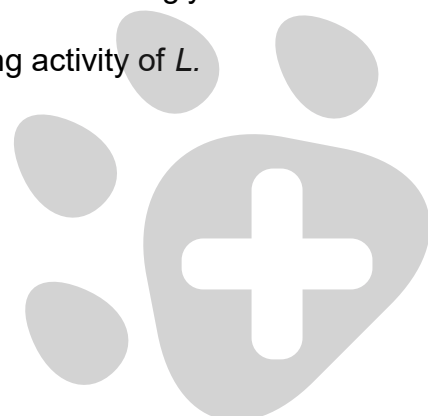


Medicinal mushrooms and cancer chemoprevention

While the foregoing antitumour studies on animal models and human clinical trials (Chapters 6 and 7) have used relatively pure extracted polysaccharides it has also been possible to demonstrate antitumour effects when the animal diet has been enriched with either powdered fruit-bodies or liquid concentrates from various edible medicinal mushrooms.

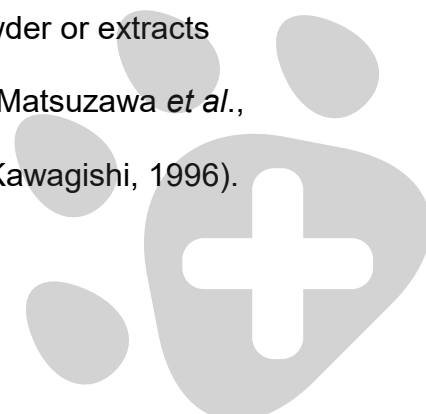
Powdered fruit-bodies of *Lentinus edodes* were supplied orally in the diet (20%) of CDF₁ mice who had been inoculated with synergistic IMC carcinoma cells and C3H/He mice inoculated with MM-46 carcinoma cells (Nanba *et al.*, 1987). The MM-46 carcinoma growth was strongly inhibited (79%) whereas the IMC carcinoma growth was much less affected (21% inhibition). A further series of experiments examined macrophage spreading and phagocytosis of latex beads in both normal and tumour-bearing mice fed on a diet supplemented with powdered *L. edodes* (Nanba and Kuroda, 1987). A decreased spreading rate of macrophage in CDF₁ mice but an increase in C₃H mice were observed. However, both the spreading rates and phagocytosis of macrophages in tumour-bearing mice of either strain were significantly depressed when compared to non-tumour bearing animals. Cytotoxicity activity of natural killer cells (NK) and/or lymphokine-activated killer cells (LAK) was significantly increased in mice on feed enhanced with powdered *L. edodes* when compared to mice on normal feed. Pre-treatment of the cells with anti-Thy 12 monoclonal antibodies and complement reduced the cytotoxicity activity by approximately 50% in both mushroom-fed mice and mice on normal feed strongly implying that cytotoxic T cells also participate in the tumour-inhibiting activity of *L. edodes*.



In a similar series of experiments using dietary supplementation (5%) with dried powdered fruit-bodies of either *L. edodes*, *Grifola frondosa* or *Pleurotus ostreatus* it was demonstrated that the incidence of urinary bladder carcinoma in female six-week old ICR mice previously treated with the carcinogen N-butyl-N-butanolnitrosamine (BBN) was decreased in all cases (Kuroshiga *et al.*, 1997). While the chemostatic activity of macrophages and the mitogenic response of lymphocytes to concanavalin A were severely suppressed by BBN treatments all of the mushroom-enriched diets restored these activities to almost normal levels. The cytotoxic activity of LAK and NK cells depressed in tumour bearing mice was augmented significantly beyond even the level in non-tumour bearing mice not fed the mushroom supplemented diet.

Hypsizygus marmoreus is a relatively new edible medicinal mushroom now available in the Japanese food market and concentrated extracts have shown a strong inhibition ratio for the solid Sarcoma 180 cancer cells and also for tumour metastasis in mice (Ikekawa *et al.*, 1992a; Saitho *et al.*, 1997). Studies have shown that when mice were fed on a normal diet plus 5% dried fruit-bodies of *H. marmoreus* they displayed strong cancer prevention ability. Mice were injected with the strong carcinogen, methylcholanthrene and examined over a 76-week period. In the control group 21 of 36 mice developed tumours while only 3 of 36 mice in the mushroom-augmented group developed tumours (Ikekawa *et al.*, 1992b; Ikekawa, 2001).

While it has been well noted in previous Chapters that the antitumour effect of medicinal mushrooms is largely due to immunomodulation effects several studies in particular involving animal diets supplemented with mushroom powder or extracts are now also implicating antioxidative activity, e.g. *H. marmoreus* (Matsuzawa *et al.*, 1997, 1998), *F. velutipes* (Hiramatsu *et al.*, 1989) and *L. edodes* (Kawagishi, 1996).

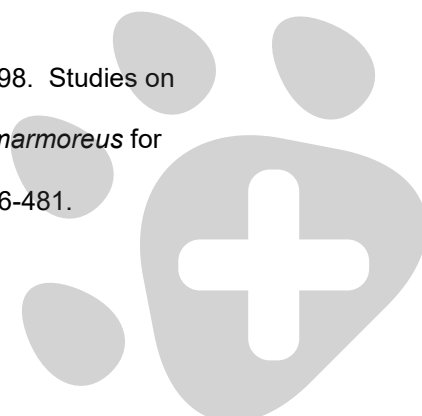


The antioxidant activity of the medicinal mushrooms has previously been outlined in Chapter 8. Thus while there is an abundance of peer-reviewed scientific evidence confirming that the antitumour effects of extracts of medicinal mushrooms are primarily by immunomodulation it would now appear that antioxidative effects are also contributing to the overall antitumour activity.

Epidemiological studies reported in Chapter 10 have highlighted some extremely interesting but as yet limited observations on cancer chemoprevention in humans through consumption of certain medicinal mushrooms. Whether regular and prolonged consumption of medicinal mushroom concentrates as dietary supplements could serve as an important approach for cancer chemoprevention in man must be subjected to critical controlled study.

References

- Ikekawa, T. 2001. Beneficial effects of edible and medicinal mushrooms on health care. *International Journal of Medicinal Mushrooms* **3**, 291-298.
- Ikekawa, T., Saitoh, H., Feng, W., Zhang, H., Li, L. and Matsuzawa, T. 1992a. Antitumour activity of *Hypsizygus marmoreus*. 1. Antitumour activity of extracts and polysaccharides. *Chemical and Pharmaceutical Bulletin* **40**, 1954-1957.
- Ikekawa, T., Saitoh, H., Feng, W., Zhang, H., Li, L. and Matsuzawa, T. 1992b. Preventive effects of *Hypsizygus marmoreus*. *51st Anniversary Meeting of the Japanese Society for Cancer Research*. Abstract.
- Kawagishi, S. 1996. Active oxygen and Ishoku Dougeu. Inone. *Kyanrita Shuppan*, Japan. P. 240.
- Kurashiga, S., Akuzawa, Y. and Endo, F. 1997. Effects of *Lentinus edodes*, *Grifola frondosa* and *Pleurotus ostreatus* administration in cancer outbreaks and activities of macrophages and lymphocytes in mice treated with a carcinogen, N-butyl-N-butamolinitrosoamine. *Immunopharmacology and Immunotoxicology* **19**, 175-183.
- Matsuzawa, T., Saitoh, H., Sano, M., Tomita, I., Ohkawa, M. and Ikekawa, T. 1998. Studies on antioxidant effect of *Hypsizygus marmoreus*. II. Effects fo *Hypozygus marmoreus* for antioxidant activities of tumour-bearing mice. *Yakogaku Zasshi* **188**, 476-481.



Matsuzawa, T., Sano, M., Tomata, I., Saitoh, J. and Ikekawa, T. 1997. Studies on the antioxidant effect of *Hypsizygus marmoreus*. 1. Effects of *Hypsizygus marmoreus* for antioxidant activities of mice plasma. *Yakugaku Zasshi* **118**, 623-628.

Nanba, H. and Kuroda, H. 1987. Antitumour mechanisms of orally administered Shiitake fruit-bodies. *Chemical and Pharmaceutical Bulletin* **35**, 2459-2464.

Nanba, H., Mori, K., Toyomasu, T. and Kuroda, H. 1987. Antitumour action of shiitake (*Lentinus edodes*) fruit-bodies orally administered to mice. *Chemical and Pharmaceutical Bulletin* **35**, 2453-2558.

Saitoh, H., Feng, W., Matsuzawa, T. and Ikekawa, T. 1997. Antitumour activity of *Hypsizygus marmoreus*. 11. Preventive effect against lung metastasis of Lewin lung carcinoma. *Yakugaku Zasshi* **117**, 1006-1010.

