

EXPLORING THE POTENCY OF WILD MUSHROOMS: A COMPRESSIVE REVIEW OF ANTIFUNGAL ACTIVITY IN THE REPUBLIC OF NORTH MACEDONIA

Emri MURATI^{1*}, Mitko KARADELEV² Adelina MURATI³

¹ Faculty of Agriculture and biotechnology, University of Tetova, Tetovo,

² Faculty of Natural Sciences and Mathematics, Ss. Cyril and Methodius University, Skopje

³ Faculty of Pharmacy- Ss. Cyril and Methodius University, Skopje

Corresponding author: emri-murati@uite.edu.mk

ABSTRACT

In the Republic of North Macedonia, according to the latest official data from the mycological research of macromycetes, close to 2,000 species are registered. The largest number belongs to basidiomycetes with 1735 species and the rest belongs to ascomycetes with 255 species. These mushrooms are used in nutrition, biotechnology, medicine, and pharmacy. A large number of these wild mushrooms also have antibacterial, antifungal, and antiviral effects. In this paper, we will mention only the types of fungi that have antifungal effects and activity that have been recorded in the research so far in the Republic of Northern Macedonia. In the paper, we present 26 species of wild and cultivated high fungi that have antifungal activity. The most popular species of macromycetes with antifungal effect are: *Agaricus bisporus*, *Agrocybe cylindracea*, *Boletus edulis*, *Ganoderma lucidum*, *Flammulina velutipes*, *Laetiporus sulphureus*, *Lactarius deterrimus*, *Lentinus edodes*, *Meripilus giganteus* and *Tricholoma giganteum*, mainly belong to the phylum *Basidiomycota*. In these mushrooms have been found isolated compounds with antifungal activity affecting certain pathogenic fungi as we can mention: *Alternaria alternate*, *A. brassicae*, *Candida albicans*, *Aspergillus niger*, *Aspergillus fumigates*, *Fusarium gramineum*, *Microsporus canis*, *Neurospora crassa*, *Penicillium inflatum*, *Sacharomyces cerevisiae*. These fungi mainly belong to the phylum *Ascomycota*.

Keywords: wild mushrooms, macromycetes, antifungal activity, Republic of Northern Macedonia.

INTRODUCTION

Fungi are organisms that belong to the kingdom of fungi named *Mycota*, *Mycetes*, and *Mycetalia*, which do not belong to either plants or animals. Mushrooms have great use both in the nutritional aspect as well as in the medicinal-pharmacological one. Medicinal mushrooms have an established history of use in traditional oriental therapies. Modern clinical practice in Japan, China, Korea, and other Asian countries continues to rely on mushroom-derived preparations [1]. Mushrooms have been used for many years in oriental culture as tea and nutritional food, and because of their special fragrance and texture. Some types of mushrooms through their chemical components can have an antimicrobial effect (antibacterial, antifungal, and antiviral). Mushrooms are one of the most important natural sources of bioactive compounds for the presence of numerous products with therapeutic properties. Commonly used in traditional Chinese medicine for centuries, mushrooms are rich in natural antioxidative, antitumor, antiviral, antimicrobial, and immunomodulatory agents, with medicinal effects proven by researchers [2]. Early civilizations,

by trial and error built up a practical knowledge of those suitable to eat and those to be avoided, e.g. poisonous or even psychotropic. In many parts of the world, especially Europe, wild mushrooms are regularly collected and used directly as a main source of food or added to soups, stews, and teas. Mushrooms are considered to be a good source of digestible proteins with protein content above most vegetables and somewhat less than most meats and milk [3].

Natural compounds with biological activity are normally present in plants, mushrooms, and other natural sources. Mushrooms need antibacterial and antifungal compounds to survive in their natural environments. Therefore, antifungal compounds with more or less strong activities could be isolated from many mushroom species and could be beneficial for humans [4]. A certain number of these mushrooms even have activity as an antioxidant, anticancer and antitumor, antiallergic, antidiabetic, antiglycemic, etc. In this paper, great importance is given to the exceptional use of a large number of macromycota (high) fungi that have antifungal activity. Pathogenic fungi are mushrooms that cause serious fungal diseases in plants, animals, and humans. Antifungal proteins have been isolated from a sizeable number of animals and plants. Although all these proteins serve the same function of protecting organisms from the deleterious consequences of fungal assault, they display a spectacular diversity of structures [5]. From the total number of macromycetes fungi, a certain number of them, according to numerous analyses and notes by various European and world authors, are also registered in the Republic of North Macedonia.

The aim of this paper

- The purpose of this paper is to present the fungi from the general list of the Republic of North Macedonia (RNM) that have been researched so far but that also have antifungal effects and activity.

- Only a certain number of fungi will be presented in the list, which, based on research so far, has proven their influence on a certain number of pathogenic and parasitic fungi.

MATERIAL AND METHODS

In the Republic of North Macedonia, based on research so far, of the total number of macromycetes, more than 2300 types of fungi have been described, which have been described in Karadelev et al. (2018, 2019) [6], [7]. The data are verified and determined in the database located in the Mycological Laboratory at the Faculty of Natural and Mathematical Sciences in UKIM. The list and table are compiled in alphabetical order and not by importance as well as the antifungal effect that they have on medicine and pharmacy. The same criterion was used in the table list of pathogenic fungi. We used the same criterion in the table of bacteria. Due to taking up more space, we have not been able to bring photos of all the mushrooms, but only of a small number, while the reader will be able to find them in the local and world literature through the name and scientific determination. In the table, in addition to the scientific name of the fungus, there are data on the spread, the name of the author who published it, and the pathogenic fungus on which it acts. For the determination of these fungi were using the newest keys and monographs while for some types we used [17]; [18]

RESULTS AND DISCUSSIONS

Recently, researchers have been searching for new antibacterial, antifungal, and antiviral agents from medicinal plants and medicinal fungi due to the unwanted side effects of antibiotics and the emergent emergence of resistant and mutant strains. Different components with protein and peptide content are isolated from the fruiting bodies of these mushrooms, which influence and have antibiotic and primarily antifungal effects.

Isolation of these compounds in the form of peptides from certain fungi is done with the help of various reagents in certain laboratories such as: Laboratory Techniques in Biochemistry and Molecular Biology [8]. An antifungal peptide with a molecular mass of 10 kDa (10 kiloDalton) was isolated from fruiting bodies of the mushroom *Pleurotus eryngii*. The peptide, designated as eryngin, inhibited mycelial growth in *Fusarium oxysporum* and *Mycosphaerella arachidicola*. Fresh fruiting bodies of the mushroom *P. eryngii* were obtained from a local vendor. They were homogenized in distilled water, and the homogenate was centrifuged [9]. *Ganoderma lucidum* is a medicinal mushroom that has antidiabetic, antioxidant, immunomodulatory, antitumor and antimetastatic activities. An antifungal protein, designated ganodermin, was isolated from the medicinal mushroom *Ganoderma lucidum*. Ganodermin was obtained with a yield of 12 mg/kg fruiting bodies. It exerted antifungal action on *B. cinerea*, *P. piricola*, and *F. oxysporum* [10]. Pleurostrin is an antifungal peptide isolated from the mushroom *Pleurotus ostreatus* (oyster) [11]. Agrocybin is an antifungal peptide with a molecular mass of 9 kDa that was isolated from fresh fruiting bodies of the mushroom *Agrocybe cylindracea* [5]. Lentin, which had a molecular mass of 27.5 kDa, inhibited mycelial growth in a variety of fungal species including *Physalospora piricola*, *Botrytis cinerea* and *Mycosphaerella arachidicola* [12]. Researching scientific papers by different authors can present newly published data regarding the antifungal action of *Laetiporus sulphureus* mushroom extract against phytopathogenic fungi including: *Aspergillus niger*, *Botrytis cinerea*, *Fusarium oxysporum f. sp. tulipae*, *Penicillium gladioli* and *Sclerotinia sclerotiorum*. *L. sulphureus* extract has inhibitory action against the germination and growth of some common phytopathogenic fungi comparable to the antifungal fluconazole and will be used further [13]. The present work detailed and evaluate the effect of aqueous and alcoholic extract of edible mushroom (*Agaricus bisporus*) against pathogenic fungus *Aspergillus flavus*, the random use of drugs using commercial antimicrobial it results in drug resistance into human pathogenic microorganisms which encourage the scientists to search new substance act as active antimicrobial from different sources [14]. The extracts were obtained from six *Lactarius* species (*Lactarius deterrimus*, *L. sanguifluus*, *L. semisanguifluus*, *L. piperatus*, *L. deliciosus*).

L. salmonicolor) have been investigated for

their antimicrobial activity (gram+ and gram- bacteria) have antifungal activity and effect in two mushrooms but with a smaller activity such as: *Candida albicans* and *Saccharomyces cerevisiae* [15]. Cordimyn is also a peptide that inhibited the growth of *Bipolaris maydis*, *Mycosphaerella arachidicola*, *Rhizoctonia solani* and *Candida albicans* (IC₅₀ 50 µM, 10 µM, 80 µM and 0.75 mM, respectively). Nevertheless, there were no effects observed against *Aspergillus fumigatus*, *Fusarium oxysporum*, and *Valsa mali*. Cordimin isolated on *Cordyceps militaris* [16].

List of wild mushrooms with antifungal activity in the Republic of Northern Macedonia

Agaricus bisporus

Agaricus bitorquis

Agrocybe cylindracea

Armillaria mellea
Boletus edulis
Cordiceps militaris.
Flammulina velutipes
Ganoderma lucidum.
Ganoderma australis
Ganoderma annulare
Hericium erinaceus
Hygrocybe cylindracea
Hygrophorus agathosmus
Hygrophorus chrysodon
Hypsizigus marmoreus
Laetiporus sulphureus
Lentinus edodes
Lyophilum shineijii
Lepista nuda
Meripilus giganteus
Paxillus involutus
Suillus collinitus
Pleurotus eryngii
Pleurotus sajor-caju
Pleurotus ostreatus
Tricholoma giganteum

Based on most of the scientific works analyzed so far, we have found that 26 types of macromycota fungi have been mentioned, mainly of the Basidiomycota type, which has an antifungal effect or activity on 22 types of parasitic and pathogenic fungi, most of the Ascomycota type, which affects living organisms such as plants, animals, and humans. This is just the beginning, our work will certainly continue with the lists of mushrooms that have antibacterial and antiviral effects or activity, etc.

List of parasitic and pathogenic fungi affected by the antifungal activity of a large group of macromycota fungi:

Alternaria alternate
Alternaria brassica
Aspergillus niger
Aspergillus fumigatus
Botrytis cinerea,
Candida albicans,
Fusarium graminearum
Fusarium oxysporum,
Fusarium verticillioides
Microsporium canis
Neurospora crassa
Penicillium inflatum
Penicillium chrysogenum
Phytophthora capsici
Physalospora paricola

Physalospora piricola
Sacharomyces cerevisiae
Sclerotinia sclerotiorum
Trichoderma viride
Trichophyton mentagrophytes
Tolypocladium inflatum
Valsa mali, var.mali

The paper presents 26 types of high wild mushrooms that have antifungal activity from which we can distinguish.: *Agaricus bisporus*, *Agrocybe cylindracea*, *Boletus edulis*, *Ganoderma lucidum*, *Flammulina velutipes*, *Laetiporus sulphureus*, *Lactarius deterrimus*, *Lentinus edodes*, *Meripilus giganteus* dhe *Tricholoma giganteum*. These fungi mainly belong to the phylum Basidiomycota. In these mushrooms, compounds with antifungal activity have been found that affect some pathogenic fungi. In the paper, we also present 22 species of pathogenic fungi affected by the aforementioned fungi. The most important are as follows: *Alternaria alternate*, *A. brassicae*, *Candida albicans*, *Aspergillus niger*, *Aspergillus fumigates*, *Fusarium gramineum*, *Microsporus canis*, *Neurospora crassa*, *Penicillium inflatum*, *Sacharomyces cerevisiae* which mainly belong to the phylum Ascomycota.

The list of fungi with antifungal effect and activity is not definitive as this number increases every day and this allows the number of parasitic and pathogenic fungi to increase simultaneously. With the increase in their use and application in Pharmacy, veterinary medicine, and agriculture, the number of antifungal and antimicrobial mushrooms will surely increase

Conclusions

Based on the scientific data so far, we can emphasize that 26 types of macromycetes mushrooms with antifungal effects and activity have been presented.

In addition to this number of fungi with an antifungal effect, we also presented 22 types of fungi that have a pathogenic effect that causes diseases in humans, plants, and animals.

The most popular species with antifungal effect are: *Agaricus bisporus*, *Agrocybe cylindracea*, *Boletus edulis*, *Ganoderma lucidum*, *Flammulina velutipes*, *Laetiporus sulphureus*, *Lactarius deterrimus*, *Lentinus edodes*, *Meripilus giganteus* dhe *Tricholoma giganteum*.

These fungi with antifungal activity are affecting certain pathogen fungi such as: *Alternaria alternate*, *A. brassicae*, *Candida albicans*, *Aspergillus niger*, *Aspergillus fumigates*, *Fusarium gramineum*, *Microsporus canis*, *Neurospora crassa*, *Penicillium inflatum*, *Sacharomyces cerevisiae* which mainly belong to the phylum Ascomycota. etc.

The number of mushrooms with antifungal activity in our Republic of Northern Macedonia is increasing day by day.

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