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RESEARCH ARTICLE

Antimicrobial properties of the button mushroom, *Agaricus bisporus*: A mini-review

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Abstract

The button mushroom, *Agaricus bisporus*, is the most important commercially cultivated mushroom in the world. However, as compared to other mushrooms recognized as medicinal mushrooms, fewer studies have been undertaken on antimicrobial activity of *A. bisporus.* Particularly, there is inadequate data in the literature regarding identity and chemical structure of components that are responsible for the antimicrobial activity in this mushroom.Moreover, very few studies have been undertaken to investigate the antibacterial potential of wild isolates of*A. bisporus* in different countries, while wild mushrooms provide a significant source of nutritional and medicinal bioactive compounds. In this mini-review, an overview of antimicrobial properties of the button mushroom has been presented. Recent achievements on possible bioactive compounds conferring the antimicrobial activity have also been highlighted here. This mini-review may encourage more research on various fields, including investigation of antimicrobial capabilities of wild sources of *A. bisporus*, characterization of active components responsible for the antimicrobial activity, exploring mechanism of action of antibacterial activity of *A. bisporus,*and the potential inhibitory effect of *A. bisporus*-derived compounds towards antibiotic-resistant bacteria.

INTRODUCTION

The ongoing threat of antibiotic-resistant microorganisms urges a continuing priority on the search for novel antimicrobial agents (Bush, 2004). Various natural sources may be investigated for antimicrobial compound discovery, including marines, plants, prokaryotes, fungi, and animals (Fallarero et al., 2014). Edible mushrooms are well-known to possess fiber, essential oils, protein (including all the essential amino acids), vitamins, minerals, lectins, and pharmacologically important bioactive compounds. In recent years, mushrooms have also been seen as one of the most interesting subjects of the search for natural antimicrobial agents (Singh et al., 2014).

The button mushroom, *Agaricus bisporus*,is still the most important commercially cultivated mushroom in the world. At the present, *A. bisporus*, accounts for 35 to 45 percent of total worldwide production of edible mushrooms (Masoumi et al., 2015). Research findings demonstrate that the button mushroom possesses bioactive components of nutritional and medicinal importance. However, this species is usually considered to be of lesser nutritional and medicinal value as compared to the other medicinal edible mushrooms particularly in Asia (Beelman et al., 2003). Accordingly, there is no recent review article exclusively compiling studies on medicinal properties of *A. bisporus,* as opposed to other mushroom species even in the same genus, such as *A. blazei* (Firenzuoli et al., 2008) or *A. subrufescens (*Wisitrassameewong et al., 2012*).* Antimicrobial activities of different mushroom species have been reviewed by Alves et al. (2012). Nevertheless, the existing knowledge on the antimicrobial potential of the button mushroom has recently been advanced. Therefore, this mini review outlines recent developments on the antimicrobial properties of *A. bisporus* in order to update the existingknowledge. In addition, it tries to discuss limitations and possible avenues for further research on antibacterial properties of *A. bsiporus*.

2. Current knowledge on antibacterial potential of mushrooms

So far, many species of mushrooms have been studied for their antibacterial activities, including species belonging to *Agaricus, Boletus, Cantharellus, Clitocybe, Cortinarius, Ganoderma, Pycnoporus, Hygrophorus, Hypholoma, Lactarius, Tricholoma,* and *Lentinus*.The majority of these mushrooms have been well known for their medicinal and therapeutic properties. Both Gram-positive and Gram-negative pathogenic microorganisms have been tested for their sensitivity to these mushrooms.In addition, few antibiotic-resistant bacterial strains have also been investigated for their susceptibility to mushroom extracts or isolated compounds. Mushrooms possess natural bioactive compounds that confer antibacterial activity, comprising low molecular weight (LMW) and high molecular weight (HMW) compounds. LMW compounds include a range of secondary metabolites (such as sesquiterpenes and other terpenes, steroids, anthraquinone and benzoic acid derivatives, and quinolones) and also primary metabolites (such as oxalic acid). HMV largely include peptides and proteins (Alves et al., 2012).

Antibacterial activities of mushrooms have been evaluated using various approaches, including conventional micro-dilution methods, micro-dilution methods coupled with a chromogenic reagent, the disk diffusion method, and a method with theincorporation of the extract in the culture medium and furtherdetermination of colonies. While numerous studies have been conducted on antibacterial activities of crude extracts of mushrooms, less information is available regarding compounds conferring antibacterial activity. Furthermore, very few studies have been undertakento assess antibacterial potential of mushrooms in animal models (Soltanian et al., 2016).

3. Antibacterial properties of wild and cultivated *A. bisporus*

Several studies have reported antibacterial activities of crude extracts of *A. bisporus* against Gram-positive or Gram-negative bacteria. Barros et al. (2008) demonstrated that the methanolic extract of a wild strain of *A. bisporus* isolated from Northeast of Portugal exerted antibacterial activity at a MIC of 5 μg/mL against *Bacillus subtilis,*whilst the tested Gram-negative bacteria were not susceptible to *A. bisporus* (Barros et al., 2008).

The methanol extract of a wild strain of *A. bisporus* collected from Turkey was also shown to inhibit several Gram-positive bacteria more effectively than Gram-negative bacteria (Öztürk et al., 2011). Similar recent findings were obtained with a Chinese strain of *A. bisporus,* where Gram-negative bacteria were not effectively inhibited by the button mushroom extract (Shang et al., 2013). In addition, our recent findings showed that the button mushroom crude extract (isolated from both wild and cultivated strains) showed quantifiable inhibition effects only towards the Gram-positive bacteria (Soltanian et al., 2016). Controversially, there are other studies reporting susceptibility of Gram-negative bacteria to crude extracts of *A. bisporus* (Tambekar et al., 2006; Ozen et al., 2011; Stojkovi´c et al., 2014). The main susceptible Gram-negative bacteria have been *Escherichia coli*, *Psudomonas aeroginosa*, *Klebsiella pneumoniae,* and *Listeria monocytogenes*.

Both wild and cultivated strains of the button mushroom, *A. bisporus,* have been investigated for antibacterial properties. However, very limited studies have compared antibacterial potential of the wild mushrooms with the cultivated strains. So far, wild *A. bisporus* mushroom isolates from Northeast of Portugal (Barros et al., 2008), Northeastern Iran (Soltanian et al., 2016), Turkey (Öztürk et al., 2011; Ozen et al., 2011), and China (Shang et al., 2013)have been reported to exert antibacterial activitiesagainst pathogenic bacteria.To the best of our knowledge, the only comparative study on cultivated and commercial strains of *A. bisporus* was conducted by our research group, where the cultivated strain of *A. bisporus* inhibited more Gram-positive bacteria as compared to the wild strain (Soltanian et al., 2016). Except for the wild *A. bisporus* reported from Turkey (Ozen et al., 2011), other reported wild *A. bisporus* isolates could not inhibit Gram-negative bacteria. There is a shortage of information on the antibacterial potency of wild *A. bisporus* in different countries. Further investigations might be warranted to discover their antibacterial potency in comparison with commercially cultivated strains of *A. bisporus*.

In addition to crude extracts isolated from the cap of *A. bisporus,* antibacterial properties of extracts isolated from the stipe of the button mushroom have also been investigated. The stipe of *A. bisporus* is a by-product in the fresh mushroom industry, and thus their medicinal and nutritional properties might be worth investigating.The stipes extracts prepared by different solvents significantly inhibited *E. coli* and *Staphylococcus aureus*. These findings promisingly suggested further applicationsfor *A. bisporus* stipe extracts as a functional food additive (Ndungutse et al., 2015).

The literature shows that qualitative methods or conventional micro-dilution have been employed in the majority of studies conducted to investigate antibacterial activity of *A. bisporus*. However, it should be noted that micro-dilution methods coupled with a chromogenic reagent generate quantitative data and improve reliability and reproducibility, as only living microorganisms react with the chromogen reagent (Jorgensen et al., 2009).

4. Antimicrobial fractions or compounds isolated from *A. bisporus*

The information about compounds conferring antibacterial activity in mushrooms is limited (Alves et al., 2012). There are few compounds that have been well-identified to confer antimicrobial activity to a range of mushrooms. The majority of these compounds belong to the group of terpens. However, very limited studies have been undertaken to investigate compounds responsible for antibacterial activity in *A. bisporus*. In recent years, promising findings have been added to theexisting knowledge regarding possible constituents that play a role in antibacterial activity in *A. bisporus.*

Aqueous total protein extracts of the cultivated *A. bisporus* was shown to possess significant antibacterial activity, particularly against *S. aureus* and m*ethicillin-resistant S. aureus* (*MRSA*) (HoushdarTehrani et al., 2012). Fractionation of the total protein resulted in three fractions, one of which showed antibacterial activities. Further purification of this fraction was carried out using DEAE-A50 ion-exchange column with a stepwise salt gradient elution. The fraction gave almost a pure protein fraction demonstrated by SDS-PAGE. The molecular weight of this protein was measured to be 22,500 Dalton. This purified peptide showed a $MIC_{50}$of 100 µg/mL against *S.aureus*and *MRSA* (HoushdarTehrani et al., 2012).

In the search among phenolic compounds, Alves et al. (2013) showed potent antibacterial activities for 2,4-dihydroxybenzoic and protocatechuic acids, which have been previously isolated from several wild mushroom species including *A. bisporus*. 2,4-dihydroxybenzoic and protocatechuic acids exhibited antibacterial activity (MIC = 1 mg/ml) against clinical isolates of Gram-negative bacteria including *E. coli*, *Pasteurella multocida*, and *Neisseria gonorrhoeae* (Alves et al., 2013). However, direct association of these phenolic compounds to *A. bisporus* has not been elucidated.

Recently, we reported fractionation of the methanol-dichloromethane (1:1) extract of the cultivated *A. bisporus*. Totally, over 200 initial eluates were eluted through step-wise gradient elution, of which six different fractions were prepared based on their thin layer chromatography band patterns. One of the fractions (eluted by two eluent systems: e*thyl acetate* and e*thyl acetate*/methanol 1:1) showed quantifiable and dose-dependent antibacterial activities. While the crude extract of *A. bisporus* inhibited only Gram-positive bacteria, the fraction significantly inhibited both the Gram-positive and the Gram-negative bacteria particularly *E.coli* at a MIC_{50} of 8 mg/ml. These findings could be an initial step towards elucidation of the chemical structuresof constituents that may confer the antibacterial activity to *A. bisporus* (Soltanian et al., 2016).

5. Conclusions and further research

Currently, there is a knowledge gap in the identification of active components that are responsible for the antibacterial activity in *A. bisporus.* So far, only initial steps have been taken towards characterization of bioactive compounds in *A. bisporus* that may play a role in the antibacterial activity. Among high molecular weight compounds, a purified 22,500 Dalton peptide fraction has promisingly been shown to exert antibacterial activity. Among low molecular weight compounds, phenol derivatives might be considered as good candidates for further investigations.

Further investigations are required to explore mechanismof action of pure antibacterial compounds isolated from *A. bisporus*. These myco- constitutes could be used to develop further nutraceutical or effective drugs. Their efficacy should also be tested towards antibiotic-resistant microorganisms. Furthermore, the in vitro antibacterial activity of *A. bisporus* should be confirmed through animal studies.

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Declaration of interest

There is no conflict of interest. The authors alone are responsible for the content and writing of the paper.

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