

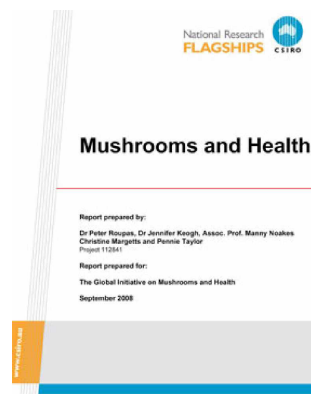
## ***Effects of mushrooms and mushroom components on health***



### **Background**

***Compiled by Initiative Team Member Glenn Cardwell APD***

As mentioned in the Introduction, mushrooms have been a part of the human diet for millennia. The majority of research has been conducted *in vitro* or with animal models. Researchers are now venturing into human studies, as the current research indicates that mushrooms have great potential in human health, especially for long-term benefits. Mushrooms have been studied for their effect on blood lipids, blood glucose, immune function, modulation of cancer cells and satiation.



## ***Scientific Investigation from Mushrooms and Health 2008***

### **From the Executive Summary**

Although there are very few direct intervention trials, trials on the safety of mushroom consumption in humans indicate that mushrooms and their extracts are generally well-tolerated with few, if any, side-effects. Studies in humans have shown an increase in the antioxidant capacity in urine and no evidence of liver, renal or DNA toxicity, and no clinical problems with regard to blood test results, liver and renal function, glucose and lipid metabolism, or blood pressure. Mushroom components/extracts have had stronger health effects/benefits than whole mushrooms in the limited number of direct human trials to date.

## ***Studies in Humans***

A series of trials evaluating *Ganoderma lucidum* in several disease states have been carried out. The trials evaluated effects on cancer, Type II diabetes, coronary heart disease, chronic hepatitis B, and neurasthenia. Treatment with Ganopoly for 12 weeks showed hypoglycemic activity and produced some anti-viral and liver protective effects in patients with chronic hepatitis B infection. However, the same treatment regimen did not result in any objective response in late-stage cancer patients (Zhou et al. 2005). Overall, the findings suggest that Ganopoly may have some pharmacological activities, although clinical proof is lacking.

Polysaccharide fractions of *Ganoderma lucidum* have been shown to have potent immunomodulating effects in pre-clinical trials. A clinical study of healthy volunteers demonstrated that *G. lucidum* did not affect their immune functions. Subsequently, an open-labeled study (i.e. not double-blind or placebo controlled) aimed to evaluate the effects of water-soluble *G. lucidum* polysaccharides (Ganopoly) in patients with advanced colorectal cancer. Forty-seven patients were enrolled and treated with Ganopoly at 5.4 g/day for 12 weeks. In 41 assessable cancer patients, treatment with Ganopoly tended to increase mitogenic reactivity to phytohemagglutinin. Larger double-blind trials are required to show if this is a real effect and further studies are needed to determine the mechanism of action, efficacy, and safety of the water-soluble *G.lucidum* polysaccharides in cancer patients (Gao et al. 2005).

A double-blind, placebo-controlled, cross-over intervention study has investigated the effects of 4 weeks *Ganoderma lucidum* (Lingzhi) supplementation on a range of biomarkers for antioxidant status, coronary heart disease (CHD) risk, DNA damage, immune status, and inflammation, as well as for markers of liver and renal toxicity. The study was performed as a follow-up to a previous study that showed that antioxidant power in plasma increased after Lingzhi ingestion, and that 10d supplementation was associated with a trend towards an improved CHD biomarker profile. Fasting blood and urine from healthy, consenting adults (n=18; ages 22-52 years) was collected before and after 4 weeks supplementation with a commercially available encapsulated Lingzhi preparation (1.44g Lingzhi/d; equivalent to 13.2g fresh mushroom/d) or placebo. No significant change in any of the variables was found. The results showed no evidence of liver, renal or DNA toxicity with Lingzhi intake. This study is one of the few intervention studies in humans, albeit with a mushroom supplement (Wachtel-Galor et al. 2004).

Yunzhi (*Coriolus versicolor*) has been reported to modulate various immunological functions *in vitro*, *in vivo*, and in human clinical trials, while Danshen (*Salvia miltiorrhiza*) has been shown to benefit the circulatory system by its vasodilating activity. A clinical trial has been carried out to evaluate the immunomodulatory effects of Yunzhi-Danshen capsules in post-treatment breast cancer patients. Eighty-two patients with breast cancer were recruited to take Yunzhi and Danshen capsules with the data showing that the percentage and the absolute counts of B-lymphocytes were significantly elevated in patients with breast cancer after taking Yunzhi-Danshen capsules, while plasma sIL-2R concentration was significantly decreased (Wong et al. 2005). The significance of these findings is not yet clear.

An extract of Hatakeshimeji (*Lyophyllum decastes* Sing., 2.88g) administered orally to 11 adults for two weeks was assessed for its safety by conducting blood tests, urine tests, blood pressure and body measurement checks. There were no clinical problems observed with regard to blood test results, hepatic and renal function, glucose and lipid metabolism, and blood pressure. Similarly, analysis of agaritine from hot-water extracts of Hatakeshimeji showed no such problems. These results suggest that the extract of Hatakeshimeji is a safe food for human consumption (Ukawa et al. 2007).

A Phase I trial and pharmacokinetic study of irofulven, a mushroom-derived cytotoxin has been carried out. Irofulven was administered via 5 minute intravenous (i.v.) infusion for five consecutive days every four weeks in patients (n=46) with advanced solid malignancies. Pharmacokinetic studies were performed on days 1 and 5 to characterize the plasma disposition of irofulven. While the highest dose used was not tolerated well (grade 4 neutropenia and renal toxicity), the authors recommended a lower dose of irofulven (10.64mg/m<sup>2</sup>) as a 5-minute i.v. infusion daily for 5 days every 4 weeks. The preliminary anti-tumour activity documented in a patient with advanced pancreatic cancer and the striking preclinical anti-tumour effects of irofulven observed on intermittent dosing schedules support further disease-directed evaluations of this agent (Eckhardt et al. 2000). Irofulven was also shown to have a rapid elimination half-life of 2 to 10 minutes.

A series of (as yet unpublished) randomized, placebo-controlled, double-blind clinical trials from Brazil in which patients with colorectal cancer were supplemented with *Agaricus sylvaticus* mushroom, orally, twice daily (30mg/kg/day), for six months was presented at the 2007 World Congress on Gastrointestinal Cancer in Spain (Garbi Novaes et al. 2007b; Garbi Novaes et al. 2007d; Garbi Novaes et al. 2007a; Garbi Novaes et al. 2007c; Garbi Novaes et al. 2007e). The trials evaluated haematological and

immunological parameters, fasting glycaemia levels and general 'quality of life' indices. As indicated, the studies are not yet published, and therefore cannot be adequately evaluated at this stage; however, it appears that the analyses were done comparing the groups with baseline values with no comparison of the groups with one another which significantly decreases the value of the analyses. A detailed evaluation of the outcomes will need to wait until the results of the trials are published.

A placebo-controlled trial of the immune modulator, lentinan, a beta-glucan isolated from *Lentinus edodes* (Shiitake mushroom), in HIV-positive patients has been reported. Two phase I/II placebo-controlled trials on a total of 98 patients were completed. In the first study, ten patients each were administered 2, 5, or 10mg of lentinan or placebo intravenously (i.v.) once a week for eight weeks. In the second study, two groups of 20 patients each were administered 1 or 5mg of lentinan i.v. twice a week for 12 weeks, and ten patients were administered placebo (vehicle containing mannitol plus dextran 40) i.v. twice a week. The study confirmed, in Caucasian subjects, the good tolerability of lentinan observed in Japanese cancer patients. Side effects were mainly mild, especially when infusion was carried out over a 30-minute period. In the first study, where administration was over a 10 minute period, there were nine side effects severe enough to be reported to the FDA (one case each of anaphylactoid reaction, back pain, leg pain, depression, rigor, fever, chills, granulocytopenia and elevated liver enzymes) and there were four patients who discontinued therapy because of side effects. In the second study, where infusion was over a 30-minute period, there were no side effects reportable to the FDA and there were four dropouts due to side effects or personal preference. Most side effects resolved promptly after the discontinuation of medication, and all of them were relieved within 24 hours. Due to the small number of patients in the study groups, the data on possible increases in CD4 cell and neutrophil activity were inconclusive (not statistically significant) (Gordon et al. 1998).

A double-blind, placebo-controlled, randomized, and dose-ranging study has been carried out in men with lower urinary tract symptoms (LUTS) to evaluate the safety and efficacy of an extract of *Ganoderma lucidum* that showed the strongest 5-alpha-reductase inhibitory activity among extracts of 19 edible and medicinal mushrooms. In this trial, 88 men over the age of 49 years who had slight-to-moderate LUTS were randomly assigned to 12 weeks of treatment with *G. lucidum* extract (6mg once per day) or placebo. The primary outcome measures were changes in the International Prostate Symptom Score (IPSS) and variables of uroflowmetry. Secondary outcome measures included changes in prostate size, residual urinary volume after voiding, laboratory values, and the reported adverse effects. *G. lucidum* was effective and significantly superior to placebo for improving total IPSS with

2.1 points decreasing at the end of treatment. No changes were observed with respect to quality of life scores, peak urinary flow, mean urinary flow, residual urine, prostate volume, serum prostate-specific antigen, or testosterone levels. Overall treatment was well tolerated with no severe adverse effects (Noguchi et al. 2008).

A randomized, double-blinded, and placebo-controlled clinical trial (72 patients) has evaluated the effects of *Agaricus blazei* Murill in combination with metformin and gliclazide on insulin resistance in type 2 diabetes. Supplementation of *Agaricus blazei* Murill extract improved insulin resistance among subjects with type 2 diabetes. The increase in adiponectin concentration after taking *Agaricus blazei* Murill extract for 12 weeks may be the mechanism that resulted in the observed effect (Hsu et al. 2007).

Clinical effects and safety evaluation of *Agaricus Blazei* Condensed Liquid (*Agaricus* Mushroom Extract; ABCL) on human volunteers with C-type hepatitis has been studied. A total of 20 patients (10 male, 10 female) with chronic C-type hepatitis received the ABCL orally twice per day for 8 weeks. No toxicological effects, nor other side effects were observed (Inuzuka and Yoshida, 2002).

Increasing intake of low energy density (ED) foods in place of high ED foods has been proposed as a strategy for preventing or treating obesity. A study (Cheskin et al, 2008) has investigated how substituting mushrooms for beef in a test lunch affected energy intake, fat intake, palatability, appetite, satiation and satiety in normal weight, overweight and obese adults. Each subject consumed a total of eight test lunches over two consecutive weeks. Energy content of meat and mushroom lunches varied (783kcal versus 339kcal), while volume was held constant. Energy intakes were significantly higher during meat lunches than mushroom lunches ( $730 \pm 7.9$ kcal versus  $310 \pm 5.8$ kcal). Subjects exhibited only partial compensation ( $11.4 \pm 12.0\%$ ) for this difference over 4 days. Total daily energy intake and fat intake were significantly greater with meat lunches than with mushroom lunches, while ratings of palatability, appetite, satiation and satiety did not differ significantly. The results suggest that substituting low energy density foods for high energy density foods in otherwise similar eating patterns can be an effective method for reducing daily energy and fat intake.