EDIBLE MUSHROOMS IN PROPHYLAXIS AND TREATMENT OF HUMAN DISEASES

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Abstract

In recent years an increase in the consumption of edible mushrooms has been observed. In many countries mushrooms have been a popular delicacy, as they add flavor and texture to a meal. Mushrooms are able to accumulate both primary and secondary metabolites. Some of them may play an antioxidant role, e.g. phenolic and indole compounds, flavonoids, terpenoids, sterols, ascorbic acid, ergothioneine and carotenoids and are a source of elements, e.g. selenium. Indole compounds fulfill the role of neurotransmitters or their precursors, exhibit antioxidant, anticancer, anti-inflammatory and anti-aging actions, regulate the diurnal cycle in humans and take part in blood coagulation. Biologically and therapeutically active metabolites of fungi are used to treat such serious diseases as cardiovascular diseases, diabetes, atherosclerosis and cancer. The intake of mushrooms clearly has a cholesterol-lowering effect or hypocholesterolemic effect by different mechanisms such as decreasing VLDL, improving lipid metabolism, inhibiting of activity of HMG-CoA reductase, and consequently preventing the development of atherosclerosis. The antioxidant and anti-inflammatory compounds occurring in mushrooms also may contribute to reduce the atherosclerosis risk.

Keywords: Basidiomycota, chitosans, ergothioneine, hypercholesterolemia, statins

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Introduction

Mushrooms are a large group of organisms playing a significant role in the environment. Mushrooms in daily life are mostly seen as a food product. Nowadays, cultivated and wild edible mushrooms, used directly or indirectly as food or ingredient, have been clearly separated from medical mushrooms by the industry [1,2]. Edible mushrooms are widely consumed in many countries as a food. Owing to their attractive taste, aroma and nutritional values, edible mushrooms are valuable components of the diet, whose culinary and commercial value is mainly due to their organoleptic properties such as their texture and flavor, being possible to distinguish edible mushroom species on the basis of their characteristic odor or aroma [3]. What's more, they are a source of essential nutrients: protein, carbohydrates, vitamins, especially vitamins B_1 and B_2, vitamin D, A, C, E, H, K and PP, and pantothenic acid. The content of vitamins in mushrooms is often much higher than in most vegetables [4,5]. Fat content is low within the limits of 5-8%, and in most species less than 1% and only in a few up to 15% [5,6,7]. The medicinal use of mushroom polysaccharides has a very long tradition. Fruiting bodies of mushrooms are a known source of a variety of biologically active compounds. Mushrooms are a source of both primary and secondary metabolites

[2,3,5]. Biologically and therapeutically active metabolites of fungi are used to treat such serious illnesses as cardiovascular diseases, diabetes, atherosclerosis and cancer [2]. Some of the metabolites exhibit antiviral and antibacterial activity [8,9]. Other widely studied groups of compounds contained in mushrooms are phenolic compounds, terpenoids, indole compounds, vitamins and bioelements (eg. selenium) [10-17].

Cardiovascular diseases (CVDs) are the leading cause of death for both men and women in the world. CVDs have a multifactorial etiology being mainly caused by atherosclerosis, and have identified potential risk biomarkers such as lipid and lipoprotein metabolism, hemostatic function, oxidative damage, homocysteine metabolism, and blood pressure. The hypocholesterolemic action of edible mushrooms has been reported in some mushrooms species from Basidiomycota taxon: *Lentinus edodes* (Shitake), *Auricularria polytricha* (Mun mushroom), *Flammulina velutipes* (golden needle mushroom) and *Agaricus bisporus* (white bottom mushroom) [17-23]. Besides, some mushrooms have shown hypotensive effect when blood pressure is already high. On the other hand, the presence of antioxidant and anti-inflammatory compounds in mushrooms may be clinically relevant in the management of heart and circulation health complications. There are some mushroom components involved in prevention or treatment of cardiovascular diseases (proteins, lipids, vitamins, fibers, phenolic compounds and minerals). However, the implicated mechanisms are not yet completely elucidated. The aim of the present review is to summarize the existing knowledge about the beneficial effects of consuming the fruiting bodies of edible mushrooms used as food or ingredient on cardiovascular diseases risks, with special emphasis in the various mechanisms potentially involved.

Nutritional composition in mushrooms

Today, in many Asian and European countries a group of mushrooms was isolated, which due to its medicinal and / or dietary properties is referred as medicinal mushrooms. An important group of medicinal mushrooms are edible species. Based on the analysis of chemical composition of fruit bodies of edible mushrooms it can be said that they are a wholesome food product that contains all the basic ingredients that are essential for growth and development of the human body and to support its life processes. The edible mushrooms contain a high moisture percentage (81.8–94.8%) whose variability in content depends on the mushroom species and other parameters related to harvest, growth, culinary and storage conditions. Dried mushrooms contain 3-25% digestible protein, and 5% carbohydrate, 0.5-3.5% fat and enzymes to help digestion. Very beneficial is the presence of enzymes in fruiting bodies. Even in small quantities, they stimulate the appetite, help digestion and absorption of food [19].

The high levels of essential aminoacids in mushrooms have been reported to vary widely among species. They are considered to be rich in glutamic acid, aspartic acid and arginine, however, their proteins are deficient

in methionine and cysteine. Interestingly, two uncommon amino acids: γ-amino butyric acid (GABA) and ornithine have been detected, which have shown important physiological activities. In fruiting bodies of *Agaricus bisporus* 33% of the total nitrogen is in the non-protein combinations. The high nitrogen content is influenced mainly by high contents of free amino acids. In fruiting bodies of this species seventeen free amino acids were found, of which the largest quantities are: alanine, arginine, aspartic acid, gluatamic acid, leucine, lysine, phenylalanine, proline, tyrosine, valine and tryptophan [19].

Edible mushrooms provide low amounts of fat. In general, unsaturated fatty acids are predominant over saturated fatty acids, especially palmitic acid (C16:0), oleic acid (C18:1) and linoleic acid (C18:2). Linolenic acid (C18:3) is the precursor for 1-octen-3-ol (also known as mushroom alcohol), which is the principal aromatic compound in most fungi, which characteristically and distinctively contributes to mushroom flavor [24,25]. Unsaturated fatty acids are essential for the proper functioning of the human body because they are precursors of bile components, they are essential for the synthesis of prostacyclin and prostaglandins and they have anti-atherosclerotic function. For example, the total content of fatty acids in the fruiting bodies of edible species *Cantharellus cibarius* (Fot. 1) is 3.6 g/100 g of dry weight (DW).

Fot. 1 *Cantharellus cibarius* - The Chantarelle (fot. Andrzej Józef Bossowski)

Carbohydrates constitute 1-6% of fruiting bodies of fungi (mainly glycogen, mannitol, sorbitol, arabitol). Of the monosaccharides in the fruiting bodies of *Basidiomycota* in free form are compounds such as glucose, galactose, mannose, fructose and sedoheptulose. Commonly there is also a sugar alcohol - mannitol. Disaccharide occurring in the largest quantities is trehalose. The presence of another disaccharide – lactose was confirmed, inter alia, in the fruiting bodies of *Cantharellus cibarius* [26-28].

Polysaccharides are one of the best known groups of fungal carbohydrates because of its importance in medicine, including fiber. It is a valuable source of fiber, which includes a number of compounds characterized by a variety of chemical, physical and physiological properties. Due to the water solubility of dietary fiber, fiber is divided into insoluble chitin, cellulose, lignin, and soluble, which major components are β-glucans and chitosans (Fig. 1) [19].

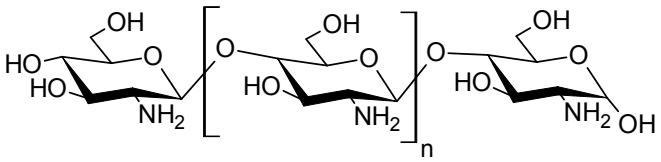

Figure 1. Chitosan, the basic compounds in mushrooms cell walls

Another very important group of carbohydrates are polysaccharides with anticancer properties. Antitumor activity of polysaccharides is multi-faceted and comprehensive. They limit the damage of DNA of cells, lower levels of carcinogens in the human body and inhibit their activation and the development of cancer cells. They bind free radicals, stimulate the immune system and induce apoptosis. The ability to activate the immune system can help to treat not only cancer, but also infectious diseases. An important advantage of polysaccharides is that they abolish the side effects of chemotherapy and also show no toxic effects on the human body [29-31].

Lentinan from *Lentinus edodes* is considered to be the most active among known polysaccharides endowed with antitumor potential. This polysaccharide is most often used in the treatment of solid tumors of the stomach, large intestine, breast, lungs and malignant leukemia. It is used in combination with chemi- and radioteraphy [32].

Krestin (Polysaccharide-K, PSK) is the second most frequently used antitumor polysaccharide. It is obtained from mycelium of an arboreal fungus, *Trametes versicolor*. This compound is a branched heteroglucan composed of glucose (74.6%), mannose (15.5%), xylose (4.8%), galactose (2.5%) and fructose (2.2%). Krestin shows a considerable antitumor activity against allogenic and syngenic animal tumors. PSK increases lymphocyte activation and stimulates cytokine production by the cells. This substance was also proven to inhibit activity of metaloproteinases and other enzymes participating in metastasizing of tumor cells.

Schizophyllan is a neutral extracellular antitumor polysaccharide produced by *Schizophyllum commune*, consisting of a 1,3-β-D-linked backbone of glucose residues with 1,6-β-D-glucosyl side groups. Studies with this compound showed that it inhibited Sarcoma-180 in mice. Further studies also indicated that it was active against tumors of the lung, digestive tract, breast and uterus. It can be assumed that its effects rely mostly upon activation of the natural defense of the body against pathological changes [33].

A polysaccharide isolated from *Tylopilus felleus* named tylopilan has a structure of homoglycan of β (1→3) type with branches at β (1→6). In laboratory tests, it exhibited antitumor activity against transplantable Sarcoma-180 in mice (more than 98% inhibition), and destroyed glioma cells. It showed immunomodulatory properties, influencing non-specific cellular immunity and some stages of specific humoral response. It also showed mitostatic effect at cellular level [33].

Recent studies prove that edible species of mushrooms contain non hallucinogenic indole compounds and their derivatives. Indole compounds are neurotransmitters or their precursors, have antitumor, anti-aging activity, they regulate the diurnal cycle in the human body and they participate in the

process of blood clotting. Indole compounds have also antioxidant activity [34, 35].

Based on the high levels of riboflavin (vitamin B_2), niacin and folates and traces of vitamin C, vitamin B_1, vitaminD, β-carotene (precursor of vitamin A), vitamin E and vitamin B_{12}, mushrooms are a good source of vitamins. Mushrooms appear as the only non-animal-based food source containing vitamin D, and hence they are the only natural vitamin D source for vegetarians. *Cantharellus cibarius* is a rich source of ergocalciferol. In addition, even after several years of storage of the dried fruiting bodies the level of vitamin D_2 is high – in average about 1.43 μg/g dry weight. *Agaricus bisporus* contains a lot of ergosterol (an average of 61.5 mg/100 g). In small quantities in mushrooms ergosta-7-enol (1.73 mg/100 g), ergosta-5,7-dienol (6.05 mg/100 g) and ergosta-7,22-dienol (2.45 mg/100 g) were found [36].

As compared with vegetables, mushrooms proved to provide a reasonable content of many mineral elements (6–10.5% DW). The main constituents in the ash are potassium and, depending on the mushroom, phosphorus or magnesium, in addition to calcium, copper, iron and zinc. Special attention should be paid to the accumulation in the mushroom of trace heavy metals, particularly toxic elements such as cadmium, lead and mercury, commonly present in the culture substrates. Indeed, *L. edodes* proved as an efficient cadmium accumulator, while *A. bisporus*, *P. ostreatus* (Fot. 2), *L. edodes* and some species of the genus Boletus are naturally rich in selenium [17].

Fot. 2 *Pleurotus ostreatus* - Oyster mushroom (fot. Bożena Muszyńska)

In the Department of Pharmaceutical Botany, Jagiellonian University Medical College, an analysis of accumulation of bioelements was performed. Concentrations of the chosen elements (Zn, Cu, Fe, Mg) in mycelium samples of *Boletus badius* (Bay bolete) and *Cantharellus cibarius* (Chantharelle) were measured by means of the atomic absorption spectrometry (AAS) method. Fe concentration in the analyzed mushroom materials was in the range 215.4 - 680.3 μg/g dry weight. Iron is an integral part of many proteins and enzymes that maintain good health. In humans, iron is an essential component of proteins involved in oxygen transport. It is also essential for the regulation of cell growth and differentiation. A deficiency of iron limits oxygen delivery to cells, resulting in fatigue, poor work performance, and decreased immunity. On the other hand, excess amounts of iron can result in toxicity and even death.

Mean values of Mg were respectively (in μg/g dry weight): mycelium of *C. cibarius* cultured in vitro 541.8, fruiting bodies 1004.1, mycelium of *B. badius* cultured in vitro 928.9 and fruiting bodies 906.4. Magnesium is an essential mineral for human nutrition. Magnesium in the body serves several important functions: contraction and relaxation of muscles, function of certain enzymes in the body, production and transport of energy and production of protein.

Mean concentrations of Zn were: in mycelium from in vitro cultures of *B. badius* 442.7 μg/g dry weight and in fruiting bodies 172.1; in case of *C. cibarius* in mycelium from in vitro cultures 131.9 and 95.5 (fruiting bodies). Zinc is an essential mineral that is naturally present in some foods, added to others, and available as a dietary supplement. Zinc is involved in numerous aspects of cellular metabolism. It is required for the catalytic activity of approximately 100 enzymes and it plays a role in immune function, protein synthesis, wound healing, DNA synthesis, preventing of depression and cell division.

Cu exhibited a reversal tendency i.e. significantly higher were the element concentrations in naturally grown mushrooms (*C. cibarius* 43.57 μg/g dry weight and *B. badius* 43.54 μg/g) than in cultured in vitro mycelium (*C. cibarius* 12.47 μg/g and *B. badius* 4.17 μg/g).

Copper, along with iron, helps in the formation of red blood cells. It also helps in keeping the blood vessels, nerves, immune system, and bones healthy. Lack of copper may lead to anemia and osteoporosis [17].

Reactive forms of oxygen and nitrogen are responsible for the oxidative deterioration of food products, as well as the pathogenesis of many human diseases such as atherosclerosis, diabetes, chronic inflammation, neurodegenerative diseases and some types of cancer. Mushrooms are a rich source of antioxidants such as phenolic compounds (eg. phenolic acids and flavonoids) and tocopherols.

Phenolic acids represent the largest percentage of phenolic compounds found in mushrooms. This is because their potent antioxidant activity and ability to protect against oxidative damage of important vital structures (cell membranes, structural proteins, enzymes, membrane lipids or nucleic acids) is related to their broad spectrum of biological activity. The strongest antioxidant activity (as the protection of cells against hydrogen peroxide) exhibit vanillic acid and cinnamic acid derivative - caffeic acid. Acids: *p*-hydroxybenzoic, gallic and protocatechuic, found in mushrooms have documented *in vitro* and *in vivo* activities: antioxidant, antibacterial, antiviral, antifungal, anti-inflammatory, and they stimulate the stomach secretion. Protocatechic acid also has immunomodulatory, spasmolytic, cardioprotective, anticoagulant and chemo-preventive activity [37].

Ergothioneine [Fig. 2] is a natural amino-acid and is a thiourea derivative of histidine, containing a sulfur atom in the imidazole ring. Ergothioneine was discovered in 1909 and named after the ergot fungus from which it was first purified, with its structure being determined later, in 1911.

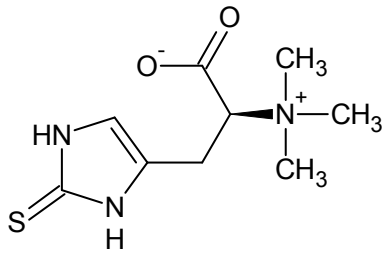

Figure 2. Chemical structure of ergothioneine

Ergothioneine fulfills protective functions both to the mushrooms which synthesize it, plants and animals. In the human body the highest level of ergothioneine is in erythrocytes, lens of the eye, semen and skin. It has the ability to capture hydrogen peroxide, hydroxyl radicals, mutagens, electrophilic particles and chloric acid and can chelate Cu^{2+} and Fe^{3+} ions. Another advantage of ergothioneine is its ability to protect the cells against oxidative stress caused by reactive forms of nitrogen such as nitric oxide. It is valued for its ability to reduce damage caused by irradiation, hypoxia after organ transplantation and brain and heart strokes. Ergothioneine can be used in thetreatment of humans, fulfilling following functions: protection against oxidative damages that arise as a result of the disease process. Its use is suggested in the treatment of malaria, thalassemia and disorders of red cells which were oxidative damaged. The addition of ergothioneine to infusion fluid may protect cardiac muscle cells from damage due to ischemia and reperfusion. The richest species in this compound are: *Agaricus bisporus* and *Pleurotus ostreatus.* [38,39,40].

The antioxidant activity of flavonoids depends on the conjugated double bonds in the position C-2 and C-3, hydroxyl groups and carboxyl group at position C-4. The direct antioxidant mechanism of action of these compounds consists of the capture of free radicals and reactive oxygen species and reduces their production in cells by inhibiting oxidative enzymes (eg. lipoxygenase) and by easily passing the hydrogen reduction of the carboxyl group of peroxides and hydroxides. An indirect mechanism of action is the chelation of transition metal ions (Cu and Fe), which prevents the formation of reactive hydroxyl radical in the cells. In addition, flavonoids may interrupt the cascade of free radical reactions during lipid peroxidation. These compounds protect the genetic material, cell membranes and enzymes.

Physiology of mushrooms, especially the way of nutrition, consisting of osmotic extraction of previously distributed dead matter associated with the presence of various enzymes in the mycelium. Most species of *Basidiomycota* produce hemicellulases, cellulases and ligninases facilitate digestion of plant cell walls. Many of the species produce specific enzymes [41].

The pharmacological potential of mushrooms

Until discovery of antibiotics, studies on chemical composition of mushrooms had not been very popular. People preferred to look for medicinal compounds in plants, while fungi remained distrusted and wrapped in superstitious fear. Wild mushroom can be found in old books of traditional medicine, especially in the Orient, as specific pharmacological agents, but almost all important medicinal mushrooms are under a large-scale artificial cultivation. Folk European medicine

also utilized fungi as a source of medicinal substances used in such diseases as tumors, hepatitis, hemorrhoids and asthma [1,2]. Discovery of penicillin scientifically confirmed the fact that fungi can be a very rich source of natural medicinal substances, including life-saving drugs [42].

The increased interest in chemical composition of fungi in the search for biologically active metabolites led to discovery of substances endowed with diverse actions. According to the definition of functional food by the International Life Sciences Institute in Europe, the mushroom is now gaining worldwide recognition as a functional food concerning improvement, prevention or treatment of some diseases. Different bioactive compounds of edible mushrooms are responsible for their antioxidant, antitumor and anticancer, antimicrobial, immunomodulatory, antiatherogenic, anthelmintic and hypoglycemic reported properties [43,44,45].

Cardiovascular disease includes numerous problems, many of which are related to a process called atherosclerosis. Atherosclerosis is a condition that develops when a substance called plaque builds up in the walls of the arteries. This buildup narrows the arteries, making it harder for blood to flow through. If a blood clot forms, it can stop the blood flow. This can cause a heart attack or stroke. The aetiological risk markers that have been shown to be specially modified by the diet are related to lipid and lipoprotein metabolism, haemostatic function, oxidative damage, homocysteine metabolism and blood pressure changes. LDL and HDL cholesterol, triacylglycerol, homocysteine and blood pressure are well-validated and generally accepted biomarkers. However, currently only LDL and blood pressure are considered diet-related biomarkers. In the folk medicine of the east mushrooms have been used in the treatment of high level cholesterol. Edible mushrooms reduce the risk of cardiovascular diseases due to specific substances included in them [Table 1.] [18,45-52].

Table 1.: Antiatherosclerotic effects and potential involved mechanisms of different edible mushrooms [18,45-52]

ANTIATHEROSCLEROTIC EFFECT OF EDIBLE MUSHROOMS			
Improvement of vascular reactivity Anti-inflammatory effects	Anti-hypertensive effects	Anti-oxidative effects Inhibition of LDL oxidation	Anti-platelet aggregating effects Inhibition of adenosin 5'diphosphate
Grifola frondosa	*Ganoderma lucidum*	*Agrocibe aegerita*	*Lentinula edodes*
Hypsizigus marmoreus	*Grifola frondosa*	*Boletus edulis*	*Pleurotus florida*
Pleurotus eryngii	*Lentinula edodes*	*Flammulina velutipes*	*Pleurotus ostreatus*
P. florida	*Pleurotus narbonensis*	*Lactarius deterrimus*	
P. ostreatus		*Lentinula edodes*	
		Pleurotus citrinopileatus	
		Pleurotus ostreatus	
		Serocomus chrysebteron	
		Suillus collitinus	
		Volvariella volvacea	

Lipids are the term given to fats in our body. Our body needs a certain amount of lipids, such as cholesterol and triglycerides, to work properly. Too much of certain lipids, on the other hand, can lead to cardiovascular problems. Lipids can be found as part of larger complexes known as lipoproteins, which are made by the liver. Lipids are made of fats and do not mix well with water, causing them to be classified as "hydrophobic." Because the blood is a water-based substance, lipids will not mix well in the blood. Consequently, lipids are transported in compounds known as lipoproteins. Lipoproteins are made of a combination of lipids and proteins which can be classified as "amphipathic," Rensselaer Polytechnic Institute explains. Amphipathic proteins contain hydrophobic segments, but they also contain hydrophilic segments, which are portions of the protein that mix well with water. This allows these proteins to serve as bridges between the blood and the lipids. The fatty acid pattern of edible mushrooms seems to contribute to reduce serum cholesterol. The predominant acid in mushrooms is palmitic acid, and in smaller amounts stearic acid. The unsaturated fatty acids are linoleic acid and oleic acid (Fig. 3).

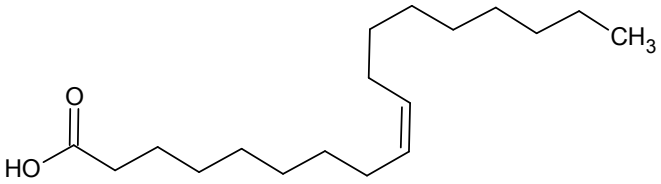

Figure 3. Oleic acid

The presence of trans isomers of unsaturated fatty acids is associated with the strongest effects on raising the serum total cholesterol to high-density lipoprotein ratio, increasing cardiovascular diseases risk. The trans isomers of unsaturated fatty acids have not been detected in mushrooms.

The dietary fiber intake may affect plasma lipid concentrations and lower the cardiovascular disease risks. The soluble dietary fiber has shown healthy effects on serum lipid levels, reducing total cholesterol and LDL-cholesterol amounts [19].

The total fiber content varies between 2.7 to 4 g/100 g of the edible part of the fruiting bodies. The percentage content of chitin in the fruiting bodies of *Armillaria mellea* (Pic. 3) calculated on the basis of determinations of glucosamine in hydrolysates of the dry weight of the fungus is 6.4% [53]. Physical and chemical properties and molecular weight of chitosans isolated from the fungus is identical with chitin isolated from crustacean cuticle. Chitosans lower LDL cholesterol (in blood and in liver) and the content of triglycerides in human serum. In this way they reduce the risk of cardiovascular disease. They also affected the absorption of cholesterol from the digestive tract. They cause decrease in its total concentration in blood and they low LDL, while they don't change the level of HDL [54, 55]. Due to the presence of large amounts of dietary fiber in edible mushrooms, particularly glucans (they increase the viscosity of gastric contents) and chitin the excretion of bile acids and neutral steroids is increased. Glucans and chitin also affect the immune system, lower blood pressure, have hypoglycemic activity, antibacterial, anti-inflammatory activity [19].

The statins are inhibitors of 3-methylglutaryl coenzyme A reductase, which

is the basic biosynthetic enzyme of endogenous cholesterol. Acting on this enzyme, they inhibit the synthesis of endogenous cholesterol [56].

Fot. 3 *Armillaria mellea* - Honey mushroom (fot. Katarzyna Sułkowska-Ziaja)

They block the mevalonic acid pathway, which lowers cholesterol levels in the body. Hypolipemic properties of statins are used in the treatment of hypercholesterolemia, stroke and cardiovascular disease. Other proven *in vitro* and *in vivo* biological effects of statins are cytotoxic and cytostatic activity against various tumor cell lines. The natural statins include lovastatin, among others, which occurs in high levels in *Pleurotus ostreatus*, especially in the gill hymenophore.

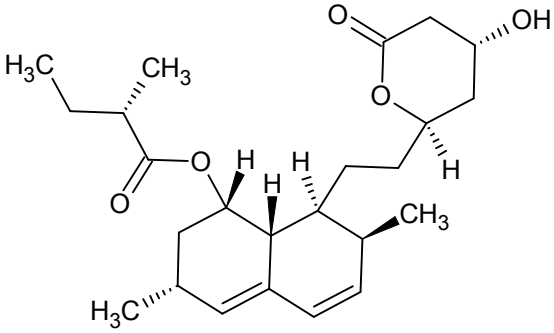

Figure 4. Lovastatin – compounds isolated from fruiting bodies of *Pleurotus ostreatus* (Jacq.: Fr.) Kummer – Oyster mushroom

The addition of this species to the diet effectively reduces the accumulation of cholesterol in blood serum and the liver. It also reduces the production of VLDL and LDL in favor of increasing the level of HDL, but also reduces the absorption of cholesterol and activity of HMG-CoA in the liver. Another statin with these properties - eritadermine - occurs in the Asian species *Lentinula edodes* [56-59].

Table 2: Edible mushrooms with reported hypocholesterolemic properties

EDIBLE MUSHROOM	HYPOCHOLESTEROLEMIC PROPERTIES	
	Lower	Raise
Agaricus bisporus	LDL cholesterol Serum total cholesterol HDL cholesterol Triglycerides in liver	Hepatic LDL receptor mRNA
Auricularia auricula	LDL cholesterol and serum total cholesterol	
Lentinula edodes	Cholesterol levels Phospholipids of plasma Other: Modification of hepatic phospholipids metabolism Hyperhomocysteinemic effect	
Pleurotus citrinopiletus *Pleurotus florida*	Triglycerides in liver and plasma Total cholesterol Total lipids Other: Inhibition of HMG-CoA reductase	Bile acid excretion

Pleurotus ostreatus	VLDL cholesterol LDL cholesterol Serum total cholesterol Plasma triglycerides Blood pressure Antioxidative glutation peroxidase activity Other: Inhibition of HMG-CoA reductase
Tremella fuciformis	LDL cholesterol Plasma triglycerides Serum total cholesterol Hepatic total cholesterol

Atherosclerosis, a progressive disease characterized by the accumulation of lipids and fibrous elements in the large arteries, constitutes the single most important contributor to the growing burden of cardiovascular diseases. Some fungi species are known to provide significant anti-inflammatory properties and natural anti-inflammatory substances have been isolated from some edible mushrooms. In addition, it has been reported that ergosterol and ergosterol peroxide from the edible mushroom *Hypsizigus marmoreus* can inhibit inflammatory processes [60].

The consumption of dietary antioxidants could be important in the prevention of cardiovascular diseases and there is evidence that the oxidative modification of LDL (lipids or protein components) play a crucial role in atherogenesis. Different antioxidant compounds have been found in mushrooms such as the polysaccharides, ergosterol, nicotinic acid, triterpenes and phenolic compounds. Polysaccharides from *L. edodes* decreased the expression level of VCAM-1mRNA of thoracic aorta endothelial cell in rats, with an increased antioxidant enzyme activity and significantly reduced serum total cholesterol, triglyceride, lipoprotein cholesterol and inhibited the oxidative injury caused by oxidation stress induced by intake of a high fat diet.

Bobek et al. [46] have observed that oyster mushroom prevented the formation of atheromatous plaques and reduced the incidence and extent of atherosclerotic lesions in aorta and coronary arteries as well as of focal fibrosis of myocardium in rabbits. The methanol extract from *P. florida* exhibited anti-platelet aggregating activity by an inhibition of adenosine 5′-diphosphate. Eritadenine is a very potent inhibitor of S-adenosylmethionine hydrolase. An increase of the level of this hydrolase or a decrease of the S-adenosylmethionine: S-adenosylmethionine hydrolase ratio inhibits phosphatylethanolamine methylation, which could contribute to reduce the synthesis of one of the major phospholipids of plasma lipoproteins.

Several studies have investigated the antihypertensive effects of some edible mushroom species such as *L. edodes*, *Ganoderma lucidum*, *Pleurotus narbonensis* and *G. frondosa.* Concerning the effects on blood pressure, the low concentration of sodium and the presence

of a great amount of potassium (182-395 mg/100 g) supports the utilization of mushroom within an antihypertensive diet [51,52].

Conclusion

There is no doubt that edible mushrooms can be used as a functional food, due to the content of representative nutritional composition as well as numerous bioactive compounds, which may promote human well-being as well as the prevention and treatment of several illnesses. The intake of mushrooms clearly has a cholesterol-lowering or hypocholesterolemic effect by different mechanisms such as decreasing VLDL, improving lipid metabolism, inhibiting of activity of HMG-CoA reductase, and consequently preventing the development of atherosclerosis. Edible mushrooms contain an impressive amount of compounds with antioxidant activity. The antioxidant and anti-inflammatory compounds occurring in mushrooms also may contribute to reduce the risk of atherosclerosis.

Resumo

Dum la pasintaj jaroj oni povis noti plialtiĝon de la konsumo de manĝeblaj fungoj. En multaj landoj fungoj kutime estas populara delikataĵo, ĉar ili aldonas guston kaj mordsenteblecon al kuiraĵoj. Fungoj eblas kolekti kaj primarajn kaj sekundarajn metabolaĵojn. Kelkaj el ili eble havas la rolon de antioksidantoj (ekz. fenolaj kaj indolaj substancoj, flavonoidoj, terpenoidoj, steroloj, askorbata acido, ergotioneinoj, karetenoidoj) kaj estas la fonto de elementoj, ekz. seleno. Indolaj substancoj ludas la rolon de neŭrotransmisiloj aŭ de iliaj prekursoroj kaj montras antioksidantajn, antikancerajn, kontraŭinflamajn kaj antimaljunigajn aktivecojn, regulas la diurnan variadon de korpaj funkcioj en homoj kaj partoprenas la koaguladon de la sango. Biologie kaj kuracade aktivaj metabolaĵoj de fungoj estas uzataj por kuraci tiajn gravajn malsanojn kiel ekz. kardiovazajn malsanojn, diabeton, aterosklerozon kaj kanceron. La enigo de fungoj evidente havas kolesterolmalplialtiĝintan aŭ hipokolesterolemiigan efikon pere de diversaj mekanismoj kiel malpliigo de VLDL, plibonigo de lipida metabolismo, malhelpo de la aktiveco de la HMG-CoA-reduktazo kaj sekve la prevento de la evoluo de aterosklerozo. La antioksidantaj kaj kontraŭinflamaj substancoj, kiuj troviĝas en fungoj, eble krome kontribuas al redukto de la ateroskleroza risko.

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