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

MARIA JOSÉ ALVES[1,2,3,4], ISABEL C.F.R. FERREIRA[3,*], JOANA DIAS[4], VÂNIA TEIXEIRA[4] , ANABELA MARTINS[3], MANUELA PINTADO[1,*]

[1]CBQF-Escola Superior de Biotecnologia, Universidade Católica Portuguesa Porto, Rua Dr. António Bernardino de Almeida, 4200-072 Porto, Portugal.

[2]Centro Hospitalar de Trás-os-Montes e Alto Douro- Unidade de Chaves, Av. Dr. Francisco Sá Carneiro, 5400-249 Chaves, Portugal.

[3]CIMO-Escola Superior Agrária, Instituto Politécnico de Bragança, Campus de Santa Apolónia, Apartado 1172, 5301-855 Bragança, Portugal.

[4]Escola Superior de Saúde, Instituto Politécnico de Bragança, Av. D. Afonso V, 5300-121 Bragança, Portugal.

* Authors to whom correspondence should be addressed (e-mail: iferreira@ipb.pt, telephone +351-273-303219, fax +351-273-325405; e-mail: mpintado@porto.ucp.pt, telephone +351-22-5580097, fax +351-22-5090351).

Abstract

Despite the huge diversity of antibacterial compounds, bacterial resistance to first choice antibiotics has been drastically increasing. Moreover, the association between multi-resistant microorganisms and nosocomial infections highlight the problem, and the urgent need for solutions. Natural resources have been exploited in the last years and among them mushrooms could be an alternative as source of new antimicrobials. In this review we present an overview about the antimicrobial properties of mushroom extracts, highlight some of the active compounds identified including low and high molecular weight (LMW and HMW, respectively) compounds. LMW compounds are mainly secondary metabolites, such as sesquiterpenes and other terpenes, steroids, anthraquinones, benzoic acid derivatives, and quinolines, but also primary metabolites such as oxalic acid. HMW compounds are mainly peptides and proteins. Data available from literature indicate a higher antimicrobial activity of mushroom extracts against Gram-positive bacteria. Among all the mushrooms, *Lentinus edodes* is the most studied species and seems to have a broad antimicrobial action against both Gram-postive and Gram-negative bacteria. Plectasin peptide, obtained from *Pseudoplectania nigrella*, is the isolated compound with highest antimicrobial activity against Gram-positive bacteria, while 2-aminoquinoline, isolated from *Leucopaxillus albissimus*, presents the highest antimicrobial activity against Gram-negative bacteria.

Key words: Mushrooms; Basidiomycetes; Antimicrobials; Gram positive bacteria; Gram negative bacteria

Abbreviations

CSAP	*Cordyceps sinensis* antibacterial protein
CFU	Colony-forming unities
ERSP	Erythromycin-resistant *Streptococcus pyogenes*
HMW	High molecular weight compounds
IC_{50}	Concentration inhibiting 50% of the growth
IZD	Internal zone diameter
LMW	Low molecular weight compounds
M	Mycelium
MIC	Minimal inhibitory concentration
MRSA	Methicillin-resistant *Staphylococcus aureus*
MRSE	Methicillin-resistant *Staphylococcus epidermidis*
PABA	*para*-Aminobenzoic acid
PRSP	Penicillin-resistant *Streptococcus pneumonia*
VREF	Vancomycin-resistant *Enterococcus faecium*

Introduction

Mushrooms bioactivity

For a long time mushrooms have been playing an important role in several aspects of the human activity. Edible mushrooms, for example, are used extensively in cooking and make part of low calorie diets. Mythology is extensively garnished by mushrooms, typically associated with gnomes, fairies and other fairytale personages. The psychedelic and consciousness expansion properties of some species have pushed mushrooms to become part of some religions. Even toxic mushrooms have found a place of relevance, because of the uniqueness of their compounds that evolved naturally as a protection against consumption [1].

Wild and cultivated mushrooms contain a huge diversity of biomolecules with nutritional [2] and/or medicinal properties [3-5]. Due to these properties, they have been recognized as functional foods, and as a source for the development of medicines and nutraceuticals. Fruiting bodies, mycelia and spores accumulate a variety of bioactive metabolites with immunomodulatory, cardiovascular, liver protective, anti-fibrotic, anti-inflammatory, anti-diabetic, anti-viral, antioxidant, antitumor, and antimicrobial properties [3-14]

The frequent use of mushrooms is based on three main assumptions: first they are used as part of regular diet for their nutritional value (since they are rich in water, minerals, proteins, fibers and carbohydrates, and are low caloric foods due to low content in fat [2]); secondly, fruiting bodies are also appreciated for their delicacy (they are palatability enhancers of flavor and aroma when associated to other foods); thirdly, mushrooms are widely used for medicinal purposes. Their pharmacological action and therapeutic interest in promoting human health have been known for thousands of years [5, 15,16].

In particular, mushrooms could be a source of natural antibiotics, which can be low or high molecular weight (LMW and HMW, respectively) compounds. LMW compounds are mainly secondary metabolites such as sesquiterpenes and other terpenes, steroids, antraquinone and benzoic acid derivatives, and quinolines, but also primary metabolites such as oxalic acid (**Figure 1**). HMW compounds include mainly peptides and proteins.

It is estimated that there are about 140,000 species of mushrooms on earth and of these only 22,000 are known and only a small percentage (5%) was investigated. Therefore, there is much to explore about mushrooms properties and potential applications [4].

Bacteria and drug discovery

The development of antibiotics has been one of the most important scientific achievements of the last seventy years. These compounds act in several ways, by interfering in metabolic processes or in the organism structures [17]. The mechanism of action is mostly related with interferences in the synthesis of cell wall, modification of plasmatic membrane permeability, interferences in chromosomes replication or in protein synthesis [18]. The cell wall is responsible for the shape and rigidity of bacterial cells, acting as osmotic barrier [19]. The peptidoglycan content in the cell wall varies between 10% and 60% for Gram negative and Gram positive bacteria, respectively [20, 21].

Antiparietal antibiotics act in one of the phases of peptidoglycan synthesis, being classified according to that phase. Phosphomycin, D-cycloserine, glycopeptides (bacitracin, vancomycin, teicoplanin) and beta-lactams (penicillins, cephalosporins, carbapenemics and monobactamics) are some examples of this group [22].

Otherwise, other antibiotics such as ascolistin and daptomycin act at the cell membrane level. Aminoglycosides and tetracyclines, macrolides, oxazolidines, quinupristin and

dalfopristin, clindamycin and chloramphenicol inibhit protein synthesis by interfering with 30s or 50s ribosomal subunits. Quinolones, rifampicin and metronidazol inibhit nucleic acids synthesis..Sulfonamides and trimetoprim are antimetabolic antibiotics that inhibit the metabolic chain of *para*-aminobenzoic acid (PABA), essential to cell growth [23].

Despite the huge diversity of antibacterial compounds, bacterial resistance to first choice antibiotics has been drastically increasing. Some examples are microorganisms such as *Klebsiella* spp. and *Escherichia coli* producing broad spectrum beta-lactamase or presenting resistance to third generation cephalosporins. Other examples include methicillin-resistant *Staphylococcus aureus* (MRSA), *Enterococcus* spp. resistant to vancomycin [24, 25], *Acinetobacter* spp. with increasing resistance to carbapenems and colistin [26], and also *Pseudomonas* spp. resistant to aminoglycosides, carbapenemics and/or cephalosporins [24].

Diseases that were easily healed are nowadays becoming a serious problem due to the emergent antibiotics resistance [27,28]. The association between multi-resistant microorganisms and hospital infections certainly highlighted the problem and the urgent need for solutions [29]. In 2010, the World Health Organization advised all the countries to implement control procedures for the propagation of drug multi-resistant bacteria, highlighting the risks associated to the absence of alternative therapies against those microorganisms [30].

Therefore, the research of new antimicrobial substances effective against pathogenic microorganisms resistant to current drugs is crucial. New groups of organisms such as marine have been increasingly exploredin the last years and among them mushrooms could be an alternative as source of new antimicrobials. In this review we provide an overview about the antimicrobial properties of mushroom extracts and highlight

selected compounds. The databases searched were Medline (1980 to March 2012) and Web of Science (2001 to March 2012) including scientific articles and conference proceedings. Search terms were: 'mushrooms', 'antimicrobial activity' and 'antimicrobials'. An exhaustive literature search was performed but only mushroom extracts and isolated compounds with positive results were included.

Antimicrobial activity against gram positive bacteria

Methodologies

Different methodologies have been used to acess 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 incorportation of the extract in the culture medium and further determination of colonies. Therefore, the results for antimicrobial activity are expressed in different unities (Tables **1** and **2**).

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 difusion 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 unities (CFU) are determined.

Mushroom extracts with antimicrobial activity

Numerous mushroom extracts have been reported as having antimicrobial activity against Gram-positive bacteria (**Table 1**).

Agaricus bisporus, the most cultivated mushroom in the world, should be highlighted. Its methanolic extract revealed MIC = 5µg/mL against *Bacillus subtilis* even lower than the standard ampicillin (MIC = 12.5 µg/mL) [31] and also showed activity against *Bacillus cereus, Micrococcus luteus*, *Micrococcus flavus*, *Staphylococcus aureus* and *Staphylococcus epidermidis* [15, 32, 33]. Other *Agaricus* species also demonstrate antimicrobial activity. *Agaricus bitorquis* and *Agaricus essettei* methanolic extracts showed inhibitory effect upon all the tested Gram-positive bacteria [15]. *Agaricus silvicola* methanolic extract also revealed antimicrobial properties against *Bacillus cereus* (MIC = 5µg/mL), *Bacillus subtilis* (MIC = 50µg/mL), and against *Staphylococcus aureus* (MIC = 5µg/mL), lower than the standard ampicillin (MIC = 6.25µg/mL) [31]. The mycelium of *Agaricus* cf. *nigrecentulus* and *Tyromyces duracinus* (ethyl acetate extracts) showed activity only against *Staphylococcus saprophyticus* [34].

The ethanolic extracts of *Armillaria mellea* mycelium showed antibacterial effect against *Sarcina lutea*, however no activity was observed upon other Gram-positive bacteria [35]. However, ethanolic extract of their fruiting bodies showed broad-spectrum antimicrobial activity [36].

The most studied mushrooms of the genus Boletus is *Boletus edulis*. Its methanolic mushroom showed lower antimicrobial activity than other species studied by Ozen et al. [32]. Nevertheless, Barros et al. [31] reported MIC = 5µg/mL against *Staphylococcus aureus* lower than ampicilin (MIC = 6.25µg/mL).

Cantharellus cibarius methanolic extract demonstrated good activity against *Bacillus subtilis* and *Staphylococcus aureus* [31, 32, 37]. This mushroom had activity against

Bacillus cereus in some studies [32, 37], but it was not so effective in other report [31], which could be related to the different methodologies used to evaluate antimicrobial activity.

Clitocybe alexandri methanolic extract presented significant activity against *Bacillus subtilis* and *Micrococcus luteus* [38]. Kalyoncu et al. [36] tested antimicrobial activity of chloroform and ethanolic extracts from *Clitocybe geotropa*, the latter showing significant capacity against *Bacillus cereus*.

The genus *Cortinarius* is one of the most diverse genera of mushrooms. Ethyl acetate extracts of *C. ardesiacus*, *C. archeri*, *C. atrosanguineus*, *C. austrovenetus*, *C. austroviolaceus*, *C. coelopus*, *C.* [*Dermocybe canaria*], *C. clelandii*, *C.* [*D. kula*], *C. memoria-annae*, *C. persplendidus*, *C. sinapicolor*, *C. vinosipes* and others 47 collection samples not identified to species level, exhibited IC_{50} values of ≤ 0.09 mg/mL against *Staphylococcus aureus* [10]. However in a study reported by Ozen et al. [32], *Cortinarius* sp. methanolic extracts showed lower activity against *Staphylococcus aureus*. This demonstrates the effect of solvent extraction in the type and concentration of compounds present in the final extract and consequently the spectrum of antimicrobial activity.

Ganoderma lucidum is one of the most famous traditional medicinal mushrooms. Various extracts have been found to be equally effective when compared with gentamycin sulphate, the acetone extract being the most effective. This mushroom had moderate inhibition against *Bacillus subtilis* and *Staphylococcus aureus* for any extract [39], but in the study reported by Sheena et al. [40] its methanolic extract showed poor antimicrobial activity. Other authors described the capacity of the aqueous extract to inhibit 15 types of Gram-positive and Gram-negative bacteria, with the highest inhibition exhibited against *Micrococcus luteus* [41].

Ethyl acetate extracts of *Phellinus* sp., *Gloeoporus thelephoroides* and *Hexagonia hydnoides* inhibited *Bacillus cereus* growth while the same extract of *Nothopanus hygrophanus* mycelium presented inhibitory activity against *Listeria monocytogenes* and *Staphylococcus aureus*. *Irpex lacteus* mycelium extract was the most effective presenting a broad spectrum of activity [34].

The antimicrobial activity of *Pycnoporus sanguineus* has been known since 1946, when Bose isolated poliporin, a compound active against Gram-positive and Gram-negative bacteria and without toxicity in experimental animals. Rosa et al. reported inhibition against *Listeria monocytogenes* and *Staphylococcus aureus* [34]. Smânia et al. [42, 43] showed that this mushroom produces cinnabarine, an orange pigment active against *Bacillus cereus*, *Staphylococcus aureus, Leuconostoc mesenteroides, Lactobacillus plantarum* and several *Streptococcus* spp. Cinnabarine was more active against Gram-positive than Gram-negative bacteria [34].

The chloroform extract of *Hygrophorus agathosmus* and dichloromethane of *Suillus collitinus* were active against all the tested Gram-positive bacteria. The highest antibacterial activity was seen in the extract of *H. agathosmus* against *Staphylococcus epidermidis* and *Bacillus subtilis*, with MIC values 7.81 µg/mL lower than the reference antibiotic streptomycin (MIC = 15.62 µg/mL). MIC values (15.62 µg/mL) against *Staphylococcus aureus* were equal to the ones of streptomycin. *Suillus collitinus* showed MIC values much higher than the standard [44].

One non-edible mushroom, *Hypholoma fasciculare* (methanolic extract) presented high antimicrobial activity against Gram-positive bacteria namely *Bacillus cereus*, *Bacillus subtilis* and *Staphylococcus aureus* [37].

All the tested Gram-positive bacteria were susceptible to methanolic extracts of *Lactarius* species and *Tricholoma portentosum* [32, 45, 46]. Among *Lactarius* species

(*L. piperatus*, *L. camphorates*, *L. volemus*, *L. delicious*), *L. camphoratus* methanolic extract was the one with greater antimicrobial activity [32]. Methanolic extracts of *Ramaria botrytis* and ethanolic extract of *Ramaria flava* inhibited the growth of Gram-positive bacteria better than Gram-negative bacteria [47]. The antimicrobial effect of ethanolic extract of *Laetiporus sulphureus* was tested by Turkoglu et al. [48] and strongly inhibited the growth of the Gram-positive tested, including *Bacillus subtilis*, *Bacillus cereus*, *Micrococcus luteus* and *Micrococcus flavus*.

Lepista nuda methanolic extract had a good action on Gram-positive bacteria, more specifically on *Bacillus cereus*, *Bacillus subtilis* and *Staphylococcus aureus* [37, 49].

Ishikawa et al. reported the inhibitory activity of *Lentinus edodes* ethyl acetate extract against *Bacillus cereus*, *Bacillus subtilis*, *Staphylococcus aureus*, and *Staphylococcus* epidermidis [11]. This mushroom (aqueous extract) as also the n-BuOH fraction of *Phellinus linteus* methanol extract demonstrated good activity against MRSA [50, 51]. Furthermore, *Streptococcus pyogenes* was very sensitive to *Lentinus edodes* chloroform extract [52]. The ability of *L. edodes* extracts to improve oral health has also been extensively researched, since it showed strong bactericidal effect upon *Streptococcus mutans* that is strongly implicated in dental caries and tooth decay [53, 54].

Mycelium of *Leucopaxillus giganteus* (methanolic extract) presented antimicrobial capacity, inhibiting only Gram-positive bacteria and in the decreasing order *Staphylococcus* aureus > *Bacillus cereus* > *Bacillus subtilis* [55]. The authors stated that the most promising nitrogen source to produce mushrooms with increased content in bioactive compounds that inhibit Gram positive bacteria growth was $(NH_4)_2HPO_4$.

Methanolic extract of *Phellinus rimosus* and *Navesporus floccosa* showed moderate inhibition of *Bacillus subtilis* and *Staphylococcus aureus* [40].

Pleurotus ostreatus and *Meripilus giganteus* showed broad-spectrum antimicrobial activity. The maximum effect was shown by ethanolic extracts of *Pleurotus ostreatus* against *Sarcina lutea* [35].

Ether extract of *Pleurotus sajor-caju* showed high antibacterial activity against *Staphylococcus aureus*, whereas *Staphylococcus epidermidis* showed high sensitivity for ethanol extract [33].

Overall, it should be pointed out that the most susceptible Gram positive bacteria to mushrooms inhibitory action are *Staphylococos aureus*, *Bacillus cereus* and *Bacillus subtilis*. *Agaricus bisporus* [15, 32, 33], *Agaricus bitorquis* [15], *Boletus edulis* [31, 32], *Cantharellus cibarius* [31, 32, 37], *Lentinus edodes* [11, 50, 54], and different *Cortinarius* sp. [10], seem to be a good option to inhibit *Staphylococos aureus*, and in some cases *Bacillus cereus* and *Bacillus subtilis*. Studies with microorganisms related to nosocomial infections and multiresistance cases such as *Enterococcus faecalis, Enterococcus faecium* and MRSA are scarce. Nevertheless, in the few studies available, *Lentinus edodes* [50] was reported to inhibit *Enterococcus faecalis*, *Enterococcus faecium* and MRSA. The latter micrrorganism was also inhibited by *Phellinus linteus* [51] and *Pleurotus ostreatus* [50]. It is important to develop new studies with different mushroom species and, moreover, with these microorganisms so problematic to human health.

Antimicrobial compounds from mushrooms

Most studies on mushrooms with antibacterial activity, describes the action of its extracts without identifying the compounds responsible for this activity. However, some compounds have been described as active against Gram-positive bacteria (**Table 2**). Five of these compounds are terpenes. Confluentin **(1a)**, Grifolin **(1b)** and Neogrifolin

(1c) from *Albatrellus fletti* had activity against *Bacillus cereus* and *Enterococcus faecalis*. The best result was for *Enterococcus faecalis* (MIC 0.5 to 1.0 mg/mL) [56]. Ganomycin A and B **(5 a, b)**, isolated from *Ganoderma pfeifferi*, showed activity against *Bacillus subtilis, Micrococcus flavus* and *Staphylococcus aureus* (15-25 mm zones of inhibition at a concentration of 250µg/mL [57].

A steroid, 3,11-dioxolanosta-8,24(Z)-diene-26-oic acid **(2)**, was isolated from *Jahnoporus hirtus* mushroom and revealed activity against *Bacillus cereus* and *Enterococcus faecalis* [56].

Four sesquiterpenes with antimicrobial activity were described. The Enokipodins A, B, C and D **(4a-d)**, isolated from mycelium of *Flammulina velutipes,* with activity against *Bacillus subtilis,* but only Enokipodins A and C showed activity against *Staphylococcus aureus* [58].

Oxalic acid **(3)**, an organic acid, isolated from mycelium of *Lentinus edodes,* showed activity against *Bacillus cereus, Staphylococcus aureus* and *Streptococcus faecalis* [59].

Coloratin A **(10)**, a benzoic acid derivative isolated from *Xylaria intracolarata,* inhibited *Staphylococcus aureus* [60].

Eight compounds anthraquinones derivatives were also reported due to their antibacterial activities. 6-Methylxanthopurpurin-3-*O*-methyl ether **(7)**, (1*S,* 3*S)*-Austrocortilutein **(8a)**, (*1S,3R*)-Austrocortilutein **(8b)**, (*1S,3S*)-Austrocortirubin **(8c)** and Torosachrysone **(8d)**, isolated from the mushroom *Cortinarius basirubencens*, and Physcion **(9a)**, Erythroglaucin **(9b)** and Emodin **(9c)** isolated from other species of *Cortinarius* were all effective against *Staphylococcus aureus* [10].

In addition to the LMW compounds already mentioned, several antimicrobial compounds with HMW have also been described, in particular proteins and peptides.

CSAP (*Cordyceps sinensis* Antibacterial Protein-N-terminal sequence ALATQHGAP) isolated from *Cordyceps sinensis,* showed strong activity against *Staphylococcus aureus* and poor activity against *Bacillus subtilis.* However, the antibacterial action of this protein was bacteriostatic [61].

The Ribonuclease isolated from *Pleurotus sajor-caju* had activity against *Staphylococcus aureus,* acting on RNA [62].

The peptide Plectasin, isolated from *Pseudoplectania nigrella*, is a macromolecule belonging to the class of defensins, present in animals and plants, which acts at the cell wall, more specifically in the synthesis of peptidoglycan. This peptide showed activity against *Bacillus cereus, Bacillus thuringiensis, Corynebacterium diphtheriae, Corynebacterium jeikeium, Enterococcus faecalis, Enterococcus faecium,* vancomycin-resistant *Enterococcus faecium* (VREF), *Staphylococcus aureus,* MRSA, *Staphylococcus epidermidis,* methicillin-resistant *Staphylococcus epidermidis* (MRSE), *Streptococcus pneumonia,* penicillin-resistant *Streptococcus pneumonia* (PRSP), *Streptococcus pyogenes* and erythromycin-resistant *Streptococcus pyogenes* (ERSP). The *in vitro* action of Plectasin against *Streptococcus pneumoniae* is comparable to the action of penicillin and vancomycin [63].

The peptides Peptaibol Boletusin, Pepteibol Chrysospermin 3 and Peptaibol Chrysospermin 5 (isolated from *Boletus spp.*), allow the opening of pores for ions transport, and showed activity against *Bacillus subtilis*, *Corynebacterium lilium* and *Staphylococcus aureus*. The Peptaibol Chrysospermin 3 also had activity against *Streptococcus* sp. [64].

Fraction B from *Pycnoporus sanguineus* obtained by Smânia et al. [42], whose main constituent is a phenoxazin-3-one type pigment, showed activity against *Staphylococcus*

aureus and *Streptococcus* A, B, C and G. Lower values of MIC were obtained against *Streptococcus* strains.

The mechanisms of action of most of the compounds described above are not available in literature.

Antimicrobial activity against gram negative bacteria

Methodologies

The same methodologies already described for Gram positive bacteria are also used in the evaluation of mushroom extracts or compounds antimicrobial activity against Gram negative bactéria. The results are presented in Tables **3** and **4**.

Mushroom extracts with antimicrobial activity

The antimicrobial activity against Gram negative bacteria showed by different mushroom extracts is not so extensive and is shown in Table **3**.

The results for *Agaricus bisporus* are contradictory. Barros et al. [31] and Öztürk et al. [15] found no activity against Gram negative bacteria, while Ozen et al. [32] and Tambeker et al. [33] reported positive activity mainly against *Escherichia coli*, but also against *Pseudomonas aeruginosa*, *Enterobacter aerogenes*, *Klebsiella pneumoniae*, *Proteus vulgaris*, *Salmonella typhi* and *Salmonella typhimurium*. However, these divergences may be due to different methods and concentrations used. *Agaricus bitorquis* methanolic extract had some effects against three of Gram negative bacteria namely *Yersinia enterocolitica*, *Klebsiella pneumoniae* and *Proteus vulgaris* [15]. *Agaricus essettei*, *Agaricus silvicola*, *Agaricus silvaticus* and *Agaricus* cf. *nigrecentulus* did not show any antibacterial activity against Gram negative bacteria [15, 31, 34].

Ethanolic extracts of *Armillaria mellea* fruiting bodies revealed better antimicrobial activity than chloroform extracts and mycelium extract upon Gram negative bacteria [35, 36].

According to Barros et al. [31, 37] *Cantharellus cibarius* showed no activity against Gram negative bacteria as opposed to Ozen et al. [32] which showed activity against *Escherichia coli* and *Pseudomonas aeruginosa*.

Enterobacter aerogenes and *Escherichia coli* were inhibited by methanolic extract of *Clitocybe alexandri* [38]. *Clitocybe geotropa* chloroform and ethanolic extracts inhibited the growth of all Gram-negative bacteria tested, being *Proteus vulgaris* the most sensitive [36].

Beatttie et al. [10] report the anti-*Pseudomonas aeruginosa* activity of the genus *Cortinarius* and its subgenus, *Dermocybe* (methanolic extracts). The species tested were four, namely *C. abnormis*, *C. austroalbidus*, *C.* [*D. kula*], *C. persplendidus*, and eleven *Cortinarius* collection samples not identified to species level, obtaining IC_{50} values ≤ 0.09 mg/mL against *P. aeruginosa*.

Acetone extract from *Ganoderma lucidum* had strong antibacterial activity mainly against *Klebsiella pneumonia* [39]. Further studies indicate that the antimicrobial combination of *G. lucidum* extracts with chemotherapeutic agents (ampicillin, cefazolin, oxytetracycline, and chloramphenicol) resulted in synergism or antagonism, with synergism observed when combined with cefazolin against *Bacillus subtilis* and *Klebsiella oxytoca* [40, 65].

Mycelium extract from *Leucoagaricus* cf. *cinereus*, *Marasmius* cf. *bellus* and *Marasmius* sp. were capable of inhibiting the growth of *Escherichia coli*. Within the family *Tricholomataceae*, species from the genus *Marasmius* have long been known to produce interesting secondary metabolites [66].

Hydnum repandum methanolic extract was mainly active against *Pseudomonas aeruginosa*. *Escherichia coli* was found to be the most sensitive bacteria to methanolic extracts of *Lactarius* species [32]. However, it was not observed activity of *Lactarius delicious* against *E. coli* [45, 46].

Laetiporus sulphureus ethanolic extract had a lower antibacterial spectrum against Gram negative bacteria, having no activity against *Klebsiella pneumonia* [48].

On three occasions, namely with the *Pseudomonas* sp., *Lentinus edodes* aqueous extract was significantly more active than ciprofloxacin (positive control), whereby it gave markedly greater zones of inhibition. This result is of important clinical significance, as *P. aeruginosa* is emerging as a major aetiological of nosocomial infection [50]. *L. edodes* mycelium had no effect on *Escherichia coli*, *Pseudomonas fluorescens*, *Klebsiella pneumoniae* and *Camphylobacter jejuni* [52].

Extracts from *Lentinus edodes* showed strong bactericidal effect against *Prevotella intermedia*, which is associated with gingivitis. This mushroom was capable of significantly reducing dental plaque deposition [53, 54, 67, 68].

Lepista nuda methanolic extract was effective against *Escherichia coli* and *Pseudomonas aeruginosa* [49].

Tambeker et al. [33] reported the antimicrobial ability of several extracts of *Pleurotus sajor-caju. Escherichia coli*, *Enterococcus aerogenes*, *Pseudomonas aeruginosa* and *Klebsiella pneumoniae* were most sensitive to ethanolic, methanolic and xylene extracts.

Overall, among the tested Gram negative bacteria, *Escherichia coli* and *Klebsiella pneumoniae* are the most susceptible to mushrooms inhibitory effect. *Agaricus bisporus* [32, 33], *Lentinus edodes* [50, 54], *Ganoderma lucidum* [39, 40] and *Lepista nuda* [49] seem to have the higher antimicrobial activity against those microorganisms.

Pseudomonas aeruginosa was inhibited by *Clitocybe alexandri* [38], *Boletus edulis, Cantharellus cibarius* [32], *Ganoderma lucidum* [39] and *Cortinarius* sp. [10] extracts. Studies with *Enterobacter aerogenes* and *Serratia marcescens* are scarce, and due to the importance in multiresistance area, they should be carrried out to assess sensibility to extracts from mushroom species.

Antimicrobial compounds from mushrooms

Some of the compounds discussed in section 2.2. and other have also been described for their action against Gram-negative bacteria (**Table 4**).

Terpenes **5a** and **5b** isolated from *Ganoderma pfeifferi*, showed moderate activity against *Escherichia coli*, *Proteus mirabilis* and *Serratia marcescens* [57].

The organic acid **3**, isolated from mycelium of *Lentinus edodes,* showed activity against *Klebsiella pneumoniae, Proteus vulgaris, Pseudomonas aeruginosa* and *Pseudomonas fluorescens* [59].

The benzoic acid derivative **10** isolated from *Xylaria intracolarata*, showed activity against *Escherichia coli, Klebsiella pneumonia, Pseudomonas aeruginosa* and *Salmonella enteritidis.* For this compound the highest inhibition (22 mm) was found in *Klebsiella pneumonia,* higher than the control (gentamicin, 14 mm) [60].

Compounds **7, 8a-d** (*Cortinarius basirubescens*) and **9a-c** (*Cortinarius* spp.) were effective against *Pseudomonas aeruginosa* [10].

The quinoline **6**, isolated from *Leucopaxillus albissimus*, showed activity against *Achromobacter xyloxidans, Acinetobacter baumannii, Burkholderia cenocepacia, Burkholderia cepacia, Burkholderia multivorans, Cytophaga johnsonae,* and *Pseudomonas aeruginosa.* Among the thirteen microorganisms tested, *Cytophaga johnsonae* was the most strongly inhibited (16 mm) [69].

Some proteins have also been reported against Gram-negative bacteria. The protein CSAP isolated from *Cordyceps sinensis* and already mentioned above, showed activity against *Escherichia coli, Proteus vulgaris and Salmonella typhi* [61], while the protein (N-terminal sequence SVQATVNGDKML) isolated from *Clitocybe sinopica* was active against *Agrobacterium rhizogenes, Agrobacterium tumefaciens, Agrobacterium vitis, Xanthomonas malvacearum* and *Xanthomonas oryzae* [70].

Ribonuclease (*Pleurotus sajor-caju*) had activity against *Pseudomonas aeruginosa* and *Pseudomonas fluorescens,* acting at RNA level [62].

Fraction B (*Pycnoporus sanguineus*) showed activity against *Escherichia coli, Klebsiella pneumoniae, Pseudomonas aeruginosa* and *Salmonella typhi* [42].

Unfortunatly, the mechanism of action of each one of the isolated compounds is not completly clear and described in the available reports.

Concluding remarks

The present review focuses on antimicrobial effects of mushrooms from all over the world, and their isolated compounds. It will be certainly useful for future scientific studies. Both edible and not edible mushrooms show antimicrobial activity against pathogenic microorganisms, including bacteria associated with nosocomial infections (*Pseudomonas aeruginosa, Pseudomonas maltophila, Listeria monocytogenes, Staphylococcus aureus, Klebsiella pneumoniae, Morganella morganii, Proteus mirabilis*, *Serratia marcescens*) and multi-resistance (MRSA, MRSE, VREF, PRSP, ERSP).

Data available from literature indicates that mushroom extracts and isolated compounds exhibit higher antimicrobial activity against Gram-positive than Gram-negative bacteria. Among all the mushrooms, *Lentinus edodes* is the best studied species and seems to

possess broad antimicrobial action against both Gram-positive and Gram-negative bacteria. Species from the genera *Boletus*, *Ganoderma* and *Lepista* appear promising for future studies, if one considers the good activity and limited number of publications. Considering the low number of studies with individual compounds, Plectasin peptide, isolated from *Pseudoplectania nigrella*, revealed the highest antimicrobial activity against Gram-positive bacteria.

The comparison of the results reported by different authors is dificult, due to the diverse methodologies used to evaluate antimicrobial activity of mushroom extracts or isolated compounds. Therefore, the standardization of methods and establishment of cut-off values is urgent. The knowledge about the mechanisms of action of different compounds might leads to the discovery of new active principles for antimicrobial activity. Furthermore, the application of citotoxicity assays is also important to evaluate the effects on human in the range of the *in vitro* tested concentrations.

The research on mushrooms is extensive and hundreds of species have been demonstrated a broad spectrum of pharmacological activities, including antimicrobial activity. Although there are a number of studies available in literature, they are almost entirely focused on screening of antibacterial properties of mushroom extracts. In fact, there is a gap on identification of individual compounds responsible for those properties, and only a few low molecular weight compounds and some peptides and proteins have been described. After eluciadation of their mechanism of action, these mushroom metabolites or other related compounds could be used to develop nutraceuticals or drugs effective against pathogenic microorganisms resistant to conventional treatments.

Aknowledgements

This work was funded by Fundação para a Ciência e a Tecnologia (FCT, Portugal) and COMPETE/QREN/EU (research project PTDC/AGR-ALI/110062/2009; CIMO strategic project PEst-OE/AGR/UI0690/2011 and project PEst-OE/EQB/LA0016/2011. It was also supported by CHTAD – Hospital Center of Trás-os-Montes e Alto Douro and Siemens.

Conflict of Interest

The authors have no conflicts of interest.

References

[1] *Bala N, Aitken EAB, Fechner N, Cusack A, Steadman KJ.* Evaluation of antibacterial activity of Australian basidiomycetous macrofungi using a high-throughput 96-well plate assay. Pharm Biol 2011; 1–9.

[2] *Kalač P*. Chemical composition and nutritional value of European species of wild growing mushrooms: A review. Food Chem. 2009; 113: 9–16.

[3] *Borchers A, Keen CL, Gershwin ME*. Mushrooms, tumors, and immunity: an update. Exp Biol Med 2004; 229: 393-406.

[4] *Lindequist U, Niedermeyer THJ, Jülich W-D*.The pharmacological potential of mushrooms. eCAM 2005; 2: 285-299.

[5] *Poucheret P, Fons F, Rapior S*. Biological and pharmacological activity of higher fungi: 20-Year retrospective analysis. Mycologie 2006; 27: 311-333.

[6] *Zaidman B-Z, Yassin M, Mahajana J, Wasser SP*. Medicinal mushroom modulators of molecular targets as cancer therapeutics. Appl Microbiol Biotechnol 2005; 67: 453-468.

[7] *Moradali M-F, Mostafavi H, Ghods S, Hedjaroude G-A*. Immunomodulating and anticancer agents in the realm of macromycetes fungi (macrofungi). Int Immunopharmacol 2007; 7: 701-724.

[8] *Zhang M, Cui SW, Cheung PCK, Wang Q*. Antitumor polysaccharides from mushrooms: a review on their isolation process, structural characteristics and antitumor activity. Trends Food Sci Technol 2007; 18: 4-19.

[9] *Wasser SP, Weis AL*. Medicinal properties of substances occurring in higher Basidiomycetes mushrooms: Current perspectives (Review). Int J Med Mushrooms 1999; 1: 31-62.

[10] *Beattie KD, Rouf R, Gander L, May TW, Ratkowsky D, Donner CD, Gill M, Grice ID, Tiralongo E*. Antibacterial metabolites from Australian macrofungi from the genus *Cortinarius*. Phytochemistry 2010; 71: 948–955.

[11] *Ishikawa NK, Kasuya MCM, Vanetti MCD*. Antibacterial activity of *Lentinula edodes* grown in liquid medium. Braz J Microbiol. 2001; 32: 206-210.

[12] *Shittu OB, Alofe FV, Onawunmi GO, Ogundaini AO, Tiwalade TA*. Mycelial growth and antibacterial metabolite production by wild mushrooms. Afr J Biomed Res 2005; 8: 157-162.

[13] *Suay I, Arenal F, Asensio FJ, Basilio A, Cabello MA, Díez MT, García JB*, Del Val AG, Gorrochategui J, Hernández P, Peláez F, Vicente MF. Screening of basidiomycetes for antimicrobial activities. Antonie van Leeuwenhoek 2000; 78: 129–139.

[14] *Gonçalves O, Pereira R, Gonçalves F, Mendo S, Coimbra MA, Rocha SM*. Evaluation of the mutagenicity of sesquiterpenic compounds and their influence on the susceptibility towards antibiotics of two clinically relevant bacterial strains. Mutat Res 2011; 723: 18–25.

[15] *Öztürk M, Duru ME, Kivrak S, Mercan-Doğan N, Türkoglu A, Özler MA*. *In vitro* antioxidant, anticholinesterase and antimicrobial activity studies on three *Agaricus* species with fatty acid compositions and iron contents: A comparative study on the three most edible mushrooms. Food Chem Toxicol 2011; 49: 1353-1360.

[16] *Xu X, Yan H, Chen J, Zhang X*. Bioactive proteins from mushrooms. Biotechnol Adv 2011; 29: 667–674.

[17] *Fuchs FD*. Princípios Gerais do Uso de Antimicrobianos. In: Fuchs F, Wannamacher L, Ferreira M, editors. Farmacologia Clínica – Fundamentos da terapêutica Racional. 3ª ed. Rio de Janeiro, Guanabara Koogan; 2004, p. 342.

[18] *Tenover FC*. Mechanisms of antimicrobial resistance in bacteria. Am J Infect Control 2006; 34(5 Suppl 1): S3-10.

[19] *Koch AL*. Bacterial wall as target for attack: past, present, and future research. Clin Microbiol Rev 2003; 16: 673-687.

[20] *Opal SM, Cohen J*. Clinical gram-positive sepsis: does it fundamentally differ from gram-negative bacterial sepsis? Crit Care Med 1999; 27: 1608-1616.

[21] *Ginsburg I*. Role of lipoteichoic acid in infection and inflammation. Lancet Infect Dis 2002; 2: 171-179.

[22] *Silveira G, Nome F, Gesser JC, Sá MM, Terenzi H*. Estratégias utilizadas no combate a resistência bacteriana. Quím Nova 2006; 29: 3-7.

[23] *Craig WA*. Antibacterial Therapy. In: Goldman & Ausiell, editor. Cecil Textbook of Medicine. 22 ed. Saunders: Copyright 2004, p. 1853-1926.

[24] *Harbarth S, Harris AD, Carmeli Y, Samore MH*. Parallel analysis of individual and aggregated data on antibiotic exposure and resistance in gram-negative bacilli. Clin Infect Dis 2001; 33: 1462-1468.

[25] *Segal-Maurer S, Urban C, Rahal J.J.Jr*. Current perspectives on multidrugresistant bacteria. Epidemiology and control. Infect Dis Clin North Am 1996; 10: 939-957.

[26] *Kempf M, Rolain JM*. Emergence of resistance to carbapenems in Acinetobacter baumannii in Europe: clinical impact and therapeutic options. Int J Antimicrobiol Agents 2012; 39: 105-114.

[27] World Health Organization report on infectious diseases 2000- Overcoming antimicrobial resistance. Available at http://www.who.int/infectious-disease-report. Accessed January 21, 2012.

[28] *Peres-Bota D, Rodriguez H, Dimopoulos G, DaRos A, Mélot C, Struelens MJ, Vincent JL*. Are infections due to resistant pathogens associated with a worse outcome in critically ill patients? J Infect 2003; 47: 307-316.

[29] *Pittet D*. Infection control and quality heath care in the new millennium. Am J Infect Control 2005; 33: 258-267.

[30] World Health Organization report antimicrobial resistance (AMR). Available at http://www.who.int/mediacentre/news/releases/2010/amr_20100820/en/index.html. Accessed January 21, 2012.

[31] *Barros L, Cruz T, Baptista P, Estevinho LM, Ferreira ICFR*. Wild and commercial mushrooms as source of nutrients and nutraceuticals. Food ChemToxicol 2008; 46: 2742–2747.

[32] *Ozen T, Darcan C, Aktop O, Turkekul I*. Screening of antioxidant, antimicrobial activities and chemical contents of edible mushrooms wildly grown in the Black Sea region of Turkey. Comb Chem High Throughput Screen 2011; 14: 72-84.

[33] *Tambekar DH, Sonar TP, Khodke MV, Khante BS*. The Novel antibacterials from two edible mushrooms: *Agaricus bisporus* and *Pleurotus sajor* caju. Int J Pharmacol 2006; 2: 584 – 587.

[34] *Rosa LH, Machado KMG, Jacob CC, Capelari M, Rosa CA, Zani CL*. Screening of Brazilian Basidiomycetes for antimicrobial activity. Mem Inst Oswaldo Cruz 2003; 98: 967-974.

[35] *Kalyoncu F, Oskay M, Sağlam H, Erdoğan TF, Tamer AÜ*. Antimicrobial and antioxidant activities of mycelia of 10 wild mushroom species. J Med Food 2010; 13: 415-419.

[36] *Kalyoncu F, Oskay M*. Antimicrobial activities of four wild mushroom species collected from Turkey. Proceeding of the 6th International Conference on Mushroom Biology and Mushroom Products, 2008 Edited by J.I. LelleyGAMU GmbH, Institut für Pilzforschung, Krefeld, Germany.

[37] *Barros L, Venturini BA, Baptista P, Estevinho LM, Ferreira ICFR*. Chemical composition and biological properties of Portuguese wild mushrooms: A comprehensive study. J Agric Food Chem 2008; 56: 3856-3862.

[38] *Solak MH, Kalmis E, Saglam H, Kalyoncu F*. Antimicrobial activity of two wild mushrooms *Clitocybe alexandri* (Gill.) Konr. and *Rhizopogon roseolus* (Corda) T.M. Fries collected from Turkey. Phytother Res 2006; 20: 1085–1087.

[39] *Quereshi S, Pandey AK, Sandhu SS*. Evaluation of antibacterial activity of different *Ganoderma lucidum* extracts. J Sci Res 2010; 3: 9-13.

[40] *Sheena N, Ajith TA, Mathew AT, Janardhanan KK*. Antibacterial activity of three macrofungi, *Ganoderma lucidum*, *Navesporus floccosa* and *Phellinus rimosus* occurring in South India. Pharm Biol 2003; 41: 564–567.

[41] *Gao Y, Tang W, Gao H, Chan E, Lan J, Li X, Zhou S*. Antimicrobial activity of the medicinal mushroom Ganoderma. Food Rev Int 2005; 21: 211-229.

[42] *Smânia A, Monache FD, Smânia EFA, Gil ML, Benchetrit LC, Cruz FS*. Antibacterial activity of a substance produced by the fungus *Pycnoporus sanguineus* (Fr.) Murr. J Ethnopharmacol 1995; 45: 177-181.

[43] *Smânia EFA, Smânia A, Loguercio-Leite C, Gil ML*. Optimal parameters for cinnabarin synthesis by *Pycnoporus sanguineus*. J Chem Technol Biotechnol 1997; 70: 57-59.

[44] *Yamac M, Bilgili F*. Antimicrobial activities of fruit bodies and/or mycelial cultures of some mushroom isolates. Pharm Biol 2006; 44: 660–667.

[45] *Barros L, Calhelha RC, Vaz JA, Ferreira ICFR, Baptista P, Estevinho LM*. Antimicrobial activity and bioactive compounds of Portuguese wild edible mushrooms methanolic extracts. Eur Food Res Technol 2007; 225: 151–156.

[46] *Barros L, Baptista P, Estevinho LM, Ferreira ICFR*. Effect of fruiting body maturity stage on chemical composition and antimicrobial activity of Lactarius sp. mushrooms. J Agric Food Chem 2007; 55: 8766–8771.

[47] *Gezer K, Duru ME, Kivrak I, Turkoglu A, Mercan N, Turkoglu H, Gulcan S*. Free-radical scavenging capacity and antimicrobial activity of wild edible mushroom from Turkey. Afr J Biotechnol 2006; 5: 1924-1928.

[48] *Turkoglu A, Duru ME, Mercan N, Kivrak I, Gezer K*. Antioxidant and antimicrobial activities of *Laetiporus sulphureus* (Bull.) Murrill. Food Chem 2007; 101: 267–273.

[49] *Dulger B, Ergul CC, Gucin F*. Antimicrobial activity of the macrofungus *Lepista nuda*. Fitoterapia 2002; 73: 695–697.

[50] *Hearst R, Nelson D, McCollum G, Millar BC, Maeda Y, Goldsmith CE, Rooney PJ, Loughrey A, Rao JR, Moore JE.* An examination of antibacterial and antifungal properties of constituents of Shiitake (*Lentinula edodes*) and Oyster (*Pleurotus ostreatus*) mushrooms. Complement Ther Clin Pract 2009; 15: 5–7.

[51] *Hur J-M, Yang C-H, Han S-H, Lee S-H, You Y-O, Park J-C, Kim K-J*. Antibacterial effect of *Phellinus linteus* against methicillin-resistant *Staphylococcus aureus*. Fitoterapia 2004; 75: 603– 605.

[52] *Hatvani N*. Antibacterial effect of the culture fluid of *Lentinus edodes* mycelium grown in submerged liquid culture. Int J Antimicrob Agents 2001; 17: 71–74.

[53] *Signoretto C, Burlacchini G, Marchi A, Grillenzoni M, Cavalleri G, Ciric L, Lingström P, Pezzati E, Daglia M, Zaura E, Pratten J, Spratt DA, Wilson M, Canepari P*. Testing a low molecular mass fraction of a mushroom (*Lentinus edodes*) extract formulated as an oral rinse in a cohort of volunteers. J Biomed Biotechnol 2011 doi:10.1155/2011/857987.

[54] *Hirasawa M, Shouji N, Neta T, Fukushima K, Takada K*. Three kinds of antibacterial substances from *Lentinus edodes* (Berk.) Sing. (Shiitake, an edible mushroom). Int J Antimicrob Agents 1999; 11: 151–157.

[55] *Barros L, Baptista P, Estevinho LM, Ferreira ICFR*. Bioactive properties of the medicinal mushroom *Leucopaxillus giganteus* mycelium obtained in the presence of different nitrogen sources. Food Chem 2007; 105: 179–186.

[56] *Liu XT, Winkler AL, Schwan WR, Volk TJ, Rott MA, Monte A*. Antibacterial compounds from mushrooms I: A Lanostane-type triterpene and prenylphenol derivates from *Jahnoporus hiritus* and *Albatrellus flettii* and their activities against *Bacillus cereus* and *Enterococcus faecalis*. Planta Med 2010; 76: 182-185.

[57] *Mothana RAA, Jansen R, Jülich W-D, Lindequist U*. Ganomycins A and B, new antimicrobial Farnesyl hydroquinones from the Basidiomycete *Ganoderma pfeifferi*. J Nat Prod 2000; 63: 416-418.

[58] *Ishikawa NK, Fukushi Y, Yamaji K, Tahara S, Takahashi K*. Antimicrobial Cuparene-type sesquiterpenes, Enokipodins C and D, from a mycelial culture of *Flammulina velutipes*. J Nat Prod 2001; 64: 932-934.

[59] *Bender S, Dumitrache CN, Backhaus J, Christie G, Cross RF, Lonergan GT, Baker WL*. A case for caution in assessing the antibiotic activity of extracts of culinary-medicinal Shiitake mushroom [*Lentinus edodes* (Berk.) Singer] (Agaricomycetideae). Int J Med Mushrooms 2003; 5: 31–35.

[60] *Quang DN, Bach DD, Hashimoto T, Asakawa Y*. Chemical constituents of the Vietnamese inedible mushroom *Xylaria intracolorata*. Nat Prod Res 2006; 20: 317-321.

[61] *Zheng H, Maoqing Y, Liqiu X, Wenjuan T, Lian L, Guolin Z*. Purification and characterization of an antibacterial protein from the cultured mycelia of *Cordyceps sinensis*. Wuhan University J Nat Sci 2006; 11: 709-714.

[62] *Ngai PHK, Ng TB*. A ribonuclease with antimicrobial, antimitogenic and antiproliferative activities from the edible mushroom *Pleurotus sajor-caju*. Peptides 2004; 25: 11–17.

[63] *Mygind PH, Fischer RL, Schnorr KM, Hansen MT, Sönksen CP, Ludvigsen S, Raventós D, Buskov S, Christensen B, De Maria L, Taboureau O, Yaver D, Elvig-Jørgensen SG, Sørensen MV, Christensen BE, Kjærulff S, Frimodt-Moller N, Lehrer RI, Zasloff M, Kristensen, H-H*. Plectasin is a peptide antibiotic with therapeutic potential from a saprophytic fungu. Nature 2005; 437: 975-980.

[64] *Lee S-J, Yeo W-H, Yun B-S, Yoo I-D*. Isolation and sequence analysis of new Peptaibol, Boletusin, from Boletus spp. J Pept Sci 1999; 5: 374–378.

[65] *Yoon SY, Eo SK, Kim YS, Lee CK, Han SS*. Antimicrobial activity of *Ganoderma lucidum* extract alone and in combination with some antibiotics. Arch Pharm Res 1994; 17: 438–442.

[66] *Anke T, Kupka J, Schramm G, Steglich W*. Antibiotics from basidiomycetes. X. Scorodonin, a new antibacterial and antifungal metabolite from Marasmius scorononius (Fr.). J Antibiot 1980; 33: 463-467.

[67] *Ciric L, Tymon A, Zaura E, Lingström P, Stauder M, Papetti A, Signoretto C, Pratten J, Wilson M, Spratt D*. *In Vitro* assessment of Shiitake mushroom (*Lentinula edodes*) extract for its antigingivitis activity. J Biomed Biotechnol 2011; doi:10.1155/2011/507908.

[68] *Signoretto C, Marchi A, Bertoncelli A, Burlacchini G, Tessarolo F, Caola I, Pezzati E, Zaura E, Papetti A, Lingström P, Pratten J, Spratt DA, Wilson M, Canepari P*. Effects of mushroom and chicory extracts on the physiology and shape of *Prevotella intermedia*, a Periodontopathogenic bacterium. J Biomed Biotechnol 2011; doi:10.1155/2011/635348.

[69] *SchwanWR, Dunek C, Gebhardt M, Engelbrecht K, Klett T, Monte A, Toce J, Rott M, Volk TJ, LiPuma JJ, Liu X-T, McKelvey R*. Screening a mushroom extract library for activity against *Acinetobacter baumannii* and *Burkholderia cepacia* and the identification of a compound with anti-Burkholderia activity. Ann Clin Microb Antimicrob 2010; 9:4

[70] *Zheng S, Liu Q, Zhang G, Wang H, Ng TB*. Purification and characterization of an antibacterial protein from dried fruiting bodies of the wild mushroom *Clitocybe sinopica*. Acta Biochim Pol 2010; 51: 43–48.

Table 1. Mushroom extracts with antimicrobial activity against Gram-positive bacteria.

Microorganism	Mushroom[a]	Results	References
Actinomyces naeslundii	*Lentinus edodes*	CFU = 0 – 3.30 (±5.48)×10^6 MIC = 0.05 – 20 mg/mL	[53,54,67]
Actinomyces viscosus	*Lentinus edodes*	MIC = 0.05 – 20 mg/mL	[54]
Bacillus cereus	*Agaricus bisporus*, *Agaricus bitorquis*, *Agaricus essettei*, *Agaricus silvicola*, *Armillaria mellea*, *Boletus edulis*, *Cantharellus cibarius*, *Clitocybe alexandri*, *Clitocybe geotropa*, *Cortinarius* sp., *Gloeoporus thelephoroides*, *Hexagonia hydnoides*, *Hydnum repandum*, *Hypholoma fasciculare*, *Irpex lacteus* (M), *Lactarius camphorates*, *Lactarius delicious*, *Lactarius piperatus*, *Lactarius volemus*, *Laetiporus sulphureus*, *Lentinus edodes*, *Lepista nuda*, *Leucopaxillus giganteus* (M), *Macrolepiota procera*, *Meripilus giganteus* (M), *Meripilus giganteus*, *Phellinus* sp., *Pleurotus ostreatus* (M), *Pleurotus ostreatus*, *Ramaria botrytis*, *Ramaria flava*, *Rhizopogon roseolus*, *Sarcodon imbricatus*, *Sparassis crispa*, *Tricholoma portentosum*	IZD = 5 – 21 mm MIC = 5 µg/mL – 100 mg/mL	[11,15, 31,32, 34-38,45-48, 50, 55]
Bacillus megaterium	*Lentinus edodes*	CFU = 0 (total inhibition)	[52]
Bacillus pumilis	*Lentinus edodes*	IZD = 14 mm	[50]
Bacillus subtilis	*Agaricus bisporus*, *Agaricus bitorquis*, *Agaricus essettei*, *Agaricus silvicola*, *Armillaria mellea*, *Cantharellus cibarius*, *Clitocybe alexandri*, *Clitocybe geotropa*, *Cortinarius* sp., *Ganoderma lucidum*, *Hygrophorus agathosmus*, *Hypholoma fasciculare*, *Lactarius delicious*, *Lactarius piperatus*, *Laetiporus sulphureus*, *Lentinus edodes*, *Lepista nuda*, *Leucopaxillus giganteus* (M), *Meripilus giganteus* (M), *Navesporus floccosa*, *Paxillus involutus* (M), *Phellinus rimosus*, *Pleurotus ostreatus* (M), *Pleurotus ostreatus*, *Ramaria botrytis*, *Ramaria flava*, *Rhizopogon roseolus*, *Sparassis crispa*, *Suillus collitinus*, *Tricholoma acerbum*, *Tricholoma portentosum*	IZD = 5 –28mm MIC = 5 µg/mL – 300 mg/mL	[11,15,31, 35-40,44-50,54, 55,71]
Enterococcus faecalis	*Lentinus edodes*	IZD = 8 mm	[50]
Enterococcus faecium	*Lentinus edodes*	MIC >1.5 – >50 mg/mL	[54]
Lactobacillus casei	*Lentinus edodes*	CFU = 5.00 (±7.07)×10^{-1} – 9.28 (±2.76)×10^2 MIC = 0.05 – 15 mg/mL	[53,54,67]
Listeria innocua	*Lentinus edodes*	IZD = 8 mm	[11]
Listeria monocytogenes	*Lentinus edodes*, *Pycnoporus sanguineus* (M),	IZD = 11 – 13mm	[11,34,50]
Staphylococcus sp.	*Lentinus edodes*	IZD = 12 mm	[50]
Staphylococcus aureus	*Agaricus bisporus*, *Agaricus bitorquis*, *Agaricus essettei*, *Agaricus silvícola*, *Armillaria mellea*, *Boletus edulis*, *Cantharellus cibarius*, *Clitocybe geotropa*, *Cortinarius* sp., *Cortinarius abnormis*, *Cortinarius ardesiacus*, *Cortinarius archeri*, *Cortinarius austroalbidus*, *Cortinarius austrovenetus*, *Cortinarius austroviolaceus*, *Cortinarius coelopus*, *Cortinarius clelandii*, *Cortinarius* [*Dermocybe* sp, *Dermocybe canaria*, *Dermocybe kula*], *Cortinarius fulvoiubatus*, *Cortinarius ianthinus*, *Cortinarius memoria-annae*,	CFU = 2.1×10^4 IZD = 8 – 24 mm MIC = 5µg/mL –50 mg/mL IC_{50} <0.01 – ≥2.00 mg/mL	[10,11,15,31-37,39,40, 44, 46-50,52,54, 55]

	Cortinarius persplendidus, *Cortinarius sinapicolor*, *Cortinarius submagellanicus*, *Cortinarius tricholomoides*, *Cortinarius vinosipes*, *Ganoderma lucidum*, *Hydnum repandum*, *Hygrophorus agathosmus*, *Hypholoma fasciculare*, *Irpex lacteus* (M), *Lactarius camphoratus*, *Lactarius delicious*, *Lactarius piperatus*, *Lactarius volemus*, *Laetiporus sulphureus*, *Lentinus edodes*, *Lepista nuda*, *Leucopaxillus giganteus* (M), *Macrolepiota procera*, *Meripilus giganteus* (M), *Meripilus giganteus*, *Morchella elata* (M), *Morchella esculenta* var. *vulgaris* (M), *Navesporus floccosa*, *Nothopanus hygrophanus* (M), *Paxillus involutus* (M), *Phellinus rimosus*, *Pleurotus eryngii* (M), *Pleurotus ostreatus* (M), *Pleurotus sajor-caju*, *Pycnoporus sanguineus* (M), *Ramaria botrytis*, *Ramaria flava*, *Sparassis crispa*, *Suillus collitinus*		
MRSA	*Lentinus edodes*, *Phellinus linteus*	IZD = 12 mm MIC = 500 μg/mL	[50,51]
Staphylococcus epidermidis	*Agaricus bisporus*, *Hygrophorus agathosmus*, *Lentinus edodes*, *Pleurotus sajor-caju*, *Suillus collitinus*	IZD = 11 – 27mm MIC = 7.81 – 62.5 μg/mL	[11,33,44,50]
Streptococcus gordonii	*Lentinus edodes*	MIC = 0.075 – 50 mg/mL	[54]
Streptococcus mitis	*Lentinus edodes*	MIC = 0.075 – 15 mg/mL	[54]
Streptococcus mutans	*Lentinus edodes*	CFU = 2.15 (±5.58)×10^5 MIC = 0.1 – 10 mg/mL	[53,54,67]
Streptococcus oralis	*Lentinus edodes*	MIC = 0.1 – >50 mg/mL	[54]
Staphylococcus saprophyticus	*Agaricus* cf. *nigrecentulus* (M), *Tyromyces duracinus* (M)	IZD >12 mm	[34]
Streptococcus pyogenes	*Lentinus edodes*	CFU = 6.0×10^4	[52]
Streptococcus salivarius	*Lentinus edodes*	MIC = 0.1 – 10 mg/mL	[54]
Streptococcus sanguinis	*Lentinus edodes*	CFU = 2.53 (±0.62)×10^6 – 5.06 (±1,58)×10^6 MIC = 0.075 – 50 mg/mL	[53,54,67]
Streptococcus sobrinus	*Lentinus edodes*	MIC = 0.075 – 20 mg/mL	[54]
Micrococcus flavus	*Agaricus bisporus*, *Agaricus bitorquis*, *Agaricus essettei*, *Laetiporus sulphurous*, *Ramaria flava*	IZD = 20 – 23 ± 1 mm	[15,47,48]
Micrococcus luteus	*Agaricus bisporus*, *Agaricus bitorquis*, *Agaricus essettei*, *Clitocybe alexandri*, *Laetiporus sulphurous*, *Lentinus edodes*, *Ramaria flava*	IZD = 10 – 21±1mm	[15,38,47,48, 52]
Sarcina lutea	*Armillaria mellea* (M), *Armillaria mellea*, *Clitocybe geotropa*, *Meripilus giganteus* (M), *Meripilus giganteus*, *Morchella costata* (M), *Morchella esculenta* var. *vulgaris* (M), *Paxillus involutus* (M), *Pleurotus ostreatus* (M), *Sparassis crispa*	IZD = 8 – 27 mm	[35,36]

[a] Acetone, chloroform, ethanol, ethyl acetate, methanol, dichloromethane, ether, xylene or water extracts.
M- mycelium, the other samples refer to fruiting body; MRSA- Methicillin-resistant *Staphylococcus aureus*.
The antimicrobial activity was expressed in CFU (colony-forming unities), MIC (minimal inhibitory concentrations), IZD (internal zone diameter) or IC_{50} (concentrations inhibiting 50% of the growth) values.

Table 2. Mushroom compounds with antimicrobial activity against Gram-positive bacteria.

Microorganism	Compound (mushroom)	Results	References
Bacillus cereus	Confluentin (**1a**), Grifolin (**1b**) and Neogrifolin (**1c**) (*Albatrellus flettii*); 3,11-Dioxolanosta-8,24(*Z*)-diene-26-oic acid (**2**) (*Jahnoporus hirtus*); Oxalic acid (**3**) (*Lentinus edodes* M); Proteins and peptides: Plectasin (*Pseudoplectania nigrella*)	IZD = 17 mm MIC = 10 μg/mL – ≥128 mg/L	[56,59,63]
Bacillus subtilis	Peptides: Peptaibol Boletusin, Peptaibol Chrysospermin 3 and Peptaibol Chrysospermin 5 (*Boletus* spp.); Protein (*Cordyceps sinensis*); Enokipodins A, B, C and D (**4a-d**) (*Flammulina velutipes* M); Ganomycin A and B (**5a,b**) (*Ganoderma pfeifferi*)	MIC > 100000 g/L IZD = 11 – 28 mm	[57,58,61,64]
Bacillus thuringiensis	Plectasin (*Pseudoplectania nigrella*)	MIC = 0.5 mg/L	[63]
Corynebacterium diphtheriae	Plectasin (*Pseudoplectania nigrella*)	MIC = 8 mg/L	[63]
Corynebacterium jeikeium	Plectasin (*Pseudoplectania nigrella*)	MIC = 2 mg/L	[63]
Corynebacterium lilium	Peptaibol Boletusin, Peptaibol Chrysospermin 3 and Peptaibol Chrysospermin 5 (*Boletus* spp.)	IZD = 23 – 25 mm	[64]
Enterococcus faecalis	**1a**, **1b** and **1c** (*Albatrellus flettii*); **2** (*Jahnoporus hirtus*); Plectasin (*Pseudoplectania nigrella*)	MIC = 0.5μg/mL – ≥128 mg/L	[56,63]
Enterococcus faecium; VREF	Plectasin (*Pseudoplectania nigrella*)	MIC = 32 – 64 mg/L	[63]
Micrococcus flavus	**5a,b** (*Ganoderma pfeifferi*)	IZD = 25 – 26 mm	[57]
Staphylococcus aureus	Peptaibol Boletusin, Peptaibol Chrysospermin 3 and Peptaibol Chrysospermin 5 (*Boletus* spp.); Proteins (*Cordyceps sinensis*); 6-Methylxanthopurpurin-3-*O*-methyl ether (**7**), (1S,3S)-Austrocortilutein (**8a**), (1S,3R)- Austrocortilutein (**8b**), (1S,3S)-Austrocortirubin (**8c**) and Torosachrysone (**8d**) (*Cortinarius basirubencens*); Physcion (**9a**), Erythroglaucin (**9b**) and Emodin (**9c**) (*Cortinarius* sp.); **4a-d** (*Flammulina velutipes* M); **5a,b** (*Ganoderma pfeifferi*); **3** (*Lentinus edodes* M);; Ribonuclease (*Pleurotus sajor-caju*); Plectasin (*Pseudoplectania nigrella*);Fraction B (*Pycnoporus sanguineus*); Coloratin A (**10**) (*Xylaria intracolarata*)	IZD = 12 – 24 mm MIC = 0.156 mg/L – 50000 g/L IC_{50} = 0.7 – >50 μg/mL IC_{50} = 34 ± 4 μM	[10,42,57-64]
MRSA	Plectasin (*Pseudoplectania nigrella*);	MIC = 32 mg/L	[63]
Staphylococcus epidermidis; MRSE	Plectasin (*Pseudoplectania nigrella*)	MIC = 8 mg/L	[63]
Streptococcus sp.	Peptaibol Chrysospermin 3 (*Boletus* spp.)	IZD = 9 mm	[60]
Streptococcus faecalis	**3** (*Lentinus edodes* M)	IZD = 13 mm	[59]
Streptococcus group A.B,C,G	Fraction B (*Pycnoporus sanguineus*)	MIC = 0.019 – 0.039 mg/mL	[42]
Streptococcus pneumonia; PRSP	Plectasin (*Pseudoplectania nigrella*)	MIC = 0.5 mg/L	[63]
Streptococcus pyogenes; ERSP	Plectasin (*Pseudoplectania nigrella*)	MIC = 0.125 mg/L	[63]

M- mycelium, the other samples refer to fruiting body. The antimicrobial activity was expressed in MIC (minimal inhibitory concentrations), IZD (internal zone diameter) or IC_{50} (concentrations inhibiting 50% of the growth) values. VREF - Vancomycin-resistant *Enterococcus faecium ;* MRSA- Methicillin-resistant *Staphylococcus aureus*;

MRSE - Methicillin-resistant *Staphylococcus epidermidis*; PRSP - Penicillin-resistant *Streptococcus pneumonia;* ERSP - Erythromycin – resistant *Streptococcus pyogenes*

Table 3. Mushroom extracts with antimicrobial activity against Gram-negative bacteria.

Microorganism	Mushroom[a]	Results	References
Cupriavidis	*Lentinus edodes*	IZD = 15 mm	[50]
Enterobacter aerogenes	*Agaricus bisporus*, *Clitocybe alexandri*, *Hygrophorus agathosmus*, *Meripilus giganteus* (M), *Paxillus involutus* (M), *Pleurotus ostreatus* (M), *Pleurotus sajor-caju*, *Rhizopogon roseolus*, *Suillus collitinus*	IZD = 8 – 22mm MIC = 15.62 – 125 μg/mL	[33,35,38,44]
Enterobacter cloacae	*Armillaria mellea*, *Clitocybe geotropa*, *Meripilus giganteus* (M), *Meripilus giganteus*, *Paxillus involutus* (M), *Pleurotus ostreatus* (M), *Sparassis crispa*	IZD = 10 – 20 mm	[35,36]
Enterobacter faecalis	*Armillaria mellea*, *Clitocybe geotropa*, *Meripilus giganteus* (M), *Meripilus giganteus*, *Sparassis crispa*	IZD = 8 – 14 mm	[35,36]
Escherichia coli	*Agaricus bisporus*, *Armillaria mellea* (M), *Armillaria mellea*, *Boletus edulis*, *Cantharellus cibarius*, *Clitocybe alexandri*, *Clitocybe geotropa*, *Cortinarius* sp., *Ganoderma lucidum*, *Hydnum repandum*, *Irpex lacteus* (M), *Lactarius camphoratus*, *Lactarius delicious*, *Lactarius piperatus*, *Lactarius volemus*, *Laetiporus sulphureus*, *Lentinus edodes*, *Lepista nuda*, *Leucoagaricus* cf. *cinereus* (M), *Macrolepiota procera*, *Marasmius* sp. (M), *Marasmius* cf. *bellus* (M), *Meripilus giganteus* (M), *Meripilus giganteus*, *Morchella costata (*(M), *Morchella hortensis* (M), *Navesporus floccosa*, *Paxillus involutus* (M), *Phellinus rimosus*, *Pleurotus eryngii* (M), *Pleurotus ostreatus* (M), *Pleurotus sajor-caju*, *Rhizopogon roseolus*, *Sparassis crispa*, *Suillus collitinus*	IZD = 8 – 27.40 ± 0.19 mm MIC = 250 μg/mL – >50mg/mL	[32-36,38-40, 44, 46,48-50,54,71]
Fusobacterium nucleatum	*Lentinus edodes*	CFU = 2.40 (±3,11)×10^2 – 7.56 (±4.28)×10^6 MIC = 0.9 – 20 mg/mL	[53,54,67]
Klebsiella aerogenes	*Lentinus edodes*	IZD = 9 mm	[50]
Klebsiella pneumoniae	*Agaricus bisporus*, *Agaricus bitorquis*, *Ganoderma lucidum*, *Lactarius piperatus*, *Lentinus edodes*, *Lepista nuda*, *Pleurotus sajor-caju*, *Ramaria flava*	IZD = 4 – 31.60 ± 0.10 mm MIC = 0.5 mg/mL	[11,15,33,39, 46,47,49,50, 55]
Morganella morganii	*Agaricus bisporus*, *Agaricus bitorquis*, *Agaricus essettei*, *Laetiporus sulphurous*	IZD = 4.5 ± 0.5 mm	[15,48]
Neisseria subflava	*Lentinus edodes*	CFU = 9.49 (±2.60)×10^6 – 1.50 (±0,50)×10^8	[53,67]
Porphyromonas gingivalis	*Lentinus edodes*	MIC = 0.05 – 10 mg/mL	[45]
Prevotella intermedia	*Lentinus edodes*	CFU = 2.00 (±2.83)×10^1 – 2.60 (±6.66)×10^5 MIC = 0.05 – 15mg/mL	[53,54,67,68]
Prevotella nigrescens	*Lentinus edodes*	MIC = 0.1 – 15mg/mL	[54]
Proteus mirabilis	*Lentinus edodes*	IZD = 4 mm	[11]

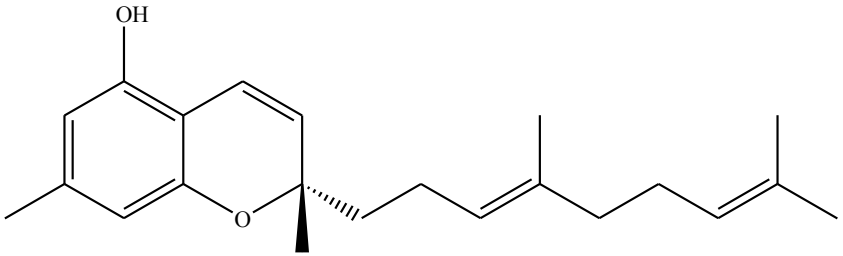
Proteus vulgaris	*Agaricus bisporus*, *Agaricus bitorquis*, *Armillaria mellea*, *Clitocybe geotropa*, *Laetiporus sulphureus*, *Meripilus giganteus* (M), *Meripilus giganteus*, *Pleurotus ostreatus* (M), *Pleurotus sajor-caju*, *Sparassis crispa*	IZD = 5.5 ± 0.5 – 19 mm	[15,33,35,36, 48]
Pseudomonas aeruginosa	*Agaricus bisporus*, *Boletus edulis*, *Cantharellus cibariusCortinarius* sp., *Cortinarius abnormis*, *Cortinarius ardesiacus*, *Cortinarius archeri*, *Cortinarius austroalbidus*, *Cortinarius austrovenetus*, *Cortinarius austroviolaceus*, *Cortinarius coelopus*, *Cortinarius clelandii*, *Cortinarius* [*Dermocybe* sp., *Dermocybe canaria*, *Dermocybe kula*], *Cortinarius fulvoiubatus*, *Cortinarius ianthinus*, *Cortinarius memoria-annae*, *Cortinarius persplendidus*, *Cortinarius sinapicolor*, *Cortinarius submagellanicus*, *Cortinarius tricholomoides*, *Cortinarius vinosipes*, *Ganoderma lucidum*, *Hydnum repandum*, *Lactarius camphoratus*, *Lactarius delicious*, *Lactarius piperatus*, *Lactarius volemus*, *Laetiporus sulphureus*, *Lentinus edodes*, *Lepista nuda*, *Macrolepiota procera*, *Navesporus floccosa*, *Phellinus rimosus*, *Pleurotus sajor-caju*, *Ramaria flava*	IZD = 6 – 20 mm MIC = 0.5 – 100 mg/mL IC_{50} = 0.04 – >2.00 mg/mL	[10,32,33,39, 40,45,46,48-50]
Pseudomonas maltophila	*Lentinus edodes*	IZD = 6 mm	[11]
Salmonella enteritidis	*Laetiporus sulphureus*, *Ramaria flava*	IZD = 4 – 5 ± 1 mm	[37,40]
Salmonella poona	*Lentinus edodes*	IZD = 9 mm	[50]
Salmonella typhi	*Agaricus bisporus*, *Ganoderma lucidum*, *Pleurotus sajor-caju*	IZD = 7.00 ± 0.18 – 20.60 ± 0.14 mm	[33,39]
Salmonella typhimurium	*Agaricus bisporus*, *Armillaria mellea* (M), *Armillaria mellea*, *Clitocybe geotropa*, *Ganoderma lucidum*, *Hygrophorus agathosmus*, *Irpex lacteus* (M), *Lepista nuda*, *Meripilus giganteus* (M), *Meripilus giganteus*, *Morchella costata* (M), *Morchella elata* (M), *Morchella esculenta* var. *vulgaris* (M), *Morchella hortensis* (M), *Navesporus floccosa*, *Paxillus involutus* (M), *Phellinus rimosus*, *Pleurotus ostreatus* (M), *Pleurotus sajor-caju*, *Sparassis crispa*, *Suillus collitinus*,	IZD = 6 – 16 mm MIC = 15.62 – 125 µg/mL	[33-36, 40,44,49]
Serratia marcescens	*Lentinus edodes*	IZD = 10 mm	[50]
Veillonella dispar	*Lentinus edodes*	CFU = 1.37 (±0.31)×10^7 – 2.35 (±1.09)×10^7	[53,67]
Veillonella parvula	*Lentinus edodes*	MIC = 0.3 – 20 mg/mL	[54]
Yersinia enterecolitica	*Agaricus bitorquis*, *Laetiporus sulphureus*, *Lentinus edodes*, *Ramaria flava*	IZD = 5 – 16 mm	[11,15,47]

[a] Acetone, chloroform, ethanol, ethyl acetate, methanol, dichloromethane, ether, xylene or water extracts.
M- mycelium, the other samples refer to fruiting body.
The antimicrobial activity was expressed in CFU (colony-forming unities), MIC (minimal inhibitory concentrations), IZD (internal zone diameter) or IC_{50} (concentrations inhibiting 50% of the growth) values.

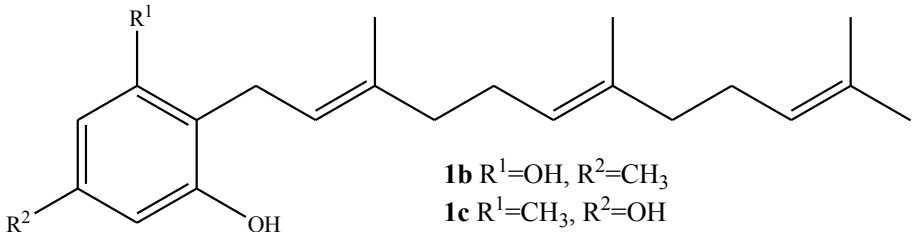
Table 4. Mushroom compounds with antimicrobial activity against Gram-negative bacteria.

Microorganism	Compound (mushroom)	Results	References
Achromobacter xyloxidans	**6** (*Leucopaxillus albissimus*)	MIC = 32 µg/mL	[69]
Acinetobacter baumannii	**6** (*Leucopaxillus albissimus*)	MIC = 128 µg/mL	[69]
Agrobacterium rhizogenes	Protein (*Clitocybe sinopica*)	MIC = 0.14 µM	[70]
Agrobacterium tumefaciens	Protein (*Clitocybe sinopica*)	MIC = 0.14 µM	[70]
Agrobacterium vitis	Protein (*Clitocybe sinopica*)	MIC = 0.28 µM	[70]
Burkholderia cenocepacia	**6** (*Leucopaxillus albissimus*)	MIC = 16 µg/mL	[69]
Burkholderia cepacia	**6** (*Leucopaxillus albissimus*)	MIC = 32 µg/mL	[69]
Burkholderia multivorans	**6** (*Leucopaxillus albissimus*)	MIC = 16 µg/mL	[69]
Cytophaga johnsonae	**6** (*Leucopaxillus albissimus*)	IZD = 16 mm	[69]
Escherichia coli	Proteins (*Cordyceps sinensis*); **5a,b** (*Ganoderma pfeifferi*); Fraction B (*Pycnoporus sanguineus*); **10** (*Xylaria intracolarata*)	IZD = 4 – 16 mm MIC = 0.625 mg/mL – 100000 g/L	[42,57,60,61]
Klebsiella pneumoniae	**3** (*Lentinus edodes* M); Fraction B (*Pycnoporus sanguineus*); **10** (*Xylaria intracolarata*)	IZD = 12 – 22 mm MIC = 0.625 mg/mL	[42,59,60]
Proteus mirabilis	**5a,b** (*Ganoderma pfeifferi*)	IZD = 15 mm	[57]
Proteus vulgaris	Protein (*Cordyceps sinensis*); **3** (*Lentinus edodes* M)	IZD = 12 mm MIC = 75000 g/L	[59,61]
Pseudomonas aeruginosa	**7**, **8a-8d** (*Cortinarius basirubencens*); **9a-c** (*Cortinarius* sp.); **3** (*Lentinus edodes* M); **6** (*Leucopaxillus albissimus*); Ribonuclease (*Pleurotus sajor-caju*); Fraction B (*Pycnoporus sanguineus*); **10** (*Xylaria intracolarata*)	IZD = 15 – 16 mm MIC = 128 µg/mL – 1.250 mg/mL IC_{50} = 1.5 – >50 µg/mL IC_{50} = 51 ± 6 µM	[10, 42,59,62, 64,68]
Pseudomonas fluorescens	**3** (*Lentinus edodes* M); Ribonuclease (*Pleurotus sajor-caju*)	IZD = 13 mm IC_{50} = 186 ± 12 µM	[59,62]
Serratia marcescens	**5a,b** (*Ganoderma pfeifferi*)	IZD = 15 – 16mm	[57]
Salmonella enteritidis	**10** (*Xylaria intracolarata*)	IZD = 16 mm	[60]
Salmonella typhi	Protein (*Cordyceps sinensis*); Fraction B (*Pycnoporus sanguineus*)	MIC = 0.312 mg/mL – 50000 g/L	[42,61]
Stenotrophomonas maltophilia	**6** (*Leucopaxillus albissimus*)	MIC = 32 µg/mL	[69]
Xanthomonas malvacearum	Protein (*Clitocybe sinopica*)	MIC = 0.56 µM	[70]
Xanthomonas oryzae	Protein (*Clitocybe sinopica*)	MIC = 0.56 µM	[70]

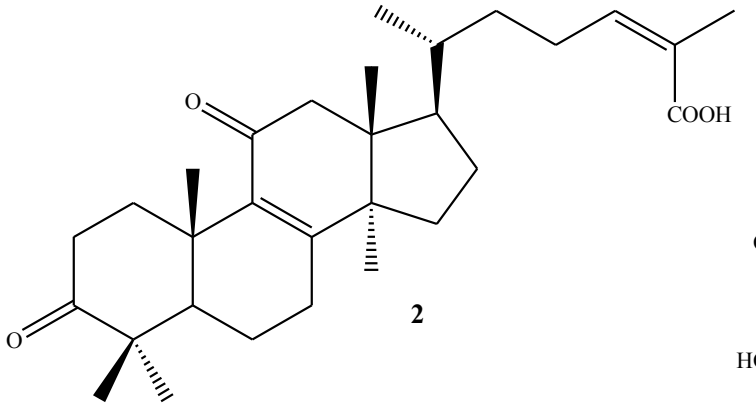
M- mycelium, the other samples refer to fruiting body. The antimicrobial activity was expressed in MIC (minimal inhibitory concentrations), IZD (internal zone diameter) or IC_{50} (concentrations inhibiting 50% of the growth) values.



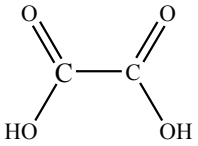
1a



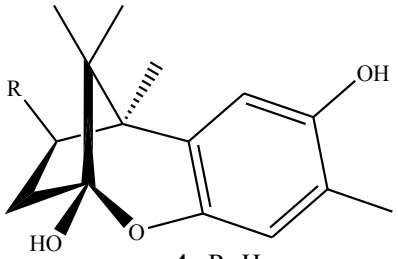
1b R^1=OH, R^2=CH_3
1c R^1=CH_3, R^2=OH



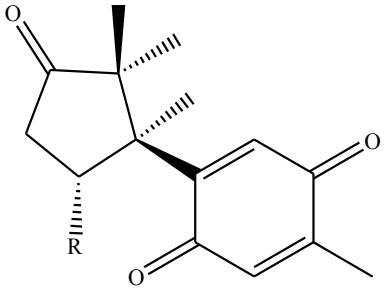
2



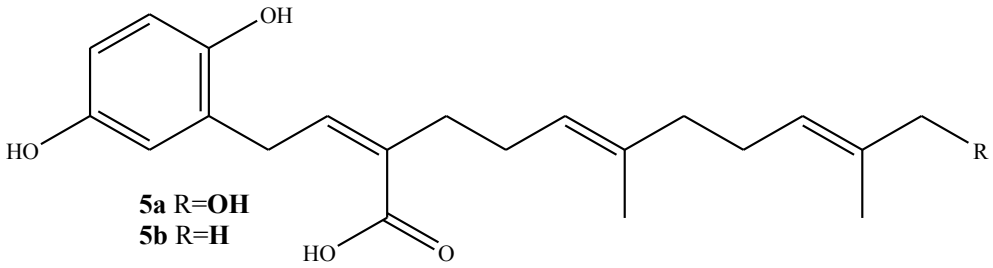
3



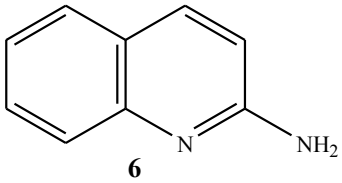
4a R=H
4c R=OH



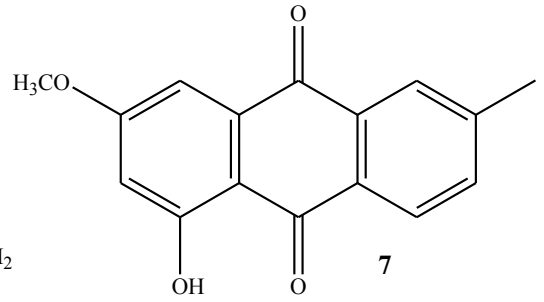
4b R=H
4d R=OH



5a R=**OH**
5b R=**H**



6



7

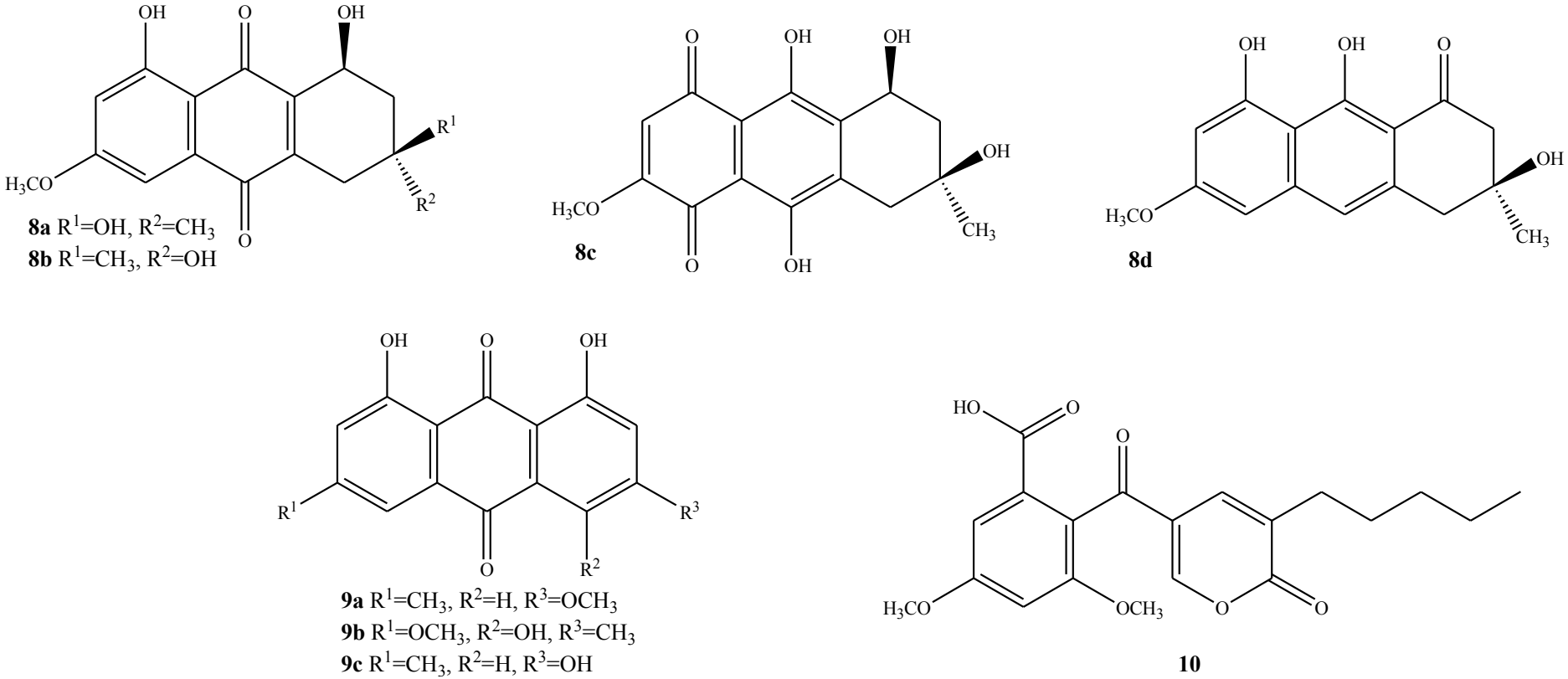


Figure 1. Chemical structure of the low-molecular-weight (LMW) compounds with antimicrobial potential found in mushrooms.