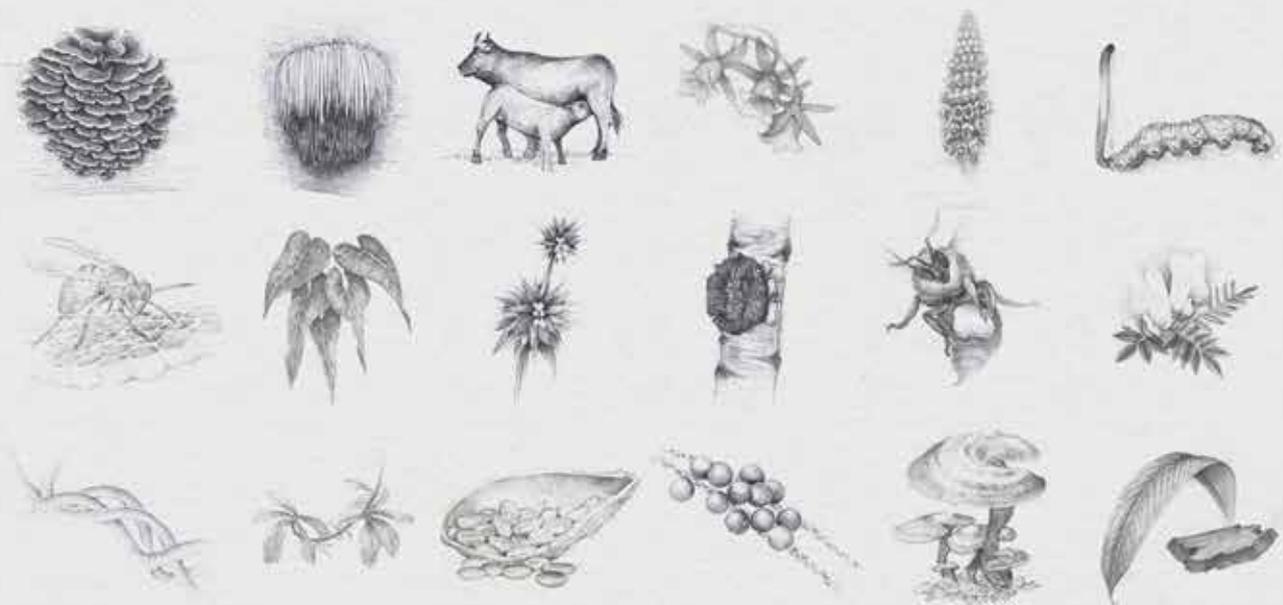




SCIENCE

SHIITAKE MUSHROOM



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LENTINULA EDODES



Shiitake, *Lentinula edodes*, is one of the most heavily cultivated and widely consumed edible mushrooms in the world. Total annual production of shiitake in the year 2000 was 7.5 million tons, second only to the white button mushroom ⁽¹⁾. The name shiitake is derived from a combination of the Japanese words for a variety of chestnut tree, the shita, and mushroom, or take. Shiitake may also be referred to as forest mushroom, or black forest mushroom. In China it is known under different names; for example, Xianggu which means fragrant mushroom. Interest in shiitake is increasing due to its high nutritional value and medicinal properties that have long been appreciated by traditional oriental cultures, especially in China and Japan, and dating back over 2000 years.

Shiitake is a wood-decaying basidiomycetes that proliferates within the sapwood of dead or dying chestnut, beech, oak, Japanese alder, or mulberry, among other hardwood species. In its natural habitat, shiitake is found in damp, forested areas with deep shade. Mushrooms are produced in the fall, early winter, and spring when changes in temperature and moisture induce the reproductive cycle. When mushrooms first emerge through the tree bark, the cap of the mushroom is a shade of dark brown and then becomes lighter in color with age. The spores are white and the edges of the gills are serrated. This species is native to Japan, China, the Korean peninsula, and other regions in eastern Asia.

This brief summary of shiitake takes a look at the bioactive compounds found in this popular, edible mushroom. Shiitake is known to have strong antimicrobial and antibacterial effects and may also reduce growth of cancerous tumors via immunomodulatory properties. Shiitake is also a natural source of antioxidants.

COMPOUNDS AND TOXICITY

Shiitake naturally contains many important contributions to human nutrition and health. Among these are proteins that are built by a total of 18 different amino acids, including essential amino acids, lipids (primarily linoleic acid), carbohydrates, fiber, minerals, vitamins B1, B2, B3, and B12 (in trace amounts), vitamin C, and ergosterol, and the D2 provitamin. Each of these nutritional factors has been isolated from fruiting bodies (i.e., the mushroom) and mycelia.

Modern research indicates that polysaccharides are the main chemical components related to the bioactivity and pharmacological properties of shiitake ^(2, 3, 6, 7). In particular, one of the most medically significant compounds isolated from the shiitake mushroom is lentinan, a polysaccharide that has a mean molecular mass of 500 kDa. Lentinan activates macrophage T-lymphocytes and other immune effector cells that in turn modulate the release of cytokines. This molecular mechanism may account for the indirect antitumor and antimicrobial properties of this polysaccharide. Other compounds with biological activity are lentinacin and lentysine, which each have been reported to show hypocholesterolemic and hypoglycaemic effects

The aromatic components in shiitake include alcohols, ketones, sulfides, alkanes, and fatty acids. The major volatile flavor contributors are matsutakeol and ethyl-n-amyl ketone ⁽⁵⁾. Therapeutic effects and bioactive compounds are presented in *table 1*.

Although shiitake is an edible mushroom, some individuals may experience minor side effects such as allergic reactions. Hypoallergenicity to the spores of shiitake have been reported in workers picking mushrooms within indoor cultivation facilities. Symptoms include fever, headache, congestion, coughing, sneezing, nausea, and general malaise. However, there is no evidence to indicate that shiitake mycelium is acutely toxic, even in massive doses, though mild side effects such as diarrhea and skin rash may occur.

BIOACTIVE COMPOUND	BIOACTIVE COMPOUND
Lentinan (β -D-glucans), KS-2- α -mannan-peptide, LEM, LAP (heteroglucan-protein), EP3	Antitumor
Mannoglucan, polysaccharide protein complex, glucan, Lentinan, polysaccharide L-II, (1-3)- β -D glucan	Immunomodulation
Lentinamicin	Antimicrobial
Lentinan, LEM, JLS-18, EP3, EPS4	Antiviral
LEM, Lenthionine, chloroform and ethylacetate extracts	Antibacterial
Lentin	Antifungal
Eritadenine, lentinacin, lentysine	Cardiovascular and hypolipidemic
Lentinan, LEM, hot water extraction and ethanol extraction	Hepatoprotective
Lectin	Hemagglutinating
Methanol and water extracts, polyphenolic compounds	Antioxidant

Table 1.

Bioactive compounds of shiitake mushroom and reported therapeutic effects. LEM = Lentinula edodes mushroom mycelin; EP3 and EPS4 = lignins of shiitake; JLS-18 = water-soluble extract of mycelium ref.

ANTIMICROBIAL, ANTIBACTERIAL, AND ANTIVIRAL PROPERTIES

Antimicrobial activity of shiitake has been found in liquid cultures, chloroform or ethyl acetate extracts, water extracts and dried fruiting body. These extracts are active against gram-positive and gram-negative bacteria, and yeasts and mycelial fungi including dermatophytes and phytopathogens. Mycelial-free culture of shiitake exhibited greater antimicrobial effect against gram-positive than gram-negative bacteria, with *Bacillus subtilis* and *Staphylococcus aureus* among the most strongly inhibited bacteria. Antimicrobial compounds isolated from shiitake liquid cultures include compounds such as lentinamycin .

In a study conducted by Hearst et al. ⁽²⁾, shiitake extract demonstrated antimicrobial activity against 33 of 39 species (84.6%) of microorganisms. Moreover, 5 of 10 yeast and mould species (50%) were inhibited, while 26 of 39 microorganisms (66.6%) showed a zone of inhibition when tested against positive controls (e.g., a ciprofloxacin 5 mg disk). Further work to isolate and identify the active shiitake compound(s) is on-going.

The results of experiments by Hatvani ⁽⁸⁾ showed that sterile, mycelium-free culture fluid of fermented shiitake mycelium, had inhibitory effects on microbes. Specifically, the culture fluid was bacteriostatic against *Streptococcus pyogenes*, *S. aureus* and *B. megaterium*. The culture fluid was less toxic to human tissue culture cells than to microbes. The antibacterial activity and the toxicity cannot be attributed to the same component of the culture fluid because the chloroform fraction contained the bacteriostatic compound and the aqueous fraction had some toxic effect but did not affect bacterial growth. It is probable that the active component of the culture fluid in this extraction was lenthionine, an antibacterial and antifungal sulphur-containing compound.

Studies have shown that shiitake extracts obtained with supercritical fluids were effective against the growth of *Micrococcus luteus* and *B. cereus* but ineffective against *S. aureus* (contra previous work) and *Escherichia coli*. For the yeast *Candida albicans*, the shiitake extracts that showed antifungal activity were obtained from supercritical CO₂ at 15 MPa and 30 and 40°C.

Lentinan and its derivatives are effective against infection by several kinds of bacteria, viruses (including HIV), and parasites. An important area of research targeting this polysaccharide addresses its ability to



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mobilize the body's humoral immunity to ward off bacterial infections that are resistant to antibiotics⁽⁹⁾. Research also suggests that shiitake extracts can improve the beneficial contributions of intestinal flora and reduce harmful effects of bacterial enzymes such as β -glucosidase, β -glucuronidase, and tryptophanase, as well as reduce the risk of colon cancer .

ANTITUMOR ACTIVITY AND IMMUNOMODULATORY EFFECTS

The carcinostatic effect of shiitake lentinan results from activation of the host's immune system. This β -D-glucan lentinan binds to lymphocyte surfaces or serum-specific proteins which activate macrophage, T-helper cells, natural killer (NK) cells, and other effector cells. Each of these immune factors in turn increase production of antibodies as well as interleukins (IL-1, IL-2) and interferon (IFN- γ). The antitumor studies conducted with shiitake thus far are very interesting and do show a potential for providing therapeutic control over cancer⁽⁵⁾.

Lentinan was demonstrated to have antitumor activity and to increase survival time of patients with inoperable gastric cancer and women with recurrent breast cancer following surgical therapy. Specifically, when shiitake lentinan was administered once or twice each week along with chemotherapy to patients with progressive cancer who otherwise showed no signs of serious liver, kidney, or bone marrow dysfunction, there was a statistically significant improvement in immune and anticancer activity when compared to chemotherapy alone.

Ethanol extracts of shiitake fruiting body, spores, and mushroom culture broth, were assessed for their effects on modulation of cell proliferation and apoptosis in murine skin carcinoma cells (CH72) and non-tumorigenic epidermal cells (C50). Shiitake extracts significantly decreased rates of proliferation of CH72 cells, but there were no such effects on C50 cells. Similarly, fluorescent DNA-microscopy with ethidium bromide and acridine-orange staining of cells revealed that shiitake extract reduced cell proliferation and induced apoptosis in a time- and dose-dependent manner in carcinoma cells but not in non-tumorigenic C50 cells. Cell cycle analysis also demonstrated that shiitake extract induced a transient G1 arrest with no changes observed in the non-tumorigenic cells.

Immunomodulatory effects of shiitake lentinan has attracted considerable attention because of its role as a biological response modifier (BRM). Augmentations of NK, CTL (cytotoxic T lymphocyte), LAK (lymphokine-activated killer) activities and DTH (delayed-type hypersensitivity) responses against tumor antigen were observed after administration of lentinan. These mechanisms are the likely cause of the antitumor effects of lentinan. Antitumor polysaccharide L-II was isolated and purified from the fruiting body of shiitake. The antitumor activity of the polysaccharide L-II on mice-transplanted sarcoma 180 was mediated by inducing T-cells and macrophage-dependent immune system responses.

ANTIOXIDANT ACTIVITY

A study by Kitzberger et al.⁽¹⁾ demonstrates that supercritical fluid extraction very efficiently recovers antioxidant and antimicrobial activities of shiitake. Results of the biological activity of shiitake extracts obtained with high-pressure and low-pressure techniques indicate that both extraction methods were adequate in terms of antioxidant activity.

An earlier study investigated the pharmacological effect of polysaccharides from shiitake on the serum oxidative status in rats fed a diet high in fat. Control rats were fed a standard diet and had ad libitum access to water. The administration of shiitake polysaccharides significantly reduced serum total cholesterol along with levels of triglycerides and low-density lipoprotein (LDL) cholesterol, and enhanced serum antioxidant enzyme activity while improving thymus and liver indices in high-fat-diet rats. In conclusion, the data suggest that administration of polysaccharides of shiitake decreases oxidative stress induced by a high-fat diet.

Selenium is one of the trace elements of fundamental importance to human health, and a key component of the antioxidant enzymes that protect cells against the damaging effects of free radicals. Another important health effect of selenium relates to proper functioning of the immune system. Selenium appears to be a key nutrient in cancer prevention and the inhibition of HIV progression to AIDS. The mechanism by which selenium exerts anticancer and immunomodulatory activity differs from that of shiitake extracts and polysaccharide fractions, but a similar pharmacological effect suggests a possible synergism of these two agents. Incorporation of selenium into shiitake mycelium significantly increases antioxidant activity by improving free-radical scavenging ability of mycelial extracts. Selenated extracts are highly active even when selenium is present in very low concentrations (i.e., 0.1–0.5 mg/ml), an effect that may be realized when selenium is in –II and 0 oxidation states. These results suggest that submerged cultivation of shiitake mycelia in selenium-enriched media is a useful method for enhancing human dietary supplements or for obtaining novel selenium-derived chemopreventive agents.

The effect of heat treatment, on changes in the overall antioxidant activity and polyphenolic compounds of shiitake extract, was investigated by Choi et al ⁽¹¹⁾. Raw shiitake was heated at 100 and 121 °C for 15 or 30 min using an autoclave. After heat treatment, the free and bound polyphenols and flavonoids in the mushroom extracts were analyzed. ABTS radical and DPPH radical scavenging activities were measured to evaluate antioxidant activity of the extracts. The polyphenolic contents and antioxidant activities in the extracts increased as temperature and time increased. For example, the free polyphenolic content in the extract heated at 121 °C for 30 min was increased by 1.9-fold compared to that in the extract from the raw sample. The ABTS and DPPH radical scavenging activities were increased by 2.0-fold and 2.2-fold compared to the raw sample, respectively. There was a good correlation between total polyphenolic contents and ascorbic acid equivalent antioxidant capacity (AEAC). Results showed that heat treatment significantly enhanced the overall antioxidant activities of shiitake mushroom. ⁽¹¹⁾

CONCLUSIONS

SHIITAKE MUSHROOM



Shiitake is the second most cultivated and among the most popular edible mushrooms in the world. It grows on dead or dying hardwood trees and is native to Japan, China, the Korean peninsula, and other areas of East Asia. The cap is dark brown at emergence and grows lighter with age. One of the most important biological compounds found in shiitake is lentinan, a polysaccharide that activates immune effector cells. Lentinan and its derivatives reduce infection by gram-positive bacteria, viruses including HIV, and other parasites. Research also suggests that shiitake extract enhances beneficial activity of intestinal flora and reduces the harmful effects of certain bacterial enzymes. Shiitake has antitumor activity and the carcinostatic effect of lentinan results from the activation of the host's immune system. This β -D-glucan binds to lymphocyte surfaces or serum-specific proteins, which activate macrophage, T-helper cells, natural killer (NK) cells, and other effector cells.

Moreover, shiitake has antioxidant activities that are enhanced with heat treatment. Even incorporation of selenium into shiitake mycelium significantly increases antioxidant activity by increasing the free radical scavenging ability. Finally, administration of shiitake polysaccharides significantly reduces serum total cholesterol, lowers levels of triglycerides and LDL-cholesterol, and enhances serum antioxidant enzyme activity while improving thymus and liver indices in high-fat-diet rats.

DISCLAIMER

Statements throughout this publication have not been evaluated by the FDA. These products are not intended to diagnose, treat, cure or prevent any disease process.

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SHIITAKE MUSHROOM

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