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Cultivating Edible Fungi

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ANTITUMOR ACTIVITIES OF EDIBLE MUSHROOMS BY ORAL ADMINISTRATION

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ABSTRACT

Antitumor activities of edible mushrooms were investigated by breeding mice with the feed containing 10-30% (w/w) powdered fruit bodies. In allogeneic tumor systems (Sarcoma-180 in ICR mice), the tumor growth was suppressed to 40-50% by oral administration of edible mushrooms. While in syngeneic systems (B-16 melanoma or Lewis Lung carcinoma in C57BL/6, Meth-A fibrosarcoma in BALB/C), the feed containing Lentinus edodes(Shiitake) did not suppress the growth of all tumors, but the breeding with Grifola frondosa (Maitake)elongated the live time of mice to 145% in the case of Meth-A fibrosarcoma in BALB/C.

1 INTRODUCTION

Chihara and Hamuro[1,2] have been reporting the lentinan (ß-1,3 glucan having branching of 1,6 bond), prepared from the fruit bodies of Lentinus edodes(Shiitake), to have antitumor activities against allogeneic tumor as well as certain species of syngeneic tumor in mice by intraperitoneal injection. It still remains to be clarified whether this mushroom, when orally administered to mice, has such effects. For clarificaton of this problem, tumor-bearing mice were fed the dried powdered form of edible mushrooms containing Lentinus edodes. This present research describes the remarkable suppressive action of these mushrooms against tumor growth.

2 MATERIAL and METHODS

Four-week old mice were obtained from Charles River Japan. After they had been maintained for a week on an ordinary diet, $2x10^4$ tumor cells(Sarcoma-180 in ICR mice), were transplanted to each mouse. The mice were then devided into experimental groups and a control group. Control groups were bred for one month with a commercial food, (Nihon Clea,CE-2), which was made of 20% mushroom powder only in the case of the experimental group. After the mouse had been sacrificed, the weights of the growing tumors were measured. Antitumor activities were expressed in a way that would allow a comparison of the tumor weights of both groups. There were 10 mice in each group and the experiment was conducted three times. For the determination of antitumor material in mushroom, glucan was removed from the dried mushroom powder by hot water extraction. The defatted powder was then prepared by treatment with ether

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and ethanol.

3 RESULTS and DISCUSSION

Figure 1 shows the antitumor effects of orally administered Lentinus edodes-feed (L-feed) and Grifola frondosa-feed(G-feed) against the allogeneic tumor, Sarcoma-180 in ICR mice. Tumor suppression was noted to increase in proportion to the amount of L-feed administered to the mice, being a maximal 58.3% for L-feed in the case of 20% G-feed, the growth inhibition was 43.3%.

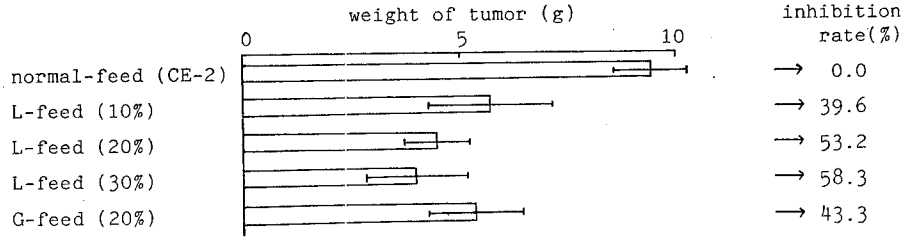


Fig. 1. Effect of the content of mushrooms in the feed on the Sarcoma-180 in ICR mice

An examination was then conducted to determine the best time to administer the L-feed (TABLE 1). No tumor suppression was noted at all either when the mice were fed L-feed prior to inoculation or when gived food without this powder following tumor cell transplantation. Suppression action was found strongest when L-feed was provided at the same time as the tumor cell inocula - tion. But even when the mice were provided this food one week following inoculation, the suppression was 53.9%.

Based on the above results, it is clear that edible mushroom powder administered orally has suppressive action against tumor growth in mice. Experiments were also conducted to determine if such effects were expressed only by the polysaccharides present in the fruit bodies of Lentinus edodes. The results are summarized in TABLE 2. Tumor growth inhibition was 66.7% by the L-feed, 57.2% by its defatted form and only 38.9% when devoid of polysaccharides. Following the removal of both lipids and polysaccharides, the powder failed to have any suppressive action at all. When commercial food (N-feed), was supplemented with the lipid content extracted from Lentinus edodes and administered to mice, 24.7% tumor growth inhibition was determined. These results indicate that the polysaccharides and lipid content in Lentinus edodes fruit bodies is responsible for the suppressive activities against tumor growth.

TABLE 1

Effect of Different Schedules of L-feed (20%) breeding on the Growth of Sarcoma-180 in ICR mice

Conmencement of breeding with L-feed	Weight of tumor (g)	Inhibition rate (%)
control (never) ←normal-feed——→ 1st 8th 32th(days) ↑tumor	4.75± 0.88	0.0
7 days befor and returned feed since the day tumor implated ←L-feed——✳——normal-feed→ 1st 8th 32th(days) ↑tumor	4.67± 2.14	1.7
simultaneous day with tumor implantation ←normal-feed——✳——L-feed→ 1st 8th 32th(days) ↑tumor	1.31±0.98	72.4
7 days after tumor implantation ←normal-feed——✳——L-feed→ 1st 8th 15th 32th(days) ↑tumor	2.19±1.47	53.9

TABLE 2

Growth inhibition of various L-feed (Shiitake) on Sarcoma-180 in ICR mice

Sample	Inhibition (%)
Normal-feed	0.0
(A) Shiitake powder + Normal-feed	66.7
(B) Shiitake-lipid + Normal-feed	24.7
(C) -Lipid Shiitake + Normal-feed	57.2
(D) -Glucan Shiitake + Normal-feed	38.9
(E) -Glucan,-Lipid Shiitake + Normal-feed	-0.4

Since orally administered Lentinus edodes and Grifola frondosa was found to inhibit tumor growth in ICR mice, research was also carried out on other species of mushrooms such as Hiratake, Enokitake, Nameko, Kikurage, Mushroom and Fukurotake for confirmation of similar effects.

All these species showed as much as 60% suppression of Sarcoma-180 growth. In the case of Maitake, growth inhibition was as much as 86.3%, (two out of eight mice completely recovered from their tumors), and for Shirokikurage(Tremella fuciformis), 81% (TABLE 3). It is widely accepted that tumor suppression activity by polysaccharides comes about through their activation of macrophages and T-cells in the cellular immune system. Possibly a certain period of time must precede the expression of such effects following the oral administration was conducted on the relation between the expression of these effects and the time at which mushroom containing food was administered to mice. Suppressive effects become stronger in proportion to the period(duration) of the feeding time (TABLE 4). Thus, the presence of mushrooms in the food may possibly activate the cellular immune system.

TABLE 3
Antitumor activities of edible mushrooms by oral administration on Sarcoma-180 in ICR mice

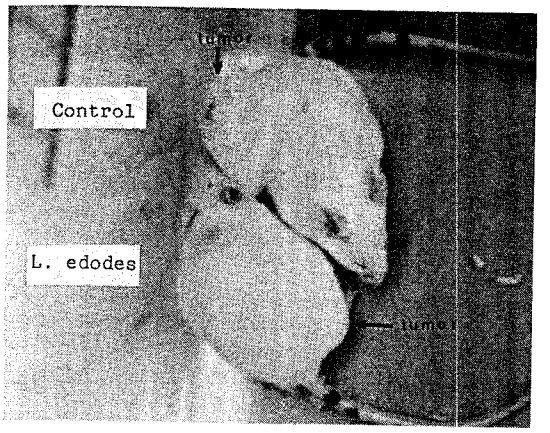
	31 days after tumor implantation		
	No. of mouse	Weight of tumor (g)	Inhibition (%)
Control	10	18.11 ± 0.07	0.0
Lentinus edodes	10	4.01 ± 0.91	77.9
Grifola frondosa	8	2.48 ± 0.04	86.3(2/8 complete)
Agaricus bisporus	9	5.20 ± 0.19	71.3
Pleurotus ostreatus	9	6.76 ± 0.75	62.7
Flammulina velutipes	8	6.94 ± 0.03	61.7
Pholiota glutinosa	8	6.75 ± 0.84	62.7
Tremella fuciformis	10	3.44 ± 0.59	81.0
Auricularia minor	8	5.72 ± 1.12	68.4
Volvariella volvaces	10	5.86 ± 0.09	67.6

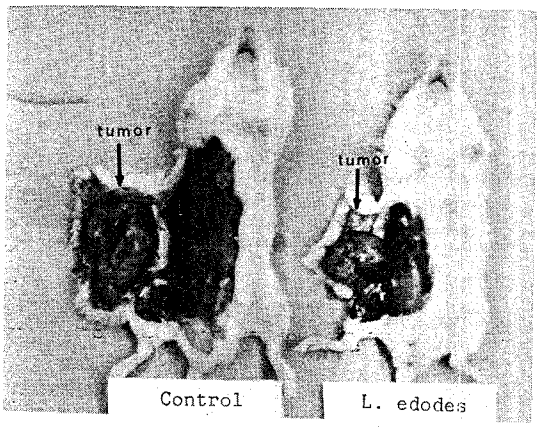
TABLE 4
Antitumor effects of edible mushrooms by oral administration on Sarcoma-180 in ICR mice (Time course of antitumor effect)

	days after tumor implantation		
	28	31	42
Control	0.0 % [a]	0.0 %	0.0 %
Agaricus bisporus	51.1	67.5	53.2
Pleurotus ostreatus	58.3	64.4	79.4
Pholiota glutinosa	-	62.7	74.9
Tremella fuciformis	26.6	81.0	-
Auricularia minor	33.5	68.4	-
Volvariella volvacea	47.6	67.6	-

[a] Inhibition ratio

Analysis was also made of the antitumor effects of mushroom on syngeneic tumors such as MM-46 in C3H, IMC-carcinoma in CDF1 and Lewis Lung carcinoma in C57BL mice. As indicated in TABLE 5, Mushroom (Agaricus bisporus), Hiratake (Pleurotus ostreatus) and Nameko (Pholiota glutinosa) showed respective inhibitions of 97.9, 89.7 and 99.0% of MM-46 cell growth. None of the edible


tumor
Control
L. edodes
tumor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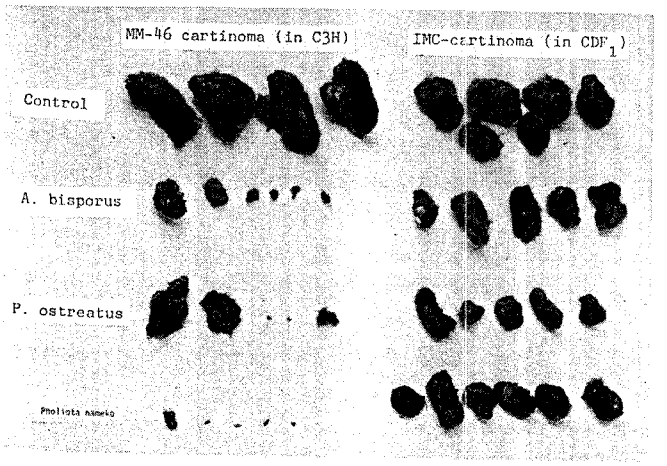
MM-46 cartinoma (in C3H)
IMC-cartinoma (in CDF1)
Control
A. bisporus
P. ostreatus
Pholiota nameko

mushrooms in the present research was found capable of suppressing Lewis Lung carcinoma. Hiratake alone expressed antitumor activity against IMC carcinoma. Shirokikurage and Kurokikurage (Auricularia minor) were ineffective for inhibiting the growth of any tumor.

TABLE 5

Antitumor activities of edible mushrooms by oral administration

	MM-46 (in C3H)	IMC-carcinoma (in CDF1)	Lewis Lung carcinoma (in C57BL)
Control	0.0 % [a]	0.0 %	0.0 %
Agaricus bisporus	97.9	33.3	17.9
Pleurotus ostreatus	89.7	65.6	-
Pholiota glutinosa	99.0 (4/8)	41.1	-
Tremella fuciformis	78.7	-30.3	15.2
Auricularia minor	43.0	-21.5	1.4
Volvariella volvacea	41.6	31.1	8.7

[a] Inhibition ratio, ( ) complete

Based on the present data, orally administered edible mushroom may be concluded to have suppressive activities against allogeneic tumors and syngeneic tumors. Additional research should be carried out to clarify the mechanism of this activities by the oral administration of edible mushrooms. As a part of studies to elucidate mechanisms of antitumor activities of edible mushrooms, effects on macrophage, which play an important role as effector in cellular immuno response systems, were investigated.

4 REFERENCES

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