Archives of Razi Institute, Vol. 75, No. 1 (2020) 123-130

DOI: 10.22092/ARI.2019.128088.1403

Short Communication

Assessment of Agaricus Bisporus S-II Extract as a Bio-Controlling Agent against Human Pathogenic Bacterial Species

Karnwal [1]*, A., Kaur [2], M.

1. Department of Microbiology, School of Bioengineering and Biosciences, Lovely Professional University, Punjab, India
2. Department of Biotechnology, School of Bioengineering and Biosciences, Lovely Professional University, Punjab, India

Received 14 October 2019; Accepted 01 December 2019
Corresponding Author: runkarnwal@gmail.com

ABSTRACT

Agaricus bisporus mushrooms are well known for their nutritional and medicinal values. *A. bisporus* is a source of protein (about 40% on a dry basis), ergosterol, several minerals, carbohydrate, and fat. The present study was conducted to investigate the effect of *A. bisporus* S-II extracts on human pathogenic bacteria *in-vitro* condition. Totally, three human pathogenic bacterial strains (MTCC culture type) were procured from the Institute of Microbial Technology, India. Out of these three bacterial strains, one was Gram-negative (namely *P. aeruginosa* MTCC741), and the other two were Gram-positive (*B. cereus* MTCC9786 and *S. aureus* MTCC740). Microdilution assay was applied for the evaluation of the minimum inhibitory concentration (MIC). The highest antimicrobial activity was observed in methanol extract (26.5%) against *S. aureus* MTCC740, compared to ethanol extract (17%). Similar results were obtained for *P. aeruginosa* MTCC741 (21.8%) and *B. cereus* MTCC9786 (15%) in methanol extract. Least microbial growth inhibition observed for *B. cereus* MTCC9786 (13.82%) followed by *P. aeruginosa* MTCC741 (14%), compared to control in ethanol extract. The highest antimicrobial activity up to 17% with ethanolic extracts recorded against *S. aureus* MTCC740. The MIC results in microtitre plates showed the growth inhibition of *P. aeruginosa* MTCC741 and *S. aureus* MTCC740 at extract concentrations of 15 mg/ml and 20 mg/ml, respectively. However, no MIC detected for *B. cereus* MTCC9786 below 20 mg/ml extract concentration. Regarding minimum bactericidal concentration, the bactericidal value for *P. aeruginosa* MTCC741 and *S. aureus* MTCC740 was obtained at 10 mg/ml concentration. The present study indicated that the extracts of the *A. bisporus* S-II mushrooms had promising antimicrobial activities against the tested organisms.

Keywords: Antibacterial, *Bacillus cereus,* Button mushroom, Human pathogens, Mushroom extract

Évaluation de l'extrait d'*agaricus bisporus* S-II dans la lutte biologique contre les espèces bactériennes pathogènes pour l'homme

Résumé: *Agaricus bisporus* est une espèce de champignons qui sont bien connus pour leurs valeurs nutritionnelles et médicinales. *A. bisporus* est une source de protéines (environ 40% sur base sèche), d'ergostérol, de plusieurs minéraux, de glucides et de lipides. La présente étude a été menée pour étudier l'effet des extraits d′ *A. bisporus* S-II sur certaines bactéries pathogènes pour l'hommedans des conditions in vitro. Au total, trois souches bactériennes pathogènes (type de culture MTCC) ont été obtenues auprès de l'Institut de technologie microbienne (Inde). Sur ces trois souches bactériennes, une était à Gram négatif (*P. aeruginosa* MTCC741) et les deux autres étaient Gram positifs (*B. cereus* MTCC9786 et *S. aureus* MTCC740). La concentration minimale inhibitrice (CMI) a été évaluée par la méthode de microdilution. L'extrait méthanolique montrait une 'activité antimicrobienne plus élevée contre *S. aureus* MTCC740 (26.5%), comparé à l'extrait 'éthanolique (17%). Des.

résultats similaires ont été obtenus pour *P. aeruginosa* MTCC741 (21.8%) et *B. cereus* MTCC9786 (15%) avec une efficacité plus importante des extraits méthanoliques. Pour l'extrait éthanolique une moindre inhibition de la croissance microbienne a été observée pour *B. cereus* MTCC9786 (13.82%) ainsi que pour *P. aeruginosa* MTCC741 (14%), par rapport au témoin. L'activité antimicrobienne la plus élevée des extraits éthanoliques a été observée contre *S. aureus* MTCC740 (17%l) La détermination de la CMI des extraits sur des plaques de microtitration montre une inhibition de la croissance de *P. aeruginosa* MTCC741 et *S. aureus* MTCC740 à des concentrations d'extrait de 15 mg/ml et 20 mg/ml, respectivement. Cependant, aucune CMI n'a été observée pour *B. cereus* MTCC9786 en dessous de la concentration d'extrait de 20 mg/ml. Concernant la concentration bactéricide minimale, la valeur bactéricide pour *P. aeruginosa* MTCC741 et *S. aureus* MTCC740 a été obtenue à une concentration de 10 mg/ml. Cetteétude montre que les extraits des champignons *A. bisporus* S-II présentent une activité antimicrobienne prometteuse contre les organismes testés.
Mots-clés: Antibactérien, *Bacillus cereus*, Champignon bouton, Pathogènes humains, Extrait de champignon

INTRODUCTION

Mushrooms have been considered a delicacy and are preferred both for taste and flavor with a long history of medicinal uses. A new term was coined as "nutraceutical" (Bassarello et al., 2004) to explain their therapeutic components. The availability of low-molecular-weight (LMW) and high-molecular-weight (HMW) compounds in mushroom makes it a natural antibiotic source (Castillo et al., 2018). The HMW compounds are peptides and proteins (Glamoclija et al., 2015), whereas LMW compounds are primarily categorized in secondary metabolites (Bassarello et al., 2004) including various types of steroids, sesqui-terpenes and other terpenes, anthraquinone, quinolines, and benzoic acid derivatives (Abenavoli et al., 2018). However, the LMW also carries few primary metabolites (i.e., oxalic acid and those that can be used as antimicrobial agents (Bassarello et al., 2004; Atri et al., 2013; da Silva de Souza et al., 2017). *Agaricus bisporus* consists of a wide variety of these kinds of biomolecules having dietary and/or therapeutic traits (Bassarello et al., 2004; Atri et al., 2013; Inbakani and Siva, 2017). As a result of all these traits, they have been known for valuable dietary foods, as well as a resource intended for the production of remedies and nutraceuticals (Acharya et al., 2015). Fruiting bodies, mycelia, and spores of *A. bisporus* hold a complete range of bioactive biomolecules that has immuno-modulatory, cardiovascular, liver protective, anti-fibrotic, anti-inflammatory, antidiabetic, antiviral, antioxidant, antitumor, and antimicrobial properties (Alves et al., 2013; Alves et al., 2014; Ali et al., 2019).

A. bisporus, which is one of the most common white button mushrooms, contributes about 40-45% to the world mushroom production (Glamoclija et al., 2015). *A. bisporus* is a low-temperature species requiring 20±23 C° for its vegetative growth and 16±20 C° for its fruiting. Moreover, it is a widely consumed mushroom in the world which is cultivated in more than 70 countries (Castillo et al., 2018; Ali et al., 2019). The anti-microbial property of *A. bisporus* is due to essential bioactive components (i.e. Catechin) which is one of the significant phenolic elements contributing to anti-microbial, anti-oxidant, anti-cancer, and anti-allergy properties of *A. bisporus (Breene, 1990; Glamoclija et al., 2015)*. Caffeic acid and rutin have been shown to exhibit anti-microbial activity (Glamoclija et al., 2015). Gallic acid is another bioactive constituent vastly available in various plants and also in *A. bisporus*. It has a potent natural anti-oxidant, anti-inflammatory, anti-tumor, anti-bacterial, and anti-fungal property (Bassarello et al., 2004; Inbakani and Siva, 2017). Methanolic extract of *A.*

bisporus exhibits higher activity against *Bacillus subtilis*, *B. cereus*, *Staphylococcus aureus*, and *S. epidermidis*. In addition, it has lower actions against *Micrococcus luteus* and *M. flavus*. Atri et al. (2013) (Castillo et al., 2018) reported the anti-microbial activity of different *Agaricus* species against various bacterial species (spp). They demonstrated that *A. bitorquis* and *A. essettei* methanolic extracts had an inhibitory effect on various Gram-positive bacteria in lab conditions. *A. silvicola* methanolic extract also revealed anti-microbial properties against *B. cereus*, *B. subtilis*, and *S. aureus* although they were lower than the standard ampicillin (Atri et al., 2013; Castillo et al., 2018). The mycelium of *A. cf. nigrecentulus* and *Tyromyces duracinus* (ethyl acetate extracts) showed activity only against *S. saprophyticus* (Rosa et al., 2003). *A. bisporus* mushrooms are well known for their nutritional and medicinal values. They are also valued for waste management since most of them grow on lignocellulosic materials of agricultural origin, forest litter, and garden litter. *A. bisporus* is a source of protein (about 40% on a dry basis), ergosterol, as well as a precursor of vitamin D, several minerals, carbohydrates, and fat. It was demonstrated that the extract of *A. bisporus* exhibited anti-microbial and anti-oxidant properties against some Gram-positive as well as Gram-negative bacteria (Boda et al., 2012; da Silva de Souza et al., 2017; Castillo et al., 2018). They used different assay methods to determine the anti-microbial property of *A. bisporus* extracts (i.e., micro-dilution assay, Disc-diffusion method, Agar-streak dilution assay) (Cebin et al., 2018). The above-cited description points to the nutritional and medicinal values and subsequent studies on *A. bisporus* S-II-anti-microbial properties; however, there is hardly such a report available in the vicinity of the industrial hub of Himachal Pradesh, India. Therefore, the present study aimed to highlight the anti-microbial activity of mushroom under prevalent environmental conditions using regional resources and human pathogenic bacterial isolates.

MATERIAL AND METHODS

Procurement of Human Pathogenic Bacteria. In the present study, three human pathogenic bacterial strains (MTCC culture type) were selected and procured from the Institute of Microbial Technology, Chandigarh, India. Out of these three bacterial strains, one was Gram-negative (namely *P. aeruginosa* MTCC741), and two were Gram-positive (*B. cereus* MTCC9786 and *S. aureus* MTCC740).

Standardization of Test Microorganisms. Standardization of all three procured bacterial cultures was carried out using 0.5 Mc Farland Standard (cell density: 1.5 x 10^8 CFU/ml at the wavelength of 600 nm). Mc Farland Standard was considered as the benchmark to regulate the final turbidity of bacterial culture to ensure that bacterial count would be present in a specific range. All bacterial suspensions were maintained in their appropriate liquid culture medium and compared by measuring the absorbance with that of the standard.

Collection of *A. Bisporus S-II*. Fresh and healthy fruiting bodies of *A. bisporus* S-II was grown in laboratory condition at Bhojia Institute of Life Sciences, Himachal Pradesh, India, and were collected for antimicrobial assay.

Drying and Pulverization. About 1 kg of *A. bisporus* S-II mushroom was shredded in small pieces and sun-dried for 7-10 days under a controlled condition. Sun-dried mushroom pieces were finally dried in the oven at 40 °C for 72 h. After 72 h of drying, completely dried mushroom pieces were pulverized with the help of grinding machine into coarse powder and maintained in the hermetically sealed storage container for further application.

Preparation for Extract. One gram powder of dried *A. bisporus* S-II mushroom was suspended in 9 ml ethanol and methanol separately. Extraction was carried out by stirring the mixture at 150 rpm for 48h at 20±1 °C. After 48 h, the mixture (mushroom+solvent) was centrifuged for 10 min at 4000 g. Furthermore, the centrifuged mixture was filtered using Whatman No. 1

paper, and the extracts were collected in pre-sterilized micro-centrifuge vials. The extracts were then stored at 40±1°C for the study of antibacterial activity. For MIC and minimum bactericidal concentration (MBC) experiments, 4 gm of *A. bisporus* S-II samples (lyophilized) was extracted at -20°C for 6 h using methanol/water (80: 20; 30 ml) mixture. The mushroom+solvent mixture was kept in the ultrasonic bath for 20 min and then further centrifuged in a cooling centrifuge for 10 min at 4000 g. In addition, the centrifuged extract was filtered using Whatman No. 1 paper. The residue was then extracted with two additional 30 ml portions of the methanol/water mixture. The combined extract was dried in a rotary evaporator at 40±1 °C and lyophilized. The dried extract was dissolved at a concentration of 200 mg/ml in water and stored at -20 °C for further application.

Screening of Antibacterial Activity of *A. bisporus* S-II. *In-vitro* antibacterial susceptibility tests were performed using identified pathogenic microorganisms following the agar well diffusion method (Glamoclija et al., 2015). Cetrimide *agar* medium was utilized throughout the study for the cultivation of bacterial spp. The plates were left overnight at 37±1 °C for pre-incubation to check for any contamination to appear. In the next stage, freshly grown bacteria were seeded on the medium to prepare bacterial lawns, and two agar wells of 8 mm diameter were made opposite to each other. One well served as a control, and others served as tests. In total, 10 µl of the extract was pipetted in one well, and its respective solvent without extract was pipetted in other wells. After pipetting, the plates were kept at 20±1 °C for 1 h so that the medium absorbed the extracts. Inoculated plates were then incubated at 37±1°C for 24 h to observe the effect of the extract on the bacterial lawn, and the obtained results were then compared to the control treatment. Percentage inhibition of the growth of bacterial microorganisms was calculated after subtracting control from the values of inhibition diameter using control as standard (Kuete et al., 2011).

% growth inhibition=Control - Test/Control x 100

Control=average diameter of a bacterial colony in control.

Test=average diameter of a bacterial colony in treatment sets.

Assessment of Anti-microbial Activity of Mushroom Extracts. Microdilution assay was applied for the evaluation of the MIC for methanol extract of *A. bisporus* S-II followed by the application of rapid iodonitrotetrazolium chloride (INT) colorimetric method as described by Kuete et al. (2011). Regarding the microdilution assay, 450 µl of Müller-Hinton broth (MHB) was mixed with 50 microliters of *A. bisporus* S-II extract (200 mg/ml) for all bacterial pathogens (final concentration of 20 mg/ml). Following that, each well of microplate was poured with 200 µl of this extract solution under aseptic condition. Dilutions had been performed through the wells having 100 µl of MHB, and subsequently, 10 µl of bacterial inoculum (with 0.5 Mc Farland value or 1×10^8 CFU/ml) was inoculated in all wells. Inoculated microplates were placed in the incubator for proper incubation of bacterial culture for 24 h at 37±1 °C. In the same manner, two negative (with MHB and mushroom extract) and one positive (with MHB+bacterial inoculum) controls were also performed. After 24 h of incubation, 40 µl of 0.2 mg/ml INT was added in all wells to detect the MIC of the sample and incubated for 30 min at 37±1 °C. Viable bacteria reduced INT in samples and identified as a change in INT color from yellow to pink. The MIC was defined as the minimum *A. bisporus* S-II extract amount that stopped this color transformation and displayed complete inhibition of microbial growth. Additionally, 50 µl content from each well with no color changes was spread on Cetrimide *agar* (CA) plates and incubated for 24 h at 37±1 °C for MBC. Least concentration of methanolic extract that produced zero microbial growth on CA plats considered as MBC. All of the experiments were carried out in triplicates.

RESULTS AND DISCUSSION

A large number of pharmaceutic chemicals with exceptional and robust health-boosting benefits have been separated from mushrooms and marketed globally (Atri et al., 2013; Glamoclija et al., 2015). Mushroom oriented remedies isolated from the mycelia or fruiting bodies are utilized in the form of tablets, capsules, or concentrates. In the present study, the concentrated methanolic and ethanolic extracts of *A. bisporus* S-II were tested to screen the potential antibacterial properties against three human pathogens. The level of antimicrobial action was evaluated through the MIC value towards the bacterial strains (Alves et al., 2014). The well diffusion approach primarily applied to reveal the antibacterial ability associated with mushroom extracts against chosen three human pathogenic bacteria (i.e., *Pseudomonas aeruginosa* MTCC741, *Bacillus cereus* MTCC9786, and *Staphylococcus aureus* MTCC740).

Mushroom Mycelial Properties. *A. bisporus* S-II fruiting bodies used for the extraction of extracts were cultivated in the laboratory under controlled conditions. The color of mushroom fruiting bodies was white. Mushroom spores were ovoid to circular with brown color spore print. Mycelial growth was radial longitudinally and bright white; moreover, it elevated in the beginning and turning into compactly twisted and cottony inconsistency.

Antibacterial Activity of *Agaricus Bisporus* S-II. Nowadays, the cases of multi-drug tolerance in microorganisms are elevating and limiting the management of a large percentage of contagious infections (Bassarello et al., 2004; Atri et al., 2013). Therefore, there is an immediate requirement for the production of fresh and robust medicines to protect against current antibiotic-tolerant infections. Fungal varieties have revealed excellent potential as a resource of bioactive molecules of high remedial importance (Boda et al., 2012; Alves et al., 2013). Moreover, they are the wealthiest resources of secondary metabolites. The antimicrobial activities of the methanolic and 70% ethanolic extracts of *A. bisporus* S-II were quantitatively analyzed towards three bacterial isolates (i.e., *P. aeruginosa* MTCC741, *B. cereus* MTCC9786, and *S. aureus* MTCC740). Methanolic and ethanolic extracts of *A. bisporus* S-II showed substantial inhibition in the development of three tested bacteria at various concentrations (i.e., 25%, 50%, 75%, and 100%). According to the obtained results, the methanolic extract of *A. bisporus* S-II showed the maximum level of growth inhibition up to 21.8%, 15%, and 26.5% at 100% extract strength against *P. aeruginosa* MTCC741, *B. cereus* MTCC9786, and *S. aureus* MTCC740, respectively (Table 1). However, 100% concentrated ethanolic extract was recorded with maximum growth inhibition up to 14%, 13.82%, and 17% against *P. aeruginosa* MTCC741, *B. cereus* MTCC9786, and *S. aureus* MTCC740, respectively (Table 2). The MIC results collected during screening the effect of *A. bisporus* S-II methanolic extract against human pathogenic bacteria are presented in Table 3. It has been noted during experimentation that at 20 mg ml^{-1} concentration, mushroom extract only showed growth inhibition for *P. aeruginosa* MTCC741 and *S. aureus* MTCC740, whereas no antimicrobial activity was recorded for *B. cereus* MTCC9786. The findings in this study are in line with the previously mentioned results by various studies (Kuete et al., 2011; Chen et al., 2019) investigating the effect of the mushroom extract on different human pathogens. Ozen et al. (2011) assessed mushroom extracts antibacterial property through the disc diffusion method and reported that *A. bisporus* and *C. cibarius* methanolic extracts had high antibacterial activity against human pathogenic *Escherichia coli*. The methanolic extract showed a powerful antibacterial effect in the microtitre plate on the growth of *P. aeruginosa* MTCC741 at 15 mg/ml concentration, whereas the growth inhibition of *S. aureus* MTCC740 was recorded with 20 mg/ml concentration of extract. Methanolic extract at 20 mg/ml concentration has not shown any growth inhibition for *B. cereus* MTCC9786. Amongst all three pathogens, *P. aeruginosa* MTCC741 was highly

sensitive for mushroom methanolic extract. In the current study, the bactericidal effect of the extract was also analyzed for all three tested pathogens (Table 3). The lowest MBC values (10 mg/ml) were recorded for *P. aeruginosa* MTCC741 and *S. aureus* MTCC740, whereas in the MBC experiment, no bactericidal effect of the extract was noticed on *B. cereus* MTCC9786. The results of the present study demonstrated that extracts (i.e., methanolic and ethanolic) of *A. bisporus* S-II had maximum % growth inhibition towards *S. aureus* MTCC740. Mushroom extract prepared in methanol as the solvent has shown maximum bacterial inhibition activity up to 26.5% against *S. aureus,* compared to ethanolic extract of *Agaricus bisporus* S-II for *S. aureus* MTCC740 (17%). Earlier findings revealed that mushroom extracts demonstrated diversified antibacterial properties to protect against Gram-positive and Gram-negative infections (Kuete et al., 2011; Chen et al., 2019). The findings in this study are consistent with those of a previous study (Bassarello et al., 2004; Ozen et al., 2011) conducted by many researchers on antibacterial actions of mushrooms. In the present study, *P. aeruginosa* MTCC741 and *S. aureus* MTCC740 are identified as remarkably sensitive, and their growth was more inhibited due to methanolic extracts, compared to ethanolic extract and other tested organisms (*B. cereus* MTCC9786). Similar observations investigated the ethanolic extract of *Agaricus bisporus* S-II *against P. aeruginosa* MTCC741 and *S. aureus* MTCC740. The results of the present study are in line with the findings of earlier studies (Bassarello et al., 2004; Abenavoli et al., 2018) in which methanolic and ethanolic extracts of outdoor mushrooms possess active antibacterial activities against Gram-negative and Gram-positive bacteria. An earlier study carried out by scholars on

Table 1. Percent inhibition of growth of bacterial isolates at various % concentration of *A. bisporus* S-II methanolic extract

S. no.	% Concentration methanolic extract	% Inhibition of bacterial growth		
		P. aeruginosa MTCC741	***B. cereus*** MTCC9786	***S. aureus*** MTCC740
1	Control	0	0	0
2	25	12.1±0.18	7±0.12	8±0.12
3	50	13±0.22	7.4±0.08	11±0.08
4	75	16.5±0.04	`10.6±0.18	19±0.04
5	100	21.8±0.26	15±0.04	26.5±0.14

Table 2. Percent inhibition of growth of bacterial isolates at various % concentration of *A. bisporus* S-II ethanolic extract

S. no.	% Concentration ethanolic extract	% Inhibition of bacterial growth		
		P. aeruginosa MTCC741	***B. cereus*** MTCC9786	***S. aureus*** MTCC740
1	Control	0	0	0
2	25	0±0.00	2.8±0.06	4±0.14
3	50	6.8±0.2	5.32±0.08	10±0.12
4	75	10.2±0.02	`11.8±0.12	16.5±0.14
5	100	14±0.16	13.82±0.18	17±0.08

Table 3. Minimum inhibitory concentration and minimum bactericidal concentration values (mg/ml) of the *A. bisporus* S-II methanolic extract against pathogenic bacterial strains

Bacterial pathogens	*MIC value (mg/ml)	**MBC value (mg/ml)
P. aeruginosa MTCC741	15	10
B. cereus MTCC9786	>20	-
S. aureus MTCC740	20	10

*MIC: Minimum inhibitory concentration
** MBC: Minimum bactericidal concentration

mushroom extract confirmed the intense antibacterial activity of *G. lucidum* against Gram-negative bacteria (Sharma and Karnwal, 2018). The aforementioned study reported the antimicrobial effect of methanolic extract of *Lactarius delicious* (Chen et al., 2019) and *Sparassis crispa* (Ali et al., 2019) against human pathogenic bacteria. The similar antimicrobial tendency of *Morchella esculenta* and *Ganoderma lucidum* (Abenavoli et al., 2018; Castillo et al., 2018) were reported against *S. aureus* and *E. coli*. It was observed that the extract of *C. vermicularis* and *M. oreades* presented even more growth inhibition to Gram-negative bacteria (i.e., *E. coli* and *P. aeruginosa*), compared to Gram-positive bacteria (i.e., *B. subtilis* and *S. aureus*) (Ali et al., 2019). Acharya et al. (2015) and Castillo et al. (2018) also claimed the antibacterial capability of ethanolic extract of *P. florida* and *P. ostreatus* against various bacterial spp.

According to the obtained results, it was concluded that *A. bisporus* S-II had good antibacterial activity against different pathogens (i.e., *P. aeruginosa* MTCC741, *B. cereus* MTCC9786, and *S. aureus* MTCC740). Moreover, it was found that the extract of this mushroom was more or less inhibitory to all three bacterial isolates. Therefore, there is a need for the exploitation of S-II strain on a large scale for therapeutic use, which is still in the infancy stage.

Ethics

We hereby declare all ethical standards have been respected in preparation of the submitted article.

Conflict of Interest

The authors declare that there is no conflict of interest regarding the publication of the study.

Grant Support

The authors received no direct funding for this study.

Authors' Contribution

Study concept and design: Arun Karnwal

Acquisition of data: Arun Karnwal, Manpreet Kaur

Analysis and interpretation of data: Arun Karnwal

Drafting of the manuscript: Arun Karnwal, Manpreet Kaur

Critical revision of the manuscript for important intellectual

Content: Arun Karnwal

Statistical analysis: Arun Karnwal, Manpreet Kaur

Acknowledgment

The authors are thankful to Bhojia Institute of Life Sciences, Budh, Baddi, H.P., India, for its technical support and contribution to conducting this study.

References

Abenavoli, L., Izzo, A.A., Milic, N., Cicala, C., Santini, A., Capasso, R., 2018. Milk thistle (Silybum marianum): A concise overview on its chemistry, pharmacological, and nutraceutical uses in liver diseases. Phytother Res 32, 2202-2213.

Acharya, K., Khatua, S., Sahid, S., 2015. Pharmacognostic standardization of Macrocybe crassa: an imminent medicinal mushroom. Res J Pharm Technol 8, 860-866.

Ali, A., Ashraf, Z., Rafiq, M., Kumar, A., Jabeen, F., Lee, G.J., *et al.*, 2019. Novel Amide Derivatives as Potent Tyrosinase Inhibitors; In-vitro, In-vivo Antimelanogenic Activity and Computational Studies. Med Chem 15, 715-728.

Alves, M.J., Ferreira, I.C., Dias, J., Teixeira, V., Martins, A., Pintado, M., 2013. A review on antifungal activity of mushroom (basidiomycetes) extracts and isolated compounds. Curr Top Med Chem 13, 2648-2659.

Alves, M.J., Ferreira, I.C., Lourenco, I., Castro, A., Pereira, L., Martins, A., *et al.*, 2014. Wild mushroom extracts potentiate the action of standard antibiotics against multiresistant bacteria. J Appl Microbiol 116, 32-38.

Atri, N., Sharma, S.K., Joshi, R., Gulati, A., Gulati, A., 2013. Nutritional and neutraceutical composition of five wild culinary-medicinal species of genus Pleurotus (higher Basidiomycetes) from northwest India. Int J Med Mushrooms 15, 49-56.

Bassarello, C., Lazzaroni, S., Bifulco, G., Lo Cantore, P., Iacobellis, N.S., Riccio, R., *et al.*, 2004. Tolaasins A--E, five new lipodepsipeptides produced by Pseudomonas tolaasii. J Nat Prod 67, 811-816.

Boda, R.H., Wani, A.H., Zargar, M.A., Ganie, B.A., Wani, B.A., Ganie, S.A., 2012. Nutritional values and antioxidant potential of some edible mushrooms of Kashmir valley. Pak J Pharm Sci 25, 623-627.

Breene, W.M., 1990. Nutritional and Medicinal Value of Specialty Mushrooms. J Food Prot 53, 883-894.

Castillo, T.A., Lemos, R.A., Pereira, J.R.G., Alves, J.M.A., Teixeira, M.F.S., 2018. Mycelial Growth and Antimicrobial Activity of Pleurotus Species (Agaricomycetes). Int J Med Mushrooms 20, 191-200.

Cebin, A.V., Petravic-Tominac, V., Djakovic, S., Srecec, S., Zechner-Krpan, V., Piljac-Zegarac, J., *et al.*, 2018. Polysaccharides and Antioxidants from Culinary-Medicinal White Button Mushroom, Agaricus bisporus (Agaricomycetes), Waste Biomass. Int J Med Mushrooms 20, 797-808.

Chen, W., Tan, H., Liu, Q., Zheng, X., Zhang, H., Liu, Y., *et al.*, 2019. A Review: The bioactivities and pharmacological applications of phellinus linteus. Molecules 24, 1888.

da Silva de Souza, A.C., Correa, V.G., Goncalves, G.A., Soares, A.A., Bracht, A., Peralta, R.M., 2017. Agaricus blazei Bioactive Compounds and their Effects on Human Health: Benefits and Controversies. Curr Pharm Des 23, 2807-2834.

Glamoclija, J., Ciric, A., Nikolic, M., Fernandes, A., Barros, L., Calhelha, R.C., *et al.*, 2015. Chemical characterization and biological activity of Chaga (Inonotus obliquus), a medicinal "mushroom". J Ethnopharmacol 162, 323-332.

Inbakani, S.A., Siva, R., 2017. Biosynthesis of silver nanoparticles using edible mushrooms and it's bactericidal activities. Res J Pharm Technol 10, 467-472.

Kuete, V., Ango, P.Y., Fotso, G.W., Kapche, G.D., Dzoyem, J.P., Wouking, A.G., *et al.*, 2011. Antimicrobial activities of the methanol extract and compounds from Artocarpus communis (Moraceae). BMC Complement Altern Med 11, 42.

Ozen, T., Darcan, C., Aktop, O., Turkekul, I., 2011. Screening of antioxidant, antimicrobial activities and chemical contents of edible mushrooms wildly grown in the black sea region of Turkey. Comb Chem High Throughput Screen 14, 72-84.

Rosa, L.H., Machado, K.M., Jacob, C.C., Capelari, M., Rosa, C.A., Zani, C.L., 2003. Screening of Brazilian basidiomycetes for antimicrobial activity. Mem Inst Oswaldo Cruz 98, 967-974.

Sharma, H., Karnwal, A., 2018. Impact of Herbal Extracts in Biocontroling of Four Human Pathogenic Bacteria-an in-vitro Study. Res J Pharm Technol 11, 2895-2900.