A review on antifungal activity of mushroom (Basidiomycetes) extracts and isolated compounds

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Abstract

The present review reports the antifungal activity of mushroom extracts and isolated compounds including high (e.g. peptides and proteins) and low (e.g. sesquiterpenes and other terpenes, steroids, organic acids, acylcyclopentenediones and quinolines) molecular weight compounds. Most of the studies available on literature focused on screening of antifungal activity of mushroom extracts, rather than of isolated compounds. Data indicate that mushroom extracts are mainly tested against different *Candida* species, while mushroom compounds are mostly tested upon other fungi. Therefore, the potential of these compounds might be more useful in food industry than in clinics. *Oudemansiella canarii* and *Agaricus bisporus* methanolic extracts proved to be the most active mushroom extracts against *Candida* spp. Grifolin, isolated from *Albatrellus dispansus,* seemed to be the most active compound against phytopathogenic fungi. Further studies should be performed in order to better understand the mechanism of action of this and other antifungal compounds as well as safety issues.

Key words: Antifungal activity; Antifungal proteins; Basidiomycetes; Grifolin

Introduction

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. Mushrooms have been used for many years in oriental culture as tea and nutritional food and because of their special fragrance and texture [1]. While the usage of medicinal mushrooms has a long tradition in Eastern countries, in Western countries it has increased only slightly since the last decades [2].

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 [3].

Pathogenic fungi cause considerable damage in humans, farm animals, crops, and other organisms. Fungal infections can be devastating with a serious effect on health or lead to enormous economic losses. The organism has the innate ability to fight fungal invasions producing antifungal substances; however in immunocompromised individuals, this innate ability is diminished and fungal infections assume greater relevance. Furthermore, in agriculture, fungal invasion brings about serious reduction in the quality and yield of crops and incurs enormous economic losses. Research on antifungal compounds may provide ways to tackle the problem, introducing genes encoding antifungal proteins into crops to boost their resistance against fungal pathogens [4,5].

So, the use of mushrooms with potential therapeutic properties raises global interests from the scientific and clinical community based on two main reasons. First,

mushrooms demonstrate their efficiency against numerous diseases and metabolic disorders as serious as cancer or degenerative diseases. Secondly, fungal bioactive metabolites can be obtained from many origins (wild and cultivated fruiting bodies or from mycelial biomass and supernatant of submerged cultured using bioreactors) [6].

Following our previous review on antibacterial activity of mushroom extracts and isolated compounds [7], in the present report we intend to give an overview about the antifungal potential of mushrooms and highlight some of the compounds identified and isolated from them.

The databases searched were Medline (1999 to August 2012) and Web of Science (1999 to August 2012) including scientific articles and conference proceedings. Search terms were: 'mushrooms', 'antifungal activity' and 'antifungal'. An exhaustive literature search was performed, but only mushroom extracts and isolated compounds with positive results were included.

In the scientific articles revised, different methodologies have been used to access antimicrobial activity of mushrooms extracts and compounds, including microdilution method, disk diffusion method, agar streak dilution method based in radial diffusion and a method with incorporation of the extract in the culture medium and further determination of viable cell numbers. Therefore, the results for antimicrobial activity may be expressed in different units.

Microdilution method comprises microdilutions of the extract in liquid medium using microplates to determine MIC (minimal inhibitory concentration) or IC_{50} (concentration inhibiting 50% of the growth) values. In disk diffusion method, the extract is incorporated in disks at different concentrations, and the halo of growth inhibition is determined and represented by IZD (internal zone diameter) values. The agar streak dilution method based in radial diffusion is most widely used in extracts and implies the

extract application in circular holes made in solid medium. The result might be expressed in IZD or MIC values. Regarding the fourth method, the extract is incorporated in the culture medium and, then, colony-forming units (CFU) are determined. Mycelial Growth Inhibition Test is the method based in Poison Food Technique. Percentage inhibition of mycelial growth is calculated by comparing the colony diameter of poisoned plate and non-poisoned plate [7]. Most of conventional antifungal drugs act in the plasmatic membrane, mainly in ergosterol metabolism. Two examples are fluconazole and ketoconazole, from the azoles group, which is characterized by inhibiting P-450 enzyme responsible for the ergosterol synthesis; ninestine interfers in the permeability and transport functions [8].

Antifungal activity

Mushroom species with reported antifungal activity

As far as we know, 52 species were reported as having antifungal activity (Table **1**); most of them are edible mushrooms (44 referenced from among 52 species). Despite the lower interest of researchers for non-edible mushrooms in comparison with edible species, they also contain different metabolites that can be used in pharmaceutical products.

Most of the mushrooms that revealed antifungal activity are wild, allowing a higher diversity among the studied species. Mushrooms cultivation requires several specific conditions, being hard to obtain them. There are several factors influencing mushrooms cultivation, mainly environmental and physiological conditions, as also the existence of plagues. According to *Pinna* et al. [9], the soil conditions affect the phenotype of all mushrooms, although each species has a specific answer. A good example is the soil humidity that can stimulate (*e.g. Boletus edulis* and *Lactarius deterrimus*) or delay

(*Cortinarius caperatus* and *Catathelasma ventricosum*) the initial fructification period. Furthermore, the presence of insects, mites, crustaceans and other arthropods decomposing synthetic substrates or wood used in mushrooms cultivation, has been reported as compromising their growth [10]. Other study also reports that substrates supplemented with sodium carbonate precipitate ($CaCO_3$) increase the yield and size of shiitake mushroom (*Lentinus edodes*) [11]. Therefore, due to all mentioned problems, only a limited number of species is cultivated and the best way to get a wide variety of mushrooms is collecting them from the natural and original habitats.

As Table **1** shows, the most studied mushrooms regarding antifungal properties are from Turkey and China. Twenty one species are exclusively saprotrophic, decomposing dead organic matter, and being very important to the ecosystem balance. Sixteen species are mycorrhizal, which establish symbiotic relationships with the roots of plants and trees, and six are biotrophic parasites, infecting a host and taking benefit from this relationship. Four species are necrotrophic parasite fungi that kill the host and then continue to feed on dead matter, passing to saprotrophic; finally five species are saprotrophic but also mycorrhizal.

Mushroom extracts with reported antifungal activity

Different extracts obtained from several mushroom species were described in literature as possessing antifungal activity (Table **2**).

Regarding *Agaricus* species, Öztürk et al. [12] reported antifungal activity of *A. bisporus*, *A. bitorquis* and *A. essettei* methanolic extracts against *Candida albicans* and *C. tropicalis*, being *Agaricus bitorquis* the most active one for both species. Nevertheless, Barros et al. [13] did not found activity of *Agaricus bisporus* against *Candida albicans*.

Methanolic extract of *Ganoderma lucidum* gave an activity against *Trichoderma viride* (MIC = 0.005 mg/mL) higher than the one of the tested standards, bifonazole (MIC = 0.15 mg/mL) and ketoconazole (MIC = 1.0 mg/mL). Furthermore, it showed demelanizing activity against *Aspergillus niger* [14].

Ethyl acetate and water extracts with 5% DMSO of *Agrocybe perfecta*, *Climadocon pulcherrimus*, *Oudemansiella canarii* and *Pycnoporus sanguineus* showed antifungal activity against *Candida krusei*. Among these species, only *Oudemansiella canarii* extract exhibited activity against other *Candida* species (*C. albicans, C. glabrata* and *C. tropicalis*) [15].

Albatrellus dispansus mushroom ethanolic extract showed the highest activity against *Sclerotinina sclerotiorum* and *Fusarium graminearum* [16].

The ethanolic extract of *Armillaria mellea* showed higher activity (IZD=19 mm) than the chloroform extract (IZD=2 mm) against *Candida albicans*, using nistatyn (IZD=22mm) as positive control [17].

The antifungal activity of *Hygrophorus agathosmus* chloroform extract was low for *Saccharomyces cerevisae* (MIC=250 µg/mL) in comparison to the positive control (fluconazole, MIC 62.5 µg/mL). The same was observed for *Suillus collitinus* dichloromethane extract against *Saccharomyces cerevisae* and *Candida albicans* [18].

Despite the low antifungal activity revealed by *Lactarius* species, *L. camphoratus* was the one that demonstrated activity against *Candida albicans* [19].

Laetiporus sulphureus ethanolic extract seems to be promising against *Candida albicans* (IZD = 21 ± 1mm), showing higher activity than the positive control, nystatin (IZD=19 mm) [20]. *Lentinus edodes* chloroform extract showed higher activity against *Candida albicans* than the ethyl acetate and aqueous extracts [21]. *Lepista nuda*

methanolic extract also revealed antifungal activity against *Candida albicans* and *Rhodotorula rubra* (IZD=6mm for both cases) [22].

Kalyoncu et al. [17] described a higher antifungal activity of the ethanolic extract of *Meripilus giganteus* fruiting bodies (IZD=20 mm) than of chloroform extract (IZD=10 mm) or ethanolic extract of its mycelium [23]. These authors [23] studied several mushrooms, and the best one against *Candida albicans* was *Paxillus involutus* mycelium ethanolic extract (IZD=15 mm).

Mushroom isolated compounds with reported antifungal activity

Most studies on mushrooms with antifungal activity describe the action of its extracts without identifying the compounds responsible for this activity. However, some low molecular weight (LMW; Figure **1**) and high molecular weight (HMW) compounds have been described as active against fungi (Table **3**).

The LMW terpene compound grifolin (**1**) seems to have the highest antifungal activity [15], but other LMW compounds also showed some activity (e.g., rufuslactone (**2**), enokipodim F,G,I (**3a-c**), cloratin A (**5**) and 2-aminoquinoline (**13**).

The sesquiterpene rufuslactone (**2**), showed activity against some phytopathogenic fungi such as *Alternaria alternata*, *A. brassicae*, *Botrytis cinerea* and *Fusarium graminearum.* Furthermore, the growth inhibition percentage of this compound in *Alternaria alternata* (38.9%) was higher than the one obtained for the positive control, carbendazim (~10%) [24]. Other sesquiterpenes, enokipodim F, G and I (**3a-c**), isolated from *Flammulina velutipes* mycelium presented low activity against *Aspergillus fumigatus* with IC_{50} values 229.1 ± 3.6, 233.4 ± 3.8 and 235.1 ± 4.2 µM, respectively [25].

Phenolic acids and related compounds such as *p*-hydroxybenzoic and cinnamic acids (**4a,b**) identified in *Ganoderma lucidum* also revealed activity against different fungi

species, as in the case of *Aspergillus fumigatus*, *A. versicolor*, *A. ochraceus*, *A. niger*, *Trichoderma viride*, *Penicillium funiculosum*, *P. ochrochloron* and *P. verrucosum* (with MICs of 0.003-0.12 mg/mL and 0.007-0.03 mg/mL for compounds **4a** and **4b**, respectively). Moreover, the mentioned compounds gave higher activity than the standards, bifonazole (MIC = 0.15 mg/mL) and ketoconazole (MIC = 1.0 mg/mL) [14]

Cloratin A (**5**), a derivative of benzoic acid, was isolated from *Xylaria intracolarata* and showed activity against *Aspergillus niger* (IZD=15 mm) and *Candida albicans* (IZD=17 mm); similar to the control (nystatin; with a IZD= 17 mm [26].

Smânia et al. [27] reported a reduced activity of two LMW compounds isolated from *Ganoderma australe* (australic acid (**6a**) and methyl australate (**6b**)) against *Candida albicans*, *Microsporum canis* and *Trichophytom mentagrophytes*. Australic acid proved to be more active against filamentous fungi.

Chrysotriones A and B (**7a,b**), two acylcyclopentenediones isolated from *Hygrophorus chrysodon* exhibited activity against *Fusarium verticillioides* [28].

Three steroids: 5α-ergost-7-en-3β-ol (**8**), 5α-ergost-7,22-dien-3β-ol (**9**) and 5,8-epidioxy-5α,8α-ergosta-6,22-dien-3β-ol (**10**) and five terpenes: applanoxidic acid A, C, F, G and H (**11a,b; 12a-c**), isolated from *Ganoderma annulare*, revealed activity against *Microsporum canis* and *Trichophyton mentagrophytes.* Applanoxidic acid A (**11a**) showed the best activity against the mentioned fungi, and particularly for *Trichophyton mentagrophytes* it showed higher activity (MIC=500 µg/mL) than the positive control (fluconazole; MIC= 0.6 µg/mL). According to the obtained data, the antifungal activity observed for the mentioned compounds is not comparable to the most used antibiotics for fungal diseases; nevertheless, future studies can modify the mentioned compounds in order to increase their antifungal activity [29].

2-Aminoquinoline (**13**) has been described in several studies showing broad spectra of biological activities. A weak activity of this LMW compound was reported against *Penicillium inflatum* and *Streptomyces galilaeus*. The concentration of this quinoline in the mushroom is 40 times higher than the one used in the assay [30].

HMW compounds with antifungal properties were also isolated from mushrooms (Table **3**). Gonodermim is an antifungal protein isolated from *Ganoderma lucidum* with activity against phytopathogenic fungi such as *Botrytis cinerea* (IC_{50}=15.2 µM), *Fusarium oxysporum* (IC_{50}=12.4 µM) and *Physalospora paricola* (IC_{50}=18.1 µM). This protein does not have inhibitory activity of protease, desoxyribonuclease, ribonuclease, or (lectin) hemagglutinin. The mentioned pathogens are commonly present in food, including cotton, cucumber and apple, respectively. Therefore, the isolation of antifungal proteins with activity upon those toxin producers' fungi might have important applications in food industry [31].

Another antifungal protein is ribonuclease, obtained from *Pleurotus sajor-caju*, which showed activity against *Fusarium oxysporum* and *Mycosphaerella arachidicola* (IC_{50} values 95 and 75 µM, respectively) [32].

Trichogin is also an antifungal protein, isolated from the mushroom *Tricholoma giganteum*. It showed antifungal activity against *Fusarium oxysporum*, *Mycosphaerella arachidicola* and *Physalospora piricola* [33]. Guo et al. [33] reported this protein as being significantly different from other antifungal proteins such as LAP (Lyophyllum antifungal protein) [34] and eryngin [35].

Eryngin, an antifungal peptide isolated from *Pleurotus eryngii* fruiting bodies, gave activity against *Fusarium oxysporum* and *Mycosphaerella arachidicola* [35]. Its N-terminal sequence showed some similarity with the antifungal protein of the mushroom *Lyophyllum shimeiji* [34].

Hypsin, isolated from *Hypsizigus marmoreus* fruiting bodies, showed activity against *Botrytis cinerea*, *Fusarium oxysporum*, *Mycosphaerella arachidicola* and *Physalospora piricola* [36]. Lyophyllin and LAP isolated from *Lyophyllum shimeji* revealed activity against *Physalospora piricola* [34]. Lentin, isolated from *Lentinus edodes*, showed activity against *Mycosphaerella arachidicola* [36].

Peptides with antifungal activity were also described as pleurostrin, isolated from *Pleurotus ostreatus*, which showed activity against *Fusarium oxysporum*, *Mycosphaerella arachidicola* and *Physalospora piricola* [4].

Agrocybin, an antifungal peptide isolated from *Agrocybe cylindracea* fruiting bodies, showed activity against *Mycosphaerella arachidicola* [38].

Cordimin is also a peptide that inhibited the growth of *Bipolaris maydis*, *Mycosphaerella arachidicola*, *Rhizoctonia solani* and *Candida albicans* (IC_{50} 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* [39].

The mechanisms of action of most of the LMW compounds described above are not available in literature. Regarding proteins, mainly lyophyllin [34] and hypsin [36], the mechanism of action involves ribosomal inactivation. Nevertheless, the mode of action of many other proteins remains unknown being extensively researched [40]. In literature, the authors compare the studied compounds with others revealing antifungal activity. Ribonuclease presents a N-terminal sequence similar to the one present in the bacteriocine peptide of *Lactobacillus plantanum* and also enzymes involved in RNA metabolism [32]. Lentin N-terminal sequence revealed similarities with sequences of some endoglucanases near the C-terminal [37].

Concluding remarks

The present review focuses on antifungal effects of mushrooms from all over the world, and their isolated compounds; it will be certainly useful for future scientific studies. Nonetheless, the comparison of the results reported by different authors is difficult, due to the diverse methodologies used to evaluate antifungal activity of mushroom extracts or isolated compounds. Therefore, the standardization of methods and establishment of cut-off values is necessary.

Data available from literature indicates that mushroom extracts are mainly tested against different *Candida* species, while mushroom compounds are mostly tested in other fungi (e.g., food contaminants). Therefore, most of those compounds might be more useful in food industry than in clinics.

Oudemansiella canarii and *Agaricus bisporus* methanolic extracts proved to be the best ones against *Candida* sp.. Regarding mushroom compounds, grifolin (**2**) isolated from *Albatrellus dispansus* seemed to be the best option against phytopathogenic fungi.

Further studies should be performed in order to deeply understand the activity of some mushroom extracts against *Candida* sp. and the mechanism of action of these compounds against phytopathogenic fungi. Cytotoxicity assays will also be important to evaluate the effects on human in the range of the *in vitro* tested concentrations.

Most of the studies available on literature focused on screening of antifungal activity of mushroom extracts, rather than of isolated compounds. After elucidation of their mechanism of action, LMW or HMW mushroom compounds could be used to develop antifungals for pathogenic or contaminant microorganisms.

Abbreviations

CFU	Colony-forming units
GI	Growth inhibition
HMW	High-molecular weight

IC_{50}	Concentration inhibiting 50% of the growth
IZD	Internal zone diameter
LAP	Lyophyllum antifungal protein
LMW	Low-molecular weight
M	Mycelium
MIC	Minimal inhibitory concentration

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Authors' contributions

Conducted bibliographic research: M.J. Alves, J. Dias and V. Teixeira; Conducted data organization: M.J. Alves and I.C.F.R. Ferreira; Performed data analysis regarding mushrooms: M.J. Alves, I.C.F.R. Ferreira and A. Martins; Performed data analysis regarding antifungal activity: M.J. Alves, I.C.F.R. Ferreira and M. Pintado; Wrote or contributed to the writing of the manuscript: M.J. Alves, I.C.F.F. Ferreira, J. Dias and V. Teixeira; Revised the manuscript writing: I.C.F.F. Ferreira, A. Martins and M. Pintado.

Conflict of Interest

The authors have no conflicts of interest.

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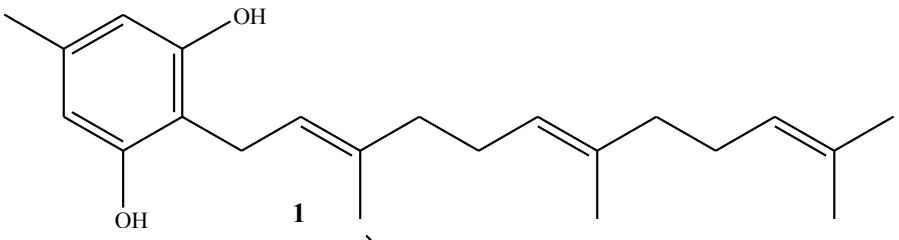

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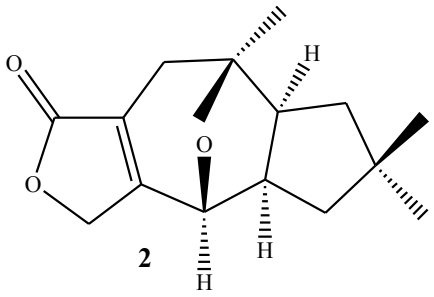

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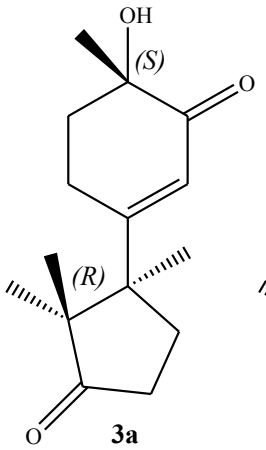

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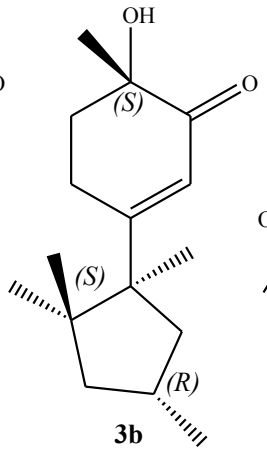

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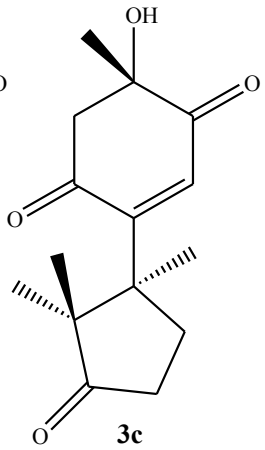

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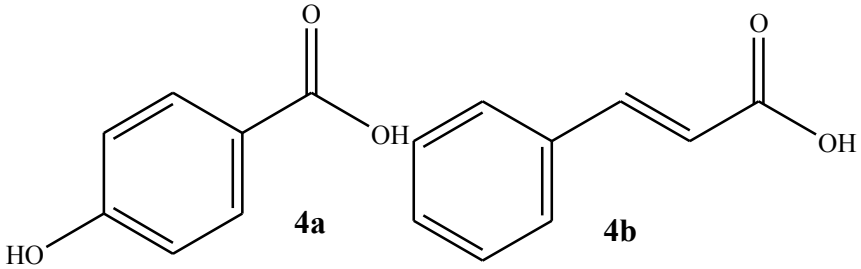
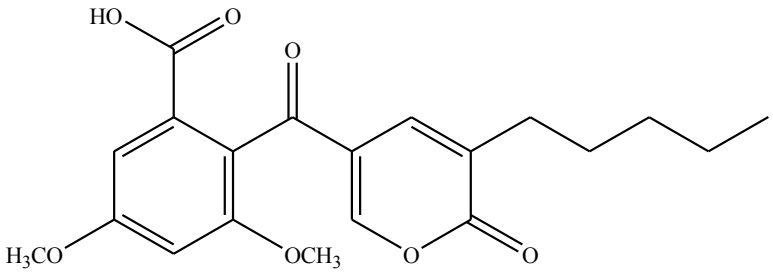


4a **4b**



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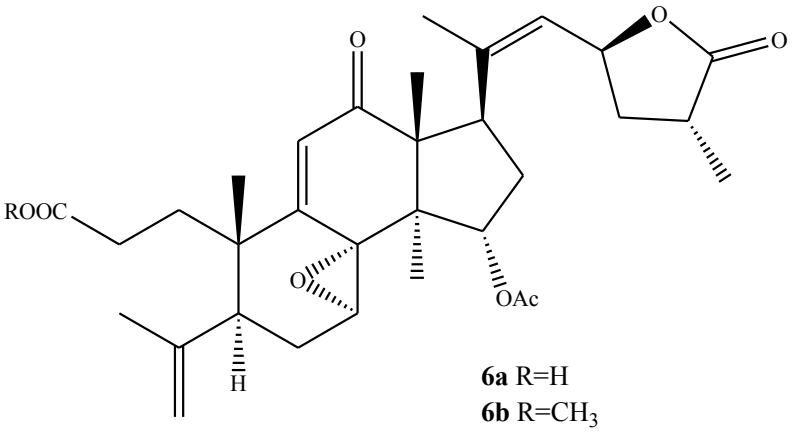
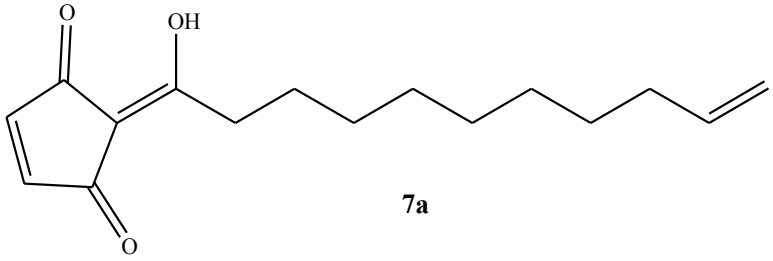


6a R=H
6b R=CH_3



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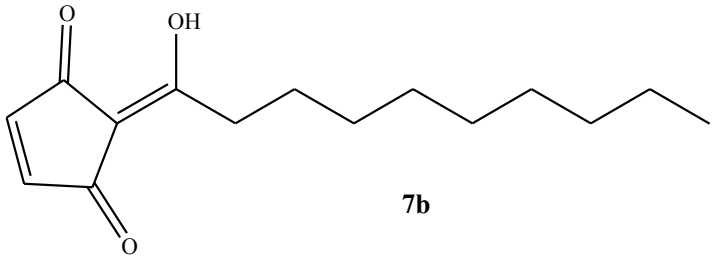

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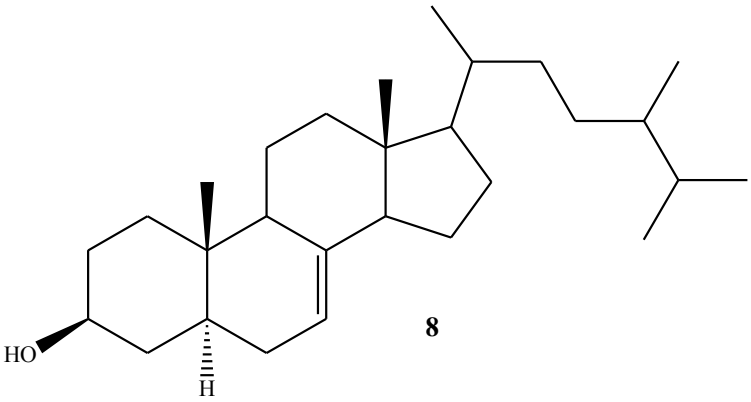

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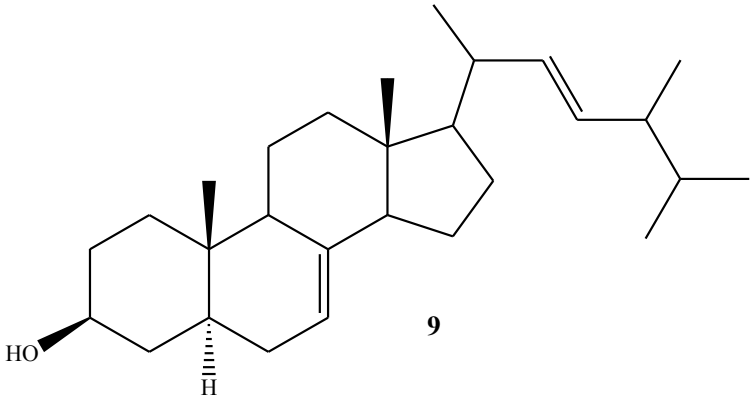

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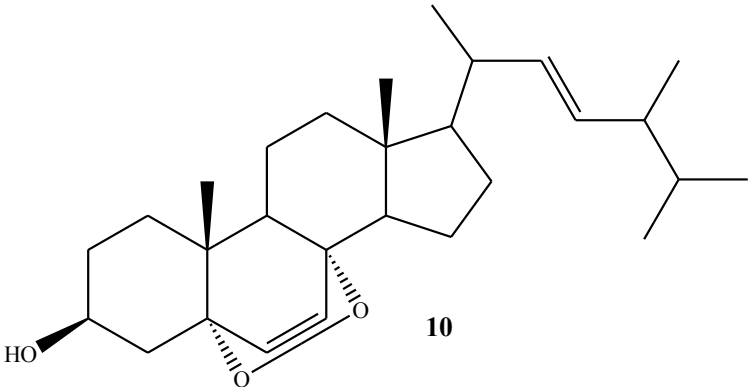

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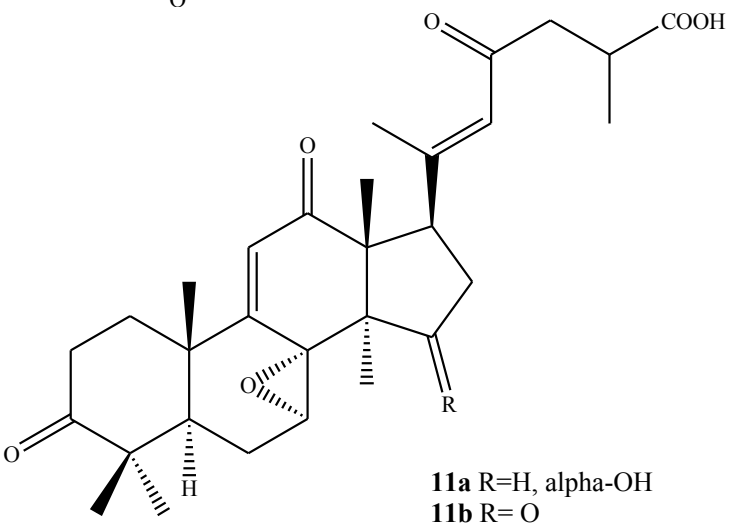

11a R=H, alpha-OH
11b R= O

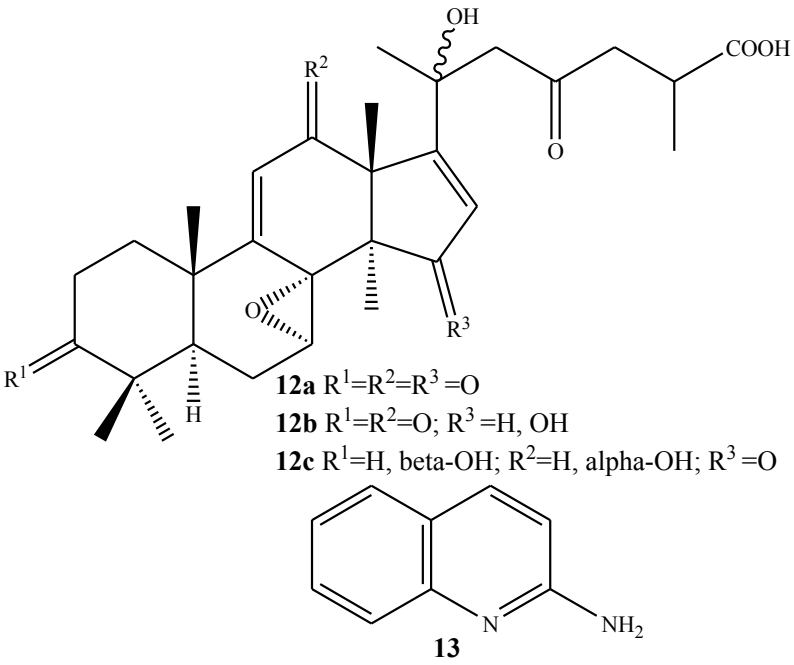

Figure 1. Chemical structure of the low-molecular-weight (LMW) compounds with antifungal properties identified in mushrooms. 1. Grifolin; 2. Rufuslactone; 3a. Enokipodim F; 3b. EnokipodimG; 3c. Enokipodim I; 4a. *p*-Hydroxybenzoic acid; 4b. Cinnamic acid; 5. Cloratin A; 6a. Australic acid; 6b. Methyl australate; 7a. Chrysotrione A; 7b. Chrysotrione B; 8. 5α-Ergost-7-en-3β-ol; 9. 5α-Ergost-7,22-dien-3β-ol; 10. 5,8-Epidioxy-5α,8α-ergosta-6,22-dien-3β-ol; 11a. Applanoxidic acid A; 11b. Applanoxidic acid F; 12a. Applanoxidic acid C; 12b. Applanoxidic acid G; 12c. Applanoxidic acid H; 13. 2-Aminoquinoline.

Table **1.** Mushroom species with reported antifungal activity.

Scientific name	Common name	Edibility	Habitat	Country	Date of collection	Ecology
Agaricus bisporus (J.E.Lange) Emil J. Imbach	Commercial button mushroom	Edible	Marketed/ cultivated	Turkey [12] Turkey [19]	December 2007 Not available	Saprotrophic
Agaricus bitorquis (Quélet) Sacc.	Pavement mushroom	Edible	Marketed/ cultivated	Turkey [12]	December 2007	Saprotrophic
Agaricus bohusii Bom	Unknown	Edible	Wild/woodland/ pastures	Portugal [45]	July of 2011	Saprotrophic
Agaricus essettei Bom	Unknown	Edible	Grasslands/ forest	Turkey [12]	December 2007	Saprotrophic
Agrocybe cylindracea (V. Brig.) Singer	Poplar fieldcap	Edible	Marketed/ cultivated	China [38]	Not available	Saprotrophic/ parasitic
Agrocybe perfecta (Rick.) Singer	Unknown	Edible	Grasslands/ forest	Brazil [15]	Not available	Saprotrophic
Albatrellus dispansus (Lloyd) Canf.& Gilb	Unknown	Edible	Wild	China [16]	July 2001	Mycorrhizal
Armillaria mellea (Vahl) P.Kumm	Honey fungus	Edible	Wild	Turkey [23]	Not available	Parasitic
Armillaria mellea, (Vahl) P.Kumm	Honey fungus	Edible	Wild	Turkey [17]	Between 2006 and 2007	Parasitic
Cantharellus cibarius Fr.	Chanterelle, yellow chanterelle, golden chanterelle	Edible	Wild	Turkey [19]	Not available	Mycorrhizal
Clitocybe geotropa (Bull.) Quél.	Trooping funnel	Edible	Wild	Turkey [17]	Between 2006 and 2007	Saprotrophic
Climacodon pulcherrimus (Berk. & M.A. Curtis) M.I. Nikol.	Unknown	Inedible	Wild	Brazil [15]	Not available	Saprotrophic
Cordyceps militaris (L.) Link	Caterpillar fungus	Inedible	Wild	China[39]	Not available	Parasitic

Ganoderma australe (Fr.) Pat.	Southern Bracket	Edible	Wild	Brazil [27]	1999	Parasitic
Ganoderma lucidum (Curtis) P. Karst	Lacquered Bracket, Reishi	Edible	Marketed/ cultivated	China [31]	Not available	Saprotrophic/ Parasitic
			Wild	Portugal [14]	July 2011	
Hygrophorus agathosmus E. Fries	Gray almond waxy cap, almond woodwax	Edible	Marketed/ cultivated	Turkey [18]	Not available	Mycorrhizal
Hygrophorus chrysodon Fr.	Unknown	Edible	Wild	Italy [28]	October 2005	Mycorrhizal
Hydnum repandum L., Pe.	Wood hedgehog	Edible	Wild	Turkey [19]	Not available	Mycorrhizal
Hypsizygus marmoreus (Peck) Bigelow	Beech shimeji	Edible	Cultivated	China [36]	Not available	Saprotrophic
Irpex lacteus (Fr.) Fr.	White rot fungus	Inedible	Wild	Brazil [15]	Not available	Parasitic
Lactarius camphoratus (Bull.) Fr.	Candy cap, curry milkcap	Edible	Wild	Turkey [19]	Not available	Mycorrhizal
Lactarius delicious (L. ex Fr.) S.F.Gray	Saffron milk cap, red pine mushroom	Edible	Wild	Portugal [43]	Autumn 2004	Mycorrhizal
Lactarius piperatus (L.) Pers.	Peppery milk-cap	Edible	Wild	Turkey [19]	Not available	Mycorrhizal
Lactarius rufus (Scop.) Fr.	Rufous milkcap	Edible	Wild	China [24]	July 2003	Mycorrhizal
Lactarius volemus (Fr.) Fr.	Weeping milk cap, voluminous-latex milky	Edible	Wild	Turkey [19]	Not available	Mycorrhizal
Laetiporus sulphureus (Bull.) Murrill	Sulphur polypore, sulphur shelf, chicken of the woods	Edible	Wild	Turkey [20]	Spring and autumn of 2004	Saprotrophic/parasitic
				Turkey [19]	Not available	
Lentinus edodes (Berk.) Pegler	Shiitake	Edible	Marketed/ cultivated	Ireland [41]	Not available	Saprotrophic
				Hungary [44]	Not available	

				Japan [21]	Not available	
Lepista nuda (Bull.) HEBigelow & AHSm.	Wood blewit, blue stalk	Edible	Marketed/ cultivated	Turkey [22]	1995	Saprotrophic
Leucopaxillus albissimus (Sowerby) Singer	Unknown	Inedible	Wild	EUA [30]	Not available	Saprotrophic
Lyophyllum shimeji (Kawam.) Hongo	"Hon-shimeji"	Edible	Wild	China [34]	Not available	Mycorrhizal
Meripilus giganteus Karst.	Giant polypore, black-staining polypore	Edible	Wild	Turkey [17, 23]	Not available	Saprotrophic
Morchella costata (Vent.) Pers.	Morel	Edible	Wild	Turkey [23]	Not available	Mycorrhizal/ Saprotrophic
Morchella elata Fr.	Black morel	Edible	Wild	Turkey [23]	Not available	Mycorrhizal/ Saprotrophic
Morchella esculenta var. v*ulgaris* Pers.	Yellow morel	Edible	Wild	Turkey [23]	Not available	Mycorrhizal/ Saprotrophic
Morchella hortensis Boud.	Morel	Edible	Wild	Turkey [23]	Not available	Mycorrhizal/ Saprotrophic
Morchella rotunda (Pers.: Fr) Boudier	Yellow morel	Edible	Marketed/ cultivated	Turkey [23]	Not available	Mycorrhizal/ Saprotrophic
Oudemansiella canarii (Jungh.) Höhn	Porcelain slimecap	Edible	Marketed/ cultivated	Brazil [15]	Not available	Saprotrophic
Paxillus involutus (Batsch) Fr.	Brown roll-rim, common roll-rim, poison pax	Inedible	Wild	Turkey [23]	Not available	Mycorrhizal
Pleurotus eryngii (DC.) Quél.	King trumpet mushroom	Edible	Marketed/ cultivated	Turkey [23]	Not available	Parasitic
Pleurotus sajor-caju Fr.	Houbitake	Edible	Marketed/ cultivated	China [32]	Not available	Saprotrophic
Pycnoporus sanguineus (L.) Murrill	Cinnabar bracket	Inedible	Wild	Brazil [15]	Not available	Saprotrophic
Pleurotus ostreatus (Jacq. ex Fr.) P. Kumm.	Oyster mushroom	Edible	Marketed/ cultivated	China [4]; Turkey [23]	Not available	Saprotrophic
Ramaria flava (Schaeff.) Quél.	Changle	Edible	Wild	Turkey [19]	Not available	Mycorrhizal
Rhizopogon roseolus Th. Fr.	Unknown	Edible	Wild	Turkey [47]	Between 2004 and 2005	Mycorrhizal

Sparassis crispa (Wulfen)	Wood cauliflower	Edible	Wild	Turkey [17]	Between 2006 and 2007	Saprotrophic
Suillus collitinus (Fr.) Kuntze	Slippery jacks	Edible	Wild	Turkey [18]	Navailable	Mycorrhizal
Sarcodon imbricatus (L.) P.Karst.	Shingled hedgehog, scaly hedgehog	Edible	Wild	Portugal [43]	Autumn 2004	Mycorrhizal
Schizophyllum commune (Frie)	Split gill	Inedible	Wild	Malaysia [45]	Not available	Saprotrophic
Tricholoma giganteum Massee	Giant mushroom	Edible	Marketed/ cultivated	China [33]	Not available	Saprotrophic
Xylaria intracolarata Unknown	Unknown	Unknown	Wild	Vietnam [26]	July 2004	Saprotrophic

Table **2.** Target microorganisms, mushroom extracts[a] and resulting antifungal activity.

Microorganism	**Mushroom**	**Results**	**References**
Alternaria alternata	*Albatrellus dispansus*	GI = 40 - 80 %	[16]
Aspergillus fumigatus	*Ganoderma lucidum*, *Lentinus edodes*	MIC = 1.5 mg/mL IZD = 20 mm	[14, 41]
Aspergillus niger	*Ganoderma lucidum*, *Lentinus edodes*	MIC = 1.5 mg/mL IZD = 10 mm	[14, 41]
Aspergillus versicolor	*Ganoderma lucidum*	MIC = 0.1 mg/mL	[14]
Aspergillus ochraceus	*Ganoderma lucidum*	MIC = 0.75 mg/mL	[14]
Botrytis cinerea	*Albatrellus dispansus*	GI = 40 - 80 %	[16]
Candida albicans	*Agaricus bisporus, Agaricus bitorquis, Agaricus essettei, Armillaria mellea* (M)*, Armillaria mellea, Cantharellus cibarius, Clitocybe geotropa, Cortinarius* sp.*, Hydnum repandum, Irpex lacteus* (M)*, Lactarius camphoratus, Lactarius delicious, Lactarius piperatus, Lactarius volemus, Laetiporus sulphureus, Lentinus edodes, Lepista nuda, Meripilus giganteus* (M)*, Meripilus giganteus, Morchella costata* (M)*, Morchella elata* (M)*, Morchella esculenta* var. v*ulgaris* (M)*, Morchella hortensis* (M)*, Morchella rotunda* (M)*, Oudemansiella canarii* (M)*, Paxillus involutus* (M)*, Pleurotus eryngii* (M)*, Pleurotus ostreatus* (M)*, Ramaria flava, Sparassis crispa, Suillus collitinus*	CFU = 6.8×10^5 IZD = 2-21±1 mm MIC = 250 µg/mL – >50 mg/mL	[13, 15, 17, 18, 19, 20, 21, 22, 23, 42, 43, 44]
Candida glabrata	*Irpex lacteus* (M)*, Oudemansiella canarii* (M)	IZD >12 mm	[15]
Candida krusei	*Agrocybe perfecta* (M)*, Climadocon pulcherrimus* (M)*, Lentinus edodes, Oudemansiella canarii* (M), *Pycnoporus sanguineus* (M)	IZD >12 mm	[15, 41]
Candida parapsilosis	*Irpex lacteus* (M)*, Lentinus edodes*	IZD = 11 – >12 mm	[15,41]
Candida tropicalis	*Agaricus bisporus, Agaricus bitorquis, Agaricus essettei, Oudemansiella canarii* (M)	IZD = 11 – 14 ± 0 mm	[13, 15]
Cladosporium resinae	*Cortinarius* sp.	IZD = 5 - 15 mm	[42]
Cryptococcus neoformans	*Lactarius delicious, Sarcodon imbricatus*	MIC = 10 – 300 mg/mL	[43]
Fulria fulva	*Albatrellus dispansus*	GI = 40 - 80 %	[16]
Fusarium graminearum	*Albatrellus dispansus*	GI >80 %	[16]
Gaeumannomyces graminis	*Albatrellus dispansus*	GI = 20 - 40 %	[16]
Gloeophyllum trabeum	*Schizophyllum commune*	MIC = 2.5 - 5 µg/µL	[45]
Gloeosporium fructigenum	*Albatrellus dispansus*	GI = 40 - 80 %	[16]
Lentinus sp.	*Schizophyllum commune*	MIC = 0.16 – 0.31 µg/µL	[45]

Lentinus sajor-caju	*Schizophyllum commune*	MIC = 1.25 - > 5 µg/µL	[45]
Lentinus strigosus	*Schizophyllum commune*	MIC = 2.5 - > 5 µg/µL	[45]
Microporus affinis	*Schizophyllum commune*	MIC = 0.31 – 0.61 µg/µL	[45]
Microporus xanthopus	*Schizophyllum commune*	MIC = 0.31 – 0.61 µg/µL	[45]
Penicillium funiculosum	*Ganoderma lucidum*	MIC = 0.09 mg/mL	[14]
Penicillium ochrochloron	*Ganoderma lucidum*	MIC = 0.35 mg/mL	[14]
Penicillium verrucosum	*Agaricus bohusii*, *Ganoderma lucidum*	GI= 3.3 ± 1.9 – 100 % MIC = 1.5 mg/mL	[14, 46]
Pycnoporus sanguineus	*Schizophyllum commune*	MIC = 5 - > 5 µg/µL	[45]
Pyricularia oryzae	*Albatrellus dispansus*	GI = 20 - 40 %	[16]
Rhizoctonia solani	*Albatrellus dispansus*	GI = 40 - 80 %	[16]
Saccharomyces cerevisae	*Hygrophorus agathosmus, Rhizopogon roseolus, Suillus collitinus*	IZD = 11 mm MIC = 250 µg/mL	[18, 47]
Scedosporium apiospermum	*Lentinus edodes*	IZD = 12 mm	[41]
Trametes feei	*Schizophyllum commune*	MIC = 1.25 - 5 µg/µL	[45]
Trametes menziezi	*Schizophyllum commune*	MIC = 0.31 – 5 µg/µL	[45]
Trametes versicolor	*Schizophyllum commune*	MIC = 1.25 - > 5 µg/µL	[45]
Trichoderma viride	*Ganoderma lucidum*	MIC = 0.005 mg/mL	[14]
Trichophyton mentagrophytes	*Cortinarius* sp.	IZD = 5 - 15 mm	[42]

[a]Chloroform, ethanol, ethyl acetate, methanol or water extracts.
M- mycelium, the other samples refer to fruiting body.
The antimicrobial activity was expressed in GI (growth inhibition percentages), CFU (colony-forming unities), MIC (minimal inhibitory concentrations) or IZD (internal zone diameter) values.

Table **3.** Target microorganisms, mushroom compounds and resulting with antifungal activity.

Microorganism	**Compound (mushroom)**	**Results**	**References**
Alternaria alternata	Grifolin (**1**) (*Albatrellus dispansus*); Rufuslactone (**2**) (*Lactarius rufus*)	GI = 38.9% – 70.2%	[16, 24]
Alternaria brassicae	**2** (*Lactarius rufus*)	GI = 68.3 %	[24]
Aspergillus fumigatus	Enokipodins F, G, I (**3a-c**) (*Flammulina velutipes* M); *p*-Hydroxybenzoic and Cinnamic acids (**4a,b**) (*Ganoderma lucidum*)	IC_{50} = 229.1 ± 3.6 – 235.1 ± 4.2 µM MIC = 0.12 and 0.007 mg/mL	[14, 25]
Aspergillus niger	**4a,b** (*Ganoderma lucidum*); Coloratin A (**5**) (*Xylaria intracolarata*)	MIC = 0.03 mg/mL IZD = 15 mm	[14,26]
Aspergillus ochraceus	**4a,b** (*Ganoderma lucidum*)	MIC = 0.015 and 0.007 mg/mL	[14]
Aspergillus versicolor	**4a,b** (*Ganoderma lucidum*)	MIC = 0.003 and 0.007 mg/Ml	[14]
Bipolaris maydis	Cordymin (*Cordyceps militaris*)	IC_{50} = 50 µM	[39]
Botrytis cinerea	**1** (*Albatrellus dispansus*); Ganodermin *(Ganoderma lucidum*); Hypsin (*Hypsizigus marmoreus*); **2** (*Lactarius rufus)*	GI = 40 - 68 % IC_{50} = 0.66 – 15.2 ± 0.7 µM	[16,24,31, 36]
Candida albicans	Cordymin (*Cordyceps militaris);* Australic acid and Methyl australate (**6a,b**) (*Ganoderma australe*); Coloratin A (**5**) (*Xylaria intracolarata*)	IZD = 17 mm MIC = 2.0 mg/mL IC_{50} = 0.75 µM	[26,27,39]
Fusarium graminearum	**1** (*Albatrellus dispansus*); **2** (*Lactarius rufus*)	GI ≈ 45 – 80.9%	[16, 24]
Fusarium oxysporum	Ganodermin (*Ganoderma lucidum*); Hypsin (*Hypsizigus marmoreus*); Eryngin (*Pleurotus eryngii*); Pleurostrin (*Pleurotus ostreatus*); Ribonuclease (*Pleurotus sajor-caju*)	GI = 20% IC_{50} = 1.35 ± 0.15 – 95 µM	[4,31,32, 35, 36]
Fusarium verticillioides	Chrysotrione A and B (**7a,b**) *(Hygrophorus chrysodon*)	IZD = 3 mm	[28]
Gaeumannomyces graminis	**1** (*Albatrellus dispansus*)	GI ≈ 42%	[16]
Gloeosporium fructigenum	**1** *(Albatrellus dispansus)*	GI ≈ 70%	[16]
Microsporum canis	5α-Ergost-7-en-3β-ol (**8**), 5α-Ergost-7,22-dien-3β-ol (**9**), 5,8-Epidioxy-5α,8α-ergosta-6,22-dien-3β-ol (**10**), Applanoxidic acid A (**11a**), C (**12a**), F (**11b**), G (**12b**) and H (**12c**) (*Ganoderma annulare*); (**6a,b**) (*Ganoderma australe*)	MIC = 1.0 – 2.0 mg/mL	[27, 29]
Mucor ramannianus	Peptides: Peptaibol Boletusin, Peptaibol Chrysospermin 3 and Peptaibol Chrysospermin 5 (*Boletus* spp.)	IZD = 10 – 12 mm	[43]
Mycosphaerella arachidicola	Agrocybin (*Agrocybe cylindracea*); Cordymin (*Cordyceps militaris*); Hypsin (*Hypsizigus marmoreus*); Lentin (*Lentinus edodes*); Eryngin (*Pleurotus eryngii*); Pleurostrin (*Pleurotus ostreatus);* Ribonuclease (*Pleurotus sajor-caju*); Trichogin (*Tricholoma giganteum*)	GI = 45% IC_{50} = 2.5 – 125 µM	[4,32, 33, 35, 36, 37, 38, 39]
Penicillium inflatum	2- aminoquinoline (**13**) (*Leucopaxillus albissimus*)	IZD = 6 mm	[30]

Penicillium funiculosum	**4a,b** (*Ganoderma lucidum*)	MIC = 0.03 and 0.015 mg/mL	[14]
Penicillium notatum	Peptaibol Boletusin, Peptaibol Chrysospermin 3 and Peptaibol Chrysospermin 5 (*Boletus* spp.)	IZD = 10 – 12 mm	[48]
Penicillium ochrochloron	**4a,b** (*Ganoderma lucidum*)	MIC = 0.06 and 0.03 mg/mL	[14]
Penicillium verrucosum	**4a,b** (*Ganoderma lucidum*)	MIC = 0.06 and 0.007 mg/mL	[14]
Physalospora piricola	Ganodermin (*Ganoderma lucidum*); Hypsin (*Hypsizigus marmoreus);* Protein: LAP (*Lyophyllum shimeji* antifungal protein) and Lyophyllin (*Lyophyllum shimeji*); Pleurostrin (*Pleurotus ostreatus*)	GI = 63% IC_{50} = 70 nM – 18.1 ± 0.5 μM	[4,31, 34,36]
Pyricularia oryzae	**1** (*Albatrellus dispansus*)	GI ≈ 35%	[16]
Rhizoctonia solani	Cordymin (*Cordyceps militaris*); **1** (*Albatrellus dispansus*)	GI ≈ 34% IC_{50} = 80 μM	[16, 39]
Saccharomyces cerevisae	Peptaibol Boletusin, Peptaibol Chrysospermin 3 and Peptaibol Chrysospermin 5 (*Boletus* spp.)	IZD = 10-11 mm	[48]
Sclerotinina sclerotiorum	**1** (*Albatrellus dispansus*)	GI = 86.4%	[16]
Streptomyces galilaeus	**13** (*Leucopaxillus albissimus*)	IZD = 6 mm	[30]
Trichoderma viride	**4a,b** (*Ganoderma lucidum*)	MIC = 0.007 and 0.015 mg/mL	[14]
Trichophyton mentagrophytes	**8-12** (*Ganoderma annulare*); **6a,b** (*Ganoderma australe*)	MIC = 500 μg/mL – 2.0 mg/mL	[27, 29]

M- mycelium, the other samples refer to fruiting body.

The antimicrobial activity was expressed in GI (growth inhibition percentages), CFU (colony-forming unities), MIC (minimal inhibitory concentrations), IZD (internal zone diameter) or IC_{50} (concentrations inhibiting 50% of the growth).