The Use of Mushrooms and Their Extracts and Compounds in Functional Foods and Nutraceuticals

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Abstract

Functional foods are conventional or everyday foods consumed as part of daily diet. They exert positive effects on target function(s) beyond their nutritive value, enhancing the well-being and quality of life, and/or reducing disease risks. Nutraceuticals are defined as a food or part of a food providing medical or health benefits including the prevention and treatment of a disease. Mushrooms are considered as a delicacy with a high nutritional and functional value and accepted as functional and nutraceutical food ingredients. They are of considerable interest because of their organoleptic value, medicinal properties, and economic significance. The nutritional value of edible mushrooms is due to their high protein, fiber, vitamin and mineral contents, and low-fat levels. Besides, they include several bioactive compounds giving them the ability to exert beneficial effects at different levels. Numerous molecules of mushrooms known to be bioactive and found in fruit bodies, cultured mycelium and broth are polysaccharides, proteins, fats, minerals, glycosides, alkaloids, volatile oils, terpenoids, tocopherols, phenolics, flavonoids, carotenoids, folates, lectins, enzymes, ascorbic, and organic acids. Bioactive properties include immunomodulating, antitumour, anti-hypercholesterolemia, antibacterial, antifungal, anti-inflammatory, antiviral, anti-diabetic, and cardiovascular health promoting effects. Nowadays, mushroom extracts are commercialized as dietary supplements, mainly for antitumour activity and the enhancement of immune function. In addition, it is possible to find foods in the markets including edible wild and cultivated mushrooms and their compounds as an ingredient. This review focuses on the enhancement of biochemical and biological properties by adding mushrooms, mushroom extracts and compounds to produce value-added mushroom-related products.

Keywords: Mushroom extracts, mushroom compounds, nutritional, bioactivity, functional, nutraceutical.

1. Introduction

According to current estimates, mushrooms constitute at least 12.000 species worldwide and 2.000 of these species are reported as edible. About 35 edible mushroom species are commercially cultivated whereas nearly 200 wild species are being used for medicinal purposes (Beulah et al., 2013). Many researchers have documented that edible mushrooms are the source of a variety of nutraceutical compounds such as polysaccharides (β-glucans), dietary fibers, unsaturated fatty acids, terpenes, peptides, glycoproteins, alcohols, mineral elements and antioxidants like phenolic compounds, tocopherols, ascorbic acid (Pardeshi and Pardeshi, 2009). Mushrooms are excellent functional foods containing Se, ergothioneine, vitamin D_2, vitamin B_1 and Fe, etc. The amount and the bioavailability of any nutrient and bioactive biomolecule primarily depend on the mushroom variety (Ruiz-Rodriguez et al., 2009; Yokota et al., 2016). Higher Basidiomycetes mushrooms contain biologically active compounds in fruit bodies, cultured mycelium and cultured broth (Wasser, 2014). Thus, they might be used directly in diet and promote health, taking advantage of the additive and synergistic effects of all the bioactive compounds they included (Vaz et al., 2010; Pereira et al., 2012; Badalyan, 2014).

The presence of specific bioactive compounds makes these mushrooms valuable, from the strengthening of the immune system to the treatment and prevention of life-threatening diseases such as heart disease, hypertension, cerebral stroke and cancers. Mushrooms are also known to exhibit antiviral, antibacterial, antifungal, antiinflammatory, antitumour and immunomodulating, cardiovascular, hepatoprotective, antidiabetic, hypolipidemic, antithrombotic and hypotensive effects (Wasser and Weis, 1999a and b; Singh, 2017). The properties and mechanisms of extracts and bioactive compounds from mushrooms have already been evaluated in a human population or human cell lines and animal model or animal cell lines (Rathee et al., 2012; Roupas, et al., 2012; Giavasis, 2014a, b; Kothari et al., 2018).

Mushrooms are basically consumed for their texture and flavor. The rich source of proteins, vitamins and minerals, low in fat content (2-8%) and having unique biochemicals make mushrooms low calorie food and choice diet for those suffering from hypertension, arthrosclerosis, diabetes and obesity. Additionally, they have recently become attractive as health-beneficent food and as sources for the development of drugs (Singh, 2017). There is a wide usage of mushroom from their traditional uses to medicinal purposes (Aida et al., 2009). Modern clinical practice in Japan, China, Korea, Russia, and several other countries have

relied on mushroom-derived preparations (Wasser, 2010; Chang and Wasser, 2012). Moreover, *in vitro* and *in vivo* studies on functional foods and nutraceuticals derived from edible and medicinal mushrooms were previously conducted (Giavasis, 2014a,b; Prasad et al., 2015; Morris et al., 2016; Taofiq et al., 2016a; Rathore et al., 2017; Reis et al., 2017; Ma et al., 2018).

2. Nutraceutically Important Bioactive Compounds of Mushrooms

Recent scientific studies reported that many edible mushrooms, described before by the traditional folklore of Asian culture, especially in China, Japan, Korea and India as medicinal remedies towards a variety of disorders and diseases, contained specific bioactive compounds. These compounds were confirmed to protect against tumours and other disorders, microbes, and viruses and to lower cholesterol levels, (Ruiz-Rodriguez et al., 2009). Moreover the presence of wonder molecules like polysaccharides, low molecular weight proteins, terpenes, glycoprotein and bioactive compounds again reinforce the usage of such magic food for the better mankind (Rathore et al., 2017).

2.1. Polysaccharides

Oyster mushrooms possess bioactive compounds with hypocholesterolemic activities, such as polysaccharides, mevinolin and other statins (Gunde-Cimerman and Plemenitas, 2001). Also, proteoglycans from *Agaricus blazei* are known to have strong immuno-modulatory properties which are therapeutically important in controlling cancers and immune deficient diseases through the up-regulation of dendritic cells maturation (Kim et al., 2005). Mushroom polysaccharide extracted from *Agaricus bisporus* exhibits excellent inhibiting activity against human breast cancer (Jeong et al., 2012). Pleuran from *Pleurotus* species, lentinan from *Lentinula edodes*, schizophyllan from *Schizophyllum commune*, calocyban from *Calocybe indica*, or ganoderan and ganopoly from *Ganoderma lucidum* are various β-linked glucans isolated from mushrooms (Villares et al., 2012).

The anti fatigue activities observed in the polysaccharides extract of *Hericium erinaceus* extends the utilization of these kinds of novel polysaccharides for sports nutrition (Liu et al., 2015). These polysaccharides are known to possess various physiological activities such as

antitumour, antioxidant, antiviral activities; immunomodulatory, antiinflammatory and anticarcinogenic actions (Rathore et al., 2017).

2.2. Bioactive Protein Molecules

Mushroom bioactive proteins and peptides such as lectins, mushroom immunomodulatory proteins, ribosome inactivating proteins, antimicrobial proteins, ribonucleases, and laccases are an important part of functional components with great value of pharmaceutical potential (Xu et al., 2011). Lectins are the non-immune proteins or glycoproteins binding specifically to cell surface carbohydrates and have been previously studied for their antiproliferative, antitumour, and immunomodulatory activities in *Agaricus bisporus* (Chang et al., 2007) and *Ganoderma lucidum* (Tong et al., 2008). Furthermore, there is no effect of thermal, freezing, acid, alkali and dehydration treatments on the properties of lectin protein (ABL) isolated from *A. bisporus*, hence indicating their usage as a stable immune stimulant for nutraceutical and functional food development (Chang et al., 2007).

2.3. Terpenes

Terpenes are basically a group of volatile unsaturated hydro-carbons which are responsible for the antiinflammatory activities and have been isolated from the mushrooms widely and these terpenoids are responsible for many pharmacological activities like anticancer antimalarial, anticholinesterase, antiviral, antibacterial and anti-inflammatory activities (Duru and Tel Çayan, 2015). The isolated terpenoids were monoterpenes and sesquiterpenoids, sesquiterpenoids such as flammulinol, flammulinolides, and triterpenoids such as lanostane were isolated from *Pleurotus cornicopiae*, *Flammulina velutipes* and *Ganoderma lucidum*, respectively (Rathore et al., 2017). Basically, these terpenes can be effectively utilized in developing drugs for curing Alzheimer's and other degenerative diseases.

2.4. Antioxidants

Antioxidant compounds prevent oxidative damage related to aging and diseases, such as atherosclerosis, diabetes, cancer and cirrhosis. Mushrooms that contain antioxidants or increase antioxidant enzyme activity may be used to reduce oxidative damage in humans

(Yang et al., 2002). The antioxidant activities of edible and medicinal mushrooms have been associated with minerals such as Se and Zn. In addition, biomolecules such as ergothioneine, polysaccharide-protein complexes (β-D-glucans, etc.) phenolic compounds, flavonoids and, in lower amounts, peptides, carotenoids, ascorbic acid and tocopherol have been determined which are the responsible compounds isolated from the different species of mushrooms and reported to boost the immune system, have anticancerous, antihypercholesterolaemic and anti-viral activities, and ameliorate the toxic effect of chemotherapy and radiotherapy (Ruiz-Rodriguez et al., 2009; Valverde et al., 2015). The radical scavenging activities of mushrooms have been extensively studied and documented for the species such as *Pleurotus* spp., *Agaricus* spp., *Ganoderma lucidum* and *Lentinula edodes* known for their profound antioxidant activities. *Phellinus rimosus*, *Hericium erinaceus* and *Cordyseps sinensis* can be used as nutraceuticals having natural antioxidants and healthy commercial preparations (Rathore et al., 2017).

2.5. Other Biologically Active Nutraceutical Compounds Present in Mushrooms

Some of the identified bioactive molecules in mushrooms are β-glucan, dietary fibre, proteoglycan, lectin, phenolic compounds, flavonoids, volatile oils, tocopherols, carotenoids, alkaloids, glycopeptides, folates and organic acids (Prasad et al., 2015). Because of these bioactive compounds contents, the mushrooms have antitumour, anticancer, antidiabetic, cardio-protector, hepato-protective, neuro-protective, antibacterial, antiviral, etc. functions. *Cordyceps militaris* contains a natural immunostimulating polysaccharide having potential to cure various kinds of cancers and tumours. The isolated active molecules dictyophorine A and B from *Dictyophora indusiata* account for curing neurodegenerative diseases by improving Nerve Growth Factor. *Hericium erinaceus* contains hericenones and erinancines that prevent or treat human chronic, cognitive, and neurological diseases. Furthermore, the tablet formulations of *H. erinaceus* have been extensively used for strengthening the gastrointestinal and immune function. *Phellinus rimosus* has an activity against tumour and for refreshing human body to improve longevity. *Panellus serotinus* (Mukitake) prevents the development of nonalcoholic fatty liver disease. *Pleurotus* spp., *Lentinula edodes*, *Agaricus bisporus* and *Tremella fuciformis* possess strong prebiotic activities (Aida et al., 2009; Rathore et al., 2017).

3. Therapeutical Potential of Mushroom Bioactive Compounds

The reported biological activity of some mushrooms and their active constituents were given in Table 1.

Table 1. Biological activities of biocompounds in some commonly consumed edible and medicinal mushrooms

Mushroom species	Active principle/constituent/extract	Reported biological activity
Agaricus bisporus	Fibers, lectins, fucogalactan, 2-amino-3H-phenoxazin-3-one, lectin	Hypocholesterolemic, hypoglycemic, anti-aging property, anticancer, anti-inflammatory
Agaricus blazei	Glucan-protein complex, soluble polysaccharide	Activation of T lymphocytes
Amanita muscaria	Fucomannogalactan	Anti-inflammatory
Auricularia auricula-judae	Methanolic extracts, dietary fiber, acidic polysaccharides, glucan	Antioxidant, antitumour, hypocholesterolemic, antiviral, antiradiative, hypoglycemic
Boletus edulis	Extracts of fruiting bodies, lectin, polysaccharides, polyphenols, ergothioneine, BE3, BSF-A	Antitumour, immune-modulating, antibacterial, antifungal, antiviral, anti-inflammatory, antioxidant, mitogenic, neurotropic
Cantharellus cibarius	Polysaccharides, cibaric acid, phenolic compounds	Antioxidant, antimicrobial, antifungal, insecticidal, nematicidal
Cordyceps sinensis	Adenosine, cordycepin, and ergosterol	Hypoglycemic activity, anti-depressant activity, cures lung infections, antioxidant
Dictyophora indusiata	Heteroglycan, mannan, glucan	Antitumour, hyperlipidemia
Flammulina velutipes	Fibers, ethanolic extracts, flammulin, FVP2, peptide glycans, prolamin, proflamin, enokipodin J, velutin protein, alcoholic and hot water extracts of its sporophores, FIPs, RIPs	Antioxidant, anti-cancer, hypocholesterolemic, antiviral, antiallergic, anti-ageing, cytotoxic, antibacterial, antitumour, antifungal, antiallergic, anticomplementary
Ganoderma lucidum	Ganoderan A, B, C, β-glucans, lanostane triterpenoids, ganosporeric acid A, ganopoly, the polysaccharide-containing preparation, germanium, nucleotides and nucleosides, ribonucleas, ganoderic acid B, C1, E, Y, DM, ganolucidic acid A, ganodermadiol, lucidenic acid N, A, lucidadiol	Hypoglycemic, antitumour, antiviral (HIV-1), antiallergic, anti-inflammatory, cytotoxic, antihepatotoxic, anti-cancer, anticholinesterase, antioxidative free radical scavenging effects, immunomodulating, induction of apoptosis, anti-invasive
Grifola frondosa	MD-fraction, ergosterol, grifolan, lectins, α-glucan, GFP1, mannogalactofucan, heteroxylan, galactomannoglycan, xyloglucan, fucomannoglucan, heteroglucan proteins	Antioxidant, hypotensive, antitumour, hypoglycemic, immunotherapy, antidiabetic, anti-inflammatory activity, improves ovulation, antiviral
Grifola gargal	Ergothioneine	Anti-inflammatory
Hericium erinaceus	Phenol-analogous compounds, erinacine A, hericenones, HEP3	Antioxidant, ameliorative effect in Alzheimer's dementia, antitumour, hypoglycemic
Inonotus obliquus	β-glucan, triterpenes	Antitumour, antioxidant, immunomodulating, anti-inflammatory

Table 1. *(continued)*

Mushroom species	Active principle/constituent/extract	Reported biological activity
Lactarius deliciosus	Sesquiterpenoids, lectin, phenolic compounds	Antibacterial, antifungal, cytotoxic, anti-inflammatory, insecticidal, nematocidal, antioxidant
Lactarius volemus	Phenolic acids, lectin	Antioxidant
Laetiporus sulphureus	Dehydrotrametenolic acid, acetyl eburicoic acid	Hypoglycemic, anti-inflammatory
Lentinula edodes	Methanolic and water extracts, eritadenine, lentinan, oxalic acid, ethanolic mycelial extracts, eritadenine, LT2, heterogalactan, emitanin	Antioxidant, anticancer, hypocholesterolemic, immunotherapy, antimicrobial, antiprotozoal, antitumour, anti-inflammatory
Morchella esculenta	Galactomannan (α-d-glucan), proteins, enzymes, vitamins, minerals, and amino acids	Immune-modulating, antitumour, hypoglycemic, cures pneumonia, fever, cough, cold, and stomachache
Pleurotus eryngii	Ethanolic extracts, eryngiolide A, laccases, diterpenoids	Antiallergic, antiproliferative, antiviral, cytotoxic
Pleurotus ostreatus	Water and 30% ethanolic extract, lovastatin, lectin	Antioxidant, antitumour, arhterosclerotic, hypocholesterolemic, increases gastrointestinal motility, immuno-modulatory activity
Pleurotus sajor-caju	Lovastatin, proteins having polysaccharide, xyloglucan, xyloproteins	Hypocholesterolemic, cardio-protective, anti-inflammatory, antitumour
Poria cocos	β-glucans, 29-hydroxypolyporenic acid C, polyporenic acid C	Anticancer, prebiotic, anti-inflammatory
Russula delica	Lectin	Antiproliferative, antiviral
Schizophyllum commune	β-D-glucan (Schizophyllan)	Immunotherapy, antitumour
Sparassis crispa	Bioactive β-D-glucan, phenyl derivatives, chalcones, and sesquiterpenoids	Lipid peroxidation inhibition, immunomodulation
Trametes versicolor	Coriolan, a β-glucan-protein complex, krestin (PSK), glycoproteins, PSP, CVP	Hypoglycemic, immunotherapy, anticancer, antifungal, antiviral (HIV-1), liver protective
Tremella fuciformis	Heteroglycan	Hypolipidemic, hypoglycemic, immunomodulating, antitumour, antidecrepitude, antithrombus
Tricholoma spp.	Tricholomalide A, B, C	Cytotoxic, anticancer
Volvariella volvacea	Methanolic and water extracts, exopolysaccharides, glycoproteins	Antioxidant, hypotensive, hypocholesterolemic, cardio-protective

References: Lakhanpal and Rana, 2005; Zhang et al., 2007; Rathee et al., 2012; Badalyan, 2014; Rahi and Malik, 2016; Taofiq et al., 2016a; Rathore et al., 2017; Kothari et al., 2018; Ma et al., 2018.

Supplementation of products with dried mushroom powders like *Lentinula edodes* (Regula et al., 2010) and *Pleurotus* spp. (Regula et al., 2016a; b) have been confirmed to increase the blood hemoglobin concentration, liver, and kidney Fe levels in *in vivo* models. These functional foods might also have a big potential for the prevention or cure of diabetes more than in other plant species (Perera and Li, 2011).

4. Health Promoting Novel Mushroom-Derived Products

Functional food is defined as natural or formulated food that enhances a physiological performance or prevents or treats a particular disease, and is consumed as part of the normal daily diet. Nutraceutical refers to a medicinal or nutritional component of food, plant, or naturally occurring material that is used for the improvement of health, by preventing or treating a disease in the form of extract, compound, nutrient or pharmaceutic such as pills, tablets (Doyon and Labrecque, 2008; El Sohaimy, 2012). Food supplements have essentially a feed function, taking the form of medicines as pills or capsules (Howlett, 2008). Today, mushrooms are consumed in various forms, as foods, in the form of dietary supplement (DS), as a nutraceutical or medicine, usually called "mushroom pharmaceuticals". Moreover, they are used as natural bio-control agents in plant protection (acting as insecticides, fungicides, bactericides, etc.) and in cosmetics (due to their film forming capability, antioxidant, anti-allergic or antibacterial activities, stimulation of collagen activity among others) (Wasser, 2014; Taofiq et al., 2016b).

Most mushroom-derived preparates and substances are used as a novel class of "dietary supplements" (DS) or "nutraceutical" not as "pharmaceutical". A "mushroom nutraceutical" is a refined or partially refined extract or dried biomass from either the mycelium or the fruiting body of the mushroom, which is consumed in the form of capsule or tablets as a dietary supplement and which may enhance the immune response of human body, thereby increasing resistance to disease and in some cases causing regression of a disease state (Wasser et al., 2000; Giavasis, 2014a; Wasser, 2014). As functional foods, mushrooms represent a paradigm of integrating traditional and novelty, due to their wide spectrum of pharmacological properties. Their bioactive components can be extracted or can be concentrated as nutraceuticals, and/or as a diverse class of dietary supplements. "Functional foods" and "nutraceuticals" particularly mushrooms, are immunoceuticals with antitumour and immunomodulatory effects which target and modulate biological processes that foster the development of diseases (Morris et al., 2016). Due to the limited supply and high price of wild mushrooms, artificial cultivation has become the major source of many edible mushroom-based products on the market (Smith et al., 2002).

Despite the studies developed in the field of mushroom incorporation to foods, these products have not got into market, yet. There is still a lack of information regarding the bioaccessibility/bioavailability of the compounds and possible interactions with the food

matrix. Therefore, most of the mushrooms and their compounds are mainly consumed in natural form or in dietary supplements (Reis et al., 2017).

4.1. The Use of Mushroom Extracts and Compounds in Functional Foods

As part of a healthy diet, functional foods, can be consumed not only in their natural state, but also after biotechnical modification. It is suggested that these foods will enrich a healthy diet and improve the nutritional value of other foodstuffs (Martins et al., 2016). In Table 2, some studies on functional foods derived from various mushrooms were given. By the production of these products, it was aimed to get high nutritional value, high-fibre and low-calorie novel functional foods and beverages having some functionalities such as improving the pasting properties of wheat flour, getting and increasing antioxidant, antimicrobial, antithrombotic and hypocholesterolemic properties, decreasing the potential glycemic response, inhibition of food contaminants, avoiding food deterioration and protection from lipid peroxidation (Giavasis, 2014b; Reis et al., 2017; Ma et al., 2018).

Table 2. Studies on mushroom-based functional foods with their powders, extracts, compounds and mycelia

Mushroom species	Functional food	References
Agaricus aegerita	Cream cheese	Petrovic et al., 2015
Agrocybe aegerita	Snack food	Brennan et al., 2012; 2013
Auricularia auricula	Bread	Fan et al., 2006
Agaricus bisporus	Snack food	Singla et al., 2009
	Bread	Ahmad and Singh, 2016
	Sponge cake	Arora et al., 2017
Agaricus blazei	Yoghurt	Stojkovic et al., 2014
	Milk	Vital et al., 2017
Agaricus blazei, Antrodia camphorata, Hericium erinaceus and *Phellinus linteus*	Bread	Ulziijargal et al., 2013
Agaricus bohusii	Cream cheese	Reis et al., 2012
Boletus aereus	Pork meat product	Stojkovic et al., 2015
Boletus edulis	Beef burger	Barros et al., 2011
Cordyceps militaris	Extruded product	Zhong et al., 2017
Ganoderma amboinense, *Agaricus* spp. or *Fomes yucatensis* or mixed mushrooms	Soup and sauce	Laroche and Michaud, 2007
Laetiporus sulphureus	Chicken pate	Petrovic et al., 2014
Lentinula edodes	Baked food	Kim et al., 2011
	Noodle	Kim et al., 2008; 2009
	Frying batter	Kim et al., 2010
Pleurotus sajor-caju	Papad (An Indian snack food)	Parab et al., 2012
Schizophyllum commune	Cheese-like food	Okamura-Matsui et al., 2001
Suillus luteus and *Coprinopsis atramentaria*	Cottage cheese	Ribeiro et al., 2015
Tirmania pinoyi	Soup	Stojkovic et al., 2013

References: Giavasis, 2014b; Reis et al., 2017; Ma et al., 2018.

Moreover, some novel mushroom-based functional foods and beverages strengthening energy, vitality and immunity have been producted such as blend of burger beef with mushrooms by Sonic Drive-In, *Hericium erinaceus*-flavored ice cream by Unframed Ice Cream and functional beverage by Koios, collogen-rich beverage containing *Auricularia auricula* by Simply Auri, *Inonotus obliquus*-blended lemonade mix by Four Sigmatic and bottled tea by Sol-ti, *Ganoderma lucidum*-based bottled mushroom-chocolate beverage, cold brew drink by REBBL and probiotic-rich fermented tea by Health-Ade, and also mushroom coffee mixes by Four Sigmatic, medicinal mushroom-infused cold-brewed coffee by Love Grace, medicinal mushroom-enriched teas by Choice and cold green teas by Mudra Mushroom in recent years (URL-1, 2018).

With regard to sensory characteristics and consumer acceptance, a potential additional advantage of using mushroom polysaccharides in functional foods may be the fact that some mushroom crude extracts also contain monosodium glutamate-like components and an intense umami taste that might improve the flavor of the final product (Tsai et al., 2006). However, bioaccessibility and bioavailability studies are required to be performed because of the changes occurred in the digestive tract (Reis et al., 2017). There is a need of *in vivo* studies to be carried out using realistic food matrices, rather than pure/crude polysaccharide solutions, before a health claim is made for the functional foods where they are added. Another concern with the food applications of mushroom polysaccharides is to determine the appropriate dose for bioactivity without any kind of toxic effect so that a food can be declared as functional (Wasser, 2011). Although some of the most studied polysaccharides such as schizophyllan and lentinan produced by mushrooms are already available and marketed as nutraceuticals (pharmaceutical formulation), their addition to food in their purified form has not been commercialized worldwide, yet (Giavasis, 2013). It is considered that some subjects of production economics, quality standardization, and stable availability need to be resolved and clinical studies on the therapeutic effects and the effective doses of functional foods need to be performed in order to allow a more global commercialization (Wasser, 2011; Giavasis, 2013).

4.2. The Use of Mushroom Extracts and Compounds in Nutraceuticals

The principal nutraceuticals found in mushrooms include: i) lipids, especially unsaturated fatty acids; ii) vitamins, such as vitamin E and vitamin C; iii) proteins, peptides and amino acids, including lectins, leucine and valine; iv) carbohydrates, especially

polysaccharides (Wasser, 2014). In addition to the participation in the production of functional food, the mushroom bioactive nutraceuticals were majoringly studied and developed as dietary supplements, which could inhibit the high risking of some threaten disease and protect the body from the damage of some disadvantageous environment (Ma et al., 2018).

Medical mushrooms have been used for a long time in countries such as China and Japan, but western countries have already recognized the therapeutic properties of mushrooms. Several different polysaccharides antitumour agents have been developed from the fruiting body, mycelia, and culture medium of various medicinal mushrooms (*Agaricus bisporus*, *A. brasiliensis*, *Auricularia auricula*, *Flammulina velutipes*, Ganoderma *lucidum*, *Grifola frondosa*, *Inonotus obliquus*, *Lentinula edodes*, *Pleurotus ostreatus*, *Schizophyllum commune*, *Trametes versicolor*, and *Tricholoma matsutake*) (Prasad et al., 2015; Sokovic et al., 2016). They possess a wide range of bioactivities such as anticancerous, antibacterial, antiviral, antifungal, antidiabetic and antiinflammatory. These are also used in cardiovascular disorders. The mushrooms are usually administered orally or intraperitoneally (Sokovic et al., 2016).

Today, there are some pharmaceutical companies developing and marketing mushroom polysaccharide based extracts, drugs, and supplements for anticancer uses such as Zhejiang Fangge Pharmaceutical Co., Ltd. in China, FineCo Ltd. in South Korea, ecoNugenics, Mushroom Wisdom, MycoFormulas, Gourmet Mushrooms, Healing Edge Sciences, Inc. and Aloha Medicinal Inc. in USA, linkNUTRITION in UK, Myko San in Crotia, Pleuran, s.r.o. in Slovakia, GlycaNova AS in Norway, and Concord Mushroom Supplements in Australia (Patel and Goyal, 2012; Reis et al., 2017; URL-2, 2018).

Medicinal mushrooms are regulated by food law and not by pharmaceutical law in Germany. The main criteria that must be provided by pharmaceutical companies to the authorities before authorization are pharmaceutical quality, efficacy, and safety of the product (Lindequist, 2013). In China, there are several commercial nutraceutical products based on medicinal mushroom extracts and mushrooms biopolymers. For instance, a tonic liquor made of extracts of *Ganoderma lucidum*, *Lentinula edodes,* and *Poria cocos*, which is claimed to have anticarcinogenic, antiviral, and hypolipidemic effects, and a similar potable extract of *Cordyceps sinensis*, *Ganoderma lucidum*, and some medicinal herbs, which is marketed as an antiageing dietary supplement that improves cardiovascular function and reduces blood lipids. Additionally, in a traditional Chinese medicine recipe, a soup of *Auricularia auricula-judae*

and *Tremella* spp. mushrooms is recommended for the treatment of hypertension and this could form the basis of a novel nutraceutical (Xu, 2001).

Today, some dietary supplements based on mushrooms are available on the market. These include i) artificially cultivated fruiting body powders, hot water or alcohol extracts of these fruiting bodies; ii) dried and pulverized preparations of the combined substrate, mycelium and primordial mushroom; iii) biomass or extracts from mycelium harvested from submerged liquid culture grown in a fermentation tank or bioreactor; iv) naturally grown, dried mushroom fruiting bodies in the form of capsules or tablets; and v) spores and their extracts (Wasser, 2014).

In the last two decades there has been an upsurge on the use of mushrooms as nutraceuticals and many edible species have been thoroughly investigated and authenticated for medicinal use. The species that have been properly analysed for medicinal value *in vivo* are *Agaricus blazei*, *A. brasiliensis*, *Cordyceps militaris*, *Flammulina velutipes*, *Ganoderma lucidum*, *Grifola frondosa*, *Hericium erinaceus*, *Lentinula edodes*, and *Pleurotus ostreatus*, (Lakhanpal and Rana, 2005; Rathore et al., 2017). In order to promote a health claim for nutraceuticals based on mushroom polysaccharides, there is a need to consider the potential influence of food processing such as heating, high-pressure and irradiation, and food physicochemical properties and composition such as pH, moisture, presence of other biocompounds, enzymes and organic acids on the bioactivity of the medicinal biocompounds (Giavasis, 2014b).

Many commercial products derived from these mushrooms such as Lentinan from *Lentinula edodes*, Concord Sunchih and Reishi Plus from *Ganoderma lucidum*, Grifon from *Grifola frondosa* and Didanosine from *Cordyceps militaris* are available on the market (Lakhanpal and Rana, 2005). In Table 3, there are some other mushroom-based nutraceuticals and dietary supplements available in the market and their health claims. Furthermore, there have been some clinical studies on therapeutic effects of mushroom-derived nutraceuticals and dietary supplements in the literature such as *Agaricus blazei* extract, Active hexose correlated compound (AHCC), Ganopoly®, Hispidin, Hispolon, Immune Assist™, and SX-Fraction® (Reis et al., 2017).

Although recognizing the great potential of mushrooms being the basis of such formulations, some problems which affect their preparation and subsequent marketing such as safety issues, standardization, regulation, efficacy and mechanism of action, still await to be solved (Wasser, 2014). In addition there is a strong necessity of performing clinical trials for

these nutraceutical products in order to be accepted by the global market (Rathore et al., 2017).

Table 3. Some commercial mushroom-based nutraceuticals/dietary supplements available on the market

Mushroom species	Product in the market	Health benefit claim
Agaricus blazei	*Agaricus blazie* capsules	Immune support supplement
Agaricus blazei, Cordyceps sinensis, Coriolus versicolor, Ganoderma lucidum, Grifola frondosa and *Lentinula edodes*	Immune Assist complete	Immunity supporter
Agaricus blazei, Cordyceps sinensis, Ganoderma lucidum and *Lentinula edodes*	CocoaMojo-cocoa powder	Immunity supporter
Agaricus blazei, Ganoderma Lucidum, Grifola frondosa, Lentinula edodes and *Pleurotus ostreatus*	Agarikon.1	Enhancement of immune system
Cordyceps sinensis	Mycoformulas Endurance™	Enhancement of intracellular energy exchange, increases oxygenation and natural endurance
Cordyceps sinensis and *Ganoderma lucidum*	Nutricafe-organic performance coffee	Increases physical endurance and helps to remove toxins from your body
Cordyceps sinensis, Ganoderma lucidum, Hericium erinaceus and *Inonotus obliquus*	Mushroom Plus	Combines some of the most popular mushrooms for an overall health boost by supporting immune system, energy levels, and cognition
Ganoderma lucidum	Pure Red Reishi - capsules Organic Reishi tablets - MRL GanoSuper - concentrated extracts for coffee	Increases the body's resistance to stress and helps it overcome all health challenges more quickly, supports the body's normal cellular immune system
Ganoderma lucidum only or combined with *Cordyceps sinensis*	GanoPoly®	Helpful for assisting recovery after illness, supports healthy nervous system and quality of sleep, promotes calmness and sense of well-being, beneficial for healthy menstrual function, supports health of the heart and blood vessels, supports a healthy immune system, protects the body against cellular damage, helps support normal cholesterol balance and blood sugar levels
Ganoderma lucidum and *Lentinula edodes*	Organic ReiShi-Gen (synergestic formulations)	Immune support supplement
Grifola frondosa	MaitakeGold 404®	Providing daily immune protection
Grifola frondosa and *Lentinula edodes*	OsteoMykon	Maintenance of bone health (indicated for osteoporosis)
Grifola frondosa and *Phellinus linteus*	Breast-Mate®	Supports healthy breast tissue
Hericium erinaceus	MycoFormulas Memory™	Memory support and daily mental clarity
Lentinula edodes	Shiitake gold - capsules	For complete physical health
Pleurotus ostreatus	Imunoglukan P4H® capsules	Immune system enhancement
Trametes versicolor	ORIVEDA® PSP-50	Immune supporter

References: Morris et al., 2016; Reis et al., 2017; URL-2, 2018; URL-3, 2018.

Despite interest in such products having grown over the years, the market in Asian countries has been exploited more. In the West, this remains a market requiring greater investment and exploitation (Giavasis, 2014a). On the European markets, products containing medicinal mushrooms are sold as food or dietary supplements and not as licensed drugs. It means that the declaration of medicinal indication is not allowed (Chang and Wasser, 2012).

5. Conclusion

Mushrooms are traditional medicines which are ignored today due to the lack of maintaining the proper standards during manufacturing, the purity system, and insufficient clinical trials. Whereas they possess bioactive molecules such as polysaccharides, terpenoids, low molecular weight proteins, glycoproteins, and antioxidants etc., which have a great role to play in boosting immune strength, lowering risks of cancers, inhibition of tumoural growth, blood sugar maintenance and much more. Therefore, it should be created awareness amongst the consumers regarding the proper utilization of this golden drug for the future. This can only be obtained by choosing the appropriate standard protocols and practices for making the drugs out of them, and comparing with available medicines around the world. Moreover, with respect to their high nutritional and therapeutic potential, mushrooms can find different applications, namely as functional foods or as a source of nutraceuticals for maintenance and promotion of health and life quality.

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