Maitake D-fraction: Healing and Preventive Potential for Cancer

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Abstract

I have been studying medicinal mushrooms for the last 15 years and have reported that of all mushrooms studied, Maitake Mushroom (Grifola frondosa) has the strongest activity in tumor growth inhibition both in administered orally and intraperi-toneally.[1,2,3] *In this report, Maitake extract D-fraction was investigated to determine its effectiveness not only on the inhibition against tumors already growing, but also on the inhibition of formation of the secondary focus due to metastasis of tumor cells in lymph and/or blood. In the tests of cancer inhibition rates on mice bearing MM46 (breast cancer), they were bred for one month with foods containing 20% edible mushroom powder. The result was that Maitake outperformed all other mushrooms. Through the 31 day oral administration, total remission of the tumor was visibly confirmed on four out of ten Maitake fed mice. The remaining six rodents also indicated almost 90% suppression rate compared to untreated (control) mice. Most other mushroom extracts are reported ineffective when given orally.*[4,5] *The results of human studies on Maitake D-fraction is reported which indicated strong potential of Maitake D-fraction for cancer treatment.*

Introduction

Maitake (Pron. "my-tah-key") is indigenous to northern part of Japan. The basket-ball sized mushroom, weighing sometimes over 50 pounds, grows on the foot of old Japanese oak trees. For hundreds of years, this rare and tasty mushroom has been prized in traditional Japanese herbology. Maitake literally means "Dancing Mushroom". People who found the mushroom in deep mountain valleys started dancing with joy since they knew its delicious taste and the health benefits. Also, in the feudal era, it could be exchanged with the same weight of silver. Maitake was, and still is, one of the most valuable and expensive mushrooms.

This legendary giant mushroom has been available by cultivation since the mid 1980s which gave opportunities for mycologists and pharmacologists to study the various medicinal properties on the mushroom as claimed in anecdotes and folklore. In addition to its antitumor effect, anti-hypertension, anti-diabetes, anti-obesity and anti-hepatitis activities have been found in Maitake. Its anti-HIV activity was also confirmed by both Japan National Institute of Health and U.S. National Cancer Institute in early 1992.

Maitake D-fraction

Among the various fractions in the process of standardization of the mushroom extraction, it is known that Maitake D-fraction is most potent in enhancing the immune system, demonstrating highest cancer inhibition in oral administration.[3,6] The protein-bound Maitake D-fraction is the acid-insoluble, alkali-soluble and hot water extractable fraction (1,6 beta-glucans carrying 1,3 branched chains) with molecular weight of about one million. Maitake D-fraction has strong ability to potentiate and activate the cellular immune system. We investigated how much each immune-competent cell is activated by the administration of Maitake D-fraction. Mice in experiment groups were administered either 0.5 mg/Kg of D-fraction by I.P. injection for 10 days or 1.0 mg/Kg of D-fraction by oral administration for 10

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days. The activity of Natural Killer cells, cytotoxic T-cells and delayed-hypersensitive T-cells were all increased by 1.5-2.2 times by Maitake D-fraction. Also, it was observed that production of interleukin-1 (which activates T cells), and super-oxide anion (which damages tumor cells) were enhanced. The production of interleukin-2 was also observed to increase by 1.7 fold (**Table 1**). From these results it may be concluded that the cellular immune-competent cells ability to inhibit tumor growth may be potentiated by Maitake D-fraction.

The purified D-fraction extract and Maitake crude tablets were tested using mice to investigate acute and chronic toxicity. Based on a previous animal test which indicates the optimal dose of 1mg/kg of D-fraction for anti-tumor activity, ten times more dosage was employed intraperitoneally for 30 days. On the 31st day, no abnormal symptoms were observed, when mice were sacrificed and their organs and blood were checked. Furthermore, 5 mg/kg of D-fraction was injected for 120 days and the toxicity was investigated in the same manner. Since no abnormality was found in this test, we came to the conclusion that there is no toxicity in the D-fraction. At present, it is not permitted to inject D-fraction into the human body, therefore, in our study the D-fraction was used via oral administration. Maitake tablets were also investigated for possible toxicity. Maitake has been appreciated by the Japanese people as the premier culinary mushroom for hundreds of years, and it is therefore unlikely to exhibit any toxicity. However, we did the same test as was done with the D-fraction, by feeding it to mice by mixing it in their diet at a 1:4 ratio for a period of 13 months. After completion of these tests, we concluded that both Maitake D-fraction and the tablets made of Maitake crude powder were safe with no toxicity.

Clinical Results

A number of animal tests have confirmed Maitake's strong ability in cancer inhibition.[7-10] but human trials have not been conducted until recently. 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 the western part of Japan. Patients were either taking Maitake D-fraction with crude powder tablets only, or Maitake D-fraction, crude tablets in addition to chemotherapy. Tumor regression or significant symptom improvements was observed in 11 out of 15 breast cancer patients, 12 out of 18 lung cancer patients and 7 out of 15 liver cancer patients. If Maitake was taken in addition to chemotherapy together, these response rates improved by 12-28 percent.

Figure 1 is the summary of the trial results against various cancer patients. The criteria to judge the effectiveness are established as follows. A positive response is defined as one of the following:

1) if the size of tumor in CT or MRI screen reduced or stayed unchanged.
2) if the value of tumor mark decreased.
3) if T, N or M factors reduced or remained unchanged.
4) if the remaining life expectancy indicated by the doctor was prolonged by more than 4 times.

As can be seen, these 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 following are some of the typical cases which demonstrated improvements by taking Maitake D-fraction and tablets. **Table 2** (page 46) summarizes the results of these cases.

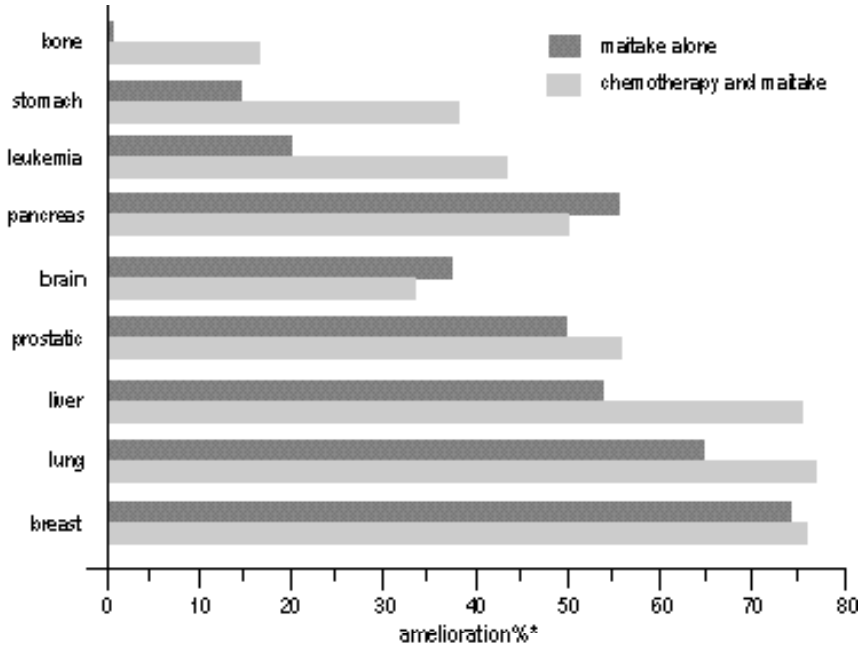
51 years old, male, Liver cancer (hepatocellular carcinoma)

He had received Adriamycin (ADM)

Table 1. Activation Ratio of Immune-competent Cells and Interleukin Products by D-Fraction Treatment

	Ratio (treatment/control)
Saline injection (as control)	1.00
D-fraction injection	
Natural killer cells	1.52
Lymphokine activated killer cell	1.64
Cytotoxic T cell	2.22
Interleukin-1 (IL-1)	1.98
Interleukin-2 (IL-2)	1.73

Figure 1. Effects of Maitake D-Fraction on Cancer Patients



*Tumor regression and/or significant symptomatic improvement

since 1993, but refused it because of little effectiveness and severe side effects of chemotherapy. He took 35 mg of D-fraction and 4 g of Maitake caplet per day. After 8 months, the level of bilirubin and albumin are improved as well as T and N factors. The value of bilirubin reduced to 1.8 mg/dL from 4.7 mg/dL. Also, albumin improved from 2.1 g/dL to 3.7 g/dL and the prothrombin activation was increased to 92% from 36%. Meanwhile, T-factor improved from 3-4 to 1-2 and N-factor changed from 0-1 to 0. T-factor 3 means that tumor diameter is more than 2 cm and some tumors remove into blood vessels. N-factor 1 means that the tumors

Patient		Cancer Type	Treatment Start date		Remarks
Age	Sex		Before	D-Fraction + Tablet	
51	Male	Liver Cancer (hepatocellular carcinoma)	3/93 Adriamycin (ADM)	12/93 35 mg + 4.0g	as of 5/95 stage III to stage II
56	Female	Liver Cancer (hepatocellular carcinoma)	1/94 TAE, CP, AMD, 5FU	12/94 55mg + 6.0g (+5FU)	as of 7/95 stage III to stage I
53	Female	lung Cancer (epidermoid carcinoma)	11/93 CP, AMD, CDDP	3/94 50mg + 6.0g	as of 5/95 stage IIIb to stage I
71	Male	lung Cancer (epidermoid carcinoma)	No Treatment	8/93–4/95 (died) 70mg + 6.0g	as of 3/95 stage IV to stage IIb bid only three months before treatment
45	Female	BreastCancer (intraductal carcinoma) ER+	4/92 focus dia 1.8 cm removed 4/94 focus dia 0.9 cm recurred	5/94 100 mg + 5.0 g	as of 6/95 focus disappeared
44	Male	Brain Tumor (astocytoma)	2/94 CCNU (lomustine)	10/94 100 mg + 6.0 g	as of 1/95 Egg sized tumor disappeared

Table 2 : Cases of Typical Improvement by Maitake Treatment

metastasized to lymph nodes.

56 years old, female, Liver cancer (hepatocellular carcinoma)

She was diagnosed in stage III with serum bilirubin of 3.5 mg/dl, albumin of 2.8 g/dl and prothrombia activation of 48%. By eye observation, T-factor was 3, N-factor as 1 and M-factor as 0. She received transcatheter arterial embolization (TAE) in January, 1994, and 10 mil of lipiodol, 15 mg of ADM and 100 mg of Cisplatin (CDDP) were administered by injection. Then, 200 mg of 5-FU was orally administered for 60 consecutive days but no improvements were observed. In December, 1994, she started taking 55 mg of D-fraction liquid and 6 g of Maitake tablets everyday. As of July, 1995, value of bilirubin was 2.7, albumin 3.1, and prothrombia activation was improved to 63%. She is now diagnosed as stage I.

53 years old, female, Lung cancer (epidermoid carcinoma)

In November, 1993, she was diagnosed as stage III-A according to the TNM classification by UICC (Unia Intern Contra Cancrum). CDDP 80 mg/m, CPA 350 mg/m and ADM 50 mg/m were administered. However, she gave up taking these chemos in March, 1994, because of severe side effects. Since then, she took 100 mg/m of Etoposide with 50 mg of D-fraction and 4 g of tablets. After 14 months, she improved to stage I.

71 years old, male, Lung cancer (epidermoid carcinoma)

He was diagnosed as advanced stage IV but refused to take chemotherapy. He had taken D-fraction 70 mg and 6 g tablets everyday but unfortunately died 20 months later. However, he showed improvement and was diagnosed as stage III-A before he died. As he was told he had only 3 months to live by his doctor, Maitake must have contributed to extending his life for 17 more months. T-factor 2 means that tumor size

is more than 3 cm and tumors advanced to the hilus. N-factor 2 means that tumor metastasized to lymph nodes (homolaceral mediaspinum). M-factor1 means that there is remote metastasis.

45 years old, female, Breast cancer (intraductal carcinoma)

ER+ (Estrogen receptor positive) was observed on this patient who had 1.8 cm dia. of tumor focus and had the rigid pleura. In April, 1992, she had surgery to remove the focus and then received mild chemotherapy such as 5-FU and ADM until February, 1994, but a cancer recurrence (diameter of focus 0.9 cm) was found in April, 1994. She refused to undergo surgery at this time, and started taking 100 mg of D-fraction and 5 g of Maitake tablets every day for 6 months. After 6 months, the dose of D-fraction reduced to 50 mg a day. As of may, 1995, it was confirmed that the recurred tumor focus disappeared.

44 years old male, Brain tumor (astrocytoma)

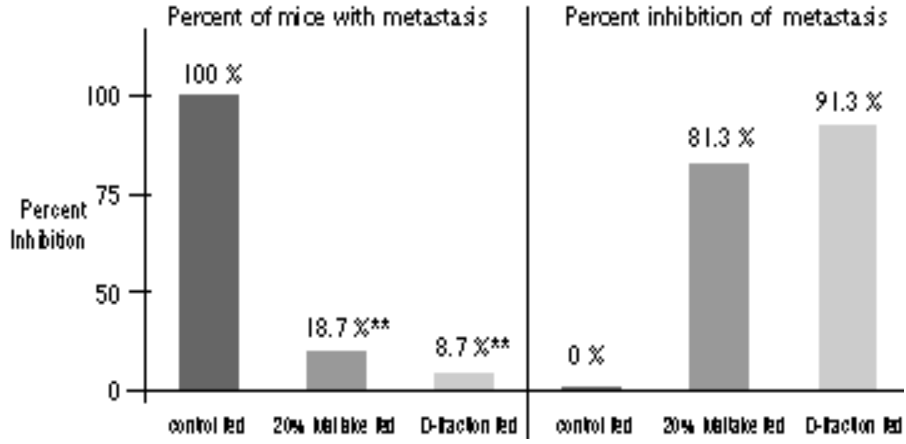
This is an example of an effective trial of D-fraction therapy against a brain tumor. The patient has taken 100 mg of D-fraction and 6 g of Maitake tablets every day for 4 months without taking any other medication including chemotherapy or radiation. In this case, the patient showed dramatic improvement. He had received chemotherapy (CCNU) in four cycles since February, 1994. But he could not accept it because of severe side effects and received no treatment for four months before starting Maitake administration. After 4 months since he started taking Maitake, a complete regression of an egg-sized tumor focus was confirmed (See **Table 1**)

It can not be concluded that Maitake D-fraction and crude powder alone have the strong anti-cancer activities in human cancer. 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% of the patients. Reduction of the pain was also reported by 83% of the patients.

Preventing Cancer Metastasis

Another interesting of investigation was whether the formation of secondary fo-

Figure 2. Effect of Maitake D-fraction on Cancer Metastasis



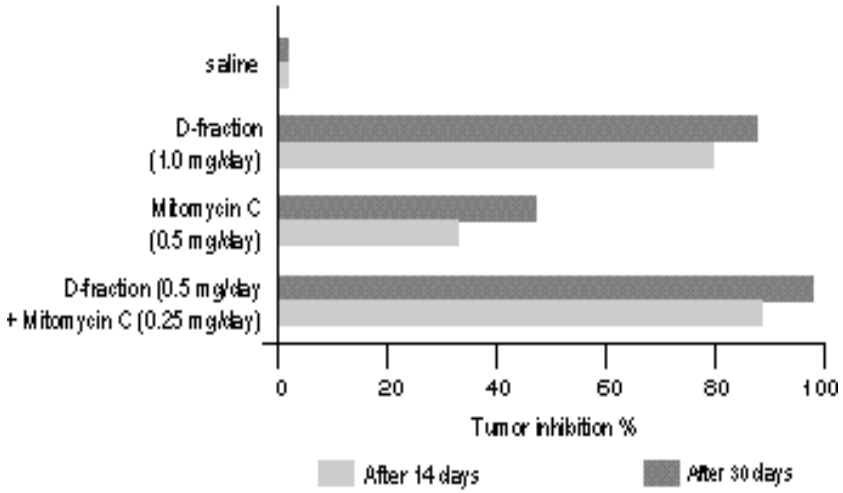


Figure 3. Tumor Inhibition by Mitomycin C with D-Fraction

cus due to metastasis of cancer cells could be inhibited. This test was conducted using mice in the following manner; MM-164 liver carcinoma (1 x 107 cells) was injected to left rear footpad of mice and the footpad was cut off after 48 hours. Then, normal feed was given to the control group (A), 20% Maitake powder was given to group (B) and 1 mg/Kg of D-fraction was given to group (C) with normal food. All three groups were bred for another 30 days, and the number of tumor focus metastasized in the liver was counted by microscope, the result is shown in **Figure 3**. It was observed that the metastasis to the liver was prevented by 91.3% by the administration of D-fraction and by 81.3% by Maitake powder. It is believed that tumor cells present in blood and/or lymph were necrotized by the activated cellular immune-competent cells. The result of this animal test indicates that cancer metastases could be reduced to less than one tenth by the use of Maitake D-fraction daily. (See **Figure 2**).

Synergistic Effect with Chemotherapy

Maitake does not kill cancer cells directly. It stimulates the activities of immune-competent cells and potentiates their action against cancer cells. Chemotherapy is supposed to kill cancer cells directly. Which is more effective in terms of cancer growth inhibition? Here are some interesting results from our study on this effect. We used Mitomycin C (MMC), probably the most popular antibiotic used for various cancer treatments, despite its very severe side effects. In this animal test, Maitake D-fraction, MMC , and D-fraction and MMC together (cutting each dose by half) were injected into tumor-bearing mice respectively. As can be seen in **Figure 3**, D-fraction alone demonstrated superior tumor growth inhibition to that of MMC (about 80% vs 45%). When MMC and D-fraction were given together, cutting each dose by half, tumor inhibition was further enhanced (nearly 98%). The result indicates some synergistic effect between MMC and Maitake, i.e., tumor cells are directly attacked by MMC while the immune system is activated by D-fraction. Chemotherapy is sometimes very harmful as it significantly lowers the immune system of the patients. We have seen many advanced cancer patients recover from severe side-effects caused by chemotherapy by taking Maitake D-fraction (orally) as an

adjuvant. From the above studies, it appears that Maitake and chemotherapy work together, and Maitake has proven to be a valuable adjuvant in the chemotherapeutic treatment of cancer.

Conclusion

Since the cultivation method of Maitake mushroom was established in mid 1980's, this legendary and delicious mushroom has gained much popularity among Japanese people. Anecdotes and folklore on its medicinal values have also been elucidated by a number of mycologists and pharmacologists and its strong anti-tumor activity has attracted many researchers. It should be noted that, unlike many other mushroom extracts that have to be injected intravenously, Maitake D-fraction has a strong ability to inhibit tumor growth when given orally as well. In this context, various tests were conducted focusing on inhibition of growth and metastasis of cancer after surgery, by oral administration of Maitake. Even though this was a limited and non-controlled trial, the clinical study indicated that Maitake D-fraction is effective against such cancers of the breast, lung, liver, prostate and brain. Both human and animal tests demonstrate a synergistic effect with chemotherapy while ameliorating severe side effects from chemotherapy. Though the data is preliminary, the results of animal (and limited clinical) studies based on Maitake D-fraction suggest significant healing and preventing potential for cancers and other immune-related health disorders. It is important to note that even among Maitake Mushrooms (Grifola-frondosa), there are many strains and some contain very little Beta-glucan, the active ingredient to stimulate the immune system. From such strains of Maitake, D-fraction may not be obtained.

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