which are obtained from fruiting bodies, mycelium and spores of this species. The therapeutic effect of *G. lucidum* extracts has been demonstrated in many scientific studies. The most important pharmacological and physiological effects include: immunomodulatory, anti-cancer, anti-inflammatory, antiviral, anti-atherosclerosis, antidiabetic and anti-aging. Reishi has also a beneficial effect on liver cells and the cardiovascular system

and protects in case of stomach ulcers. Due to its properties *G. lucidum* can be used in the prevention and treatment of life-threatening diseases, such as cancer, stroke and heart diseases.

**Key words:** *Reishi, medicinal mushrooms, bioactive compounds, polysaccharides, triterpenoids*

## INTRODUCTION

Medicinal properties of mushrooms have been known and used for centuries. In the Far East, where herbal medicine and other natural methods have been applied in the treatment of many diseases, fungi traditionally have been also included in therapy. In Orient, mainly two species have been used: *Ganoderma lucidum* and *Lentinula edodes*. Folk medicine in Eastern Europe was based on four mushroom species: *Inonotus obliquus*, *Fomitopsis officinalis*, *Piptoporus betulinus* and *Fomes fomentarius*. These species were used in gastrointestinal disorders, as well as various cancers, asthma and night sweats. Medicinal use of mushroom also has a long history in Central America and Africa. Health-promoting potential of mushrooms has increased when fruitbodies started to be collected not only from the natural environment, but also from large-scale production cultures [1].

At present, approximately 270 species of fungi are known to possess various therapeutic properties. The most important species include the previously mentioned Reishi *Ganoderma lucidum* and Shiitake mushroom *Lentinula edodes*, as well as Maitake mushroom *Grifola frondosa*, almond mushroom *Agaricus brasiliensis*, Turkey tail mushroom *Coriolus versicolor* and caterpillar fungus *Cordyceps sinensis*. Contemporary research on medicinal fungi was initiated in the 1960's in Japan, China and Korea. A little later, also Western researchers started such studies, particularly in the USA. These studies verified earlier knowledge on the potential therapeutic use of mushrooms [2]. According to the latest studies, mushrooms owe their health-promoting action to the contents of biologically active compounds, such as polysaccharides, triterpenoids, specific proteins, phenolic compounds, vitamins and minerals [3]. A beneficial health effect results from the interaction of all active components of mushrooms.

Fruitbodies of medicinal mushrooms constitute raw materials for the production of dietary supplements, particularly in Far East. Several hundred preparations are commercially available in the form of tablets, capsules or teas, which are used mainly to boost the immune system [4]. The market offer includes also preparations containing extracts from one or several different species of fungi [5]. At present, conventional medicine in many countries, e.g. Japan, China, Korea and Russia, allows for the use of fungal preparations in treatment of many diseases, e.g. in cancer therapy in combination with chemo- or radiotherapy [1].

*Ganoderma lucidum* (Reishi) is the best known representative of medicinal mushrooms in the world. The aim of the study is to characterize the therapeutic value of the species with focus on bioactive substances determining its health-promoting properties. The paper is based on research results published in scientific works in last two decades.

### *Ganoderma lucidum* – characteristics of the species

According to Index Fungorum, the current taxonomy of *Ganoderma lucidum* (Curt.: Fr.) Karst. is presented as follows: kingdom Fungi, phylum Basidiomycota, subphylum Agaricomycotina, class Agaricomycetes, order Polyporales, family Ganodermataceae [6]. This species is referred in literature using following synonyms: *Boletus lucidus* (Fr.), *Polyporus lucidus* Curt. (Fr.), *Polyporus polychromus* Curt. (Fr.), *Ganoderma polychromum* Curt. (Fr.), *Ganoderma sessile* Curt. (Fr.), *Fomes lucidus* (Curt.:Fr.) Sacc. Japanese names of this species are Reishi, Mannentake, Mannen Dake and Sachi Dake. In Korea Reishi is known as Youngzi, while in China it is named Ling Zhi, Ling Chi, Ling Chih and Ling Qi. Due to its rare occurrence in natural sites, it is also called the “supernatural mushroom” [7]. In Asian countries, this species is considered to be a symbol of good health and immortality, referred as “the magic mushroom, which enhances the spirit” or “the mushroom of spiritual potency”. In Far East, it is also used as a talisman protecting people and homes against evil.

Reishi is found on living and dead wood of deciduous species. It is a saprophyte or facultative parasite. In the wild, it grows in the subtropical and temperate climate zones, in the forests of Asia, USA, Europe and South America. In North America, it is found mainly on the East Coast and in the South-West [8]. In Far East, it grows most often on dead trees of Japanese plum *Prunus salicina*. In Europe, the mushroom is found in Summer and Autumn on different species of deciduous trees. In Poland, Reishi is rare in nature, e.g. in the Świętokrzyskie Mountains. It grows mainly on oaks and alders, less often on other deciduous species and only occasionally on softwood, e.g. spruce. It causes white rot of wood [9]. In Poland, the mushroom is a strictly protected species.

Reishi produces fruitbodies with a cap diameter ranging from 30 to 250 mm. The cap is flat, rounded or kidney-shaped, shiny, red, cherry-red, reddish-brown or reddish-black in colour, offset on the stipe. Young fruitbodies are yellow-brown, yellow-red and with age they take on darker colours. The cap surface is irregularly knobby, with concentric serration and the cap margin is typically lighter in colour. The stipe is shiny, irregularly twisted, of 50-120 x 10-20 mm in size, assumes the same colour as the cap or darker. The hymenophore is trimitic, spongy or corky, powdery, of whitish, beige or brown colour. Spores of Reishi are ellipsoid or oval, composed of two covering layers: external, colourless, smooth, and internal yellowish-brown, lumpy, ranging in size from 6 to 11  $\mu\text{m}$  [10].

## ***Ganoderma lucidum* as a source of active substances**

*Ganoderma lucidum* is a particularly valuable source of biologically active substances [11]. According to the latest study by Grienke *et al.* [12], so far 279 bioactive secondary metabolites have been isolated from Reishi. Polysaccharides (*Ganoderma lucidum* polysaccharides – GLP) are considered to be the main group of active compounds in Reishi, determining its health-promoting properties. Polysaccharides found in Reishi account for 10–50% of dry matter of fruitbodies [13]. Polysaccharides exhibit the capacity to boost the immune system and act as anticarcinogens [14, 15]. To date, over 200 different polysaccharides have been isolated from fruitbodies, spores, and mycelia or from liquid cultures of Reishi [1]. They include e.g.  $\beta$ -D-glucans,  $\alpha$ -D-glucans,  $\alpha$ -D-mannans and polysaccharide-protein complexes. Biological activity of glucans is determined by their water solubility, molecular size, branching and form. The effectiveness of  $\beta$ -glucans is also influenced by the number of lateral branches in the main chain, the length of the lateral chain and the ratio of the number of bonds (1.4) to (1.6) and (1.3) [2]. According to latest studies,  $\alpha$ -D-glucans found in the cell walls of Reishi exhibit a cytotoxic action in relation to HeLa cancer cells [16]. Zhu *et al.* [17] showed the capacity to boost the immune system by low-molecular-weight polysaccharides contained in the water extract from fruitbodies of *G. lucidum*.

Chen *et al.* [18] showed the antioxidant activity of polysaccharides isolated from fruitbodies of Reishi. It was also found that H-GLP obtained by structural modification of slightly water-soluble polysaccharides (GLP), showed a stronger antioxidative effect than the original polysaccharides [19]. Meng *et al.* [20] reported the effectiveness of application of polysaccharides from *G. lucidum* in the prevention of cardiac complications in diabetics. Pillai *et al.* [21] showed that polysaccharides from Reishi exhibit a strong protective effect against damage caused by gamma radiation. Kozarski *et al.* [22] confirmed the immunomodulatory effect of polysaccharides extracted from *G. lucidum* spores. Yamin *et al.* [23] showed that polysaccharides isolated from Reishi (GLCP) and the PF-2 fraction are prebiotics stimulating growth of probiotic *Bifidobacterium* spp. The most important bioactive polysaccharides isolated from *G. lucidum* are given in table 1 [24].

Triterpenoids found in Reishi, which contain the carboxyl group, are called generally ganoderic acids. These compounds are characterised by a complex structure, high lipophilicity and molecular mass ranging from 450 to 650 kDa. In terms of their chemical structure, they are highly oxidized derivatives of lanostane [25]. These triterpenoids may contain 30, 27 or 24 carbon atoms in the molecule. To date, over 150 ganoderic acid derivatives and other triterpenoids have been isolated from *G. lucidum* and other fungi from the *Ganoderma* genus [26]. They include ergosterol and its derivatives as well as lanostane derivatives, such as ganoderic acids (A, AM1, B, C1, C2, D, DM, F, G, H, K, Me, Mk, S, T, TR, Y), ganoderenic

acids (A, B, D), ganoderols (A, B), ganoderiol F, ganoderatriol, ganoderal A, Me ganoderate D, ganoderate G, and lucideric acid A [27]. Characteristics of selected terpenoids are presented in table 2 [28].

Table 1.

Bioactive polysaccharides isolated from *Ganoderma lucidum* [24-adapted]

Polysaccharide	Molecular weight	Source	
		Fruiting body	Spores
SP	1.0 x 10 <sup>4</sup>		+
PL-1	8.3 x 10 <sup>3</sup>	+	
PL-3	6.3 x 10 <sup>4</sup>	+	
PL-4	2.0 x 10 <sup>5</sup>	+	
PSGL-I-1A	7.18 x 10 <sup>5</sup>		+
Ganoderan A	2.3 x 10 <sup>4</sup>	+	
Ganoderan B	7.4 x 10 <sup>3</sup>	+	
Ganoderan C	5.8 x 10 <sup>3</sup>	+	
GL-1	4.0 x 10 <sup>4</sup>	+	

Table 2.

Triterpenoids content in *Ganoderma lucidum* extract [28 – adapted]

Ganoderic acids	Structure
Ganoderic acid E	C <sub>37</sub> H <sub>36</sub> O <sub>7</sub>
Ganoderic acid C6	C <sub>30</sub> H <sub>42</sub> O <sub>8</sub>
Ganoderic acid G	C <sub>30</sub> H <sub>44</sub> O <sub>8</sub>
Ganoderic acid A	C <sub>30</sub> H <sub>44</sub> O <sub>7</sub>
Ganoderic acid C2	C <sub>30</sub> H <sub>46</sub> O <sub>7</sub>
Ganoderic acid D	C <sub>30</sub> H <sub>40</sub> O <sub>7</sub>
Ganoderic acid B	C <sub>30</sub> H <sub>44</sub> O <sub>7</sub>
Ganoderic acid H	C <sub>32</sub> H <sub>44</sub> O <sub>9</sub>
Ganoderic acid F	C <sub>32</sub> H <sub>42</sub> O <sub>9</sub>
Ganoderic acid J	C <sub>30</sub> H <sub>42</sub> O <sub>7</sub>
Ganodermanontriol	C <sub>30</sub> H <sub>48</sub> O <sub>4</sub>

Triterpenoids have a hepatoprotective effect and reduce blood pressure and cholesterol level in blood. They exhibit antihistamine, anticancer and anti-HIV effects [29]. They also inhibit angiogenesis and platelet aggregation [30]. Ganoderic acids also exhibit antiandrogenic [31], anti-inflammatory and anticancer effects [32]. Liu *et al.* [27] showed a cytotoxic action of ganoderic acids in relation to androgen-dependent prostate cancer and estrogen-dependent breast cancer cells. Triterpenoids have a positive effect on cognitive functions and memory [33].

Proteins of therapeutic effects were also isolated from *G. lucidum*. Mycelium of this species contains the LZ-8 protein, a polypeptide with a molecular mass of 12 kDa, composed of 110 amino acids. LZ-8 exhibits an immunomodulatory action and mitogenic activity [34]. Ganodermin, a protein of 15 kDa exhibiting antifungal effects, was isolated from fruitbodies of Reishi [35]. A considerable health-promoting role is also ascribed to substances formed as complexes of proteins and polysaccharides. Reishi is a source of ganoderan, which is a proteoglycan containing (1→3)- $\beta$ -glucans and 4% protein [36]. Ganoderan was found to have anticancer properties [37].

Reishi contains also nucleosides, e.g. adenosine, cystidine, guanosine, inosine, thymidine, uridine and nucleotides, including adenine, guanine, hypoxanthine, thymine and uracil [38]. Adenosine and its derivatives may inhibit platelet aggregation [39]. Fruitbodies and spores of Reishi contain sterols, e.g. ergosterol (provitamin D<sub>2</sub>) and ergosterol peroxide, which inhibits the growth of breast cancer cells [40, 41]. Among minerals contained in fruitbodies of Reishi particularly selenium and germanium are worth mentioning, which enhance the anticancer effect.

At present, therapeutic substances are collected from fruitbodies of *G. lucidum* coming from commercial cultures and from so-called submerged cultures. They constitute raw material for the production of therapeutic preparations in the form of extracts, powdered fruitbodies or teas. Preparations presently available on the market are dietary supplements. They are used mainly to stimulate the immune system and act as tonics. They are highly valued not only in traditional Chinese medicine, but also in conventional medicine. At present, the use of *G. lucidum* is admissible in the treatment of different diseases, e.g. cancers, when it is recommended to take Reishi during chemo- or radiotherapy.

## HEALTH-PROMOTING PROPERTIES OF REISHI

The tradition of therapeutic use of *G. lucidum* dates back to 4000 years. Reports on health effects of this species were found in “Compendium of Materia Medica” in 16<sup>th</sup> century (the Ming Dynasty). Currently, *G. lucidum* is included in the Pharmacopoeia of the People’s Republic of China [42]. Reishi is approved for the treatment of dizziness, insomnia, palpitation, shortness of breath, cough and asthma. Reishi is also present in the American Herbal Pharmacopoeia, where this mushroom is regulated as a dietary supplement [43].

At present, Reishi is the best known species of medicinal fungi in the world. In last decades, numerous *in vitro* and animal studies have been conducted, which confirmed the multifaceted health-promoting effect of *G. lucidum*. The most important effects of Reishi include immunomodulatory, anticancer, anti-inflammatory, antibacterial, antiviral, antiatherogenic, anti-diabetic, anti-ageing and hepatoprotective effects [44]. Reishi also has a beneficial effect on the cardiovascular system and exhibits a protective effect in gastric ulcers [45]. Medicinal value of *G. lucidum* is given below and summarized in table 3.

Table 3.

Medicinal value of *Ganoderma lucidum*

Bioactive compounds	Activity	Treatment
Polysaccharides	immunomodulatory	cancers
	anticancer	breast and ovarian cancers, leukemia
	anti-viral	hepatitis B
	cholesterol and triglycerides lowering	hyperlipidemia
	antioxidant	anti-aging
	blood glucose lowering	diabetes
Triterpenoids	anti-platelet aggregation	vascular diseases, stroke, thrombosis
	cytotoxic	prostate and breast cancers
	hepatoprotective	hepatic tissue damage, chronic hepatitis B
	antihistamine	allergies
	cholesterol and triglyceride lowering	hyperlipidemia
	blood pressure reduction	hypertension
	antiviral	HIV and Epstein-Barr virus infections, influenza
	anti-inflammatory	inflammatory diseases
LZ-8 Protein	memory improvement	dementia
Adenosine	immunomodulatory	cancers
	anti-platelet aggregation	vascular diseases
Sterols	anticancer	breast cancer

## Immunomodulatory effect

*G. lucidum* contains several substances with a potential immunomodulatory action, e.g.  $\beta$ -D-glucans, the Zhi-8 proteins and triterpenoids. First of all, the action of these substances consists of the stimulation of the activity of immune system cells such as macrophages, natural killer (NK) cells and T lymphocytes. *In vitro* tests showed that water extract from *G. lucidum* stimulates the production of such cytokines as interleukins IL-2, IL-10, IL-1 $\beta$  IL-6, the tumour necrosis factor (TNF- $\alpha$ ) and interferon [46]. It was found that extract from Reishi spores influenced an increased the number of macrophages and NK cells in mice and inhibited the development of cancer [47]. Substances contained in Reishi inhibit also allergic reactions thanks to their effect on mast cells and B lymphocytes [48].

## Anticancer effects

Promising effects were observed when using *G. lucidum* extract against cancer cells. It was found that the administration of *G. lucidum* reduced the growth of K562 leukemia cells [49], MCF-7 breast cancer cells [40] and ovarian cancer [50].

The reduction of tumours in animal studies was caused by destruction of blood vessels and the resulting reduced blood supply to the tumour, necrosis induced by T lymphocytes and localised production of TNF- $\alpha$ . It was shown that the anticancer effect consisted also in the inhibition of DNA polymerase. The administration of oil from Reishi spores in mice enhanced immune response against cancer cells, increasing their proliferation and improving survival rates of animals [51]. It was found that the LZ-8 protein from Reishi inhibited proliferation and induced apoptosis of HL60 human leukemia cells [52].

### Antibiotic activity

Substances extracted from *G. lucidum* exhibit antibiotic properties. They inhibit the development of gram-positive and gram-negative bacteria [53]. Extract from Reishi inhibited also the development of *Helicobacter pylori*, the bacterium responsible for the formation of gastric ulcers and gastric cancer [54]. Several substances with antifungal action were also isolated from *G. lucidum* [46]. Ganodermin obtained from mycelium inhibited mycelial growth of *Botrytis cinerea*, *Fusarium oxysporum* and *Physalospora piricola* [33]. A study by Heleno *et al.* [55] showed antibacterial and antifungal properties of Reishi extract. The extract showed a higher activity against *S. aureus* and *B. cereus* than the antibiotics ampicillin and streptomycin. The extract antifungal activity against *Trichoderma viride* exceeded that of the standards, i.e. bifonazole and ketoconazole. In a study by Shah *et al.* [56], methanol extract of *G. lucidum* showed antimicrobial activity against such bacteria as *Bacillus cereus*, *Enterobacter aerogenes*, *Staphylococcus aureus*, *Escherichia coli* and *Pseudomonas aeruginosa*.

### Antiviral properties

Ganoderic acids isolated from fruitbodies of Reishi exhibit antiviral activity e.g. against HIV and Epstein-Barr virus [57]. Water soluble substances GLhw and GLlw, and methanol soluble GLMe-1-8 isolated from fruitbodies inhibited replication of influenza A virus. Polysaccharides showed a direct action towards hepatitis B virus (HBV) by inhibiting DNA polymerase. Ganodermediol exhibited activity against herpes simplex virus type 1 [58]. Water extract from *G. lucidum* inhibited proliferation of VPH transformed cells [59].

### Antidiabetic activity

Reishi induces an antidiabetic effect. Studies on animals showed that the polysaccharide fraction from *G. lucidum* (ganoderans B and D) showed a hypoglycemic



potential. Clinical studies involving patients with diabetes type II confirmed that extract from Reishi is effective in lowering blood glucose levels comparable to oral antidiabetic drugs and insulin [60]. Pre-clinical studies in rats showed that administration of a Reishi preparation protected against diabetic nephropathy [61].

### Hepatoprotective activity

*Ganoderma lucidum* protects liver cells. Extract from Reishi containing triterpenoids in studies on mice showed a hepatoprotective effect, resulting probably from an enhanced capacity to remove free radicals from this organ [62]. In clinical trials within 6 months, preparation from *G. lucidum* containing polysaccharides normalised levels of aminotransferases in patients with chronic hepatitis B [63].

### Cardiovascular system protection

Reishi has a positive effect on the cardiovascular system, which results e.g. from the capacity to reduce blood cholesterol and triglyceride levels and to normalise blood pressure. In clinical trials involving patients with primary stage of hypertension, normalisation of blood pressure was observed after 2 months of *G. lucidum* extract administration [64]. Other studies showed that extract from Reishi reduced blood lipid level and prevented the development of atherosclerosis in rats [65]. It was shown that compounds formed as polysaccharide and peptide complexes exhibited a protective action in relation to endothelial cells of blood vessels in humans [66].

### Anti-inflammatory activity

Animal studies showed an anti-inflammatory action of Reishi extract and its protective effect against colitis [67]. Gupta *et al.* [68] confirmed that aqueous lyophilized extract of *G. lucidum* possessed significant wound-healing activity.

### CONCLUSIONS

Reishi is regarded as a very promising pharmaceutical source due to the abundance of bioactive compounds. Substances of potentially health-promoting properties could be obtained from fruit bodies, mycelium, as well as from spores of the species. This fungus is traditionally used in Chinese medicine in chronic diseases. Recently, the interest of *Ganoderma* in West countries has been increasing

intensively. Dietary supplements containing Reishi are very popular therapeutic agents all over the world. Substances obtained from *Ganoderma* could potentially support the conventional medicine in the treatment of severe diseases, including cancer. This requires further clinical trials to confirm the efficacy and safety. It is expected that in the nearest future studies on this medicinal mushroom will be conducted on broad scale.

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## LAKOWNICA LŚNIĄCA *GANODERMA LUCIDUM* (CURT.: FR.) KARST. – WŁAŚCIWOŚCI PROZDROWOTNE. PRZEGLĄD

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### Streszczenie

Opracowanie przedstawia charakterystykę lakownicy lśniącej (*Ganoderma lucidum*) pod względem właściwości prozdrowotnych. Gatunek ten w Polsce występuje rzadko i jest objęty całkowitą ochroną. Lakownica lśniąca zaliczana jest do grzybów leczniczych, których owocniki charakteryzują się zawartością substancji aktywnych o wielokierunkowym pozytywnym wpływie na zdrowie człowieka. *G. lucidum* jest wyjątkowo bogatym źródłem związków bioaktywnych, które pozyskuje się z owocników, grzybni oraz zarodników tego gatunku. W wielu badaniach naukowych wykazano efekt leczniczy ekstraktów z lakowni-

cy lśniące. Do najważniejszych farmakologicznych i fizjologicznych oddziaływań należy zaliczyć: immunomodulujące, antynowotworowe, przeciwzapalne, przeciwbakteryjne, przeciwwirusowe, antymiażdżycowe, przeciwcukrzycowe oraz przeciwstarzeniowe. Lakownica lśniąca wywiera również korzystny wpływ na komórki wątroby oraz układ krążenia, a także działa ochronnie w przypadku wrzodów żołądka. Ze względu na wymienione właściwości, *G. lucidum* może być wykorzystana w profilaktyce i leczeniu zagrażających życiu chorób, takich jak nowotwory, udar mózgu oraz choroby serca.

**Słowa kluczowe:** *Reishi, grzyby lecznicze, substancje bioaktywne, polisacharydy, triterpenoidy*