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Antioxidant and Antimicrobial Activities of *Armillaria mellea* and *Macrolepiota procera* Extracts

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Abstract: Mushrooms have been used extensively, owing to their nutritional and medicinal value, for thousands of years. This study designed for the determine of antioxidant and antimicrobial potential of two edible mushrooms *Armillaria mellea* (Vahl) P.Kumm. and *Macrolepiota procera* (Scop.) Singer. Antioxidant activity was detected method by DPHH free radical scavenging. *M.procera* extract had more potent free radical scavenging activity than *A.mellea* extract (IC_{50}: 0.191, 1.19 mg/mL). The concent of the components with antioxidant properties, such as total phenols,β-caratone and lycopene were determined by spectrophotometric methods. Finally, the antimicrobial potential was determined with a agar well diffusion method on 14 microorganisms. *A. mellea* methanol extract formed against to *Klebsiella pneumaniae* ATCC 13883, *Bacillus subtilis* ATCC 6633, *Staphylococcus aureus* ATCC 25923,10±1 mm inhibition zone diameter. *M.procera* methanol extract formed against to *Enterococcus faecalis* ATCC 29212, *Klebsiella pneumaniae* ATCC 13883, 9±1 mm inhibition zone diameter. This research has shown that these two edible mushrooms have potential as natural antioxidants.

Key words: Antimicrobial activity, Antioxidant activity, *Armillaria mellea, Macrolepiota procera,* Mushroom

Armillaria mellea and *Macrolepiota procera* Ekstrelerinin Antioksidan ve Antimikrobiyal Etkileri

Öz: Mantarlar, binlerce yıldır besin ve tıbbi değerleri nedeniyle yaygın olarak kullanılmaktadır. Bu çalışma iki yenilebilir mantar olan *Armillaria mellea* (Vahl) P.Kumm ve *Macrolepiota procera* (Scop.) antioksidan ve antimikrobiyal potansiyelinin belirlenmesi için tasarlanmıştır Antioksidan aktivitesi DPHH serbest radikal süpürme yöntemi ile tespit edildi. *M.procera* methanol ekstresi *A.mellea* methanol ekstresinden daha güçlü serbest radikal süpürücü aktivitesine sahiptir (IC_{50}: 0.191, 1.19 mg/mL). Toplam fenol, β-karoten ve likopen gibi antioksidan özelliklere sahip bileşenlerin konsantrasyonu spektrofotometrik yöntemlerle belirlendi. Son olarak, antimikrobiyal aktivitesi 14 mikroorganizma üzerinde denenmiş olup agar difüzyon yöntemi ile kullanılmıştır. *A. mellea* metanol ekstraktı *Klebsiella pneumaniae* ATCC 13883, *Bacillus subtilis* ATCC 6633, *Staphylococcus aureus* ATCC 25923 mikroorganizmlarına karşı 10 ± 1 mm inhibisyon zon çapı oluşturdu. *M.procera* metanol ekstresi ise *Enterococcus faecalis* ATCC 29212, *Klebsiella pneumaniae* ATCC 13883 mikroorganizmlarına karşı 9 ± 1 mm inhibisyon zon çapı oluşturdu Bu araştırma, iki yenilebilir mantarın doğal antioksidanlar olarak potansiyele sahip olduğunu göstermiştir.

Anahtar Kelimeler: Antimikrobiyal aktivite, Antioksidan aktivite, *Armillaria mellea, Macrolepiota procera*, Mantar

Introduction

Free radicals are atoms or molecules that have one or more unpaired electrons. Free radicals can form homolytic and heterolytic products or redox reactions as well as reactive oxygen species and reactive nitrogens. Reactive oxygen species include oxygen-bearing free radicals (Turpaev, 2002). Due to their unbalanced nature, reactive oxygen and nitrogen species (including free radicals) may trigger many biochemical reactions in cell. There must be a balance between the production and accumulation of these reagents in cells and tissues and the inactivation of these forms in living organisms (Son 2012; Pizzino et al. 2017). This unbalanced situation causes oxidative stress that affects the structure of cells membranes, lipids, proteins, lipoproteins and DNA (Young and Woodside 2001; Droge 2002). In addition, overproduction of free radicals can cause oxidative damage to biomolecules, (lipids, proteins, DNA), eventually leading to many chronic diseases such as cancer, cardio-vascular diseases and inflammation in humans. Oxidative stress in cells can result from either an increase in the levels of reactive oxygen species, or a reduction of the natural cell antioxidant capacities (Racchi et al. 2002).

Antioxidants can be defined as molecules that can delay or prevent oxidation of the substrate when they encounter a low amount of oxidizable substrate (Becker et al. 2004). In some cases, the amount of antioxidant in cell may be insufficient for intracellular protection. In such cases, external antioxidant supplementation will contribute to the renovation of this balance again (Valko et al. 2007).

In recent decades, the presence of antimicrobial resistance in pathogenic bacteria has been one of the most worrying human health issues. It is estimated that antibiotic resistance causes 25,000 deaths per year in the European Union and 700,000 deaths worldwide. In addition, antimicrobial resistance in bacteria can cause serious economic damage, with an estimated cost of 1.5 trillion dollars worldwide in health costs and lost productivity (Arteaga et al. 2019).

Mushrooms are distinctive organisms which constitute their own kingdom. Some characteristics relate them more closely to animals than to plants. In many ways fungi are important supporters of life on earth, as decomposers of dead matter and nutrient recyclers. On the other hand, benefits from edible (wild and grown) mushrooms and truffles are widely recognized (Willis 2018). Mushrooms have been used extensively for medical properties for centuries (Muszyńska et al. 2017). Mushrooms contain many non-toxic and bioactive compounds that can be used as a source in the pharmaceutical and nutrition (Dong et al. 2006; Ji et al. 2007; Sevındık et al. 2017). They can produce a large variety of secondary metabolities, such as steroids, alkoloids, terpenoids, organic acids and phenolic compounds (Kosanic et al. 2016; Bal et al.2019). Nowadays, especially in Japan, Korea and China, various mushroom extracts are used as potential additives in chemotherapy and radiation treatments (Sullivan et al. 2006; Borchers et al. 2008). The mushroom's compounds possess anticancer and antiviral effects, immunosuppressive, and lipid-lowering effects in the blood (Bobek and Galbavy 2001; Nowacka et al. 2015; Aytar and Ozmen 2020). Therefore, antimicrobial compounds are a rich source of natural antibiotics since they can be isolated from many mushroom species (Yamaç and Bilgili 2006; Barros et al. 2007;Sevindik et al.2018). For example, glucans found in cell walls are known for their immunomodulatory properties and their secondary metabolites have been shown to be effective against bacteria and viruses (Suzuki et al. 1990).

A. mellea is used in traditional medicine. These species that grow naturally in our country are known as honey mushrooms. Traditional medicine is used as a treatment for dizziness, headache, nerve weakness, insomnia, numbness in the arms and legs, and remittance in elderly patients with stroke (Yang et al. 1989). In modern pharmacology, the effects of polysaccharides isolated from *A. mellea* against vertigo, aging and allergy have also been demonstrated in many studies (Yang et al. 2007; Lai and Ng 2013). *M. procera* is a kind of saprobic fungi. It is popularly known as the parasol mushroom (Arora et al. 2003). *M. procera* is a rich source for carbohydrates (glycerol, mannitol, glucose, trehalose, lepiotan) 15.9%, saturated acids 81.95%, unsaturated fatty acid 19.51%, monosaturated acids 62.44%, polysaturated acids 10.95%, palmitic acid 62.44%, dien 17.40%, oleic acid 62.44%, linoleic acid, chitin, proteins, fiber, vitamins, minerals.(Kumari and Atri 2004;Ouzouni and Riganakos 2007; Falandysz et al. 2008; Yılmaz et al. 2013).

The main objectives of the current study were to evaluate the phenolic, β-Carotene and lycopene profıle, antioxidant and antimicrobial properties of *A. mellea* and *M. procera* in Turkey (popular edible mushroom species).

Material and Method

Mushrooms material

A. mellea and *M. procera* samples were collected from Bozkır district of Konya in 2012. The mushroom samples used in this study was identified by Dr. Ilgaz AKATA from Ankara University.

Preparation of mushroom extracts

The dried mushroom samples were extracted by maceration in 1:4 (w/v) biomass /solvent ratio with methanol for 2 weeks at room temperature in a dark environment. The obtained methanolic extracts were filtered through filter paper. After filtration the solvent was evaporated in a rotary evaporator (Heidolph, Germany) at 50 °C under reduced pressure and the solid extracts were stored at +4°C until further use.

Determination of total phenolic content

Total phenolic of each mushroom extract was quantified according to the method of Folin-Ciocalteu (Siddhuraju and Becker, 2003) using gallic acid as standard. Briefly, 0.1 mL of extracts (1 mg/mL) were mixed with 0.2 mL of diluted Folin-Ciocalteu reagent (1:1 with water). After incubation at room temperature for 3 min,1 mL 2% sodium carbonate was added to the reaction mixture. The absorbance was read at 760 nm by spectrophotometer after 1 h of incubation at room temperature in the dark. The total phenolic concent values are expressed as gallic equivalent (GAE) in milligrams per gram of dried extract (mg GAE/g). All measurements were performed in triplicate.

Determination of β-carotene and lycopene content

β-Carotene and lycopene content of the extracts were determined according to the method described by (Nagata and Yamashita,1992) with slight modification. Briefly, dried samples (100 mg) were mixed with acetone/hexane (4:6, v/v). After incubation for 1 min. The absorbance of the supernatants was read at 453, 505, 645 and 663 nm by spectrophotometer. Contents of β-carotene and lycopene were calculated according to the following equation:

Lycopene (mg/100 ml) = −0.0458 A_{663} + 0.372 A_{505} − 0.0806 A_{453}; β-carotene (mg/100 ml) = 0.216 A_{663} − 0.304 A_{505} + 0.452 A_{453}.

1-Diphenyl-2-picrylhydrazyl (DPPH) radical scavenging activity

The free radical scavenging capacity of the extracts were analyzed according to the method described by (Braca et al. 2001) with slight modifications. Briefly,0.5 mL extracts with different concentrations were mixed with a methanolic solution of DPPH radical (0.1mM) freshly prepared. After incubation for 30 min at room temperature in the dark, absorbance was read at was added to extracts solutions at 517 nm by spectrophotometer (Shimadzu UV-1800,Japan) against a blank (extract only). Same procedure with a solution without the extract was applied as a control group. Butylated hydroxytoluene (BHT) was used as a reference standard. The percentage of DPPH radical scavenging effect was calculated according to the following equation:

DPHH scavenging activity (%inhibation)= [($A_{control}$-A_{sample})/$A_{conrtol}$]×100, where $A_{conrtol}$ is the absorbance of the control and A_{sample} is the absorbance of the reaction mixture or standard. A curve of extract concentration versus %inhibation was created to determine the concentration of the extract needed to cause a %50 decrease of the beginning DPHH concentration. This value calculated by linear regression analysis is known as a IC_{50}.

Antimicrobial activity

The antimicrobial activities of mushroom extracts were determined by agar well method and evaluated against bacterial strains on *Staphylococcus aureus* ATCC 25923, *Bacillus cereus* NRRL B-3711, *Bacillus subtilis* ATCC 6633, *Escherichia coli* ATCC 35218, *Escherichia coli* ATCC 25922, *Enterococcus faecalis* ATCC 29212, *Enterococcus hirae* ATCC 9790, *Klebsiella pneumaniae* ATCC 13883, *Pseudomonas aeruginosa* ATCC 27853, *Proteus vulgaris* RSKK 96029, *Salmonella typhimurium* ATCC 14028 and fungal strains *Candida tropicalis* Y-12968, *Candida albicans* ATCC 10231, *Candida krusei* ATCC 6258. For comparison ampicillin and chloramphenicol were used a standard antibiotics.

In the agar well method, bacterial strains were allowed to incubate at 37 ° C for 24 hours in Nutrient Agar medium and yeast strains were incubated for 48 hours at 30 ° C in Malt Extract Agar medium. The post-incubation microorganisms were adjusted to 0.5 McFarland blur. Muller – Hinton Agar (for bacterial strains) and Malt Extract Agar (for yeast strains) were spread on a petri with a 1% suspension of microorganism suspension. With the punch, 6 mm in diameter wells are opened at specific points of the medium. The opened wells were placed in a volume of 50 µL from mushroom extracts at a concentration of 150 mg/mL and left to incubate. The diameter of the inhibition zones formed after incubation is measured in mm. Chloramphenicol, ampicillin were used for antimicrobial activity.

Results

Determination of total phenolic content

The total phenolic contents of the methanolic extracts of mushrooms, evaluated by Folin-Ciocalteu method, are shown in Table 1. As a shown in table, the mushrooms *A. mellea* and *M. procera* presented phenolic contents with 20.87 ± 0.88 and 36.25±0.35 mg GAE/g extract, respectively.

Determination of β-carotene and lycopene content

The β-carotene and lycopene content of *A. mellea* and *M. procera* methanol extracts are shown in Table 1. As a shown in table, the mushrooms *A. mellea* and *M. procera* demonstrated β-carotene contents with 0.032 ± 0.04 and 0.091 ± 0.09 µg/mL, respectively. The content of lycopene was lower than the concentration of β-carotene in the mushrooms studied. The mushrooms *A. mellea* and *M. procera* content of lycopene were found 0.011 ± 0.02 and 0.059 ± 0.02 µg/mL, respectively.

Determination of DPPH radical scavenging activity

The scavenging DPPH radicals of the studied methanol extracts are indicated in Table 2. As a shown in table, the free radical scavenging activity of the mushroom extracts was evaluated by DPPH assay comparing the IC_{50} value of synthetic chemical BHT, which was 0.096 ± 0.005 mg/mL. *M. procera* methanol extract revealed the best antioxidant properties (IC_{50} 0.191 ± 0.07 mg/mL).*A.mellea* methanol extract exhibited the lowest IC_{50} 1.19 ± 0.03 mg/mL.

Antimicrobial activity

Antimicrobial activities of the mushrooms extract against the test microorganisms is shown in Table 3. *A. mellea* methanol extract formed against to *K.pneumaniae* ATCC 13883, *B.subtilis* ATCC 6633, *S. aureus* ATCC 25923,10±1 mm inhibition zone diameter. *M.procera* methanol extract formed against to *E. faecalis* ATCC 29212, *K.pneumaniae* ATCC 13883, 9±1 mm inhibition zone diameter.

The antimicrobial activity was compared with the standard antibiotics, ampicillin and chloramphenicol. The results showed that standard antibiotics had stronger activity than tested samples as shown in Table 3. In a negative control, DMSO had no inhibitory effect on the tested organisms.

Table1. Total phenolic contents of the MeOH extracts as mg GAE $g^{-1}$and β-Carotene and lycopene content.

Sample	Total phenolic content (mg GAE/g extract)	β -Carotene (µg/mL)	Lycopene (µg/mL)
A.mellea	20.87±0.88	0.032±0.04	0.011±0.02
M.procera	36.25±0.35	0.091±0.09	0.059±0.02

Values epresent the mean with the error bars representing standard deviation, n = 3.

Table 2. DPPH radical scavenging activities of the extracts. Scavenging activity is expressed as IC_{50} (µg/mL) ± SD (n=3)

Sample	IC_{50} (mg/mL)
A.mellea	1.19±0.03
M.procera	0.191±0.07
BHT	0.09647±0.005

Table 3. Antimicrobial activity results (zone diameter / mm)

Test microorganisms	*A.mellea*	*M.procera*	Amphicillin	Chloramphenicol
E. faecalis ATCC 29212	-	9 ± 0	27±0	20±0
K. pneumaniae ATCC 13883	10± 1	9 ± 0	-	31±1
B. subtilis ATCC 6633	10± 1	-	23±1	21±0
S. aureus ATCC 25923	10± 1	-	44±1	24±0

Discussions

Metabolic syndromes affect people of all age groups. Natural compounds are noteworthy because chemical compounds are perceived to be incompatible with the human body. Therefore, the search for new and natural bioactive compounds has been become of great interest (Asatiani et al. 2018). In this study, the antioxidant and antimicrobial activity of methanolic extracts of mushrooms *A. mellea* and *M. procera* have been evaluated.

The antioxidant activity of mushrooms increased with the increased in the concentration of samples, higher the antioxidant property lower the IC_{50} values. A lower IC_{50} values means better radical scavenging activity (Abdelaaty et al. 2015). The scavenging DPPH radicals of the studied methanol extracts are indicated in Table 2. *M.procera* extract had more potent free radical scavenging activity (IC_{50}: 0.191 mg/mL) than *A.mellea* extract (IC_{50}:1.19 mg/mL). In previous studies, the antioxidant activities of *A.mellea* and *M.procera* extracts have been reported. In the study of Akata et al. 2012, found that the DPPH radical scavenging effect methanolic extract of *A. mellea* IC_{50}: 4.51 mg/mL. In another study Strapac et al. 2016 reported that the DPPH radical scavenging effect methanolic extract of *A. mellea* IC_{50}: 6.44 mg/mL. Lung and Chang 2011, Popescu et al. 2016 demonstrated the DPPH radical scavenging effect methanolic extract of *A. mellea* IC_{50} 7.83, 4.03 mg/mL, respectively. In addition, Lung and Chang 2011, investigated that dried mycelia and mycelia-free broths obtained by *A. mellea* submerged cultures are extracted with methanol and hot water and investigated for antioxidant properties. Methanolic extracts from dried mycelia and mycelia-free broth and hot water extracts from dried mycelia by *A. mellea* submerged cultures show good antioxidant properties as evidenced by low IC_{50} values (<10 mg/mL). In a anathor study of Kalyonu et al. 2010, found that the DPHH radical inhibition value ethanolic extract mycelia of *A.mellea* %2.85 (extract 1mg/mL). On the other hand, similar studies of *M. procera* conducted previously. In the study of Akata and Zengin 2019, found that the DPPH radical scavenging effect methanolic extract of *M. procera* IC_{50} 14.73 ± 0.55 mg/mL. In another study Kosanic et al. 2016, raported that methanolic extract *M. procera* IC_{50}: 0.311 ± 0.3 mg/mL. It was also Fernandes et al. 2013, reported that different extraction methods in the dry, fresh, freeze and irradiated methanol extracts of *M. procera* were 2.7, 4.9, 3.7, 7.9 mg/mL, respectively. The differences observed in this studys could be due to the growing conditions and the extraction method. This current study also indicated that *A.mellea* and *M.procera* extract possesses DPPH free radical scavenging activity which has demonstrated the antioxidant potential of the studied mushrooms.

Phenolic compounds are aromatic hydroxylated compounds with one or more aromatic rings and one or more hydroxyl groups. They include phenolic acids, flavonoids, hydroxybenzoic acids, hydroxycinnamic acids, lignans, tannins, stilbenes and oxidized polyphenols. Furthermore, some of them stimulate synthesis of endogenous antioxidant molecules in the cell (Shanchez 2017). The total phenolic contents of the methanolic extracts of mushrooms, evaluated by Folin-Ciocalteu method, are shown in Table 1. The mushrooms *A. mellea* and *M. procera* presented phenolic contents with 20.87 ± 0.88 and 36.25±0.35 mg GAE/g extract, respectively. The results suggest that most of the phenolic compounds in *M. procera.* Phenolic content in extracs of *A.mellea* was reported before as having 21.68 mg GAE/g (Zavastin et al. 2015), and this value is very similar to what we obtained in this study (20.87 mg GAE/g). On the other hand, Sarıkurkcu et al. 2015 reported that total phenolic content of 2.56, 4.24 mg GAE/g for methanol and water extract of *M.procera* from Turkey. Hussein et al. 2015 found that a phenolic content of 136 mg GAE/g for *M.procera* from Tanzania. The differences observed in this studys could be due to the growing regions.

β-carotene is a light yellow or orange pigment and the precursor of vitamin A. Antioxidant β-carotene prevents oxidation of unsaturated fats and the formation of free radicals. Carotenoids have been reported to act as radical scavengers due to the extensive system of conjugated double bonds in their molecule, and β-carotene is an excellent scavenger of singlet oxygen (Heinonen et al. 1994). Lycopene, which is an important derivative of carotenoids, is the most powerful antioxidant and has more radical aggregation activity (Kelkel et al. 2011). In this study, the amount of β-carotene and lycopene were considerably different among two studied samples (Table 1). Similar results also reported by Lung and Chang 2011;Strapac et al. 2016; Vishwakarma et al. 2016.

The antimicrobial activities of mushroom extracts were determined by agar well method. Antimicrobial activities of the mushrooms extract against the test microorganisms are shown in Table 3. *A. mellea* methanol extract formed against to *K.pneumaniae* ATCC 13883, *B.subtilis* ATCC 6633, *S. aureus* ATCC 25923,10±1 mm inhibition zone diameter. *M.procera* methanol extract formed against to *E. faecalis* ATCC 29212, *K.pneumaniae* ATCC 13883, 9±1 mm inhibition zone diameter. Similar to our results, numerous researchers found antimicrobial activity for *A. mellea* and *M. procera.* (Yamac and Bilgili 2006; Barranco et al.2010; Kalyoncu et al.2010; Kosanic et al. 2016). In this study, methanol extract of tested mushrooms exhibited a same antimicrobial effect than previously reported for other studies.

As a result, *A. mellea* and *M. procera* have high antioxidant activity at low concentrations of methanol extracts. However, both mushroom have low

antimicrobial activity. Wild mushroom samples have high free radical scavenging activity, they can be used health beneficial antioxidant supplement.

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