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FILE:▪Mushrooms - Medicinal
▪Fungi - Medicinal

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RE: Major Review of Health Benefits of Medicinal Mushrooms

Wasser SP, Weis AL. Medicinal Properties of Substances Occurring in Higher Basidiomycetes Mushrooms: Current Perspectives (Review). *International Journal of Medicinal Mushrooms* 1999;1:31-62.

Medicinal mushrooms have been used since ancient times in folk medicine throughout the world. Some authors combine nutritional uses of mushrooms with medicinal properties. This extraordinarily comprehensive review highlights some substances from higher Basidiomycetes (mushrooms and toadstools) with antitumor, immunomodulating, cardiovascular and antihypercholesterolemic, antiviral, antibacterial, antiparasitic, hepatoprotective, and antidiabetic effects. The higher Basidiomycetes include about 10,000 species from 550 genera and 80 families in the Basidiomycetes class with macroscopic fruiting bodies. Mushrooms are often used as adaptogens and immunostimulants. Cellular components and secondary metabolites of many mushrooms have been shown to affect host immune systems and might be used to treat a variety of diseases including cancer, immunodeficiency disease, and immunosuppression after drug treatment.

Cancer is the second largest cause of death in children and adults, taking more than 6 million lives annually worldwide. Chemoprevention (ingestion of chemical agents that reduce the risk of carcinogenesis) is one direct way to reduce this toll. Mushrooms useful against cancers of the stomach, esophagus, lungs, etc. are known in China, Russia, Japan and Korea, as well as the United States and Canada. Approximately 200 species of mushrooms have been found to markedly inhibit tumor growth, although most mushroom-origin antitumor substances have not been clearly identified. Antitumor activity of higher Basidiomycetes was first demonstrated by Lucas and his collaborators in 1957, who used extracts of fruiting bodies of *Boletus edulis* and other Homobasidiomycetes against sarcoma in mice. In the 1960s, calvacin was isolated form the giant puffball *(Calvatia gigantea)* and became the most commonly cited natural product isolated from mushrooms, used in many laboratories as an anticancer agent. Calvacin emerged indirectly from the recorded ancient application and verification of folk medicine. During the 1960s and 1970s, a number of potentially useful anticancer substances were isolated from *Lampteromyces japonicus, Flammulina velutipes, Pholiota nameko,* oyster mushroom *(Pluerotys ostreatus), P. spodoleucus, Tricholoma matsutake,* shiitake mushroom *(Lentinus edodes),* and others. Gregory and collaborators surveyed more than 7000 cultures of higher Basidiomycetes for antitumor activity against rodent tumors. Fifty cultures representing 22 species produced inhibitory materials. In Japan, Russia, China, and the United States, polysaccharide antitumor agents have been developed form the fruiting body, mycelia, and culture medium of various

mushrooms: shiitake, reishi (*Ganoderma lucidum*), split gill (*Schizohlyllum commune*), turkey tails (*Trametes versicolor*), *Inonotus obliquus,* and *F. velutipes).*

A water-soluble polysaccharide, lentinan, derived from shiitake mushrooms, was reported by Chihara "to almost completely regress the solid type of tumors in synergic host-tumor system A." Numerous researchers have since isolated other essential polysaccharides, each of which has been found to be a β-D-glucan, yielding D-glucose by acid hydrolysis. In addition to water-soluble β-D-glucans, these include β-D-glucans with heteropolysaccharide chains of xylose, mannose, galactose, and uronic acid extracted by salt and alkali, and β-D-glucan-protein complexes present at 10% to 50% in dry matter. Some have shown remarkable carcinostatic effects not only by intraperitoneal injection, but also by oral ingestion. While not all of these substances demonstrate antitumor properties, those that have done so are listed in Table 2.

Polysaccharides from mushrooms do not attack cancer cells directly, but activate different immune responses in the host. Immunomodulators increase the activity of macrophages (white blood cells that destroy pathogens) found in the mucous membranes of the body and the reticuloendothelial system, centered in the spleen, liver, and lymphoid tissues. Many mushroom polysaccharides have an ability to stimulate macrophage (scavenger cell) activity.

Most of the active polysaccharides isolated from mushrooms can be classified as dietary fiber (high molecular weight materials excreted without digestion and absorption by human beings. A lot of immune tissue is in the gut and can be affected as the mushroom compounds travel through the gut.). β-glucans and chitinous substances with carcinostatic activity, contained primarily in the dietary fiber of mushrooms, absorb hazardous materials. They prevent absorption and hastening excretion and may help prevent cancer of the colon and rectum. Lectins have been isolated and purified from several higher Basidiomycetes. These materials can be used for affinity chromatography, for diagnosis of cancer cells, or as specific binding moieties (one of two parts) for targeted cancer therapy. For instance, an N-acetylgalactosamine specific lectin from the fruiting body of maitake, or hen-of-the-woods mushroom *(Grifola frondosa),* GFL, is cytotoxic against cervical cancer cells. Additionally, some terpenoids and their derivatives, isolated from Polyporales and Ganodermatales mushrooms, are cytotoxic. About 100 different terpenoids are found in the fruiting bodies of reishi and *G. applanatum* and related species of *Ganoderma.*

Of these anticancer and immunomodulating substances, lentinan has been studied most extensively and is discussed throughout the text. Table 3 summarizes antitumor activity currently known to be induced by lentinan. Lentinan has been found to have a number of other beneficial properties, also discussed at length. Table 4 lists the activities of lentinan in potentiating host defenses. Table 6 lists antiviral, antibacterial, and antiparasitic effects of lentinan and related shiitake derivatives. Most studies with lentinan use injectable dose forms, which are normally not available in the U.S.

The major cause of death in Western countries is coronary artery disease. A primary risk factor, hypercholesterolemia (high cholesterol), contributes to hardening of the arteries. The initial step in lowering cholesterol is a diet low in fat and saturated fatty acids and rich in fiber. This is followed by drug therapy. The best known pharmacologic agent currently available is lovastatin and its analogs. Potential producers of lovastatin from edible higher Basidiomycetes are species of *Pleurotus,* with the highest concentrations found in the fruiting bodies of oyster mushroom. Experiments conduced by Bobek and collaborators found that the addition of 2% to 4% of oyster mushroom to the hyperlipidemic diet efficiently prevented accumulation of C and triacly-glycerols in both the blood and livers of animals with hyperlipemia. Mature fruiting bodies of oyster mushroom "could be recommended for consumption as a natural cholesterol lowering agent." Other heart protective mushrooms may include *Auricularia auricula-judae* (traditionally used as an immune tonic; has shown anticoagulatory effects; lowered total cholesterol, triglyceride, and lipid levels in rat studies; and antiaggregatory activity on blood platelets); *Tremella fuciformis* (demonstrated antilipemic activity, lowered LDL-cholesterol, and positively influenced blood coagulation in animal studies); *Armillariella mellea* (decreased heart rate, reduced vascular resistance, increased cerebral blood flow, and increased coronary oxygen efficiency in animal studies); maitake (reduced blood pressure, reduced serum cholesterol levels in rats); *Trametes* spp. (showed activity against hypertension and thrombosis, inhibited blood platelet aggregation, is antihyperlipemic and antiarrhythmic,

lowered serum cholesterol, decreased LDL-cholesterol in animal studies); *Wolfporia cocos* (useful in treating arrhythmia), and *Volvariella volvacea* (lowered blood pressure in animals).

Several substances in the higher Basidiomycetes act against various viral, bacterial, and parasitic infections, including AIDS and the opportunistic infections to which AIDS patients are highly susceptible. Use of these compounds — here again, lentinan and other substances from Shiitake mushrooms have been studied extensively — to boost the immune system are of great value in treating AIDS. Table 5 provides a sampling of mycoses and mycetes seen in AIDS patients, and the text augments this with discussion of numerous antibacterial, antibiotic, and antiviral compounds from mushrooms which have been found effective against these and other infections.

Animal experiments and human clinical studies have demonstrated beneficial effects of mushrooms and their extracts on a wide variety of liver disorders, including hepatitis. Hepatitis B, which the World Health Organization says now infects 350 million people worldwide, can lead to complications believed to kill over one million people annually. Here again, lentinan and other compounds from shiitake mushroom have been found to have hepatoprotective effects, some in combination with polysaccharides from reishi and turkey tails. Maitake, *Dendropolyporus umbellatus,* split gill, turkey tails, *Tremella fuciformis,* and *Wolfporia cocos* have also been reported to exert positive effects on the hepatic system.

Diabetes, one of the oldest known diseases, currently affects 250 million people worldwide. Diabetes has become the fourth leading cause of death in the U.S. and the leading cause of related disorders such as kidney disease, vessel disease, blindness, impotence, and gangrene. Cases of insulin resistance and side effects from conventional drugs have triggered a search for alternatives. Some animal studies have shown that Maitake mushroom may have an antidiabetic effect. Glucans from reishi mushroom and a β-glucan-protein from turkey tails have also shown antidiabetic promise in animal and in vitro tests.

The information presented in this review, a part of which appeared earlier in *Critical Reviews in Immunology* (1999;1) will be helpful in seeking valuable compounds to treat a variety of diseases and conditions. Wasser and Weis are internationally known and respected mycologists and their article cites over 250sources from many countries and laboratories. The Tables provide a vast amount of information, not all of which is included in the text. Table 1 cross-indexes medically active higher Basidiomycetes (28 mushrooms organized by taxa) with 15 therapeutic effects.

The article includes information on the life cycle and characteristics of the higher Basidiomycetes, the cancer preventive effects of nonsteroidal antiinflammatories (NSAIDS), and how investigation of their mechanism of action led to the discovery of the cancer inhibiting effects of resveratrol, and much more detailed information on investigational research into many of the mushroom-derived substances mentioned.

¾ *Mariann Garner-Wizard*

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