Therapeutic Potential of Mushrooms

Mahendra Rai[1]*, Girish Tidke[1] and Soloman P Wasser[2]

[1]Department of Biotechnology, Amravati University, Amravati – 444 602, Maharashtra, India

[2]International 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.

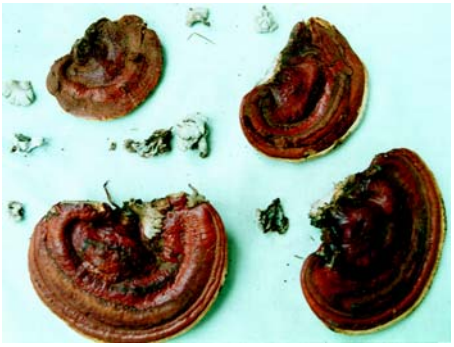
IPC code; Int. cl.[7]— A61K 35/84, A61P 9/00, A61P 31/00, A61P 35/00

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.**

Agaricus sp.



Ganoderma sp.

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, leukopenia, 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***, ***Dendropolyporus 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, antiinflammatory, antidiabetic, 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 (***Lycoperdon pusilum*** 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 pusilum*** 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, antidiabetic, 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, antidiabetic 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 heteroglycans 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 has also shown 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 immunostimulative 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 anti-tumour 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

Pleurotus sajor-caju

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 hypercholesteromia 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

Lentinus edodes

Lentinus edodes

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 strobilurin 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 1 : Compounds showing antimicrobial activity

Mushrooms	Bioactive compounds	Bioactivity	Reference
Cheimonophylum candissimum	Cheimonophyllon A-E	Antibacterial, weak antifungal	Stadler *et al*, 1994
Clitocybe cyathiformis	Cyathiformine A	Antibacterial and antifungal	Arnone *et al,* 1993
Clitocybe diatreta	Diatretol	Antibacterial	Arnone *et al,* 1996
Coprinus atramentarius	Illudin C2, Illudin C3	Antimicrobial	Lee *et al,* 1996
Crepidotus fulvotomentosus	Strobilurin E	Antifungal	Weber *et al,* 1989
Favolaschia pustulosa	9-methoxystrobilurin L	Antifungal and Antibacterial	Wood *et al,* 1996
***Favolaschia* sp.**	Favolon	Antifungal	Anke *et al,* 1995
Flagelloscypha pilatii	Pilatin	Antibiotic	Heim *et al,* 1988
Ganoderma lucidum	Ganoderan	Antiviral	Wasser, 2005
Lentinus edodes	Lentinan	Antiviral	Mizuno, 2000
***Mniopetalum* sp.**	Mniopetals	Antimicrobial	Kuschel *et al*, 1994
***Mycena* sp.**	Strobilurin M, Tetrachloropyrocatechol	Antifungal, Cytostatic, Antifungal, Antibacterial	Daferner *et al*, 1998
Omphalotus illudens	Illudinic acid	Antibacterial	Dufresne *et al*, 1997
Oudemansiella radicata	Oudemansin x	Antifungal	Anke *et al*, 1990
Poria cocos	Lanostane	Phospholipase A2 inhibitor (group of antiinflammatory agents)	Cuellar *et al*, 1996

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 myotonous 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*

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

Ref. Willard, 1990; Chen & Yu, 1993; Wasser, 2005a, 2005b

The Royal sun, ***Agaricus brasiliensis*** 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. brasiliensis*** 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 adrenalpituitary 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 immunoactive 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 cerevisae*.

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 3 : Mushroom products with their doses compensations for the cure of respective diseases

Mushroom	Disease	Dose	Reference
Oral Administration			
Trametes versicolor (PSK)	Lung cancer	3 capsules 340 mg three times daily	Tsang *et al,* 2003
Trametes versicolor (PSP)	Immunosuppression	2g/kg/day	Qian *et al*, 1997
Trametes versicolor (PSP)	HIV-1	6.25 mg/ml	Collins & Ng, 1997
Ganoderma lucidum (Ganopoly)	Advanced cancer	600 mg three times daily	Gao *et al,* 2002
Grifola frondosa D-fraction	Various cancers	100 mg/day for 34 months	Kodama *et al,* 2002
Intraperitoneal Administration			
Sparassis crispa	Cancer	250 µg/ mouse 1000 µg/ mouse	Harada *et al,* 2002
Phellinus linteus	Cancer	100 mg/kg of an acidic polysaccharide	Kim *et al,* 2003
Agaricus brasiliensis (F III-2-b and 5-FU)	Meth A tumour cells	10mg/kg/day × 30	Itoh *et al*, 1994

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

References

1. Alberts AW, MacDonald JS, Till AE and Tobert JA, Lovastatin, *Cardiovasc Drug Rev,* 1989, **7**, 89-109.
2. Alexeev V and Kupin V, *Ganoderma lucidum* administration in air-spacemedicine, 5thInternational Symposium on *Ganoderma lucidum,* Seoul, 1993, pp. 60-63.
3. Anke T, Basidiomycetes: a source of new bioactive secondary metabolites, *Prog Ind Microbiol,* 1989, **27**, 51-66.
4. Anke T, Werle A, Bross M and Steglich W, Antibiotics from basidiomycetes XXXIII, Oudemansin X, a new antifungal *E-β*-Methoxyacrylate from *Oudemansiella radicata* (Rehlan EX FR.) Sing, *J Antibiot* (Tokyo), 1990, **43**(8), 1010-1011.
5. Anke T, Werle A, Zapf S, Velten R and Steglich W, Favolon, a new antifungal triterpenoid from a *Favolaschia* species, *J Antibiot* (Tokyo), 1995, **48**, 725-726.
6. Aoki T, 1984a, Antibodies to HTLV I and HTLV III in sera from two Japanese patients one with possible pre-AIDS, *Lancet,* 1984, **20**, 936-937.
7. Aoki T, 1984b, Lentinan, *In*: Immune Modulating Agents and their Mechanisms, RL Fenichel, and MA Chirgis (Eds), *Immunol Studies,* 1984, **25**, 62-77.
8. Arnone A, Cardillo R, Nasini G and Pava OVD, Cyathiformines A-D, new chorismate-derived metabolites from the fungus *Clitocybe cyathiformis, Tetrahedron,* 1993, **49**, 7251- 7258.
9. Arnone A, Capelli S, Nasini G, Meille SV and Pava OVD, Secondary mould metabolites II Structure elucidation of diatretol - A new Diketopiperzine metabolite from the fungus *Clitocybe diatreata*, *Liebigs Ann*, 1996, 1875-1877.
10. Bae EA, Kim DH and Han M J, Effect of *Lentinus edodes* on the growth of intestinal lactic acid bacteria, *Arch Pharm Res,* 1997, **20**, 443-447.
11. Buswell JA and Chang ST, Edible mushrooms, Attributes and applications. In a Genetics and breeding of edible mushrooms Chang ST, Buswell, JA, Miles PG Gordon and Breach, Philadelphia, 1993, 297-394.
12. Berkeley Rev. MJ, Introduction to Cryptogamic Botany, London, H Bailliere, *Food Ingred J* (Japan), 1857, **167**, 69-85.
13. Chang H and But P (Eds.), Lingzhi, Pharmacology and application of Chinese materia medica, World Scientific publishing, Singapore, 1986, pp. 642-653.
14. Chang R, Limitations and Potential applications of *Ganoderma* and related fungal polyglycans in clinical ontology; First International Conference on Mushroom Biology and Mushroom products, 1993, 96.
15. Chang R, Effective dose of *Ganoderma* in humans, *In*: Proceedings Contributed Symposium 59A, B. 5th *Int Mycol Congr*, Buchanan PK, Hseu RS and Moncalvo JM (Eds), Taipei, 1994, pp.101-13.
16. Chang R, Functional properties of edible mushrooms, *Nutr Rev,* 1996, **54**(11), S91-S93.
17. Chen RY and Yu DQ, Studies on the triterpenoid constituents of the spores from *Ganoderma lucidum*, *Yao Hsueh Hsueh Pao* (*Acta Pharm Sinica),* 1993, **26**, 267-273.
18. Cheng HH, Hou WC and Lu ML, Interactions of lipid metabolism and intestinal physiology with *Tremella fuciformis* Berk. edible mushroom in rats fed a high-cholesterol diet with or without Nebacitin, *J Agric Food Chem,* 1993, **50**(25), 7438-7443.
19. Chihara G, Antitumour and immunological properties of polysaccharides from fungal origin, *Mushr Sci,* 1978, **9**, 797-814.
20. Chihara G, Hamuro J, Maeda YY, Arai Y and Fukoeka F, Fractionation and purification of the polysaccharides with marked antitumour activity, especially lentinan from *Lentinus edodes* (Berk.) Sing (an edible mushroom), *Cancer Res*, 1970, **30**, 2776 -2781.
21. Collins RA and Ng TB, Polysaccharopeptide from *Coriolus versicolor* has potential for use against human immunodeficiency virus type 1 infection, *Life Sci*, 1997, **60**(25), 383-387.
22. Cuellar MJ, Giner RM, Recio MC, Just MJ, Manez S and Rios JL, Two Fungal lanostane derivative as Phospholipase A2 Inhibitors, *J Nat Prod*, 1996, **59**, 977-979.
23. Daferner M, Anke T, Hellwig V, Steglich W and Sterner O, Strobilurin M, Tetrachloropyrocatechol and Tetrachloropyrocatechol methyl ether: new antibiotics from *Mycena* species, *J Antibiot* (Tokyo), 1998, **51**, 816-822.
24. Dharmananda S, Medicinal Mushrooms, Best ways Magazine, July 1988, pp. 54-58.
25. Didukh MY, Wasser SP and Eviatar N, Medicinal value of species of the family Agaricaceae Cohn (Higher Basidiomycetes); Current Stage of knowledge and future perspectives, *Int J Med Mushr,* 2003, **5**, 133-152.
26. Ding G, Antiarrhythmia agents in Traditional Chinese Medicines, *Abstr Chin Med*, 1987, **1**, 287-308.
27. Dufresne C, Young K, Pelaez F, Val AGD, Valentino D, Graham A, Platas G, Bernard A and Zink D, Illudinic acid, a novel Illudane sesquiterpine antibiotic, *J Nat Prod,* 1997, **60**, 188-190.
28. Gao Y, Zhou S, Chen G, Dai X and Ye J, A phase I/II study of a *Ganoderma lucidum* (Curt. Fr.)P. Karst. extract (*Ganopoly*) in patients with advanced cancer, *Int J Med Mushr,* 2002, **4**, 207–214.
29. Gunde-Cimerman N, Medicinal value of the genus *Pleurotus* (Fr.) P. Krast (Agaricales S. R., Basidiomycetes), *Int J Med Mushr,* 1999, **1**, 69-80.
30. Hamada C, Inhibitory effect of lentinan on the tumourigenesis of adenovirus type 12 in mice, *In*: Manipulation of Host Defense Mechanisms, Akoi, T *et al* (Eds.) Amsterdam, *Excerpta Med Int Congr Ser*, 576, 1981, pp. 76-87.
31. Hamuro J and Chihara G, Lentinan a T- cell oriented immunopotentiator: Its experimental and clinical applications and possible mechanism of immune modulation, *In*: Fenichel R L, Chirigos M A (Eds.), Immunomodulating agents and their mechanism of action. Dekker, New York, 1985, pp. 409-434.
32. Harada T, Miura N, Adachi Y, Nakajima M, Yadomae T and Ohn N, Effect of SCG, 1, 3-ß-D-glucan from *Sparassis crispa* on the hematopoietic response in cyclophosphamide induced leukopenic

mice, *Biol Pharm Bull*, 2002, **25**, 931–939.

33. Heim J, Anke T, Mocek U, Steffan B and Steglich W, Antibiotics from Basidiomycetes XXIX: Pilatin, A new antibiotically active marasmane derivative from cultures of *Flagelloscypha pilatii* Agerer., *J Antibiot* (Tokyo), 1988, **41**, 1752-1757.
34. Hu B and But P, Chinese materia medica for radiation protection, *Abstr Chin Med*, 1987, **1**, 475-490.
35. *Chem Abstr*, 1992, **116**, 160396.
36. Ikekawa T, Enokitake *Flammulina velutipes*: Antitumour activity of extracts and polysaccharides, *Food Rev Int*, 1995, **11**, 203-206.
37. Ishikawa NK, Kasua M and Vanetti MC, Antibacterial activity of *Lentinus edodes*, grown in liquid medium, *Braz J Microbiol*, 2001, **32**, 206-210.
38. Ikekawa T, Maruyama H, Miyano T, Okura A, Sawasaki Y, Naito K, Kawamura K and Shiratori K, Proflamin a new antitumour agent: preparation, physicochemical properties and antitumour activity, *Jpn J Cancer Res (Gann)*, 1985, **76**, 142-148.
39. Itoh H, Ito H, Amano H and Noda H, Inhibitory action of a (1>6)-beta-D-glucan-protein complex (F III-2-b) isolated from Agaricus blazei Murill ("himematsutake") on Meth A fibrosarcoma-bearing mice and its antitumour mechanism, *Jpn J Pharmacol,* 1994, **66**(2), 265-271.
40. Jeong H, Lee JW and Lee KH, Studies on anticomplimentary activity of Korean higher fungi, *Hanguk Kyunhakhoechi*, 1990, **18**, 145-148; *Chem Abstr*, 1991, **115**, 218446.
41. Kawagishi H, Inagaki R, Kamao T, Mizuino T, Shimura K, Ito H, Hagiwara T and Nakamura T, Fractionation and antitumour activity of the water-insoluble residue of *Agaricus blazei* fruiting body, *Carbohydr Res*, 1989, **186**, 267-273.
42. Kim GY, Roh SI, Park SK, Ahn SC, Oh YH, Lee JD and Park YM, Alleviation of experimental septic shock in mice by acidic polysaccharide isolated from the medicinal mushroom *Phellinus linteus*, *Biol Pharm Bull*, 2003, **26**, 1418–1423.
43. Kim BK, Kim HW and Choi EC, Anti-HIV effects of *Ganoderma lucidum. In* : *Ganoderma*: Systematics, Phytopathology & Pharmacology: Proceedings of Contributed Symposium 59 A, B. 5th Int *Mycol Congr,* 1994, Vancouver.
44. Kodama N, Komuta K and Nanba H, Can maitake MD-fraction aid cancer patients? *Altern Med Rev,* 2002, **7**, 236-239.
45. Kuschel A, Anke T, Velten R, Klostermeyer D, Steglich W and Konig B, The Mniopetals, New Inhibitors of reverse transcriptases from a *Mniopetalum* species (Basidiomycetes), *J Antibiot (Tokyo),* 1994, **47**, 733-739.
46. Lee IK, Jeong CY, Cho SM, Yun BS, KimYS, Yu SH, Koshino H and Yoo ID, Illudins C2 and C3, new illudin C derivates from *Coprinus atramentarius* AST20013, *J Antibiot (Tokyo),* 1996, **49**, 821-822.
47. Misaki A, Kakuta M, Sasaki T, Tanaka M and Miyaji H, Studies on the interrelation of structure and antitumour effects of polysaccharides: Antitumour action of periodate-modified, branched(1-3)-B-d-Glucan of Auricularia auricula-judae and other polysaccharides containing (1-3)-Glycosidic Kikurages, *Carbohydr Res*, 1981, **92**,115-129.
48. Mizuno T, 1995a, Shiitake, *Lentinus edodes*: functional properties for medicinal and food purposes, *Food Rev Int,* 1995, **11**(1), 111-128.
49. Mizuno T, 1995b, Bioactive biomolecules of mushrooms: food function and medicinal effect of mushroom fungi, *Food Rev Int,* 1995, **11**(1), 7-21.
50. Mizuno T, 1995c, Kawariharatake, *Agaricus blazei* Murrill: Medicinal and dietary effects, *Food Rev Int,* 1995, **11**(1), 167-172.
51. Mizuno T, Antitumour Mushrooms *Ganoderma lucidum*, *Grifola frondosa, Lentinus edodes* and *Agaricus blazei, Gendai-shorin*, Tokyo, 1997, 188p.
52. Mizuno T, Immunological special diets, *Agaricus blazei, Ganoderma lucidum, Cordyceps sinensis, Grifola frondosa* and *Lentinus edodes, Gendai-shorin*, Tokyo 1998, 188p.
53. Mizuno T, Development of an antitumour biological response modifier from *Phellinus linteus* (Berk. et Curt.) Teng (Aphyllophoromycetedeae), *Int J Med Mushr,* 2000, **2**, 21-33.
54. Mizuno T, Medicinal properties and clinical effects of *Agaricus blazei* Murill (review), *Int J Med Mushr,* 2002, **4**, 299-313.
55. Mizuno T, Kato L, Totsuka A, Shinkai K and Shimizu M, Fractionation, structural features and antitumour activity of water soluble polysaccharide from "Reishi": The Fruit body of *Ganoderma lucidum, Nippon Nogei Kagaku Kaishi*, 1984, **58**, 871-880.
56. Mizuno T, Hagiwara T, Nakamura T, Ito H, Shimura K, Sumiya T and Asakura A, 1990a, Antitumour activity and some properties of water soluble polysaccharides from "Himematsutake" the fruiting body of *Agaricus blazei* Murrill, *Agric Biol Chem*, 1990, **54**, 2889-2896.
57. Mizuno T, Inagaki R, Kanao T, Hagiwara T, Nakamura T, Ito H, Shimura K, Sumiya T and Asakura A, 1990b, Antitumour activity and some properties of water soluble hetero-glycans from "Himematsutake" the fruiting body of *Agaricus blazei* Murrill, *Agric Biol Chem*, 1990, **54**, 2897-2906.
58. Nanba H, Maitake mushroom — The king of mushrooms, *Mushr News*, 1993, **41**, 21-25.
59. Ooi VEC and Liu F, A review of pharmacological activities of mushroom polysaccharides, *Int J Med Mushr*, 1999, **3**, 361-394.
60. Qian ZM, Xu MF and Tang PL, Polysaccharide peptide (PSP) restores immunosuppression induced by cyclophosphamide in rats, *Am J Chin Med,* 1997, **25**(1), 27-35.
61. Sakagami H and Aoki T, Induction of immuno potentiation activity by a protein-bound polysaccharide, PSK (Review), *Anticancer Res,* 1991, **11**, 993-1000.
62. Sakagami H and Takeda M, Diverse biological activity of PSK (Krestin), a protein bound polysaccharide from *Coriolus versicolor*. *In*:Mushroom Biology and Mushroom Products. ST Chang, JA Buswell and SW Chiu (Eds), Chinese University Press, Hong Kong, 1993, pp. 237- 245.
63. Soo TS, The therapeutic value of *Ganoderma lucidum*, 8th *Int Mycol*

Congr (IMC5), Abstracts, Vancouver, B.C., 1994, pp. 95.

64. Soo TS, Effective Dosage of the extract of *Ganoderma lucidum* in the Treatment of Various Ailments, *In*: DJ Royse, (Ed), Mushroom Biology and Mushroom Products. Proceedings of the Second International Congress, 1996, pp. 177-186,
65. Stadler M, Anke H and Sterner O, New nematicidal and antimicrobial compounds from the basidiomycete *Cheimonophyllum candidissimum* (Berk and Curt) Sing, *J Antibiot* (Tokyo), 1994, **47**, 1284-1289.
66. Suzuki M, Higuchi S, Taki Y, Taki S, Miwa K and Hamuro J, Induction of endogenous lymphokine-activated killer activity by combined administration of Lentinan and interleukin 2, *Int J Immunopharmacol*, 1990, **12**, 613-623.
67. Suzuki S and Oshima S, Influence of Shiitake, *Lentinus edodes,* on human serum cholesterol, *Ann Rep Natl Inst Nutr,* 1974, **25**, 89-94.
68. Suzuki S and Oshima S, Influence of shiitake, *Lentinus edodes,* on human serum cholesterol, *Mushr Sci,* 1976, **9**(1), 463-467.
69. Toth JO, Luu B, Beck J and Ourission G, 1983a, Chemistry and biochemistry of oriental drugs, Part IX, Cytotoxic Triterpines from *Ganoderma lucidum* (Polyporaceae): structures of ganoderic acids U-Z, *J Chem Res Synpo*, 1983, 299;*Chem Abstr*,1984, **100**, 117512.
70. Toth JO, Luu B and Ourission G, 1983b, Les acides ganoderiques T a Z: Triterpenes cytotoxiques de *Ganoderma lucidum* (Polyporaceae), *Tetrahedron Lett*, 1983, **24**, 1081-1084.
71. Tsang KW, Lam CL, Yan C, Mak JC, Ooi GC, Ho JC, Lam B, Man R, Sham JS and Lam WK, *Coriolus versicolor* polysaccharide peptide slows progression of advanced non-small cell lung cancer, *Respir Med*, 2003, **97**, 618–624.
72. Tsukagoshi S, Krestin (PSK), *Cancer Treatment Rev*, 1984, **11**, 131-155.
73. Ukai S, Kiho T, Hara C, Morita M, Gao A and Naomi HY, Polysaccharides in Fungi XIII Antitumour activity of various polysaccharides isolated from *Dictyophora indusiata, Ganoderma japonicum, Cordyceps cicadae, Auricularia auricula- Judae* and *Auricularia* Species, *Chem Pharm Bull*, 1983, **31**, 741-744.
74. Ventura HO and Messerli FH, Abgiotensine converting enzyme inhibitors: a new class of hypertensive drugs, *In*: Drugs therapy in hypertension, JIM Drayer *et al* (Eds.), Marcel Deccer, Inc., 1987, pp. 139-161.
75. Wasser SP, Dietary supplements from medicinal mushrooms: Diversity of types and variety of regulations, *Int J Med Mushr,* 2000, **2**, 20-21.
76. Wasser SP, 2005a, Reishi or Ling Zhi *(Ganoderma lucidum)*, *In*: Encyclopedia of Dietary supplements, Marcel Dekker, N.Y., 2005, pp. 603-620.
77. Wasser SP, 2005b, Shiitake (*Lentinus edodes*), *In*: Encyclopedia of Dietary supplements, Marcel Dekker, N.Y., 2005, pp. 653-664.
78. Wasser SP and Didukh MYA,Culinary-medicinal higher basidiomycete mushrooms as a prominent source of dietary supplements and drugs for the 21st century, Proceedings of the 5th International Conference of Mushroom Biology and Mushroom Products, Q Tan, J Zhang MChen, HCao and JA(Eds), Buswell, Sanghai, China, 2005, **12**, 20-34.
79. Wasser SP and Weis AL 1997a, Shiitake mushroom [*Lentinus edodes* (berk.) Sing.], *In*: E Nevo (Ed) Medicinal mushrooms, Peledfus, Haifa, Israel, 1997.
80. Wasser S P and Weis AL, 1997b, Reishi Mushroom [*Ganoderma lucidum* (Curt.: Fr.) P.Karst.]. *In*: E Nevo (Ed) Medicinal mushrooms. Peledfus, Haifa, Israel, 1997.
81. Wasser SP and Weis AL, 1999a, Medicinal properties of substances occurring in higher Basidiomycetes mushrooms: current perspective, *Int J Med Mushr,* 1999, **1**, 31-62.
82. Wasser SP and Weis AL, 1999b, Therapeutic effects of substances occurring in higher Basidiomycetes mushrooms: a modern perspective, *Crit Rev Immunol,* 1999, **19**, 65-96.
83. Weber W, Anke T, Steffan B and Steglich W, Antibiotics from Basidiomycetes XXXII Strobilurin E: A New Cytostatic and Antifungal (E)-Methoxyacrylate Antibiotic from *Crepidotus fulvotomentosus* Peck, *J Antibiot* (Tokyo), 1989, **43**, 207-212.
84. Willard T, Reishi Mushroom: Herb of Spiritual Potency and Medical Wonder, Sylvan Press, Washington, 1990, pp.110.
85. Yang QY and Wang MM, The effect of *Ganoderma lucidum* extract against fatigue and endurance in the absence of oxygen. 5th International Mycological Congress (IMC5), Abstract, Vancouver, BC, Canada, August, 14-21,1994, pp. 249.
86. Ying J, Mao X, Ma Q, Zong Z and Wen H, Icons of Medicinal fungi from China, X Yuehan, (Ed), Science Press, Beijing, Translated.
87. Yoon SY, Eo SK, Kim YS, Lee CK and Han SS, Antimicrobial activity of *Ganoderma lucidum* extract alone and in combination with some antibiotics, *Arch Pharm Res*,1994, **17**, 438-442.
88. Zhuang C, Mizuno T, Shimada A, Ito H, Suzuki C, Mayuzumi Y, Okamoto H, MaY and Li J, Antitumour Protein-containing polysaccharides from a Chinese mushroom Fengweigu or Houbitake, *Pleurotus sajor-caju* (Fr.) Sing, *Biosci Biotechnol Biochem,* 1993, **57**, 901-906.
89. Zhuang C, Mizuno T, Ito H, Shimura K, Sumiya T and Kawade M, 1994a, Fractionation and antitumour activity of polysaccharides from *Grifola frondosa* mycelium, *Biosci Biotechnol Biochem,* 1994, **58**, 185-188.
90. Zhuang C, Mizuno T, Ito H and Shimura K, 1994b,Chemical modifications and anti-tumour activity of polysaccharides from mycelium of liquid-cultured *Grifola frondosa*, *Nippon Shokuhin Kogyo Gakkaishi*,1994, **41**, 733 -740.