Review Article

Therapeutic Potential of Mushrooms

Mahendra Rai1*, Girish Tidke1 and Soloman P Wasser2
1Department of Biotechnology, Amravati University, Amravati – 444 602, Maharashtra, India
2International Centre for Cryptogamic Plants and Fungi, Institute of Evolution University of Haifa, Mt. Carmel, Haifa, 31905, Israel
*Correspondent author, E-mail: pmkrai@hotmail.com
Received 15 April 2004; Revised 16 March 2005

Abstract

Mushrooms are an important natural source of foods and medicines. Traditional aboriginals knew the medicinal importance of edible and wild mushrooms and these are now being screened for their bioactivity in various ailments. Mushrooms represent a major and untapped source of potent new pharmaceutical products. A wide range of activities including antitumour, cardiovascular and antimicrobial are reported in mushrooms. In developing countries like India mushroom progress is a boon in the field of food, medicine, and in generating employment. The alternative systems of medicine utilize the curative properties of mushrooms. The present review is aimed to discuss biological activities of mushrooms and their roles in various human diseases.

Keywords: Mushrooms, Antimicrobial, Bioactivity, Biomedical, Cardiovascular, Therapeutics.

IPC code; Int. cl.7—A61K 35/84, A61P 9/00, A61P 31/00, A61P 35/00

Introduction

Mushrooms can be either hypogeous or epigeous, large enough to be seen with the naked eye and usually picked by hands. They produce fleshy fruit bodies belonging to Basidiomycotina and Ascomycotina. The edible nature of mushrooms is now well-known. Usually Agaricus, Pleurotus and Volvariella spp. are eaten all over the world in general, and tropical countries, in particular. However, the medicinal uses of the mushroom still need to be worked out for their biological activities due to a fast increasing number of multidrug resistance in pathogenic microbes like Candida spp., Staphylococcus aureus, S. epidermidis, Streptococcus spp., Enterococcus spp. and Escherichia coli (Ishikawa et al, 2001). The use of mushrooms as medicine was mentioned by Berkeley (1857), who reported that Calvatia gigantea (Giant Puffball) and C. caelata can be used in burnt cases due to their anaesthetic nature. Calvatia spp. are also used to stop bleeding from wounds. A wood decaying fungus, Fomitopsis officinalis, which contains agaricin, is used in many medicines.

Mushrooms represent a major and as yet, largely untapped source of potent new pharmaceutical products. Out of approximately 15,000 known species, 2,000 are safe for human consumption, and about 650 of these possess medicinal properties. In the second half of twentieth century, the mushroom producing technologies have grown enormously and the value of world mushroom production was estimated to be worth about eighteen billion US dollar. Many pharmaceutical substances with potent and unique properties were recently extracted from mushrooms and make their way all around the world. The Ganodermataceae family includes about forty species with hard basidiocarp (fruit bodies). In Chinese folklore the fruit body of Ganoderma lucidum (Fr.) P.
Karst. (Lingzhi) has been regarded as a panacea for all types of diseases like hepatopathy, chronic hepatitis, nephritis, hypertension, hyperlipidemic, arthritis, neurasthenia, insomnia, bronchitis, asthma, gastric ulcer, arteriosclerosis, leukaopenia, diabetes and anorexia.

In developing countries like India, mushrooms are a boon for progress in the fields of food, medicine and unemployment. Mushrooms in the twentieth century are well-known to people all over the Asian countries as an important bio-source of novel secondary metabolites. In India, particularly the alternative systems of medicine, utilize the curative properties of mushrooms. The secondary metabolites of these mushrooms are chemically diverse and possess a wide spectrum of biological activities, which are explored in traditional medicines and in new targets of molecular biology. They have important present status and possess a potential to design future strategies for human health values. Pharmaceuticals worth $700 million US dollars are produced annually in Japan alone from Lentinus, Trametes, Schizophyllum, and Ganoderma. Extracts of various edible fungi, viz. Lentinus edodes, Flammulina velutipes, Pleurotus ostreatus, Agaricus bisporus, Pholiota nameko, Tricholoma matsutake and Auricularia auricula-judae possess antitumour effects also. In USA and Japan, Maitake (Grifola frondosa) and Shiitake (Lentinus edodes) have been reported to be inhibitory to the AIDS virus. The important medicinal mushroom species with antitumour polysaccharides in fruit bodies and cultured mycelium are: Tremella fuciformis, Schizophyllum commune, Dendro polyporus umbellatus, Grifola frondosa, Hericium erinaceus, Inonotus obliquus, Ganoderma lucidum, G. applanatum, Lentinus edodes, Flammulina velutipes, etc. They stimulate macrophage activity and strengthen immune systems.

In traditional Chinese medicine, extracts from many medicinal mushrooms have long been used for a wide range of diseases. Modern scientific and medical studies support many of these claims. The main areas of medicinal studies include anticancer, cholesterol and blood pressure lowering, liver protective, antifibrotic, antinflammatory, anti-diabetic, and antimicrobial activity (Ooi & Liu, 1999; Wasser & Weis, 1999a, 1999b; Gunde-Cimerman, 1999; Wasser, 2005 a, 2005 b; Wasser & Didukh, 2005).

In addition to the therapeutic potential, hundreds of the mushrooms are being explored the world over to study and reveal their biotechnological potential. Wasser (2002) has screened more than one hundred Agaricales species for their antimicrobial and other such properties. The product made from the mushroom is being sold in the national and international markets. They are available with prior clinical trials and doses recommended by various doctors and physicians.

The traditional uses of the mushroom are known to the aboriginals of Africa, India, Brazil and other countries. In Nigeria, Puff balls (Lycomperdon pusillum and Calvatia gigantea) are used to cure sores, abrasion or bruises, deep cut, haemorrhages, and urinary infections (Buswell & Chang, 1993). In India, Ganoderma lucidum is used in asthma by the Baiga tribe of Central India, Agaricus spp. is used in goiter and Lycoperdon pusillum in wound healing and also for controlling bleeding.

The medicinal and commercial potential of bioactive substances derived from higher Basidiomycetes mushrooms (edible and medicinal) and its proprietary biotechnology process in order to produce new dietary supplements and, at a later stage, new pharmaceutical products, have been exploited. Extensive tests to obtain substances for anticancer, anticholesterol, anti-diabetic, hepatoprotective and sexual potential activities have been performed in vitro and in vivo. Several dietary supplements from fungal biomass are produced and tested. These supplements contain many bioactive substances with mild health promoting and sustaining effects. They do not specifically treat disease, rather, they are used as functional food, on a daily basis, strengthening and perfecting many different physiological systems of the human body. Two new dietary supplements with cholesterol lowering, anti-diabetic and immunostimulating properties have been produced and patented (Wasser, 2000).

The present review is aimed to summarize the therapeutic importance of...
various mushrooms and explore further research in various areas and the future prospects in order to develop a new generation of modern drugs.

Antitumour properties

The fruiting body of mushroom Agaricus brasiliensis S. Wasser et al (＝blazei Murrill ss. Heinem) having a glycoprotein (50.2% sugar and 43.3% protein) and three ergosterol derivatives (I, II, III), showed antitumour activity. A β-D-glucan polysaccharide isolated from this mushroom also exhibited immunostimulative and antitumour activity (Mizuno et al, 1990; Kawagishi et al, 1989). However, a higher antitumour activity was observed in another xyloglucan protein complex obtained from the 5% NaOH solution (Mizuno et al, 1990). A glycoprotein fraction obtained from A. campestris also exhibited antitumour activity against Sarcoma 180 in ICR mice; the protein moiety was composed of 17 amino acids (Jeong et al, 1990). Along with ergosterol, six steroids are also isolated from an acetone extract of A. brasiliensis fruit bodies. Out of the six steroids, three of them effectively inhibited cell proliferation of cervical cancer cell (HeLa cells) (Mizuno, 2002). The acidic heteroglucans isolated from Auricularia auricula-judae exhibited antitumour activity on implanted Sarcoma 180 (Ukai et al, 1983; Misaki et al, 1981).

Extracts of fruiting bodies of Boletus edulis have shown 100% inhibition against Sarcoma 180 and 90% inhibition against Ehrlich carcinoma in mice (Ying et al, 1987). Calvacin was isolated from Calvatia gigantea with antitumour activity. Flammulina velutipes, exhibits strong antitumour activity against Sarcoma 180, Lewis cancer of lung, and B-16 melanoma (Ikekawa, 1995). The antitumour glycoprotein proflamin found in mycelia of F. velutipes is effective against allogeneic and syngeneic tumours by oral administration. Proflamin augments antibody formation and activates lymphocyte blastogenesis (Ikekawa, 1995; Ikekawa et al, 1985). A polysaccharide, PA3 DE, isolated from this fungus also showed inhibitory activity against implanted Sarcoma 180 (solid tumour) in mice.

The triterpenoids isolated from Ganoderma lucidum are C3 epimers and C-3/C-15 positional isomers in pairs. A β-D-glucan isolated from this fungus showed immunostimululative antitumour activity. A glycoprotein fraction GL isolated from the hot water soluble components of the basidiocarp of G. lucidum showed 81% inhibition of tumour growth in mice. GL exerted the antitumour activity through immunopotentiation and not through direct cytotoxicity against the tumours. (Chem Abstr, 1992). From the culture mycelium of G. lucidum, Toth et al (1983a, 1983b) isolated ganoderic acids Z, Y, X, W, V and U which were found to be cytotoxic to hepatoma cells in vitro. Glucuronoglucan, xyloglucan, mannoglucan, xylomannoglucan and other active heteroglucans and their potential complexes, extracted from this species were purified using salts, alkali and DMSO (Mizuno et al, 1984; Willard, 1990; Wasser & Weis, 1997b).

A protein with β-glucan isolated from Grifola frondosa extract exhibits antitumour activity by potentiating antitumour cellular functions by directly enhancing various mediators such as lymphokines and IL-1 (Nanba, 1993). Grifolan (β-glucan), xyloglucan, annoglucan, fucomannoglucan, compounds isolated from this fungus possess antitumour property (Mizuno, 1997, 1998). Heteroglucan protein, mannogalactofucan, heteroxylan, galactomannoglucan, compounds isolated from submerged cultures of G. frondosa have also shown antitumour activity (Zhuang et al, 1994a, 1994b). The antitumour properties of Lentinus edodes are attributed to the polysaccharide lentinan and emitanin. Lentinan is now used as an antitumour drug (Chihara et al, 1970). Lentinan is nontoxic to tumour cells, but inhibits tumour growth by stimulating the immune system (Chihara, 1978).

The mushroom Pleurotus sajor-caju contains protein having polysaccharide xyloglucan, xylanproteins, has shown antitumour activity against Sarcoma 180 tumour cells in vivo (Zhuang et al, 1993). Trametes (Coriolus) versicolor was found to possess antitumour and immunostimulant properties. From the carpophores of this fungus, a polysaccharide fraction, built up of glucose (96.44%), xylose (2.16%) and mannose (1.73%), exhibiting antitumour activity was isolated. PSP, a glycopeptide
possessing antitumour and immunostimulant activities was also obtained from the ethanol extract of *T. versicolor* mycelium (Yang & Wang, 1994).

**Cardiovascular and hypercholesterolemic properties**

*Lentinus edodes* can lower both blood pressure and free cholesterol in plasma, as well as accelerate accumulation of lipids in liver by removing them from circulation. In most developed countries, the common cause of death is coronary artery disease. The main risk factors are hypercholesteremia and dislipoproteinemia, diabetes, disturbance in blood platelet binding and high blood pressure. The initial steps for the prevention and treatment of CAD and hypercholesterolemia are the modification in regime with a diet low in fats and saturated fatty acids in crude fibers. Clinical intervention studies have clearly demonstrated therapeutic importance of correcting hypercholesterolemia (Albert *et al.*, 1989).

Mevinolin is produced commercially from the filamentous fungus *Aspergillus tereus*. This is the first specific inhibitor of microzomal enzyme that occurs early in the biosynthetic pathway to cholesterol formation. The addition of 4% dried *Pleurotus* to a high cholesterol diet reduced cholesterol accumulation in the serum effectively and liver of experimental rats. Cholesterol lowering effect of the mushroom *Pleurotus ostreatus* in hypercholesterolemic rats is also reported. It has been suggested that *Pleurotus* mushrooms could be recommended as a natural cholesterol lowering substance within the human diet (Gunde-Cimerman, 1999).

In western countries coronary artery disease is the major cause of death, while hypercholesterolemia is a risk factor, which causes the hardening of the arteries. In humans, 50% or more of total cholesterol I is derived from *de novo* synthesis. It has been proven that Shiitake mushroom is used to lower blood serum cholesterol (BSC) via a factor known as eritadenine, which is also called “Lentinacin” or “Lyntisine”. It is known that, apparently, eritadenine reduces BSC in mice, not by inhibition of cholesterol biosynthesis, but by the acceleration of excretion of ingested cholesterol and its metabolic decomposition (Suzuki & Oshima, 1974, 1976). Eritadenine also lower the blood levels of cholesterol and lipids in animals.

**Antimicrobial properties**

In recent years *Basidiomycetes* and other higher fungi including some recognized medicinal mushrooms have been re-investigated as sources of novel antibiotics mainly as a result of increasing difficulty and the cost of isolating novel bioactive compounds from the Actinomycetes and Streptomycetes. The water extract of *Lentinus edodes* demonstrated growth-enhancing effects on colon inhabiting beneficial lactic acid bacteria, *Lactobacillus brevis* and *Bifidobacteria brevie*. The effective factor in the extract is considered to be the disaccharide sugar, trehalose. The *L. edodes* extract can improve the beneficial intestinal flora of the gut and reduced harmful effects of certain bacterial enzymes such as β-glucosidase, β-glucorinidase and tryptophase as well as reducing colon cancer formation (Bae, 1997). It is clear from the results that mushrooms also have antimicrobial properties.

The bioactive compounds like mniopetals, oudemansin, lanostane and stroblurin possess potent antimicrobial activity (Table 1). Their dose compensation and the mode of action is subject for research for new generation researchers. Clearly, the antimicrobial potential of extract of several medicinal mushroom type and indeed other *Basidiomycetes* not yet exploited, must warrant further examination.

The heavy molecular weight cell wall polysaccharides, for example, PSP from *Trametes versicolor* inhibits...
growth of infectious yeast, such as *Candida albicans* (Tsukagoshi, 1984; Sakagami, 1991, 1993). Antitumour polysaccharides inhibit bacteria such as *Bacillus subtilis, Staphylococcus aureus, Escherichia coli* and *Pseudomonas aeruginosa*. *Hericium erinaceus* shows strong antimicrobial activity against a broad range of infectious agents. Compounds extracted from *Agaricus bisporus,* *Lentinus edodes,* *Coprinus comatus* and *Oudemansiella mucida* have been reported to have antifungal and antibacterial properties.

### Clinical trials and other uses of mushrooms

Clinical trials were conducted on 56 cancer patients, 30 were chosen to receive the medicinal mushroom extract mix and another 26 comparable patients receiving the accepted pharmaceutical drug Polyactin-A as a control group. All patients were in the middle-late stages (stage 3 and 4) of cancer. The experiment concludes that the tablets of mixed polysaccharides, made up of the six species of medicinal mushrooms, can become a new health product to improve immunity with high effectiveness and nontoxicity. However, further trials are needed.

<table>
<thead>
<tr>
<th>Mushrooms</th>
<th>Bioactive compounds</th>
<th>Bioactivity</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cheimonophyllum candeissimum</td>
<td>Cheimonophyllon A-E</td>
<td>Antibacterial, weak antifungal</td>
<td>Stadler <em>et al.</em>, 1994</td>
</tr>
<tr>
<td>Clitocybe cyathiformis</td>
<td>Cyathiformine A</td>
<td>Antibacterial and antifungal</td>
<td>Arnone <em>et al.</em>, 1993</td>
</tr>
<tr>
<td>Clitocybe diatreta</td>
<td>Diatretol</td>
<td>Antibacterial</td>
<td>Arnone <em>et al.</em>, 1996</td>
</tr>
<tr>
<td>Coprinus atramentarius</td>
<td>Illudin C2, Illudin C3</td>
<td>Antimicrobial</td>
<td>Lee <em>et al.</em>, 1996</td>
</tr>
<tr>
<td>Crepidotus fulvotomentosus</td>
<td>Strobilurin E</td>
<td>Antifungal</td>
<td>Weber <em>et al.</em>, 1989</td>
</tr>
<tr>
<td>Favolaschia pustulosa</td>
<td>9-methoxystrobilurin L</td>
<td>Antifungal and Antibacterial</td>
<td>Wood <em>et al.</em>, 1996</td>
</tr>
<tr>
<td>Favolaschia sp.</td>
<td>Favolon</td>
<td>Antifungal</td>
<td>Anke <em>et al.</em>, 1995</td>
</tr>
<tr>
<td>Flagelloscypha pilatii</td>
<td>Pilatin</td>
<td>Antibiotic</td>
<td>Heim <em>et al.</em>, 1988</td>
</tr>
<tr>
<td>Ganoderma lucidum</td>
<td>Ganoderan</td>
<td>Antiviral</td>
<td>Wasser, 2005</td>
</tr>
<tr>
<td>Lentinus edodes</td>
<td>Lentinan</td>
<td>Antiviral</td>
<td>Mizuno, 2000</td>
</tr>
<tr>
<td>Mniopetalum sp.</td>
<td>Mniopetals</td>
<td>Antimicrobial</td>
<td>Kuschel <em>et al.</em>, 1994</td>
</tr>
<tr>
<td>Mycena sp.</td>
<td>Strobilurin M, Tetrachloropyrocatechol</td>
<td>Antifungal, Cytostatic, Antifungal, Antibacterial</td>
<td>Daferner <em>et al.</em>, 1998</td>
</tr>
<tr>
<td>Omphalotus illudens</td>
<td>Illudinic acid</td>
<td>Antibacterial</td>
<td>Dufresne <em>et al.</em>, 1997</td>
</tr>
<tr>
<td>Oudemansiella radicata</td>
<td>Oudemansin x</td>
<td>Antifungal</td>
<td>Anke <em>et al.</em>, 1990</td>
</tr>
<tr>
<td>Poria cocos</td>
<td>Lanostane</td>
<td>Phospholipase A2 inhibitor (group of antiinflammatory agents)</td>
<td>Cuellar <em>et al.</em>, 1996</td>
</tr>
</tbody>
</table>
The polysaccharides extracted from *Agaricus brasiliensis*, *Grifola frondosa*, *Lentinus edodes*, *Ganoderma lucidum*, *Trametes versicolor* and *Cordyceps sinensis* are used to produce tablets for inhibiting the growth of tumours and improving the immunity.

The products of *Ganoderma lucidum* are prescribed in various forms; it can be injected as a solution of powdered spores or given as syrup. It can be taken as tea, soup, capsules, tinctures, or bolus. In tincture form, the dose given is 10 ml thrice daily. In case of syrup the dose is 4-6 ml/day. The dried mushroom (200-300 g) is prepared in water and given as a drink, the recommended dose is 3-5 times daily (Ying et al, 1987; Zhuang, 1993).

In Japan, *Ganoderma lucidum* is used for the treatment of the cancer (Willard, 1990). The results obtained after application shows that the patient sleeps well with a healthier feeling and has an increased appetite; Reishi also provides relief from angina pectoris. Injection of spore powder is effective in curing progressive deterioration, atrophy and muscles stiffness. The effect of elevation changes has been prevented and cured by tablets of mushroom spores.

In an experimental study for therapeutic application of *G. lucidum*, 143 patients with advanced previously treated cancer were given an oral *G. lucidum* polysaccharide extract of 1800 mg three times daily for 12 weeks. Twenty-seven patients were not assessable for response and toxicity, because they were unable to track for follow-up or refused further therapy before the 12 weeks of treatment were up. Of the 100 fully assessable patients, 46 (32.2%) had progressive disease before or at the six weeks evaluation point (range: 5 days-6 weeks). There was no significant change in the Functional Assessment of Cancer Therapy-General (FACT-G) scores in 85 assessable patients. In the group with stable disease, FACT-G scores improved in 23 patients, remained unchanged in five, and declined in one. Within this group, the median change from the baseline score to the 6 and 12 weeks was +7.6 and +10.3, both statistically significant ($P < 0.05$). For the 38 patients with SD, the median change from the baseline score was 28.1 ± 10.2 weeks. This indicates that Ganopoly may have an adjunct role in the treatment of patients with advanced cancer although objective responses were not observed in the study (Wasser & Weis, 1997a).

*G. lucidum* and other mushrooms like *G. applanatum*, *Lentinus edodes*, *Flammulina velutipes*, *Grifola frondosa* from China, Korea, Japan and India have been used in many clinical studies with animals and humans, reporting the beneficial results. The high-molecular-weight polysaccharides from the cell walls of *G. lucidum* are physiologically active. They are used against various diseases like diabetes, Alzheimer’s disease, retinal pigmentary degeneration, atrophic myotonomus hepatodymia, rhinitis, leucopoenia, insomnia, dyspnea, neurasthenia and duodenal ulcers. The water extract from fruit body had inhibitory activity on histamine release from rat peritoneal mast cells, induced by compound 48/80 or antigen-antibody reaction and on passive cutaneous anaphylaxis reaction in guinea pigs and the rats. This activity is due to the Ganoderic acids C and D, which are also responsible for the treatment of asthma and allergy. The polysaccharides and triterpenoids have also shown the anti-HIV activity. They also show protective effects on liver in animal and human studies (Wasser & Weis, 1997b).

Ganopoly is well-tolerated and appears to be active against HBV patients with chronic hepatitis B. The mechanism for hepatoprotective effects of *G. lucidum* have been largely undefined. However, accumulating evidence suggests several possible mechanisms, which include antioxidants and radical scavenging activity, modulation of hepatic Phase I and II enzymes inhibition of β-glucuronidase, antifibrotic and antiviral activity, modulation of NO production, maintenance of hepatocellular calcium homeostasis and immunomodulating effects. *G. lucidum* also cures lung and heart dysfunction. Clinical studies on this were conducted in China in which 200 patients with chronic bronchitis were given *G. lucidum* in tablet form and 60-90% patients showed marked improvement with increased appetite. It also reduced blood and plasma viscosity in hypertensive patients with hyperlipidaemia. The extracts of this mushroom were reported to reduce blood cholesterol and blood pressure and also treat arrhythmia (Ding, 1987; Cheng et al, 1993). *G. lucidum* has also shown hypoglycaemic and hypolipidemic activities. In a study, 71 patients with confirmed type II diabetes mellitus were cured and had best results. This study demonstrated that Ganopoly is efficacious and safe in lowering blood glucose concentrations.
The practitioner experiences along with preliminary clinical reports indicate that immunostimulating polysaccharides of *G. lucidum* are useful in treating certain viral diseases, inducing HIV and Epstein Barr Virus (EBV), the cause of mononucleosis. The *G. lucidum* is one of the ingredients in skin lotions produced for protection against UV radiation. (Ying *et al*, 1987). Current biomedical applications of *G. lucidum* are given in Table 2.

**Table 2 : Current biomedical applications of Ganoderma lucidum**

<table>
<thead>
<tr>
<th>Applications</th>
<th>References</th>
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<tbody>
<tr>
<td>A. Immunomodulating effects</td>
<td>Chang, 1994</td>
</tr>
<tr>
<td>1. Anticancer</td>
<td>Mizuno, 1995a, 1995b, 1995c</td>
</tr>
<tr>
<td>2. Antiviral (e.g., anti-HIV)</td>
<td>Kim <em>et al</em>, 1994</td>
</tr>
<tr>
<td>3. Antibacterial</td>
<td>Yoon <em>et al</em>, 1994</td>
</tr>
<tr>
<td>B. Cardiovascular disorders</td>
<td>Soo, 1994, 1996</td>
</tr>
<tr>
<td>1. Coronary dilation and increasing coronary circulation</td>
<td>Chang &amp; But, 1986</td>
</tr>
<tr>
<td>2. Anti-hyperlipidemic, and antiplatelet hypoglycaemic aggregation (blood clots)</td>
<td>Chang, 1994; Soo, 1994</td>
</tr>
<tr>
<td>C. Cancer therapy</td>
<td>Chang &amp; But, 1986; Hu &amp; But, 1987; Chen &amp; Yu, 1993; Mizuno, 1995 a, 1995 b, 1995 c</td>
</tr>
<tr>
<td>1. Maintain leucocyte count</td>
<td>Soo, 1996</td>
</tr>
<tr>
<td>2. Enhance the immune system</td>
<td>Chang &amp; But, 1994</td>
</tr>
<tr>
<td>3. Reduction of chemotherapy toxicity and elimination of induced leucopenia (low blood leucocytes) by chemotherapy</td>
<td>Chang &amp; But, 1995 a, 1995 b, 1995 c</td>
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<tr>
<td>4. Remission to prevent relapses</td>
<td>Chang, 1994</td>
</tr>
<tr>
<td>D. Remission of cancer and hepatitis B treatment</td>
<td>Ventura &amp; Messerli, 1987; Chang, 1993; Mizuno, 1995a, 1995b, 1995c</td>
</tr>
<tr>
<td>E. Enhancing oxygen utilization</td>
<td>Dharmananda, 1988</td>
</tr>
<tr>
<td>1. Relief of discomfort of high altitude stress, headaches, dizziness, nausea &amp; insomnia</td>
<td>Mizuno, 1995c</td>
</tr>
<tr>
<td>2. Relief of oxygen deprivation caused by coronary arteries blocked by atheromas, spasms or clots</td>
<td>Mizuno, 1995a, 1995b, 1995c</td>
</tr>
<tr>
<td>F. Anti-ageing, anti-oxidant free radical scavengers</td>
<td>Gunde-Cimerman, 1999</td>
</tr>
<tr>
<td>G. Antidiabetic</td>
<td></td>
</tr>
<tr>
<td>H. Other examples</td>
<td></td>
</tr>
<tr>
<td>1. Physical exercise</td>
<td>Alexeev &amp; Kupin, 1993</td>
</tr>
<tr>
<td>2. Improving work capacity</td>
<td>Mizuno, 1995a, 1995b, 1995c</td>
</tr>
<tr>
<td>3. Rapid recovery of normal physiology</td>
<td>Mizuno, 1995a, 1995b, 1995c</td>
</tr>
</tbody>
</table>

Ref. Willard, 1990; Chen & Yu, 1993; Wasser, 2005a, 2005b
The Royal sun, *Agaricus brasiiliensis* modulates the immune system against cancer. The active substance and mechanism of their action is under way to be studied in detail. The hot water soluble fraction from *A. brasiiliensis* fruit bodies significantly increased positive cells such as Pan T-cells, helper T-cells, cytotoxic T-cells population (Mizuno *et al.*, 1990a). The polysaccharides from this mushroom is considered to be an effective prophylactic, protecting humans against cancer by stimulating lymphocytes such as cytotoxic T-cells, they are considered to be the active principles like polysaccharides present in boiled water extract. Another preparation obtained with fine particles from fruit bodies (ABP-F) and from mycelium (ABP-M), prepared by mechanical disruption, activates the human complement system in human serum via the alternative pathways, which depends on time and dose given. Thus, the extracts of fruit body and mycelium and the culture broth possess compounds exhibiting antitumour, antiviral, antigenotoxic/antimutagenic and immunostimulatory activities.

Thirty seven species of 8 genera out of 912 species belonging to 57 genera have been screened from family *Agaricaceae* for obtaining biologically active substances by cultivation. In view of the rapidly growing popularity of mushroom-based products, including numerous products of species from family *Agaricaceae*, the further elucidation of active principles, mechanism of action, and their possible adverse effect as well as the quest for other biological response modifiers by means of the screening programs was crucial in implementing safety measures for public health (Didukh *et al.*, 2003).

The schizophyllan derived from *Schizophyllum commune*, shown to activate macrophage *in vitro* and *in vivo*, which results in augmentation of T-cell activities and increases sensitivity of cytotoxic LAK and NK cells to IL-2 (Mizuno *et al.*, 1990). The laboratory tests seem to indicate the role for the adrenalinpituitary axis and central peripheral nervous system including serotonin, 5HT, histamine and catecholamine in lentinans antitumour activity.

The lentinan from *Lentinus edodes* is also an important compound. It acts as the host defense potentiator and is able to store or augment the responsiveness of host cells by stimulating maturation, differentiation, or proliferation of cells involved in host defense mechanisms (Chihara *et al.*, 1970). In one case the noble increase in several serum protein components in α- and β-globulin regions is observed mainly in complement C3, hemopexin and ceruloplasmin. The immunomodulating action of mushroom polysaccharides is especially valuable as a prophylactic, a mild and non-invasive form of treatment, and in the prevention of metastatic tumours, etc.

The immunostimulatory substance EP3, obtained from the fractionation of *Lentinus edodes* mycelium is a lignin complex (80%), 10% carbohydrates and 10% protein. When lignin is removed from the above components the activity was reduced. This means the activity was due to the water-soluble lignin containing numerous carboxyl groups. These host defense potentiators (HDP’s) are functionally different from the biological response modifiers. Many other interesting biological activities of lentinan are reported by various investigators (Hamada, 1981; Aoki, 1984b; Hamuro & Chihara, 1985).

The mushroom can lower blood pressure and free cholesterol in plasma, as well as accelerate the accumulation of lipids in the liver by removing them from circulation. It helps in liver protection, improves liver function and enhances the production of antibodies to hepatitis B. The 9g/day intake of dried Shiitake mushroom decrease the serum cholesterol by 7-10% in patients suffering from hypercholesterolaemia. The older patients (60 years or more) with hyperlipidaemia have experienced a decrease in total cholesterol levels by 9-10% by taking 90g/day in 7 days. Lentinan has actively exerted an inhibitory activity on the HIV-1 reverse transcriptase and proliferation of leukaemia cells.

Mushroom products with their dose compensations for the cure of respective disease are given in Table 3.

The lipid fractions isolated from the fruiting bodies are highly effective against Sarcoma 180 and highly metastatic, drug resistant mouse Lewis Lung Carcinoma (LIC) cells via oral administration. The active substance ergosterol is devoid of side effects that are usually caused by cancer Chemotherapy drugs. The ergosterol is an anti-angiogenic substance.

The water soluble extracts of Shiitake mushroom mycelium has shown antiviral and immunomodulating effects and lentinan has shown various activities against various diseases, viz. antiviral activity in mice against VSV (vesicular somatitis virus), encephalitis virus,
abelson virus, and adenovirus type 12. Stimulated nonspecific resistance against respiratory viral infections in mice, enhanced bronchoalveolar, macrophage activity and increased resistance against the parasites Schistosoma japonicum and S. mansoni. Lentinan has also exhibited activity against Mycobacterium tuberculosis bacilli (resistant to antituberculosis drugs), Bacillus subtilis, Staphylococcus aureus, Micrococcus lentius, Candida albicans and Saccharomyces cerevisiae.

*Ganoderma lucidum* contains 800-2000 ppm of germanium, which can promote blood circulation, can increase the oxygen absorbing capacity of the body and regulate the oxygen supply. The medicine called PSK is used in cancer immunotherapy has been extracted from ‘Yung-Jong’, which belongs to the *Ganodermataceae* family.

**Conclusion**

The research reports summarized in this article have highlighted the medicinal importance of mushrooms as new anticancer, anticholesterolenic, antidiabetic, hepatoprotective and immunomodulative drug. However, the screening of mushrooms from different ecological and geographical regions of the world is still required to identify, isolate, design, develop, modify or prepare new pharmacologically active compounds from wild mushrooms. The development of a novel biotechnological process for growing pure cultures of higher *Basidiomycetes* under controlled conditions on surfaces especially in submerged cultures and the determination of optimal conditions of growth in submerged cultures are needed. The mechanism of action of various secondary metabolites isolated from medicinal and wild edible mushrooms is yet to be elucidated.

**Acknowledgements**

We are grateful to the Honorable Dr. S.N. Patil, Vice-Chancellor, Amravati University, Amravati, for valuable guidance and for encouragement; and to Dr. S. K. Deshmukh for supplying the literature.

<table>
<thead>
<tr>
<th>Mushroom Product</th>
<th>Disease</th>
<th>Dose</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Oral Administration</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>Trametes versicolor</em> (PSK)</td>
<td>Lung cancer</td>
<td>3 capsules 340 mg three times daily</td>
<td>Tsang <em>et al</em>, 2003</td>
</tr>
<tr>
<td><em>Trametes versicolor</em> (PSP)</td>
<td>Immunosuppression</td>
<td>2g/kg/day</td>
<td>Qian <em>et al</em>, 1997</td>
</tr>
<tr>
<td><em>Trametes versicolor</em> (PSP)</td>
<td>HIV-1</td>
<td>6.25 mg/ml</td>
<td>Collins &amp; Ng, 1997</td>
</tr>
<tr>
<td><strong>Ganoderma lucidum</strong> (Ganopoly)</td>
<td>Advanced cancer</td>
<td>600 mg three times daily</td>
<td>Gao <em>et al</em>, 2002</td>
</tr>
<tr>
<td><strong>Grifola frondosa</strong> D-fraction</td>
<td>Various cancers</td>
<td>100 mg/day for 34 months</td>
<td>Kodama <em>et al</em>, 2002</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Mushroom Product</th>
<th>Disease</th>
<th>Dose</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Intraperitoneal Administration</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>Sparassis crispa</em></td>
<td>Cancer</td>
<td>250 µg/ mouse 1000 µg/ mouse</td>
<td>Harada <em>et al</em>, 2002</td>
</tr>
<tr>
<td><strong>Phellinus linteus</strong></td>
<td>Cancer</td>
<td>100 mg/kg of an acidic polysaccharide</td>
<td>Kim <em>et al</em>, 2003</td>
</tr>
<tr>
<td><strong>Agaricus brasiliensis</strong> (F III-2-b and 5-FU)</td>
<td>Meth A tumour cells</td>
<td>10mg/kg/day × 30</td>
<td>Itoh <em>et al</em>, 1994</td>
</tr>
</tbody>
</table>

PSP = polysaccharide peptide; PSK = Krestin
Ganopoly = A crude polysaccharide fraction of *Ganoderma lucidum*
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