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Antimicrobials from Mushrooms for Assuring Food Safety

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Abstract: The interest in discovering and developing natural antimicrobials has significantly increased due to consumer preferences for foods that are free of chemical preservatives while still microbiologically safe. One of the best sources of natural antimicrobials is certain mushrooms (fungi) as many of them not only have nutraceutical functions but also possess antimicrobial properties. This article reviews the available information on mushroom antimicrobials for food safety control. It includes available resources, extraction procedures, antimicrobial activities, and the status of their applications to food safety. The review indicates that there are great potential benefits to be gained from mushroom antimicrobials in food production, processing, and preservation as a biosolution to meet the increasing demands for food quality and safety.

Keywords: antimicrobials, food safety, mushroom, natural preservatives

Introduction

Mushrooms are any of various rapid-growing, often wood-colonizing fleshy fungi, belonging to Basidiomycetes, a subdivision belonging to the division Eumycota, characterized by the formation of basidiospores. They can live as independent saprophytes or in association with other plants. Although some of these macrofungi are edible, with highly desirable culinary, nutritional, and medicinal characteristics, many mushrooms are poisonous or not palatable. Mushrooms have developed and/or adapted their metabolism in their habitat for survival and for competing with other organisms. Many secondary or specific metabolites produced in the life cycle of mushrooms have been discovered and demonstrated to have antimicrobial, antioxidation, and anti-inflammation functions in addition to their nutritional and culinary properties (Zjawiony 2004; Sridhar and others 2011; Alves and others 2012b). Many wild mushrooms have been considered to have antimicrobial properties and are more often used as bioresources for identifying antimicrobials than are cultivated mushrooms.

Because of public health threats by foodborne pathogens, food safety as a global issue has been challenging the food processing and preservation technologies in recent years. In addition to the favorable nutritional and culinary properties of mushrooms, their antimicrobial properties become more and more attractive to people who are looking for natural solutions to meet the urgent need for food safety (Venturini and others 2008). However, compared to the great amount of information on mushroom cultivation and nutrition, the reports on mushroom antimicrobial properties, especially on their applications for food safety, are relatively few.

This review yielded from literatures on mushroom antimicrobials from several databases including Agricola (from 1970 to 2016), Biological abstract (from 1984 to 2016), CAB abstracts (from 1990 to 2016), and Food Science and Technology Abstracts (from 1980 to 2016). It summarizes the available data on mushroom antimicrobials with a focus on their potential applications in food safety management. It particularly focuses on sources, extraction procedures for mushroom antimicrobials, antimicrobial properties of mushrooms against foodborne microorganisms, the diversity of mushroom antimicrobial metabolites, and the status of applications of mushroom antimicrobials for food safety purposes.

Sources of Mushroom Antimicrobials

Although many varieties of mushrooms have been discovered, only 2000 among 140000 identified mushroom species are safe as food (Balakumar and others 2011), and only 158 species from 88 genera have been recognized to have antimicrobial properties. To identify novel sources of mushroom antimicrobials, an initial screening process for mushroom species with antimicrobial properties is often based on the ecology of the region where the mushrooms grow or on local usage of the mushrooms (Rosa and others 2003; Yamac and Bilgili 2006; Venturini and others 2008; Fagade and Oyelade 2009; Giri and others 2012). For example, Rosa and others (2003) screened over 100 mushroom isolates from various Brazilian ecosystems and identified 13 isolates with antimicrobial activities. Giri and others (2012) evaluated 30 edible wild mushroom species from West Bengal, India, and found that all their methanol extracts showed different levels of antimicrobial activities. Table 1 lists the mushrooms with antimicrobial properties. Those mushrooms belong to 88 fungal genera and are distributed widely in various ecosystems within different regions in the world, specifically, Bangladesh (Chowdhury and others 2015), Brazil (Rosa and others 2003), China (Cao and others 2003), India

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Table 1–Mushroom genera with antimicrobial properties.

Code	Genus (main species)	Extraction solvents	References[a]
1	*Agaricus* (*A. arvensis, A. bisporus, A. blazei, A. brasiliensis, A. campestris, A. devoniensis, A. gennadii, A. silvicola, A. nigrecentulus*)	Water, methanol, ethanol, and ethyl acetate DCM- MeOH (1:1, v/v)	Beelman and others (2003); Rosa and others (2003); Venturini and others (2008); Santoyo and others (2009); Akyuz and others (2010); Alves and others (2012a); Giri and others (2012); Dundar and others (2016); Soltanian and others (2016)
2	*Agrocybe* (*A. aegerita, A. perfecta*)	Ethanol, ethylacetate, and culture filtration	Coletto and Lelli (1998); Cao and others (2003); Rosa and others (2003)
3	*Amanita* (*A. caesarea, A. castanopsidis, A. cokeri, A.zambiana*)	Water and methanol	Yamac and Bilgili (2006); Santoyo and others (2009); Giri and others (2012); Reid and others (2016)
4	*Armillaria* (*A. mellea*)	Methanol and ethanol	Yamac and Bilgili (2006); Kalyoncu and Oskay (2008); Giri and others (2012); Dundar and others (2016)
5	*Astraeus*(*A. hygrometricus*)	Methanol	Giri and others (2012)
6	*Auricularia* (*A. auricula-judae, A. polytricha*)	Water, ethanol, and chloroform	Gbolagade and Fasidi (2005); Nwachukwu and Uzoeto (2010)
7	*Boletus* (*B. edulis*)	Water and ethanol	Santoyo and others (2009); Reid and others (2016)
8	*Calocybe* (*C. indica*)	Methanol	Giri and others (2012)
9	*Cantharellus*(*C. cibarius*, *C. heinemannianus, C. miomboensis, C. symoensii*)	Water, methanol, and ethanol	Barros and others (2007b); Santoyo and others (2009); Alves and others (2012b); Reid and others (2016)
10	*Chroogomphus*(*C. rutilus*)	Ethanol, chloroform, and ethyl acetate, Acetone and dichloromethane	Yamac and Bilgili (2006)
11	*Clavariadelphus*(*C. truncates*)	Same as above	Yamac and Bilgili (2006)
12	*Clavaria* (*C. vermicularis*)	Methanol	Ramesh and Pattar (2010)
13	*Climadocon* (*C. pulcherrimus*)	Ethyl acetate	Rosa and others (2003)
14	*Clitocybe* (*C. alexandri, C. geotropa, C. maxima, C. nebularis, C. sinopica*)	Water, methanol, ethanol, and ethyl acetate, Diethylether and N-hexane	Solak and others (2006); Yamac and Bilgili (2006); Kim and others (2008); Kalyoncu and Oskay (2008); Zheng and others (2010)
15	*Collybia* (*C. albuminosa*)	Cultural filtration	Coletto and Lelli (1998)
16	*Coprinellus* (*C. mecaceus*)	Culture filtration	Ayodele and Idoko (2011)
17	*Coprinus* (*C. cinereus, C. micaceus, C. Sp.*)	Methanol, ethanol, and ethyl acetate	Mwita and others (2010); Ndyetabura and others (2010); Dundar and others (2016); Reid and others (2016)
18	*Cordyceps* (*C. militaris, C. sobolifera*)	Tris-HCl (pH 8.0) and culture filtration	Cao and others (2003); Imtiaj and others (2007b); Park and others (2009)
19	*Corilopsis*(*C. occidentalis*)	Methanol	Gbolagade and Fasidi (2005)
20	*Cortinarius* (*C. sp*)	Cultural filtration	Coletto and Lelli (1998)
21	*Craterellus* (*C. cornucopioides*)	Water, methanol, hexane, and ethyl acetate	Venturini and others (2008)
22	*Daedalea* (*D. elegans*)	Methanol	Coletto and Lelli (1998); Gbolagade and Fasidi (2005)
23	*Daldinia* (*D. concentrica*)	Methanol	Gbolagade and Fasidi (2005)
24	*Dictyophora* (*D. duplicate*, *D. Echino-volvatus*, *D. indusiata, D. rubrovalvata*)	Water, ethanol, ethyl acetate, and n-hexane, Cultural filtration	Tan and others (2002, 2007); Han and others (2008); Yang and others (2008); Lu and others (2009); Oyetayo and others (2009); Chen and others (2012)
25	*Entoloma* (*E.lividum*)	Cultural filtration	Coletto and Lelli (1998)
26	*Fistulina* (*F. hepatica*)	Methanol	Karaman and others (2009); Alves and others (2012a); Giri and others (2012)
27	*Flammulina* (*F. velutipes*)	Methanol	Ishikawa and others (2001a); Karaman and others (2009)
28	*Fomes* (*F. lignosus, F. fomentarius*)	Methanal and ethanol	Fagade and Oyelade (2009); Dundar and others (2016)
29	*Fomitopsis* (*F. officinalis, F. pinicola*)	Ethanol and chloroform	Guler and others (2009)
30	*Galera* (*G. sphagnorum*)	Culture filtration	Coletto and Lelli (1998)
31	*Ganoderma* (*G. applanatum, G. australe, G. carnosum, G. lucidum, G. pfeifferi, G. sinense*)	Water, ethyl alcohol, methanol, and acetone	Gao and others (2005); Yamac and Bilgili (2006); Smania and others (2007); Moradali and others (2008); Subbraj and others (2008); Jonathan and Awotona (2010); Sridhar and others (2011); Reid and others (2016)
32	*Glocostereum* (*G. incarnatum*)	Culture filtration	Cao and others (2003)
33	*Gloeoporus* (*G. thelephoroides*)	Ethyl alcohol	Rosa and others (2003)
34	*Gomphidius* (*G. viscidus*)	Methanol	Venturini and others (2008)
35	*Gyromitra* (*G. esculenta*)	Methanol	Venturini and others (2008)
36	*Hericium* (*H. erinaceus*)	Methanol	Wong and others (2009)
37	*Hexagonia* (*H. hydnoides*)	Ethyl alcohol	Rosa and others (2003)
38	*Hydnum* (*H. repandum*)	Ethanol, chloroform, ethyl acetate, and acetone, Dichloromethane	Yamac and Bilgili (2006)
39	*Hygrophorus* (*H. agathosmus*)	Methanol and chloroform	Yamac and Bilgili (2006); Giri and others (2012)
40	*Hypholoma* (*H. fasciculare, H. sublateritium*)	Ethanol	Coletto and Lelli (1998); Barros and others (2008b)
41	*Hypsizeygus* (*H. tessulatus*)	Methanol	Chowdhury and others (2015)
42	*Irpex* (*I. lacteus*)	Ethyl alcohol	Rosa and others (2003)
43	*Lactarius* (*L. camphoratus, L.deliciosus, L. deterrimus, L. kabansus, L. necator, L. piperatus , L. salmonicolor, L. sanguifluus, L. vellereus*)	Methanol and culture filtration	Anke and others (1989); Barros and others (2007b); Guler and others (2009); Karaman and others (2009); Santoyo and others (2009); Alves and others (2012b); Dundar and others (2016); Reid and others (2016)
44	*Laetiporus* (*L. sulphureus*)	Ethanol	Turkoglu and others (2007); Karaman and others (2009)

(*Continued*)

Table 1–Continued.

Code	Genus (main species)	Extraction solvents	References[a]
45	*Lentinus* (*L. edodes, L. conatus, L. cladopus, L. squarrosulus*)	Water, methanol, ethanol, and chloroform, Culture filtration	Ishikawa and others (2001b); Beelman and others (2003); Cao and others (2003); Guo and others (2004); Yamac and Bilgili (2006); Rao and others (2009); Giri and others (2012)
46	*Lenzites* (*L. betulina*)	Ethanol, chloroform, ethyl acetate, acetone, Dichloromethane	Chowdhury and others (2015)
47	*Lepiota* (*L. procera, L. sp*)	Methanol	Giri and others (2012)
48	*Lepista* (*L. nuda*)	Methanol	Yamac and Bilgili (2006); Alves and others (2012a)
49	*Leucoagaricus* (*L. pudicus*)	Ethanol, chloroform, ethyl acetate, Acetone and dichloromethane	Rosa and others (2003); Yamac and Bilgili (2006)
50	*Leucopaxillus* (*L. giganteus*)	Methanol	Barros and others (2007a); Alves and others (2012a)
51	*Lycoperdon*(*L. molle, L. perlatum*)	Methanol	Barros and others (2008b); Ramesh and Pattar (2010)
52	*Lyophillium* (*L. agregatum*)	Water	Venturini and others (2008)
53	*Macrolepiota* (*M. procera*)	Methanol and ethyl acetate	Venturini and others (2008)
54	*Marasmius* (*M. bellus, M. oreades, M.* sp)	Methanol, ethyl acetate, and culture filtration	Cao and others (2003); Rosa and others (2003); Ramesh and Pattar (2010)
55	*Meripilus* (*M. giganteus*)	Ethanol	Kalyoncu and Oskay (2008); Karaman and others (2009)
56	*Merulius* (*M. tremellosus*)	Culture fluid	Giannetti (1978)
57	*Morchella* (*M. deliciosa*)	Culture filtration	Cao and others (2003)
58	*Mutinus* (*M. elegans, M. caninus*)	Culture filtration	Coletto and Lelli (1998)
59	*Mycena* (*M. rosea*)	Methanol	Alves and others (2012a)
60	*Nothopanus* (*N. hygrophanus*)	Ethyl acetate	Rosa and others (2003)
61	*Oudemansiella* (*O. mucida, O. canarii*)	Methanol and ethyl acetate	Rosa and others (2003); Imtiaj and others (2007b)
62	*Panus* (*P. tigrinus, P. fulvus*)	Methanol and ethanol	Fagade and Oyelade (2009); Karaman and others (2009)
63	*Paxillus* (*P. involutus*)	Ethanol, chloroform, ethyl acetate, Acetone and dichloromethane	Coletto and Lelli (1998); Yamac and Bilgili (2006)
64	*Phellinus* (*P. baumii, P.*sp)	Methanol and ethyl acetate	Rosa and others (2003); Balakumar and others (2011); Lee and others (2013)
65	*Pholiota* (*P.mutabilis*)	Culture filtration	Coletto and Lelli (1998)
66	*Piptoporus* (*P. betulinus*)	Methanol and chloroform	Karaman and others (2009)
67	*Pleurotus* (*P. eryngii, P. ferulae, P. ostreatus, P. pulmonarius, P. sajor-caju, P. squarrosolus*)	Water, methanol, ethanol, and petroleum ether	Gerasimenya and others (2002); Ngai nd Ng (2004); Akyuz and Kirbag (2009); Fagade and Oyelade (2009); Ramesh and Pattar (2010); Nwachukwu and Uzoeto (2010); Chowdhury and others (2015)
68	*Polyporus* (*P. arcularius, P. Grammocephalus*)	Methanol, chloroform, ethyl acetate, acetone, and dichloromethane	Yamac and Bilgili (2006); Giri and others (2012); Dundar and others (2016)
69	*Polystictus* (*P. hirsutus*)	Culture filtration	Coletto and Lelli (1998)
70	*Psathyrella* (*P. candolleana*)	Culture filtration	Coletto and Lelli (1998)
71	*Pycnoporus* (*P. cinnabarinus, P.sanguineus*)	Ethyl acetate	Rosa and others (2003); Shittu and others (2006); Imtiaj and others (2007b)
72	*Ramaria* (*R. flava, R. formosa, R. botrytis*)	Methanol	Barros and others (2008b); Ramesh and Pattar (2010); Giri and others (2012)
73	*Russula* (*R. delica, R. laurocerasi, R. vesca*)	Water, methanol, and ethanol	Nwachukwu and Uzoeto (2010); Alves and others (2012a); Giri and others (2012)
74	*Rhizopogon* (*R. roseolus*)	Water, methanol, ethanol, diethyl ether; Ethyl acetate and N-hexane	Solak and others (2006); Yamac and Bilgili (2006)
75	*Sarcodon* (*S. imbricatus*)	Ethanol, chloroform, ethyl acetate, Acetone and dichloromethane	Yamac and Bilgili (2006); Barros and others (2007cc)
76	*Schizophyllum* (*S. commune*)	Methanol	Giri and others (2012)
77	*Sparassis* (*S. crispa*)	Ethanol	Kalyoncu and Oskay (2008)
78	*Stereum* (*S. ostrea*)	Water, ethanol, and culture filtration	Imtiaj and others (2007a, b)
79	*Strobilurus* (*S. ohshimae*)	Culture filtration	Shiono and others (2007)
80	*Stropharia* (*S. rugoso-annulata*)	Ethanol	Chen and others (2010b)
81	*Suillus* (*S. collitinus*)	Ethanol, chloroform, ethyl acetate, acetone, Dichloromethane	Yamac and Bilgili (2006)
82	*Terfezia* (*T. boudieri*)	Methanol	Akyuz and others (2010)
83	*Termitomyces* (*T. clypeatus, T. eurhizus, T. microcarpus*)	Methanol	Giri and others (2012)
84	*Trametes* (*T. versicolor, T. Saepiara, T. strumosa*)	Ethanol	Yamac and Bilgili (2006); Fagade and Oyelade (2009); Reid and others (2016)
85	*Tremella* (*T. fuciformis*)	Water	Guo and others (2004)
86	*Tricholoma* (*T. lobayensis, T. mongolicum, T. portentosum*)	Ethanol, chloroform, ethyl acetate, Acetone and dichloromethane	Gbolagade and Fasidi (2005); Yamac and Bilgili (2006); Barros and others (2007cc; 2008b); Alves and others (2012b); Giri and others (2012)
87	*Tyromyces* (*T. duracinus*)	Ethyl acetate	Rosa and others (2003)
88	*Volvariella* (*V. vulvae*)	Water, methanol, and ethanol	Nwachukwu and Uzoeto (2010); Giri and others (2012)

[a] Cited by 1st author's name.

(Ramesh and Pattar 2010; Giri and others 2012), Korea (Imtiaj and others 2007b), Nigeria (Fagade and Oyelade 2009), Northern Serbia (Karaman and others 2009), Portugal (Alves and others 2012a), Turkey (Yamac and Bilgili 2006), and Spain (Venturini and others 2008). Those mushrooms include both naturally occurring wild mushrooms, especially wood-decay species, such as *Agrocybe* spp., *Panus fulvus*, and *Auricularia auricula-judae* (Rosa and others 2003; Fagade and Oyelade 2009; Nwachukwu and Uzoeto 2010) and commercially cultivated mushrooms, such as *Agaricus bisporus* and *Pleurotus* spp. (Gerasimenya and others 2002; Jagadish and others 2009), and worldwide well-known medicinal mushrooms, such as *Ganoderma* spp., *Lentinus edodes*, and *Cordyceps militaris* (Ishikawa and others 2001b; Gao and others 2005; Park and others 2009). Some of the 1st research studies that included the antitumor

and antimicrobial compounds from *Ganoderma* species, *L. edodes*, *Schizophyllum commune*, and *Grifola frondosa* had been the main research subjects (Zjawiony 2004; Rai and others 2005). However, more recently, an increasing number of studies on mushrooms have incorporated their antimicrobial properties and the research focus now is shifting from traditional medicinal mushrooms to edible mushroom species, such as *Pleurotus* spp., *Dictyophora* spp., *Lentinus* spp., and *Agaricus* spp. (Cao and others 2003; Han and others 2008; Aida and others 2009; Akyuz and others 2010).

Extraction of Mushroom Antimicrobials

Extracting active compounds and determining their antimicrobial properties are now common practice. Classic solvent extraction is still the most widely used method for the extraction of active compounds from natural sources, though other technologies are gaining recognition, such as supercritical and microwave extraction. The solvent used for extraction determines the specific components, but it may also affect the quality, quantity, and safety of the recovered products. Therefore, studies have compared the effect of different solvents on the extraction of mushroom antimicrobial compounds (Yamac and Bilgili 2006; Venturini and others 2008).

Water and methanol (or ethanol) are the most commonly used solvents in extracting mushroom antimicrobial components (Table 1). Water is a common medium for biochemical reactions and has a strong polarity, facilitating the extraction of active ingredients from biological materials. Water can be used for extracting water-soluble small-molecular-weight phenolic compounds and certain other compounds with strong polarity, such as saccharides and polysaccharide-binding proteins. Suortti (1986) reported that the water extracts from *Lactarius necator* showed antibacterial activity through compounds with phenolic characteristics. Moreover, Santoyo and others (2009) found that water extracts of *L. edodes*, *Boletus edulis*, and *Pleurotus ostreatus* had stronger antibacterial activities as compared to their methanol extracts. One of the major factors that affects water extraction is temperature. Although a higher temperature may increase extraction efficiency, it may also result in degradation of temperature-sensitive antimicrobials. As an example, the hot-water extracts (boiling for 4 h) from *Russula vesca* and *Pleurotus squarrosulus* had greater antibacterial activity than the warm water extracts (room temperature, 28 ± 2 °C, for 36 h); in contrast, antibacterial activities of the hot-water extracts from *Volvariella vulvae* and *A. auricula-judae* were weaker than the warm water extracts (Nwachukwu and Uzoeto 2010).

Methanol (or ethanol) is another common solvent used for extracting phenolic compounds from mushrooms. In Ramesh and Pattar's research (2010), the antimicrobial properties of methanol extracts of *Lycoperdon perlatum, Clavaria vermicularis, Marasmius oreades*, and *Pleurotus pulmonarius* were directly influenced by phenolic contents. Barros and others (2007c) also reported that the antimicrobial activity levels were positively associated with the portion of phenolic and/or flavonoid compounds in the methanol extracts of *Lactarius deliciosus, Sarcodon imbricatus*, and *Tricholoma portentosum*. Temperature can also affect the extraction efficiency of menthol (or ethanol) and has effects on the yield of total phenolic compounds. Extracting *A. bisporus* samples with ethanol at room temperature resulted in higher total phenolic and flavonoid contents and stronger antibacterial activities than extracting the same samples with boiling ethanol (Jagadish and others 2009).

Other than water and methanol (or ethanol), several other organic solvents, such as chloroform, dichloromethane, acetone, ethyl acetate, and hexane, can also be used to extract various active compounds. The chemical profile of the extracts obtained with different solvents can vary and result in variations of their antimicrobial properties (Venturini and others 2008; Reid and others 2016). The fruiting bodies of *L. edodes* were extracted with methanol, hexane, ethyl acetate, and water, respectively, and the extracts from each of the solvents revealed different antibacterial spectra. The water extract inhibited a great number of bacterial species, including *Bacillus cereus, Listeria monocytogenes, Staphylococcus aureus, Clostridium perfringens, Vibrio parahaemolyticus,* and *Yersinia enterocolitica*. The methanol extract was active against *L. monocytogenes* and *C. perfringens,* while the ethyl acetate extract was only slightly inhibitory to *C. perfringens* and the hexane extract showed no any antimicrobial action (Venturini and others 2008).

Serial extraction, using more than one solvent with different polarities, may increase the extraction efficiency and help in identifying active components in the extracted fractions (Yamac and Bilgili 2006; Basunia and others 2007; Venturini and others 2008). To determine the antimicrobial activities of steroids from *Ganoderma lucidum*, Subbraj and others (2008) extracted fruiting bodies of this mushroom with petroleum ether, benzene, chloroform, ethyl acetate, and ethanol in the sequence of increasing polarity, and found that the antibacterial activities were only detected in the extracts of the 1st 3 solvents, which contained steroids, but not from the extracts of ethyl acetate and ethanol.

In addition to classic solvent extraction, current physical techniques such as microwave, ultrasonic wave, microfilter, and supercritical fluid extraction are now being used to enhance extraction efficiency. Microwave and ultrasonic uses are now common techniques for assisting extractions. For example, to increase the polysaccharide yield from *Clitocybe maxima* water extract, an 8-min microwave exposure was done before a normal water extraction procedure. This increased total extract amount and polysaccharide content by 60% and 30.7%, respectively (Chen and others 2013). For the extraction of phenolic compounds from *Agrocybe chaxingu,* ultrasonic wave-assisted extraction significantly reduced extracting time to 30 min from the overnight time needed with regular ethanol extraction for a similar extraction efficacy (Shen, unpublished data, 2016). Kitzberger and others (2007) compared antimicrobial activities of *L. edodes* obtained by classical extraction and supercritical extraction, and they noticed that only supercritical extracts showed antibacterial activity against *Micrococcus luteus* and *B. cereus*.

The antimicrobial activities of mushroom extracts are commonly determined using bioassays, including agar diffusion tests and disk or agar cup assays. Those assays determine the inhibitive activities against targeted microorganisms. Minimum inhibitory concentration (MIC) or minimum bactericidal concentration is frequently used to quantitatively express the activity levels of mushroom antimicrobials (Ishikawa and others 2001b; Giri and others 2012). In some cases, thin layer chromatography is also applied for separating and determining antimicrobial compounds in selected fraction/extracts (Shittu and others 2006; Sudirman 2010).

Antimicrobial Properties of Mushrooms

The currently known mushroom genera with antimicrobial properties are listed in Table 2. Among the 88 fungal genera listed, 45 of them are known to have antibacterial properties and 42 genera demonstrated both antibacterial and antifungal properties. Only one genus *Climacodon pulcherrimus* was found to only have antifungal properties (Rosa and others 2003). The extract of mushroom fruiting bodies or/and mycelia is usually used for evaluating

Table 2–Antimicrobial properties of mushrooms against pathogenic or nonpathogenic foodborne bacteria and molds.[a]

		Foodborne/health-related bacterial[b]									Foodborne/health-related molds[c]						
	Mushroom genus	Bac	Clo	Lis	Sta	Ecol	Kle	Pse	Sal	Shi	Can	Sac	Asp	Bot	Fus	Pen	Tri
1	*Agaricus*	+	+		+	+	+	+			+					+	+
2	*Agrocybe*	+			+	+				+	+		+			+	
3	*Amanita*		+		+	+	+		+			+					
4	*Armillaria*		+			+	+			+		+					
5	*Astraeus*						+		+			+					
6	*Auricularia*		+			+	+	+	+	+		+					+
7	*Boletus*		+	+	+	+			+	+							
8	*Calocybe*							+									
9	*Cantharellus*		+	+	+	+			+								
10	*Chroogomphus*		+			+	+		+	+							
11	*Clavariadelphus*		+			+	+			+							
12	*Clavaria*		+			+	+		+			+					
13	*Climadocon*											+					
14	*Clitocybe*	+		+	+	+		+	+	+	+	+		+			+
15	*Collybia*		+														
16	*Coprinellus*					+	+							+			+
17	*Coprinus*				+	+		+	+		+		+				
18	*Cordyceps*					+	+		+						+	+	
19	*Corilopsis*		+			+	+	+									
20	*Cortinarius*		+														
21	*Craterellus*		+	+		+											
22	*Daedalea*	+			+	+	+										
23	*Daldinia*		+			+	+	+									
24	*Dictyophora*		+		+	+	+		+	+	+	+	+	+			+
25	*Entoloma*	+															
26	*Fistulina*			+	+	+											
27	*Flammulina*		+			+											
28	*Fomes*					+	+	+									
29	*Fomitopsis*		+														
30	*Galera*		+														
31	*Ganoderma*		+			+	+	+	+	+		+		+	+		+
32	*Glocostereum*		+			+	+				+						+
33	*Gloeoporus*		+														
34	*Gomphidius*		+		+						+						
35	*Gyromitra*				+												
36	*Hericium*	+			+	+		+	+	+	+						
37	*Hexagonia*		+														
38	*Hydnum*		+	+		+											
39	*Hygrophorus*		+	+		+			+	+							
40	*Hypholoma*		+			+						+					
41	*Hypsizigus*	+			+	+	+	+	+		+						
42	*Irpex*		+					+			+						
43	*Lactarius*	+	+		+	+	+	+	+	+	+		+		+	+	
44	*Laetiporus*		+			+	+		+	+		+					
45	*Lentinus*	+	+	+	+	+	+	+	+		+	+		+	+		+
46	*Lenzites*		+			+	+										
47	*Lepiota*		+				+		+			+					
48	*Lepista*		+		+	+	+										
49	*Leucoagaricus*		+			+	+			+		+	+				
50	*Leucopaxillus*		+		+	+	+										
51	*Lycoperdon*		+			+	+					+					
52	*Lyophillium*				+												
53	*Macrolepiota*		+	+													
54	*Marasmius*		+	+		+	+		+	+	+	+		+			+
55	*Meripilus*	+			+	+			+		+						
56	*Merulius*		+														
57	*Morchella*		+				+										
58	*Mutinus*		+			+	+			+		+					
59	*Mycena*				+	+											
60	*Nothopanus*				+	+											
61	*Oudemansiella*					+	+		+			+			+		
62	*Panus*					+	+	+									
63	*Paxillus*		+			+				+							
64	*Phellinus*	+			+	+		+	+				+			+	
65	*Pholiota*		+			+											
66	*Piptoporus* (*P. betulinus*)	+															
67	*Pleurotus*	+	+		+	+	+	+	+		+	+	+		+		+
68	*Polyporus*	+			+	+		+	+								
69	*Polystictus*		+			+											
70	*Psathyrella*		+			+								+			+
71	*Pycnoporus*				+	+	+		+			+			+		
72	*Ramaria*		+	+	+	+											
73	*Russula*		+		+	+	+	+	+	+		+					
74	*Rhizopogon*					+	+		+								
75	*Sarcodon*	+		+	+	+			+								
76	*Schizophyllum*		+				+		+			+					

(*Continued*)

Table 2–Continued.

	Mushroom genus	Foodborne/health-related bacterial[b]									Foodborne/health-related molds[c]						
		Bac	Clo	Lis	Sta	Ecol	Kle	Pse	Sal	Shi	Can	Sac	Asp	Bot	Fus	Pen	Tri
77	*Sparassis*	+			+	+			+		+						
78	*Stereum*		+			+	+	+	+						+		
79	*Strobilurus*					+			+								
80	*Stropharia*						+										+
81	*Suillus*		+			+	+			+		+	+				
82	*Terfezia*						+										
83	*Termitomyces*		+				+		+								
84	*Trametes*				+	+		+	+			+					
85	*Tremella*					+											
86	*Tricholoma*		+		+	+	+	+	+			+					
87	*Tyromyces*					+											
88	*Volvariaella*					+	+				+						

[a] Pathogens listed in Table 2 are the same targets used to determine the antimicrobial activities of mushroom species from same genus (same row), "+" indicates active against targets.
[b] Gram-positive bacteria: *Bacillus* spp., Bac; *Clostridium perfringens*, Clo; *Listeria monocytogenes*, Lis; *Staphylococcus* spp., Sta.
Gram-negative bacteria: *Escherichia coli*, Ecol; *Klebsiella pneumonia*, Kle; *Pseudomonas aeruginosa*, Pse; *Salmonella* spp., Sal; *Shigella* spp, Shi.
[c] Yeast species: *Candida* spp., Can; *Saccharomyces cerevisiae*, Sac.
Filamental mold species: *Aspergillus* spp., Asp; *Botrytis* spp., Bot; *Fusarium* spp., Fus; *Penicillium* spp., Pen; *Trichophyton mentagrophytes*, Tri.

antimicrobial properties, though in certain cases, mycelial cultural broth has also been tested. The antimicrobial activities are usually challenging to compare among genera as the reports are usually obtained from different research groups and great variations exist in the microorganisms and bioassays used by different researchers. Therefore, we summarized the available reports and listed the food pathogens to which each mushroom genus has positive antimicrobial activities (Table 2), and our efforts were not focused on those "not tested" or "tested but not active." In this review, the antibacterial and antifungal properties will be discussed separately.

Antibacterial property

Foodborne bacteria that are usually used for the evaluations of the antibacterial activities of mushroom extracts include *Acinetobacter baumannii*, *Aeromonas* spp., *Bacillus* spp., *Campylobacter* spp., *C. perfringens*, *Escherichia coli* 0157:H7, *Klebsiella pneumoniae*, *L. monocytogenes*, *Pseudomonas aeruginosa*, *Salmonella enteritidis*, *Shigella* spp., *Staphylococcus* spp., *V. parahaemolyticus*, and *Yersinia* spp.. Different mushroom genera have usually demonstrated different antibacterial spectra, as shown in Table 2. Even in the same genus, different mushroom species may exhibit different antibacterial activities. Additionally, mushroom extracts with different extraction solvents also had different antibacterial activities. For example, Jonathan and Awotona (2010) in comparing antibacterial activities of *G. lucidum* and *Ganoderma applanatum* against *B. cereus*, *S. aureus*, *P. aeruginosa*, and *K. pneumoniae*, found that the water extract of *G. lucidum* had much greater activity than that of *G. applanatum*; however, their ethanol extract of *G. lucidum* was less active than that of *G. applanatum*.

Mushroom antibacterial activities summarized in Table 2 indicated that the number of mushrooms with activities against Gram-positive bacteria is much greater than that with activity against Gram-negative bacteria, which agreed with the review of Alves and others (2012b). This phenomenon was also noticed by Venturini and others (2008) and Yamac and Bilgili (2006), who studied 48 and 20 mushroom species, respectively.

Antibacterial products of mushrooms can be their intracellular or/and extracellular metabolites. Extracts from the fruiting body and mycelial culture filtrate (cell-free) of the same mushroom species may result in different antibacterial properties. From a submerged culture of 14 *P. ostreatus* strains, Gerasimenya and others (2002) confirmed that the mycelial extracts were more active against tested bacteria than the extracts of their culture filtrates. Yamac and Bilgili (2006) compared the extracts of fruiting bodies and extracts of mycelial culture filtrates, finding among the 20 mushroom species/genera tested, that 16 fruiting body extracts and 10 mycelial culture filtrate extracts showed antibacterial activities. The antibacterial activities of the extracts from fruiting bodies were generally greater than those of the extracts from mycelial culture filtrates. In *Ganoderma carnosum*, *Lenzites betulina*, *Leucoagaricus pudicus*, *Polyporus arcularius*, *Rhizopogon roseolus, Trametes versicolor*, and *Tricholoma auratum*, both the extracts of fruiting body and culture filtrate showed antibacterial activities. In *Amanita caesarea, Armillaria mellea, Chroogomphus rutilus, Clitocybe geotropa, Hydnum repandum, Hygrophorus agathosmus, S. imbricatus, Suillus collitinus*, and *Tricholoma fracticum,* only the extracts from the fruiting body demonstrated antibacterial activities, while antibacterial activities of *Clavariadelphus truncatus, Ganoderma* sp. T-99, and *Lepista nuda* were only found in the extracts of their culture filtrate.

Antibacterial properties of mushrooms may also vary with the maturation of their fruiting bodies. Barros and others (2007b) in comparing the antibacterial activity and the contents of phenols, flavonoids, ascorbic acid, β-carotene, and lycopene of *L. deliciosus* at different maturity stages discovered that the immature fruiting bodies of *L. deliciosus* were more active against *B. cereus*, *S. aureus*, and *P. aeruginosa* than the mature fruiting bodies, which corresponded to the decrease in the phenolic, flavonoid, and ascorbic acid contents as the fruiting bodies aged. However, a report on *Coprinus cinereus* showed a different trend. The ethyl acetate extracts of its capping and postcapping fruiting bodies exhibited stronger antibacterial activities as compared to the extracts of precapping fruiting bodies (Mwita and others 2010).

Antifungal property

Antifungal activities of mushrooms are usually determined by evaluating the inhibition of fungal mycelial growth. Common foodborne fungi used for such determination include the filamentous fungi *Aspergillus* spp., *Botrytis cinerea*, *Cladosporium herbarum*, *Fusarium* spp., *Magnaphorthe grisea*, *Mycosphaerella arachidicola*, *Penicillium* spp., *Physalospora piricola*, and *Trichophyton mentagrophytes,* and the yeasts *Candida albicans* and *Saccharomyces cerevisiae*. Mushrooms with antifungal properties are summarized in Table 2. Among the 43 genera listed with antifungal activity, only 20 of them have been tested against yeast species. *Fusarium* species, important foodborne pathogens with potential of producing mycotoxins, have frequently been used to test the antifungal activity of many mushroom species. Extracts from cultured *P. ostreatus* (Okamoto and others 2002), wild species of *Pleurotus* (Ngai and Ng

2004), *Ganoderma* spp. (Jonathan and Awotona 2010), *C. militaris* (Park and others 2009), and wild mushrooms of *Fomitopsis pinicola* and *Lactarius vellereus* (Guler and others 2009), have demonstrated antifungal activities against various *Fusarium* spp.

The antifungal properties of mushrooms also provide an additional advantage by lowering food safety risks associated with fungicide use in cultivated mushrooms, as mushrooms with antifungal property can suppress undesirable fungi, such as *Trichoderma* spp., *Aspergillus* spp., and *Penicillium* spp., during growth, thus leading to reduced fungicide use (Choi and others 2010). Eleven mushroom genera have been identified with antifungal properties against *Aspergillus* spp. or *Penicillium* spp., including *Agaricus*, *Agrocybe*, *Coprinus, Cordyceps, Dictyophora*, *Hygrophorus, Lactarius*, *Leucoagaricus, Ganoderma*, *Pleurotus*, and *Phellinus*. Among these genera, only *Agrocybe*, *Lactarius*, and *Phellinus* mushrooms have antifungal activity against both *Aspergillus* spp. and *Penicillum* spp. Although cultivated mushrooms, such as *A. bisporus* and *P. ostreatus*, have been intensively studied for their antifungal property against undesirable fungi, only less than half of the mushroom genera listed in Table 1 have been evaluated for their antifungal property (Table 2). Therefore, there are great potentials in discovering more mushroom species with antifungal properties.

Diversity of Mushroom Antimicrobial Metabolites

A mushroom metabolite profile is species-unique and related to its growth condition. Thus, there is a great diversity in the mushroom antimicrobial metabolites due to the many different species and that mushrooms can live in a wide range of ecological niches with great variations in nutrients and physical and biological conditions (Lindequist and others 2005). Wild mushrooms are usually evaluated as initial material sources in many screenings for identifying antimicrobials (Rosa and others 2003; Yamac and Bilgili 2006; Venturini and others 2008; Giri and others 2012), although antimicrobial compounds may also be produced from cultivated mushrooms (Wong and others 2009). During mushroom growth, a variety of primary and secondary metabolites can be accumulated as intracellular and extracellular products, including phenolics, polyketides, terpenoids, steroids, nonprotein amino oxide, antibacterial or antifungal proteins, and volatile fatty acids (Che and others 1998; Zjawiony 2004; Alves and others 2012b, 2013). The production of such metabolites, especially secondary metabolites, is associated with mushroom living environments and nutrient sources, which all lead to the great diversity of the metabolites (Table 3). Different mushroom species usually have characteristic metabolite profiles, although they may show similar antimicrobial activities. As summarized in the review by Zjawiony (2004), the secondary metabolites of more than 75% of the screened medicinal polypores, including *Ganoderma* spp., *Laetiporus* spp., *Trametes* spp., and *Grifola umbellate*, showed similar and strong antimicrobial activities.

Many phenolic compounds, especially the low-molecular-weight phenolic compounds, have been identified in various mushrooms, and their antimicrobial properties have been demonstrated. Alves and others (2013) have shown the antibacterial activities of 2,4-dihydroxybenzoic, protocatechuic, vanillic, and *p*-coumaric acids from different wild mushrooms; Chen and others (2010b), and Chowdhury and others (2015) have confirmed the antimicrobial activity of total flavonoid compounds in mushrooms. The intensity of antimicrobial activities of methanol extracts from mushrooms such as *L. deliciosus*, *S. imbricatus*, and *T. portentosum* corresponded positively to the total content of phenols and flavonoids in the extracts (Barros and others 2007c). Phenolic antimicrobial compounds can greatly vary in their chemical structures, including the molecular functional groups (Figure 1). The type of phenolic components and their ratios in a mushroom determine their antimicrobial activities (Kim and others 2008; Alves and others 2013). Phenolic components may exhibit activity against both bacteria and fungi, such as *p*-anisaldehyde, obtained from the sweet flavor extract of *P. ostreatus*, which inhibited the growth of *Bacillus subtilis, P. aeruginosa, Aspergillus niger*, and *Fusarium oxysporum* (Okamoto and others 2002).

Mushroom terpenoids are a large group of secondary metabolites belonging to terpenes with different functional groups (Figure 1), which have been identified in various mushroom genera/species, including sesquiterpenoids from *Lentinus connatus* (Vatcharin and others 2005), *Lactarius* spp. (Anke and others 1989), *Flammulina velutipes* (Ishikawa and others 2001a), strobilactones from *Strobilurus ohshimae* (Shiono and others 2007), triterpenoids from *Ganoderma sinense* (Sato and others 2009) and *Ganoderma pfeifferi* (Mothana and others 2000), and lanostanoid (1-4) from *Flammulina pinicola* (Keller and others 1996). This group of chemical compounds has exhibited antibacterial properties, although the functional groups are different (Table 3 and Figure 1). In addition to the antibacterial activity, cuparene-type sesquiterpenes, such as enokipodins C and D from *F. velutipes*, are also inhibitory to *C. herbarum* mycelial growth (Ishikawa and others 2001a). Compared to the knowledge on antimicrobial properties of terpenoids, the information on their biosynthetic mechanisms in mushrooms is very scarce. However, the sesquiterpene synthase homologues are widespread among fungi (Agger and others 2009), indicating the great potential in cultivating mushrooms as biosources for antimicrobial terpenoids.

The nonprotein amino oxides are another group of secondary metabolites that have antimicrobial activities. Cortamidine oxide extracted from wild *Cortinarius* spp. showed significant antimicrobial activity against *E. coli*, *B. subtilis*, *C. albicans*, *T. mentagrophytes*, and *Cladosporium resinae* (Nicholas and others 2001), and 2-amino-3-cyclopropylbutanoic acid from *Amanita cokeri* was active against *Cercospora kikuchii, Agrobacterium tumefaciens*, *Erwinia amylovora*, and *Xanthomonas campestris* (Drehmel and Chilton 2002).

Fatty acids and fatty alcohols are another group of secondary metabolites from mushrooms that have demonstrated antimicrobial activities against foodborne bacteria and molds. The fatty acids extracted from *Dictyophora echino-volvatus* showed strong antimicrobial activity against *S. aureus*, *E. coli, S. cerevisiae*, *C. albicans*, *Penicillium citrinum*, and *A. niger* (Tan and others 2007). Two secondary metabolites with strong antimicrobial activities, 1-octen-3-ol and 10-oxo-trans-8-decenoic acid (ODA), which were initially extracted from *A. bisporus,* have also been identified in many other mushroom species, such as *L. edodes*, *P. ostreatus*, and *Portabellas* spp. (Beelman and others 2003). These 2 metabolites have the function of stimulating mycelial growth of mushrooms themselves, while also possessing antimicrobial properties against bacteria such as *E. coli* O157: H7 (Morawicki and others 2005) and molds, including *Penicillium expansum* (Okull and others 2003). Palmitic acid from *G. applanatum* fruiting bodies, which plays an important role in mushroom growth, has also shown antibacterial activity (Moradali and others 2008). Other secondary metabolites, such as 2 farnesyl hydroquinones (ganomycin A and B) from *Ganoderma* spp. and polyketide from *Merulius tremellosus*, have also demonstrated antibacterial activities (Giannetti and others 1978; Mothana and others 2000; Gao and others 2005).

Some primary metabolites of mushrooms may also contribute to their antimicrobial properties (Table 3). For example, the

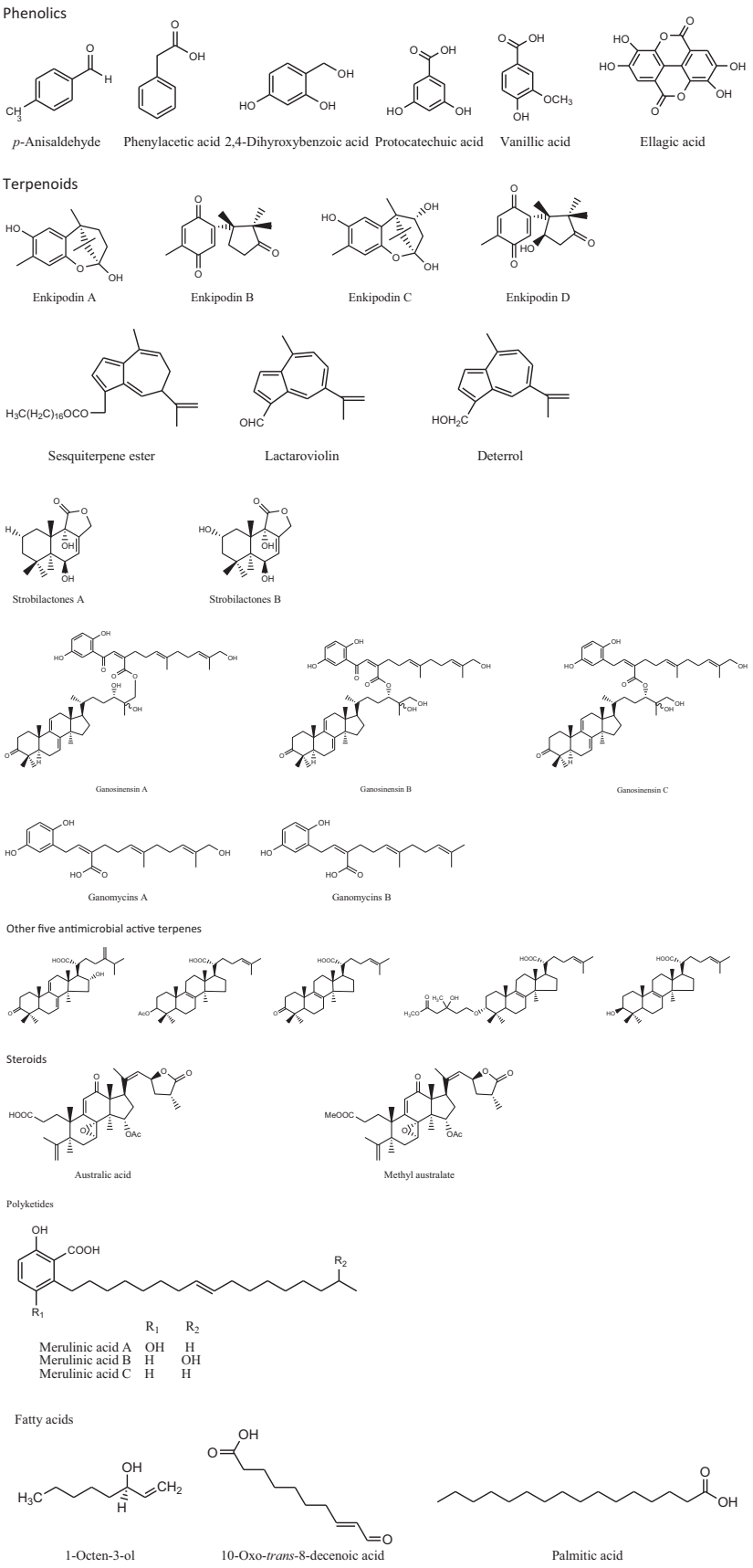

Figure 1–Chemical structures of antimicrobial secondary metabolites from mushrooms (compounds in Table 3).

Table 3–Antimicrobial compounds from mushrooms

Chemical group	Active compounds	Antimicrobial property	Mushrooms	References[a]
Phenolics	*p*-Anisaldehyde	Antibacterial and antifungal	*Pleurotus ostreatus*	Okamoto and others (2002)
	Phenylacetic acid	Antifungal	*Clitocybe nebularis*	Kim and others (2008)
	Protocatechuic acid	Antibacterial	*A. bisporus*	Alves and others (2013)
	Vanillic acid	Antibacterial	*Auricularia auricula-judae*	Alves and others (2013)
	Tannins	Antibacterial and antifungal	*Lentinus edodes*	Rao and others (2009)
	Ellagic acid	Antibacterial and antifungal	*L. edodes*	Rao and others (2009)
	Flavonoids	Antibacterial	*Leucopaxillus giganteus, Lactarius deliciosus*	Barros and others (2007a, 2007c)
Terpenoids	Terpene		*Pleurotus*	Vatcharin and others (2005)
Sesquiterpenoids	Sesquiterpenoids		*Lentinus connatus*, *Dictyophora*	Vatcharin and others (2005)
	Enokipodins A-D	Gram-positive bacterial	*Flammulina velutipes*	Ishikawa and others (2001a); Saito and Kuwahara (2005)
	Guaiol stearic acid ester Lactaroviolin, deterrol	Weak antibacterial	*Lactarius* spp.	Anke and others (1989)
	Strobilactones A and B	Antibacterial	*Strobilurus ohshimae*	Shiono and others (2007)
Triterpenoids	Ganosinensins A-C	Antibacterial	*Ganoderma sinense*	Gao and others (2005); Sato and others (2009)
	Ganomycins A, B	Antibacterial	*Ganoderma pfeifferi*	Mothana and others (2000)
Steroids	Other triterpenes	Antibacterial	*Fomitopsis pinicola Ganoderma*	Keller and others (1996)
	Methyl australate, australic acid	Antibacterial and antifungal	*Ganoderma australe*	Smania and others (2007)
Polyketides	Merulinic acids A-C	Antimicrobial	*Merulius tremellosus*	Giannetti and others (1978)
Fatty acids	1-Octen-3-ol 10-Oxo-trans-8-decenoic acid	Antibacterial and antifungal	*Agaricus bisporus, P. ostreatus*	Okull and others (2003)
	Palmitic acid	Antibacterial	*Ganoderma applanatum*	Moradali and others (2008)
	Pinicolic acid (1-3)	Antibacterial	*F. pinicola*	Keller and others (1996)
Fatty alcohol	Lentinamycin	Antibacterial and antifungal	*L. edodes*	Ishikawa and others (2001b)
Proteins	Lentin	Antifungal	*L. edodes*	Ngai and Ng (2003)
	Ganodermin	Antifungal	*Ganoderma lucidum*	Wang and Ng (2006)
(Carbohydrate-binding protein)	Lectin	Antifungal	*Dictyophora duplicate, L. edodes*	Ngai and Ng (2003); Lin and Su (2005)
(Nonprotein amino acid)	Cyclopropyl amino acid	Antibacterial and antifungal	*Amanitacokeri*	Drehmel and Chilton (2002)
	Disulfide cortamidine oxide	Antibacterial and antifungal	*Cortinarius sp.*	Nicholas and others (2001)
	2,2′-Dithiobis(pyridine *N*-oxide)	Antibacterial and antifungal	same above	Same as above
	Nebularine	Antifungal	*C. nebularis*	Kim and others (2008)
Enzymes	Ribonuclease	Antibacterail and antifungal	*P. sajor-caju*, *Dictyophora indusiata*	Ngai and Ng (2003); Wang and Ng (2003)
Sulfur heterocyclics	Lenthionine	Antibacterial and antifungal	*L. edodes*	Hatvani (2010)
Quinazoline compounds	Dictyoquinazols A-C		*D. indusiata*	Lee and others (2002)
Alkaloid	Sinensines A-E		*G. sinense*	Liu and others (2011)

[a] Cited by 1st author's name.

strong antimicrobial activity of some polypores resulted from high-molecular-weight polysaccharides (Zjawiony 2004) and proteins (Ngai and Ng 2003; Wang and Ng 2006). For example, the antifungal protein lentin, obtained from *L. edodes*, exhibited inhibition of mycelial growth of *P. piricola*, *B. cinerea*, and *M. arachidicola* (Ngai and Ng 2003). The ribonuclease from fresh *Pleurotus sajor-caju* has been shown to be inhibitory against *F. oxysporum* and *M. arachidicola*, as well as *P. aeruginosa* and *S. aureus* (Ngai and Ng 2004); ganodermin, another antifungal protein from *G. lucidum*, displayed inhibitory activity against the mycelial growth of *B. cinerea*, *F. oxysporum*, and *P. piricola* (Wang and Ng 2006), and the *G. lucidum* extracts combined with antibiotic ampicillin and cefazolin resulted in additive antimicrobial activity effects (Gao and others 2005). A protein from the wild mushroom *Clitocybe sinopica* has shown strong activity against *Agrobacterium* spp. and *Xanthomonas* spp. (Zheng and others 2010).

The antimicrobial properties of mushrooms are mainly determined by their genetic background. For example, the bamboo-mushroom *Dictyophora* spp. is known for its antimicrobial function and has been widely used as a preservative in food preservation (Tan and others 2002; Han and others 2008). The antimicrobial properties of the species *Dictyophora indusiatus* and *D. echino-volvatus* have been found to be significantly different from one another (Luo and others 2012). The extracts from *D. indusiatus* were more effective against bacteria than against yeasts and molds, while extracts of *D. echino-volvatus* showed the opposite (Luo and others 2012).

The antimicrobial properties of mushrooms can be significantly affected by environmental or nutritional factors, as such factors

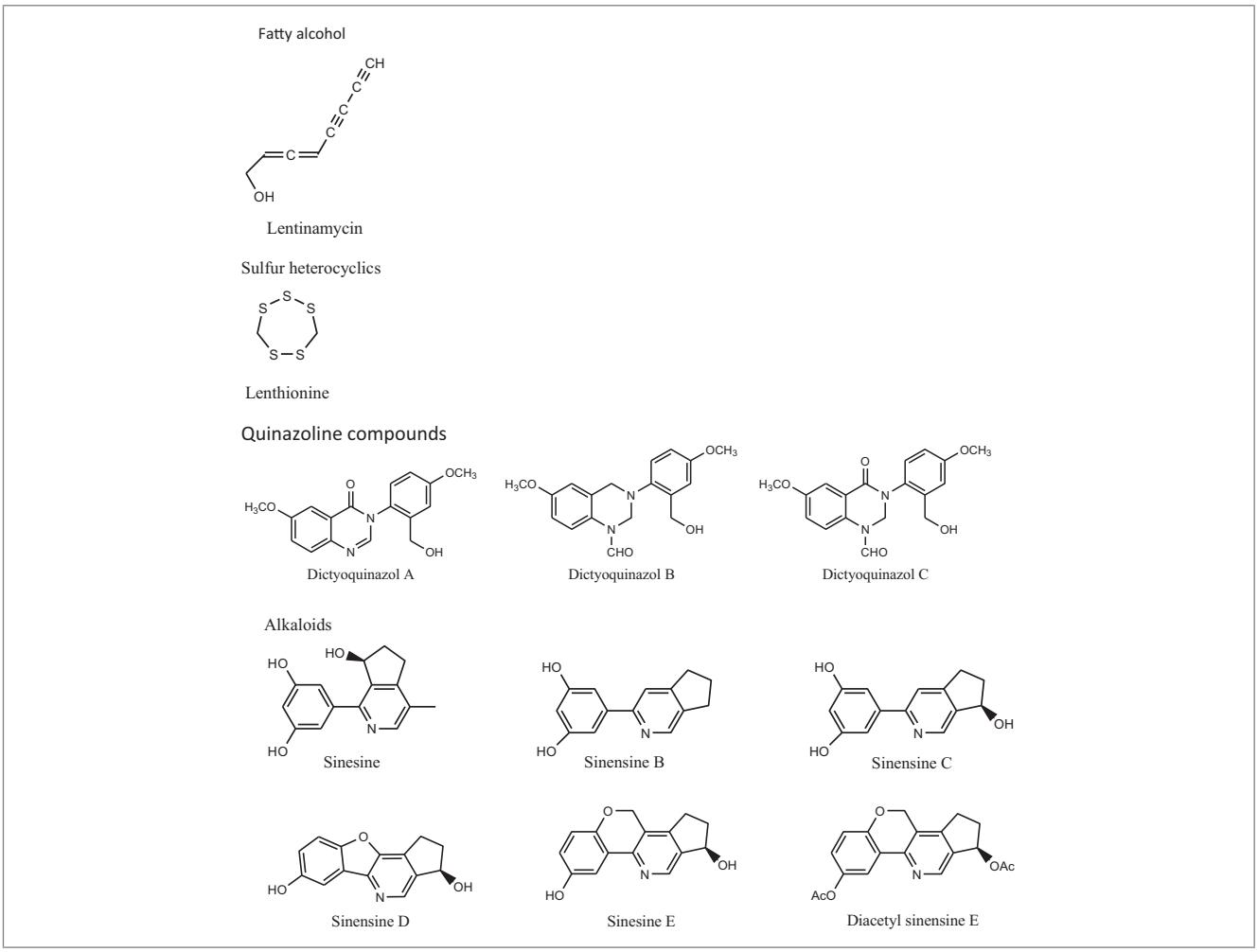

Figure 1–*Continued.*

can change mushroom metabolism, leading to variations in the production of their secondary metabolites. Wild mushrooms from different ecosystems and cultivated mushrooms from different cultivation substrates may produce very different antimicrobials (Barros and others 2007a; Akyuz and Kirbag 2009; Ndyetabura and others 2010). Crude ethyl acetate extracts of wild *C. cinereus* grown on dry grasses and cow dung in different ratios exhibited great difference in their activities against foodborne *E. coli, C. albicans*, and *A. niger* (Ndyetabura and others 2010). Barros and others (2008) compared a great number of wild and cultivated mushroom species and found that the contents of phenolic compounds were higher in wild mushrooms than in cultivated ones. However, the contents of protein and sugar were lower in wild mushrooms as compared to cultivated mushrooms. It is possible that mushrooms in the wild may consume nutrients for producing more secondary metabolites to resist abiotic stresses and biotic competitions. Also, the changes in mushroom growth conditions, for example, solid-cultivation and liquid-cultivation, may result in differences in the production of secondary metabolites (Shittu and others 2006).

Applications of Mushroom Antimicrobials to Assure Food Safety

In recent decades, the use of synthetic preservatives in food processing has been a common practice to control foodborne microorganisms. However, a public antipathy has developed recently against synthetic chemicals in foods, but not against naturally occurring chemicals. Therefore, discovering and applying natural and presumably safe antimicrobials as alternatives, especially from traditional food materials themselves, such as edible mushrooms, has become attractive to researchers and the food industry. Although the reports on successful applications of mushroom antimicrobials as food safety control agents are considerably few, more and more studies have started in this area and the number of patents on the use of mushroom antimicrobials for food safety purposes has been increasing significantly (Zjawiony 2004; Gao and others 2005; Alves and others 2012b).

The advances in large-scale processing techniques have now made it possible to prepare mushroom antimicrobials, or mushrooms with antimicrobial properties, for food use at an industrial scale. With spray-drying or freeze-drying technologies, those mushrooms and mushroom products, whether they are liquid or solid, and heat-stable or sensitive, can all be processed as food products or food supplements. Through a rotary concentration system, and followed by spray-drying, water extracts of mushrooms, including *Ganoderma, Tremella*, and *Agaricus* species, which mainly contain antimicrobial polysaccharides, have been made into polysaccharide powders as food supplements (Chen and others 2010a). This procedure has been developed to an industrial scale and now used for producing several mushroom nutraceutical products (Chen and others 2014). Freeze-drying technology is a

dehydration process generally used to preserve perishable materials, and it has been used to prepare heat-sensitive mushroom compounds (Shen and others 2006). The prepared mushroom antimicrobial products can be directly used in food to play a similar, or even better, function than synthetic antibiotics and preservatives. Such functions of mushroom antimicrobials have been demonstrated for their effects on modulating the gut microbiota when used as antibiotic treatment, and on prolonging the shelf-life of products when used as food preservatives.

Applied as an alternative for antibiotics, mushroom antimicrobial compounds have shown prebiotic functions by stimulating the growth of intestinal beneficial bacteria, while suppressing the growth of pathogenic ones (Aida and others 2009). Mushroom extracts have been used as feed supplements for experimental animals such as broiler chickens (Guo and others 2004; Willis and others 2009), piglets (Zhang and others 2008), and mice (Shen and others 2012). Feeding polysaccharide extracts of *L. edodes* and *Tremella fuciformis,* respectively, to broiler chickens infected with avian *Mycoplasma gallisepticum* stimulated the populations of beneficial bacteria such as *bifidobacteria* and *lactobacilli* and reduced the number of harmful or undesirable bacteria such as *Bacteroides* spp. and *E. coli* (Guo and others 2004). A similar experiment using healthy broiler chickens also indicated that mushroom extracts decreased *salmonella* populations in the chickens (Willis and others 2009). In another application of mushroom antimicrobials, Zhang and others (2008) fed weaned piglets with the *Agaricus blazei* liquid culture along with the usual feed to replace 50% of the antibiotic additive and found that the rate of animals with diarrhea was reduced by about 70%, lower than the rate in animals fed with antibiotics only, and the growth performance of piglets fed with *A. blazei* substitute was better than that fed with the antibiotics. This application has demonstrated the benefits of using a mushroom supplement to substitute for synthetic antibiotics in livestock to reduce food safety risks of many animal-based foods (Zhang and Shen 2007).

Mushroom material/extracts with antimicrobial compounds can be directly added to food as preservatives to prolong shelf-life by inhibiting spoilage bacteria. This effect of mushroom antimicrobials has been demonstrated with several applications. For instance, the antimicrobial polysaccharides of *Tremella* mushrooms (Guo and others 2004) have been used in *Tremella* drink products (Li and others 2011), and the shelf-life of these products without any addition of synthetic preservative was over 2 y, with no microbial spoilage or color or flavor changes (Chen and others, unpublished data, 2016). The bamboo mushroom (*Dictyophora*) is another noteworthy alternative for food preservatives. In southeast China, *Dictyophora* spp. are traditionally used in household cooking, especially in making stews, as a natural preservative to prevent microbial spoilage, and to maintain the freshness and delicate taste of the stews (Tan and others 2002; Han and others 2008). The keeping quality of tofu, meat, and rice can be maintained for several days with the addition of *Dictyophora* extracts or its fruiting body materials, while food without such an addition spoiled much more quickly (Han and others 2008).

Unlike synthetic antibiotics, which act by directly killing or inhibiting targeted microbes, antimicrobial functions of mushrooms often result from their multifunctional properties. Mushroom compounds with antimicrobial properties usually also have nutraceutical and pharmaceutical properties. Mushroom antimicrobial polysaccharides may improve human/animal immunity, and certain phenolic compounds have both antioxidant and antimicrobial functions (Rai and others 2005; Aida and others 2009; Pala and Wani 2011). When mushroom antimicrobials are used as alternatives to antibiotics or food preservatives, their various properties will provide multibenefits. For example, one of phenolic mushroom antimicrobials, *p*-anisaldehyde, isolated from *P. ostreatus* mushroom (Okamoto and others 2002), can function as both a preservative and a sweet flavor when added to processed food products. Substituting an antibiotic with *A. blazei* liquid culture complex in the feed not only significantly reduced the number of piglets with diarrhea, but the growth performance of the piglets was also better than those fed with antibiotics (Zhang and others 2008). Further study showed that feeding the liquid culture improved the development of the animal intestine, which is a nonspecial immunity organ, implying that certain mushroom antimicrobials may also be able to stimulate the immunity response of animals (Shen and others 2012). Strengthening immunity by the application of mushroom antimicrobials would significantly decrease the adverse effects of pathogens on animals and thus reduce the necessity for the use of antibiotics (Zhang and others 2008; Pala and Wani 2011). Mushroom antimicrobial active compounds such as polysaccharides may also play a prebiotic role in humans when used in food (Aida and others 2009). Mushroom antimicrobials used as preservative in food are usually made from water extracts of the fruiting body or mushroom materials, and they are rich in glucan-containing compounds, such as polysaccharides and glycoproteins. These compounds are well-known natural prebiotics (Aida and others 2009).

However, there are also challenges for the wide use of mushroom antimicrobials in food industry. The 1st one is that the productivity of the active antimicrobial compounds is relatively small. For example, the concentration of the extractable active flavonoids from *Stropharia rugoso-annulata* is only 7.94 g kg^{-1} fruiting body (dry weight), while the MIC of the extract against *E. coli* and *Penicillium* spp. is 20 and 40 mg mL^{-1} (Chen and others 2010b). A large quantity of mushrooms would be needed to produce enough antimicrobial compounds through traditional cultivation methods. By using the liquid culture rather than the production of fruiting bodies, the production volume could be increased and that would be more practical for industrial production. The 2nd challenge is the management of waste generated after the bioactive component extraction from the mushrooms. Research has been started on recycling the large amounts of these residues. Another issue with the production of the bioactive compounds is the use of nonenvironmentally friendly organic solvents. Emerging technologies have attempted to reduce or even omit the use of organic solvent, such as supercritical extraction. Another more important aspect when using mushroom antimicrobials for assuring food safety is the safety of the antimicrobials itself. Currently, there is a deficiency of references in reporting the food safety properties of those identified mushroom antimicrobial compounds (or extracts). This is not a so critical issue when the compounds or extract was from an edible material, but it is imperative that inedible species or even poisonous species be evaluated for the safety of the mushroom metabolites. For example, Drehmel and Chilton (2002) isolated 2 nonprotein amino acids from poisonous *A. cokeri* and also demonstrated their antimicrobial properties. However, strict and accurate tests will be required to verify their safety before use for food safety. Common strategy used by food industry to ensure the safety of mushroom extracts is the combination of using edible mushroom species (Beelman and others 2003; Cao and others 2003; Han and others 2008; Lu and others 2009) and water extraction (Jagadish and others 2009; Chen and others 2010a). It has become an emerging but challenging research topic to determine the food

safety properties of mushroom antimicrobials (Chen and others 2016).

Conclusion

Mushroom components are gaining increasing interest in their application as antimicrobials agents in food safety. Although there are quite many edible mushrooms, the number of mushroom species that have been identified with antimicrobial properties is quite small. Only 158 species from 88 mushroom genera have been reported to possess antimicrobial properties against important foodborne pathogens. The most common mushrooms genera with antimicrobial properties include *Lentinus*, *Pleurotus*, *Dictyophora*, *Cordyceps*, *Ganoderma*, and *Tremella*. The antimicrobial activities of mushrooms are mainly derived from their secondary metabolites with inhibitory activity against targeted microorganisms. Some nutritive metabolites, including polysaccharides, proteins, and enzymes, have also been shown to have antimicrobial activities. Since many mushrooms have been eaten safely for years, there is a significant advantage in using these multifunctional mushroom antimicrobials as alternatives to currently used antibiotics and synthetic food preservatives. To expand their applications and to maximize the advantages of mushroom antimicrobials, innovative strategies and techniques need to be developed for their mass production and improving their effectiveness in food processing and food preservation.

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Author Contributions

H. Shen and J. Chen searched the literature and drafted the manuscript; S. Shao and T. Zhou reviewed and revised the manuscript.

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