

REISHI

Ganoderma lucidum (Curtis:Fr.) P. Karst

Family

Ganodermataceae.

The family Ganodermataceae describes polypore basidiomycetous fungi having a double-walled basidiospore (a reproductive spore produced by Basidiomycete fungi). In all, 219 species within the family have been assigned to the genus *Ganoderma*. Both *Ganoderma lucidum* and *Ganoderma japonicum* are officially accepted in the Chinese pharmacopoeia as reishi, the former producing red reishi (hong ling zhi) and the latter black reishi (he ling zhi).^{1,2}

Parts Used

Fruiting body.

Description

Reishi, an annual fungus, is a large (35cm broad), kidney-shaped dark mushroom with a glossy exterior and a woody texture. It is dark red to reddish-brown or black in the centre and ochre or yellowish towards the margin. The stalk, if present, can be up to 13cm long and four centimetres thick. Its growth form is highly variable with specimens from North America typically large and shelf-like while those from the tropics and Old World are usually smaller with cap and stalk; intermediate forms exist, including a rare antlered form highly prized medicinally in China and Japan. Strains high in triterpenes are characteristically intensely bitter. Reishi is found primarily on the base, roots or stumps of hardwoods, such as oak and maple, and rarely on conifers. It is collected after the fruiting body has fully matured.



In Traditional Chinese Medicine (TCM) the quality of the reishi mushroom is predominantly determined by colour, shape and size with the large, deep red mushrooms with a swirled ram's horn pattern generally considered to be the highest quality.³

Traditional Use

Reishi is an oriental fungus which has a long history of use, spanning 2000 years, for promoting health and longevity in China, Japan and other Asian countries. The Latin word *lucidus* means "shiny" or "brilliant" and refers to the varnished appearance of the surface of the mushroom. In Japan the name for the Ganodermataceae family is reishi, or mannentake, whereas in China it is called lingzhi. In Chinese, the name lingzhi represents a combination of spiritual potency and essence of immortality, and is regarded as the "herb of spiritual potency," symbolizing success, well-being, divine power and longevity. Reishi mushroom has also been commonly referred to as "the mushroom of immortality", "ten-thousand-year mushroom" and "spirit plant".

Reishi is classed as one of the great original adaptogen medicines. Its reputation has even surpassed ginseng as one of the most valuable herbs of the Orient. Wild reishi is rare, with only two to three mushrooms found for every 10,000 dead plum or hemlock logs, which might explain some of the mystical qualities attributed to this herb. In the years before it was cultivated only the nobility could afford it. It was believed that the sacred fungus grew in the home of the immortals on the "three aisles of the blest" off the coast of China. Traditionally it was used in China by Taoist monks to promote a centered calmness, improve meditative practices and attain a long and healthy life. Chinese royalty, seeking longevity, held reishi mushroom in high esteem. However, its reputation as a panacea may have been earned more by virtue of its irregular distribution, rarity and use by the rich and privileged members of Chinese society than by its actual effects. Nevertheless, the *Ganoderma* species continue to be a popular traditional medicine in Asia and their use is growing throughout the world.

Among cultivated mushrooms, reishi is unique in that its pharmaceutical rather than nutritional value is paramount. A variety of commercial reishi products are available in various forms, such as powders, dietary supplements and tea.

These are produced from different parts of the mushroom, including mycelia, spores and fruit body. The specific applications and attributed health benefits of reishi include supporting immune resistance in patients undergoing chemotherapy and/or radiation treatment for various forms of cancer, chronic hepatitis, nervousness, nephritis, insomnia, high blood pressure, high cholesterol, AIDS, diabetes, enhancing longevity and more. The various beliefs regarding the health benefits of reishi are based largely on anecdotal evidence, traditional use and cultural mores. However, recent reports provide scientific support to some of the ancient claims of the health benefits of reishi.

Reishi was documented as far back as 56BC in the Shen Nung Ben Cao Jing (the first book wholly devoted to the description of herbs and their medicinal value written in the Eastern Han dynasty of China (206 BC to AD 8)) where it was described as having extensive healing powers. Reishi was listed as the most respected out of 120 superior tonics (shang pin) cited. 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 heaven. Interestingly reishi was not often included in many common materia medicas throughout Chinese history, possibly due to its relative rarity or perhaps to it being reserved only for use by royalty. Similarly it is not included in many standard English language materia medicas.^{4,5,6,7}

In modern herbal therapies, reishi is applied in two primary ways: according to traditional principles of Chinese herbalism and incorporated into Western herbal therapies based on its pharmacological activities, irrespective of traditional Chinese diagnostic and therapeutic indications. In TCM the energetics are: bland, sweet or bitter depending on the cultivar, mild flavour with neutral to warm property. It's action is nourishing, supplementing, tonifying, removes toxins, disperses accumulation and stops tightness in the chest. Reishi is primarily used for its tonic properties In Western herbal therapies, especially its use as an immunomodulator. For this purpose, it is often used in conjunction with chemo and/or radiation therapies in the treatment of cancer as a means to help in the prevention of opportunistic infections and to counter side effects associated with conventional therapies.

Reishi is also integrated into many treatment protocols for those infected with HIV with the primary goal being to enhance immune resistance and prevent opportunistic infections. For both of these purposes reishi is most often combined with other similarly acting immune modulating botanicals such as astragalus (*Astragalus membranaceus*), schisandra (*Schisandra chinensis*) and other mushrooms and polypores. Reishi is additionally used as a general tonic for deficiency syndromes associated with tiredness and fatigue and, conversely, as a calmative for insomnia due to restlessness and an overactive mind. Occasionally reishi is used as a mild analgesic when pain is associated with stress and tension.⁸

Constituents

Immunostimulating polysaccharides, peptidoglycans and triterpenes are three major physiologically active constituents in reishi. The predominant triterpenes are ganoderic acids A-Z. The triterpenes are insoluble in cold water but are extractable in ethanol and water. Other active ingredients include lanostans, coumarin, ergosterol, adenosine, uridine, uracil, small amounts of germanium, organic acids, resins and the polysaccharide chitin. Chitin is largely indigestible by the human body and is partly responsible for the physical hardness of reishi. To assure bioavailability the mushroom must be ground into a fine powder. However, the amount and percentage of each component can be very diverse in natural and commercial products. Such variations can occur for several reasons, including differences in the species or strains of mushroom used and differences in production methods. Most mushrooms are composed of around 90% water by weight. The remaining 10% consists of 10 to 40% protein, 2 to 8% fat, 3 to 28% carbohydrate, 3 to 32% fibre, 8 to 10% ash and some vitamins and minerals, with potassium, calcium, phosphorus, magnesium, selenium, iron, zinc and copper accounting for most of the mineral content. In a study of the nonvolatile components of reishi, it was found that the mushroom contains 1.8% ash, 26 to 28% carbohydrate, 3 to 5% crude fat, 59% crude fibre and 7 to 8% crude protein. In addition to these, mushrooms contain a wide variety of bioactive molecules, such as steroids, phenols, nucleotides and their derivatives, glycoproteins.

Mushroom proteins contain all the essential amino acids and are especially rich in lysine and leucine. The low total fat content and high proportion of polyunsaturated fatty acids relative to the total fatty acids of mushrooms are considered significant contributors to the health value of mushrooms.^{9,10,11}

Actions

Immune modulating and enhancing, antitumour, adaptogen, tonic, antioxidant, anti-inflammatory, antiviral, nervine, relaxant, stimulant, antiallergic.

Pharmacological Activity

Reishi has been examined extensively through both traditional and scientific methods and is one of the most widely researched botanicals in Asia. Numerous pharmacological studies have been conducted, most of them in China and Japan, primarily evaluating the polysaccharide and triterpene fractions. Several scientific congresses have focused on the chemistry and medical applications of reishi, and several research organisations are dedicated to this subject. Most of the reported activity of reishi mushroom has been centred on four therapeutic actions: immune enhancing, cardiovascular-regulating, hypoglycaemic and hepatoprotectant. Since the majority of research has been reported in Asian-language journals it has been difficult for non-native Asian researchers to assess the quality of study design and to interpret the conclusions. Most of the English language reports are in abstract form or presentation summaries. Such reports are not subject to peer review as occurs in formal journal submissions. The preparations of reishi used in these studies are poorly defined. Therefore, in the absence of more extensive translation, non-Asian reviewers are unable to make full use of the extensive data that are available. The research provided here is based on the information in the available English-language studies and English-language reports from Asian studies.¹² We will also focus predominantly on whole herb studies.

Immunomodulatory Activity

In the United States, reishi mushroom is most often recommended for its immune-supporting effects. This is based primarily on animal studies showing a host-mediated attack against implanted tumours

and on the use of reishi and other mushroom polysaccharide fractions in supporting immune resistance of patients undergoing conventional chemo and/or radiation therapy for various forms of cancer. English-language reports of clinical studies are quite limited in this area for reishi mushroom.

A 2012 systemic review evaluated the clinical effects of reishi on long-term survival, tumour response, host immune functions and quality of life in cancer patients, as well as adverse events associated with its use. To be eligible for being included in this review, studies had to be RCTs comparing the efficacy of reishi medications to active or placebo control in patients with cancer that had been diagnosed by pathology. All types and stages of cancer were eligible for inclusion. Five RCTs met the inclusion criteria and were included in this review. The review did not find sufficient evidence to justify the use of reishi as a first-line treatment for cancer. It remains uncertain whether reishi helps prolong long-term cancer survival. However, reishi could be administered as an alternative adjunct to conventional treatment in consideration of its potential of enhancing tumour response and stimulating host immunity.¹³

In one placebo-controlled study, it was reported that three grams of a reishi mushroom extract (10:1 concentration of hot water extract) was administered orally to 48 patients with advanced tumours (breast, renal, gastric) for 30 days. A marked immune-modulating effect with an increase in T lymphocytes, including T helpers, as well as a decrease in CD8s, was reported in patients whose immunologic parameters were initially compromised. Little effect was seen in patients with normal immune indices. The extract was also reported to lessen side effects due to chemo- and/or radiation therapy and enhanced post operation patient recovery as compared to controls. No specific values or statistical analysis were provided.¹⁴

There is considerable evidence to support the immunostimulating activities of reishi via induction of cytokines and enhancement of immunological effector. Different components, typically polysaccharides, from reishi were proved to enhance the proliferation and maturation of T and B lymphocytes, splenic mononuclear cells, NK cells, and dendritic cells in culture *in vitro* and in animal studies *in vivo*.^{15,16,17}

The 2015 article presents the results of the investigation of the effect of biomass powder of reishi on T-cell-mediated immunity in normal and immunosuppressed mice. Results of the study show that the administration of reishi in a dose of 0.5mg/kg orally for 10 days increases the delayed-type hypersensitivity response in normal mice. Administration of 0.5mg/kg of reishi for 10 days blocked the development of the T-cell-mediated immunosuppression and restored the delayed-type hypersensitivity response in immunosuppressed mice.¹⁸

The antimetastatic benefits of reishi warrant further clinical studies following a 2014 study suggesting that an oral administration of reishi can inhibit breast-to-lung cancer metastases through the downregulation of genes responsible for cell invasiveness. Breast cancer metastasis is one of the major reasons for the high morbidity and mortality of breast cancer patients. In spite of surgical interventions, chemotherapy, radiation therapy and targeted therapy, some patients are considering alternative therapies with herbal/natural products. Human breast cancer cells were implanted into the mammary fat pads of mice. Although an oral administration of reishi only slightly suppressed the growth of large tumours, the same treatment significantly inhibited the number of breast-to-lung cancer metastases. Reishi also downregulated the expression of genes associated with invasive behaviour.¹⁹

Based on the analysis of more than 270 patents and scientific articles, a 2013 state-of-the-art review presented reishi with immunomodulatory and anticancer effects. Cultivation methods for the commercial production of reishi fruit bodies and mycelia were summarised, with main active compounds of triterpenoids, polysaccharides, and proteins, often found in forms of proteoglycans or glycopeptides. Pharmacological effects with emphasis on anticancer and immunomodulatory functions were presented, separately for spores and dry mycelia, and for the groups of triterpenoids, polysaccharides, proteins and glycoproteins. Patents disclosing preparation methods of extracts and purified pharmaceutical isolates were reviewed, and examples of anticancer formulations, used as pharmaceuticals or nutraceuticals, were given. The review suggested that according to the present understanding, the anticancer activity of reishi may

be attributed to at least five groups of mechanisms: (1) activation/modulation of the immune response of the host, (2) direct cytotoxicity to cancer cells, (3) inhibition of tumour-induced angiogenesis, (4) inhibition of cancer cells proliferation and invasive metastasis behaviour, and (5) carcinogens deactivation with protection of cells. Although, the data from recent *in vitro* and *in vivo* studies demonstrates promising anticancer effects, a need is identified to further (1) isolate and purify compounds, with a deeper understanding of their individual and synergistic pharmacological effects, (2) molecular level studies of the antitumour and immuno-supportive mechanisms, (3) well designed *in vivo* tests and controlled clinical studies, and (4) standardisation and quality control for reishi strains, cultivation processes, extracts and commercial formulations.²⁰

Antitumour Activity

In humans, whether the antitumour effect of reishi is a direct one or is mediated via effects on the immune system is a key question to address. Only a few clinical trials have used reishi as a single agent on cancer patients and that was not using the whole herb. Two randomised, controlled trials have been conducted using a GLPS (*Ganoderma lucidum* polysaccharide)-rich extract (a patented over-the-counter product, Ganopoly). The study recruited 134 patients with advanced cancers of different sites and supplemented them with reishi capsules at a dosage of 1800mg/day for 12 weeks. Cellular immunity in 80% of these patients was significantly enhanced in terms of elevated plasma interleukin (IL)-2, IL-6, and interferon γ (IFN- γ) levels and natural killer (NK) cell activity. In another study, the same protocol was followed with 68 lung cancer patients in whom immune parameters including total T cells, NK cells, and CD4/CD8 ratio were significantly enhanced in the reishi-treated group. In addition, quality of life in terms of Karnofsky score was improved in about 65% of these patients. Ganopoly was also demonstrated to enhance mitogenic activity and NK cells in patients with advanced cancer in a before-and-after comparison study. These results provide some evidence that the antitumour effects of reishi are mediated via effects on the immune system. However, it must be noted that all studies were conducted by the same

research group and that other direct antitumour effects of reishi have not yet been studied on humans *in vivo*.^{21,22,23}

Numerous studies have reported the antitumour activity of reishi mushroom in animals. This activity is primarily associated with polysaccharides in general and, specifically, polysaccharides with the branched (1–3)- β -D-glucan moiety. Antitumour activity has also been reported for reishi triterpenes. In one study, polysaccharides from various species of *Ganoderma* were administered to mice with implanted tumour cells. Considerable antitumour activity was reported for all species with varying degrees of inhibitory activity elicited by the polysaccharides.²⁴

The findings of a 2016 animal study strongly suggest that reishi, used in combination with other agents that target Epidermal Growth Factor Receptor (EGFR), may enhance therapeutic responsiveness in breast cancer patients with abnormal EGFR signaling.²⁵

In the first study of its kind it was proved that, in gastric adenocarcinoma cell line (AGS), the methanolic extract of reishi causes an induction of autophagy, rather than a reduction in the autophagic flux. Autophagy is the normal process of destruction of cells in the body. Previous studies have shown some evidence that the methanolic extract of reishi affects cellular autophagy. However, it was not known if it induces autophagy or decreases the autophagic flux. The treatment of a (AGS) with the mushroom extract increased the formation of autophagosomes (vacuoles typical from autophagy). Moreover, the cellular levels of LC3-II were also increased, and the cellular levels of p62 decreased, confirming that the extract affects cellular autophagy. Treating the cells with the extract together with lysosomal protease inhibitors, the cellular levels of LC3-II and p62 increased.²⁶

Of 58 basidiomycetes mushrooms tested in a French study reishi was shown to be the most effective in killing cancer cells. Reishi induced cell-cycle arrest and apoptosis in more than 30 human and rodent tumour cells.²⁷

An ethanol extract of reishi decreased cyclooxygenase 2 (COX)-2 enzyme expression and increased nitric oxide synthesis in colon HT-29 cells. The study was designed to evaluate the

claims that reishi is useful for the prevention and treatment of various cancers in human colon cancer cells in terms of cancer preventive mechanisms. Results have demonstrated induction of apoptosis, anti-inflammatory action and differential cytokine expression during induced inflammation in the human colonic carcinoma cell line, HT-29. The results suggested that reishi has pro-apoptotic and anti-inflammatory functions, as well as inhibitory effects on cytokine expression during early inflammation in colonic carcinoma cells, which may be of significance in the use of herbal alternative medicines for cancer prevention.²⁸

A tumour mass requires a continuous nutrient supply via new blood vessels formed by the process of angiogenesis. Invasive cancer cells spread to distant sites through blood and lymphoid vessels. Therefore, agents that inhibit angiogenesis inhibit tumour growth and spread. The potential antiangiogenic activities of reishi have been demonstrated in *ex vivo* chick embryo chorioallantoic membrane (CAM) assay. Fresh fruit bodies of reishi were extracted with 70% ethanol at room temperature.²⁹

Reishi could have potential therapeutic use for the treatment of prostate cancer. In a recent study the researchers examined the effect of reishi on angiogenesis related to prostate cancer. They found that reishi inhibits the early event in angiogenesis, capillary morphogenesis of the human aortic endothelial cells. Polysaccharide peptide and ethanol extract from reishi have been proven to decrease microvessels around a microfiber filter disc containing an embryo with intact yolks. Using a prostate cancer cell line, two angiogenic factors, known as vascular endothelial growth factor (VEGF) and transforming growth factor (TGF)- β 1, were suppressed by reishi through inhibition of the ras/extracellular signal-regulated kinase (Erk1/2) and Akt signaling pathways.³⁰

Cell adhesion, invasion, and migration are the key factors in determining the aggressiveness of cancer; hence, control of cell motility is effective in avoiding cancer metastasis. An American study investigated the effect of reishi on highly invasive breast and prostate cancer cells. Cell adhesion, invasion and colony formation of breast cancer cells were significantly inhibited on exposure to reishi extracts.³¹

In addition, another study at the Centre for Nutrition in Los Angeles was conducted to investigate chemopreventive effects of reishi using a unique *in vitro* human urothelial cell (HUC) model. Ethanol and water extracts of fruiting bodies and spores of the reishi were used to examine growth inhibition, actin polymerization status and impact of actin remodeling on cell migration and adhesion. Results showed that ethanol extracts had a stronger growth inhibition effect than water extracts. Water and ethanol extracts of reishi modulated the F/G-actin ratio, which, in turn, reduced the formation of stress fiber and focal adhesion complexes of bladder cancer cells, suggesting the actin remodeling was associated with the inhibition of carcinogen-induced cell migration.³²

Antioxidant Activity

Consumption of antioxidant-rich plants may help prevent cancer and other chronic diseases.³³ Antioxidants protect cellular components from oxidative damage, which is likely to decrease risk of mutations and carcinogenesis and also protect immune cells, allowing them to maintain immune surveillance and response. Various components of reishi, in particular polysaccharides and triterpenoids, show antioxidant activity *in vitro*. However, a direct link has not been established between the antioxidant properties of reishi and its immunomodulatory and anticancer effects, and whether reishi acts as an antioxidant or pro-oxidant may depend on concentration and environment.^{34,35,36}

Reishi may improve physical fitness in women with fibromyalgia and might be a useful dietary supplement to enhance physical performance of the patients suffering from fibromyalgia a 2015 study has found. Fibromyalgia is a chronic rheumatic disease of unknown etiology characterised by generalised pain, stiffness, poor physical conditioning, non-restorative sleep and poor health-related quality of life. The objective of the study was to evaluate the effects of a six week treatment of reishi on the physical fitness in patients suffering from fibromyalgia. There were 64 women with fibromyalgia who participated in the study and they took six grams of reishi per day for six weeks. Different fitness tests were selected in order to evaluate functional capacity. After the six week

treatment period, reishi significantly improved aerobic endurance, lower body flexibility and velocity ($p < .05$).³⁷

Medications produced from natural products are widely used as prophylactics for sickness induced by alcohol consumption. Because of its antioxidant properties the neuroprotective prophylactic effects of reishi-based medications were studied in alcohol-treated animals. Regular administration of reishi improved the energy supply to the brain cortex and decreased the prevalence of inhibitory neurotransmitters that are characteristic of alcohol consumption the 2015 study found. The alcohol-induced increase in liver proliferation was significantly suppressed by regular administration of the reishi water suspension.³⁸

Antioxidants from reishi were found to be absorbed quickly after ingestion, resulting in an increase in the plasma total antioxidant activity of human subjects. The aim of a Chinese study was to investigate *in vitro* antioxidant capacity of reishi, absorption and systemic distribution of reishi antioxidants, and effects of short-term (10 days) supplementation on biomarkers of antioxidant status, coronary heart disease (CHD) risk and DNA damage. In this double-blinded, placebo-controlled, cross-over intervention study, blood and urine samples were collected from 10 healthy volunteers at 0 (fasting) and 45, 90, 135 and 180min post-ingestion of a single dose (1.1g) of reishi. Repeat fasting samples were collected after 10 days' supplementation with 0.72g/d reishi. The acute response (up to 3 hours) was also investigated with a larger dose (3.3g) of reishi (n=7). Results showed that the total antioxidant capacity (as the FRAP value) of an aqueous suspension of reishi was 360 micromol/g. Ingestion of reishi caused a significant post-ingestion increase in plasma antioxidant capacity, with peak response at 90 minutes.³⁹

Anti-inflammatory Activity

In 14 renal patients with increased blood levels of TNF-alpha and reduced levels of IL-10, glomerular dysfunction and proteinuria, 900 to 1125mg/day reishi was shown to reduce TNF-alpha and increase IL-10 and correct renal dysfunction, including suppressing proteinuria. A persistent proteinuria is commonly observed in nephrotic patients with focal segmental glomerulosclerosis (FSGS) under

treatment with prednisolone+/-cyclophosphamide or with vasodilators (ACEI+All receptor antagonist, calcium channel blocker and antiplatelet agent). Fourteen such patients with persistent proteinuria were treated with reishi. The study revealed an enhanced endothelial cell cytotoxicity induced by patient's serum, and an altered immunocirculatory balance with predominant proinflammatory cytokine TNF alpha activity in the presence of defective anti-inflammatory cytokine interleukin-10. Treatment with reishi suppressed endothelial cell cytotoxicity, restored immunocirculatory balance and successfully suppressed proteinuria in all of these 14 patients.⁴⁰

A 2013 study has discovered that reishi may be useful in the treatment of neurodegenerative diseases by inhibiting inflammatory mediator responses in activated microglia. Although a great deal of work has been carried out on the therapeutic potential of reishi, the pharmacological mechanisms of its anti-inflammatory actions remain unclear. Several studies have demonstrated that various reishi extracts interfere with cell cycle progression, induce apoptosis and suppress angiogenesis in human cancer cells and thus act as anticancer agents. Additionally, it has also been suggested that reishi extracts have a neuroprotective effect and may be useful in future studies on the pathogenesis and prevention of Alzheimer's disease and Parkinson's disease. However, the precise biochemical mechanisms underlying the reishi extract-induced anti-inflammatory effects have not yet been clarified in microglial cells. In the Korean study scientists evaluated the inhibitory effects of reishi ethanol extract on the production of inflammatory mediators and cytokines in rodents. They identified that reishi significantly inhibits the excessive production of nitric oxide, prostaglandin E(2) and pro-inflammatory cytokines, including interleukin (IL)-1 β and tumour necrosis factor- α , in a concentration-dependent manner without causing cytotoxicity. The results indicate that the inhibitory effects of reishi on inflammatory responses in are associated with the suppression of the nuclear factor kappaB and toll-like receptor signaling pathways.⁴¹

Cardiovascular Activity

The ability of reishi mushroom to inhibit platelet aggregation after oral administration, as revealed by

human peripheral blood samples, has been reported. This activity has been associated with a water-soluble component from reishi that is a derivative of adenosine.⁴²

A 2015 Cochrane review to evaluate the effectiveness of reishi for the treatment of pharmacologically modifiable risk factors of cardiovascular disease in adults found that evidence from a small number of randomised controlled trials does not support the use of reishi for treatment of cardiovascular risk factors in people with type 2 diabetes mellitus.⁴³

In one clinical trial of 15 healthy volunteers and 33 patients with atherosclerotic disease, statistically significant ($p < .01$) inhibition of platelet aggregation was observed following administration of one gram of reishi mushroom three times daily for two weeks. After treatment with reishi, the length and width of induced thrombi was reduced by approximately 10% to 15%.⁴⁴

In a study of hypertensive patients, which included a placebo control group, whole blood viscosity, plasma viscosity and blood pressure were significantly reduced ($p < .01$ compared with pretreatment values) in 33 patients (15 male, 18 female) given oral doses equivalent to 1.3g reishi (110mg of dried reishi mushroom extract) each time, four times daily for two weeks. A reduction in a variety of symptoms including dizziness (58.8%), headache (75.0%), chest tightness (53.8%), and insomnia (64.7%), was also observed in the reishi-treated group while no significant changes were observed in the placebo group.⁴⁵

In a study of patients with heart disease, a cold water infusion of reishi mushroom (concentration and dosage undefined) was administered to 35 patients. Symptoms (undefined), electrocardiogram (ECG), and primary blood dynamic parameters reportedly improved in 85.7% of patients.⁴⁶

Spontaneously hypertensive rats were given an undisclosed amount of reishi mushroom powder as part of the diet. After four weeks the systolic blood pressure in treated rats was reported to be significantly lower than that of the controls though no statistical analysis was provided.⁴⁷

Hypoglycemic Activity

Overall, the data from different studies suggest that reishi intake helps in modulating blood glucose

levels. However the studies were performed mostly on animals. More support from well-planned human clinical studies is needed with and without combination with conventional medicines.⁴⁸

In one study reported in the literature, 71 adult patients with confirmed type 2 diabetes mellitus were supplemented with Ganopoly (polysaccharide fractions extracted from reishi). The patients received either Ganopoly or placebo orally at 1800mg, three times daily for 12 weeks. Glycosylated hemoglobin (HbA1C) and plasma glucose decreased significantly after 12 weeks, indicating a hypoglycemic effect of the extract.⁴⁹

The results of a 2015 study indicate that reishi and its high molecular weight polysaccharides may be used as prebiotic agents to prevent gut dysbiosis and obesity-related metabolic disorders in obese individuals. Obesity is associated with low-grade chronic inflammation and intestinal dysbiosis. A water extract of reishi was shown to reduce body weight, inflammation and insulin resistance in mice fed a high-fat diet. The data indicated that reishi not only reversed high fat diet-induced gut dysbiosis but also maintained intestinal barrier integrity and reduced metabolic endotoxemia.⁵⁰

In a recent Chinese study oral administration of reishi hot water extract (0.03 and 0.3g/kg BW) for four weeks was found to lower the serum glucose levels in obese/diabetic mice, with effects seen after the first week of treatment. However the glucose levels were still higher in these animals than in the control animals and insulin levels were not altered. The extract markedly reduced levels of phosphoenol-pyruvate carboxykinase (PEPCK), which are usually high in obese/diabetic mice. The suggested mechanism, according to the authors, is that of lowering the serum glucose levels through suppression of the hepatic PEPCK gene expression.⁵¹

Antiviral and Antibacterial Activity

A small study in human patients reported beneficial effects with the use of reishi to decrease herpes zoster pain and lesions in four individuals. A dried hot water extract of reishi taken orally (equivalent to 36 or 72g of dried mushroom per day) was used as the sole treatment for postherpetic (varicella zoster virus) neuralgia in the elderly patients (mean age of 65). This treatment was reported to dramatically

decrease pain and promote the healing of lesions without any toxicity even at very high doses.⁵²

A 2016 study has shown that the use of reishi extract prior to *Mycobacterium tuberculosis* infection may protect the host against bacterial replication to some extent.⁵³

In another *in vitro* study, the direct antimicrobial effect of a reishi water extract was examined against 15 species of bacteria alone and in combination with four kinds of antibiotics. Reishi was found to be more effective than antibiotics against *E. coli*, *Micrococcus luteus*, *S. aureus*, *B. cereus*, *Proteus vulgaris* and *Salmonella typhi*, but less effective against other species tested. The antimicrobial combination of reishi with four commonly used antibiotics resulted in an additive or synergistic effect in most, but not all, instances, with apparent antagonism against cefazolin and ampicillin effects on *Proteus vulgaris*.⁵⁴

Hepatoprotective Activity

A number of studies have focused on the ability of reishi to protect the liver from chemical damage and enhance its detoxifying activity.

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 (serum glutamic-pyruvic transaminase)/SGOT (serum glutamic-oxaloacetic transaminase) levels were given six grams of a reishi extract (concentration undefined) for three months. After one month, bilirubin, SGPT and SGOT levels were significantly reduced ($p < .01$); after 90 days all values returned to within normal ranges.⁵⁵

A 2014 study found that reishi pharmacopuncture (treatment) is effective in protecting against ethanol-induced acute hepatic injury in rats by modulating the activities of ethanol-metabolizing enzymes and by attenuating oxidative stress. Pharmacopuncture is an effective therapy in Oriental medicine. A solution extracted from medicinal herbs is injected into acupuncture points according to the condition of the patient. Pharmacopuncture, or herbal acupuncture, is a new form of therapy derived from a combination of two traditional therapeutic methods, herbal medicine and acupuncture therapy. Recently, pharmacopuncture

therapies in Korea have developed into quite a unique and systematic framework for the diagnosis and treatment of various diseases.⁵⁶

Hot water and water-ether extracts of the fruit body of reishi were found to have a potent hepatoprotective effect on liver injury induced by carbon tetrachloride (CCl₄) given orally and intraperitoneally to rats. The measured markers for liver injury included aspartate and alanine transaminases (AST and ALT) and lactate dehydrogenase (LDH). One active compound of the extract was separated and identified as ganoderenic acid A. This was found to have a potent inhibitory effect on β -glucuronidase, and the authors suggest that this inhibitory effect may have mediated the hepatoprotection seen when this isolated compound was given.^{57,58}

The hepatic and renal protective mechanism of reishi might be due, at least in part, to its prominent superoxide scavenging effect. A recent study found that reishi could protect the liver and kidney from superoxide induced hepatic and renal damages. The antioxidative effect of hot water extract of reishi on ethanol-induced free radical generation was studied. Hot water extract of reishi was given orally to mice 30 minutes before administration of ethanol. The extract was found to have an inhibitory effect against the formation of malondialdehyde (MDA), a degradation product of lipid peroxides, in mouse liver and renal homogenate, with evidence of a dose response seen.⁵⁹

A reishi methanolic extract was reported to show hepatic protection. The extract was given orally to rats (500mg/kg/day) for 30 days before hepatic damage was caused by benzo(a) pyrene. The extract prevented the increase of serum AST, ALT, and alkaline phosphatase (ALP) activities that result from benzo(a)pyrene challenge, and enhanced the levels of GSH, SOD, GpX, CAT, and glutathione S-transferase (GST).⁶⁰

Respiratory Activity

Reishi has a long history of use in TCM for treatment of chronic bronchitis. In one small uncontrolled study of 20 patients with chronic bronchitis, reishi mushroom was administered for four months. According to the review, in all but two patients there

was a significant decline in blood cholinesterase activity, suggesting a reduction in the excitability of the parasympathetic nerves.⁶¹

Wound Healing Activity

A 2016 study presents a case of a 44-year-old male patient who used soap enriched with reishi and goat's milk for three days in treating annular cutaneous sarcoidosis. The patient showed almost complete regression of the lesions.⁶²

Scientific reports have shown that the wound healing effects of reishi were partly attributed to its rich polysaccharides. However, little attention has been paid to its potential effects on wounds associated with diabetes mellitus. In a 2013 study the wound healing activity of the hot aqueous extract of reishi in streptozotocin-induced diabetic rats was evaluated. The extract of reishi was standardised based on chemical contents of total polysaccharides (25.1%), ganoderic acid A (0.45%), and adenosine (0.069%). Six groups of six rats were experimentally wounded in the posterior neck region. Intrasite gel was used as a positive control and aqueous cream as the placebo. Topical application with 10% of mushroom extract-incorporated aqueous cream was more effective than that with Intrasite gel in terms of wound closure. The antioxidant activity in serum of rats treated with aqueous extract of reishi was significantly higher; whereas the oxidative protein products and lipid damage were lower when compared to those of the controls. These findings strongly support the beneficial effects of standardised aqueous extract of reishi in accelerating wound healing in streptozotocin-induced diabetic rats.⁶³

Other Activity

Consumption of reishi could be used as one of the prophylactic means to reduce the body-burden of toxic lead and lead-toxicity-related early hemolysis and hence to combat anemia a 2015 study has found. The animal study investigated the effect of chronic oral exposure to lead acetate on the sensitivity of red blood cells to hemolysis and whether the sensitivity could be decreased by feeding rats with reishi.⁶⁴

Another 2015 study examined fermentation by lactic acid bacteria as a method to improve the memory-

enhancing effects as well as maximize the efficacy of reishi water extracts by two-step fermentation with *Bifidobacterium bifidum* and *Lactobacillus sakei*. This study investigated the anti-amnesic effect of fermented reishi water extracts on scopolamine-induced memory impairment in rats. The results suggest that secondary fermented extract could be useful to enhance learning memory and cognitive function via cholinergic dysfunction.⁶⁵

Indications

- Chronic fatigue, weakened immunity, chronic infections or inflammation, convalescence, autoimmune disease, fibromyalgia, HIV/AIDS
- As a relaxing adaptogen for anxiety or overstimulation in constipation predominant irritable bowel syndrome.
- Adjunct therapy in cancer during chemotherapy and radiation
- Tonic for the elderly

Energetics

Bitter, warming, drying.

Use in Pregnancy

No data available.

Contraindications

None known.

Drug Interactions

Monitor with anticoagulant/antiplatelet, antidiabetic and antihypertensive drugs. Combination may be beneficial with antimicrobial and antiviral therapy – medical supervision recommended.

Administration and Dosage

Liquid Extract:	1:5
Alcohol:	30%
Weekly Dosage:	20 to 100mL

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