

Shiitake Mushroom: A Tool of Medicine

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ABSTRACT

Medicinal mushrooms have an established history of use in traditional oriental therapies. Contemporary research has validated and documented much of the ancient knowledge. Over the last three decades, the interdisciplinary fields of science that study medicinal mushrooms has sprung up and has increasingly demonstrated the potent and unique properties of compounds extracted from a range of species. Currently, the field is being developed into a very fruitful area. Modern clinical practice in Japan, China, Korea and other Asian countries rely on mushroom-derived preparations.

Mushrooms have been studied for nutritional and medical purposes for its various potential anti-tumoral and immunomodulatory componests like polysaccharides that have been identified. For medical purposes, mushrooms have been consumed to prevent cancer and cardiac diseases, to improve blood circulation and to reduce blood cholesterol level. Some of these mushrooms have also been used for the treatment of physical and emotional stress, osteoporosis, gastric ulcers and chronic hepatitis, for the improvement of the quality of life of patients with diabetes and especially for the stimulation of immunity.

Shiitake has a history of medicinal uses. The mushroom is used as anticarcinogenic, anti-inflammatory, antioxidant, antifungal, antibacterial, antiviral as well as antithrombotic in cardiovascular disorders. This article has been written to throw some light on Shiitake mushroom which has many nutritional values. Many Shiitake preparations came in market containing the active ingredients which can replace many other marketed synthetic medicines and may prove to have promising results with fewer side effects.

Key words: *Lentinus edodes*, lentinan, beta-glucan, eritadenine

Introduction

Shiitake mushroom, the common Japanese name for *Lentinus edodes*, is derived from the mushroom associated with the shii tree (*Castanopsis cuspidate* Schottky). Because Japan is the world leader in production of this type of mushroom, the mushroom is now widely known by this name. These mushrooms are renowned in Far East countries (e.g. Japan, China and Korea) as a food and medicine for thousands of years. In the year 199 A.D., Kyusuyu, a native tribe of Japan, offered the Japanese Emperor Chuai a shiitake mushroom. Even older documents record its use in ancient China where it was referred to as 'ko-ko' or 'hoang-mo'¹.

The cultivation of this mushroom has been practiced for a thousand years with its cultivation originating in China during the Sung Dynasty (960-1127). Both history and legend credit Wu San Kwung as the originator of shiitake cultivation. Almost every mushroom-growing village in China has a temple in his honor². In 1313, Chinese author Wang Cheng recorded shiitake-growing techniques in his Book of Agriculture. He described how to select a suitable site, choose appropriate tools and cut down the trees on which one could cultivate the mushrooms. He outlined the basic methods as follows: Cut the bark with a hatchet and cover

the logs with soil. After 1 year, top the soil and water frequently, beat the logs with a wooden club to induce mushroom production. The mushrooms will appear after a rain^{2,3}. Shiitake mushroom cultivation techniques were probably introduced to Japanese farmers by the Chinese between 1500 and 1600 A.D⁴. At present, shiitake is one of the five most cultivated edible mushrooms in the world⁵. Its production (2 million tons) is second only to button mushroom *Agaricus bisporus*, grown mainly in East Asia. Shiitake is now arousing interest worldwide^{5,6,7,8}. Increasing markets have been spawned, partly by the exotic and well appreciated taste of shiitake and partly by advances in research that has demonstrated its significant medicinal properties. Shiitake mushroom is becoming popular in nutritional and medicinal products throughout Asia, Europe and North America.

Discussion

Shiitake are traditionally well-known edible mushrooms of high nutritional value. Raw or dried forms used in Chinese curative powers of shiitake mushroom are legendary. It was stated in *Ri Youg Ben Cao*, Vol. 3 (1620), written by Wu-Rui of the Ming Dynasty, "shiitake accelerates vital energy, wards off hunger, cures colds and defeats body fluid energy." In later years, it was found that the mushroom contained various important nutrients. Moreover, recent scientific investigations have isolated many compounds and have found evidence of their health promotion activities^{1,7,8,9,10}.

Shiitake mushrooms have excellent nutritional value. Their raw fruit bodies contain water, protein, lipids, carbohydrates as well as vitamins and minerals. It should be noted that amounts of nutrients and biologically active compounds differ in various strains and are affected by substrate, fruiting conditions and methods of cultivation. On a dry weight basis, they have a relatively high nutritional value when compared to commonly consumed vegetables.

Dried shiitake mushrooms are rich in carbohydrates and protein. They contain 58-60% carbohydrates, 20-23% protein (digestibility of

which is 80-87%), 9-10% fiber, 3-4% lipids and 4-5% ash. The mushroom is a good source of vitamins, especially pro-vitamin D₂ (ergosterol) 325 mg % which under ultraviolet (UV) light and heat yields calcitriol. It also contains B vitamins, including B₁, B₂, B₁₂ and pantothenic acid^{1,3,9,10}. Minerals found include Fe, Mn, K, Ca, Mg, Cd, Cu, P, and Zn. Analysis of dried cultured shiitake mycelium gives the following mineral concentrations (in mg/g of dry weight): K, 15.1; Ca, 22; Mg, 44-78; Mn, 1.2; Cd, 0.96; Fe, 2.36; Ni, 52.5; Cu, 89.1; P, 281; Zn, 282; Ge, 3; Br, 11.4 and Sr, 164. Water-soluble polysaccharides amount to 1-5% of the dry weight of the shiitake mushroom. In addition to glycogen-like polysaccharides, (1-4)→(1-6)-α-D-glucans and antitumor polysaccharides, lentinan, (1-3)→(1-6)-β-bonded heteroglucans, heterogalactans, heteromannans, xyloglucans, etc. have been identified. The mushrooms' indigestible polysaccharides which serve as dietary fiber include heteroglycan, polyuronide, β-glucan as well as chitin. Among the free sugars present are trehalose, glycerol, mannitol, arabitol, mannose, and arabinose^{1,7,8,9,10}.

In shiitake mushrooms, dietary fiber consists of water-soluble materials such as β-glucan and protein and water-insoluble substances extractable only with salts, acids, and alkalies such as polyuronide (acidic polysaccharide), hemicellulose, β-glucan with heterosaccharide chains, lignin and chitin present as cell wall constituents. The fatty acids account for 3.38% of the total lipids^{10,11}. Their composition is as follows: linoleic acid (18 : 2), 72.8%; palmitic acid (16 : 0), 14.7%; oleic acid (18 : 1), 3.0%; tetradecenoic acid (14 : 1), 1.6%; stearic acid (18 : 0), 0.9%; and myristic acid (14 : 0), 0.1%.

The aroma components include alcohols, ketones, sulfides, alkanes, fatty acids etc. The major volatile flavor contributors are matsutakeol (octen-1-ol-3) and ethyl-n-amyl ketone. The characteristic aroma of shiitake mushrooms was identified as 1,2,3,5,6-pentathiepane. According to Mizuno¹⁰, the components responsible for the delicious flavor

are monosodium glutamate, free amino acids, low molecular weight peptides, organic acids, and sugars. Their relative ratios are responsible for the variation in flavor naturally seen in this mushroom. Organic acids contributing to the flavor of shiitake mushroom include malic acid fumaric acid α -keto-glutaric acid, oxalic acid, lactic acid, acetic acid, formic acid and glycolic acid.

Anticarcinogenic and Antitumor Effects

Using methods of fractionation and purification of polysaccharides, Chihara *et al.*^{12,13,14} isolated a watersoluble antitumor polysaccharide from fruiting bodies of shiitake which was named "lentinan" after the genus *Lentinus* to which the shiitake mushroom belongs. Chihara was one of the first to report on the antitumor properties of the mushroom stating that lentinan "was found to almost completely regress the solid type tumors of Sarcoma 180 and several kinds of tumors including methylchloranthrene-induced fibrosarcoma in synergic host-tumor system A^{13,14}". The antitumor effect of lentinan was originally confirmed by using Sarcoma 180 transplanted in CD-1/ICD mice¹². Later it showed prominent antitumor activity not only against allogenic tumors such as Sarcoma 180 but also against various synergic and autochthonous tumors and it prevented chemical and viral oncogenesis¹⁵. The molecular formula of β -D-glucan lentinan is $(C_6H_{10}O_5)_n$ and the mean molecular weight is about one million. Its structure was confirmed as β - \rightarrow (1-3)-D-glucopyranan with a branched chain of β - \rightarrow (1-6)-monoglycosyl (branching degree: 2.5), a right-handed triple helix^{7,10,15,16}. It is water soluble, heat stable and alkali labile. That is, β -D-glucan binds to lymphocyte surfaces or serum-specific proteins which activate macrophage, T-helper cells, natural killer (NK) cells and other effectors cells. All these increase the production of antibodies as well as interleukins (IL-1, IL-2) and interferon (IFN-g) released upon activation of effectors cells^{17,18}. Thus, the carcinostatic effect of lentinan results from the activation of the host's immune system. In animal testing of carcinostatic activity,

intraperitoneal administration is used but oral administration is occasionally effective.

The purified polysaccharide has been shown in animal studies to produce strong tumor regression and even the disappearance of sarcoma tumors in 5 weeks, ascitic hepatoma^{13,16,17,19} and Ehrlich carcinoma as well as a number of other experimentally induced cancers in allogenic, syngenic and autologous hosts. It also exhibits preventive activity against chemical carcinogenesis. Injections of lentinan into mice produced either an 80% reduction in tumor size or complete regression in most of the animals tested. However, an intact immune system and a functioning thymus gland were found to be requisite for its anticancer effect^{20,21}. When immunosuppressive agents such as b-benzylthioguanosine or X-radiation were given with lentinan, the antitumor effect decreased. The polysaccharide has also been found to restore the enzyme activity of X-prolyl-dipeptidyl-aminopeptidase which can be depressed in cancer patients and in mice with implanted tumors²². Laboratory tests seem to indicate a role for the adrenal-pituitary axis and central peripheral nervous system including serotonin, 5HT, histamine and catecholamines in lentinan's antitumor activity^{1,9,15,18}.

The oral administration of the polysaccharide to AKR mice exerted strong antitumor activity resulting in raised levels of lymphocytokines, such as IFN-g, tumor necrosis factor (TNF- α) and IL-1 α . Tissue cultures of murine macrophages CRL-2019, β -lymphocytes HB-284 and T-lymphocytes DRL-8179 which were treated with lentinan, showed high levels of activation using flow cytometry. Lentinan-activated immunocytes particularly the T-helper cells, might render the physiological constitutions of the host highly cancer and infection resistant. Adoptive immunotherapy of the immunodeficient mice such as the nude (athymic) mice, β -cell deficient mice and severe combined immunodeficient (SCID) mice via the transfer of the lentinan-activated immunocytes resulted in the inhibition of tumor growth. Lentinan appeared to represent

a unique class of host defense potentiators (HDP), protecting the hosts from the side effects of conventional therapeutic measures and improving various kinds of immunological parameters with no toxic side effects in animal models^{17,18,23,24}.

Hepatoprotective Effects

The injection of lentinan slowed the growth of cancerous liver tumor in rats^{11,16,25}. A polysaccharide fraction from shiitake mushrooms demonstrated liver protection in animals as well as the ability to improve liver function and enhance the production of antibodies to hepatitis B^{7,26}. Lentinan improved serum glutamic pyruvic transaminase (SGPT) and completely restored GPT levels in mice with toxic hepatitis. Crude extracts of shiitake mushroom cultures have demonstrated liver-protecting actions.^{9,11,16,26}

Cardiovascular Effects

The major cause of death in western countries is coronary artery disease, a primary risk factor for which is hypercholesterolemia that contributes to hardening of the arteries. In humans, 50% or more of the total serum cholesterol is derived from de novo synthesis^{16,26,27}. It is known that shiitake mushroom is able to lower serum cholesterol via a factor known as eritadenine (also called 'lentinacin' or 'lentisine'). Apparently, eritadenine reduces serum cholesterol in mice, not by the inhibition of cholesterol biosynthesis but by the acceleration of the excretion of ingested cholesterol and its metabolic decomposition. It has been shown to lower blood levels of cholesterol and lipids in animals. When added to the diet of rats, eritadenine (0.005%) caused a 25% decrease in total serum cholesterol in as little as one week. The cholesterol-lowering activity of this substance is more pronounced in rats fed a high-fat diet than in those on a low-fat diet. Although feeding studies with humans have indicated a similar effect further research is needed. Hobbs^{1,9} and Yang *et al.*²⁷ have shown that shiitake

mushrooms lowered serum cholesterol levels. Various studies have confirmed^{1,7,9,11}, that the mushroom can lower blood pressure and free cholesterol in plasma as well as accelerate the accumulation of lipids in the liver by removing them from circulation.

Immune-Modulating Effects

As was stated earlier, lentinan and other polysaccharides from shiitake mushrooms do not attack cancer cells directly, but produce their antitumor effects by activating different immune responses in the host. Lentinan, for example, appears to act as an HDP, which is able to restore or augment the responsiveness of host cells to lymphocytokines, hormones and other biologically active substances by stimulating maturation differentiation or proliferation of cells involved in host defense mechanisms^{17,18}. Host defense potentiators are functionally different from biological response modifiers. Thus, lentinan is able to increase host resistance against various kinds of cancer and infectious diseases including acquired immuno deficiency syndrome (AIDS)^{7,24}. The initial interactions of lentinan in the human body or animals are not presently known. However, there is a transitory but notable increase in several serum protein components in the α - and β -globulin region, namely, complement C₃, hemopexin, and ceruloplasmin^{7,9,17,18}.

Lentinan can activate NK cells in vitro in the same concentrations that are achieved in the blood plasma of patients treated clinically with lentinan.^{11,18} Natural killer-cell activity is involved in tumor suppression and while these cells do not stimulate T-killer cell activity or do so only under certain conditions, they are strong T-helper cell stimulants both in vitro and in vivo^{1,7,9,11,17,18}. Using the blood of healthy donors and cancer patients, some authors have shown that the polysaccharide is able to stimulate peripheral blood lymphocytes in vitro to increase IL-2 mediated lymphokine-activated killer cell (LAK-cell) and NK cell activity at levels achievable in vivo by administration of clinical doses of lentinan. It has been shown to

inhibit suppressor T cell activity in vivo and to increase the ratio of activated T cells and cytotoxic T-cells in the spleen when administered to gastric cancer patients undergoing chemotherapy^{7,9,18}.

Many interesting biological activities of lentinan have been reported including: a) an increase in the activation of nonspecific inflammatory responses such as acute phase protein (APP) production, b) vascular dilation and hemorrhage in vivo, c) activation and generation of helper and cytotoxic T-cells, b) augmentation of immune mediators like IL-1 and IL-3, colony stimulating factor(s) and migration inhibitory factor, and e) increasing the capacity of peripheral blood mononuclear (PBM) cells of patients with gastric cancer and producing IL-1 α , IL-1 β , and a TNF- α ^{7,9,17,18,23}.

In an in vivo study of rats with peritonitis, combined lentinan-gentamicin treatment had a significantly better survival rate than the controls. Lentinan activated the peritoneal macrophages' secretory activity of active oxygen and produced cytokines, thus enhancing the ability of polymorphonuclear leukocytes (PMNs) to produce active oxygen, which has a bactericidal effect²⁸. It also increases peritoneal macrophage cytotoxicity against metastatic tumor cells in mice, but not against a highly metastatic tumor type²⁹. Some patients treated with lentinan for carcinomatous pleuritis or carcinomatous peritonitis has improved with the disappearance of malignancy, while in another group their condition deteriorated or diminished³⁰. The polysaccharide can activate the normal and alternative pathways of the complement system and can split C3 into C3a and C3b enhancing macrophage activation³¹. Many biological reactions are accelerated and induced by lentinan including the very important phenomenon of infiltration of eosinophils, neutrophils and granulocytes around target tissues.

Lentinan's immune-activating ability may be linked with its modulation of hormonal factors,

which are known to play a role in tumor growth. Aoki³¹ showed that the antitumor activity of lentinan is strongly reduced by administration of thyroxin or hydrocortisone. It can also restore tumor-specific antigen-directed delayed-type hypersensitivity reaction (DTHR). Lentinan is not formally included among the nonspecific immunostimulants (RES stimulants), but it augments the induction of antigen-specific cytotoxic T-lymphocytes, macrophages and other nonspecific immune responses.

Antibacterial Property

Lentinan is therapeutically effective against *Mycobacterium tuberculosis* and *Listeria monocytogenes*.³² Oxalic acid is an agent responsible for the antimicrobial effect of *Lentinula edodes*³³ grown in submerged liquid culture was bacteriostatic against *Streptococcus pyogenes*, *Staphylococcus aureus* and *Bacillus megaterium*³⁴. Lentinan inhibits *Candida albicans* and *S.aureus*³⁵. Lentinan helps to regulate the inflammatory response in the host when encounter pathogens. It also activates the complement system which split C3 into C3a and C3b, enhancing macrophage activation.³⁶

Antiviral Property

Lentinan is able to inhibit replication of Adenovirus type 12, Abelson virus and VSV-encephalitis virus³². Although lentinan itself has no ability to block HIV infection, concomitant treatment with 3'-azido-3'- deoxythymidine suppresses the surface expression of HIV antigens more than does AZT alone.³² *Lentinula edodes* naturally contain antiviral agents known as proteinase inhibitors. Anti HIV activities were reported for mycelia culture medium of *L. edodes* (LEM) and water soluble lignin in LEM^{37,38}. Sulfated lentinan from *L. edodes* completely prevented HIV induced cytopathic effect³⁸. The polysaccharide Lentinan demonstrates effects against influenza virus and polio virus as well as against some bacteria and parasites. These effects are mediated by immune system induction that even delays AIDS

symptomatology appearance. This action would be linked to induction of increased level of interferon. *L. edodes* seems to be one of the most promising stimulator of immunofunctions. This mushroom is tested on HIV positive patients in the USA and in Japan.³⁹

Antioxidant Property

Oxidative damage caused by free radicals may be related to aging and diseases, such as atherosclerosis, diabetes, cancer and cirrhosis⁴⁰. Antioxidant compounds reduce the action of reactive oxygen species (ROS) in damaged tissues during the recovery process⁴¹. Kitzberger *et al* used extracts of *L. edodes* obtained by organic solvents to test the antioxidant activity⁴². Cheung and Cheung⁴³ also reported the antioxidant activity of *L. edodes* against lipid peroxidation. They found that the low molecular weight sub fraction of water extracts of *L. edodes* had the highest antioxidant activity against lipid peroxidation of rat brain homogenate, with IC₅₀ values of 1.05 mg/ml¹⁹. Shiitake enhance the host's antioxidant capacity or upregulating phase-1 and phase-2 enzymes involved in the metabolic transformation and detoxification of mutagenic compounds.⁴⁴ *L. edodes* is also inducer of superoxide dismutase and glutathione peroxidase, the two antioxidant enzymes³⁸. *Lentinula edodes* filtrates and mycelia exhibit Aflatoxin inhibiting effects⁴⁵. They act as an external stimulus affecting the antioxidant states in the toxin producing fungus and leads to inhibition of Aflatoxin⁴⁶.

Antifungal Property

From the fruiting bodies of the shiitake mushroom, a novel protein designated lentin with potent antifungal activity was isolated in 2003.²⁴ It was unadsorbed on DEAE-cellulose, and adsorbed on Affi-gel, blue gel and Mono S. The N-terminal sequence of the protein showed similarity to endoglucanase. Lentin with a molecular mass of 27.5 kDa, inhibited mycelia growth in a variety of fungal species including *Physalosporia piricola*, *Botrytis cinerea* and *Mycosphaerella arachidicola*²⁴.

Anti-thrombotic Effects

Thrombosis, has been shown to be significantly reduced in individuals consuming Shiitake mushroom oil.⁴⁵ The department of Agricultural and Biological Chemistry at Nihon University in Japan has demonstrated that the levels of Lenthionine found in Shiitake mushrooms inhibited platelet aggregation⁴⁵.

Antihypercholesterolemic Effects

Scientific studies involving animals have proved that eritadenine found in shiitake mushrooms is beneficial in reducing the cholesterol levels in the blood vessels as well as low density lipoproteins or LDL cholesterol that are harmful for the body. These researches have confirmed that eritadenine in shiitake has the ability to reduce the cholesterol levels in the blood vessels by 25% in just one week²⁶. And surprisingly, the results after the usage of eritadenine was found to be better in subjects that consumed high protein food compared to those who took low protein food stuff. According to researches by Japanese medical scientists, chemicals present in shiitake help in building up the harmful low density lipoproteins in the liver, where they are modified into high density lipoproteins or HDL cholesterol that are useful for the human system.

Antihypertensive Effects

High blood pressure means your heart has to do extra work and can lead to, if unchecked, a stroke or heart attack. Preliminary studies have suggested that dietary shiitake and other types of mushroom consumption may prevent blood pressure increase⁹.

Antiobesity Effects

Shiitake mushrooms possess many health benefits that can aid weight loss. Eating a well-balanced diet that contains these healthful mushrooms will be the best way to lose weight and keep it off, according to the American Heart Association⁴⁷. Remember to prepare the mushrooms using a low fat, heart-healthy cooking method on your way to weight loss success.

Improves Appearance of Skin

Applying shiitake mushroom extract to your skin may improve its appearance, according to Skincare-News.com⁴⁷. Beauty products aimed at brightening your skin may contain mushroom extract because of its concentration of kojic acid, a natural alternative to hydroquinone, a chemical that bleaches your skin to fade scars and age spots. The antioxidant effects of shiitake are not limited only to protect your internal organs but skin creams and lotions that contains mushroom extract as an ingredient may be able to minimize inflammation of the skin.

Toxicity and Side Effects

Shiitake mushroom is edible, but some individuals may experience minor side effects or allergic reactions. Literature describes^{7,9,12,46} cases of shiitake-induced toxicodermia and shiitake dermatitis. Allergic reactions to the spores of shiitake mushrooms have been reported in workers picking mushrooms indoors, who are prone to an immune reaction to spores called "mushroom worker's lung". Symptoms include fever, headache, congestion, coughing, sneezing, nausea and general malaise⁴⁸. A water extract of the fruiting body was found⁴⁹ to decrease the effectiveness of blood platelets in initiating coagulation. *L. edodes* mycelium has shown no evidence of being acutely toxic, even in massive doses of over 50 mg/day for 1 week, though mild side effects such as diarrhoea and skin rash may occur. As a rule, symptoms disappear after a short period when the body has adapted to the extract. Lentinan has no known serious side effects. However, in clinical trials of patients with advanced cancer, minor side reactions occurred such as a slight increase in glutamate-oxaloacetate transaminase (GOT) and GPT liver enzymes and a feeling of mild pressure on the chest. But these changes disappeared after lentinan administration was stopped.⁴⁹

Dosage and Preparation of Shiitake Mushroom

Shiitake mushroom is prescribed in various

forms. It may be injected as a solution (1 mg/vial) or ingested as a sugar-coated tablet, capsule, concentrate, powdered extract, syrup, tea, wine, and/or as a medicinal dish. Lentinan's anticancer effect is highly dose dependent. The standard dose of the dried fruiting body in tea or in mushroom dishes is given as 6-16 gm, equivalent to about 90 gm of fresh fruiting body. As a tablet, the dosage is usually in the form of 2 gm tablets 2-4/day. Commercial preparations can be found in many countries in health food stores and supermarkets. The tablets are usually made from a dried water extract of the mycelia or fruiting bodies because drying concentrates the lentinan and other active principles. Standardized extracts are also available and they are preferred because the amount of lentinan present is certified and clearly stated on the bottle. Although the fresh form can be a valuable dietary supplement, the quantities one would require for therapeutic doses are so great that its consumption could cause digestive upset. That is why LEM, which is concentrated and easily absorbed, is preferred for medicinal use.^{7,8,9} Fresh and dried shiitake mushrooms are used in medicinal mushroom dishes (Yakuzen). Certain medicinal effects have been recently studied¹¹ and found to reduce the ill effects of certain gourmet diets. These dishes can be prepared in many ways, limited only by one's ingenuity: boiled, grilled, skewered, or on aluminum foil with different types of seasoning. To obtain a concentrate, whole fruit bodies or powdered mushrooms are boiled in water. The extract is then concentrated and is used as a drink. It can also be consumed as a tea: canned "shiitake tea" which contains a concentrated extract or many other shiitake "healthy tea" products sold as mushroom containing tea bags. Shiitake mushroom concentrate can be freeze-dried or spray-dried to form a granular powder. There are many products containing powdered shiitake mushroom extract, such as a mixture of this powder with vitamin C crystals or with medicinal plants such as ginseng. In Eastern countries, the mushroom is mainly used as a concentrate when extracted with boiling water.

Residues from these processes still contain substantial amounts of useful polysaccharide substances, including those effective as antitumor compounds such as β -glucans, nucleic acids, dietary fiber etc. An alcohol extraction product is obtained by preserving fresh or dried shiitake mushroom in alcohol, which has been mixed with sugar or molasses. Some products, including 'healthy shiitake wine' are sold as a nightcap or as a tonic drink^{8,10}.

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