Maitake Extracts and Their Therapeutic Potential – A Review

Mark Mayell

Abstract
Maitake *(Grifola frondosa)* is the Japanese name for an edible fungus with a large fruiting body characterized by overlapping caps. It is a premier culinary as well as medicinal mushroom. Maitake is increasingly being recognized as a potent source of polysaccharide compounds with dramatic health-promoting potential. The most recent development is the MD-fraction, a proprietary maitake extract its Japanese inventors consider to be a notable advance upon the preceding D-fraction. The D-fraction, the MD-fraction, and other extracts, often in combination with whole maitake powder, have shown particular promise as immunomodulating agents, and as an adjunct to cancer and HIV therapy. They may also provide some benefit in the treatment of hyperlipidemia, hypertension, and hepatitis.
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Maitake: A Premier Mushroom

The scientific name *Grifola frondosa* is derived from the griffin, the beast from Greek mythology with the head and wings of an eagle and the body of a lion, and frondosa, meaning leaflike. In Japanese, *mai* means dance and *take* means mushroom, thus "dancing mushroom." It is not known whether the name came about because the fruiting bodies of adjacent fungi overlap each other, looking like nymphs or butterflies in a wild dance, or because mushroom seekers who were lucky enough to come upon maitake in the wild would dance for joy. In feudal times maitake apparently was so valued it was worth its weight in silver. Even in recent times maitake hunters have been known to jealously guard the location of their maitake grounds, sometimes revealing secret spots (where it may fruit for many years) only in a will. Maitake remains highly sought after by chefs and gourmands for its excellent taste and texture (somewhat like chicken or game hen)[1] and for non-culinary reasons by others for its beneficial health effects.

Maitake often occurs as a heavy mass (clumps may weigh many pounds) at the base of stumps and on the roots of oaks, elms, persimmons, and other trees. Like many other fungi, maitake's optimal growing conditions exist within a limited range for temperature, moisture, humidity, and other environmental factors. Parts of northeastern Japan are especially hospitable for maitake, although foraging and development have combined to limit its availability in the wild. Maitake can also be found in the northern temperate forests of Asia, Europe, and eastern North America. While relatively rare in the wild in Japan, maitake is not an uncommon forest

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mushroom in the United States and Canada, where it is known as hen of the woods (because the shape and color of its clusters bear a likeness to the tail feathers of a hen) and sheep's head. Only rarely is it found in the western United States.

Closely related species include *Grifola umbellata*, which the Chinese call zhu ling or chuling, *G. albicans*, and *G. gigantea*. The Chinese sometimes include zhu ling (they use the sclerotium rather than the fruiting body) as an ingredient in herbal tonic formulas. Although zhu ling and the other Grifolas are not as thoroughly studied as maitake, they are thought to have similar compounds and health effects.

Maitake cultivation is a recent development. Only within the past two decades have producers been able to switch from a reliance on foraged maitake to offering cultivated maitake. Current bottle- or bag-culture often makes use of a bed of sawdust/bran/soybean cake (in an 80:10:10 ratio) as the base.[2] Japanese commercial cultivation, mainly for food, started in 1981 with 325 tons.[3] It grew to 1,500 tons in 1985, 8,000 tons in 1991, and almost 10,000 tons in 1993. Commercial maitake production worldwide may now be in excess of 40,000 tons.

Within the past two decades maitake has also begun to be cultivated for use as a dietary supplement. It may be the most versatile and promising medicinal mushroom supplement, though currently less well-known than shiitake (*Lentinus edodes*) and reishi *(Ganoderma lucidum)*.

Mushrooms' Unique and Active Compounds

Some 50 of the 38,000 species of mushrooms have been found to have medicinal properties, according to mushroom researcher Cun Zhuang, PhD. Three have been used as the source for extracts now employed clinically as anticancer drugs in Japan:

◆ Kawaratake (*Coriolus versicolor*) is the source for PSK (Krestin). Developed in the late 1970s, PSK was the first mushroom-based anticancer drug and is now one of the most popular anticancer drugs in Japan. It is taken orally for gastric and other cancers.

◆ Shiitake is the source for Lentinan, which has been approved since the mid-1980s to treat gastric cancer. Because of poor absorption when taken orally, this compound is best administered by injection.

◆ Suehirotake (*Schizophyllum commune*) is used to derive Shizophyllan, which is used to treat cervical cancer (it also is injected).

These anticancer medications, as well as many additional medicinal mushrooms such as reishi, hiratake or oyster (*Pleurotus ostreatus*), and enokitake (*Flammulina velutipes*), contain various compounds with diverse biological and therapeutic effects. The content and bioactivity of these compounds depend on how the mushroom is prepared and consumed.[4] Among the most important constituents are certain polysaccharides, known as beta-glucans, which are bound to proteins. PSK, Lentinan, and Shizophyllan are all forms of beta-glucan. Maitake's prominent immune-boosting effects are thought to be due predominantly to these polysaccharides.

Polysaccharides such as beta-glucans found in a number of medicinal mushrooms (as well as other polysaccharides found in medicinal herbs such as *Echinacea angustifolia*) are increasingly being recognized for their non-specific immunomodulatory effects. These so-called biological response modifiers can be potent antiviral and antitumor agents, not by killing viruses or cancer cells directly but by stimulating the body's innate ability to marshal cellular defenses. Augmenting what Japanese cancer researchers have termed "intrinsic host defense mechanisms" is particularly promising because it is

a property generally lacking in conventional anticancer drugs.

The Immunopotentiating Maitake Fractions

In the early 1980s Japanese mycologist Hiroaki Nanba of the Pharmaceutical University at Kobe was studying various medicinal mushrooms, especially shiitake. He gradually came to the conclusion, however, that the polysaccharides in maitake have a unique structure and were among the most powerful to be studied to date, demonstrating more pronounced antitumor activity in animal tests than other mushroom extracts.[5] Maitake also demonstrated the most promise as an orally effective immunomodulator. This made it potentially much easier to use compared to, for example, shiitake extracts that worked optimally only when administered by injection. Nanba decided to focus exclusively on maitake, and he and a number of other Japanese scientists began to extract various polysaccharides from maitake and test them for antitumor and immunomodulating potential.

In 1984 Nanba identified a fraction found in both the mycelia and the fruit body of maitake with the ability to stimulate macrophages. The fraction can be derived from maitake by treating the fruit bodies with hot water and saturating the resulting water-soluble extract to 80 percent with ethyl alcohol. The precipitate is then treated with acetic acid and an alkaline material. The resulting D-fraction is a standardized form of isolated beta-glucan polysaccharide compounds (beta-1,6 glucan and beta-1,3 glucan) and protein with a molecular weight of about 1,000,000. In 1984 a patent was issued in Japan to Nanba and others.[6]

While other medicinal mushrooms have been shown to have bioactive beta-glucan constituents, Nanba notes that various beta-glucans differ and that the beta-glucans found in the maitake D-fraction have a unique and complex structure, containing both a 1,6 main chain having a greater degree of 1,3 branches, and a 1,3 main chain having 1,6 branches. Most other mushroom-derived beta-glucans have a 1,3 main chain with 1,6 branches only. Other fractions have also been derived from maitake; for example, the X-fraction is a beta-1,6 glucan having alpha-1,4 branches. One theory is that the greater the degree of branching, the higher the likelihood the fraction will reach and activate a greater number of immune cells.

The D-fraction's high molecular weight may also be a factor in its immunomodulating effects, according to research into antitumor activity and glucose consumption by macrophages. One investigation concluded, "These results suggest that an antitumor glucan is not always a multiple enhancer of host defense mechanisms and that a large molecular weight is required to augment multiple immunological activities."[7] A subsequent study by some of the same researchers suggested that "the branching ratio and molecular weight of (1—>3)-beta-D-glucans are important factors for the production of cytokines from macrophages."[8]

A recent review of the existing data on the mechanism of whole mushrooms and isolated mushroom compounds, particularly certain beta-glucans, concluded the antitumor mechanisms of several species, including maitake, are mediated largely by T-cells and macrophages. According to the researchers, "Despite the structural and functional similarities of these glucans, they differ in their effectiveness against specific tumors and in their ability to elicit various cellular responses, particularly cytokine expression and production."[9]

The Culmination of Dr. Nanba's Research

Throughout the late 1980s and into the 1990s Nanba and colleague Keiko Kubo continued to study maitake, trying to improve

upon the antitumor and immunopotentiating activity of the D-fraction. Further purification of the D-fraction yielded the MD-fraction (U.S. Patent #5,854,404), which Nanba and Kubo believe to be even more bioactive than the D-fraction. In appearance the MD-fraction is a hygroscopic powder in shades of brown, is neutral to weakly acidic, and has a molecular weight distributed around 1,000,000.

The MD-fraction is extracted and fractionated from the mycelia and fruit bodies of *Grifola frondosa* or *G. albicans*, *G. umbellata*, or *G. gigantea*. The process is similar to that described in the Japanese patent for the D-fraction; however, Nanba and Kubo added a key step to the D-fraction process, which removes floating or adhering matter by adding alcohol at a final concentration of 20 to 60 percent by volume to the water-soluble Grifola extract. Analysis shows that, like the D-fraction, the main component of the MD-fraction is a glucan/protein complex in which the glucan/protein ratio is in the range of 80:20 to 99:1.[10] Essentially, the D- and MD-fractions have the same beta-glucan configurations, but the MD-fraction is more purified.

The MD-fraction provided superior results over the D-fraction in an antitumor test described in the patent. Each solution was administered intraperitoneally into C3H mice with transplanted MM-46 carcinoma, ten times at a dosage of 0.1 mg/kg to examine its effect on tumor growth inhibition. The researchers found the group given the MD-fraction experienced a significantly stronger inhibitory effect on tumor growth than that of the group given the D-fraction. The researchers also compared the substances' effects on macrophage and killer T-cell activity five days after each test substance was given. They determined that the MD-fraction exhibited stronger antitumor activity and immunopotentiating activity than the D-fraction.[10] Both the D- and MD-fractions are considered to have low toxicity and high safety.

Antitumor Effects of Maitake Fractions

Numerous studies have confirmed that maitake has prominent beneficial effects on immune function.[9,11-16] It promotes the action of not only macrophages, but also a variety of other immune-related cells, such as natural killer (NK) cells and cytotoxic T-cells (Tc) that can attack tumor cells. Maitake also increases the immune-related efficiency of these cells by increasing interleukin-1, interleukin-2, and lymphokines. The end result is an increased defense against infections, AIDS, and cancer.

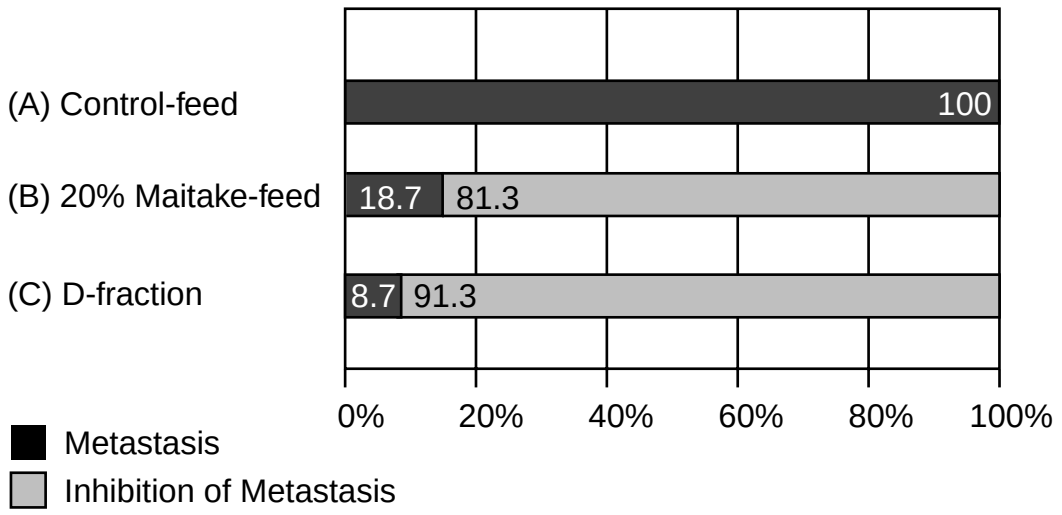
Maitake fractions in particular seem to have a specific antitumor action, potentially slowing the growth of tumors in the colon, lungs, stomach, liver, prostate, brain, and other organs. (It should be noted that any research references to the D-fraction also apply to the MD-fraction, as they are the same beta 1,6/1,3 glucan derived from *Grifola frondosa*.) Centers in the United States have begun to treat cancer patients with the D- and MD-fractions. For example, in February 1998 the U.S. Food and Drug Administration approved an Investigational New Drug Application (IND 54,589) for researchers to conduct a Phase II pilot study on the D-fraction's potential effects on advanced breast and prostate cancers.

Maitake researchers have identified several ways maitake can counter cancer:[17-25]

- By protecting healthy cells from becoming cancerous
- By helping to prevent cancer metastasis
- By slowing or stopping the growth of tumors

Studies have confirmed all three of these potential benefits. Preliminary but unpublished clinical data from a non-controlled study also suggest a fourth potential benefit: maitake may work in conjunction with chemo-therapy to lessen its side effects, such as hair loss, pain, and nausea, and to boost its positive effects.

Figure 1: Inhibition of Metastasis by Maitake.



In a study of maitake's cancer-preventive potential, 20 five-week-old mice were injected once with a carcinogenic substance (3-MCA, methylcholanthrene). Beginning on the fifteenth day after injection, 10 mice were fed 0.2 mg of maitake D-fraction for 15 consecutive days. The other 10 (the control group) received saline solution. After 30 days the number of mice with cancer was 30.7 percent in the maitake group and 93.2 percent in the control group. Nanba notes that Lentinan has also been shown to be effective against MCA, but needs to be administered through i.v. injection for 10 consecutive days to achieve a similar inhibition ratio, "suggesting that maitake D-fraction has the stronger ability to enhance the immune system."[26]

In another study, researchers exposed mice to a known urinary bladder carcinogen (N-butyl-N'-butanolnitrosoamine; BBN) every day for eight weeks and then fed them medicinal mushrooms, including maitake, shiitake, and oyster mushrooms. All 10 mice treated only with BBN developed bladder carcinoma. Mushroom feeding significantly reduced the number of bladder cancers, with maitake being the most effective. Carcinomas were observed in 46.7 percent of the maitake-treated mice compared to 52.9 percent and 65 percent for shiitake and oyster, respectively. The mushrooms also prevented a significant depression in lymphocyte and NK cell activity.[27]

In a study on the potential antimetastatic activity of maitake, researchers injected liver carcinoma cells into the rear footpad of mice. Mice were divided into three groups. The control group received normal feed, while two other groups received either whole maitake powder as 20 percent of their diet or 1 mg/kg of D-fraction intraperitoneally 10 times. After 30 days the mice were observed for tumor foci metastasized to the liver. In the control group 100 percent of the animals showed metastasis. By comparison, the D-fraction prevented 91.3 percent of that total, and the maitake-feed diet 81.3 percent ($p<0.01$) (Figure 1).[28]

Researchers administered 1 mg/kg/day of a purified maitake polysaccharide fraction (MT-2; 3-branched beta-1,6 glucan) intraperitoneally 24 hours after implantation of MM-46 tumor cells, IMC-carcinoma cells, or Meth-A fibrosarcoma cells in the axillary region of experimental male mice. On the twenty-fifth day after the cells were implanted, the solid

Table 1: Tumor Growth Inhibition of Oral and Intraperitoneal Administration of Maitake D-Fraction.

Mice	Tumor system	Growth Inhibition	
		Oral administration	Intraperitoneal
C3H	MM-46 carcinoma (breast)	64% (1.5 mg)	83.2% (1.0 mg)
CDF1	IMC carcinoma (skin)	75% (1.5 mg)	47.7% (1.0 mg)
C57BL/6	B-46 melanoma (skin)	27.3% (1.5 mg)	25.6% (1.0 mg)

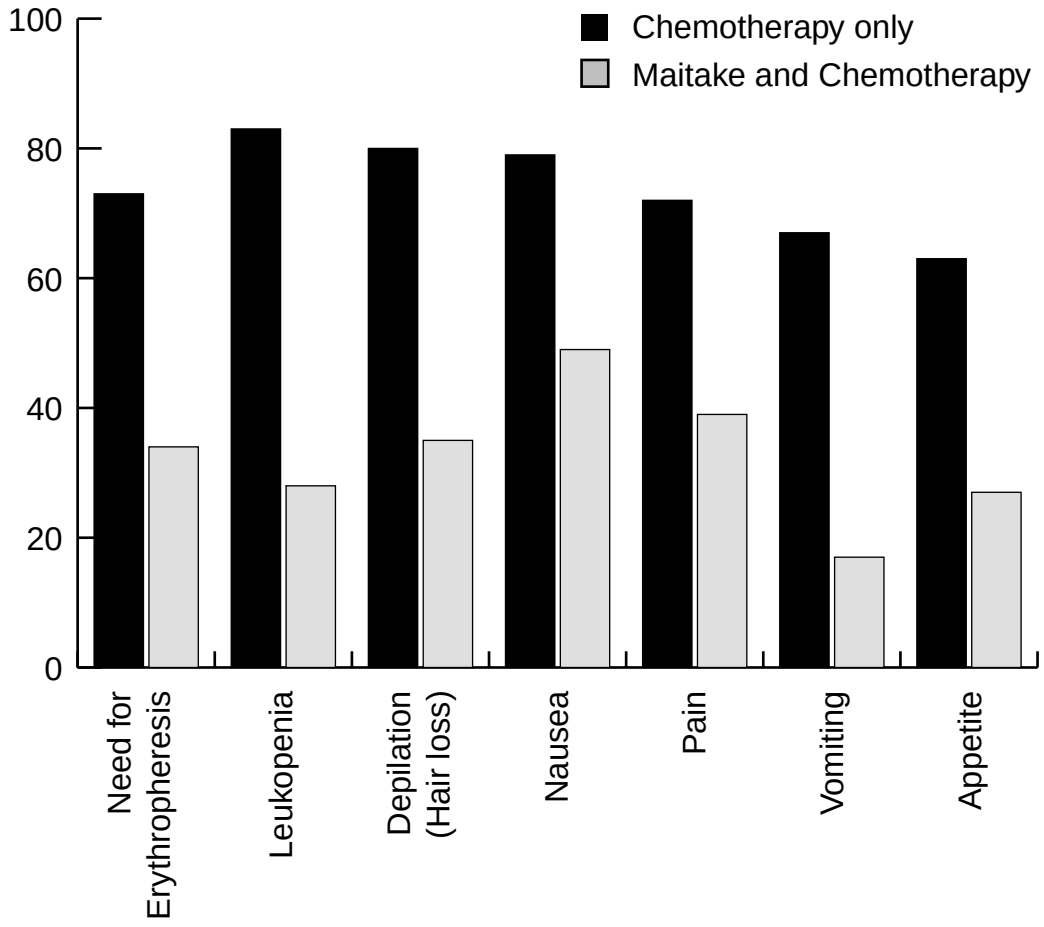
tumors were extirpated and weighed to obtain a tumor growth inhibition ratio. The maitake fraction was found to cause significant tumor growth inhibition, ranging from 25.6 percent for Meth-A fibrosarcoma to 49 percent for MM-46.[29]

A mice study with a similar syngeneic tumor design tested a 6-branched beta-1,3 glucan polysaccharide fraction (LELFD) extracted from maitake. The fraction exhibited significant antitumor effects against Meth-A fibrosarcoma cells and IMC carcinoma cells, although it did not inhibit the growth of leukemia cells.[15] Oral doses of the D-fraction have also been shown to have significant antitumor activities against allogenic and syngeneic tumors (Table 1).[30,31]

Researchers compared the effects on tumor-bearing mice of D-fraction and mitomycin-c (MMC), a popular chemotherapeutic agent, but one that often causes strong side effects. The D-fraction alone inhibited tumor growth more effectively than MMC alone (by about 80- and 45 percent, respectively), with the combination being the most effective (tumor inhibition was further enhanced by almost 98 percent). The apparent synergistic effect between maitake and MMC has been attributed to their distinct modes of action, with maitake stimulating the immune system and MMC directly attacking tumor cells.[32]

Unpublished preliminary clinical data on maitake's use as an adjunct to chemotherapy is described by Nanba.[32] He notes, "A non-randomized clinical study using D-fraction was conducted to see if it is effective against advanced cancer patients as it is against animals. A total of 165 cancer patients in stage III-IV, from 25-65 years old, participated in the study and the data was collected under the cooperation of their medical doctors with major university hospitals and cancer treatment clinics in Japan." Patients were administered either tablets containing maitake D-fraction with whole powder, or the maitake tablets along with chemotherapy. According to Nanba, "The results suggest that breast, lung, and liver cancers were improved by maitake, but it was less effective against bone and stomach cancers or leukemia." The best response rates were from combining maitake and chemotherapy. Nanba adds, "It should be noted, however, that most of the patients under the maitake treatment claimed improvement of overall symptoms, even when the tumor regression was not observed. Various side effects from chemotherapy such as lost appetite, vomiting, nausea, hair loss, and leukopenia (deficiency of white blood cells) were ameliorated by 90 percent of the patients. Reduction of the pain was also reported by 83 percent of the patients."(Figure 2)

Figure 2: Amelioration of Chemotherapeutic Side-Effects by D-Fraction (n=455).



Human Immunodeficiency Virus (HIV)

In the late 1980s Japanese researchers determined in a non-controlled animal trial that oral doses of the D-fraction exhibited an enhancing effect on helper T-cells, the target cells of HIV.[30] This was one of the earliest clinical indications that maitake may be a potential treatment for HIV.

In November 1991 a sulfated maitake fraction was found to be active in a preliminary anti-HIV drug screening test conducted by the National Cancer Institute (NCI). According to the NCI's Developmental Therapeutics Program In-Vitro Testing Results, the maitake test compound showed significant dose-related antiviral activity. Although the sulfated maitake fraction resembled the anti-HIV potency of AZT (zidovudine, formerly azidothymidine), it was not considered a promising treatment because of potential cellular toxicity *in vivo*.

Since then, much of the research into the immunomodulating effects of MD-fraction supports its potential use against HIV. The MD-fraction was also the subject of a recent long-term human study on its potential to

benefit HIV-infected patients. Nanba and colleagues looked at the effects of 6 g of tablets or 20 mg of purified MD-fraction together with 4 g of tablets per day for 360 days on 35 HIV-positive subjects. The researchers monitored CD4+ (helper T-cell) counts, viral load, symptoms of HIV infection, status of secondary disease, and subjects' sense of well-being. Effects on the helper T-cell count and viral load were variable: helper T-cells increased in 20 patients, decreased in eight patients, and remained static in four patients. Viral load decreased in ten patients, increased in nine patients, and was static in two patients. Some 85 percent of respondents, however, reported an increased sense of well-being with regard to various symptoms and secondary diseases caused by HIV. The researchers concluded that the MD-fraction appears to work on several levels: by direct inhibition of HIV, stimulation of the body's own natural defense system against HIV, and making the body less vulnerable to opportunistic disease.[33]

Preliminary unpublished clinical reports suggest a maitake D-fraction liquid extract mixed with DMSO (dimethylsulfoxide) applied topically has promise as a treatment for Kaposi's sarcoma, the skin tumor that has claimed the lives of many people suffering from AIDS.

Additional Potential Effects

The Japanese have long recognized whole maitake as a tonic or adaptogen — a substance that seems to balance bodily functions and to enhance wellness, vitality, strength, and vigor. Practitioners who have begun to use maitake in their clinical practice have reported beneficial effects on chronic fatigue syndrome,[34] persistent vaginal *Candida albicans* proliferation,[35] and uterine fibroids.[36] Studies conducted on whole maitake powder and other forms of the mushroom over the past two decades suggest it may also play a beneficial role in the treatment of other ailments.

Diabetes

At least two studies have suggested antidiabetic effects for maitake. In one, Japanese researchers fed genetically diabetic mice a diet containing 20-percent whole maitake powder for eight weeks. The maitake was shown to inhibit a rise in blood glucose. The researchers also observed glucose-lowering activity in the X-fraction. They concluded that their findings suggest maitake is effective at lowering blood sugar in diabetic animals.[37] A subsequent study by Kubo and Nanba, also done on genetically diabetic mice, sought to identify the active material and examine its mechanism. Again, maitake inhibited significant blood glucose increase, with the antidiabetic mechanism of maitake or the X-fraction being directly associated with insulin receptors. According to the researchers, their results suggest maitake could increase insulin sensitivity.[38]

Blood pressure

Powdered whole maitake has been shown in animal studies to lower blood pressure and to prevent blood pressure increase. For example, the blood pressure of spontaneously hypertensive rats (SHR) was significantly reduced by maitake powder feeding (5 percent of the diet) for nine weeks.[39] A similar feeding protocol over eight weeks, beginning when the rats were 10 weeks old and had well-established high blood pressure, was also successful. The researchers concluded the results support the contention that maitake not only suppresses the development of hypertension, but also lowers already elevated blood pressure.[40] In a third study by some of the same researchers, spontaneously hypertensive rats were fed a five-percent maitake powder diet for nine weeks and compared to control and shiitake-fed rats. Adverse histological changes, including necrosis of the medial smooth muscle cells and fatty liver development, were essentially the same in the control and shiitake-fed rats. On the other hand, except for large

amounts of glycogen observed in the livers, the maitake-fed rats were normal in all respects. According to the researchers, "Dietary maitake seems to play an important role in preventing the histological degenerative changes in SHR and thus may imply some benefits to be gained through blood pressure reduction and an improvement of lipid metabolism."[41]

Cholesterol and Triglycerides

A number of studies have examined maitake's effects on serum lipids, including cholesterol and triglycerides, with somewhat mixed results. In a study published in 1988, dried and powdered maitake, as five percent of the feed of spontaneously hypertensive rats, significantly lowered levels of VLDL and total serum cholesterol.[42] Another study conducted on spontaneously hypertensive rats fed a diet consisting of five-percent maitake powder for eight weeks, however, found no difference in plasma total and free cholesterol, tri-glyceride, and phospholipid levels compared to controls. (Shiitake did not reduce blood pressure but did lower these other factors.)[40] More recently, Japanese scientists fed rats a high-cholesterol diet and measured the effects of fortifying the diet with 20-percent maitake dried powder. The researchers found that maitake inhibited fat accumulation in the liver and caused an initial reduction in total cholesterol. By day 25, however, the difference in total cholesterol was no longer significant. The maitake-fed rats did maintain baseline values for HDL, which usually decrease on a high-cholesterol diet.[43] In a subsequent study with a similar protocol, maitake-fed rats experienced significant and lasting reductions in serum cholesterol and triglycerides, and a similar maintenance of HDL levels.[44] One observer noted the inconsistent findings may be due to lack of standardization of maitake powder in the studies, and the fact that the lipid lowering constituent apparently has not yet been completely defined.[1]

Liver Ailments

A number of studies suggest maitake may also be effective in the prevention or treatment of liver disorders. In the early 1990s Chinese researchers conducted a pilot study on 32 patients with chronic hepatitis B. At an international symposium on shiitake products held in China in 1994, the researchers revealed that those patients who took a maitake fruit body polysaccharide preparation showed positive signs (such as a higher recovery rate in alanine transferase levels) compared to patients in the control group provided routine treatment.[45] In another study, scientists fed Sprague-Dawley rats a high-cholesterol diet and measured the effects of fortifying the diet with 20-percent dried maitake powder. The researchers found maitake inhibited harmful fat accumulation in the liver.[43] Finally, researchers tested maitake (powdered fruit body, the D-fraction, and the X-fraction) as a treatment for experimental mice suffering from hepatic damage and found that autoimmune chronic hepatitis occurred more severely in control mice than in maitake-treated mice.[16]

Weight Control

Maitake provides some B vitamins, ergosterol/provitamin D2, magnesium, potassium, calcium, unsaturated fatty acids, phosphatidylserine and other phospholipids, and protein. Maitake does not contain vitamins A or C although substances with chemical properties similar to ascorbic acid have been identified in maitake.[46] Because maitake is rich in fiber yet low in calories and fat, it has been cited as a potential weight-loss aid. Animal studies have shown that maitake as a major component of the diet can inhibit weight gain. When rats were fed dried maitake powder as 20 percent (by weight) of a high-cholesterol diet, it significantly inhibited increases in body weight and body fat.[43] A similar protocol promoted improved fat metabolism among

maitake-fed rats. Maitake-fed rats weighed 24.9-percent less than control rats at the end of the study.[44] Feeding tests conducted on spontaneously hypertensive rats showed a weight-inhibiting effect for maitake.[47] In a preliminary clinical study conducted on 30 overweight patients, researchers gave subjects maitake tablets equal to 200 g fresh maitake daily for two months. Even though subjects made no changes to their regular diets, all lost weight. Average weight loss was 7-13 pounds, and one subject lost 26.4 pounds. A few patients reported slightly looser stools as a side effect.[48]

Dosage

Further research may help clarify issues relating to dosage. Data from feeding studies done on animals fed a 5-20 percent maitake diet by weight are difficult to apply to humans, since such a maitake-rich diet would be difficult for most people to follow. One recent animal study investigated the clearance of two kinds of glucans (GRN from *Grifola frondosa* and SSG from *Sclerotinia sclerotiorum*) from the blood following multiple dosing of mice with an autoimmune disease. Researchers administered 250 mcg once per week intraperitoneally to mice for 35 weeks. Blood glucan concentrations were determined to be high (about 20 mcg/mL for GRN and 200 mcg/mL for SSG). The researchers concluded, "These findings suggest that administration of a large quantity of the glucan saturated the reticuloendothelial system, resulting in circulation of the glucan in the blood."[49]

In his discussion of maitake dosing in *Medicinal Mushrooms*,[50] Hobbs notes that oral doses of the D-fraction that have been shown to be effective as antitumor and immunopotentiating agents in mice are approximately 0.75 mg/kg of mouse weight. He notes, "Although it is difficult to compare the activity in mice with humans, assuming a 1:1 activity ratio would mean that a comparable dose of D-fraction, found in the quantity of 4 mg/g of fruit body, is 47.25 mg for a 140-pound person—the amount contained in about 11.81 grams of maitake fruiting body." One product manufacturer says the therapeutic amount of maitake D-fraction is from 0.5mg to 1.0 mg/kg of body weight per day. That would amount to an approximate daily dose of 35-70 mg of the D-fraction.

Commercial preparations of the D- and MD-fractions typically provide 3-25 mg of the standardized extract along with 75-250 mg of the whole powder per capsule. Capsules of the whole powder typically range in size from 100-500 mg. Liquid extracts are also available, some standardized, for example, for 1 mg D-fraction per drop. Some capsule products are also concentrated and standardized for a minimum (such as 30 percent) of polysaccharides, including the beta-D-glucan fraction. Typical label-recommended daily disease-preventive doses range from 12-25 mg extract/200-250 mg whole powder, and 500-2,500 mg whole powder.

Conclusion

Maitake is among the most promising natural sources of immunotherapeutic products. Standardized beta-glucan extracts such as the D- and MD-fraction show particular potential as carcinostatic agents that can be used in conjunction with conventional medical treatments to treat cancer. The fraction extracts have an important ease-of-use advantage over similar anticancer mushroom derivatives, such as Lentinan and Shizophyllan, by being better absorbed when administered orally. Extracts, whole maitake powder, or a combination of both (such as is offered in most of the commercially available maitake fraction supplements) have also been shown effective in studies on HIV, diabetes, hypertension, liver ailments, and weight control. Beneficial effects on hyperlipidemia have been inconsistent.

Most of the published studies to date have been animal studies; additional human

studies and clinical trials in particular are needed. Although it may be difficult to investigate structure-activity correlations because of the structural complexity of polysaccharides and variations in the protein and amino acid composition,[2] further studies are needed to identify the unique contributory effects and mechanisms of action of fractions and other maitake constituents. Although the beta-glucans have been identified as the likely active constituents responsible for beneficial effects on cancer, immunity, and HIV, it is less clear which constituents may promote effects on blood sugar and blood lipids.

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Correction

Effects of Black Currant Anthocyanoside Intake on Dark Adaptation and VDT Work-induced Transient Refractive Alteration, *Altern Med Rev* 2000;5(6):553-562.

Due to a mistake in translation from Japanese characters to English symbols, errors were made in tables 3, 4, and 5. The Å} should have been ±.