PHENOLIC CONTENT, ANTIOXIDANT AND ANTIMICROBIAL POTENTIAL OF *MELANOLEUCA MELALEUCA* EDIBLE MUSHROOM

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ABSTRACT

Wild edible mushrooms have been gathered and consumed by humans since ancient times. In addition to their nutritional properties, many mushrooms are known to possess medicinal properties. The present study aimed to determine antioxidant and antimicrobial activities and phenolic content of the wild edible mushroom *Melanoleuca melaleuca* (Pers.) Murrill. All experiments were performed 5 times, and results expressed as mean $\pm$ standard deviation unless otherwise stated ($p \leq 0.05$). The present study findings demonstrated that the antioxidant potential of the mushroom was high. It was determined that the TAS value of ethanol extract of the *M. melaleuca* mushroom was 3.393 ± 0.098 mmol/L, TOS value was 6.460 ± 0.121 μ mol/L and OSI value was 0.190 ± 0.002 . Furthermore, it was determined that the mushroom extracts were effective against test microorganisms at 25-400 μ g/mL concentrations. HPLC scans revealed that the mushroom contained gallic, catechin, p-coumaric, syringic and protocatechuic acids. Thus, it was determined that the mushroom had antioxidant and antimicrobial potential. It was also determined that the mushroom could serve as a natural source for phenolic content.

Keywords: Antimicrobial, antioxidant, phenolic content, *Melanoleuca melaleuca*, wild edible mushroom.

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INTRODUCTION

Reactive oxygen species (ROS) produced by living organisms could be beneficial at low levels. For example, ROS play physiological roles in cellular response to noxia such as defense against infectious agents, and in the functioning of certain cellular signaling systems (Rahman, 2007). However, due to increased ROS levels, damages could occur in cellular structures such as lipids, membranes, proteins and nucleic acids (Rahman, 2007; Pham-Huy *et al.*, 2008). These harmful effects of ROS could be inhibited or reduced by endogenous antioxidants. However, oxidative stress could be observed when endogenous antioxidants are insufficient. Oxidative stress could lead to several chronic and degenerative diseases such as cancer, arthritis, aging, autoimmune, cardiovascular and neurodegenerative diseases. In cases where endogenous antioxidants are insufficient to counteract the effects of ROS, supplementary antioxidants could be beneficial in the prevention or reduction of oxidative stress. Exogenous antioxidants function as free radical scavengers by preventing and repairing the damages caused by the ROS. Thus, they could improve the immune defense and reduce the cancer and degenerative disease risks (Rahman, 2007; Pham-Huy *et al.*, 2008; Nimse and Pal, 2015; Suleman *et al.*, 2019). Natural products with antioxidant activity such as the mushrooms are used as supplementary antioxidants. In recent times, there is an increasing

interest in mushrooms used to assist endogenous antioxidants.

Microorganisms are responsible for several diseases globally. While several of these diseases could be easily treated, today, these diseases are becoming difficult to treat due to resistant microorganisms. Therefore, it became necessary to identify and investigate natural products that are effective against resistant microorganisms (Nowacka *et al.*, 2015; Sevindik, 2018). Natural mushrooms are living organisms that have not been investigated adequately. Thus, it is very important to investigate the potential of mushrooms as an antimicrobial agent.

Mushrooms have been used for many purposes in several parts of the world for a long time. They are mainly used as nutrients and for their medicinal properties. They have high protein content, are rich in vitamin B, various minerals and contain almost all essential amino acids. In addition to their nutritional properties, mushrooms are good therapeutic agents. Mushrooms could also provide health benefits as well as their nutritional values. In previous studies, it was reported that mushrooms had significant antioxidant, antibacterial, anticancer, antigenotoxic, anti-inflammatory, antifungal and DNA protective effects (Arora *et al.*, 2013; Bal *et al.*, 2019; Meng *et al.*, 2016; Yılmaz *et al.*, 2016; Muszyńska *et al.*, 2018).

Melanoleuca melaleuca (Pers.) Murrill is an edible mushroom. It is prevalent in mixed forests. The

present study aimed to determine the antioxidant and antimicrobial activities and phenolic content of the wild and edible *M. melaleuca* mushroom.

MATERIALS AND METHODS

Laboratory Studies: *M. melaleuca* samples investigated in the present study were collected in Oguzeli/Turkey. Mushroom samples were dried at +40°C (Profilo, PFD1350W, Turkey). Ten grams of the pulverized mushroom samples were macerated (24 h) with 200 mL ethanol (EtOH) using a magnetic stirrer. They were then concentrated via filtration at 40°C using a rotary evaporator.

Phenolic Content Analyses: The phenolic contents of the mushroom were determined with a RPHPLC-DAD system (Shimadzu). The presence of gallic acid, catechin, chlorogenic acid, caffeic acid, epicatechin, syringic acid, coumaric acid, benzoic acid, hydroxybenzoic acid, hesperidin, sinapic acid, protocatechuic acid and rosmarinic acid was investigated. To perform the analysis, the standards of the compounds were injected. Then, standards were scanned in the mushroom sample. Then, the peak resolution and run time was defined for each compound. A DAD detector was utilized in the process. Chromatographic processes were conducted with an Agilent Eclipse XDB-C18 column (250x4.6 mm; id 5 µm) at 30°C (Caponio *et al.*, 1999).

Antioxidant and Oxidant Analyses: TAS, TOS and OSI values of ethanol extract of *M. melaleuca* mushroom were determined with commercial Rel assay kits TAS and TOS (Rel Assay Kit Diagnostics, Turkey). Analysis was conducted on 5 replicates. Hydrogen peroxide (TOS) and Trolox (TAS) were used as the calibrator. Results are expressed as mmol Trolox equiv./L for TAS and µmol H₂O₂ equiv./L for TOS (Erel, 2004, 2005). The following formula was used to calculate the OSI (arbitrary unit: AU) (Erel, 2005).

$$O \quad (A) : \frac{T \quad (\mu\text{mol } H_2O_2 \text{ equiv./L})}{T \quad (\text{mmol Trolox equiv./L}) \times 10}$$

Antimicrobial Analyses: Antimicrobial activity analyses were conducted using the agar dilution method on mushroom extracts. Bacterial strains: *Staphylococcus aureus* ATCC 29213, *S. aureus* MRSA ATCC 43300, *Enterococcus faecalis* ATCC 29212, *Escherichia coli* ATCC 25922, *Pseudomonas aeruginosa* ATCC 27853 and *Acinetobacter baumannii* ATCC 19606. Fungal strains: *Candida albicans* ATCC 10231, *C. krusei* ATCC 34135 ATCC 13803 and *C. glabrata* ATCC 90030. Pre-cultured processes were performed in Muller Hinton Broth for bacteria and RPMI 1640 Broth for fungi. Fungi reference drugs: Fluconazole and Amphotericin B. Bacteria reference drugs: Amikacin, Ampicillin and Ciprofloxacin. Mushroom extracts were tested at 800,

400, 200, 100, 50, 25 and 12.5 µg/mL concentrations. The concentrations were adjusted using distilled water. The lowest concentration that inhibited the bacteria and fungi growth was determined as the minimum inhibitor concentration (MIC) (Bauer *et al.*, 1966; Hindler *et al.*, 1992; CLSI, 2012; EUCAST, 2014; Matuschek *et al.*, 2014; EUCAST, 2015).

Statistical Analysis: All experiments were performed 5 times, and results expressed as mean ± standard deviation unless otherwise stated. Statistical analysis was performed using Microsoft Excel. Results were considered significant (P≤0.05).

RESULTS AND DISCUSSION

Phenolic Content: The mushrooms, which have rich organic and inorganic content, synthesize secondary metabolites as a result of metabolic and physiological activities. These secondary metabolites exhibit various biological activities (Zhong and Xiao 2009; Chen and Liu 2017). Thus, it has been seemed worth to study the biological action mechanisms and activities of mushrooms. Also, analysis of the phenolic compounds that are primarily responsible in mushroom research for biological activities is very important. In the present study, phenolic acid content in *M. melaleuca* mushroom was determined. In HPLC analysis, 13 phenolic acids were screened in the mushroom. Analysis findings demonstrated that 5 compounds (Gallic acid, catechin, p-coumaric acid, syringic acid and protocatechuic acid) were present. The analysis findings are presented in Table 1.

Table 1. Phenolic Contents of *M. melaleuca*.

Phenolic Compound (ppm)	<i>M. melaleuca</i>
Gallic Acid	14.062
Catechin	5.328
Chlorogenic Acid	none
Caffeic Acid	none
Epicatechin	none
Syringic Acid	1.251
P-Coumaric Acid	26.231
Benzoic Acid	none
Hydroxybenzoic Acid	none
Hesperidin	none
Sinapic Acid	none
Rosmarinic Acid	none
Protocatechuic Acid	41.820

Previous studies reported that gallic acid is a common and important antioxidant compound found in several natural products (Zanwar *et al.*, 2014). It was also reported that gallic acid exhibits various biological properties such as anticancer, antimicrobial, anti-

inflammatory, antitumor, anti-neoplastic and anti-diabetic effects (Kroes *et al.*, 1992; Kawada *et al.*, 2001; Fiuza *et al.*, 2004; Chia *et al.*, 2010; Liu *et al.*, 2013; Sun *et al.*, 2014; Zhang *et al.*, 2019). In addition to its high antioxidant activity; catechin was reported to exhibit several activities such as anti-inflammatory, anti-pandemic, anti-metastatic, anti-ulcer, anti-angiogenic, anti-allergic, anti-mutagenic, anti-proliferative, antimicrobial effects (Nagabhushan and Bhide, 1988; Maeda-Yamamoto *et al.*, 2007; Xu *et al.*, 2008; Chunmei *et al.*, 2010; Delgado *et al.*, 2014; You *et al.*, 2018; Nakano *et al.*, 2019). It was reported that p-coumaric acid exhibited immunomodulatory activity, antioxidant, anti-inflammatory and antiangiogenic properties (Etoh *et al.*, 2004; Kong *et al.*, 2013; Pragasaam *et al.*, 2013). In previous studies, syringic acid was reported to possess hepatoprotective, anti-steatotic and anti-inflammatory effects (Itoh *et al.*, 2009; Ham *et al.*, 2016). In addition, it was evidenced that protocatechuic acid exhibited anti-inflammatory, analgesic, anti-aging, anti-glycative, anti-apoptotic, anti-influenza virus activities and anti-diabetic property (Lu *et al.*, 2002; Min *et al.*, 2010; Lende *et al.*, 2011; Tsai and Yin, 2012; Deng *et al.*, 2014; Erukainure *et al.*, 2017). Phenolic contents of *M. melaleuca* have not been previously determined. In a study on different species, it has been reported that Benzoic acid, p-Coumaric acid, p-Hydroxybenzoic acid, Protocatechuic acid, Syringic acid and trans-Cinnamic acid are within *Melanoleuca cognata* (Fr.) Konrad and Maubl. and *M. stridula* (Fr.) Singer at different levels (Bahadori *et al.*, 2019). In our study, p-coumaric acid, syringic acid and protocatechuic acid were determined in the body of *M. melaleuca* similar to these species. Unlike these species, it has been determined in Gallic acid and catechin in *M. melaleuca*. The present study findings suggested that *M. melaleuca* mushroom could be a natural source for these compounds.

Antioxidant and Oxidant Potential: Mushrooms synthesize various reduced molecules with antioxidant effects. In addition, they have the potential to contain antioxidant enzymes and coenzymes in their body. Furthermore, they are rich in vitamins A, C and E, which have antioxidant properties (Tan *et al.*, 2018; Sevindik, 2018). TAS values are indicative of the system that mushrooms potentially produce in their structure and reflect the whole enzymatic and nonenzymatic molecules they possess (Selamoglu *et al.*, 2020). Thus, determination of TAS is very important for the determination of new antioxidant natural resources. There are only a few studies in the literature that determined TAS, TOS and OSI of wild mushrooms. Furthermore, there are no studies that aimed to determine the TAS, TOS and OSI of *M. melaleuca* mushroom in the literature. In studies on edible mushrooms, TAS values for *Cyclocybe cylindracea* (DC.) Vizzini and Angelini,

Laetiporus sulphureus (Bull.) Murrill, *Lentinus tigrinus* (Bull.) Fr., *Gyrodon lividus* (Bull.) Sacc., *Cerionporus varius* (Pers.) Zmitr. and Kovalenko and *Infundibulicybe geotropa* (Bull.) Harmaja were reported as 4.325, 2.195, 1.748, 2.077, 2.312 and 1.854 mmol/L, respectively. TOS values for the same mushrooms were reported as 21.109, 1,303, 19.294, 13,465, 14.358 and 30.385 μ mol/L, respectively. OSI values for the same mushrooms were reported as 0.488, 0.059, 1.106, 0.651, 0.627 and 1.639 (Bal, 2018; Sevindik *et al.*, 2018a; Sevindik, 2018; Sevindik *et al.*, 2018b; Sevindik, 2019; Sevindik *et al.*, 2020). In the present study, it was determined that the TAS of the *M. melaleuca* mushroom EtOH extract was 3.393 ± 0.098 mmol/L, TOS was 6.460 ± 0.121 μ mol/L and OSI was 0.190 ± 0.002 . Thus, it was determined that the TAS value of *M. melaleuca* mushroom was lower when compared to that of *C. cylindracea* mushroom and higher when compared to that of *L. sulphureus*, *L. tigrinus*, *G. lividus*, *C. varius* and *I. geotropa*. It is suggested that these differences in TAS between the mushrooms were due to the differences in their capacity to produce antioxidant compounds. Furthermore, differences in the number and variety of secondary metabolites produced by mushroom defense system reactions to structural and environmental factors could have led to these findings. Thus, it was determined that *M. melaleuca* mushroom is suggested to be an important supplementary antioxidant nutrient.

In this study, it was determined that *M. melaleuca* mushroom TOS was lower than *C. cylindracea*, *L. tigrinus*, *G. lividus*, *C. varius* and *I. geotropa* mushrooms and higher than *L. sulphureus* mushroom. It is suggested that these differences were due to the differences between the regions where the mushrooms were collected, between the mushroom species, and between the substrates utilized by the mushrooms. Mushroom defense system mechanism stimulates the production of certain free radicals such as reactive oxygen species to protect itself against harmful endogenous factors in metabolite processes, particularly due to the environmental factors; thus, leading to changes in total oxidant levels in the mushroom (Kozarski *et al.*, 2015; Sevindik, 2018). Consumption of these mushrooms may lead to various physiological disorders in humans, who are among the consumers in the environmental ecosystem (Frey-Klett *et al.*, 2011). Therefore, determination of the total oxidant values of the mushroom samples collected in the regions where the mushrooms are consumed is very important. In the present study, TOS of the *M. melaleuca* mushroom was determined. The present study findings demonstrated that the analyzed mushrooms exhibited normal oxidant compound levels.

The OSI reflects the inhibition rate of oxidant compounds by the endogenous antioxidant compounds in living organisms. An increase in OSI reflects a lower

inhibition rate of the endogenous oxidant compounds by the endogenous antioxidant compounds in the mushroom (Selamoglu *et al.*, 2020). In the present study, it was determined that *M. melaleuca* mushroom OSI was lower when compared to that of *C. cylindracea*, *L. tigrinus*, *G. lividus*, *C. varius* and *I. geotropa* mushrooms and higher when compared to that of *L. sulphureus* mushroom. Since the total antioxidant system of edible *M. melaleuca* mushroom was more potent and effective against oxidant compounds in the present study, OSI values were low. Thus, it was determined that there was no significant disadvantage based on the oxidant compounds in consumption of the mushroom.

Antimicrobial activity: Today, due to the overconsumption of antibiotics, the resistance levels of microorganisms to antibiotics have increased (Stewart *et al.*, 2018). Therefore, identification of new antimicrobial

agents became mandatory. Mushrooms are exposed to several microorganisms in their natural ecosystem (Frey-Klett *et al.*, 2011). This has led to the development of defense systems for survival. Several studies demonstrated that mushrooms have significant effects on microorganisms. In studies previous studies, researchers from different parts of the world such as Chile, Brazil, Japan, Macedonia, Uruguay, Thailand, Korea, Turkey and Spain reported that mushrooms have antimicrobial effects on different types of microorganisms (Venturini *et al.*, 2008; Akyuz and Kirbag 2009; Doğan *et al.*, 2013; Kim *et al.*, 2018; Rosenberger *et al.*, 2018; Srichanun *et al.*, 2018; Angelini *et al.*, 2019; Yamada *et al.*, 2019). In the present study, the effects of *M. melaleuca* mushroom EtOH extracts on the tested microorganisms were investigated. The findings are presented in Table 2.

Table 2. Antimicrobial Activities of *M. melaleuca*.

	<i>A</i>	<i>B</i>	<i>C</i>	<i>D</i>	<i>E</i>	<i>F</i>	<i>G</i>	<i>H</i>	<i>I</i>
EtOH	400	400	200	25	25	25	50	50	50
Ampicillin	1.56	3.12	1.56	3.12	3.12	-	-	-	-
Amikacin	-	-	-	1.56	3.12	3.12	-	-	-
Ciprofloksasin	1.56	3.12	1.56	1.56	3.12	3.12	-	-	-
Flukanazol	-	-	-	-	-	-	3.12	3.12	-
Amfoterisin B	-	-	-	-	-	-	3.12	3.12	3.12

25, 50, 200, 400 µg/mL extract concentration

A: *S. aureus*, B: *S. aureus* MRSA, C: *E. faecalis*, D: *E. coli*, E: *P. aeruginosa*, F: *A. baumannii*, G: *C. albicans*, H: *C. glabrata*, I: *C. krusei*

Literature review revealed no study on the antimicrobial potential of *M. melaleuca* mushroom. It was determined that the mushroom extracts used in the present study were effective on test microorganisms at 25-400 µg/mL concentrations. It was found that mushroom extracts were particularly effective at 25 µg/mL concentration on gram negative *E. coli*, *P. aeruginosa* and *A. baumannii* bacteria. In recent years, especially gram-negative bacteria have become a health problem due to their resistance to antibiotics. Thus, mortality rates have increased in infections caused by resistant bacteria (Frey-Klett *et al.*, 2011). Researchers and the pharmaceutical industry have focused on various natural products effective on resistant bacteria (Selamoglu *et al.*, 2020). In this study, it was determined that *M. melaleuca* extracts displayed the highest impact on gram negative bacteria. Furthermore, mushroom extracts were effective on *C. albicans*, *C. glabrata* and *C. krusei* fungal strains at 50 µg/mL concentration. In addition, mushroom extracts were effective on *S. aureus*, *S. aureus* MRSA and *E. faecalis* bacteria at high concentrations (200-400 µg/mL). As a result, it was determined that *M. melaleuca* mushroom analyzed in the present study was highly effective on tested gram

negative bacterial and fungal strains. Furthermore, the antimicrobial potential of *M. melaleuca* was determined for the first time in the present study.

Conclusion: In this study, antioxidant potential, phenolic contents and antimicrobial potential of *M. melaleuca* edible mushroom, were determined. It was found that the mushroom had antioxidant properties. Furthermore, 5 compounds including gallic acid, catechin, p-coumaric acid, syringic acid and protocatechuic acid were identified in the mushroom. Antimicrobial activity of the mushroom was higher against the tested gram-negative bacteria, and fungal strains. Thus, it was concluded that edible *M. melaleuca* mushroom is a natural functional nutrient with biological potential.

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