

Maitake D-Fraction: Apoptosis Inducer and Immune Enhancer

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Maitake, The King of Mushrooms

Maitake is indigenous to Northern Japan. For hundreds of years, this rare and tasty mushroom has been praised by traditional Japanese herbalists. Maitake literally means, "dancing mushroom." 8 Maitake is a giant mushroom that often reaches 20 inches in diameter and that may weigh up to 100 pounds. Such unique characteristics and potential health benefits are why it is often considered the "king of the mushrooms." Maitake is still one of the most valuable and expensive mushrooms in Japan today.

Maitake mushroom has been available via cultivation since the mid-1980's, enabling mycologist and pharmacologists to study the medicinal properties that have been claimed in anecdotes and folklore regarding this mushroom. Numerous physiologic benefits of maitake have been postulated, ranging from antitumor effects to treatment for hypertension, diabetes, hypercholesterolemia, obesity and hepatitis B infection. 3-7,9-12

Maitake's antiviral activity against human immunodeficiency virus (HIV)/auto-immune deficiency syndrome (AIDS) was confirmed by the U.S. National Cancer Institute in 1992.

Maitake D-Fraction

Most research on maitake has been focused on the use of maitake D-fraction for treatment of various malignancies. The bioactive D-fraction that is extracted from maitake is the protein-bound polysaccharide compound and is prepared by a standardized procedure developed by Maitake Products, Inc. (Ridgefield, New Jersey). Among the various maitake fractions that have been prepared, D-fraction was found to be the most potent for enhancing the immune system via oral administration or injection, (effective regardless of route of administration) leading to the highest reduction rate in cancer proliferation. 14-16

D-fraction as an Immune Booster

Maitake D-fraction has been shown to have an antitumor effect on tumor-bearing mice, 14 with enhanced cytotoxic activity of macrophages and elevated production of interleukin-1 leading to the activation of cytotoxic T-lymphocytes (CTLs). 17. These findings are highly suggestive that D-fraction acts not only via direct activation of various immune effectors (macrophages, CTLs, natural killer

(NK) cells, etc) targeting tumor cells but also via potentiating the activity/production of various lymphokines. Thus D-fraction appears to have a potent immunostimulatory activity, which may account primarily for its anti-tumor effect on cancer cells.

D-Fraction as an Apoptosis Inducer- Prostate Cancer

Prostate cancer is the most common malignance with high mortality in elderly men in the United States. In 1999, cancer statistics noted that approximately 140,000 new cases and more than 39,000 deaths were expected to occur annually. 19

"Because of the total failure of chemotherapy treatment of prostate cancer, an improved efficacy of chemotherapy is urgently required." 22

This high mortality is attributable primarily to disease progression to a hormone-refractory or androgen-independent cancer state. ...Unfortunately current conventional therapies for hormone-refractory prostate cancer are ineffective. 22

Androgen ablation, brachytherapy (radioactive seeds implanting), and chemotherapy are viable therapeutic options but have not been able to achieve the expected level of efficacy.

To explore a more effective modality for treatment of prostate cancer, a research group from the Department of Urology at New York Medical College (Valhalla, New York), has recently conducted a study on the ability of maitake D-fraction to induce apoptosis activity against human prostatic cancer PC-3 cells (the most aggressive and metastatic cancer cells) in vitro. 23

Experiments were performed, including a dose-response study and examinations of potentiation with Vitamin C and chemosensitizing effect on anticancer drugs.

The Results:

Potent Apoptosis-Inducing Activity

When PC-3 cells were treated with D-fraction at a concentration of 480 ug/ml, almost complete cell death (>95%) was observed in 24 hours, accompanied by "cell blebbing" (vesicle formation) and considerable damage in the plasma membrane assessed by lipid peroxidation assay. These cellular alterations are indicative of oxidative stress (generation of oxygen free radicals), which appears to subsequently cause discrete DNA fragmentation in cancer cells. Histologic (in situ hybridization) and molecular analysis then confirmed that cell death induced by D-fraction had resulted most likely from apoptosis suggesting that the D-fraction is a potential apoptosis inducer.

Synergy with Vitamin C

As little as 30-60 ug/mL (one sixteenth to one eighth of 480 ug/mL) of D-fraction combined with 200uM of vitamin C was found to be nearly as effective as 480 ug/mL of D-fraction alone, resulting in a >95% cell death. It has been reported anecdotally by a number of doctors and patients that D-fraction appeared to work very well (cooperatively) with vitamin C. Such synergy has now been evidenced in this study.

Chemosensitizing Effect

It was of additional interest to explore a possible chemosensitizing effect of D-fraction on anticancer drugs that are currently in use. Because of the total failure of chemotherapy in the treatment of prostate cancer, 22, an improved efficacy of chemotherapy is urgently required. Compared to approximately a 50% reduction in cell viability induced by carmustine (a common Chemotherapeutic agent used in brain tumor treatment) alone, approximately a 90% reduction in viability was attained when 60 ug.mL of D-fraction was combined with carmustine. This study implies that D-fraction may also have a chemosensitizing activity on certain anticancer drugs, helping to improve the efficacy of chemotherapy.

D-Fraction as a Metastasis Inhibitor

Inhibition of cancer metastasis is another critical issue in the slowing down of cancer progression or prolonging the survival time. This aspect of cancer treatment was addressed in a 1995 study of maitake D-fraction.²⁵ The results suggest that maitake preparations are capable of preventing tumor metastasis, presumably by necrotizing tumor cells present in the blood and /or lymphatic vessels via the activated immune-competent cells.

Clinical Trials in Human Subjects

Although a number of animal studies have confirmed maitake's ability to inhibit cancer, not many human trials have yet been conducted. To test whether the efficacy of D-fraction demonstrated on animals 14,15 could be verified in patients with cancer, a non-randomized clinical study was conducted on 165 patients (25-65 years old) with various types of advanced cancers. **The results showed that tumor regression or significant symptomatic improvements with D-fraction were observed in 73% of patients with breast cancer, 67% of patients with lung cancer, and 47% of patients with liver cancer. When D-fraction was given with chemotherapy, the response rates improved from 12% to 28%.**

Overall, the following trends were found: the clinical status of patients with breast, prostate, lung, and liver cancers was improved significantly with D-fraction, while the D-fraction was less effective on subjects with bone and stomach cancers or with leukemia.

It is important to note that many side effects of chemotherapy on all patients with all types of cancers were ameliorated when D-fraction was given with conventional treatment. **Adverse symptoms, such as nausea, hair loss, and leukopenia, were alleviated in 90% of the patients in the study. A reduction in pain was also reported in 83% of the study patients.**

Based on the above studies and the in vitro prostate cancer study, it is conceivable that maitake D-fraction may work cooperatively with chemotherapy, implying that D-fraction should be considered as a valuable adjuvant in ongoing cancer chemotherapy.

Effects of D-fraction on HIV/AIDS and Kaposi's Sarcoma

Both the National Institute of Health in Japan (Tokyo) and the U.S. National Cancer Institute (Bethesda, Maryland) have confirmed that maitake D-Fraction was able to prevent the HIV-mediated destruction of T-helper lymphocytes up to 97% in vitro.¹³

These findings suggest that D-fraction may even help to prevent or slow down the progression of HIV to full-blown AIDS. Several physicians who used D-fraction for the treatment of patients with HIV/AIDS have also reported that oral administration of D-fraction had significantly improved the clinical conditions of patients with Kaposi's sarcoma (even those who were undergoing radiotherapy and other AIDS-related symptoms).²⁶

Toxicity

The FDA has exempted D-fraction from a phase I study of toxicology

Maitake D-fraction (liquid form) and maitake tablets (whole crude powder) were tested on mice to assess potential toxicity. ¹⁸

Based on a pilot study indication the optimal dose of 1 mg/kg of D-fraction for antitumor activity, a ten-times-higher dosage was given to mice for 30 days. On the thirty-first day, no abnormal symptoms or signs were observed when mice were killed and their organs and blood thoroughly examined.

Similar tests were repeated using maitake tablets and essentially the same results as the D-fraction tests were obtained with no toxic or adverse effects. The researchers concluded that both maitake D-fraction and tablets are safe with no toxicity. Indeed, such safety is supported further by the fact that the FDA has exempted D-fraction from a phase I study of toxicology. ²⁶

FDA Approval of the IND for D-fraction for Breast and Prostate Cancers

In 1998, the Food and Drug Administration (FDA) granted Maitake Products, IN (Paramus, New Jersey), an investigational new drug application (IND) to conduct a phase II pilot study using maitake D-fraction on patients with advanced breast and prostate cancers. These studies are currently underway at Metabolic Associates (Florham Park, New Jersey) to evaluate the immune stimulatory effect of D-fraction on tumor size, tumor makers, immune assays, clinical symptoms, and quality of life of patients. Other independent institutions are also planning to conduct similar trials.

Recommended Maitake Dosage

Fukumi Morishige, M.D., Ph.D, a renowned Japanese surgeon and a member of the Linus Pauling Institute, Corvallis, Oregon, explains that taking small amounts of vitamin C along with the mushroom supplements will facilitate absorption of polysaccharides and enhance their effectiveness further.²⁷ Such increased absorption renders polysaccharides more accessible to immune cells, including macrophages and NK cells. As, mentioned earlier, the synergy with vitamin C was also demonstrated by the study on maitake D-fraction-induced apoptosis in prostate cancer PC-3 cells. ²⁹

The following dosages of maitake D-fraction and maitake tablets for adults are recommended. (but not established)

- 1-4 per day of maitake tablets for prevention and 4-7 grams for therapeutic self-help. (e.g. for patients with chronic immune dysfunction).
- 5-6 drops of maitake D-fraction (GrifronPro D-fraction®; Maitake Products, Inc.) 3 times per day, for health maintenance and 15-20 drops, 3 times per day for therapeutic purposes.
- Optionally, 250-1000 mg of Vitamin C can be taken with maitake D-fraction or tablets as described above.

Note: Please, consult your physician/healthcare professional as to what dosage you should be taking for your condition. To learn more about this natural healing agent, see Maitake.com.

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