

Full Length Research Paper

Aqueous extracts of *Lentinula edodes*, *Pleurotus pulmonarius*, and *Pleurotus sajor-caju*: Antifungal activity and inhibition of exoenzyme production by *Candida albicans*

**Morgana Lüdtke Azevedo¹, Carolina Lambretch Gonçalves², Alessandro Menna Alves³,
Caroline Neugebauer Wille⁴, Adriana Etges³, Patrícia da Silva Nascente², and
Rafael Guerra Lund^{1,3*}**

¹Graduate Program in Biochemistry and Bioprospecting, Center for Chemical, Pharmaceutical and Food Sciences, Federal University of Pelotas, Pelotas, RS, Brazil..

²Graduate Program in Microbiology and Parasitology, Biology Institute, Federal University of Pelotas, Pelotas, RS, Brazil..

³Graduate Program in Dentistry, Pelotas Dental School, Federal University of Pelotas, Pelotas, RS, Brazil.

⁴Federal Institute of Education, Science and Technology of Rio Grande do Sul (IFSul), Campus Camaquã, RS, Brazil.

Received 27 June 2022; Accepted 6 October 2022

This study was aimed at evaluating the effects of aqueous extracts of *Lentinula edodes* (SHI), *Pleurotus pulmonarius* (PUL), and *Pleurotus sajor-caju* (PSC) on the growth of eight yeast species and the exoenzyme production by *Candida* species after exposure to the extracts, which were prepared with the cold extraction methodology and tested against yeasts by the broth microdilution method. Proteinase and phospholipase were produced *in vitro* with the plate assay method using bovine serum albumin and egg yolk, respectively. The antifungal activity of the filtered mushroom extracts at different dilutions was confirmed against non-*albicans* *Candida* and *Rhodotorula* species. Exposing *Candida* isolates to extracts significantly reduced phospholipase production ($p < 0.001$). The antifungal activity against yeasts varied among different mushroom extracts. Moreover, SHI and PUL extracts may modulate the activity of phospholipase produced by *Candida albicans*. However, further studies are required to evaluate the inhibitory effect and its mechanism, as well as complementary studies with a higher number of samples tested.

Key words: Mushrooms extracts, yeasts, *Candida* species, antifungal activity, proteinases, phospholipases.

INTRODUCTION

In recent years, various extracts and metabolites of traditionally used mushrooms have assisted in the treatment of several diseases. Medicinal mushrooms,

especially those from higher basidiomycetes such as oak (SHI) and oyster (*Pleurotus* species) mushrooms, are reservoirs of bioactive compounds with multiple therapeutic

*Corresponding author. E-mail: rafael.lund@gmail.com. Tel: +55 53 99125-7668.

properties (Badalyan et al., 2019). The search for these natural products to control microbial infections has increased in recent years due to the excessive use of antibiotics in society, resulting in the resistance of microorganisms to different drugs (Castillo et al., 2018). The same occurs with some *Candida* species. The literature has reported the resistance of *Candida albicans* and other species of this genus to some antifungals (Zida et al., 2017).

Candida spp. is a commensal member of the oral cavity of most of the population. However, local or systemic factors may disrupt this balance, causing superficial and disseminated infections in humans (Tong and Tang, 2017). Besides host factors, microorganisms require several mechanisms to colonize epithelial cells, invade deep organs, and evade the human immune system. Extracellular enzyme production, such as proteinase and phospholipase, stands out among these mechanisms (Staniszewska, 2020).

Secreted aspartyl proteinase is an enzyme family that can degrade several physiologically important substrates such as albumin, immunoglobulin, and collagen, and immune components such as antibodies, elements of the complement system, and cytokines (Dabiri et al., 2018). Phospholipases are hydrolytic enzymes that attack the phospholipids of any cell membrane and have been associated with the ability of fungus adherence to the host cell (Zhao et al., 2020; Sriphannam et al., 2019).

Using natural products aims to replace conventional chemical drugs, mushroom properties should be examined because they may show active compounds produced by these organisms. Some mushrooms have been studied for their ability to use microorganisms as a food resource and promote their activity (Bach et al., 2017; Abidin et al., 2017). Several substances have been isolated from basidiomycetes, especially *Lentinula*, which can assist host cell response to biologically active substances stimulating the maturation, differentiation, or proliferation of cells involved in defense mechanisms, increasing host resistance against various cancers and infectious diseases (Chaturvedi et al., 2018).

Recent studies have reported an increased interest in alternative medicine and natural therapies, especially using substances with antimicrobial properties, with mushrooms representing a good possibility (Fisher et al., 2018). Among these basidiomycetes, *Lentinula edodes* and *Pleurotus pulmonarius* have shown promising results as antimicrobial agents (Sakamoto et al., 2017; Válková et al., 2017). The *L. edodes* mushroom, known as 'Shiitake', has important pharmacological properties such as antimicrobial and antioxidant activities. Experiments with compounds produced during mycelial growth and substances found in basidiocarp have demonstrated this ability (Ruilova et al., 2019; Vetter, 2019). Regarding *Pleurotus* spp., investigations have shown that mushrooms of this genus can also produce antimicrobial agents (Govindaraj and Renganathan, 2017).

Therefore, this study aims to evaluate the activity of mushroom extracts from *L. edodes*, *P. pulmonarius*, and *Pleurotus sajor-caju* species against eight yeast species and evaluate proteinase and phospholipase productions in *Candida* spp. samples, verifying the effect on phospholipase production through the exposition of these samples to two mushrooms filtrates (SHI and PUL).

MATERIALS AND METHODS

Mushroom culture conditions

The mushrooms were grown in the Mycology Laboratory of the Department of Microbiology and Parasitology of the Institute of Biology, Federal University of Pelotas, RS, Brazil. After the collection for extraction, the basidiomata were washed under running water, drained on a paper towel, sliced, and put in a forced-air oven, where they remained for 15 days at 35°C for drying.

Preparation of the filtered mushroom extracts

The dried mushrooms were packed in paper bags, placed in desiccators at room temperature, and protected from light until used. Dried mushrooms were ground in a blender for 1 min (50 g mushroom/L of distilled water). The mixture remained in the refrigerator at 4°C for 24 h, then filtered through cotton, and centrifuged at 5000 g and at 4°C for 1 h. The supernatant was filtered through a Whatman No. 1 filter and cellulose acetate membranes of 0.45 and 0.25 µm in aseptic conditions in a laminar flow.

Antifungal susceptibility assay

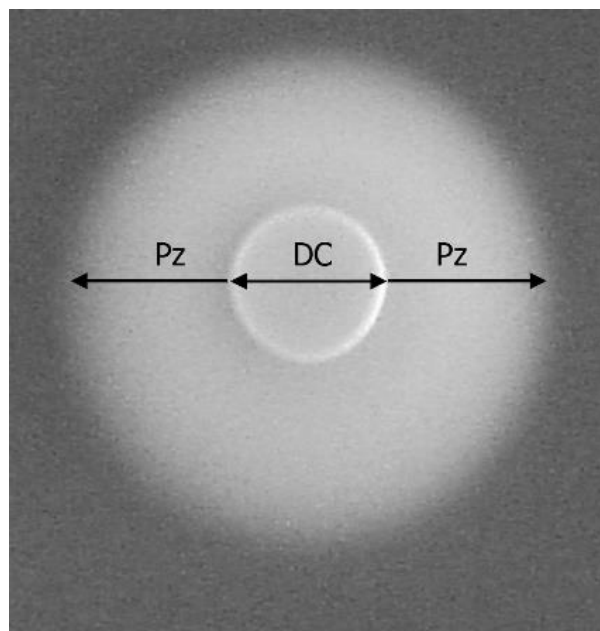
This study applied the methodology of the CLSI according to the document M27-A3 (CLSI, 2008a), which allowed testing pure and diluted extracts (50%) against eight yeasts with broth microdilution. The antifungigram assay was conducted adapted to plant protection, using the mushroom extracts diluted at 1:2 and 1:4 against *Candida sake*, *C. albicans*, *Candida parapsilosis*, *Candida glabrata*, *Rhodotorula* species, *Kloeckera japonica*, and *Cryptococcus laurentii* yeasts. The results were released after 24 and 48 h.

Sample and culture conditions

Eighty-one *C. albicans* samples were collected from individuals with denture stomatitis to evaluate the extracellular activities of phospholipase and proteinase. The samples were collected from the palate of individuals with sterile swabs. The specimens were seeded in the SDA medium with 0.2 mg/mL of chloramphenicol and incubated at 37°C for 24 to 48 h. *C. albicans* strains were identified with (1) microculture assay in corn meal agar, (2) growth in CHROMagar™ *Candida*, (3) growth in the hypertonic medium, and (4) ID 32 C assimilation assay (bioMérieux). The ATCC 62342™ strain was used as the control for phospholipase and proteinase productions.

Exposure of *Candida* samples to filtered mushroom extracts

The effect of both mushroom filtrates on phospholipase activity was evaluated with the Kadir methodology with some alterations (Kadir



$$\text{EA value} = \frac{\text{DC}}{\text{DC} + \text{PZ}}$$

Figure 1. Illustrative image of the formation of a halo measured by the division of diameter of the colony (DC) / DC + zone of precipitation (Zp).

Source: Authors

et al., 2007). Ten *C. albicans* samples with positive phospholipase production were randomly selected for the assay. A 0.5 McFarland turbidity suspension was prepared from each of the 10 isolated samples. Of these suspensions, 0.5 mL was added to tubes containing 2 mL of phosphate-buffered saline (PBS; control) and others containing 1.9 mL of PBS and 0.1 mL of filtered mushroom extract. The tubes were incubated for 30 min at 37°C. Then, the agent was removed with two rounds of washing with sterile PBS and centrifuged for 10 min at 3000 turns. The supernatant was completely removed, and the pellet was re-suspended in 2 mL of sterile PBS.

Evaluation of the extracellular activities of phospholipase and proteinase enzymes

Eighty-one *C. albicans* samples were tested in triplicate to verify phospholipase and proteinase activities. The assay medium for phospholipase was Sabouraud Dextrose Agar (SDA) with 57.3 g of sodium chloride, 0.55 g of calcium chloride, and 100 mL of sterile egg yolk (enriched egg yolk) per liter of distilled water. The assay medium for proteinase was bovine serum albumin (BSA) agar containing 5 g of BSA, 1.45 g of yeast nitrogen base (YNB), 20 g of glucose, and 20 g of Agar-Agar per liter of distilled water. All samples were cultivated in 4% SDA for 24 h. Then, they were diluted in distilled water on the scale of 0.5 McFarland, and 20 µl of each sample was applied to the assay medium. The plates were incubated at 37°C for 72 h for proteinase and phospholipase. The enzymatic activity was determined with the formation of a halo around a fungal colony and measured by the division of diameter of the colony (DC) / DC + zone of precipitation (Zp), according to the

method described by Price et al. (1982), and illustrated in Figure 1. The values obtained allowed determining whether *C. albicans* presents high, low, or no enzymatic activity. High activity had values lower than 0.63, low activity had values between 0.99 and 0.64, and no activity had a value of 1.00. These values work for the activities of both enzymes analyzed in this study.

Statistical analysis

The results were analyzed with Student t-test and ANOVA, using the SigmaStat 3.5 software for both tests to determine whether the statistical difference was calculated, considering $p < 0.05$.

RESULTS

Antifungal susceptibility assay

After reading the results at 24 and 48 h, *C. parapsilosis* was sensitive to SHI, PUL, and PSC filtered extracts diluted at 1:2 and SHI at 1:4. A *C. globose* sample was sensitive to SHI and PUL filtered extracts diluted at 1:2 and SHI at 1:4. Other specimens of *C. globose*, *C. japonica*, and *C. laurentii* were only sensitive to the PSC extract diluted at 1:2. *Rhodotorula* spp. was sensitive to SHI and PSC extracts diluted at 1:2 and PSC at 1:4. *C. sake* and *C. albicans* did not show sensitivity to any of the three filtered mushroom extracts at any dilution.

Most of the 81 isolated strains identified as *C. albicans* ($n = 70$). *C. parapsilosis* ($n = 5$), *Candida guilliermondii* ($n = 2$), *Candida lipolytic* ($n = 2$), *Candida glabrata* ($n = 1$), and *Candida tropicalis* ($n = 1$) samples were also isolated. These *C. albicans* samples presented a high proteinase production rate, with Zp values between 0.167 and 0.581. Phospholipase was produced in 55 strains of *C. albicans*, with Zp values from 0.422 to 0.905. The 11 non-*albicans* samples also showed a high proteinase production rate, with Zp from 0.217 to 0.391. Phospholipase was produced in only four non-*albicans* strains (two *C. parapsilosis*, one *C. lipolytic*, and one *C. tropicalis*). Table 1 shows the mean phospholipase and proteinase production values according to species.

Neither SHI nor PUL mushroom filtrates showed any effect on fungal growth at the concentration used for the anti-phospholipase assay. Table 2 shows the mean phospholipase activity values for the 10 strains of *C. albicans* exposed to the two mushroom filtrates.

Evaluation of the extracellular activities of phospholipase and proteinase enzymes

The mean value of phospholipase produced by *C. albicans* isolates not exposed to mushroom filtrates was 0.574.

The brief exposure to SHI and PUL filtrates reduced extracellular phospholipase with Zp values of 0.652 and 0.636, respectively. The difference in Zp values between the two groups exposed to mushroom filtrates was not

Table 1. Mean proteinase and phospholipase production values according to species.

Species	Proteinase production (Pz) (media±DP)	Phospholipase production (Pz) (media±DP)
<i>C. albicans</i> (n=70)	0.327±0.083	0.663±0.118
<i>C. parapsilosis</i> (n=5)	0.272±0.037	0.756±0.036
<i>C. lipolytic</i> (n=2)	0.325±0.065	0.743±0.050
<i>C. guilliermondii</i> (n=2)	0.331±0.039	-
<i>C. glabrata</i> (n=1)	0.342±0.016	-
<i>C. tropicalis</i> (n=1)	0.246±0.025	0.663±0.015

Source: Authors

Table 2. Mean phospholipase production values for the two groups exposed to mushroom extracts compared with the control group.

Sample	Control	Mushrooms filtrates	
		SHI	PUL
23682	0.629±0.018	0.745±0.017	0.717±0.022
25688P	0.569±0.024	0.600±0.007	0.569±0.017
24078	0.761±0.062	0.775±0.025	0.892±0.003
23783	0.551±0.030	0.642±0.050	0.582±0.011
23609B	0.534±0.014	0.745±0.017	0.576±0.010
23651D	0.517±0.025	0.549±0.011	0.569±0.002
24073	0.527±0.017	0.601±0.024	0.633±0.008
24058(2)	0.580±0.031	0.673±0.019	0.613±0.013
23559(2)	0.517±0.001	0.583±0.017	0.617±0.008
24008	0.558±0.008	0.603±0.022	0.596±0.019
Media±DP	0.574±0.075	0.652±0.080 ^a	0.636±0.098 ^b

^ap<0.001; ^bp<0.001.

Source: Authors

significant ($p = 0.991$), while there was a statistically significant difference between the two test groups and the control ($p < 0.05$).

DISCUSSION

The interest in alternative non-chemical antimicrobial agents has grown considerably in recent years worldwide. The filtered extract of the *L. edodes* culture has significant antimicrobial activity against different species of phytopathogenic bacteria such as *Ralstonia solanacearum*, and the main bioactive components responsible for this antimicrobial effect are its acids, mainly oxalic acid (Kwak et al., 2016). Moreover, another study showed that exposing *C. albicans* and *Candida neoformans* yeasts to *Lentinus subnidus* and *Lenzites* species mushroom extracts at concentrations from 12.5 g/mL to 100 mg/mL made them sensitive to the lowest concentrations (Chakraborty et al., 2019).

The antimicrobial ability of mushrooms, especially

Pleurotus spp., also seems effective against *Bacillus subtilis* bacteria. Studies have demonstrated the sensitivity of bacterial species from the fermentation broth and mycelium of *Pleurotus ostreatus* (Muszyńska et al., 2018; Al-Bahrani et al., 2017).

Pleurotus spp. is known for its high nutrient and medicinal content. The antimicrobial action of this genus occurs with the production of antibiotics such as pleurotin, produced by some species (Purnomo et al., 2017). Another study confirmed the presence of compounds such as lecithin, which also has therapeutic properties (El-Enshasy et al., 2019; Masri et al., 2017). *P. ostreatus* also showed antimicrobial activity, decreasing the bacterial adhesion of *Listeria innocua* by up to 96% (Klančnik et al., 2017). Additionally, the *Pisaster giganteus* extract associated with *Lignosus rhinocerus*, *Hericium erinaceus*, and *Schizophyllum commune* extracts was effective against the DENV-2 serotype of the dengue virus, presenting low toxicity to Vero cells when infected by the virus (Eilan et al., 2019).

L. edodes also has antitumor and antioxidant properties,

and has hypocholesterolemic activity, which was demonstrated in experiments with compounds produced during mycelial growth and substances found in the basidiocarp (Yoo et al., 2019).

Using mushrooms as antimicrobial, particularly antifungal agents is possible, as several of them can produce toxic metabolites. The results obtained in this study showed new perspectives on the use of macroscopic fungi pathogenic to humans and animals.

Regarding the *Candida* genus, several studies have been concerned with attenuating or inhibiting virulence factors instead of causing the death of this yeast. Kadir tested two subtherapeutic doses of chlorhexidine in ten *C. albicans* samples from patients with denture stomatitis and showed a significant decrease in phospholipase activity (Kadir et al., 2007).

Studies aiming to attenuate or inhibit the virulence factor of the *Candida* genus generally use antifungal agents that inhibit the ergosterol synthesis of fungal cells, such as fluconazole, itraconazole, amphotericin B, flucytosine, and nystatin. Lyon and Resende (2006) verified decreased adhesion ability and phospholipase and proteinase productions in *C. albicans* samples after exposure to fluconazole. This inhibition of virulence factors by antifungal agents seems similar among *Candida* spp.

The present study also evaluated the phospholipase activity of *C. albicans* isolates (phospholipase producers) exposed to two mushroom filtrates. Exposing the samples to the two mushroom filtrates for 30 min significantly reduced the mean value of phospholipase production (Meza-Menchaca et al., 2019). In a similar study, the anti-enzymatic activity in phospholipase is attributed to ergosterol peroxides, characterized as an ergosterol derivate, a compound present in the cell membrane of fungi. Additionally, the aqueous chloroform extract found in the fruiting bodies of mushrooms with *Lactarius matsutake* has also inhibited the enzymatic activity of phospholipase (Gao et al., 2007).

Conclusion

Thus, after verifying the filtered mushroom extracts tested, the results promise an inhibitory effect on phospholipase production. Further studies are required to evaluate the inhibitory effect and its mechanism, as well as complementary studies with a higher number of samples tested.

CONFLICT OF INTERESTS

The authors have not declared any conflict of interests.

ACKNOWLEDGEMENTS

The authors thank the Brazilian Council of Scientific and

Technological Development (CNPq).

REFERENCES

- Abidin MHZ, Abdullah N, Abidin NZ (2017). Therapeutic properties of *Pleurotus* species (oyster mushrooms) for atherosclerosis: A review. *International Journal of Food Properties* 20(6):1251-1261.
- Al-Bahrani R, Raman J, Lakshmanan H, Hassan AA, Sabaratnam V (2017). Green synthesis of silver nanoparticles using tree oyster mushroom *Pleurotus ostreatus* and its inhibitory activity against pathogenic bacteria. *Materials Letter* 186:21-25.
- Bach F, Helm CV, Bellettini MB, Maciel GM, Haminiuk CWI (2017). Edible mushrooms: a potential source of essential amino acids, glucans, and minerals. *International Journal of Food Science and Technology* 52(11):2382-2392.
- Badalyan SM, Barkhudaryan A, Rapior S (2019). Recent progress in research on the pharmacological potential of mushrooms and prospects for their clinical application. *Medicinal Mushrooms* 1-70.
- Castillo TA, Lemos RA, Pereira JRG, Alves JMA, Teixeira MFS (2018). Mycelial growth and antimicrobial activity of *Pleurotus* species (*Agaricomycetes*). *International Journal of Medicinal Mushrooms* 20(2):191-200.
- Chakraborty T, Tóth R, Gácsér A (2019). Eicosanoid production by *Candida parapsilosis* and other pathogenic yeasts: Virulence 10(1):970-975.
- Chaturvedi VK, Agarwal S, Gupta KK, Ramteke PW, Singh MP (2018). Medicinal mushroom: boon for therapeutic applications. *3 Biotech* 8(8):1-20.
- CLSI (2008a) Reference method for broth dilution antifungal susceptibility testing of yeasts; approved standard-third edition; CLSI document M27-A3. Clinical and Laboratory Standards Institute, Wayne.
- Dabiri S, Shams-Ghahtarokhi M, Razzaghi-Abyaneh M (2018). Comparative analysis of proteinase, phospholipase, hydrophobicity, and biofilm-forming ability in *Candida* species isolated from clinical specimens. *Journal of Medical Mycology* 28(3):437-442.
- El-Enshasy HA, Selvamani S, Dailin DJ, Abd Malek R, Hanapi SZ, Ambehbatu KK, Sukmawati D, Leng OM, Moloi N (2019). Antioxidant compounds of the edible mushroom *Pleurotus ostreatus*. *International Journal of Biotechnology for Wellness Industries* 8(1):1-14.
- Ellan K, Thayan R, Phan CW, Sabaratnam V (2019). Anti-inflammatory effect of mushrooms in dengue-infected human monocytes. *Tropical Biomedicine* 36(4):1087-1098.
- Fisher MC, Hawkins NJ, Sanglard D, Gurr SJ (2018). Worldwide emergence of resistance to antifungal drugs challenges human health and food security. *Science* 360(6390):739-742.
- Gao JM, Wang M, Liu LP, Wei GH, Zhang AL, Draghici C, Konish Y (2007). Ergosterol peroxides as phospholipase A2 inhibitors from the fungus *Lactarius matsutake*. *Phytomedicine* 14(2):821-824.
- Govindaraj S, Renganathan S (2017). Molecular characterization and phytochemical studies of *Pleurotus* sp. to unveil species diversity and pharmacological activities. *Journal of Pure and Applied Microbiology* 11(2):891-901.
- Kadir T, Gümrü B, Uygün-Can B (2007). Phospholipase activity of *Candida albicans* isolates from patients with denture stomatitis: the influence of chlorhexidine gluconate on phospholipase production. *Archives of Oral Biology* 52(19):691-696.
- Klančnik A, Megušar P, Sterniša M, Jeršek B, Bucar F, Možina SS, Kos J, Sabotič J (2017). Aqueous extracts of wild mushrooms show antimicrobial and antiadhesion activities against bacteria and fungi. *Phytotherapy Research* 31(12):1971-1976.
- Kwak AM, Lee IK, Lee SY, Yun BS, Kang HW (2016). Oxalic acid from *Lentinula edodes* culture filtrate: antimicrobial activity on phytopathogenic bacteria and qualitative and quantitative analyses. *Mycobiology* 44(4):338-342.
- Lyon JP, Resende MA (2006). Evaluation of adhesion to buccal epithelial cells in *Candida* species obtained from denture wearers after exposure to fluconazole. *Mycoses* 50:21-24.
- Masri HJMHJ, Maftoun PMP, Abd Malek R, Boumehira AZ, Pareek A,

- Hanapi SZ, Leng OM, El-Enshasy H (2017). The edible mushroom *Pleurotus* spp.: II. Medicinal values. *International Journal of Biotechnology for Wellness Industries* 6(1):1-11.
- Meza-Menchaca T, Ramos-Ligonio A, López-Monteon A, Limón AV, Kaluzhskiy LA, Shkel TV, Strushkevich NV, Jiménez- Garcia LF, Moreno LTA, Gallegos-Garcia V, Suárez-Medellin J, Trigos A (2019). Insights into ergosterol peroxide's trypanocidal activity. *Biomolecules* 9(9):484.
- Muszyńska B, Grzywacz-Kisielewska A, Kała K, Gdula-Argasińska J (2018). Anti-inflammatory properties of edible mushrooms: A review. *Food Chemistry* 243:373-381.
- Price MF, Wilkinson ID, Gentry LO (1982). Plate method for detection of phospholipase activity in *Candida albicans*. *Sabouraudia* 20(1):7-14.
- Purnomo AS, Ashari K, Hermansyah FT (2017). Evaluation of the synergistic effect of mixed cultures of white-rot fungus *Pleurotus ostreatus* and biosurfactant-producing bacteria on DDT biodegradation. *Journal of Microbiology and Biotechnology* 27(7):1306-1315.
- Ruilova M, Niño-Ruiz Z, Sanbria J, Montero D, Salazar S, Bayas F, Sandoval R (2019). Antimicrobial activity of *Lentinula edodes* mushroom extracts against pathogenic bacteria. *Italian Journal of Food Science* pp. 179-189.
- Sakamoto Y, Nakade K, Sato S, Yoshida K, Miyazaki K, Natsume S, Konno N (2017). *Lentinula edodes* genome survey and postharvest transcriptome analysis. *Applied and Environmental Microbiology* 83(10).
- Sriphanam C, Nuanmuang N, Saengsawang K, Amornthipayawong D, Kummasook A (2019). Anti-fungal susceptibility and virulence factors of *Candida* spp. isolated from blood cultures. *Journal of Medical Mycology* 29(4):325-330.
- Staniszewska M (2020). Virulence factors in *Candida* species. *Current Protein and Peptide Science* 21(3):313-323.
- Tong Y, Tang J (2017). *Candida albicans* infection and intestinal immunity. *Microbiology Research* 198:27-35.
- Válková H, Novotný Č, Malachová K, Šlosarčíková P, Fojtík J (2017). Effect of bacteria on the degradation ability of *Pleurotus ostreatus*. *Science of the Total Environment* 584:1114-1120.
- Vetter J (2019). Biological values of cultivated mushrooms - A review. *Acta Alimentaria* 48(2):229-240.
- Yoo SI, Lee HY, Markkandan K, Moon S, Ahn YJ, Ji S, Ko J, Seong-Jin K, Ryu H, Hong CP (2019). Comparative transcriptome analysis identified candidate genes involved in mycelium browning in *Lentinula edodes*. *BMC Genomics* 20(1):1-13.
- Zhao Z, Zhou Y, Wang R, Xie F, Zhai Z (2020). Expression, purification, and characterization of phospholipase B1 from *Candida albicans* in *Escherichia coli*. *3 Biotech* 10(12):1-7.
- Zida A, Bamba S, Yacouba A, Ouedraogo-Traore R, Guiguemdé RT (2017). Anti-*Candida albicans* natural products, sources of new antifungal drugs: A review. *Journal of Medical Mycology* 27(1):1-19.