Chapter 13
Natural Antimicrobials from Basidiomycota Mushrooms

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Abstract Basidiomycota mushrooms are one of the best and rich sources of natural bioactive compounds, including antitumor, antioxidant, antimicrobial, and many others. The search for natural sources of chemically new, safe, and effective antibiotics for biological control of invasive organisms and the development of effective and competitive technologies for their production has become a scientific and technological challenge. This chapter mostly summarizes recently published reports and own data on the occurrence of antibacterial and antifungal activities among Basidiomycota species collected from different geographical regions and ecological niches. Antibiotic activities of extracts from fruiting bodies and mycelial cultures against different groups of microorganisms are compared, focusing on the diversity, common characteristics, and unique properties of individual mushrooms, as well as on several physiological approaches and strategies that enhance the biosynthetic potential of mushrooms and their antimicrobial activity to provide a sustainable source of a safe, useful, and cheap medicine for the treatment of infectious diseases.

Keywords Basidiomycetes · Medicinal mushrooms · Antimicrobial activity · Antimicrobial compounds · Cultivation conditions

Abbreviations

ABA	Antibacterial activity
AFA	Antifungal activity
CFU	Colony-forming units
CL	Culture liquid
EPS	Exopolysaccharides
FB	Fruiting bodies

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GI	Growth inhibition
G-	Gram-negative
G+	Gram-positive
IC_{50}	Concentration inhibiting 50% of the growth
IZD	Internal zone diameter
MIC	Minimal inhibitory concentration
MRSA	Methicillin-resistant *Staphylococcus aureus*
PDA	Potato dextrose agar

1 Introduction

Bacterial and fungal infections that cause significant damage to people, farm animals, crops, and other organisms lead to health problems and huge economic losses. Over the past decades, antibiotics have been effectively used to combat infections while synthetic fungicides have been used in the fight against phytopathogenic fungi. However, their use has led to the emergence and spread of multidrug resistance of pathogenic microorganisms, environmental pollution with poorly biodegradable, toxic, and carcinogenic chemicals, as well as the penetration of these compounds into food products. Nowadays, one of the main challenges for the scientific community and pharmaceutical companies is the lack of structurally new classes of antibiotics effective against pathogens (Genilloud 2012; Shen et al. 2017). Therefore, the search for new natural sources of chemically novel, safe, and effective antimicrobial compounds for biological control of invasive organisms and the development of efficient and competitive technologies for their production has become a scientific and technological task.

Basidiomycota fungi represent taxonomically, ecologically, physiologically, and genetically extremely diverse group of eukaryotic organisms. Among them, medicinal mushrooms have a proven history of use in many countries around the world. Mushrooms are mainly used in large quantities for food because of their high nutritional value and beneficial properties for human health (Wasser 2014; Gargano et al. 2017; Badalyan et al. 2019). During the last decades, medicinal mushrooms have become an attractive source of low-calorie, low fat-containing functional food, and therapeutic products mainly because of their chemical composition and ability to synthesize many highly beneficial bioactive compounds, primary and secondary metabolites, such as proteins, essential amino acids, fatty acids, dietary fiber, polysaccharides (mainly β-glucans), vitamins, macro- and microelements, lectins, terpenoids, steroids, statins, phenols, alkaloids, and antibiotics (Lindequist et al. 2005; Cohen et al. 2014; Gargano et al. 2017; Xue et al. 2020).

The literature data provides clear evidence that many species of higher basidiomycetes from different genera, such as *Agaricus*, *Coprinus, Pleurotus*, *Lentinula, Ganoderma*, *Trametes, Schizophylum, Hericium, Grifola,* and many others produce bioactive substances with diverse pharmaceutical properties useful for the treatment and prevention of various diseases. Medicinal mushrooms are believed to have over

130 medicinal functions including antitumor, immunomodulating, anti-inflammatory, antioxidant, free radical scavenging, cholesterol-lowering, antidiabetic, antiviral, antibacterial, antifungal, and many other effects (Asatiani et al. 2007, 2018; Gargano et al. 2017; Wasser 2017; Chaturvedi et al. 2018; Hetland et al. 2020).

Among different bioactive compounds, polysaccharides and phenolic compounds represent one of the major classes of chemical substances found in mushrooms. Numerous bioactive polysaccharides or polysaccharide–protein complexes from medicinal mushrooms seem to enhance innate and cell-mediated immune responses, and they exhibit antitumor and immune-protective activities in animals and humans (Wasser 2017, Venturella et al. 2019; Hetland et al. 2020). Several of the mushroom polysaccharide compounds already have proceeded through Phase I, II, and III clinical trials and are used extensively and successfully as drugs in Asian countries to treat various cancers and other diseases. It is worth noting that the effect of polysaccharides and other substances derived from mushrooms are especially beneficial when used in conjunction with chemotherapy or radiotherapy. Pharmaceutical products derived from mushrooms, such as lentinan, schizofyllan, krestin, ganoderic acid, hericenone, grifolan have been developed as adjuvant anticancer drugs for immunotherapy in oncological clinical settings (Piotrowski et al., 2015, Wasser 2017; Wasser 2017; Gargano et al. 2017).

It has been reported that different types of phenolic compounds are effective antioxidants in biological systems, acting as free radical inhibitors, peroxide decomposers, or oxygen scavengers (Sanchez 2017). It is a very important and timely finding since in recent years it became known that synthetic antioxidants have a toxic effect and could be responsible for different types of tumor and liver damage (Panico et al. 2019). Therefore, the search for new and effective natural compounds with high antioxidant properties is a serious challenge. Both polysaccharides and phenolic compounds produced by mushrooms have been documented as antioxidants. At the same time, the phenolic extracts and polysaccharides from many mushroom exhibit antimicrobial activity against a wide range of pathogens and therefore can serve as a potential source of both antimicrobial and antioxidant compounds (Adebayo et al. 2018; Angelini et al. 2019, 2020; Özdal et al. 2019; Bach et al. 2019; Badalyan et al. 2019; Adongbede et al. 2020).

In recent years, the use of basidiomycetes with potential therapeutic properties has attracted global interest for several reasons (Lindequist et al. 2005; Wasser 2011; Alves et al. 2013; Badalyan et al. 2019; Fukushima-Sakuno 2020). First, so-called medicinal mushrooms already demonstrated their nutritional and pharmacological properties as well as efficiency against numerous diseases and metabolic disorders. Second, they are largely unexplored alternative sources of new natural myco-pharmaceuticals with unique structure and chemical composition that differ from those isolated from traditional sources of antibiotics. Third, bioactive metabolites can be easily obtained not only from wild mushrooms but also from industrially cultivated FB and mycelial biomass and supernatant of submerged cultures. Finally, medicinal mushrooms are not expensive, the majority of them are non-toxic and contain many other compounds beneficial to human health.

ABA and AFA have been identified in many mushroom extracts. In this chapter, we summarize recent advances in the study of the antimicrobial potential of *Basidiomycota* mushrooms against bacteria and fungi, focusing on the diversity, common characteristics, and unique properties of individual mushrooms, as well as on several approaches and strategies that provide enhanced production of antimicrobial metabolites.

2 The Occurrence of Antimicrobial Activity among *Basidiomycota* Mushrooms

Mushrooms exhibiting antimicrobial properties are widespread in different regions and ecosystems of the world with diverse environmental and biological conditions. It is believed that mushrooms produce antimicrobial compounds to defend themselves against various pathogenic microbes and survive in their natural environment (Lindequist et al. 2005; Rai et al. 2015). The ability to show antimicrobial activity is widespread among *Basidiomycota* species belonging to different taxonomic groups. Among them are saprotrophic, mycorrhizal (several species are capable of saprotrophic nutrition),and parasites (biotrophic and necrotrophic). Most of the mushrooms tested are wild and/or edible. Barseghyan et al. (2015) reported that the highest ABA occurred among members of the *Ganodermatales*, *Poriales*, *Agaricales*, and *Stereales* that constitute a good source for developing new antibiotics. Shen et al. (2017) summarized information on the antimicrobial properties of 158 mushroom species belonging to 88 genera, collected from various ecosystems in different regions of the world. In screening studies of hundreds of wild and edible mushrooms, important differences were observed between different strains of the same species and genera, confirming the influence of habitat and geographic location on the production of antimicrobial metabolites (Barros et al. 2007; Aqueveque et al. 2010; Bala et al. 2012; Owaid et al. 2017b; Spremo et al. 2017; Khardziani et al. 2020).

As already noted (Alves et al. 2013), the comparison of the results reported by different authors is not easy due to the diverse methodologies used to evaluate the antimicrobial activity of mushrooms. Antimicrobial activity depends on the mushroom species and even strain, mushroom form, method of extraction, and many other circumstances. Therefore, in some cases, the literature data on the antimicrobial effects of mushroom extracts are contradictory. To effectively extract the antibiotic compounds from mushrooms, a wide range of solvents with different polarity were tested while to assess the antimicrobial activity of mushrooms, mainly microdilution, disk diffusion, and agar streak dilution method have been used. Accordingly, antimicrobial activity was expressed through the determination of MIC, IC_{50}, IZD values. In some studies, a method with the incorporation of the extract in the culture medium and further determination of CFU was used.

2.1 Antimicrobial Activity of Mushroom FB

Antibacterial and antifungal activities of extracts from wild and commercially cultivated mushroom FB were the most studied. Bala et al. (2012) evaluated the antimicrobial activity of a range of Australian mushrooms from five different orders and nine different families against two Gram+ bacteria, two Gram- bacteria, and two fungi. Mushrooms belonging to the genera *Fomitopsis*, *Hohenbuehelia*, *Psathyrella*, and *Ramaria* showed promising antimicrobial activity. Alves et al. (2013) reviewed 52 mushroom species as having AFA. Among them, 44 species are edible mushrooms, 21 species are saprotrophic, 16 species are mycorrhizal, 5 species are saprotrophic but also mycorrhizal, 6 are biotrophic parasites, and 4 species are necrotrophic parasite fungi. Shen et al. (2017) summarized that among 88 mushroom genera with antimicrobial properties, 45 genera exhibited antibacterial activities and 42 genera demonstrated both antibacterial and antifungal properties. The most common mushrooms genera with antimicrobial properties include *Lentinula*, *Pleurotus*, *Dictyophora*, *Cordyceps*, *Ganoderma*, and *Tremella*. Similar to Alves et al. (2012), the authors emphasized that the number of mushrooms with activities against Gram-positive bacteria is much greater than that with activity against Gram-negative bacteria.

Barros et al. (2007) found different selectivity of methanolic extracts from Portuguese wild edible mushrooms *Lactarius deliciosus*, *Sarcodon imbricatu*s, and *Tricholoma portentosum*. Among them, *L. deliciosus* distinguished with the higher content of phenols and flavonoids and great antimicrobial activity. The extracts from the entire mushroom and the cap inhibited *Bacillus cereus*, *B. subtilis*, *Pseudomonas aeruginosa*, *Candida albicans,* and *Cryptococcus neoformans*, while the mushroom stipe extract inhibited only *B. cereus*, *P. aeruginosa,* and *C. neoformans*. The *T. portentosum* extract was effective only against Gram+ bacteria (*B. cereus*, *B. subtilis*) and *C. neoformans,* while *S. imbricatus* showed activity only against *B. cereus* and *C. neoformans* with the lowest MIC. It is worth noting that the cap extract of *S. imbricatus* was selective for *B. cereus*, while the stipe extract was not effective against the tested microorganisms. Venturini et al. (2008) evaluated the antimicrobial activity of aqueous, methanol, hexane, and ethyl acetate extracts from 48 edible wild and cultivated mushroom species against nine foodborne pathogenic bacterial strains. Extracts from 19 mushroom species did not express ABA. Of the 97 active extracts, 72.2% were active against Gram-positive bacteria and 27.8% were active against Gram-negative bacteria. *Clitocybe geotropa* appeared to be active against the majority of bacterial strains and gave inhibition zones with the largest diameters. Likewise, *L. edodes* had antimicrobial activity against all the Gram-positive bacteria and *Vibrio parahaemolyticus* and *Yersinia enterocolitica. Hygrophorus limacinus* was the only carpophore whose hexane extract resulted in an inhibition zone of more than 20 mm in diameter against *Clostridium.*

Tunisian mushrooms *Phellinus torulosus*, *Fomes fomentarius*, *Trametes versicolor*, *Pisolithus albus*, and *Fomitopsis pinicola* were extracted using ethanol and antimicrobial activities were assessed against eight bacterial species (Khadhri et al.

2017). The mushroom extracts exhibited a broad spectrum of ABA against all the tested bacterial species although with a different degree; the IZD varied from 9 mm (*E. coli*, *P. aeruginosa, A. hydrophila*, and *B. subtilis*) to 17 mm (*E. faecalis*). In particular, the IZD of *F. pinicola* extracts ranged from 10 mm (*S. typhimurium*, *L. monocytogenes*) to 16–17 mm (*P. aeruginosa*, *E. coli*, *E. faecalis*, *B. subtilis*). MIC values of *F. pinicola* extracts against the Gram+ and Gram- bacteria were 6.25–25 mg/mL and 12.5–25 mg/mL, respectively.

Of 75 mushroom samples collected in the vicinity of Oxford, Ohio (USA), the 60 °C water extracts of 25 samples had antibiotic activity against at least 1 bacterial strain tested, while water extracts of *Polyporus squamosus*, *Ganoderma applanatum*, *Lentinellus subaustralis*, *Laetiporus sulphureus*, *Ganoderma lucidum*, and *T. versicolor* exhibited strong antibiotic activity against all tested bacteria (*P. aeruginosa*, *P. fluorescens*, *B. subtilis*, *Staphylococcus epidermidis*, and *Micrococcus luteus*) (Hassan et al. 2019). The *G. lucidum* and *L. sulphureus* extracts displayed the strongest inhibition, with a MIC of 0.1 mg/mL. It is worth noting that several samples of the same mushroom species, collected from different places, showed different levels of ABA. Thus, unlike *T. versicolor* isolate 3, the extract of *T. versicolor* isolate 2 did not inhibit the growth of *P. aeruginosa.* Due to observed intraspecies differences, the researchers concluded that the local ecosystem or microenvironment can have a large impact on the antibiotic compounds that the fungus produces in the wild.

Ganoderma spp. have been considered as the best source of various secondary metabolites with antimicrobial activity. Several mushrooms exhibited exceptionally high AFA. Thus, methanolic extract from *G. lucidum* showed activity against *Trichoderma viride* and *Penicillium funiculosum* with MIC 0.005 mg/mL and 0.09 mg/mL, respectively, higher than the tested standard, bifonazole (MIC 0.15 and 0.20 mg/mL, respectively) and ketoconazole (MIC 1.0 and 0.2 mg/mL, respectively) (Heleno et al. 2013). In another study, G. *lucidum, G. applanatum, and G. australe* extracts expressed differently their antimicrobial activity depending on the solvent used for extraction (Jonathan and Awotona 2010). Compared with methanol and ethanol, water appeared to be a poor solvent while ethanol was better than methanol. The best ABA showed the crude methanol extract of *G. lucidium* against *P. mirabilis* with an IZD of 20.3 mm while the highest AFA (24.3 mm) exhibited the crude ethanol extract of *G. lucidium* against *Aspergillus niger*. For the comparison, the aqueous extract of *G. australe* showed IZD of 2.3 mm against *Escherichia coli*. The MIC values for the ethanol extract ranged between 1.7 and 5.0 mg/mL for bacteria and between 2.0 and 6.0 mg/mL for fungi. Likewise, the FB of *Ganoderma boninense* effectively suppressed the growth of tested pathogens but a degree of inhibition depended on the type of used solvent (Chan and Chong 2020). Ethyl acetate extract appeared to be the most suitable for extraction purposes exhibiting antimicrobial activity against a wide range of both Gram+ and Gram- bacteria (*Enterobacter* sp.*, P. aeruginosa, P. mirabilis, Acinetobacter* sp.*, K. pneumoniae, S. marcescens*, *S. pyogenes, coagulase negative staphylococci,* and MRSA). In this study, the effectiveness of other solvents was as follows: hot water > acetone > methanol > ethanol and chloroform extract exhibited the least antimicrobial activity.

Karnwal and Kaur (2020) assessed the *Agaricus bisporus* S-II extracts as a bio-controlling agent against human pathogens. The methanol extract of FB showed the maximum level of GI of 21.8%, 15%, and 26.5% at 100% extract strength against *P. aeruginosa*, *B. cereus*, and *S. aureus*, respectively, while 100% ethanolic extract gave GI of 14%, 13.82%, and 17% against the same bacteria, respectively. The lowest MBC values (10 mg/ml) were recorded for *P. aeruginosa* and *S. aureus*, whereas no bactericidal effect of the extract was noticed on *B. cereus*.

Pleurotus spp. are one of the best-studied mushrooms for antimicrobial activity. Some species of this genus exhibit both antifungal and antibacterial activities. Evaluation of the AFA of FB of four oyster mushrooms species revealed the best inhibition zone (16 mm) against *Trichoderma harzianum* by the dried aqueous extract (2 mg/disc) from *P. ostreatus* var. *florida* grown on the substrate containing 70% wheat straw, 20% hardwood sawdust, and 10% date palm fibers (Owaid et al. 2017a). However, as compared with *T. harzianum*, *Pythium* sp. and *Verticillium* sp. appeared to be less sensitive against mushroom extracts. Moreover, these authors (Owaid et al. 2017b) obtained liquid cultures of four *Pleurotus* spp. and revealed that the culture filtrate of *P. ostreatus* caused 55%, 43.94%, and 33.33% inhibition of growth in liquid medium of *T. harzianum*, *Verticillium* sp., and *Pythium* sp., respectively. Lesser inhibitions (13.64% and 15%) were recorded in *P. cornucopiae* filtrate against *Verticillium* sp. and *T. harzianum*, respectively. Adebayo et al. (2018) compared antibacterial properties of standardized hydro-alcoholic extracts of four *Pleurotus* species against eight clinically relevant species. Among them, *P. tuber-regium* expressed remarkable activity toward both Gram+ and Gram- bacteria with MIC of 0.006–0.048 mg/mL. Younis et al. (2015) showed that the water extracts from FB of *P. ostreatus* had the widest spectrum and the highest growth inhibitory effect against tested fungi, especially toward *C. albicans*, *Cryptococcus humicola*, and *Trichosporon cutaneum* (IZD = 30 mm). Hexane and chloroform extracts from carpophore and sclerotium of *P. tuber-regium* contained compounds that inhibited the growth of 11 Gram+ and Gram- bacteria with MIC values 6.25–12.5 mg/mL (Metsebing et al. 2020). Interestingly, the crude sclerotia extracts showed higher antimicrobial activity than that of carpophores. Likewise, the researchers observed that the tested pathogenic fungi (*C. albicans*, *Aspergillus fumigatus*, and *A. ochraceus*, MIC 3.13–6.25 mg/mL) were more sensitive to crude extracts of *P. tuber-regium* than bacteria.

Of the 35 tested wild mushrooms, *Trametes* spp. and *Microporus* spp. showed high antimicrobial activities against six bacterial pathogens and two yeast species (Gebreyohannes et al. 2019). In particular, *S. aureus*, *P. aeruginosa*, and MRSA appeared to be the most susceptible to chloroform extract of *Trametes* spp. with MIC values of 0.83 mg/mL, 1.00 mg/mL, and 1.17 mg/mL, respectively. The same extracts inhibited the growth of *C. albicans* and *C. parapsilosis* at a MIC value of 1.5 mg/mL. The authors noted that hot water extracts provided better antimicrobial activities against all of the tested organisms with MIC values of 0.67–1.0 mg/mL. Between two species of *Clitocybe*, *C. geotropa* expressed strong and better antimicrobial activity than *C. nebularis* (Kosanić et al. 2020a). MIC values of acetone extracts against *B. cereus*, *B. subtilis*, *E. coli*, *P. mirabilis*, *S. aureus* for *C.*

geotropa were in the range of 0.78–6.25 mg/mL and for *C. nebularis* from 3.12 to 25 mg/mL. Like in other studies (Alves et al. 2012; Bach et al. 2019), G+ bacteria were more susceptible to extracts than G- bacteria. In general, fungi were more resistant than bacteria. *C. geotropa* showed the lowest MIC values for fungal species against *Geotrichum candidum* (6.25 mg/mL), *A. fumigatus* (6.25 mg/mL), and *C. albicans* (6.25 mg/mL).

Rena et al. (2014) tested polysaccharides extracts of eight edible mushroom species for their ability to inhibit the growth of five common bacterial pathogens. Among them, an aqueous extract from *Pleurotus australis* inhibited the growth of *S. epidermidis* with a MIC value of 0.47 mg/mL while extract from *Cordyceps sinensis* inhibited the growth of *B. subtilis* and *S. epidermidis* with MIC values of 0.94 and 0.47 mg/mL, respectively. The recently published paper (Kosanić et al., 2020b) reports that acetone extract of *Lactarius piperatus* was active against both G+ and G- bacteria with the MIC values of 0.039 mg/mL for *S. aureus*, 0.078 mg/mL for *E. coli* and *B. cereus*, and 0.156 mg/mL for *B. subtilis* and *P. mirabilis*. The same mushroom extract inhibited cell growth of *C. albicans* (MIC - 2.5 mg/mL), *T. viride* (MIC - 5 mg/mL) as well as *A. niger, Mucor mucedo,* and *Penicillium italicum* with MIC of 10 mg/mL. Angelini et al. (2019) found out that ABA and AFA of methanolic extracts from the FB of medicinal mushroom *Inonotus hispidus* are rather higher than that of the mycelial culture. In particular, MIC of extracts from mushroom FB and mycelium against *C. albicans* and *Aspergillus tubingensis* were 1.71 and 2.56 mg/mL, respectively.

Of eight mushrooms tested, ethanol extract from *Hydnum repandum* exerted AFA toward five phytopathogenic fungal strains with MIC of 24.75 mg/ml (Spremo et al. 2017). The methanol extract of the same species exhibited activity to *Alternaria padwickii* (MIC 24.75 mg/ml) as well. Likewise, methanol extracts of *Stereum subtomentosum* and *Coprinellus truncorum* displayed AFA to all phytopathogenic fungi but with lower MIC (49.5–198.0 mg/mL). The authors consider these mushrooms as potentially efficient antifungal agents that can be used as biocontrol agents against phytopathogenic fungi. It is worth noting that the methanolic extract of *B. adusta* affected only on *Fusarium* (MIC 24.75–99.0 mg/mL), while the methanol extracts of *Coprinus comatus*, *T. versicolor*, *F. velutipes*, as well as ethanol extracts of *C. comatus*, *A. strobiliformis*, and the chloroform extract of *C. comatus* had antifungal effects on the phytopathogenic isolate *A. padwickii*. No antifungal effects on any of the tested phytopathogenic isolates were observed in the testing of the methanol extract of *Amanita strobiliformis* and chloroform extract of *C. micaceus*.

The presence of antimicrobial activity in *Ramaria* species is also well documented. Among them, *R. flava* (Liu et al. 2013) expressed activity against Gram+ bacteria but weak or no activity against Gram- bacteria. Thus, the ethanol extract from *R. flava* exhibited activity against bacteria *S. aureus*, *B. subtilis*, and *E. coli* with the MIC values of 6.25, 25, and 100 mg/ml, respectively, and toward pathogenic fungi, causing at the concentration of 2 mg/mL reduction of *Fusarium avenaceum*, *C. albo-maculans,* and *F. graminearum* growth by 36.64, 30.03, and 19.99% (as compared to standard drug clotrimazole), respectively (Liu et al. 2013). The ethanol extract of *Ramaria* sp. showed almost complete inhibition of four Gram+

and Gram- bacteria and two fungi (*Geotrichum candidum*, *Saccharomyces cerevisiae*) at 10 mg/mL (Bala et al. 2012). Moreover, at 1 mg/mL it retained activity against *B. cereus* and both fungi along with some moderate activity against *P. aeruginosa*.

Cyclohexane, dichlormethane, methanol, and aqueous extracts of *Fomes fomentarius* appeared to be very effective against nine Gram+ and Gram- bacterial strains with the MICs values in the range of 0.125–0.25 mg/mL (Kolundžić et al. 2016). Of particular interest is that methanol and aqueous extracts have shown inhibitory activity against *Helicobacter pylori* with MIC values between 0.004–0.03 mg/mL. The authors suggested that the high content of polyphenols and β-glucan in *F. fomentarius* is responsible for the significant antimicrobial activity of this basidiomycete.

2.2 Antimicrobial Activity of Mycelial Biomass and Culture Liquid

Overwhelming studies on mushroom antimicrobial activity dealt with the evaluation of extracts obtained from FB. However, wild mushrooms are seasonal and the formation of FB by some mushroom species depends on the host. Moreover, certain mushrooms are slow-growing and rare in nature. Commercial production of FB is a labor-intensive process that can last several months. Naturally, submerged cultivation is a promising alternative for the production of mycelial biomass and bioactive compounds (Aqueveque et al. 2010; Elisashvili 2012; Duvnjak et al. 2016). Indeed, both mycelia and filtrates of liquid cultures have proven to be good sources of antimicrobial compounds against various groups of microorganisms. For comparison, Tables 13.1 and 13.2 show diversity in the antibacterial and antifungal potential of fruit bodies, mycelia, and culture liquids of some mushrooms.

Suay et al. (2000) screened 204 Spain mushroom species against a range of human pathogens. It was observed that the methanol extracts from the fermentation broths of more than 40% of the total species exhibited antimicrobial activity and 20% showed AFA. Among active mushrooms, members of the *Ganodermatales* (73% of the isolates tested) followed by *Agaricales*, *Boletales*, *Poriales*, and *Stereales* (in the range of 46–49%) showed good inhibition against different microorganisms. Aqueveque et al. (2010) screened extracts from submerged cultures of 148 strains representing 68 species belonging to 44 genera and 22 families for the production of antimicrobial activities. Mushrooms of the order *Agaricales* accounted for 31.0% of active strains, followed by the orders *Polyporales* (20.6%), *Sterales* (18.3%), *Boletales* (11.4%), and *Cortinariales* (9.1%). However, no activity was observed in the representatives of the orders *Ganodermatales* and *Thelephorales*. Analyses showed that the AFA of tested mushrooms was more pronounced than ABA. Twelve extracts that exhibited strong antimicrobial activity showed MIC

Table 13.1 Antibacterial activity of extracts from some medicinal mushrooms

Mushroom	Target microorganisms, extracts/compounds, effect	References
Agaricus bisporus (FB)	Methanol extract (MIC, mg/mL): *Pseudomonas aeruginosa*, *Staphylococcus aureus* – 15–20	Karnwal and Kaur (2020)
Clitocybe geotropa (FB)	Acetone extract (MIC, mg/ml): *Bacillus cereus* – 0.78, *B. subtilis* – 1.56, *E. coli* – 6.25, *Proteus mirabilis* – 6.25, *S. aureus* – 3.12	Kosanić et al. (2020a)
Clitocybe nebularis (FB)	Acetone extract (MIC, mg/ml): *B. cereus* – 3.12, *B. subtilis* – 6.25, *E. coli* – 25, *P. mirabilis* – 12.5, *S. aureus* – 6.25	Kosanić et al. (2020a)
Coriolus versicolor (culture liquid)	Exopolysaccharides (MIC, mg/mL): *Enterococcus faecalis* – 2.5, *B. cereus* – 5.0, *B. spizizeni* – 40.0, *S. aureus* – 2.5, *S. epidermidis* – 0.3, *Listeria monocytogenes* – 40.0, *L. ivanovii* – 10.0, *L. innocua* – 40.0; *P. mirabilis* – 40.0, *Proteus hauseri* – 40.0, *P. aeruginosa* – 40.0, *Salmonella enteritidis* – 40.0, *Salmonella typhimurium* – 40.0, *Shigella sonnei* – 20.0, *Yersinia enterocolitica* – 10.0, *Citrobacter freundii* – 40.0	Duvnjak et al. (2016)
C. versicolor (mycelium)	Methanol extract (MIC, mg/mL): *E. faecalis* – 20.0, *B. cereus* – 5.0, *B. spizizeni* – 0.3, *S. aureus* – 10.0, *S. epidermidis* – 0.3, *L. monocytogenes* – 10.0, *L. ivanovii* – 40.0; *P. mirabilis* – 20.0, *P. hauseri* – 10.0, *P. aeruginosa* – 20.0, *S. enteritidis* – 20.0, *S. typhimurium* – 40.0, *S. sonnei* – 20.0, *Y. enterocolitica* – 5.0, *C freundii* – 10.0	Duvnjak et al. (2016)
Flammulina velutipes (culture liquid)	Ethyl acetate extract (IC_{50}), enokipodin B: *B. subtilis* - 13.4 nmol/mL, *E. coli* – 67 nmol/mL), *S. aureus* - 406.3 nmol/mL; enokipodins A and C: *Plasmodium falciparum* – 0.002 and 0.001 mg/mL, respectively	Tabuchi et al. (2020)
Fomitopsis pinicola strains (FB)	Ethanol extract (MIC, mg/mL): *B. subtilis* – 0.031–0.125 mg/mL, *S. aureus* – 0.031–0.500 mg/mL	Dresch et al. (2015)
F. pinicola (FB)	Ethanol extract, *S. typhimurium*, *L. monocytogenes*, *P. aeruginosa*, *E. coli*, *E. faecalis*, *B. subtilis*: IZD = 9–17 mm; MIC = 12.5–50 mg/mL	Khadhri et al. (2017)
F. pinicola (FB)	Ethyl acetate extract, 100 mg/mL (IZD, mm): *B. subtilis*, *S. aureus*, *E. coli*, *P. vulgaris*, *K. pneumoniae*, *P. aeruginosa* – 17.7–21.7	Pala et al. (2019)
Ganoderma boninense (FB)	Ethyl acetate extract, *Enterobacter* sp., *P. aeruginosa, P. mirabilis, Acinetobacter* sp., *K. pneumoniae, S. marcescens*, *S. pyogenes, coagulase negative staphylococci,* and MRSA: IZD = 9.17–14.20 mm, MIC = 1.25–2.50 mg/mL	Chan and Chong (2020)
Ganoderma lucidum (FB)	EPS, 1 mg/mL (IZD, mm): *S. aureus* – 12, *B. cereus* – 23, *B. subtilis* – 19, *Klebsiella* sp. – 9, *P. aeruginosa* – 10, *E. coli* – 19,	Mahendran et al. (2013)
Ganoderma lucidum (FB)	Aqueous extract (MIC, mg/mL): *Micrococcus luteus* – 0.75	Vazirian et al. (2014)

(continued)

Table 13.1 (continued)

Mushroom	Target microorganisms, extracts/compounds, effect	References
Ganoderma lucidum (FB)	Methanol extract (IZD, mm): *E. coli* – 18, *S. aureus* – 14, *B. subtilis* – 17, *P. aeruginosa* – 11, *E. aerogenes* – 9, *K. pneumoniae* – 19, *S. typhimurium* – 17	Mehta and Jandaik (2012)
Ganoderma lucidum (mycelium)	Methanol extract (IZD, mm): *E. coli* – 22, *S. aureus* – 16, *B. subtilis* – 11, *P. aeruginosa* – 24, *E. aerogenes* – 15, *K. pneumoniae* – 16, *S. typhimurium* – 10 Acetone extract (IZD, mm): *E. coli* – 30, *S. aureus* – 12, *B. subtilis* – 14, *P. aeruginosa* – 33, *E. aerogenes* – 24, *K. pneumoniae* – 24, *S. typhimurium* – 14	Mehta and Jandaik (2012)
Hohenbuehelia sp. (FB)	Aqueous extract, 1 mg/mL (GI): *B. cereus* – 40.1%, *Listeria monocytogenes* – 99.7%, *P. aeruginosa* – 0%, *Acinetobacter baumannii* – 90.3%; ethanol extract, 1 mg/mL (GI): *B. cereus* – 16.1%, *L. monocytogenes* – 0%, *P. aeruginosa* – 30.2%, *A. baumannii* – 31.5%	Bala et al. (2012)
Inonotus hispidus (FB)	Ethyl acetate extract, 100 mg/mL (IZD, mm): *B. subtilis*, *S. aureus*, *E. coli*, *P. vulgaris*, *K. pneumoniae*, *P. aeruginosa* – 12-17.3	Pala et al. (2019)
Inonotus hispidus (FB)	Methanol extract (MIC, mg/mL): *B. cereus, S. aureus, E. faecalis, E. coli, P. aeruginosa, S. typhi* – 0.17-0.86	Angelini et al. (2019)
Inonotus hispidus (mycelium)	Methanol extract (MIC, mg/mL): *B. cereus, S. aureus, E. faecalis, E. coli, P. aeruginosa, S. typhi* – 0.32-2.03	Angelini et al. (2019)
Lactarius piperatus (FB)	Acetone extract (MIC, mg/mL): *S. aureus* – 0.039, *E. coli* and *B. cereus* – 0.078, *B. subtilis* and *P. mirabilis* – 0.156	Kosanić et al. (2020b)
Lentinus edodes (FB)	Phenolic extract (MIC, mg/mL): *B. cereus* – 12.5, *S. aureus* – 1.56, *S. enteritidis* – 100, *E. coli* – 100	Bach et al. (2019)
Lentinus tigrinus (FB)	Ethyl acetate extract, 100 mg/mL (IZD, mm): *B. subtilis*, *S. aureus*, *E. coli*, *P. vulgaris*, *K. pneumoniae*, *P. aeruginosa* – 12.3-15.6	Pala et al. (2019)
Lepista nuda (FB)	Methanol/water (80: 20) extract (MIC, mg/mL): *Pasteurella multocida* – 5, *P. mirabilis* – 20; *Streptococcus agalactiae* – 10, *Streptococcus pyogenes* – 10	Alves et al. (2012)
Laetiporus sulphureus (FB)	The 60 °C water extract (MIC, mg/mL): *S. epidermidis* – 0.1	Hassan et al. (2019)
Mircoporus spp. (FB)	Water extract (MIC, mg/mL): *S. aureus*, MRSA, *K. pneumoniae*, *P. aeruginosa*, *E. coli* – 0.67–1.67; chloroform extract: 0.83–2.0	Gebreyohannes et al. (2019)
Phellinus linteus (FB)	Methanol extract (MIC, mg/mL): *S. aureus* – 0.12, *B. cereus* – 0.032, *M. flavus* – 0.048, *L. monocytogenes* – 0.048, *P. aeruginosa* – 0.13, *S. typhimurium* – 0.095, *E. coli* – 0.072, *E. cloacae* – 0.048	Reis et al. (2014)
Pleurotus levis (FB)	Hydroalcoholic extract (MIC, mg/mL): *B. subtilis* – 0.003, *L. monocytogenes* – >0.106, *S. aureus* – 0.026, *S. agalactiae* – 0.013, *E. coli* – >0.106, *P. aeruginosa* – >0.106, *S. typhi* – >0.106, *Stenotrophomonas* sp. – >0.106	Adebayo et al. (2018)

(continued)

Table 13.1 (continued)

Mushroom	Target microorganisms, extracts/compounds, effect	References
Pleurotus ostreatus (FB)	3-(2-aminophenylthio)-3-hydroxypropanoic acid purified from the water extract (MIC, mg/mL): *S. aureus*, *E. coli* – 0.02	Younis et al. (2015)
Pleurotus ostreatus (mycelium)	Hot water extract (IZD, mm): *S. enterica, B. thuringiensis*, *P. aeruginosa*, *S. dysenteriae*, *S. pyogenes. S. aureus*, *B. subtilis*, *E. coli*, *K. pneumoniae* - 12-17	Younis et al. (2015)
Pleurotus tuber-regium (FB)	Hydroalcoholic extract (MIC, mg/mL): *B. subtilis* – 0.048, *L. monocytogenes* – 0.024, *S. aureus* – 0.012, *S. agalactiae* – 0.006, *E. coli* – 0.048, *P. aeruginosa* – 0.012, *S. typhi* – 0.024, *Stenotrophomonas* sp. – 0.024	Adebayo et al. (2018)
Pleurotus tuber-regium (FB)	Hexane and chloroform extracts (MIC, mg/mL): *B. subtilis*, *E. faecalis*, *S. epidermidis*, *S. aureus*, *Mycobacterium smegmatis*, *E. cloacae*, *P. vulgaris*, *K. aerogenes*, *K. oxytoca*, *P. mirabilis*, *E. coli* – 6.25-12.5	Metsebing et al. (2020)
Ramaria flava (FB)	Ethanol extract (MIC, mg/mL): *S. aureus* – 6.25, *B. subtilis* – 25, *E. coli* - 100	Liu et al. (2013)
Ramaria sp. (FB)	Aqueous extract, 1 mg/mL (GI, %): *B. cereus* – 41.6, *L. monocytogenes* – 0, *P. aeruginosa* – 0, *Acinetobacter baumannii* – 0%; ethanol extract, 1 mg/mL (GI,%): *B. cereus* – 100, *L. monocytogenes* – 14.9, *P. aeruginosa* – 74.8, *A. baumannii* – 24.6	Bala et al. (2012)
Sparassis latifolia (FB)	Lectin (MIC, mg/mL): *E. coli* – 0.10, *P. aeruginosa* – 0.05, *S. typhimurium* – 0.025, *B. subtilis* – 0.05, *Listeria monocytogenes* – 0.10, *S. aureus* – 0.10	Chandrasekaran et al. (2016)
Taiwanofungus salmoneus (mycelium)	Ethanol extract (MIC, mg/mL): *B. cereus*, *L. monocytogenes*, *S. typhimurium, S. aureus*, *E. coli* – 6.25–12.50; hot water extract (MIC, mg/mL): 25–50	Chiang et al. (2013)
Trametes spp. (FB)	Chloroform extract (MIC, mg/mL): *E. coli* – 1.33, *K. pneumoniae* – 1.00, *P. aeruginosa* – 1.33, *S. aureus* – 0.67	Gebreyohannes et al. (2019)
Tricholosporum goniospermum (FB)	Methanol extract (MIC, mg/mL): *E. coli* – 0.198, *P. aeruginosa* – 0.63, *S. typhimurium*– 0.79, *B. cereus* – 0.157, *B. subtilis* – 0.314, *S. aureus* – 0.315	Angelini et al. (2020)
Tricholosporum goniospermum (mycelium)	Methanol extract (MIC, mg/mL): *E. coli* – 0.099, *P. aeruginosa* – 0.396, *S. typhimurium* – 0.62, *B. cereus* – 0.099, *B. subtilis* – 0.198, *S. aureus* – 0.198	Angelini et al. (2020)

values of 50 μL/mL against *Bacillus brevis* and 25–50 μL/mL against *Penicillium notatum* and *Paecilomyces variotii*.

Mehta and Jandaik (2012) compared ABA of methanol, acetone, and aqueous extracts of *G. lucidum* FB and mycelial biomass. The acetone extract showed maximum ABA followed by methanol and aqueous extract. Mycelial extract of the mushroom exhibited higher ABA as compared to fruiting body extract. The especially high inhibitory activity showed acetone extract of mycelial biomass against G- bacteria *P. aeruginosa* and *E. coli* with IZD of 33 and 30 mm, respectively (Table 13.1). At the same concentration, the least inhibitory effect was observed for

Table 13.2 Antifungal activity of extracts from medicinal mushrooms

Mushroom	Target microorganisms, extracts/compounds, effect	References
Agaricus bisporus (FB)	Methanol extract (IZD, mm): *Candida tropicalis, Candida albicans* – 11-14	Barros et al. (2008)
Armillaria mellea (FB)	Ethanolic extract (IZD, mm): *C. albicans* – 19	Alves et al. (2013)
Clitocybe geotropa (FB)	Acetone extract (MIC, mg/ml): *Aspergillus flavus* – 12.5, *A. fumigatus* – 6.25, *C. albicans* – 6.25, *Geotrichum candidum* – 6.25, *Fusarium solani* – 12.5, *Penicillium chrysogenum* – 25, *Paecilomyces variotii* – 25, *Trichophyton mentagrophytes* – 12.5	Kosanić et al. (2020a)
Clitocybe nebularis (FB)	Acetone extract (MIC, mg/ml): *A. flavus* – 25, *A. fumigatus* – 25, *C. albicans* – 6.25, *G. candidum* – 25, *F. solani* – 12.5, *P. chrysogenum* – 25, *P. variotii* – 12.5, *T. mentagrophytes* – 12.5	Kosanić et al. (2020a)
Flammulina velutipes (mycelium)	Enokipodins: *A. fumigatus*, IC_{50} – 232 μM, MIC – 0.12 mg/mL	Wang et al. (2012)
Fomitopsis pinicola (FB)	Ethanolic extract (MIC, mg/mL): *Absidia orchidis, A. flavus, A. fumigatus, Candida krusei* – 0.5-1.0	Dresch et al. (2015)
Fomitopsis pinicola (FB)	Ethyl acetate extract, 100 mg/mL (IZD, mm): *Saccharomyces cerevisiae*, *C. albicans*, *P. chrysogenum*, *A. fumigatus* – 15.7-19.7	Pala et al. (2019)
Hohenbuehelia sp. (FB)	Aqueous extract, 1 mg/mL (GI, %): *G. candidum* – 77.1, *S. cerevisiae* – 88.1; ethanol extract, 1 mg/mL (GI, %): *G. candidum* – 79.1, *S. cerevisiae* – 100	Bala et al. (2012)
Hygrophorus agathosmus (FB)	Chloroform extract: *Saccharomyces cerevisae*, IZD = 11 mm, MIC = 0.25 mg/mL	Yamac and Bilgili (2006)
Hericium sp. (mycelium)	Compound 4 (MIC, mg/mL): *Cryptococcus neoformans*, *C. albicans* – 0.03-0.06	Song et al. (2020)
Inonotus hispidus (FB)	Ethyl acetate extract, 100 mg/mL (IZD, mm): *S. cerevisiae*, *Candida albicans*, *P. chrysogenum*, *A. fumigatus* – 13.3-18.7	Pala et al. (2019)
Inonotus hispidus (FB)	Methanol extract (MIC, mg/mL): *C. albicans* – 1.71, *C. tropicalis* – 0.86, *C. parapsilosis* – 0.68, *A. tubingensis* – 1.71, *A. minutusi* – 0.68	Angelini et al. (2019)
Inonotus hispidus (mycelium)	Methanol extract (MIC, mg/mL): *C. albicans* – 2.56, *C. tropicalis* – 2.03, *C. parapsilosis* – 2.03, *A. tubingensis* – 2.56, *A. minutusi* - 1.01	Angelini et al. (2019)
Lactarius delicious (FB)	Methanol extracts (MIC, mg/mL): *C. albicans* – 50, *C. neoformans* – 10	Barros et al. (2007)
Lactarius piperatus (FB)	Acetone extract (MIC, mg/mL): *C. albicans* – 2.5, *T. viride* – 5.0, *A. niger, Mucor mucedo, Penicillium italicum* – 10.0	Kosanić et al. (2020b)
Morchella esculenta (FB)	Butanol extract (IZD, mm): *C. albicans* – 18, *A. fumigates* – 14, *A. niger* – 11; ethyl acetate extract: *A. fumigatus* – 18	Shameem et al. (2017)

(continued)

Table 13.2 (continued)

Mushroom	Target microorganisms, extracts/compounds, effect	References
Oudemansiella mucida (culture liquid)	Ethyl acetate extract, 40 mg/mL (IZD, mm): *Alternaria longipes, Alternaria brassicae*, *Gloesporum fructigenum*, *Fusarium graminearum*, *Alternaria alternata* – 11.36-13.11; (MIC, mg/mL): *A. longipes, A. brassicae*, and *F. graminearum* – 10.0, *G. fructigenum* and *A. alternata* – 5.0	Deng et al. (2020)
Phellinus linteus (FB)	Glucan fraction (MIC, mg/mL): *A. fumigatus* – 0.25, *A. versicolor* – 0.06, *Aspergillus ochraceus* – 0.12, *A. niger* – 0.22, *T. viride* – 0.11, *P. funiculosum* – 0.11, *Penicillium ochrochloron* – 0.27, *P. verrucosum* – 0.27	Reis et al. (2014)
Pleurotus ostreatus (FB)	Hot water extracts (IZD, mm): *C. albicans*, *Cryptococcus humicola*, and *Trichosporon cutaneum* – 30, *G. candidum*, *A. fumigatus*, and *Fusarium moniliforme* – 25, *A. niger* – 12, *Botrytis cinerea* – 0	Younis et al. (2015)
Pleurotus ostreatus (mycelium)	Hot water extracts (IZD, mm): *C. albicans* – 3, *C. humicola* – 10, *T. cutaneum* – 15, *G. candidum* – 3, *A. fumigatus* – 0, *F. moniliforme* – 3, *A. niger* – 0, *B. cinerea* – 0	Younis et al. (2015)
Pleurotus ostreatus (culture liquid)	Hot water extracts (IZD, mm): *C. albicans* – 12, *C. humicola* – 0, *T. cutaneum* – 0, *G. candidum* – 0, *A. fumigatus* – 7, *F. moniliforme* - 5, *A. niger* – 5, *B. cinerea* – 0	Younis et al. (2015)
P. ostreatus (FB)	3-(2-aminophenylthio)-3-hydroxypropanoic acid purified from the water extract (MIC mg/mL): *C. albicans*, *A. fumigatus* – 0.03	Younis et al. (2015)
Ramaria flava (FB)	Ethanol extract, 2 mg/mL (GI, %): *Fusarium auenaceum* – 36.64, *C. albo-maculans* – 30.03, *F. graminearum* – 19.99	Liu et al. (2013)
Ramaria sp. (FB)	Aqueous extract, 1 mg/mL (GI, %): *G. candidum* – 73.9, *S. cerevisiae* – 94.7; ethanol extract, 1 mg/mL (GI, %): *G. candidum* – 100, *S. cerevisiae* – 100	Bala et al. (2012)
Schizophyllum commune (mycelium)	Methanol extract (MIC, mg/mL): *Pycnoporus sanguineus* – 5.0, *Trametes feei* – 0.63, *Trametes menziezi* – 0.31, *Trametes elegans* – 0.63, *Gloephyllum trabeum* – 2.5, *Lentinus sp.* – 0.16, *Microporus affinis* – 0.31, *Microporus xanthopus* – 0.31	Teoh et al. (2015)
Stereum hirsutum (culture liquid)	Sterenin D from the ethyl acetate extract (MIC, mg/mL): *B. cinerea* – 20.0	Aqueveque et al. (2017)
Tricholosporum goniospermum (FB)	Ethyl acetate extract (MIC, mg/mL): *C. albicans* – 0.198, *C. tropicalis* – 0.157, *C. parapsilopsis* – 0.099	Angelini et al. (2020)
T. Goniospermum (mycelium)	Ethyl acetate extract (MIC, mg/mL): *C. albicans* – 0.051, *C. tropicalis* – 0.099, *C. parapsilopsis* – 0.079	Angelini et al. (2020)
Verpa bohemica	Butanol extract (IZD, mm): *C. albicans* – 22; ethyl acetate extract (IZD, mm): *A. fumigatus* – 14	Shameem et al. (2017)

Gram+ bacteria *B. subtilis* and *S. aureus* (14 and 12 mm, respectively). MIC value of mycelial biomass was found to be 4 mg/mL against *P. aeruginosa* followed by *E. coli* with a value of 6 mg/mL. In the case of the fruiting body, MIC was 15 mg/mL for *P. aeruginosa* and *E. coli*.

Comparison of antimicrobial activity of *P. ostreatus* FB and that of submerged culture mycelium and filtrate revealed that the mycelium extract had little or no inhibitory effect on the growth of bacteria, whereas the broth extract exhibited high antimicrobial activity against a wide spectrum of bacterial strains suggesting that synthesized antibacterial compounds were secreted by the mycelium (Younis et al., 2015). It is worth noting that water extracts from the mushroom FB and broth had much higher antibacterial activities in comparison to the ethanol and methanol extracts. The water extract of cultural broth gave 17 mm IZD against *S. enterica* and *B. thuringiensis*, followed by 13 mm on *P. aeruginosa*, *S. dysenteriae*, and *S. pyogenes.* However, no inhibition was observed against *B. megaterium.* Regarding antifungal activity of *P. ostreatus*, the water extracts from the mushroom FB had the widest spectrum and the highest growth inhibitory effect against tested fungi, especially against *C. albicans*, *C. humicola*, and *T. cutaneum* (Younis et al. 2015). Water extracts from cultural broth and mycelial biomass exhibited moderate activities against *C. albicans*, *C. dubliniensis*, *Curvularia clavata*, and *Fusarium moniliforme*, but the degrees of inhibition varied. It is interesting that while the mushroom broth extract inhibited *Aspergillus flavus*, *A. fumigatus*, *A. niger*, *A. terreus*, and *T. viride*, the mycelia extract had no effect at all against these species. On the other hand, the mycelia extract inhibited *Cryptococcus humicola*, *Trichosporon cutaneum*, *Geotrichum candidum*, and *Penicillium expansum*, whereas the broth extract was without an effect on them. However, *Penicillium roqueforti*, *Botrytis cinerea*, *Mucor rouxii*, and *Syncephalastrum racemosum* appeared to be resistant to the inhibition by any extracts from *P. ostreatus*.

The antimicrobial activity of 21 strains belonging to 18 species of basidiomycetes was evaluated after their submerged cultivation on 7 nutrient media (Dyakov et al. 2011). Antimicrobial substances were formed by 13 strains (81.25%) of 12 fungal species. Of them, all strains exhibited activity against Gram+ bacteria, 4 strains inhibited the growth of both Gram+ and Gram- bacteria, 4 strains were active toward *A. niger*. No activity against *P. aeruginosa* was revealed in any of the fungal strains. No antimicrobial activity was revealed in the culture fluid of the *P. aurivella, P. squarrosa* (three strains), and *S. crispa* strains, despite satisfactory growth of fungi.

Duvnjak et al. (2016) tested the sensitivity of a wide range of bacterial species to methanol extract and exopolysaccharides isolated from the submerged culture of *Coriolus versicolor*. Among the G+ strains, the most sensitive to EPS were *E. faecalis*, *S. aureus,* and *S. epidermidis* with the MIC values of 2.5 mg/mL, 2.5 mg/mL, and 0.3 mg/mL, respectively. For *B. cereus* and *L. ivanovii* MIC values were slightly higher (5 mg/mL and 10 mg/mL, respectively). Other G+ bacteria were equally sensitive with a MIC value of 40 mg/mL. Testing of G- bacteria revealed that *Y. enterocolitica* and *S. sonnei* were also susceptible to EPS but with higher MIC values ranging from 10 to 20 mg/mL, while the *E. coli* strains were resistant to the tested concentrations of EPS.

Krupodorova et al. (2016) compared ABA of 30 mushroom species mycelia and culture liquids. Among them, mycelium and culture liquid of *Phellinus igniarius* cultivated on glucose-peptone-yeast extract medium caused full inhibition of *E. coli*

growth. The antibacterial effect of this mushroom mycelium and culture liquid even exceeded the values of used antibiotics. Culture liquid of *Piptoporus betulinus* grown on synthetic medium showed the complete suppression of *B. subtilis* and *S. aureus* whereas culture liquid of *L. edodes* fully inhibited the growth of *B. subtilis*. It is worth noting that the mycelium of *Piptoporus betulinus* did not exhibit any ABA against the tested bacteria. On the whole, comparison of the ABA of mycelium and culture liquid showed that the culture liquid has a higher activity. G- bacteria *E. coli* was more resistant to tested antibiotics than G+ bacteria *B. subtilis* and *S. aureus*.

Twelve wood-degrading basidiomycetes from Malaysian forests were evaluated for antifungal activities and the possibility of using them as bio-fungicides for biological control in the rubberwood industry (Teoh et al. 2015). Among them, *S. commune* and *P. sanguineus* appeared to be the least sensitive to both aqueous and methanol extracts from mycelium of basidiomycetes (MIC values were >5 mg/mL). At the same time, the growth of *M. affinis* was inhibited by the water extract of *G. trabeum* at the MIC value of 0.63 mg/mL. The methanol extract of *P. sanguineus* exhibited considerable activities against all wood-degrading fungi tested, particularly against *Lentinus* with MIC of 0.1 mg/mL. Likewise, methanol extract of *S. commune* biomass possessed AFA with MIC values between 0.16 and 5 mg/mL against all tested wood-degrading fungi. Based on the results obtained, the authors concluded that methanol extracts from mycelia of all fungal strains provided better AFA compared with water extracts.

Angelini et al. (2020) compared activities of n-hexane, ethyl acetate, and methanol extracts from FB and liquid-cultured mycelia of *Tricholosporum goniospermum* against Gram+ and Gram- bacteria, clinical yeast, and fungal dermatophytes. All extracts showed antimicrobial activity, but with a different degree. In general, ethyl acetate and methanol extracts from mycelia exhibited rather higher antimicrobial activities as compared with those from FB. The strongest inhibition against *E. coli* was observed for ethyl acetate and methanol mycelia extracts (MIC 0.099 mg/mL), while the extracts obtained from FB showed MIC 0.157 and 0.198 mg/mL, respectively. However, methanol and ethyl acetate extracts from the mushroom FB were more efficient toward *B. cereus* and dermatophyte *T. mentagrophytes* (CCF 5930) growth, respectively. It is worth noting that the n-hexane extract of FB was the least effective against all the tested microorganisms. The authors established that the methanol extract from mycelia was the richest in gallic acid, whereas the ethyl acetate extract from FB was the sole extract containing catechin. They assumed that the antimicrobial activity of these extracts is related, at least in part, to the content of these compounds.

Dutta et al. (2019) analyzed the antimicrobial activities of *S. commune* culture filtrate against various plant pathogens. Adding even 1% of the filtrate to PDA inhibited the growth of *Alternaria solani*, *B. cinerea*, and *Colletotrichum gloeosporioides*. The IC_{50} for *C. gloeosporioides* and *B. cinerea* were 20% and 15% CF, respectively. Moreover, treatment of pepper plants with the culture filtrate of *S. commune* in field experiments significantly reduced the symptoms of anthracnose at a concentration of 12.5%. However, the CL of *S. commune* was not effective against

Rhizopus stolonifer and the bacterial pathogens, *Ralstonia solanacearum* or *Pectobacterium carotovorum* subsp. *carotovorum* at any tested concentrations. The researchers identified an active compound responsible for the antifungal and disease control activity and verified it as schizostatin.

Four samples obtained from submerged culture of *Oudemansiella mucida* were evaluated for antimicrobial activity against five common phytopathogenic fungi (Deng et al. 2020). Culture broth inhibited the growth of *Alternaria longipes, Alternaria brassicae*, *Gloesporum fructigenum*, *Fusarium graminearum*, *Alternaria alternata* with inhibition zones of 11.36–13.11 mm. The ethyl acetate extract at the concentration of 40 mg/mL gave inhibition zones from 14.96 to 16.01 mm. The MIC values for *A. longipes, A. brassicae*, and *F. graminearum* were 10 mg/mL, while for *G. fructigenum* and *A. alternata* − 5 mg/mL.

Unlike most researchers, Teoh et al. (2012) tested AFA of water and methanol extracts of *S. commune* toward a range of wood-degrading fungi. *Lentinus* sp. followed by *Microporus affinis* and *Microporus xanthopus* appeared to be the most sensitive to the water extract with MIC values of 0.31–0.61 mg/mL, whereas weak activity was revealed toward *Pycnoporus sanguineus*, *Trametes versicolor*, *Lentinus sajor-caju*, and *Lentinus strigosus* with MIC higher than 5 mg/mL. The methanol extract was most active against *Lentinus* sp. with MIC of 0.16 mg/mL but reduced growth of *P. sanguineus* only at MIC of 5 mg/mL. It is worth noting that the water extract exhibited weak activity against *Trametes menziezi* (MIC = 5 mg/mL), while the methanol extract inhibited the growth of this fungus at an MIC value of 0.31 mg/mL.

In our study, wood-rotting and litter-decomposing basidiomycetes collected on the plains and in the mountains of Georgia and isolated in pure cultures have been screened for their ABA (Khardziani et al., 2020). On agar plates, the mycelium of *S. commune* exhibited the highest inhibitory activity against *E. coli*, *P. aeruginosa*, and *S. aureus* with IZD of 17, 19, and 19 mm, respectively. Moreover, this mushroom showed activity against *S. enteritidis* (11 mm) and *S. epidermidis* (12 mm). Ethanol extract from fungal biomass, as well as ethyl acetate and ethanol extracts from CL, when analyzed on a 96-well plate, showed significant ABA, especially against *S. aureus* with MIC of 1 mg/mL. Interestingly, the ethyl acetate extract from culture liquid inhibited the growth of *E. coli* with a MIC of 0.5 mg/mL. However, the cold water extract from *S. commune* biomass showed the lowest activity against *S. aureus* and *E. coli* with MIC of 5 and 7.5 mg/mL, respectively. All extracts, except ethyl acetate extract from culture liquid, appeared to be more effective against *S. aureus* than toward *E. coli*. In our other work (Metreveli et al., 2021), we showed that the ethanolic extracts from mycelium and culture liquid of *F. pinicola* were especially active against *E. coli* with MIC of 0.5 mg/mL, whereas the MIC values against *S. aureus* were, respectively, 15 and 4 times higher. At the same time, the hot water extract from *F. pinicola* biomass and ethyl acetate extract from culture liquid showed the lowest ABA against *E. coli* and *S. aureus* with MIC of 15 and 20 mg/mL, and 7.5 and 6.0 mg/mL, respectively. In this regard, it should be noted that in experiments performed by Dresch et al. (2015), ethanolic extracts of *F.*

pinicola strains showed excellent bacteriostatic and bactericidal activities with MICs of 0.031–0.125 mg/mL against *B. subtilis* and of 0.031–0.500 mg/mL against *S. aureus*.

Summarizing, we can see that basidiomycetous medicinal mushrooms exhibiting antimicrobial activity are geographically distributed on all continents of the planet. These fungi, belonging to different taxonomic, physiological, and ecological groups, have been isolated from a wide variety of ecological niches, climatic zones, environmental conditions, and growth substrates. Therefore, it is not surprising that there are qualitative and quantitative differences in antimicrobial activity identified among strains of the same species of mushrooms. Moreover, some examples presented in Tables 13.1 and 13.2 indicate that not only fungi belonging to different species, but even strains belonging to the same species can exhibit different antibacterial activity and have a different spectrum of target microorganisms. Thus, in the study by Younis et al. (2015), the broth extract of *P. ostreatus* exhibited high antimicrobial activity against a wide spectrum of bacterial strains, whereas in experiments performed by Owaid et al. (2015) none of the filtrates of *P. ostreatus* (grey and white strains) showed any activity against pathogenic bacteria and yeast. Likewise, cordimin isolated from *Cordyceps militaris* efficiently inhibited the growth of *Bipolaris maydis*, *Mycosphaerella arachidicola*, *Rhizoctonia solani*, and *C. albicans* (IC_{50} 50 μM, 10 μM, 80 μM, and 0.75 mM, respectively) but had no effects against *A. fumigatus*, *F. oxysporum* (Wong et al. 2011).

The available literature data evidence that most of the mushrooms extracts tested are more effective against Gram+ bacteria, but there are many mushroom strains exhibiting especially high activity against Gram- bacteria. Fungal organisms usually are more resistant (Pala et al. 2019; Kosanić et al. 2020b). The extracts obtained from the mushroom cap and stipe show significant differences in the activity and antimicrobial selectivity. Furthermore, the ABA of methanol extracts from FB of *I. hispidus* appeared to be higher than that of the mycelial culture (Angelini et al. 2019). On the contrary, ethyl acetate and methanol extracts of *T. goniospermum* mycelium exhibited rather higher against most tested bacteria as compared with those from FB (Angelini et al. 2020). However, extracts from the mushroom FB were more efficient toward *B. cereus* and a dermatophyte *T. mentagrophytes*.

3 Mushroom Extracts and Isolated Compounds with Antimicrobial Activity

Analysis of literature data indicates that the antimicrobial activity of extracts depends on the mushroom species and the source of antimicrobial products (fruiting body, mycelium, culture liquid). Intracellular and extracellular compounds and extracts from the fruiting body/mycelium or culture filtrate of the same mushroom species may contain chemically different antimicrobial compounds, such as anthraquinones, aromatics, fatty acids, organic acids, peptides, proteins, polysaccharides,

steroids, terpenes, etc. (Alves et al. 2013). Certainly, these compounds significantly differ in polarity and their solubility depends on the type of solvent used for the extraction of antimicrobial substances. Ethyl acetate and methanol extracts obtained, respectively, from culture liquid and mycelia of *Stereum hirsutum* and *Stereum rameale* had considerable AFA toward *Botrytis cinerea* suppressing mycelial growth and sporogenesis of the phytopathogenic fungus (Aqueveque et al. 2016). Plate diffusion assay showed that ethyl acetate extracts were more active than methanol extracts. Ethyl acetate extract produced by *S. hirsutum* inhibited 67% of the target fungus growth at a dose of 1 mg/mL and completely inhibited the sporulation at 500 mg/mL. Subsequently, Aqueveque et al. (2017) obtained ethyl acetate extract from culture liquid and methanol extract from mycelium of *S. hirsutum* after 10 days of fungus cultivation in a fermenter containing glucose, malt extract, and yeast extract-based medium. Only ethyl acetate extract showed AFA against *B. cinerea* and fractions exhibiting a marked AFA against grey mold were isolated. Of the compounds identified, Sterenin D exhibited the highest antifungal effects with an inhibition zone of 28 mm and showed MIC at 0.02 mg/mL.

Detailed work has been carried out with *Phellinus linteus* FB (Reis et al. 2014). The methanol and ethanol extracts revealed the highest activity against eight Gram+ and Gram- bacteria with MIC values lower than those in the presence of ampicillin and streptomycin (except in the case of *S. aureus*). The triterpenoids fraction was the strongest inhibitor of bacterial growth with MIC 0.16–0.28 mg/mL whereas the glucan fraction was the less effective. However, in an evaluation of the AFA, the glucan fraction appeared to be most effective against *A. versicolor*, *A. ochraceus*, *T. viride,* and *P. funiculosum* having lower MIC values than bifonazole and ketoconazole. The methanol extract had an extremely high activity against *T. viride* (MIC = 0.0045 mg/mL, against other fungi 0.16–0.72 mg/mL). Furthermore, Pala et al. (2019) evaluated the antimicrobial activity of *L. tigrinus, F. pinicola, I. hispidus*, and *R. formosa* against two Gram+, four Gram- bacteria, and four fungi. They observed no or insignificant antimicrobial activity of aqueous extracts of these mushrooms against the tested bacteria and fungi. Both methanolic and ethyl acetate extract of *F. pinicola* and *I. hispidus* showed significant antimicrobial activity against all the bacterial (Table 13.1) and fungal (Table 13.2) strains while the ethyl acetate extract of *L. tigrinus* and *R. formosa* showed significant antimicrobial activity against the bacterial strains but mild or no activity against the fungal strains.

The ABA of ethanol extracts from *Taiwanofungus salmoneus* was more effective than that of hot-water extracts (Chiang et al. 2013). Unlike ethanol extracts, hot-water extracts at 1 mg did not show any ABA, at 5 and 20 mg the inhibition zones of 5 bacterial species were 12.8–15.5 and 21.0–23.8 mm, respectively. At the same time, ethanol extracts showed effective and dose-dependent antibacterial activities with the IZD against tested pathogenic bacteria of 12.3–15.3 mm at a dose of 1 mg. The MIC of the hot-water extract against *B. cereus* was 25 mg/mL, whereas that against the rest of the bacteria was 50 mg/mL. The MIC of the ethanolic extract against pathogenic bacteria was 6.25 mg/mL, except for that against *S. typhimurium* which was 12.5 mg/mL. Both extracts were more effective against G+ bacteria than against G- bacteria. Mycelium of the submerged cultures of *Pleurotus* species

(*P. florida*, *P. citrinopileatus, P. sajor-caju*, *P. ostreatus*, and *P. eryngii*) grown in glucose-containing medium showed significant antibacterial properties (Özdal et al. 2019). The hot-water extracts of *P. ostreatus* and *P. florida* were highly antibacterial against *A. agilis* and *H. pylori,* whereas the extract of *P. eryngii* was highly antibacterial against *K. oxycota* and *X. campestris.* The extracts were distinguished with a high content of total phenolics (9.14 mg/g in *P. ostreatus* extract) and total flavonoids (3.1 mg/g in *Pleurotus sajor-caju* extract).

In early work, Barros et al. (2007) observed that antimicrobial activity of *L. deliciosus*, *T. portentosum*, and *S. imbricatu*s directly correlates with the content in total phenols and flavonoids in the entire mushroom, the mushroom cap, and the stipe. The content in total phenols and flavonoids for the stipe methanolic extracts was always lower than in the other extracts. Phenolic (cinnamic and *p*-hydroxybenzoic) acids from *G. lucidum* revealed higher activity (MICs of 0.003–0.12 mg/mL) against *A. fumigatus*, *A. versicolor*, *A. ochraceus*, *A. niger*, *T. viride*, *P. funiculosum*, *P. ochrochloron*, and *P. verrucosum* than positive controls bifonazole (MIC = 0.15 mg/mL) and ketoconazole (MIC = 1.0 mg/mL) (Heleno et al. 2013). Triterpenoid favolon B was isolated from the fermentation broth of *Mycena* spp., it showed AFA toward *Botrytis cinerea*, *M. miehei*, *P. variotii*, and *P. notatum* (Aqueveque et al. 2005). Ethanol and methanol extracts from *Ganoderma* sp. containing lanostane triterpenes were active against the *Tubercular bacilli* with the MIC values in the range of 0.05–0.78 mg/mL (Isaka et al. 2016). Steroidal compounds isolated from FB of *G. lucidum* were effective against *S. aureus* and *B. subtilis* with a MIC value of 2.5–5 mg/mL (Vazirian et al. 2014).

Several antimicrobial compounds responsible for antimicrobial activity have been isolated earlier from higher basidiomycetes, including grifolin (Hirata and Nakanishi 1950), pleuromutilin (Kavanagh et al. 1951), striatins A, B, and C (Anke and Oberwinkler 1977), scorodonin (Anke et al. 1980), oudemansin (Anke et al. 1990), strobilurin C (Anke et al. 1983), ganomycins (Mothana et al. 2000), micaceol (Zahid et al. 2006), and other. Merulinic acids A, B, and C of polyketide origin were isolated from the FB of *Merulius tremellosus* and *Phlebia radiata* (Giannetti et al. 1978). These metabolites showed exceptionally high ABA with MIC values of 0.4–10 μg/mL against *Arthrobacter citreus*, *B. subtilis*, *Corynobacterium insidiosum*, *Micrococcus roseus*, and *Sarcina lutea*. Himanimide C (N-hydroxylated maleimide derivative) isolated from *Serpula himantoides* exhibited fungicidal effect against *Alternaria porri*, *Aspergillus ochraceus*, and *Pythium irregulare* from a concentration of 0.025 mg/mL whereas fungistatic effect was observed against *Absidia glauca*, *Cladosporium cladosporiodes*, *Curvularia lunata*, *Zygorhynchus moelleri*, *Nadsonia fulvescens*, and *S. cerevisiae* (Aqueveque et al. 2002).

Eight strains of *F. velutipes* and four strains of *F. rossica* were examined for the production of enokipodins A–D, antimicrobial sesquiterpenes (after static cultivation in 3% malt extract, 0.3% peptone, at 24 °C, 46 days in the dark) (Tabuchi et al. 2020). It was found that *F. rossica* also produces enokipodins, whereas no enokipodins were detected in some strains of *F. velutipes*. Among enokipodins, enokipodin B showed the strongest growth inhibitory activity against *B. subtilis* (IC_{50} was 13.4 nmol/mL) and *E. coli* (IC_{50} was 67 nmol/mL), while enokipodins A and C

showed relatively selective anti-malarial activities against *Plasmodium falciparum* with IC_{50} of 2.4 and 1.1 μg/mL, respectively. It is worth noting that for *S. aureus* IC_{50} was more than 406.3 nmol/mL (100 μg/mL). Enokipodin B followed by enokipodin A exhibited the highest AFA against *P. oryzae* and *C. albicans*. According to Wang et al. (2012) sesquiterpenes, enokipodin F, G, and I isolated from *F. velutipes* mycelium presented low activity against *Aspergillus fumigatus* with IC50 values 229.1, 233.4, 235.1 μM, respectively.

Song et al. (2020) isolated and identified nine pure compounds (new erinacerin alkaloid, aldehyde derivative of 4-hydroxy chroman, four chlorinated orcinol derivatives, pyran, erinaceolactone, and erinacine the extract from the culture of *Hericium* sp. grown on the Cheerios substrate). Compound 4 (2-chloro-1,3-dimethoxy-5-methyl benzene) showed inhibition against *C. albicans* and *C. neoformans*, with MIC values of 62.5 and 31.25 μg/mL, respectively. Glucosylceramide was isolated from the fruiting body of *Pleurotus citrinopileatus* and its chemical composition was identified (Meng et al., 2012). The IC_{50} value of this compound for the growth of *E. coli* and *S. aureus* was 200 μg/ml and 235 μg/ml, respectively.

An antifungal protein ganodermin was isolated from *G. lucidum* with activity against phytopathogenic toxin-producing fungi, such as *B. cinerea* (IC_{50} = 0.015 mM), *F. oxysporum* (IC_{50} = 0.012 mM), and *Physalospora paricola* (IC_{50} = 0.018 mM) (Wang and Ng 2006). Purified protein, clitocypin, from *Clytocybe geotropa* showed inhibition against *Clavibacter michiganensis* subsp. *sepedonicus* when tested on agar plates (Dreo et al. 2007). Likewise, antifungal proteins were obtained from FB of *Pleurotus eryngii* (eryngin- exhibiting activity) against *F. oxysporum* and *Mycosphaerella arachidicola* (Wang and Ng 2004) and many other mushrooms. The lectin (protein) isolated and purified from FB of the Korean cauliflower medicinal mushroom *Sparassis latifolia* displayed high activity against bacteria (resistant strains of *E. coli*, *S. aureus*, and *P. aeruginosa* with MIC of 0.1, 0.2, and 0.05 mg/mL, respectively), yeast cells of *C. albicans*, *C. catenulata*, *C. glabrata*, and *C. rugosa* and against hyphae-forming fungi of *F. oxysporum* and *F. solani* (Chandrasekaran et al. 2016).

Recently, antimicrobial peptides have gained increased interest due to their high efficacy and specificity, low drug interaction and toxicity, and the inability of developing resistance by the microorganisms (Boparai and Sharma 2020). An antifungal peptide cordymin was isolated from *C. militaris* inhibiting mycelial growth in *Mycosphaerella arachidicola*, *Bipolaris maydis*, *Rhizoctonia solani*, and *C. albicans* with the IC_{50} values of 0.01 mM, 0.05 mM, 0.08 mM, and 0.75 mM, respectively. An antifungal peptide isolated from FB of edible mushroom *Lentinus squarrosulus* appeared to be especially active against clinical isolates *Trichophyton mentagrophytes* and *T. rubrum*, with inhibition zone diameter of 25.7 mm and 22.8 mm, respectively, at a dosage of 30 μg/disc (Poompouang and Suksomtip 2016). Two peptide fractions extracted from *G. lucidum* fruiting body and mycelium showed strong antibacterial activity against *E. coli* and *S. typhi* with MIC 0.06 mg and 0.052 mg, 0.042 mg and 0.036 mg, respectively (Mishra et al. 2018).

Demiri and Yamaç (2008) compared the antimicrobial activity of extracts from basidiocarps, submerged grown mycelia, and crude EPS precipitates of eight

mushroom species. Antimicrobial activities of *Lentinus strigosus* and *Clavariadelphus truncatus* FB were higher than those in other mushrooms tested. Especially heptane, chloroform, and dichloromethane extracts of *L. strigosus* showed higher antimicrobial activity as compared to the controls. The chloroform extract of *C. truncatus* basidiocarps and submerged mycelium extracts of *Cerrena unicolor* exhibited antimicrobial activity against both bacteria and yeasts. These extracts were the most active to inhibit the growth of *S. aureus*, *M. luteus*, and *E. faecium*. The activities of *C. unicolor* and *Polyporus arcularius* EPS against *E. faecium, S. aureus*, and *M. luteus* were the same as in the positive controls (vancomycine or fluconazole). However, *C. unicolor* did not show any activity against *B. subtilis*. Moreover, the activities of *Ganoderma carnosum* EPS also were higher than positive control against *M. luteus*, *E. faecium*, and *C. albicans*. However, exopolysaccharides of other basidiomycetes did not show any activity against the test cultures. Furthermore, EPS isolated from a culture liquid of *Coriolus versicolor* inhibited the growth of *S. epidermidis*, *S. aureus*, *E. faecalis*, and *B. cereus* with MIC of 0.3, 2.5, 2.5, and 5 mg/mL, respectively (Duvnjak et al. 2016). Other tested G+ bacteria were equally sensitive with a MIC value of 40 mg/mL. Among G- bacteria, *Y. enterocolitica* and *S. sonnei* were susceptible to EPS with MIC values of 10 and 20 mg/mL, respectively, whereas the *E. coli* strains were resistant to the tested concentrations of EPS.

4 Effect of Cultivation Conditions

In the literature, there is a large number of publications reporting on the effect of cultivation conditions and medium composition on mushroom growth and bioactive compounds production. Surprisingly, very limited information is available regarding the influence of cultivation parameters on the antimicrobial activity of basidiomycetes. At the same time, both submerged and solid-state fermentations are suitable cultivation techniques for the production of mushroom biomass and various metabolites. Especially, submerged cultivation in bioreactors provides a possibility to optimize the cultivation process for maximum accumulation (intracellularly or extracellularly) of the target primary or secondary metabolites. Naturally, the production of such metabolites is species-specific, associated with metabolic features of mushrooms and their physiological response to nutrient and environmental factors.

The antimicrobial properties of mushrooms can be significantly affected by nutritional and environmental factors changing mushroom metabolism and leading to variations in the production of their secondary metabolites (Barros et al. 2007; Shen et al. 2017). Vahidi et al. (2004) were among the first who studied the effect of cultivation conditions on growth and AFA of *Mycena leptocephala*. Good growth of the mushroom and AFA against *C. lipolytica* were observed when glucose (IZD – 15.2 mm) followed by fructose and maltose were used as carbon source, whereas sucrose and starch appeared to be poor carbon sources with IZD of 8.1 mm.

Likewise, a high level of antifungal activity was observed when a complex nitrogen source (yeast extract) was used as a nitrogen source (IZD – 14.8 mm), while NH_4Cl and $NaNO_3$ gave IZD of 8.2 and 7.6 mm, respectively. It was established that optimal growth and maximum AFA were observed when the mushroom cultivation was performed in a medium with an initial pH of 5.5 at 25 °C.

Comparative analysis of *Polyporus tricholoma* ABA showed that the inhibition of *S. aureus* growth by ethyl acetate extract of the culture filtrate obtained after the fungus cultivation on a malt extract-soy peptone medium was higher than that of a medium with potato dextrose (Vieira et al. 2008). The inhibitory activity of the fungus gradually increased during cultivation and achieved the maximum in the stationary phase of growth. Moreover, the authors established that lactose is a preferred carbon source as compared to glucose for the accumulation of antibacterial substances; an increase of lactose concentration from 1% to 4%, as well as substitution of static cultivation with agitation at 150 rpm favored the increase of the extract activity against *S. aureus*.

Extracts from the FB, mycelia grown in solid (Cheerios or rice substrates) and liquid media (malt or soy media), and culture supernatants of *Hericium* sp. were evaluated for antimicrobial activity by Song et al. (2020). The fruiting body extract was inactive against all of the strains tested. Only the crude extract from the Cheerios mycelial culture showed activity against both yeast pathogens *C. albicans* and *C. neoformans* with a MIC of less than 0.25 mg/mL. Extracts from soy and malt culture supernatants showed activity against *C. neoformans* with MICs comparable to the Cheerios extract, while extracts from rice cultures were active with MIC >0.50 mg/mL. Extracts from rice, malt mycelia, and supernatant, and soy supernatant exhibited weak ABA (MIC >0.50 mg/mL) against *S. aureus*; moreover, extract from the soy culture supernatant was also active against *E. faecalis* (MIC >0.50 mg/mL).

The antimicrobial activity of a wide range of basidiomycetes was evaluated under submerged cultivation on seven nutrient media (Dyakov et al. 2011). These authors showed that the tested mushrooms' activity in many cases depended on inoculum form and medium composition. Thus, *Panellus serotinus* did not produce antibiotic activity against *B. subtilis* in malt extract medium, but this mushroom expressed it in the same medium supplemented with soybean flour and distillery dregs. However, culture liquids from both media were active against *S. aureus.*

The influence of growth substrate for mushrooms antimicrobial compounds formation has been established in several studies. Thus, evaluation of ABA of *Lentinula edodes* grown in 14 different culture media revealed that rice bran, vermiculite, and molasses favor mycelial growth of mushroom and antibacterial metabolite production against *B. subtilis* (Hassegawa et al. 2005). By contrast, the sawdust-containing medium was not suitable for producing antibacterial substance(s). It is interesting that although pH 3.0–3.5 was most favorable for mushroom biomass production, the best ABA was observed at 4.5. This result indicated that incubation conditions that enhanced growth are not optimal for the ABA accumulation.

In experiments performed by Krupodorova et al. (2016), no ABA was revealed using mushroom mycelium obtained after cultivation of *P. betulinus* on

glucose-containing medium, the culture liquid completely inhibited the growth of *B. subtilis* and *S. aureus* but didn't inhibit the growth of *E. coli*. When this mushroom was cultivated on the amaranth flour containing medium mycelial suspension expressed a moderate activity (IZD = 10 mm) against *E. coli* and *B. subtilis.* Interestingly, both mycelium and culture liquid of *S. commune* grown on the glucose-based medium exhibited ABA against *B. subtilis,* whereas no activity was revealed in the culture grown on the amaranth flour containing medium. However, the opposite response of this mushroom to the medium composition was observed in testing ABA against *E. coli.*

Accumulation of EPS in submerged cultivation of *G. lucidum* and *Lysinibacillus fusiformis* only slightly depended on media containing 10 g/L glucose or 40 g/L malt extract (Mahendran et al. 2013). However, EPS isolated from malt extract-based medium exhibited significantly higher ABA against both Gram+ and Gram- bacteria than polysaccharides obtained from the glucose-containing medium. Thus, the inhibition zones of *G. lucidum* EPS from malt extract and glucose media against *E. coli* were 18 mm and 12 mm, while the inhibition zones of *L. fusiformis* EPS from the same media against *B. cereus* were 15 mm and 7 mm, respectively.

In experiments with *F. velutipes*, the type of culture medium influenced both the mycelia growth and the antimicrobial metabolite production (de Melo et al. 2009). This mushroom produces enokipodins in the stationary stage of *F. velutipes* mycelia development in malt extract broth (MEB). The PDB medium provided the best mycelial growth but not optimum production of the antimicrobial compound. At the same time, complete Pontecorvo's medium resulted in greater antibacterial metabolite production than the control MEB culture medium. The authors suggested that exhaustion of the carbon in the Pontecorvo's medium and/or the excess of some mineral and/or vitamin component activated the enokipodins biosynthesis. This study showed that there was no correlation between biomass and antimicrobial metabolite production, but there may be a correlation between culture medium composition and enokipodins biosynthesis. It should also be mentioned that a rise in temperature from 25° to 37 °C on the 15th day of *F. velutipes* mycelia cultivation in malt extract-peptone broth favored antimicrobial metabolite production. Likewise, evaluation of the antimicrobial activity of extracts from the culture broth of *L. sulphureus* grown under different culture conditions (temperature 20 and 28 °C, shaking and static conditions, medium pH 5, 6, and 7) showed that static cultivation of mushroom at medium pH 5 and 20 °C favored the accumulation of antimicrobial activity against *X. vesicatoria* and *S. aureus* (Barneche et al., 2016).

In our studies, we exploited physiological approaches to elucidate cultivation conditions enhancing the antimicrobial activity of selected mushrooms. In particular, among carbon sources tested for the cultivation of *S. commune*, xylose ensured the highest (70%) inhibition of *S. aureus* growth, whereas the highest inhibition activity (60%) against *E. coli* was detected when the fungus was grown in the medium containing glucose (Khardziani et al. 2020). Submerged fermentation of mandarin pomace by *S. commune* provided the highest ABA toward *S. aureus* (89% growth inhibition) and *E. coli* (90% inhibition). The banana peels fermentation ensured 54% and 35% inhibition of *S. aureus.* It is worth noting that no ABA was

observed after fermentation of corn cobs, ethanol production residue (EPR), and wheat bran by *S. commune*. However, the same samples of culture liquids showed ABA against *E. coli* with an 18–36% growth inhibition effect. Testing of abiotic controls obtained after sterilization of lignocellulose-containing media did not reveal any statistically significant ABA. In this study, we showed that the method of lignocellulosic materials fermentation affects antibacterial substances production by *S. commune*. Specifically, unlike submerged fermentation, 12%, 88%, and 76% inhibitions of *S. aureus* growth were revealed, respectively, in the corncobs, EPR, and wheat bran solid-state fermentation. Interestingly, the antifungal activity of *S. commune* against *Fusarium* sp., *Aspergillus* sp., and *Guinardia bidwellii* only a little depended on the carbon source used for the mushroom submerged cultivation (unpublished results). Another picture was revealed in submerged fermentation of lignocellulosic materials. Specifically, culture filtrate obtained after fermentation of mandarin pomace caused 55, 85, and 91% inhibition of *Fusarium* sp., *Aspergillus* sp., and *Guinardia bidwellii* growth, respectively. Wheat bran also provided the high antifungal activity of *S. commune,* whereas corn cobs and wheat straw appeared to be poor substrates for secretion of antifungal compounds.

5 Conclusions

Analysis of the published data in this chapter shows that basidiomycete medicinal mushrooms are promising sources of a wide range of chemically diverse biologically active compounds, including those with antimicrobial activity against a broad spectrum of pathogen microorganisms. To effectively exploit the mushroom potential in mycopharmacology is an exciting task. Therefore, we believe that future research should focus on several interrelated aspects. In particular, the expansion of search and bioprospecting of geographically, climatically, ecologically, and biologically diverse habitats is necessary to discover new promising producers of antimicrobial substances. Certainly, to correctly evaluate and compare the results on the antimicrobial potential of mushrooms reported by different authors standardization and unification of methods for the extraction of biologically active compounds and an assay of ABA and AFA against specific pathogens is necessary.

One of the main challenges for future research is to focus on fundamental physiological studies to develop innovative approaches and strategies for the sustainable production of inexpensive antimicrobials under controlled conditions. A better understanding of the factors that regulate fungal metabolism and affect not only fungal growth but also the production of antimicrobial compounds is critical to maximizing the profitability of producing targeted drags. An interesting approach may be to create stressful cultivation conditions that can affect secondary metabolism, including the activation of silent genes involved in the production of bioactive compounds. Likewise, co-cultivating fungi with pathogens can be a promising strategy to increase their antimicrobial activity.

Finally, numerous extracts and individual compounds containing ABA and/or AFA have already been isolated from mushroom cultures. Similar to penicillin and other antibiotics, future research should establish the mechanisms of action of these natural compounds responsible for antimicrobial activity.

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