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Perspectives of Biomedical Application of Macrofungi

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Abstract. Mushrooms (macrofungi) have widely been appreciated all over the world for both their nutritional values and medicinal properties. They have been used in traditional medicine for more than 3000 years for prevention and treatment of different diseases. Modern scientific research shows that mushrooms are producers of a broad spectrum of high- and low-molecular-weight bioactive compounds, i.e., alkaloids, polysaccharides, proteins, phenolics, terpenoids, polyketides, cyclic peptides, lectins and ribosome-inactivating proteins. They have various therapeutic effects as antidiabetic, anti-inflammatory, antimicrobial, antioxidant, anti-tumorous, antiviral, cardioprotective, hepatoprotective, hypocholesterolemic, hypotensive, immunomodulatory, neuroprotective and regenerative activities, and possess promising pharmacological potential. Development of fungal biotechnological cultivation industry will support production of mushroom-derived biotech products, healthy food and pharmaceuticals. Further advances in fungal biology and biotechnology, genomics and proteomics will assist biomedical research and application of mushrooms.

Keywords: medicinal mushrooms, Basidiomycota, Ascomycota, bioactive compounds, pharmacological effect, biomedicine.

Abbreviations: **BAC**, bioactive compounds; **FIP**, fungal immunomodulatory protein; **MM**, medicinal mushrooms.

INTRODUCTION

Fungi are very diverse organisms distributed worldwide and found in almost all habitats. From estimated 1.5-3 million species of fungi about 150,000 species are mushrooms (macrofungi) taxonomically placed in two phyla, the *Basidiomycota* (class *Agaricomycetes*) and *Ascomycota* (class *Pezizomycetes*) in the subkingdom Dikarya [1]. Among the fungal species about 10%

(14,000-16,000) are scientifically well-known including, about 7000 edible species and 500 poisonous species [2,3]. There may be as many as 700 medicinal mushrooms which are regarded safe and possess around 130 different pharmacological activities [4,5].

Mushrooms have widely been appreciated all over the world not only for their nutritional values but also medicinal properties [5-12]. They have been used in traditional medicine for more than 3000 years for prevention and treatment of different diseases [13,14]. Despite available ethnomycopharmacological information and scientific data the extensive pharmacological and biotechnological potential offered by mushrooms is certainly not yet fully exploited [15-20].

BIOACTIVE MOLECULES AND PHARMACOLOGICAL ACTIVITY OF MUSHROOMS

Modern scientific data shows that agaricoid, polyporoid, and other taxonomic groups of mushrooms are producers of a broad spectrum of high- and low-molecular-weight bioactive compounds, i.e., alkaloids, polysaccharides, proteins, phenolics, terpenoids, polyketides, cyclic peptides, lectins, ribosome-inactivating proteins. [21-27] These bioactive molecules were investigated for their various therapeutic effects as analgesic, antimicrobial, antiviral, antioxidant, immunomodulatory, anti-inflammatory, anti-tumorous, mitogenic/regenerative, hypotensive, hepatoprotective, antidiabetic/hypoglycemic, hypocholesterolemic, cardio- and neuroprotective activities [28-45].

Wild and cultivable edible, and non-edible medicinal mushrooms (e.g. *Agaricus brasiliensis*, *Agrocybe cylindracea*, *Auricularia auricula-judae*, *Coprinus comatus*, *Ganoderma applanatum*, *G. lucidum*, *Grifola frondosa*, *Hericium erinaceus*, *Flammulina velutipes*, *Inonotus obliquus*, *Lentinula edodes*, *Ophiocordyceps* (syn. *Cordyceps*) *sinensis*, *Phellinus linteus*, *Pleurotus ostreatus*, *Polyporus umbellatus*, *Trametes versicolor*, *Tremella fuciformis*, *Wolfiporia cocos*, etc.) are considered as valuable sources to develop health enhancing functional food (nutraceuticals, nutraceuticals), mushrooms-derived drugs (mycopharmaceuticals), and cosmetic products (cosmeceuticals, nutricosmetics) which are perspective for biomedical application [12,18-20,46].

A wide spectrum of bioactive molecules with mushrooms origin has been recommended for a variety of therapeutic applications, such as the immunomodulatory β -glucan lentinan from *L. edodes* [27], the antimalarial alkaloid 4-hydroxymethylquinoline from *T. versicolor* [47]; pain-suppressive enkephalinase inhibitors from *Polyporus betulinus* [48]; nephroprotective polysaccharides, phenolics, and flavonoids from *Pleurotus tuber-regium* [37].

The extract derived from well-known medicinal mushrooms *Cordyceps sinensis* and *A. subrufescens* possess anticancer effects by modulating the immune system and inducing cell apoptosis [25,38]. The edible medicinal oyster mushroom *Pleurotus ostreatus* has significant hypocholesterolemic properties and other pharmacological effects [30,39,40,43]. Anticancer,

antimicrobial, antioxidant, antiviral, hypolipidemic, immunomodulatory, and estrogen-like activities were observed in *Pleurotus eryngii* due to the production of diterpenoids, as eryngiolide A, hemolysins, polysaccharides, pentacyclic triterpenoids, ubiquinone-9, and other pharmacologically active biomolecules [43,49,50]. Genome sequencing, comparative genomics, and phylogenetic analysis of medicinal polypore mushroom *Lignosus rhinocerotis* revealed sesquiterpenoid biosynthesis genes. Moreover, the genome of *L. rhinocerotis* encodes for 1,3- β - and 1,6- β -glucans, as well as for laccase, lectin, and other fungal immunomodulatory proteins (FIP) [51,52].

The *Ganoderma* species produce the highest diversity of bioactive compounds (alkaloids, fatty acids, nucleosides, polysaccharides, proteins, sterols, triterpenoids, etc.) with antiaging, antibacterial, anticancer, antidiabetic, antifungal, antihypertensive, anti-inflammatory, antioxidant, antiviral, hepatoprotective, hypoglycemic, immunomodulatory, neuroprotective, wound-healing, and other pharmacological capacities [22,23,32-34,41,42].

CONCLUSION AND FUTURE PERSPECTIVES

Nowadays, pharmaceutical companies consider the medicinal mushrooms as a rich source of innovative biomedical molecules extracted not only from fruiting bodies but also from both cultivated mycelial biomass and cultural broth. Moreover, the mycelium and the cultural broth might be considered as potential sources of bioactive compounds, due to their shorter incubation time and affordable culture conditions (e.g., requiring less space, low probability of contamination, and higher production of biomass) [12,36,43].

The advances in multidimensional biotechnological cultivation industry of mushrooms will further support development and application of mushroom-derived biotech products and pharmaceuticals in biomedicine [7,19,20].

Currently, in vitro assays, animal studies, and clinical trials justify the experience of traditional medicine and suggest a great potential of mushroom-derived compounds and pharmaceuticals for both the prevention and treatment of various diseases. However, development of high-quality mushrooms-based biotech products under controlled conditions with standardized procedures for further clinical trials are needed to substantiate the pharmacological properties or side effects of mushroom consumption before their clinical recommendation as myco-pharmaceuticals [36,53-56]. Compared to available extensive lists of mushrooms' bioactive compounds and therapeutic effects, the pathways of their biosynthesis and the genes behind are largely understudied [19]. Therefore, advances in fungal biology and biotechnology, genomics and proteomics are required for further biomedical research and application of macrofungi.

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