Current Trends in Biomedical Engineering & Biosciences
ISSN: 2572-1151

Juniper Publishers
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Review Article
Volume 19 Issue 5 - July 2020
DOI: 10.19080/CTBEB.2020.19.556024

Curr Trends Biomedical Eng & Biosci

Perspectives of Biomedical Application of Macrofungi

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Submission: March 13, 2020; **Published:** July 29, 2020

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Abstract

Macrofungi (mushrooms) have widely been appreciated all over the world for 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 macrofungi 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, antitumor, antiviral, cardioprotective, hepatoprotective, hypocholesterolemic, hypotensive, immunomodulatory, neuroprotective and regenerative, and possess promising pharmacological potential. Development of fungal biotechnological cultivation industry will support production of macrofungi-derived biotech products, healthy food and mycopharmaceuticals pharmaceuticals. Further advances in fungal biology and biotechnology, genomics and proteomics will assist biomedical research and application of macrofungi.

Keywords: Medicinal macrofungi; Basidiomycota; Ascomycota; Bioactive compounds; Pharmacological effect; Biomedicine

Abbreviations: BAC: Bioactive Compounds; FIP: Fungal Immunomodulatory Protein; MM: Medicinal Macrofungi

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 macrofungi (mushrooms) taxonomically placed in two phyla, the Basidiomycota (class *Agaricomycetes*) and *Ascomycota* (class *Pezizomycetes*) in the subkingdom Dikarya [1]. Among them 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 macrofungi (MM) which are regarded safe and possess around 130 different pharmacological activities [4,5].

Macrofungi 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 ethno-mycopharmacological information and scientific data the extensive pharmacological and biotechnological potential offered by Macrofungi is certainly not yet fully exploited [15-20].

Bioactive Compounds and Pharmacological Activity of Macrofungi

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

Wild and cultivable edible, and non-edible MM (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, nutriceuticals), macrofungi-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 macrofungi 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 *Piptoporus betulinus* [48]; nephroprotective polysaccharides, phenolics, and flavonoids from *Pleurotus tuber-regium* [37].

The extract derived from well-known medicinal species *Cordyceps sinensis* and *Agaricus subrufescens* possess anticancer effects by modulating the immune system and inducing cell apoptosis [25,38]. The edible medicinal oyster mushroom *P. 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 effects [22,23,32-34,41,42].

Conclusion and Future Perspectives

Nowadays, pharmaceutical companies consider the medicinal macrofungi 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 safe 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 macrofungi will further support development and application of myco-biotech products 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 macrofungi-derived compounds and pharmaceuticals for both the prevention and treatment of various diseases. However, development of high-quality and safe 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-pharmaceutical drugs [36,53-56]. Compared to available extensive lists of bioactive compounds of macrofungi and their therapeutic effects 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.

Acknowledgments

This review arises from a long-standing cooperation between two authors (S.M.B. and S.R.) on fungal biomedical research directed to the identification of bioactive compounds and medicinal properties of macrofungi supported by the collaboration between the Institute of Pharmacy; Yerevan State University, Armenia; and Faculty of Pharmacy of the University of Montpellier/UMR 5175 CNRS, France. The research project on medicinal mushrooms was partially sponsored by MES SCS Republic of Armenia (grant number #18T-1F115).

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How to cite this article: Susanna M Badalyan, Sylvie Rapior. Perspectives of Biomedical Application of Macrofungi. Curr Trends Biomedical Eng & Biosci. 2020; 19(5): 556024. DOI: 10.19080/CTBEB.2020.19.556024.

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How to cite this article: Susanna M Badalyan, Sylvie Rapior. Perspectives of Biomedical Application of Macrofungi. Curr Trends Biomedical Eng & Biosci. 2020; 19(5): 556024. DOI: 10.19080/CTBEB.2020.19.556024.

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DOI: 10.19080/CTBEB.2020.19.556024

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