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Original Article

BIOLOGICAL ACTIVITIES OF *AGROCYBE PRAECOX* (SPRING FIELDCAP MUSHROOM)

Ali Imran Korkmaz[1], Celal Bal[2], Emre Cem Eraslan[3], Mustafa Sevindik*[4], Hasan Akgül[3]

[1] *Health Services Vocational School, University of Gaziantep Islam Science and Technology, 27-500, Gaziantep, Türkiye.*

[2] *Oguzeli Vocational School, University of Gaziantep, 27-900, Gaziantep, Türkiye.*

[3] *Akdeniz University, Science Faculty, Biology Department, University of Akdeniz, 07-000, Antalya, Türkiye.*

[4] *Department of Biology, Faculty of Science and Literature, Osmaniye Korkut Ata University, 80-000 Osmaniye, Türkiye.*

* Correspondence, e-mail: sevindik27@gmail.com

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ABSTRACT

Mushrooms, regarded as a significant component of the ecosystem, are utilised by individuals for various purposes. The present study aimed to investigate the biological activities of *Agrocybe praecox* (Pers.) Fayod, commonly referred to as the Spring Fieldcap mushroom. The ethanol extract of the mushroom was obtained with the Soxhlet apparatus. Subsequently, the quantification of total antioxidant, total oxidant, and oxidative stress index of the mushroom extract was conducted utilizing Rel Assay kits. The total phenolic content was determined using the Folin-Ciocalteu reagent. The agar dilution method was employed to assess the antimicrobial activity of the mushroom extract. The antiproliferative activity of the compound was assessed using A549 lung cancer cells. Elemental levels of the fungus were measured using the wet digestion method. The findings of the study revealed that the levels of the elements fell within the range reported in the existing literature. In addition, it was determined that the total antioxidant value was 2.97±0.08, the total oxidant value was 7.63±0.16, the oxidative stress index was 0.26±0.01, and the total phenolic content was 49.7±3.0 mg/g. It was found to be effective against microorganisms at concentrations between 50-200 µg/mL. Furthermore, it was ascertained that this mushroom exhibited antiproliferative activity, with the degree of activity being contingent upon the concentration of the extract. Consequently, it was determined that *Agrocybe praecox* exhibits potential as an antioxidant, antimicrobial, and anticancer agent.

KEYWORDS: anticancer, antimicrobial, antioxidant, Spring Field cap mushroom, medicinal mushroom.

1. Introduction

Mushrooms spread all over the world [1]. Across various regions of the globe, diverse human societies have incorporated mushrooms into their religious ceremonies, dietary practices, medicinal endeavors, and even as toxic substances [2,3]. Mushrooms possess a diverse array of bioactive compounds, which contribute to their manifold biological activities [4]. Mushrooms occupy an important position in the diet because they contain high levels of essential nutrients, including vitamins, minerals and protein [5-7]. Numerous studies in the scientific literature have documented the diverse biological activities exhibited by mushrooms, including but not limited to anticancer, antiproliferative, antimicrobial, antioxidant, DNA protective, anti-inflammatory, hepatoprotective, and immune system regulatory properties [8-15]. The assessment of the biological activities of fungi holds significance in relation to their potential applications, owing to the diverse range of effects they exhibit [16]. The present study aimed to assess the antioxidant, antimicrobial, and antiproliferative properties of *Agrocybe praecox* (Pers.) Fayod.

A. praecox (Strophariaceae/Agaricales) is frequently observed during the spring season. The dissemination of this mushroom occurs primarily in concentrated groupings, particularly within forested regions, garden or lawn spaces, and areas containing tree remnants. The palatability of this particular mushroom variety is relatively low. However, this particular species is widely acknowledged as being suitable for consumption. Since there is no study on the gastronomic evaluation of this species, its taste and nutritional values have not been studied. The cap part can reach up to about 8 cm. Morphologically, the cap part is convex, smooth, has

colors that turn from beige to yellowish brown. Gills are whitish, brown in old specimens. Stem is between 4-7 cm. Spores are 8–10 x 5–7 µm, ellipsoid and dark brown [17].

2. Materials and methods

Specimens of *A. praecox* were collected from Trabzon (Turkey). The fruiting bodies of the samples were cut into pieces and dried in a fruit dryer (Dalle BY1159, China). Next, the mushroom biomass was pulverized using a grinder. A total mass of 30 g was measured from powder samples. The material was then extracted using 250 mL of ethanol at 50°C for 6 hours (500 rpm). Solvents present in the extracts were eliminated using a rotary evaporator (Buchi R100, Switzerland).

2.1 Total phenolic content

A stock solution of the mushroom extract at a concentration of 1 mg/mL was created using distilled water. 250 µL of stock solution was mixed with 1 mL of Folin–Ciocalteu reagent (1:9, *v*/*v*). Then, 0.75 mL of 1% Na_2CO_3 was added to this mixture. It was then incubated for 2 hours at room temperature (21°C). Then measurements were made at a wavelength of 760 nm (Shimadzu UV-1800 spectrophotometer, Japan). The quantification of the mushroom's total phenolic content was conducted by utilizing the calibration curve derived from the gallic acid standard solution, resulting in a measurement of mgGAE/g [18].

2.2 Total antioxidant and total oxidant test

Evaluation of antioxidant and oxidant potentials of mushroom extract was determined using Rel Assay (Mega Tıp/Turkey) total antioxidant status (TAS) and total oxidant status (TOS) kits. Calibrators employed in this study included Trolox for TAS kit and hydrogen peroxide for TOS kit. Total antioxidant status (TAS) was expressed as mmol Trolox equivalent/L. Total oxidant status (TOS) was expressed as µmol H_2O_2 equiv./L. [19,20]. The OSI (oxidative stress index) (Arbitrary Unit: AU) was calculated based on the ratio between TOS values and TAS values. The study involved the examination of mushroom samples in three separate replications [21]. The values were reported as the mean ± standard deviation (SD).

2.3 Antimicrobial activity test

The assessment of the antimicrobial properties of the mushroom extract was conducted using the agar dilution method. The minimum inhibitory concentration (MIC) required to inhibit the growth of the bacterial and fungal strains utilized in the study was determined. Stock solutions were prepared using the mushroom extract, with concentrations: 12.5, 25, 50, 100, 200, 400 and 800 µg/mL. These stock solutions were added to the Petri dishes prepared for microorganism growth. The bacterial strains used in this study were *Staphylococcus aureus* ATCC 29213, *Staphylococcus aureus* MRSA ATCC 43300, *Enterococcus faecalis* ATCC 29212, *Escherichia coli* ATCC 25922, *Pseudomonas aeruginosa* ATCC 27853, and *Acinetobacter baumannii* ATCC 19606. These strains were cultured in Muller Hinton Broth medium. Fungi strains (*Candida albicans* ATCC 10231, *Candida krusei* ATCC 34135 and *Candida glabrata* ATCC 90030) were cultured in RPMI 1640 Broth medium [22-25].

2.4 MTT Cell Viability Assay test

The antiproliferative activity of the mushroom extract against A549 lung cancer cell line (ATCC) was tested. For this, the MTT Cell Viability Assay test was used. Stock solutions were prepared from the mushroom extract at concentrations of 25, 50, 100 and 200 µg/mL. The cells reached 70–80% confluence. After 70-80% confluence with the cell, separation was performed using 3.0 mL of Trypsin-EDTA solution (Sigma-Aldrich, MO, USA). The solution was then incubated for 24 hours. Stock solutions were then added and incubated for further 24 hours. The supernatants were then mixed into the growth medium and replaced with 1 mg/mL MTT. It was incubated at 37°C until purple precipitate formed. It was dissolved by adding dimethyl sulfoxide (DMSO) (Sigma-Aldrich, MO, USA) to MTT. Finally, the absorbance of solutions was measured at 570 nm using Epoch spectrophotometer (BioTek Instruments, USA) [26].

2.5 Elemental analysis

The elemental contents of the fruiting bodies of the fungus were assessed by atomic absorption spectrophotometer (Agilent 240FS AA, USA). The samples were dried at 80ºC. Then, 0.5 g of mushroom sample was mineralized in a mixture of 9 mL of HNO_3 + 1 mL of H_2O_2 using a microwave solubilizer (Milestone Ethos Easy) [27].

2.6. Statistical analysis

The analyses of all assays were performed in triplicate. The data were recorded as means ± standard deviations and analyzed by using Statistical Package for Social Sciences (SPSS version 22.0). Statistically significant differences ($p<0.05$) among means of experimental results were analyzed. The value determined according to the convergence analysis is subtracted from the literature values and its absolute value is taken. Then, the standard error of the determined value is subtracted from the standard error value of the literature data and its absolute value is taken. Values are convergent if the standard error differences are greater than or equal to the differences of the values. If smaller, the values are not convergent.

3 Results and discussions

3.1 Total phenolic content

The production of numerous secondary metabolites in fungi is attributed to their defense mechanisms, which are influenced by various environmental factors [28]. The secondary metabolites in question possess medicinal significance rather than nutritional value [29]. This study aimed to assess the total phenolic content of *Agrocybe praecox*, and the results are presented in Table 1.

Table 1. Total antioxidant, total oxidant, oxidative stress index and total phenolic contents of *Agrocybe praecox*

TAS	TOS	OSI	TPC
2.97±0.08	7.63±0.16	0.26±0.01	49.7±3.0

Values are presented as mean±SD (*n=3*).
Values were rounded to two significant digits.

In the literature, the total phenolic content of *A. praecox* has been reported as 52.7±1.9 mg/g [30]. In our study, the total phenolic content of *A. praecox* was

determined as 49.7±3.0 mg/g. Based on the convergence test, there is no significant difference between the literature and here obtained value. It is thought that this difference, which emerged with the literature, is due to the region where the fungus was collected, for example, the collection time and habitat difference.

3.2 Antioxidant activity

Significant quantities of free radicals are generated through metabolic processes, occasionally attributable to external influences [31]. The antioxidant defense system is activated in response to the quantity of production, thereby mitigating the detrimental impacts of oxidant compounds [32]. Nevertheless, the antioxidant defense system may prove inadequate in effectively suppressing excessive levels of oxidant compounds [33]. In this particular scenario, oxidative stress manifests. Human beings may experience various serious diseases, including cancer, cardiological disorders, Parkinson's disease, Alzheimer's disease, and multiple sclerosis, as a consequence of oxidative stress [34-36]. The utilization of additional antioxidants has demonstrated efficacy in the prevention of these disorders. Within this particular context, it holds significant importance to ascertain the antioxidant capacity exhibited by mushrooms [37,38]. The present study aimed to assess the total antioxidant, total oxidant values, and oxidative stress index of *Agrocybe praecox*. The results obtained have been presented in Table 1. It has been reported in the literature that *A. praecox* has antioxidant potential by applying different methods [30]. The present study aimed to assess total antioxidant status of *A. praecox* through the utilization of Rel Assay kits and TAS kits, marking the first instance of such an evaluation. In previously reported studies, antioxidant and oxidant status of different wild mushrooms have been reported using TAS and TOS kits. The TAS values of *Leucoagaricus leucothites, Fomitopsis pinicola, Infundibulicybe geotropa, Leucopaxillus gentianeus, Lactifluus rugatus, Laeticutis cristata*, and *Bovista nigrescens* were previously reported as 8.291, 1.44, 1.854, 3.683, 4.140 mmol/L, respectively. The reported values for TOS were 10,797, 14.21, 30,385, 6,303, 8.178, 27,476, and 8,860 µmol/L, respectively. The OSI values have been reported as 0.130, 0.99, 1.639, 0.171, 0.254, 0.765, and 0.215, in sequential order [39-45]. In comparison to the aforementioned studies, it was observed that the TAS value of *A. praecox* was comparatively lower than that of *L. leucothites, L. gentianeus, L. rugatus, L. cristata,* and *B. nigrescens*. However, it was found to be higher than *F. pinicola* and *I. geotropa*. The TAS value serves as a metric for assessing the collective antioxidant potential of various compounds present in natural products. Elevated total antioxidant status (TAS) values are indicative of a natural product possessing significant antioxidant capacity [46]. The study revealed that the total antioxidant capacity (TAS) value of *A. praecox* was generally lower compared to the antioxidant potential of other wild mushrooms documented in existing literature. Based on the TAS values derived from our study, it was ascertained that the mushroom exhibits antioxidant potential. The TOS value serves as a quantitative measure of the collective presence of oxidant compounds within natural products [46]. The study revealed that *A. praecox* exhibited a lower TOS value compared to *L. leucothites, F. pinicola, I. geotropa, L. rugatus, L. cristata,* and *B. nigrescens*. Conversely, *A. praecox* demonstrated a higher TOS value in comparison to *L. gentianeus*. Based on the findings, it was observed that *A. praecox* exhibited a limited capacity for the production of oxidant compounds. Consequently, the fungus has demonstrated the capacity to generate a reduced quantity of deleterious compounds. The OSI value quantifies the extent to which antioxidant compounds present in natural products inhibit the activity of oxidant compounds. The consumption of natural products is not advisable due to the potential harm caused by the elevation of the OSI value [46]. In our investigation, it was observed that the OSI value of *A. praecox* exhibited a higher magnitude in comparison to *L. leucothites, L. gentianeus, L. rugatus,* and *B. nigrescens*. Conversely, the OSI value of *A. praecox* was observed to be lower than that of *F. pinicola, I. geotropa*, and *L. cristata*. In the present context, it is observed that *A. praecox* exhibits the capacity to mitigate the presence of oxidant compounds within typical ranges. Consequently, it is postulated that *A. praecox* possesses potential as a natural agent with antioxidant properties.

3.3 Antimicrobial activity

In recent years, there has been a significant surge in the prevalence of microbial diseases [47]. The emergence of drug-resistant microorganisms, primarily resulting from the inadvertent use of medications, has significantly curtailed the efficacy of pharmaceutical interventions [48]. In this particular context, researchers directed their attention towards the exploration and identification of novel antimicrobial pharmaceuticals [49]. There is a growing interest among individuals in natural antimicrobial drugs due to concerns regarding the potential adverse effects associated with synthetic drugs [50]. In the present context, conducting research on fungi assumes significant importance in the pursuit of identifying natural antimicrobial pharmaceutical agents. Our study aimed to investigate the effects of *A. praecox* on standard bacterial and fungal strains. The results obtained are presented in Table 2.

Table 2. Antimicrobial activities of *Agrocybe praecox*.

Microorganism	*S. aureus*	*S. aureus* MRSA	*E. faecalis*	*E. coli*	*P. aeruginosa*	*A. baumannii*	*C. glabrata*	*C. albicans*	*C. krusei*
Concentration of extract [µg/mL]	100	100	50	50	200	200	100	100	100

200, 100, 50 µg/mL extract concentrations
Values show the lowest concentrations that inhibit the growth of bacterial and fungal strains.

The present study aimed to determine the minimal inhibitory concentrations (MICs) of the ethanol extract derived from *A. praecox*. These MICs were assessed in relation to their ability to inhibit the growth of standard

bacterial and fungal strains. The study findings revealed that the extract demonstrated efficacy against *S. aureus*, *S. aureus* MRSA, *C. glabrata*, *C. albicans*, and *C. krusei* when they were exposed to a concentration of 100 µg/mL. Furthermore, the study demonstrated efficacy of the extract against *E. faecalis* and *E. coli* when exposed to a concentration of 50 µg/mL. The extract at a concentration of 200 µg/mL demonstrated efficacy against *P. aeruginosa* and *A. baumannii*. No previous study has been found in the literature on the antimicrobial potential of *A. praecox*. But the literature reports that various mushroom species have demonstrated efficacy against a wide range of bacterial and fungal strains [51-53]. The study revealed that *A. praecox* exhibited antimicrobial properties against the tested microorganisms when the extract concentrations ranged from 50 to 200 µg/mL. Therefore, it is hypothesized that *A. praecox* possesses the potential to serve as an antimicrobial agent in the development of pharmacological interventions.

3.4 Antiproliferative activity

In recent times, there has been a significant rise in the incidence of cancer cases [54]. Various treatment modalities have been devised based on the variations in cancer types [55]. The pharmaceutical agents employed in these therapeutic approaches are typically derived from natural sources, either directly or indirectly. Numerous natural products have gained prominence due to their beneficial properties in the context of cancer treatment [56]. The present study aimed to investigate the impact of ethanol extract derived from *A. praecox* on A549 lung cancer cells. The results obtained are depicted in Figure 1.

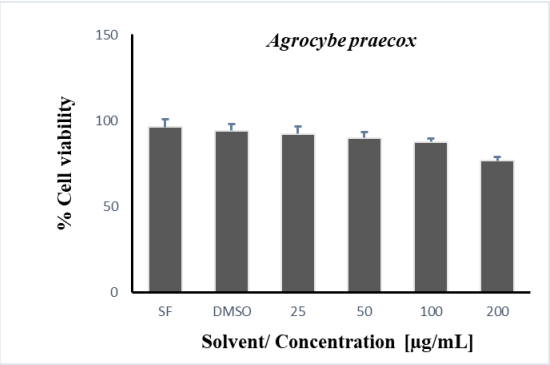

Fig 1. Antiproliferative activity of *Agrocybe praecox* (DMSO: dimethyl sulfoxide; SF: serum-free medium; 25-200: concentrations of *A. praecox* extract [µg/mL]).

The antiproliferative activity of *A. praecox* has not been reported in the literature. Antiproliferative activities of many wild fungi such as *Lignosus rhinocerus* (IC_{50}: 70.0 µg/mL) and *Inonotus obliquus* (51.61%) against A549 lung cancer cells have been reported [57,58]. In our study, the effect of ethanol extract of *A. praecox* against A549 lung cancer cells at 25, 50, 100 and 200 µg/mL concentrations was investigated. As a result of the study, it was observed that the effect of the mushroom extract increased depending on the increase in concentration. It exhibited the highest effect at the concentration of 200 µg/mL from the test concentrations. As a result, it was determined that the mushroom extract has antiproliferative activity against A549 lung cancer cells.

3.5 Element contents

Mushrooms play a crucial role as integral constituents that naturally propagate within numerous ecosystems [59]. Due to their saprotrophic nature, they contribute to the process of organic material degradation. During this particular process, a significant accumulation of various elements occurs, which is contingent upon the elemental composition of the materials being decomposed [60]. The assessment of elemental concentrations in fungi holds significant importance within the scope of their utilization [61]. The present study involved the screening of element levels in the fruiting bodies of *A. praecox*. The results obtained are presented in Table 3.

Table 3. Element contents of *Agrocybe praecox* [mg/kg]

Elements	Current research values	Literature values [62]	Literature ranges [45, 63-65]
Cr	55.17±1.98	6.0	9.63-73.01
Cu	23.81±2.34	338.00	1.90-109.95
Mn	7.10±0.68	-	5.25-103
Fe	523.93±12.25	58.8	14.6-835
Ni	0.98±0.13	1.80	0.67-5.14
Cd	3.12±0.19	0.18	0.16-8.96
Pb	8.48±0.32	36.61	0.68-16.54
Zn	48.71±1.21	68.0	29.8-158.00

Values are presented as mean±SD, n=3

In the literature, the Cr content of *A. praecox* has been reported as 6.0 mg/kg, Cu content 338.00 mg/kg, Fe content 58.8 mg/kg, Ni content 1.80 mg/kg, Cd content 0.18 mg/kg, Pb content 36.61 mg/kg and Zn content as 68.0 mg/kg [62]. Compared to this study, the Cr, Fe and Cd contents of *A. praecox* used in our study were higher, while the Cu, Ni, Pb and Zn contents were lower. The main reason for this difference is thought to be due to the differences in the habitats in which the fungi spread. In addition, element levels in various wild mushrooms in the literature are shown in Table 3. [45, 63-65]. Compared to the literature data, it was seen that the Cr, Cu, Mn, Fe, Ni, Cd, Pb and Zn contents of *A. praecox* used in our study were within the range of the literature. In this context, it is thought that the composition of this mushroom is at normal levels in terms of elements.

4 Conclusions

The present study aimed to assess the biological activities and elemental concentrations of the wild mushroom species *A. praecox*. The study findings revealed that the levels of elements in the mushroom were within the expected range based on existing literature. Moreover, the mushroom exhibited potential as an antioxidant, antimicrobial, and anticancer agent. Consequently, it has been established that *A. praecox* possesses potential as a naturally occurring substance for incorporation into pharmacological formulations.

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