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A Review on the Antibacterial Activity of Edible Mushrooms

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Abstract

Edible mushrooms produce a variety of bioactive compounds that could be used as alternatives to antibiotics. This review was aimed to evaluate the antibacterial activities of most common edible mushrooms. Extracts of oyster, button, shiitake and enokitake mushrooms showed inhibition against various gram-negative and gram-positive bacteria with the latter being more susceptible towards the mushroom extracts. The zones of inhibition differed in the disk diffusion assay and the agar well diffusion assay as it was dependent on the type and the concentration of the extract used. Larger zones of inhibition were generally seen in the studies that used agar well diffusion assays as it used larger volumes of concentrated mushroom extracts. While many solvents were used to extract the bioactive compounds from these mushrooms, the ethanolic, methanolic and aqueous were the common extraction solvents used. The methanolic and ethanolic extracts also showed the highest zone of inhibition ranging from 8.3mm to 18.4mm indicating its effectiveness in extracting the bioactive compounds with antibacterial properties. Flavonoids, tannins, fatty acids, esters and lenthionine have been identified as some of the common chemicals in the mushroom extract that exhibit antibacterial effects on tested bacteria. However, further research on these compounds is required apart from the analysis on the possible combination of mushroom extracts which could exhibit synergistic antibacterial activities eventually suggesting the potential of the mushroom extracts as possible alternatives to antibiotics.

Keywords

Edible mushrooms, bioactive compounds, antibacterial activities, antibiotics

Introduction

Fungi which have been consumed for years are rich in protein, fiber, vitamins and minerals. Nutrients found in mushrooms such as selenium, potassium, niacin, riboflavin, proteins, vitamin D and fiber are important components for traditional medicine (Valverde et al., 2015). Consuming mushrooms also provides protection against cardiovascular diseases, Alzheimer's and Parkinson's (Guillamón et al., 2010; Phan et al., 2015; Rancero & Delgado, 2017). In addition, it is also used in the treatment of cancer, stress, insomnia, asthma, allergies, and diabetes (Bhushan et al., 2018).

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The four most common edible mushrooms are oyster mushroom (*Pleurotus ostrearus*), button mushroom (*Agaricus bisporus*), shiitake mushroom (*Lentinula edodes*) and enokitake mushroom (*Flammulina velutipes*) (Valverde et al., 2015; Sande et al., 2019). Out of these four mushrooms, the commercially important mushrooms are *A. bisporus*, *P. ostreatus* and *L. edodes* (Mleczek et al., 2020). Apart from its cultivation for common consumption, edible mushrooms are also widely grown for therapeutic reasons as they are rich in bioactive compounds such as flavonoids, terpenoids, alkaloids, tannins and polysaccharides that exhibit antimicrobial, antioxidant, antiviral, anti-allergic, anti-diabetic, and anticancer properties (Ha et al., 2020; Kała et al., 2020).

There are multiple challenges faced by the medical services due to the increasing number infections caused by bacteria including the resistant ones. Hence, there is an immense search and research for effective antimicrobial agents including those from plants and fungi (Gebreyohannes et al., 2019). A study by Adeoyo & Oluborode (2020), has shown the antimicrobial activities of edible mushroom extracts of *P. florida* against *Eenterobacter aerogens, Staphylocococcus aureus* whereas, extracts of *P. ostreatus* inhibited the growth of *Klebsiella oxytoca*. In another study, the antibacterial activity of the extracts of indigenous wild mushrooms was detected against *Escherichia coli*, *Klebsiella pneumoniae, Pseudomonas aeruginosa, Staphylococcus aureus, Candida albicans,* and *Candida parapsilosis* (Gebreyohannes et al., 2019). Extracts of 13 wild mushrooms were screened against multi-resistant bacteria in which, three of the extracts were found to inhibit the resistant gram-negative and gram positive bacteria (Alves et al., 2012).

In view of the growing interest in the antibacterial properties of the edible mushroom extracts, this study aimed to review the antibacterial activities of most commonly consumed mushrooms (oyster, button, shietake, enokitake) as well as its bioactive compounds responsible for inhibiting specific metabolic pathways and for destroying the structures of bacterial cells.

Methodology

Literature Search

The scientific literature was systematically assessed and collected from PubMed, and Google Scholar, reviewing a total of 72 articles published between 2012 to 2021 (Figure 1). The keywords used in the search were "edible mushroom," and "antibacterial activity".

Inclusion and Exclusion Criteria

The article title and abstracts were manually screened to exclude unrelated studies. Only edible mushroom oyster, button, shiitake and enokitake were included in the analysis. Relevant articles were examined to determine its fit to the eligibility criteria of this review (Figure 1). The specific inclusion criteria include the following:

1. Validated source material: mushroom materials were identified to the taxonomic level of genus and species. Mushroom samples were collected and deposited in a university or a research institute.
2. Appropriate methodology: standard methods for antibacterial assays were employed using agar well diffusion method, disk diffusion method, and standard broth dilution as per the recommended procedure by CLSI.
3. Access to full-text articles written in English. Articles published only in non-English languages were excluded.

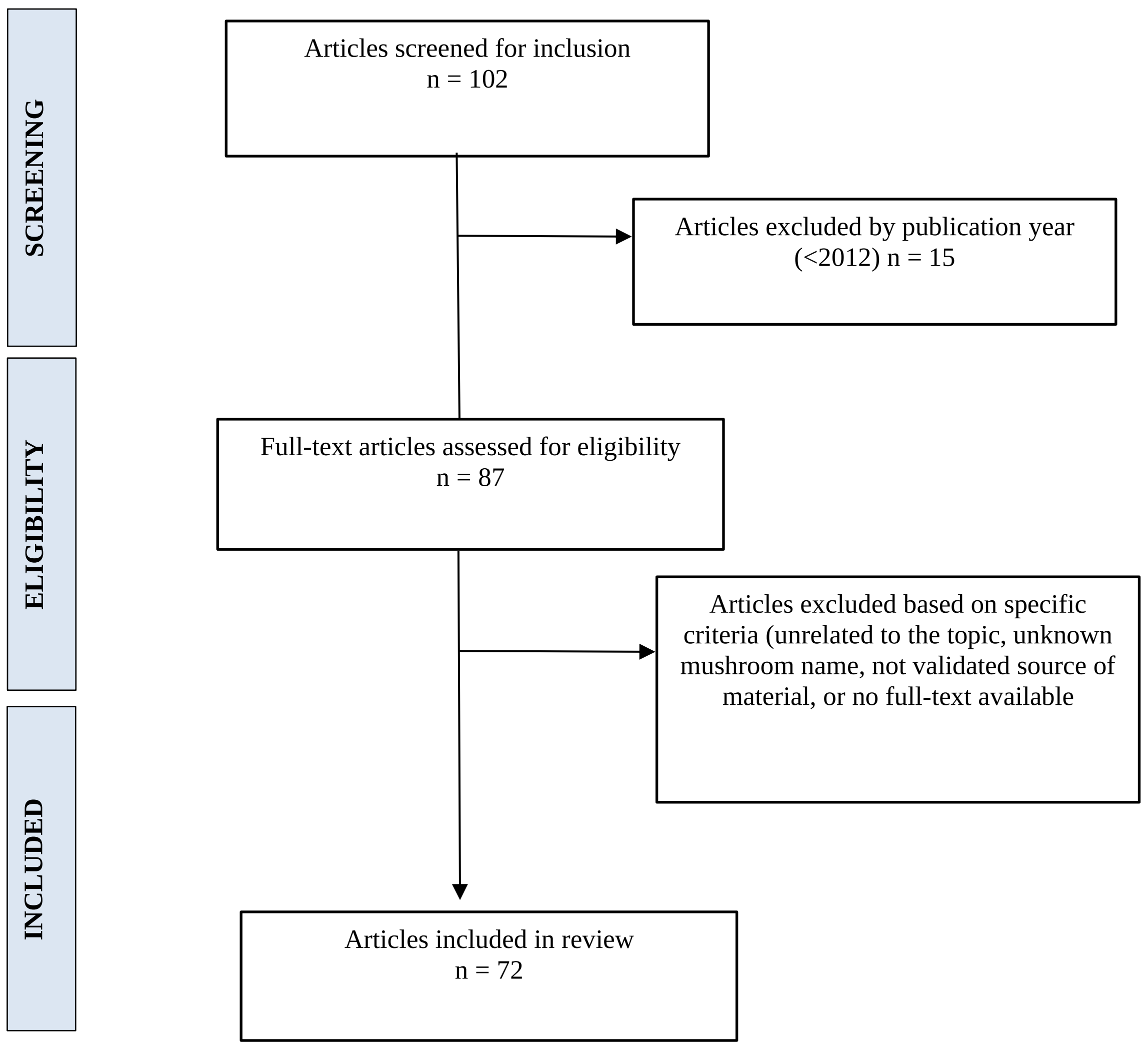

Figure 1. Representation of inclusion and exclusion criteria.

Results and Discussion

The Antibacterial Assays of the Mushroom Extracts

The common antibacterial assays used in the 12 studies indicated the use of agar well diffusion assay, the disk diffusion assay, and the standard broth dilution method (Priya & Srinivasan, 2013; Balouiri et al., 2016; Soltanian et al.,2016; Zepeda–Bastida et al., 2016; Nicolcioiu, Popa, & Matei, 2017; Lee et al.,2018; Ruilova et al., 2018; Shah et al., 2018; Krupodorova et al., 2019; Waqas et al., 2019; Gashaw et al., 2020). The mushroom extracts used in these studies were mostly dried and ground before extracting and concentrating the mushroom extracts using methanol, ethanol, water and many more. The final extracts were quantified, and filter sterilized before analyzing for its antibacterial properties. 11 studies analyzed the antibacterial activities of the extracts against both gram-positive and gram-negative whereas, one article studied only against gram-negative bacteria. Figures 2 and 3 show that *S. aureus* and *E. coli* were the most widely used bacterial cells for investigating the antibacterial activities of edible mushroom extracts which could be due to their significance as common human pathogens (Ndhlala et al., 2013). This is also in consensus with many studies on antibacterial analyses of phytochemicals (Chassagne et al., 2021).

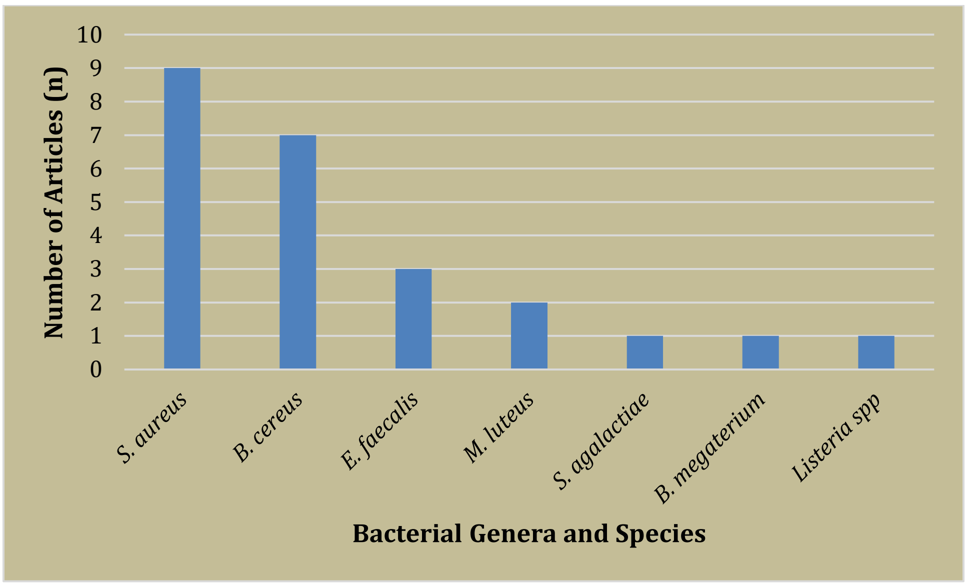

Figure 2. Common genera of gram-positive bacteria that were studied.

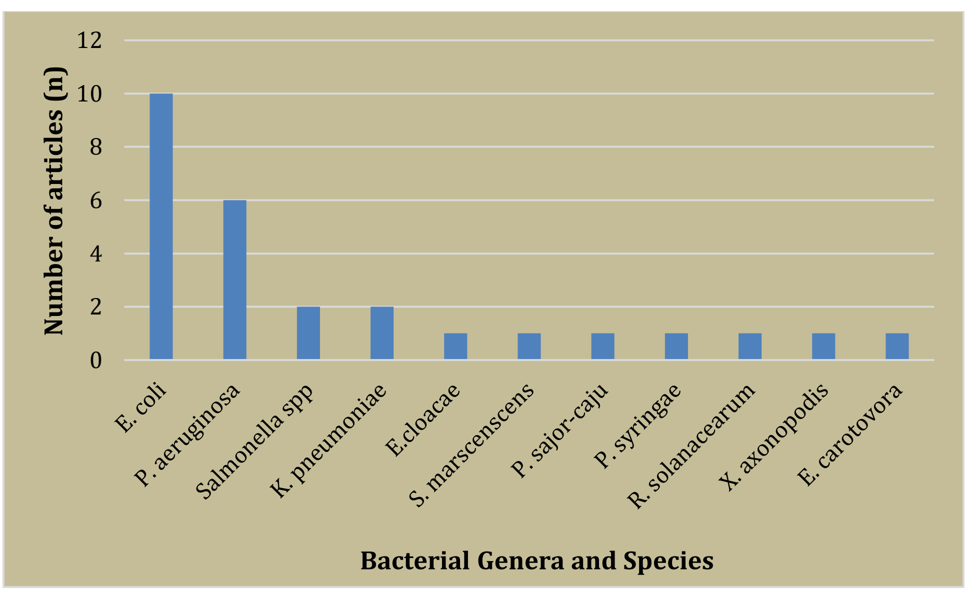

Figure 3. Common genera of gram-negative bacteria that were studied.

Table 1 summarizes the antibacterial activities of the mushroom extracts based on the extraction solvents. Overall, the ethanolic and methanolic extracts showed better antibacterial activities against the tested bacteria based on the diameter of the zones of inhibition. Study by Gashaw et al. (2020) showed that the ethanolic extracts produced zones of inhibition ranging from 8.3mm to 18.4mm indicating its effectiveness. This is because ethanol is a polar solvent and therefore, it readily mixes with water and breaks down water-soluble antibacterial bioactive compounds found in the mushroom extracts such as flavonoids, β-Glucan and many more (Ruilova et al., 2018). The antibacterial activity of the methanolic extracts could be attributed to its ability to effectively extract active antibacterial compounds in the mushrooms which exhibited higher activity with typically larger zones of inhibition (Shanmugam et al., 2014). Methanolic and ethanolic extracts are commonly used as extraction solvents in many antibacterial assays as they are widely available and have been shown to dissolve many types of antibacterial bioactive compounds (Chassagne et al., 2021). Aqueous extracts on the other hand showed the smallest zones of inhibition ranging from 4.6mm to 17.4mm indicating its inadequacy in extracting many of the antibacterial bioactive compounds (Gashaw et al., 2020; Chassagne et al., 2021).

Table 1. Overall antibacterial activity of mushroom extracts against Gram positive and Gram-negative bacteria.

Mushroom	Extracts	Gram-Negative	Gram-Positive
Oyster	Aqueous		✔
	Methanolic	✔	✔
	Ethanolic	✔	✔
Button	Aqueous		
	Methanolic		✔
	Ethanolic	✔	✔
Shiitake	Aqueous		
	Methanolic		
	Ethanolic	✔	✔
Enokitake	Aqueous		
	Methanolic		
	Ethanolic		✔

This review also indicated that the gram-negative bacteria were generally more resistant towards the mushroom extracts compared to the gram-positive bacteria based on the smaller zones of inhibition produced (Table 1). This is because of the presence of the outer membrane in gram-negative bacteria that impede the entry of many antibacterial agents including the mushroom extracts (Breijyeh et al., 2020). The review also suggests the future antibacterial potential of ethanolic extracts of shiitake mushrooms and oyster mushrooms (methanolic inclusive) on wider spectrum of bacterial species. This however, must be verified by testing the extracts against more bacterial species including resistant ones.

Antibacterial Activities of Edible Mushrooms

Younis & El Shikh (2015) showed that the aqueous extract of *Pleurotus ostreatus* exhibited growth inhibition against *Staphylococcus aureus* and *Escherichia coli*. Interestingly, the alcoholic solvents showed lower inhibition against most of the bacteria used in this study which was in contrast to study by Gashaw et al. (2020). In another study, the inhibition zones of oyster mushroom extracts (n-hexane) was large against *Bacillus cereus, Streptococcus agalactiae, Agrobacterium* and *Pseudomonas aeruginosa* whereas, no zones of inhibition were observed against *E. coli* and *Shigella dysenteriae* (Onuegbu et al., 2017). The study by Gashaw et al., 2020 showed the growth inhibition by methanolic, ethanolic and aqueous extracts of oyster mushroom against *E. coli, Bacillus subtilis, Streptococcus faecalis, P. aeruginosa,* and *Salmonella typhi.* As seen in many studies, the methanolic and ethanolic extracts of *P. ostreatus* showed higher inhibition than aqueous extract based on the zones of inhibition suggesting further exploration of these extracts as potent antibacterial activities.

The antibacterial activities of *Agaricus bisporus* (n-hexane, chloroform, and ethyl acetate extracts) ranging from 50 to 100 mg/mL were tested against four plant pathogens which showed extracts of ethyl acetate to generally exhibit a better antibacterial activity against the tested pathogens (Table 2) (Waqas et al., 2019).

Table 2. Inhibition zones of button mushroom extracts against four plant pathogens (Waqas et al., 2019)

	Types of Extracts (mg/mL)					
Bacteria	n-Hexane Extract		Chloroform Extract		Ethyl acetate Extract	
	50	100	50	100	50	100
Pseudomonas syringae	2.17mm	4.83mm	2.33mm	6.33mm	15.00mm	30.00mm
Ralstonia solanacearum	1.00mm	3.33mm	11.67mm	16.17mm	7.83mm	20.00mm
Xanthomonas axonopodis	10.67mm	16.00mm	14.00mm	17.00mm	15.17mm	19.00mm
Erwinia carotovora	1.00mm	3.33mm	1.17mm	1.67mm	16.17mm	28.67mm

In the antibacterial analysis of the aqueous extract of *A. biporus* by Priya & Srinivasan (2013), no zones of inhibition were observed against *Bacillus* sp, *S. aureus*, *E. coli*, *K. pneumoniae* and *P. aeruginosa* showing that the aqueous extract lacked the compounds required to exert antibacterial activity and this was in consensus with the study by Younis & El Shikh (2015) albeit the use of different mushrooms species. The methanolic extract of button mushroom was tested against gram-positive bacteria, *S. aureus, Enterococcus faecalis* and *B.* cereus and the resulting MIC for these bacterial strains were 0.88$\pm$0.11, 0.88$\pm$0.03, 1.25$\pm$0.16 MIC_{50} [a] (mg/ml). However, no significant MIC values were obtained against gram-negative bacteria, *E. coli*, *P. aeruginosa*, and *Salmonella Typhi* (Soltanian et al.,2016).

The ethanolic stem extract of shiitake mushroom showed the highest inhibition against *Salmonella spp* and *E. coli* which was 12.7mm inhibition compared to pileus ethanolic extract which is 10mm. The ethyl acetate extract showed only 3.7mm inhibition diameter (Ruilova et al., 2018). The differences in the antibacterial activity of the shiitake mushroom as seen in the study by Ruilova et al. (2018) could have been caused by the solubility of the chemicals in the mushroom extracts in different extraction solvents (Lapornik et al., 2005; Ruilova et al., 2018, Chassagne et al., 2021). When the ethanolic extract of shiitake mushroom was tested against Gram-positive bacteria, *Listeria* spp, the inhibition zone was 1mm whereas, it was 9.3mm for the Gram-negative bacteria *Salmonella* spp, (Ruilova et al., 2018). The study of shiitake mushroom by Zepeda–Bastida et al (2016) described the use of oats extracts and cedar extracts of *Lentinula edodes*. Both extracts were found to be effective against *E. coli*, *S. tiphymorium, S. aureus*, and *M. luteus*. However, at a lower concentration, these extracts only inhibited the growth of *E. coli* and *S. typhimurium*. This was in consensus with the study by Krupodorova et al (2019) which also showed inhibition of *E. coli*, *B. subtilis* and *S. aureus* by *L. edodes*.

The antibacterial activity of enokitake aqueous extracts showed more inhibition against gram negative bacteria compared to gram-positive bacteria. The growth inhibition (%) against gram negative bacteria S. *marcescens* and *E. coli* showed positive correlations r=0.983 and 0.809 with the total plate count (TPC) whereas, the gram-positive bacteria *B. subtilis* and *S. aureus*, showed weaker correlation towards enokitake mushroom extracts r=0.067 and 0.313 with TPC. Overall, *Flammulina velutipes* extracts had more than moderate antibacterial activity that is >68% against gram-negative bacteria *E. coli* and *S. marcescens* but a weaker antibacterial activity <45% against gram-positive bacteria *B. subtilis* and *S. aureus* (Shah et al., 2018). However, the study by Nicolcioiu, Popa & Matei (2017) showed that the ethanolic extracts of enokitake mushroom showed highest inhibition zone towards *B. subtilis* followed by *S. aureus* but with no zone of inhibition against gram negative *P. aeruginosa* and *E. coli*. *F. velutipes* extracts were evaluated by Lee at el (2018) against six strains of microbes, including *B. subtilis, S. aureus, M. luteus, E. coli, P. aeruginosa, and Enterobacter cloacae* in which, the acetone and ethyl acetate extracts showed antibacterial effects against all tested strain. The variations in the inhibition between different groups could be attributed to the use of different antibacterial assays and extraction solvents (Chassagne et al., 2021).

In general, most of the extracts from the four edible mushroom show better growth inhibition against gram positive bacteria compared to gram negative bacteria despite the differences in the extraction solvents used and the antibacterial assays. However, the inhibitions exhibited by enokitake (aqueous) and shitake mushrooms (ethanolic) against clinically-important gram negative bacteria such as *E. coli* and *Salmonella* shows its promising potential as potent antibacterial agents against these pathogens.

The Mode of Action of Bioactive Compounds

Oyster mushroom contains polysaccharides like β-glucans and α-glucans in its cell wall. The effectiveness of these β-glucans depends on its molecular weight and solubility (Deepalakshmi & Sankaran, 2014). The β-D Glucan isolated from the fruiting bodies of *Pleurotus ostreatus* promoted the survival of mice against bacterial infections. The phenolic compounds and tannin in the oyster mushroom elicit antibacterial activity characterized by cell membrane lysis, inhibition of protein synthesis, prevention of enzymatic activity of proteolytic enzymes and inhibition of adherence by microbial adhesins (Deepalakshmi & Sankaran, 2014). Polysaccharides like α-glucans are not well investigated but it is reported to have immunostimulatory and anti-oxidative properties. In addition, extracts from *P. ostreatus* was also reported to contain fatty acids and esters that could be the reason for the growth inhibition of gram-positive and gram-negative bacteria. The proteins of oyster mushroom, eryngin and pleurostrin exhibits antifungal and antibacterial properties (Golak-Siwulska et al., 2018).

Agaricus bisporus contains compounds that exhibits anti-inflammatory, antitumor, antioxidant, antibacterial, and immunomodulatory properties. The crude polysaccharides extracted from the waste biomass of *A. bisporus*, showed the presence of α-glucans and β-glucans (Cebin et al., 2018). Ammar (2019) detected alkaloids, tannins and flavonoids in the extract of button mushroom. Among these compounds, tannins are known to be the active ingredient that inhibits microbial growth by stopping the transport of water molecules into the cells resulting in deformed cell morphology and disrupted cell function. However, tannins were more found to be more effective against gram positive bacteria than gram-negative bacteria and this could be due to the absence of the outer membrane that caused the direct damage in the cell wall followed by cytoplasmic spillage and death in in gram positive bacteria (Ammar, 2019). Flavonoids are indispensable components found freely or sometimes in the form of glycoside derivatives which are inhibitor of cancer cells and antibiotic-resistant mechanisms in many bacterial pathogens (Panche et al., 2016; Ammar, 2019).

A study by Muszyńska et al. (2017) showed the presence of carbohydrates namely monosaccharides, disaccharides, trisaccharides and polysaccharides (67.5% to 78.0%) in the fruiting bodies of shiitake mushroom. The simple sugar content in shiitake mushroom is 15.87% and among these simple sugars are glucose, mannose, galactose, xylose, ribose, fucose and rhamnose. The high content of β-D-glucans polysaccharides in the shiitake mushroom contributes to the therapeutic properties of this mushroom (Gaitán-Hernández et al., 2019). The polysaccharides in *Lentinula edodes* strengthens the immune system apart from having antitumor, antiviral and antibacterial characteristics. The antibacterial properties are attributed to the presence of lentin (protein), lenthionine (exabiopolymer containing sulfur), lentysine (purine compound), lentinamycin A and B (polyacetylene derivatives). Lenthionine is a cyclic compound that contains sulfur and is responsible for antimicrobial and antifungal properties (Kupcova et al., 2018). bis [(methylsulfonyl) methyl] disulfide which is a derivative of lenthionine has strong antimicrobial properties (Muszyńska et al., 2017).

Phenols, alkaloids, steroids and saponins were detected in the enokitake mushroom extracts. However, the antibacterial activity of *Flammulina velutipes* is mainly due to the content of aldehyde and ketone. These compounds are known as electronegative compounds that interferes with the transfer of electron by reacting with nitrogenous components like proteins and nucleic acids thus, inhibiting the growth of microorganisms. In addition, flavonoids have antibacterial activity that have been reported against *S. aureus*, *S. epidermidis*, *B. subtilis*, and *C. acnes*. Sanggenon J and Moracenin C are prenylated-flavonoid derivatives which also have shown antibacterial activity towards *Streptococcus pneumoniae* (Shah et al., 2018). Polyphenols in enokitake mushroom interacts with the bacterial cell membrane and disrupts the bacterial membrane functions. Flavan-3ols, epicatechin and catechin are negatively charged compounds present in *F. velutipes* that strongly binds to the positively charged lipid bilayer of bacterial cell which results in the loss of structure and cell function. Enzyme inhibition is also another possible mechanism of polyphenol activity against bacteria or the interference of polyphenol with the production of amino acids required for bacterial growth (Shah et al., 2018).

Conclusion

Despite the challenges in reviewing diverse antibacterial assays of the mushroom extracts, the varying degrees of antibacterial activities suggests the need of further studies to underpin the antibacterial properties of the mushroom extracts against a wider range of human pathogens including the antibiotic resistant bacteria. Purification and identification of bioactive compounds responsible for antibacterial activity is needed for further development of these extracts as potent antibacterial agents. Such studies will not only improve the pharmacodynamics and pharmacokinetics of the extracts but also lead to the possibilities of producing potent antibacterial agents. In addition, this review also suggests future exploration of combined alcoholic mushroom extracts such as enokitake and shitake mushrooms for synergistic antibacterial activities against targeted pathogens. Moreover, combining more than one mushroom extracts after careful examination of the bioactive compounds is likely to increase the antibacterial activity as different compounds have different mode of actions in inhibiting bacterial growth. In-depth investigations on the mode of action of different bioactive compounds of these mushrooms might also leads to the discovery of novel antibacterial compounds.

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