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HAL Id: hal-03202984
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Submitted on 20 Apr 2021

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The Cardioprotective Properties of Agaricomycetes Mushrooms Growing in the territory of Armenia (Review)

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Short title: Cardioprotective mushrooms of Armenia

Keywords: Agaricomycetes, anti-hypertensive, anti-obesity, anti-oxidative, anti-inflammatory, Armenia, cardioprotective, hypoglycemic, hypocholesterolemic, fibrinolytic, medicinal mushrooms


ABSTRACT: Several edible and medicinal Agaricomycetes mushrooms possess biologically active compounds with different therapeutic effects, such as anti-oxidative, anti-inflammatory, hypocholesterolemic, hypoglycemic, anti-hypertensive, fibrinolytic, thrombolytic, potentially used as cardioprotective remedies. Previous studies have shown that mushrooms possessing cardioprotective effect (CPE) contain a high amount of vitamins and minerals, low contents of fat which makes them applicable as supplementary dietary and functional food for prevention and treatment of a variety of cardiovascular disease (CVD). The current review is directed to the evaluation of resource value of 31 edible and non-editable medicinal Agaricomycetes mushrooms with potential CPE growing in the
 territory of Armenia and discusses the future perspectives of their usage in biotechnology and biomedicine.

I. INTRODUCTION

Cardiovascular disease (CVD) affects the heart and circulatory system and is considered the leading cause of mortality worldwide. The main risk factors for CVD include metabolic syndrome (MS), arterial hypertension (AH), high levels of blood glucose and cholesterol. Several pathological conditions, including diabetes, obesity, drug toxicity, aging, and oxidative stress, have a significant role in the development of CVD. Among the variety of CVD, AH affects 15-20% of all adults which may be complicated by atherosclerosis, stroke and myocardial infarction. The renin-angiotensin system (RAS) plays an important role in the pathophysiology of AH. The activation of RAS leads to an increased production of angiotensin II from angiotensin I, facilitated by the angiotensin-converting enzyme (ACE), which is associated with the development of AH and myocardial remodeling. The atherosclerosis is considered a major risk factor for CVD, in particular coronary artery disease, characterized by accumulation of lipoproteins and fibrous elements in the vessel wall. Inflammation and oxidative stress are associated with atherosclerosis and play a major role in the development of CVD. Furthermore, the development of thrombosis in the coronary artery can lead to myocardial infarction due to fibrin aggregation in the blood. The thromboembolic complications may develop as a result of deep vein thrombosis, surgery, certain medications and hypodynamic lifestyle. The thrombus blocks the blood flow depriving tissues of normal blood supply and oxygen. The processes of thrombus formation and fibrinolysis (fibrin dissolution by proteolytic enzymes) are balanced in biological systems. Thus, hyperglycemia, hyperlipidemia, insulin resistance, obesity, atherosclerosis, AH and thrombosis are associated with MS and are considered risk biomarkers contributing to the development of CVD.

The existing drugs, such as insulin, inhibitors of 3-hydroxy-3-methylglutaryl Coenzyme A (HMG-CoA) reductase, aldose reductase, ACE, and α-glucosidase, used for the treatment of MS, possess limited therapeutic efficacy and several side effects. Currently, the main areas of biomedical research are directed to the prevention and treatment of CVD, and considerable effort has been made in the pharmaceutical industry to develop new preparations with natural origin to improve glucose and lipid metabolism without significant side effects.

Mushrooms are considered natural sources of different groups of bioactive compounds (phenolics, terpenoids, polysaccharides, oligopeptides, sterols, etc.) and enzymes (proteases) possessing hypocholesterolemic, hypoglycemic, hypotensive, anti-inflammatory, antioxidative, as well as fibrino- and thrombolytic effects. Furthermore, mushrooms also possess a high content of proteins,
unsaturated fatty acids, fiber, vitamins (B complex, C, D, E, H, K, PP), minerals (Fe, K, Mn, Na, Se, Zn) and a low concentration of sodium. Previous studies suggest that regular consumption of edible mushrooms may potentially reduce the risk of CVD. 

The focus of the current review is to assess the resource value of edible and non-edible Agaricomycetes medicinal mushrooms (MM) with potential CPE growing in the territory of Armenia and evaluate the perspectives for their usage in biotechnology and biomedicine.

II. THE CARDIOPROTECTIVE EFFECT OF MUSHROOMS

Mushrooms have been prescribed in traditional medicine due to their diverse bioactivity to reduce the risk of CVD (Table 1). The reported therapeutic properties of MM (e.g. anti-oxidative, anti-inflammatory, anti-atherosclerotic, anti-hypertensive, anti-obesity, hypoglycemic, hypolipidemic and fibrinolytic) may be clinically relevant in the prevention and treatment of cardiac diseases.

The maintenance of balance between free radical production and antioxidant defence is an essential condition for normal functioning of biological organisms. Free radicals may damage cellular lipids, proteins, and DNA, affect their normal function and lead to the development of various diseases. The natural products with antioxidant activity (AOA) are considered potential protective agents against oxidative damage. The development of CVD may also be prevented by the dietary intake of natural antioxidants, including mushrooms. They neutralize free radical elements by enhancing the activity of catalase and superoxide dismutase, and stabilize glutathione and malondialdehyde levels.

In this regard, *Agaricus brasiliensis*, *Agrocybe aegerita*, *Boletus edulis*, *Flammulina velutipes*, *Hericium erinaceus*, *Lentinula edodes*, *Trametes versicolor*, *Volvariella volvacea* as well as mushrooms species from genera *Pleurotus* and *Ganoderma* are considered a natural source of biomolecules (fatty acids, phenolics, polysaccharides, steroids, terpenoids, tocopherols, etc.) with anti-atherosclerotic (AAS), anti-inflammatory (AIE), antioxidant, anti-hypertension, cardioprotective, hypocholesterolemic (HCE), hypoglycemic (HGE) and hypotensive (HTE) effects.

The lanostane type triterpenoids isolated from *Ganoderma lucidum* were suggested as promising bioactive agents for the treatment of MS. In vitro study and animal assays, as well as several human trials suggest that *Agaricus bisporus*, *G. lucidum*, *H. erinaceus*, *Phellinus linteus* and *Pleurotus* species may normalize blood glucose and lipid levels. The eritadenine extracted from *L. edodes* has been identified as an anti-atherogenic compound which not only improves lipid metabolism but also inhibits in vitro activity of ACE. In vitro anti-atherogenic, ACE and HMG-CoA reductase inhibitory effects, as well
as the protection of endothelium against oxidative stress were evaluated in *Pleurotus pulmonarius.*  

Several edible MM due to a high content of unsaturated fatty acids possess AAS effect, and their consumption may have a beneficial effect on the cellular metabolism in the human body.  

Although the mechanisms of hypocholesterolemic and hypoglycemic effects of mushroom-derived metabolites are unclear, several species, such as *A. bisporus, Auricularia polytricha, F. velutipes, G. lucidum, Grifola frondosa, L. edodes, P. pulmonarius and P. ostreatus* may be recommended in nutriceutical and pharmaceutical industries to develop biotech products with HGE and HTE.  

The inhibition of ACE is considered the main mechanism of HTE of mushrooms.  

The well-known fibrinolytic agents, such as tissue-type, urokinase-type, nattokinase and streptokinase, possess a wide range of clinical applications. However, their uncontrolled usage is costly and results in a number of side effects, including internal haemorrhage, allergic reactions, and limitation in specificity towards fibrin. Therefore, the search for natural sources of fibrinolytic agents is in demand. The Agaricomycetes mushrooms, belonging to different taxonomic and ecological groups, are considered active producers of extracellular proteolytic (fibrinolytic, thrombolytic and caseinolytic) enzymes.  

Previous systematic studies have revealed the presence of fibrinolytic and thrombolytic proteases in *Armillariella mellea,*  

Coprinoid mushrooms,  

F. velutipes,  

*Fomitopsis pinicola,*  

*G. lucidum,*  

*H. erinaceus,*  

*Pleurotus eryngii var. ferulae,* and *P. ostreatus.*  

The research data provide evidence for the usage of mushrooms as a healthy food to decrease the risk of MS and CVD.  

Mushroom-rich diet regulates some risk factors associated with cardiac diseases, such as the levels of total low-density lipoprotein (LDL), high-density lipoprotein (HDL), total cholesterol, fasting triacylglycerol, homocysteine, AH, as well as the oxidative and inflammatory damage of vessels.  

With this treatment approach of CVD, several agaricoid and polyporoid MM, such as Chaga (*Inonotus obliquus*), Lion’s Mane (*H. erinaceus*), Oyster mushroom (*P. ostreatus*), Maitake (*G. frondosa*), Turkey tail [*Coriolus (=Trametes) versicolor*], Reishi (*G. lucidum*), Shiitake (*L. edodes*), and Agarikon (*Laricifomes officinalis*) are considered potential natural products to develop myco-pharmaceuticals with CPE.  

Among these species, *G. frondosa, G. lucidum, L. edodes, P. ostreatus,* and *P. pulmonarius* are considered ideal products with low-calorie healthy diet to prevent the development of CVD due to high contents of fibres, proteins, and microelements. In particular, *Pleurotus* species decrease the levels of LDL and HDL, homocysteine, total cholesterol, and fasting triglycerides, prevent the development of AH, diabetes, and other pathological conditions, as well as reduce oxidative stress.  

A pronounced HCE of *P. ostreatus* combined with inhibition of lipid peroxidation has been shown to reduce the incidence and size of atherosclerotic plaques in animals. Furthermore, lovastatin, the leading compound of statins (HMG-CoA reductase inhibitors), has been detected in this fungus. The usage of *Pleurotus*
cornucopiae, A. auricula, A. polytricha, F. velutipes, and A. bisporus the hypocholesterolemic, anti-atherosclerotic, anti-coagulant and anti-aggregant diet has been previously reported.\textsuperscript{31-33,59,61} The triterpenes, derived from \textit{G. lucidum}, have been shown to inhibit the biosynthesis of cholesterol and protect against atherosclerosis by inhibition of ACE and platelet aggregation.\textsuperscript{7,9} The dried fruiting bodies of \textit{A. aegerita} can significantly reduce the levels of total cholesterol, triacylglycerides and the atherogenic index in rats and have shown HCE and AOA.\textsuperscript{62} Therefore, they have a potential to be used in biomedicine as natural sources of phenolic antioxidants and hypocholesterolemic agents. The steroid ergosta-4-6-8(14),22-tetraen-3-one, isolated from Chinese medicinal mushroom \textit{Polyergus sclerotium}, has been shown to possess aldosterone-antagonist effects with diuretic properties \textsuperscript{63} which could also be of benefit in CVD.

Thus, mushrooms are considered a promising source of naturally-derived cardioprotective biomolecules. Further studies of their CPE for biotechnological and biomedical usages are warranted.

\section*{III. BIOLOGICAL RESOURCES OF MUSHROOMS WITH CARDIOPROTECTIVE EFFECT DISTRIBUTED IN ARMENIA}

The analysis of literature and own data to assess cardioprotective potential of agaricomicetous mushrooms in Armenia revealed 16 edible and 15 non-edible species of agaricoid, coprinoid, polyporoid and hymenochaetoid mushrooms, including \textit{A. bisporus}, \textit{A. auricula-judae}, \textit{Armillariella mellea}, \textit{Coprinus comatus}, \textit{Fomitopsis pinicola}, \textit{Ganoderma lucidum}, \textit{Hypholoma fasciculare}, \textit{P. ostreatus}, and \textit{Trametes versicolor} have been reported in all floristic regions of Armenia (Table 1). Previously, several therapeutic effects, including hypolipidemic, hypoglycemic, antioxidant, anti-inflammatory, anti-hypertensive, anti-obesity, hypotensive, and thrombolytic/fibrinolytic, have been revealed in these fungi.\textsuperscript{46-49,64-68} (Table 1).

Two wild-growing and cultivated edible mushrooms, \textit{P. ostreatus} and \textit{A. bisporus}, widely cultivated in Armenia, have been shown to possess AOA, HGE, HCE, THE and prevent the development of atherosclerosis.\textsuperscript{69}Traditionally, \textit{A. bisporus} has been used in the treatment of CVD and stroke due to its anti-diabetic and anti-aging properties.\textsuperscript{41} (Table 1). The polysaccharides isolated from \textit{P. ostreatus} and \textit{A. bisporus}, as well as from \textit{A. auricula} growing in Ijevan floristic region, showed antioxidant, hypolipidemic, anti diabetic and anticoagulant properties and may protect the heart from ischemia/reperfusion injury.\textsuperscript{43} The polysaccharides derived from \textit{A. auricula} are considered natural antioxidants that safeguard myocardial function by maintaining the redox levels in the cardiac muscle, improve the left ventricular ejection fraction (LVEF) and shot axis fractional shortening parameters of the left ventricle in experimental models.\textsuperscript{43}
The cultural liquid (CL) of eight polypores (*Fomes fomentarius*, *Fomitella fraxinea*, *Fomitopsis pinicola*, *Laetiporus sulphureus*, *Trametes gibbosa*, *T. hirsuta*, *T. ochracea*, and *T. versicolor*) has recently been screened for thrombolytic activity (TLA) on samples of thrombi obtained from human blood. The highest activity was detected in *F. fraxinea* (up to 100%), followed by *F. pinicola* (up to 85%), *F. fomentarius* (up to 83%), and *L. sulphureus* (up to 69%) strains, whereas the activity was weaker (20–55%) in *Trametes* species. The screening of fibrinolytic activity (FLA) of CL samples of two agaricoid (*F. velutipes*, *P. ostreatus*) and two polyporoid (*F. pinicola*, *G. lucidum*) mushrooms revealed the highest activity in *F. pinicola* (95%), followed by *G. lucidum* (55%), *P. ostreatus* (54.0), and *F. velutipes* (51%) (Badalyan et al. unpublished data). Thus, these findings show that mushrooms may be considered alternative natural sources of extracellular proteases to develop novel myco-pharmaceuticals with TLA and FLA.

The milk-coagulating activity was detected in CL samples of *F. pinicola* and several coprinoid mushrooms. (Table 1). The hymenochaetoid fungi, *Inonotus dryadeus*, *I. hispidus*, *I. obliquus*, *Phellinus gilvus*, *Ph. igniarius*, *Ph. pini*, *Ph. ribis*, *Ph. robustus*, and *Ph. torulosus* growing in Armenia possess AOA, whereas HGE and HCE were mainly detected in *Phellinus* species (*Ph. igniarius*, *Ph. linteus*, *Ph. pini*, *Ph. ribis*). The HGE, FLA and CPE were reported in *Coprinus comatus*, *Coprinellus micaceus*, *Volvariella volvacea*, *Coriolus versicolor* and *Lentinus tigrinus* widely distributed in Armenia (Table 1). *C. versicolor* is known for its hypoglycemic effect, however the effect of this species on myocardial function of patients with diabetic cardiomyopathy (DCM) remains unclear. The results of a recent study have shown a significant improvement of cardiac dysfunction after fungal extract treatment which decreased the extent of cardiac fibrosis in rats. This protective effect of *C. versicolor* in patients with DCM is associated with the suppression of TGF-β1/Smad signaling (transforming growth factor β-1) and attenuation of nucleotide-binding oligomerization domain (NOD)-like receptor protein 3 (NLRP3) activation, suggesting that fungal extract may be a therapeutic agent for treatment of diabetic mice. Thus, Agaricomycetes MM distributed in Armenia may be considered as a potential source of cardioprotective biomolecules to develop functional food and myco-pharmaceuticals for the prevention and treatment of CVD.

**IV. CONCLUSION AND FUTURE PERSPECTIVES**

It is known that Agaricomycetes mushrooms can be considered as a functional food and remedies, due to their nutritional value, bioactive compounds and enzymes, for the prevention and treatment of several diseases, including MS and CVD.
The current review discusses the resource value and potential CPE (hypolipidemic, hypoglycemic, antioxidant, anti-inflammatory, anti-hypertensive, anti-obesity, hypotensive, thrombolytic/fibrinolytic) of 31 species of edible and non-edible Agaricomycetes MM (e.g. *A. bisporus*, *A. auricula-judae*, *C. comatus*, *G. lucidum*, *H. erinaceus* and *P. ostreatus*) distributed in all floristic regions of Armenia. Future myco-pharmacological and clinical studies are needed to elucidate the mechanisms of cardioprotective properties of responsible bioactive compounds. The biotechnological cultivation of selected species/strains will assist in the development of cardioprotective mushroom-derived biotech products and their biomedical application in Armenia.

ACKNOWLEDGMENTS

This research was supported by the SCS RA Thematic Project #18T-1F115.

REFERENCES


Table 1: Taxonomy, bioactive compounds and medicinal (cardioprotective) effects of medicinal Agaricomycetes mushrooms growing in Armenia
<table>
<thead>
<tr>
<th>N</th>
<th>Mushrooms species</th>
<th>Floristic regions</th>
<th>Bioactive compounds</th>
<th>Medicinal effects</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td><em>Agaricus bisporus</em> (J.E. Lange) Imbach</td>
<td>GG,YE</td>
<td>Polysaccharides, ergothioneine, polyphenols, vitamins</td>
<td>Antioxidant, anti-inflammatory, hypoglycemic, pancreas protective, hypocholesterolemica, hypotensive, cardioprotective</td>
<td>5,17,42,58</td>
</tr>
<tr>
<td>2.</td>
<td><em>Agrocybe (= Cycloxybe) aegerita</em> (V. Brig.) Vizzini</td>
<td>YE</td>
<td>Polysaccharides, phenolics</td>
<td>Antioxidant, anti-atherosclerotic, hypoglycemic</td>
<td>62,37,39</td>
</tr>
<tr>
<td>6.</td>
<td><em>Cantharellus cibarius</em> Fr.</td>
<td>DI,LR</td>
<td>Polysaccharides, phenolics</td>
<td>Antioxidant, anti-inflammatory, cardioprotective, hypolipidemic, hypoglycemic</td>
<td>3</td>
</tr>
<tr>
<td>8.</td>
<td><em>Coprinellus micaceus</em> (Bull.) Vilgalys, Hopple &amp; Jacq. Johnson</td>
<td>YE,DI,LR</td>
<td>Polysaccharides, fatty acids, proteases</td>
<td>Hypoglycemic, thrombolytic</td>
<td>5,46,49,</td>
</tr>
<tr>
<td>9.</td>
<td><em>Coprinopsis strommayeri</em> (Schulzer) Redhead, Vilgalys &amp; Moncalvo</td>
<td>YE</td>
<td>Terpenoids, linoleic, palmitic, stearic, oleic acids</td>
<td>Antioxidant, casemolytic, fibrinolytic</td>
<td>5,46,49</td>
</tr>
<tr>
<td>11.</td>
<td><em>Fomes fomentarius</em> (L.) Fr.</td>
<td>ALL</td>
<td>Phenolics, flavonoids, exopolysaccharides, triterpenoids, ketones, proteases</td>
<td>Antioxidant, anti-inflammatory, hypoglycemic, hypolipidemic, fibrinolytic, thrombolytic</td>
<td>4,47,48,67</td>
</tr>
<tr>
<td>13.</td>
<td><strong>Ganoderma lucidum</strong> (Curtis) P. Karst.</td>
<td>IJ,LR,SV,ZG</td>
<td>Polysaccharides, lanostane terpenoids, phenolics, fatty acids, steroids, tocopherols</td>
<td>Antioxidant, , anti-aggregation, anti-inflammatory, anti-hypertensive, anti-obesity hypoglycemic, hypocholesterolemic, fibrinolytic, thrombolytic,</td>
<td>4-7, 9,16,36,37, 39,47,48,52,66</td>
</tr>
<tr>
<td>14.</td>
<td><strong>Ganoderma adspersum</strong> (Schulz.) Donk</td>
<td>YE, IJ</td>
<td>Polysaccharides, terpenoids, phenolics</td>
<td>Antioxidant, antihypertensive, hypoglycemic, hypocholesterolemic, fibrinolytic</td>
<td>5,47,48,67</td>
</tr>
<tr>
<td>15.</td>
<td><em>Hericium erinaceus</em> (Bull.) Pees.</td>
<td>IJ, ZG</td>
<td>Meroterpenoids, erinacerins, erinaceolactones, hericenones, herinase</td>
<td>Antioxidant, anti-inflammatory, anti-obesity, hypoglycemic, hypocholesterolemic, fibrinolytic</td>
<td>4,5,19,53</td>
</tr>
<tr>
<td>16.</td>
<td><strong>Hypholoma fasciculare</strong> (Fr.) Kumm.</td>
<td>AP, IJ, LR, YE, ZG</td>
<td>Proteases</td>
<td>Hypoglycemic, fibrinolytic, vasodilator</td>
<td>4,64</td>
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<tr>
<td>17.</td>
<td><strong>Inonotus dryadeus</strong> (Pers.) Murrill</td>
<td>IJ, ZG</td>
<td>Free fatty acids, cerevisterol, sphingosine</td>
<td>Antioxidant</td>
<td>68</td>
</tr>
<tr>
<td>18.</td>
<td><strong>Inonotus hispidus</strong> (Bull.) P. Karst.</td>
<td>YE, IJ, LR, MG, ZG</td>
<td>Phenolic compounds, hispidin</td>
<td>Antioxidant, anti-inflammatory, antidiabetic, cardioprotective</td>
<td>68</td>
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<tr>
<td>19.</td>
<td><strong>Inonotus obliquus</strong> (Ach. ex Pers.) Pilát</td>
<td>IJ, LR</td>
<td>Phenolic compounds, melanin, xylo-galactoglucan, polysaccharides, flavonoids</td>
<td>Anti-obesity, anti-diabetic, anti-oxidant, anti-inflammatory, cardioprotective</td>
<td>5,68</td>
</tr>
<tr>
<td>21.</td>
<td><em>Lentinus tigrinus</em> (Bull.) Fr.</td>
<td>YE, IJ, LR</td>
<td>Phenolics, sterols, polysaccharides, proteins</td>
<td>Antioxidant, hypoglycemic, hypocholesterolemic</td>
<td>5,67,72</td>
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<tr>
<td>22.</td>
<td><strong>Phellinus igniarius</strong> (L.) Quél.</td>
<td>All</td>
<td>Phenolic acids, polysaccharides, hispidin</td>
<td>Anti-inflammatory, antioxidant, anti-diabetes</td>
<td>68</td>
</tr>
<tr>
<td>23.</td>
<td><strong>Phellinus pini</strong> (Brot.) Bondartsev &amp; Sing.</td>
<td>IJ, LR</td>
<td>Hispidin, squarrosidine, free phenolic acids, polysaccharides</td>
<td>Antioxidant, hypoglycemic, hypolipidemic</td>
<td>68</td>
</tr>
<tr>
<td>24.</td>
<td><strong>Phellinus ribis</strong> (Schumach.) Quél.</td>
<td>IJ, MG, ZG</td>
<td>Glucan, hispidin</td>
<td>Antioxidant, anti-inflammatory, anti-diabetes</td>
<td>6868</td>
</tr>
<tr>
<td>25.</td>
<td><em>Pleurotus cornucopiae</em> (Paulet) Rolland</td>
<td>AP, YE, IJ, LR, ZG</td>
<td>Phenolics, fatty acids, mannegalactoglucons, oligopeptides</td>
<td>ACE inhibitory, Anti-inflammatory, antioxidant, hypoglycemic, hypocholesterolemic, hypotensive</td>
<td>4,5,39,67</td>
</tr>
<tr>
<td>No.</td>
<td>Species</td>
<td>Region(s)</td>
<td>Phenolacids, polysaccharides, fatty acids, proteases</td>
<td>Medicinal Properties</td>
<td>References</td>
</tr>
<tr>
<td>-----</td>
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<tr>
<td>26.</td>
<td><em>Pleurotus eryngii</em> (DC.) Quél.</td>
<td>YE</td>
<td>Phenolacids, polysaccharides, fatty acids, proteases</td>
<td>Anti-inflammatory, antioxidant, hypoglycemic, hypocholesterolemic, hypotensive, fibrinolytic</td>
<td>5,6,7,39,54,65</td>
</tr>
<tr>
<td>29.</td>
<td><em>Trametes</em> (= <em>Coriolus</em>) versicolor (L.) Lloyd</td>
<td>IJ, LR, YE</td>
<td>Polysaccharides, phenolacids, proteases</td>
<td>Antioxidant, anti-obesity, anti-diabetic, cardioprotective, thrombolytic</td>
<td>4,5,39,66,67,71</td>
</tr>
<tr>
<td>30.</td>
<td><em>Trametes hirsuta</em> (Wulfen) Pilát</td>
<td>YE</td>
<td>Polysaccharides, phenolacids, proteases</td>
<td>Antioxidant, thrombolytic</td>
<td>4</td>
</tr>
<tr>
<td>31.</td>
<td><em>Volvariella volvacea</em> (Bull.) Singer</td>
<td>YE, IJ</td>
<td>Phenolic compounds, flavonoids, ascorbic acid, β-carotene, lycopene</td>
<td>Antioxidant, hypotensive</td>
<td>4,5,37,39,70</td>
</tr>
</tbody>
</table>

(*) Edible mushroom species; Floristic regions of Armenia: (AG) – Aragats; (AP) – Aparan; (DG) – Daragez; (GG) – Gegama; (IJ) – Ijevan; (LR) – Lori; (MG) – Meghri; (SH) – Shirak; (SV) – Sevan; (UA) – Upper Akhuryan; (YE) – Yerevan; (ZG) – Zangezur