POTENTIAL OF MUSHROOM BIOACTIVE MOLECULES TO DEVELOP HEALTHCARE BIOTECH PRODUCTS

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ABSTRACT

Mushrooms are widely appreciated all over the world for their nutritional value and medicinal properties. They have low fat, high protein and vitamins contents. Mushrooms contain several minerals and trace elements, as well as substantial amount of dietary fibers. Basidiomycetes mushrooms (phylum Basidiomycota) including agaric and bracket fungi are also producers of bioactive molecules and valuable enzymes with different therapeutic effects. Therefore, they are considered as perspective organisms to develop different healthcare biotech-product. The main groups of bioactive molecules produced by different mushrooms are polysaccharides, terpenoids, phenolics, lectins etc. More than 126 therapeutic effects (immune-modulating, antimicrobial, antiviral, antioxidant, hypocholesterolemic, ect.) of these molecules were revealed.

Nowadays, interest to biotechnological cultivation of Basidiomycetes mushrooms is related with the growing demand of different mushroom-based biotech-products in pharmaceutical, food and cosmetic industries. The submerged cultivation of mycelium has significant industrial potential to obtain biomass and desired bioactive molecules for further development of consistent and safe healthcare products.

Several pharmaceuticals (krestin, lentinane, coriolan, schyzophillan, etc.) formulated from medicinal mushrooms are already available in the world market. The majority of mushroom products possesses beneficial health effects owing to the synergistic action of present bioactive molecules and can be used on a regular basis without harm. Nutritive, anti-inflammatory, regenerative and antioxidant properties of several mushrooms makes their usage perspective in manufacturing of cosmetic products. Formulation of balanced food for pets is anew area of application of mushroom biotech-products. Establishment and maintenance of culture collections play important role in studies of biodiversity, genetic resources and biotechnological potential of Basidiomycetes mushrooms.

Keywords: basidiomycetes mushrooms, bioactive molecules, biotechnological potential

INTRODUCTION

Since ancient times mushrooms were widely appreciated all over the world, particularly in China, Korea, Japan, Central and North American countries for their nutritional value and medicinal properties. Mushrooms have a low fat and high protein content, a high content of several vitamins (B, C, D, K), minerals (potassium, phosphorus) and trace elements (selenium). Mushrooms contain substantial amount of dietary fibers, as well. Modern scientific data has documented that mushrooms represent an unlimited source of bioactive molecules as an example of molecular diversity with recognized potential in drug discovery and development. Basidiomycetes mushrooms (phylum Basidiomycota) including agaric and bracket fungi are natural source of bioactive molecules and valuable enzymes with around 126 therapeutic effects [1-3]. Therefore, they are considered as perspective organisms to develop different healthcare biotech-product.

BIOACTIVE MOLECULES WITH MUSHROOM ORIGIN

Bioactive molecules produced by mushrooms are mainly belongs to the polysaccharides, glucans, terpenoids, phenolic compounds, lectins, statins, etc. [4-6]. They have immune-modulating, antioxidant, genoprotective, antitumor, hypocholesterinemic, antidiabetic, hepatoprotective and other medicinal effects [2,3,7,8]. Fungal polysaccharides are the most potent mushroom-derived substances with antitumor and immune-modulating properties. They are present in cell wall with different types of glycosidic linkages, such as (1→3) and (1→6)-β-D-glucans. Polysaccharides possess significant immune-stimulating, antitumor, antioxidant, antibacterial and antiviral activities. Fungal terpenoids (tri- and sesquiterpenes) have cytotoxic, antibacterial, antifungal, hypocholesterolemic, hypoglycemic, hypotensive and antioxidant effects. Chitin and chitosan isolated from fungal cell wall are regulating the functions of liver, gastro-intestinal tract and kidney. Fungal pigment melanin possesses antioxidant, immune-modulating, anti-mutagenic and radioprotective properties.

Wood inhabiting mushrooms from genera *Ganoderma, Fomes, Fomitopsis, Inonotus, Phellinus, Trametes, Schyzophillum* and others are reported as a source of different biomolecules, such as glucans, phenolic compounds and terpenoids with immune-modulating and antimicrobial activities [2]. About 400 bioactive molecules including different triterpenes, polysaccharides, proteins, sterols, and fatty acids have been isolated from *Ganoderma* species *G. lucidum*, *G. applanatum* and *G. tsugae*. Among them lanostan-type triterpenoids are promising candidates to develop antitumor drugs [9,10]. Two glucans grifon and grifolan isolated from maitake mushroom *Grifola frondosa* possesses immune-modulating and antitumor effects. New glycoprotein complex obtained from maitake helps to maintain healthy cardiovascular function [11]. Medicinal mushrooms *Polyporus (=Grifola umbellata) umbellatus* and *Polyporus alveolaris* contain cytotoxic steroids and polypeptides with immune-stimulating, anticancer, anti-inflammatory, antibacterial, hepatoprotective and antifungal effects [12]. An antitumor product lentinan was developed from water-soluble antitumor polysaccharide isolated from shiitake mushroom *Lentinula edodes*.The antitumor β-D-glucan extracted from cultural broth of *S. commune* was developed to anticancer biotech-product under the name schyzophillan. Polysaccharide based products from *Agaricus brasiliensis (=A. blazei)* are using to combat physical and emotional stress, stimulate immunity, reduce levels of blood cholesterol and sugar, prevent osteoporosis and gastric ulcer. Antitumor protein flammulin was isolated from enokitake mushroom *Flammulina velutipes* [5,13].

Several bioactive molecules, such as sesquiterpenes (cuparane, illudins), quinones (5-methoxy-p-toluquinone, benzoquinone, lagopodins, hydroxylagopodins), polysaccharides, proteins (hydrophobins and galectins), sterols, derivatives of imidazole, indolic (triptamine, serotonin, bufotenin, psilocin, psilocibin, ergothionin) and volatile (skatole) compounds were reported in Coprinoid mushrooms. They possess antifungal, antibacterial, antiviral, fibrino- and thrombolytic, antiprotozoal, neuro- and vasotonic effects [14].The oyster mushrooms (*Pleurotus* spp.) are potential producers of statins, which are inhibitors of HMG-CoA reductase, a key enzyme in cholesterol metabolism in the human body. Significant reduction of blood cholesterol level was observed when biotech-product plovastin obtained from submerged mycelia of *P. ostreatus* and *P. eryngii* var. *ferulae* was used as a dietary supplement [4]. Antimycotic biotech-product mucidermin was developed from antifungal compound mucidin (strobilurin A) isolated from *Oudemansiella mucida*. Antiviral agents against different types of viruses (Papilloma, H5N1, HSV-1 and 2, Hepatitis B,C,D,E, AIDS, etc.) are also actively being searched from different mushroom species (*Piptoporus betulinus, Fomitopsis officinalis, Coprinellus micaceus*, etc) to develop new class of mushroom-based antiviral biotech-products [3,14].

Bioactive proteins lectins and hydrophobins of potential medicinal interest are so far described from mushrooms. Lectins are carbohydrate-binding proteins with agglutinating properties that are widely found in eukaryotes. The hydrophobins are most interesting candidates for various medical applications, such as increasing biocompatibility of medical implants devices, immobilization of antibodies in a biosensor and stabilizing oil vesicles for drug delivery [15].

Polysaccharides, sesquiterpenes, lectins, phenolic compounds and other biomolecules with different therapeutic effects (antibacterial, antifungal, cytotoxic, anti-inflammatory, insecticidal, nematocidal, antioxidant and others) were detected in several edible medicinal ectomycorrhyzal mushrooms [3] (Table 1). Mushrooms are also producers of extracellular proteolytic enzymes with fibrinolytic and thrombolytic activities [16].

Thus, the available information about bioactive molecules and enzymes of medicinal mushrooms suggests that they are promising biological organisms to develop health enhancing biotech-products.

MUSHROOM-BASED BIOTECH-PRODUCTS

Nowadays, different mushroom-based health care commercial biotech-products with preventive and curative effects are available and largely consumable in the world market. They sold in dried forms as healthy food (“nutraceuticals”) and as functional food additives (“pharmaceuticals” or “nutriceuticals”). The majority of mushroom products possesses beneficial health effects owing to the synergistic action of present bioactive molecules and can be used on a regular basis without harm.

Mushroom polysaccharide-based biotech-product krestin (PSK) was produced from *Trametes versicolor*. Preparation befungin obtained from Chaga mushroom (*Inonotus obliquus*) was approved as an antitumor drug in Russia and reportedly successful in treating breast, lung, cervical, and stomach cancers. Healthy food developed from biotechnologically cultivated mycelia of medicinal edible mushrooms *Hericium erinaceus* and *Tremella* spp. in combination with other natural substances (medicinal plants, algae, etc.) possess antioxidant and immune-stimulating activity, regulate the level of blood lipids and sugar [17,18]. Available biotech-products from *H. erinaceus* help to control Alzheimer disease and bleeding. They are used as anti-cancer and sarcoma agents. Some mushroom products are able to decrease high glucose and lipid levels in blood and recommended as neuro- and vasotonics, hepatoprotective and thrombolytic agents [3].

Nutritive, anti-inflammatory, regenerative and antioxidant properties of several mushrooms (*Lentinula edodes*, *Ganoderma lucidum*, *Fomes officinalis*, *Hypsizygus ulmarius*,*Tremella* spp.) makes their usage perspective in manufacturing of cosmetic products [6]. Mushrooms are currently proposed as highly active ingredients in world production of hair and skin care products. *Tremella* mushrooms contain hydrophilic agent – polysaccharide glucuronoxylomannan (GXM) with anti-inflammatory and wound healing properties largely used in cosmetology [19]. *Tremella* cosmetic products are applicable in treatment of neurodermatitis and sclerodermatitis.They prevent skin pigmentation and stimulate blood circulation. Fungal chitosan is also wildly used in cosmetology as an emulgatory, gel-forming, protective and anti-bacterial agent.

A new area of application of mushroom biotech-products is formulation of balanced food for pets. Except medicinal plants and other ingredients such food additionally contains mushroom dietary fibers and polysaccharides stimulating immune activity in animals. The pet food supplements are obtaining from mycelial biomass of different mushrooms.

Thus, Basidiomycetes mushrooms have significant biotechnological potential. Biological characteristics of mycelia, particularly fast growth and easy reproduction in culture conditions is assisting biotechnological cultivation of medicinal mushrooms to obtain desired bioactive molecules and biotech-products.

BIOTECHNOLOGICAL ROLE OF CULTURE COLLECTIONS

Establishment and maintenance of cultures collections of different group of mushrooms are of valuable importance to study their biodiversity, genetic resources and biotechnological potential. Availability of culture collections is also requested for biotechnological cultivation of mycelia.

Currently, two different approaches in biotechnological cultivation of mushrooms are used. First is fruiting bodies production and second-cultivation of mycelia. The fruiting bodies production is a long-term process and takes 1-2 months, while cultivation of mycelia takes several days. The submerged cultivation of mycelia has significant industrial potential and it is the best technique to obtain biomass and desired bioactive molecules for further development of consistent and safe healthcare mushroom biotech-products.

Study of genetic resources and biotechnological potential of medicinal mushrooms and establishment of their culture collection in Armenia was initiated in 1983. Presently fungal collection at the Yerevan State University (FCC-YSU) consists around 144 species and 500 strains of Basidiomycetes mushrooms [20]. Among them 94 species and 430 strains are Basidiomycetes mushrooms. The medicinal properties (antifungal, antibacterial, antiviral, immune-modulating, antioxidant, cytotoxic, mitogenic/ regenerative etc.) of 43 species and 308 strains are reported in our publications [21,22].

Studies of mushroom collections from FCC-YSU were realized in different culture conditions (static, submerged). Favorable growth parameters (temperature, pH, medium) for biotechnological cultivation of mycelia were revealed. Colony and pellet morphology, biomass formation, characteristics of the life cycle, the presence and type(s) of asexual sporulation (anamorph), ability to form teleomorph (fruiting bodies) *in vitro* and other mycelial characters were observed and their

Table 1. Therapeutic effects of bioactive molecules in several mycorrhiza forming Basidiomycetes mushrooms [3]

Species	Bioactive molecule	Therapeutic effect
Boletus (=Xerocomus) badius	Polysaccharides, polyphenolics, N-ethyl-γ-glutamine (L-theanine analog)	Antimitotic, antitumor, immune-modulating, antioxidant, neurotropic
Boletus edulis	Lectin, polysaccharides, polyphenols, ergothioneine	Antitumor, immune-modulating, antibacterial, antifungal, antiviral, anti-inflammatory, antioxidant, mitogenic, neurotropic
Cantharellus cibarius	Polysaccharides, cibaric acid, phenolic compounds	Antioxidant, antimicrobial, antifungal, insecticidal, nematicidal
Cantharellus tubaeformis	Polysaccharides, 10-hydroxy-8-decenoic acid	Antioxidant, antimicrobial, antifungal, anti-inflammatory, insecticidal, nematicidal, hypocholesterolemic, hypoglycemic, hypotensive, antitumor
Lactarius deliciosus	Sesquiterpenoids, lectin, phenolic compounds	Antibacterial, antifungal, cytotoxic, anti-inflammatory, insecticidal, nematocidal, antioxidant
Lactarius flavidulus	Polysaccharides, flavidulols A-D	Antitumor, antibacterial, cytotoxic, anti-inflammatory, immune-suppressive
Lactarius necator	Alkaloids necatorin and necotoron	Antibacterial, antifungal
Lactarius volemus	Phenolic acids, lectin	Antioxidant
Lyophillum decastes	(1→3)- and (1→6)-beta-D-glucans, phenolics	Antitumor, anti-bacterial, hypochole-stero-lemic, hypoglycemic, hypotensive, anti-inflammatory, immune-modulating, radio-protective, antioxidant
Morchella esculenta	Galactomannan (α-d-glucan)	Immune-modulating
Russula delica	Lectin	Antiproliferative, antiviral
Russula paludosa	Peptide	Antiviral
Rusulla virescens	Polysaccharides	Antioxidant, hypoglycemic, hypocholesterolemic
Russula xerampelina	Polysaccharides	Antitumor, antiparasitic
Suillus bovines	Suillin	Immune-suppressive, antibacterial
Suillus granulatus	Tetraprenylphenols	Antitumor
Suillusluteus	Phenolics, polysaccharides	Antifungal, antioxidant, immune-modulating
Tricholoma lobayense	Polysaccharides, polysaccharide-protein complex	Immune-modulating, antitumor
Tricholoma giganteum	Polysaccharides	Immune-modulating, antitumor
Tricholoma matsutake	α-d-glucan	Immune-modulating
Tricholoma mongolicum	Lectins, polysaccharide-peptide complex	Immune-modulating, antitumor, hypotensive, vasorelaxing
Tricholoma portentosum	Polysaccharides, phenolic compounds	Antitumor, antibacterial, antifungal, fibrinolytic

taxonomic significance was evaluated [13, 23 and others]. Screening of chemical composition (polysaccharides, phenolics, terpenoids, proteins, sugars, fatty acids, etc.) of mycelial and fruiting bodies' extracts of different collections was realized [3].

Despite of commercial importance, there are gaps to be filled in the current knowledge on taxonomy and biology of medicinal mushrooms. Genetically identified collections of polypore and coprini mushrooms, as well as other agaric and bracket fungi were screened for their taxonomic verification and phylogenetic analysis. Several new species, such as

Ganoderma applanatum, *Coprinellus strossmayeri*, *Coprinellus radians* and others were originally described for Armenian mycobiota [24-26]. Studies of genetic resources and biotechnological potential of medicinal mushrooms in Armenia are in progress.

CONCLUSION

Further sustainable research of natural and genetic resources of medicinal mushrooms using improved screening methods of genomics, proteomics and metabolomics will assist further biotechnological cultivation and usage of their bioactive molecules to develop novel healthcare biotech products with a positive global impact on human welfare and environmental conservation.

ACKNOWLEDGEMENTS

The research was supported by SCSRA, joint Armenian-Russian research project 13RF-110 and RFBR grant 13-04-90607_Arm. S.M. Badalyan thanks to DAAD for technical grant (#548.104401.317).

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