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A SYSTEMATIC REVIEW ON SOME MEDICINAL MUSHROOMS SHOWING ANTIOXIDANT AND ANTICANCER ACTIVITIES

PREGLED NEKIH MEDICINSKIH GLJIVA KOJE POKAZUJU ANTIOKSIDANTNU I ANTIKANCERSKU AKTIVNOST

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Abstract

Different species of mushrooms have been found to contain various chemical constituents, micro and macronutrients as well as secondary metabolites and are commonly used for their nutritive and medicinal values. Mushrooms have a short shelf life compared with most fruits and vegetables. Intact mushrooms lose their commercial value within a few days due to senescence, water loss, microbial attack and browning. Mushrooms show a high protein content. They have shown a plethora of pharmacological activities and the main aim of this paper was to review the medicinal role of mushrooms. The different chemical constituents and pharmacological activities reported in the literature are discussed. They have shown activities like antioxidant, anticancer, antimicrobial and immunomodulatory activities etc. Different species like *Agaricus bisporus* has been tested as a nutritional supplement for bread, since it has been shown to be a good source of selenium, chromium, vitamin and antioxidant agents. *Ganoderma lucidum* contains mainly triterpenoids, polysaccharides, nucleotides, sterols, steroids, fatty acids, proteins or peptides, and trace elements and one of the most famous traditional Chinese medicinal herbs. It is believed that the active ingredients in *Agaricus blazei* are more potent than that of any other mushrooms. It has shown real promise as an immunomodulatory and a defense against tumors. It is economically the most important mushroom worldwide and shown inhibition of breast cancer development.

INTRODUCTION

Increasingly, scientific evidence is supporting the view that diet controls that modulates many functions of the human body and accordingly participates in the maintenance of the state of good health or homeostasis necessary to reduce the risk of many chronic diseases. Medicinal mushrooms have been more widely used as traditional medicinal ingredients for the treatment of various diseases and related health problems largely due to the increased ability to produce the mushrooms by artificial methods [1].

In a broad sense „mushroom is a macro fungus with a distinctive fruiting body which can be either epigeous or hypogeous and large enough to be seen with the naked eye and to be picked by hand." Thus mushrooms need not be basidiomycetes nor can aerial nor fleshy nor edible mushrooms be ascomycetes grow underground have a non fleshy texture and need not be edible [2].

Mushroom is the fruit-body of a fungus, the reproductive part of the fungus that grows above ground and releases spores, the seed like elements from which new fungi are made. Much as fruit is the reproductive organ of a fruit tree, a mushroom is the reproductive organ of a fungus. Typically, spores sprout from the gills, the thin brown tissue found on the underside of the mushroom cap. Borne by the wind, some kinds of spores are capable of traveling great distances from the fruit-body to start their own fungus colonies. Mushrooms produce prodigious numbers of spores. Not all fungi, however, produce mushrooms. Some are able to create spores and reproduce without bearing a fruit-body. Fungi that reproduce without a sexual stage are called imperfect fungi, or fungi imperfecti [3].

Ancient oriental medicine has stressed the importance of several mushroom species, mostly *Ganoderma lucidum.* (*LingZhi or Reishi*) and *Lentinus edodes* (Berk.) Singer (*Shiitake*). For instance, Ling Zhi was valued for both its medicinal and spiritual properties. The species were used in the treatment of gastrointestinal disorders, various forms of cancers, bronchial asthma, night sweats, etc. [4].

Composition of medicinal mushroom

Mushrooms are composed of polysaccharides, which are long chain molecules constructed from sugar units (poly means „many," saccharide means „sugar"). Polysaccharides present the highest capacity for carrying biological information since they have the greatest potential for structural variability. The amino acids in proteins and the nucleotides in nucleic acids can interconnect in only one way, while the monosaccharide units in polysaccharides can interconnect at several points to form a wide variety of structures [3].

D-glucan back bone of the active constituent and linked to protein forms proteoglycan. Proteoglycans have greater immune potentation activity. Sterols, phenols, terpenoids, fatty acid, proteins, vitamins, minerals and trace elements also present immune effects via stimulation of cytotoxic T cells and NK cell activity [10]. In general, the gross composition of mushrooms is water (90%), protein (240%), fat (28%), carbohydrates (155%), fiber (332%) and ash (810%) (ash is mainly Composed of salts, metals and so forth). Active metabolites can be isolated from fruiting bodies, pure culture mycelia and culture filtrate, and nowadays many attempts are being made to obtain active metabolites from mycelia through sub merged fermentation culture to obtain cheaper preparations. Kawagishi was the first to separate an active anticancer compound purified from the sodium hydroxide extract of the fruit body of *Agaricus blazei* Murril [5].

Qualitative analysis has demonstrated that mushrooms have eight essential amino acids in addition to non-essential ones. Glycosides are present in beta-glucan chains in the cell wall and cytoplasm. The fiber has a high molecular weight, is excreted practically undigested and unabsorbed, and contains chitin (N-acetyl-Glucosamine polymer, a cell wall component in most fungi), hetero polysaccharides (pectin, hemicelluloses), and beta-glucans, which are abundantly present in mushrooms. Mushrooms contain large quantities of minerals, especially phosphorus, sodium, calcium, and potassium. Heavy metals like lead, mercury, and copper can also be found in small amounts because excessive quantities of these metals are harmful, the chemical properties of the water used in the cultivation process should be carefully monitored [6].

Among cultivated mushrooms, *Ganoderma* is unique in being consumed forts medicinal, rather than nutritional value. The specific reported attributes of length include lowering the risk of cancer, heart disease and infection; these health- promoting effects are believed to be mediated via the antioxidant [7]. Any compounds that will influence body functions such as blood pressure, immune responses etc. are classified as pharmacological agents, and as such will invariably demonstrate toxicity at high dosage levels [1].

Agaricus bisporus has been tested as a nutritional supplement for bread, since it has been shown to be a good source of selenium, chromium, vitamin and antioxidant agents. *Rhizopus oligosporus* has been grown in fruit residues (solid state fermentation) aiming at increasing the concentration of free phenol compounds with antioxidant activity, since these compounds are often found in conjugate forms bearing a sugar or lipid moiety [8].

Table.1: *Levels of calcium, magnesium, zinc and iron in mushrooms from Finland, (mg/100 g of dry material)* [8].

Mushroom species	Origin	Ca	Mg	Zn	Fe
Agaricus bisporus/white	Finland	25.0	130.0	6.6	4.8
Agaricus bisporus/brown	Finland	13	141.0	4.7	2.8

SOME SELECTED MEDICINAL MUSHROOMS WITH RESPECT TO THEIR ACTIVITIES

Mushrooms are known to contain antioxidants such as ascorbic acid, tocopherols, phenolic compounds, and carotenoids. Examples of mushrooms with documented antioxidant activity include *Maitake, Agrocybe aegerita, Reishi, Agaricus blazei, Oyster mushrooms, Agaricus bisporus, Chaga,* and *Shiitake*. Chemical analysis has shown that a specific antioxidant found in some mushrooms like *Flammulina velutipes* and *Agaricus bisporus* is ergothioneine [17]. Mushrooms have been found to contain antioxidant substances that could prevent the destructive oxidative process within the organism [2].

Scientific evidences justify include heart diseases, diabetes, obesity and cancer, which could be attributed to diet. Mushrooms are extensively known for their immunomodulatory and mushrooms are helpful to human health [9].

Antioxidant activities of selected medicinal mushroom *Ganoderma lucidum*

Medicinal mushrooms occurring in South India namely *Ganoderma lucidum, Phellinus rimosus, Pleurotus florida* and *Pleurotus pulmonaris* possessed profound antioxidant and antitumor activities. This indicated that these mushrooms would be valuable sources of antioxidant and antitumor compounds. Investigations also revealed that they had significant antimutagenic and anticarcinogenic activities. Thus, Indian medicinal mushrooms are potential sources of antioxidant and anticancer compounds[10].

Ganoderma *(Reishi)*

Reishi has been called the king of herbal medicines, with many herbalists ranking it above ginseng. Although some people use reishi to brew teas, the mushroom is usually taken for medicinal purposes only, as it has a very bitter, woody taste. The name *Ganoderma lucidum* is from the Latin word gan, which means "shiny," derm means "skin," and lucidum means "brilliant." Also called the "Mushroom of immortality" belonging to family Ganodermataceae. The active ingredients are Beta- and hetero-beta-glucans; ling Zhi protein; ganodermic acids (triterpenes) [3].

Previous studies at the Amala Cancer Research Center showed that the methanolic extract of *G. lucidum* occurring in tropical South India possessed significant antioxidant and

anti inflammatory activities. Some physiological effects and distinctive properties of *Ganoderma* are strain dependent and evidence for strain specific terpenoids has been reported in this mushroom. It was reported that the chloroform extract of *G. lucidum* occurring in the tropical South India possess antioxidant and anti inflammatory activities[11].

The phytoconstituents found in *Ganoderma* efficiently scavenged the O_2, OH radical generated experimentally during *in vitro* studies and thus are found to have antioxidant and chelating activity along with reducing power and chelating abilities [2]. An increasingly popular natural remedy, *Ganoderma* is only used as a medicinal mushroom and isn't recommended for cooking [12].

Methanolic extracts of *Ganoderma lucidum* (Ling-Chih) at 0.6 mg/ml, showed an excellent antioxidant activity. *G. Lucidum* was higher in antioxidant activity, reducing power, scavenging and collecting abilities, and total phenol content[13]. The study on ethanol and water crude extracts from *G. lucidum* water extract and ethanol extract showed the highest scavenging activity against DPPH radicals (50% inhibitory concentration =0.055±0.001 mg/ml). Total phenol was the major antioxidant component found in the mushroom extracts[14].

Endogenous damaged mitochondrial DNA by free radicals is believed to be a major contributory factor to aging. A study examined the effects of the extract of important antifatigue and rejuvenating medicinal herb *G. lucidum* for their free radical scavenging effect on liver mitochondrial antioxidant activity[15].

In a study, polysaccharides were isolated from *G. lucidum* and their effects on myocardial collagen cross-linking were discussed in high-fat-diet/streptozotocin diabetic rats to investigate whether collagen-linked advanced glycation end products (AGE) and antioxidant enzymes were involved in the progress[16]. Antioxidant activities of both wild and cultivated *G. lucidum* extracts showed significant antioxidant activity, and maximum scavenging was observed in the case of methanolic extracts of wild *G. lucidum* with minimum IC50 values for DPPH, ABTS, and hydroxyl radicals[17].

In a double-blinded, placebo-controlled, crossover intervention study done on *G. lucidum* the effects of biomarkers for antioxidant status was observed. The fasting blood and urine from healthy, consenting adults was collected before and after 4 weeks supplementation. No significant change in any of the variables was found, although a slight trend toward lower lipids was again seen, and antioxidant capacity in urine increased[7].

A compound GL-1 isolated from *G. lucidum* showed high antioxidant activity of 85.7 ± 0.7%, at 10 mg/ml. Reducing power reached a plateau of 3.4 ± 0.1 at 20 mg/ml, while GL-I chelated 81.6 ± 3.6 % of ferrous ions at 20 mg/ml. At 10 mg/ml, scavenging ability on DPPH radicals of GL-I increased to 96.8 ± 2.5%. The antioxidative activities of the isolated compound GL-1 concentration dependent and increased with increasing concentration[18].

In a study done on *G. lucidum* for its antioxidant and anti-cancer properties, water-soluble extract (GLw) possessed relatively higher antioxidant capacities than the water insoluble counterpart (GLe); however, under the challenge of carcinogenic 4-aminobiphenyl (ABP), GLw reduced the 8-OHdG concentration in HUC-PC culture, while glue induced the formation of H_2O_2 and 8-OHdG in a dose-dependent manner[19].

Different extracts of *G. lucidum* were studied for its in vitro antioxidant activity using different models viz. DPPH radical scavenging, ABTS radical scavenging, FRAP assay and Superoxide Radical Scavenging Assay. The different extracts showed potent antioxidant activity and the potency has been expressed in the order as RGHW>RGHA>RGCH>RGPEt [20]. In another study administration of *G. lucidum* extract significantly ($p < 0.05$) elevated the levels of GSH as well as activities of MnSOD, GPx and GST and decreased significantly ($p < 0.05$) the levels of lipid peroxidation, AOPP and ROS [21]. The antioxidant value of *G. lucidum* was found to be highest in the order of dichloromethane followed by aqueous, methanol, ethyl acetate and hexane extract. Preliminary phytochemical analysis of methanol and aqueous extract revealed the presence of phenols, flavonoids and ascorbic acid [22].

Ethanol extracts of fruit body from *Ganoderma* cultivated in the medium supplemented with herbs were used to analyze their scavenging capabilities on different free radicals and bioactive components. The bioactive component change in *Ganoderma* due to the addition of herbs revealed an important impact to its scavenging capacity on different free radicals[23] and also a peptide isolated from *G. lucidum* is found to be unique and novel compared to other peptides fruiting body exhibiting potent antioxidant activity against various in vitro models[24].

In a recent study different kinds of extraction and cross-flow filtration of composition of 46 healthful and aromatic herbs, 8 fruits and fungi *G. lucidum* were prepared and it was concluded that Bitter 55 (EC50 = 0,387 µl/µg DPPH) possesses significantly higher antioxidant effect. The main reason for this fact arises from high concentration of herbal extract and fruit juice content[25]. *In vitro* and *in vivo* evaluation of antioxidant activities of *Ganoderma lucidum* Polysaccharides showed that GI-PS had strong scavenging activity to DPPH and superoxide radical[26] and exopolysaccharides peptides from *G. lucidum* possessed moderate scavenging ability on weak free radicals; not directly causing damage to cell, Also it was suggested that EPSP from *G. lucidum* broth had a variety of biological activity without any side effect and might be good sources for antioxidant-related functional foods and pharmaceutical industries[27].

Recent results showed that four polysaccharides exhibited antioxidant activities in a concentration-dependent manner. Among four polysaccharides, GLP-III and GLP-IV exhibited the higher scavenging effects on hydroxyl radicals, ABTS radical, DPPH free radical, and stronger reducing power and SOD-like activity than GLP-I and GLP-II. The structural characterization was conducted by Fourier transform infrared spectroscopy (FTIR), and their monosaccharide compositions were determined. Nevertheless, GLP-II was composed of three kinds of monosaccharide[28].

G. lucidum peptide (GLP) is the major antioxidant component of *G. lucidum*. Compared to butylated hydroxytoluene, GLP showed a higher antioxidant activity in the soybean oil system. Soybean lipoxygenase activity was blocked by GLP in a dose-dependent manner with an IC50 value of 27.1 íg/mL. GLP showed scavenging activity toward hydroxyl radicals produced in a deoxyribose system with an IC50 value of 25 íg/mL, and GLP effectively quenched superoxide radical anion produced by pyrogallol autoxidation in a dose-dependent manner[29].

Anticancer activities of selected medicinal mushroom *Agaricus blazei* Murrill (ABM)

Edible and medicinal mushrooms can produce variety of biologically active compounds and can be therefore described as a novel class of nutraceuticals which are widely used as dietary supplements. Recent epidemiological studies from Asia demonstrated that mushroom intake protects against cancer, specifically gastrointestinal (GI) cancer and breast cancer. The anticancer activities of mushrooms were mainly linked to the modulation of the immune system by branched polysaccharides (glucans), glycoproteins or peptide/protein-bound polysaccharides. Some of this natural mushroom compounds demonstrated specific activity against aberrantly activated signaling pathways in cancer cells and were able to modulate specific molecular targets in the cell function including cell proliferation, cell survival and angiogenesis [30].

***Table 2**: Anti-tumour Polysaccharides from Mushrooms [31]*

No.	Scientific name	Active component
1	*Agaricus blazei*	Hetero-glycan (fruiting body)
2	*Ganoderma lucidum*	Polysaccharide (fruiting body) Ganoderan (ß-glucan) (fruiting body, mycelium)
3	*Grifora frondosa*	ß-Glucan (fruiting body, mycelium, medium product)
4	*Schizophyllum commune*	Schizophyllan (ß-glucan) (medium product)

A number of bio-active molecules, including anti tumor substances, have been identified in many mushroom species. Polysaccharides are the best known and most potent mushroom-derived substances with anti tumor and immune modulating properties. Mushrooms such as *Ganoderma lucidum (Reishi), Lentinus edodes (Shiitake), Inonotus obliquus (Chaga)* and many others have been collected and used for hundreds of years in Korea, China, Japan, and eastern Russia[31].

Many drugs can be effective in the laboratory but fail in clinical practice due to either inherent toxicity when used at effective dose rates or lack of efficacy. While all of the mushroom polysaccharides successfully used in animal and human cancer treatments have been administered intravenously, several can also be effective by oral (p.o.) administration. Delivering anticancer agents by oral methods is becoming increasingly important in cost reduction of the regime for an i.v administration [1].

Recent advances in biochemical techniques have allowed the partial isolation and purification of compounds from medicinal mushrooms especially polysaccharides that exhibit anticancer activities. Most appear to act as nonspecific immuno-stimulants, though some have direct cytotoxic effects. Also recent advances in chemical technology have allowed the isolation and purification of some of the relevant compounds especially polysaccharides which possess strong immunomodulation and anti-cancer activities[32].

***Agaricus blazei* Murrill**

Agaricus blazei Murrill (ABM) popularly known as 'Cogumelo do Sol' in Brazil, or'Hime matsutake' in Japan, is a mushroom native to Brazil, and widely cultivated in Japan for its medicinal uses, so it is now considered as one of the most important edible and culinary medicinal biotechnological species. It was traditionally used to treat many common diseases like atherosclerosis, hepatitis, hyper lipidemia, diabetes, dermatitis and cancer. *In vitro* and *in vivo A. blazei* Murrill has shown immunomodulatory and antimutagenic properties; although the biological pathways and chemical substances involved in its pharmacological activities are still not clear [5].

A. blazei, a novel edible mushroom, has been used as a treatement for a long time by cancer patients, has also been reported to have antimutagenic, bactericidal and antitumor effects. Its anti tumor effects seem to be due to the restoration or augmentation of immunological responsiveness and to the potentiation of host defense system through cellular immunity [33].

The medicinal mushroom *A. blazei* Murill from the Brazilian rain forest has been used in traditional medicine and as health food for the prevention of a range of diseases, including infection, allergy, and cancer. *A. blazei* M has been shown to have antitumor, anti-infection, and antiallergic/-asthmatic properties in mouse models. These effects are mediated through the mushroom's stimulation of innate immune cells, such as monocytes, NK cells, and dendritic cells, and the amelioration of a skewed Th1/Th2 balance and inflammation[34].

The antitumor activities of various substances isolated from the lipid fraction of *A. blazei*. were examined and found that tumor growth was retarded by the oral administration of the lipid fraction with a chloroform/methanol mixture in sarcoma 180–bearing mice. Intraperitoneal administration of ergosterol at doses of 5, 10 and 20 mg/kg for 5 consecutive d inhibited the neovascularization induced by Lewis lung carcinoma cell–packed chambers, suggesting that either ergosterol or its metabolites may be involved in the inhibition of tumor-induced neovascularization. Itseems likely that the antitumor activity of ergosterol might be due to direct inhibition of angiogenesis induced by solid tumors[35].

The polysaccharides phytocomplex is thought to be responsible for its immunostimulant and antitumor properties, probably through an opsonizing biochemical pathway. Argantine is a well-known carcinogenic and toxic substance in animals that must be completely and fully evaluated [5].

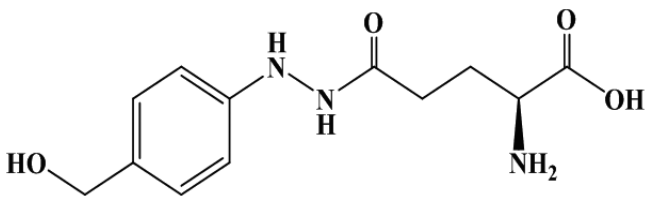


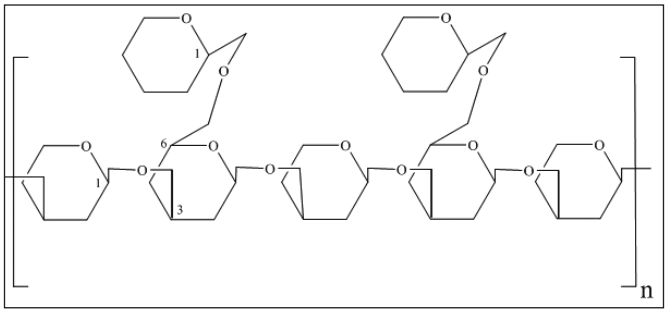
Figure 1: *Structure of* ***Agaritine***

A very recent study has demonstrated that agaritine purified from *Agaricus blazei* Murrill exerts anti-tumour activity against leukemic cells. The extract of *Agaricus blazei* Murrill (ABM) powder was fractionated by HPLC based on the anti-tumour activity against leukemic cells *in vitro*[36].

Phytochemical Constituents

The α and β-glucan Structure *A. blazei* Murrill glucans are side branches of a (1-6)-β-backbone as found by Dong and Ohno, who described that active fraction of â-glucans of ABM fruiting bodies had a (1-6)-β-backbone structure (or functional center) with (1-3)-b side branches in the ratio of 1 : 2; while the linear(1,6)-β-glucan seems to be inactive. The biochemical importance of (1-3)-β-side branches have been confirmed and have shown the enhancement of the immunomodulatory activity of polysaccharides and Mizuno [39] reported an important anti tumor.

Figure 2: *(1–6)-β-backbone structure (or functional center) with (1–3)-side branches [5]*



Many scientists believe that the active ingredients in *A. blazei* are more potent than that of any other mushrooms. It has shown real promise as an immunomodulatory and a defense against tumors. *A. blazei* Murrill is also known as Murrill's agaricus, Royal sun agaricus, and, less frequently, geesongrong and almond-flavored Portobello. The Active ingredients are Beta-(1-3)-D-glucan; beta-(1-4)-a-D-glucan; beta-(1- 6)-D-glucan; RNA-protein complex; glucomannan [3].

The whole-mushroom extracts contain compounds that may modulate tumorigenesis and carcinogenesis at different stages and/or may act at the same stage through different mechanisms. Responses to such highly different polysaccharides are likely to be mediated by different cell-surface receptors, which may be present only on specific subsets of cells, and may trigger distinct downstream responses. A combination of such responses involving different cell subsets could conceivably provide greater tumor inhibition than could be induced by single polysaccharides [5].

A. blazei Murill Kyowa (ABMK), has been reported to possess antimutagenic and antitumor effects. It was observed that natural killer cell activity was significantly higher in ABMK-treated group (ANOVA, n¼39, P<0.002) as compared with nontreated placebo group (n¼61). The reports suggest that ABMK treatment might be beneficial for gynecological cancer patients undergoing chemotherapy[37].

Mushroom species/ constituents	Dose and route of Administration	Mouse strain	Tumor model	% inhibition (or increase in life span)
Agaricus blazei ATF Fractions containing mostly (1-4) α-glucan and 1-6) β-glucan	1mg/mouse intratumorally into the right flank on Days 3,4, and 5 after MethA injection into the left flank	BALB/c	MethA, double-grafted	70% in both flanks 100% in both flanks
Agaricus blazei Polysaccahride fractions	0.5 or 2mg/mouse i.p. 5 doses on alternative days starting 7 days after tumor implantation	ICR	Sarcoma 180	No effect and 77-90
Hot water extract	2mg p.o., 35 doses (no further details provided)	ICR	Sarcoma 180	47
Sparassis crispa/ several polysaccharide fractions	0.020, 0.1 or 0.5 mg/mouse i.p., three doses on Days 7,9 and 11 after tumor implantation	ICR	Sarcoma 180	0.02 mg:54 to 84; 0.1mg: 95 to 100; 0.5mg:91-99
Lyophyllum decastes Sing. Ethanol precipitate of hot water extract	10mg/kg i.p for 10 d starting 24 hrs after tumor implantation 10mg/kg i.p for 10days starting 24hrs after tumor implantation		Sarcoma 180 Sarcoma 180	88 97 with complete regression in 9/10 mice
Lentinus edodes (Shitake) Lentinan Crude extract Lentinan	3 mg/mouse/day p.o starting 7days before K36 inoculation :Equivalent volume) to lentinan p.o. starting 7days before K36 inoculation As above	AKR	K36 murine lymphoma K36 murine lymphoma Colon carcinoma cell lines	94 55 90-93
Phellinus rimosus (Berk) Pilai. Ethyl acetate Methanol Aqueous Ethyl acetate Methanol Aqueous Ethyl acetate Methanol Aqueous	 50mg/kg p.o., for 10 consecutive days starting 24hrs after tumor implantation 50mg/kg p.o., for 10 consecutive days starting 24hrs after tumor implantation 50mg/kg p.o., for 10 days starting 13 days after tumor implantation	 Swiss albino Swiss albino Swiss albino	 Erlich ascites carcinoma Dalton's lymphoma ascites Dalton's lymphoma ascites	 65% increase in life span 33% increase in life span No effect 96 84 88 64 49 57
Pleurotus pulmonarius(Fr.) Quel. Methanol extract	250, 500 and 1000mg/kg i.p., five doses on alternate days starting 24 hrs after i.p., tumor cell injection 250, 500 and 1000mg/kg i.p., 10 doses on consecutive days starting 24 hrs after s.c., tumor cell injection	BALB/c	Erlich ascites carcinoma Erlich ascites carcinoma	No effect 52, 67 and 82(volume); 50, 64, 81(weight)
Lepista inversa(scop.: Fr.) Pat./CE= methanol crude extract	75mg/kg i.p., stating 3 days after tumor transplantation 75mg/kg i.p., stating 5 days after tumor transplantation	DBA/2	L 1210 (lymphocytic leukemia) 3LL (Lewis lung carcinoma)	50% increase in life span No significant effect

Table 2: (Borchers et al 2004) Antitumor Activities of Mushrooms and/or their constituents[46]

Polysaccharides extracted from Himematsutake (the fruiting body of *A. blazei*) and fractionated into a total of 17 polysaccharide samples thus obtained were tested for antitumour activity (Sarcoma 180/mice *i.p. p.o*. method). The water-soluble fractions showed high antitumor activities[38]. Also did not react with antibodies of anti-tumor polysaccharides such as lentinan, gliforan, and FIII-2-b which is one of anti-tumor polysaccharides from *Agaricus blazei*. This polysaccharide was completely different from the anti-tumor polysaccharide from fruiting body of *A. blazei*, *~-1, 6-glucan*[39]. Different Polysaccharide fractions prepared from cultured *A. blazei* by repeated extraction of which NaOH extracts showed antitumor activity against the solid form of Sarcoma 180 in ICR mice[40].

A study done on the extracts obtained from the fruit body of *A. blazei* Murill, the antitumor effect of intratumorally administered fraction was enhanced by oral ad lib administration. The results suggest that regression of the left non-injected tumor was due to an immune reaction, involving induction of cytotoxic cells in the spleen, and the release of chemotactic factors in the distant tumor[41].

A. blazei (H1 strain) was tested for its anticancer activity using a sarcoma 180(S180) inoculation model and the changing patterns of splenocyte subsets were examined. Its hot-water extract was administered orally to ICR and KSN mice that were inoculated with S180. The growth was significantly inhibited in *A.blazei* treated groups[42].

A recent preliminary clinical study shows that *A. blazei* Murill granulated powder is well tolerated in most patients and that supplement doses of 1.8/3.6/5.4 g per day for 6 months did not cause abnormalities within laboratory parameters. This small-scale clinical trial appears to support the previous evidence that the *A. blazei* Murill(ABM) markered product manufactured by Kyowa Wellness is generally safe except for the infrequent occurrence of allergic reaction[43].

It has been demonstrated that the *A. blazei* Murill (ABM) when combined with low doses of doxorubicin(Dox), has the potential to provide more efficient therapeutic effects against drug-resistant human hepatocellular carcinoma[44]. The antitumor activity was examined by taking isolated substances from the lipid fraction of *A. blazei*. Ergosterol inhibited the Matrigel-induced neovascularization and it seems likely that the antitumor activity of ergosterol might be due to direct inhibition of angiogenesis induced by solid tumors[45].

CONCLUSION

Mushrooms have long been valued as highly tasty and nutritional foods by many societies throughout the world. Mushrooms are composed of polysaccharides, which are long chain molecules constructed from and sugar units. Archaeological evidence indicates that humans have been eating mushrooms for thousands of years. Mushrooms are widely used for treatment of many diseases. Among these anticancer activities, antimicrobial activities, antioxidant activities and immune enhancing activities are just few examples. They also contain various active constituents which are acting on the corresponding diseases. Some potential purified biochemicals obtained from them could be used to benefit human health and disease management. The mushroom genome is potentially a natural source of novel myochemicals. That's why the intelligent use of these mushrooms can boost the host defense mechanism.

Sažetak

Poznato je da različite vrste gljiva sadrže jedinjenja različite hemijske strukture, mikro i makroelemente, kao i sekundarne metabolite koji im daju odgovarajuću nutritivnu i medicinsku vrednost. U poređenju sa većinom voća i povrća, gljive imaju kratak rok trajanja. Sveže gljive gube svoju komercijalnu vrednost tokom nekoliko dana usled stajanja, gubitka vode, pod dejstvom mikroorganizama i potamne. Gljive imaju visok sadržaj proteina. One pokazuju čitav niz farmakoloških efekata i cilj ovog rada je da prikaže medicinsku ulogu gljiva. U literaturi su opisana jedinjenja različite hemijske strukture i farmakološke aktivnosti koja su sastojci gljiva. Ova jedinjenja pokazuju antioksidativnu, antitumorsku, antimikrobnu i imunomodulatornu aktivnost. Različite vrste kao što je *Agaricus bisporus* testirane su kao hranljivi suplementi hlebu, s obzirom na to da su dobar izvor selena, hroma, vitamina i antioksidativnih agenasa. *Ganoderma lucidum* sadrži uglavnom triterpenoide, polisaharide, nukleotide, sterole, steroide, masne kiseline, proteine ili peptide, mikroelemente i spada u grupu najznačajnijih tradicionalnih kineskih biljnih lekova. Smatra se da su aktivne komponente *Agaricus blazei* aktivnije od onih koje se nalaze u drugim gljivama. Takođe, pokazana je njihova uloga kao imunomodulatora i odbrane od tumora. Širom sveta imaju veliki ekonomski značaj, jer pokazuju inhibitornu aktivnost na razvoj karcinoma dojke.

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