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Phytochemistry and biological activity of *Onosma rascheyana* (Boiss.) extracts

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ABSTRACT

In recent years, it has been determined that *Onosma* species exhibit interesting biological/pharmacological activities. The aim of this study was to analyze the chemical composition, antioxidant and enzyme inhibitory activities of the methanol (MeOH), water and ethyl acetate extracts obtained from the aerials parts of *Onosma rascheyana* (Boiss.). The chemical compositions of the extracts were determined using spectrophotometric and chromatographic methods. Biological activities of the extracts were determined using antioxidant and enzyme inhibitory test systems. The MeOH extract was found to be rich in both phenolics and flavonoids (31.55 mg GAEs/g and 15.20 mg REs/g, respectively). The MeOH extract also contained higher amounts of 4-hydroxybenzoic and *p*-coumaric acids compared to other phytochemicals. The MeOH extract exhibited remarkable activity in all antioxidant test systems. However, 2,2′-azino-bis(3-ethylbenzothiazoline-6-sulfonate) radical cation (ABTS) scavenging assay resulted in superiority of water extract (88.90 mg TEs/g). The relative antioxidant capacity indices (RACI) of the extracts and the correlations between these values and antioxidant activities confirmed the high activity of the MeOH extract. In the α-amylase, α-glucosidase, acetylcholinesterase (AChE) and butyrylcholinesterase (BChE) inhibitory activity tests, the ethyl acetate extract showed high activity, while the tyrosinase inhibitory activity assay resulted in the superiority of the MeOH extract (59.72 mg KAEs/g). It was concluded that the extracts of *O. rascheyana* could be used as alternative agents in the food, cosmetic and medical industries due to their antioxidant and enzyme inhibitory activities.

1. Introduction

Recent studies have reported that many plants have antioxidant activity (Madsen and Bertelsen, 1995; Schwarz et al., 2001; Tanabe et al., 2002). Researchers suggest that the flavonoids and phenolic compounds of plants are determinants of antioxidant activity (Madsen and Bertelsen, 1995). Concerns by health authorities about the adverse health effects of butylated hydroxyl anisole (BHA) and butylated hydroxyl toluene (BHT), which are synthetic antioxidant substances used as preservatives in food, have prompted researchers to investigate plants rich in phytochemicals (Sasaki et al., 2002). For this reason, there has been a great increase in the number of studies on the antioxidant activities of plants in recent years.

In addition to their antioxidant activities, plants also have a promising potential for the treatment of neurodegenerative diseases. Alzheimer's disease is a neurodegenerative disorder that causes cognitive and behavioral abnormalities in people. Today, a medical protocol that can fully treat this disease has not been developed yet. However, some hypotheses have been discovered that can partially eliminate the symptoms of the disease. According to the cholinergic hypothesis, which is one of the best-known of these hypotheses, inhibition of acetylcholinesterase (AChE) and butyrylcholinesterase (BChE) can help increase neuronal activity and therefore regress disease symptoms, since it causes an increase in the amount of neurotransmitter substances in the brain. Researchers are conducting intensive research on plants to discover new and highly effective cholinesterase inhibitors (Sarikurkcu et al., 2015).

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Another disease for which plants benefit medicinally is diabetes. In both type I and type II diabetes, glucose cannot pass from the bloodstream to the cells, and the blood glucose level in these patients is above the normal level (Abesundara et al., 2004). This situation causes various tissues and organs in the body to lose their functions in the medium and long term (Funke and Melzig, 2006). One of the effective ways to keep blood glucose levels at normal levels is to reduce glucose production by inhibiting the activity of α-amylase ve α-glucosidase, which are involved in carbohydrate digestion (Kim et al., 2005). Recent studies show that plants are a potential reference source for phytochemicals that can inhibit these enzymes (Kim et al., 2005).

In addition to the biological/pharmacological activities mentioned above, plants also contain phytochemicals that have an inhibitory effect on tyrosinase, which is involved in melanin biosynthesis (El-Sayed et al., 2019). Excessive melanin production can cause the development of some diseases related to hyperpigmentation in organisms. In addition, product losses due to browning may occur during the processing of vegetables and fruits due to tyrosinase activity (Asanuma et al., 2003). Researchers have focused on discovering compounds with tyrosinase inhibitory activity for use in cosmetics, medicine, and food processing (Loizzo et al., 2012). Some studies have proven that plants contain phytochemicals with significant tyrosinase inhibitory activity (Fan et al., 2017; Gheibi et al., 2015; Kamkaen et al., 2007; Kubo et al., 2000; Saghaie et al., 2013).

The aim of this study is to determine the chemical composition of methanol (MeOH), water, and ethyl acetate extracts obtained from the aerial parts of *Onosma rascheyana* (Boiss.) and to investigate their antioxidant, anti-Alzheimer, anti-diabetic, and skin whitening activities.

2. Materials and methods

2.1. Plant material

O. rascheyana was collected from the 8th km Çaglayancerit-Kahramanmaras highway, Kahramanmaras-Turkey (1550 m, 37° 44' N 37° 14' E). The plant was identified and deposited by Dr. Riza Binzet from the Department of Biology, Mersin University, Mersin-Turkey. (Herbarium no: Binzet 86).

Aerial parts of the plant was used as the study material to obtain solvent extracts. Details of the extraction procedure can be found in the supplementary file.

2.2. Determination of the phenolic compositions of the extracts

Details of the spectrophotometric and chromatographic methods were given in the supplementary file (Cittan and Çelik, 2018; Zengin et al., 2015).

2.3. Biological activity

The antioxidant and enzyme inhibitory activities of the extracts were determined using the methods specified in the literature (Apak et al., 2006; Kocak et al., 2016; Ozer et al., 2018; Tepe et al., 2011; Zengin et al., 2015). Details of the methods used were included in the supplementary file.

2.4. Statistical analysis

Details of the statistical analysis were presented in the supplementary file.

3. Results and discussion

3.1. Chemical composition

Amounts of total phenolic and flavonoid compounds of the extracts isolated from *O. rascheyana* are given in Figure 1. The MeOH and water extracts were rich in phenolic compounds (31.55 and 31.13 mg GAEs/g, respectively), while the total phenolic content of the ethyl acetate extract was 17.50 mg GAEs/g. MeOH extract was also the richest extract in terms of flavonoid compounds (15.20 mg REs/g). However, water and ethyl acetate extracts were poor in flavonoids.

Our research group has previously conducted studies on the total phenolic and flavonoid content of many endemic *Onosma* species (Kirkan et al., 2018; Ozer et al., 2018; Saravanakumar et al., 2019; Sarikurkcu et al., 2018; Sarikurkcu et al., 2020a, b; Sarikurkcu et al., 2020c; Sarikurkcu et al., 2020d; Tlili et al., 2021). The results obtained from the present study were found to be compatible with the total phenolic and flavonoid contents of the mentioned *Onosma* species (6.55-69.06 mg TEs/g and 65.57 mg QEs/g, respectively).

Results of LC–ESI–MS/MS analysis are given in Table 1. According to the data in the table, the MeOH extract contained higher amounts of 4-hydroxybenzoic acid and *p*-coumaric acid compared to other phytochemicals. The amounts of these compounds in the MeOH extract were 4002 and 349 µg/g, respectively. Similarly, there was a high amount of 4-hydroxybenzoic acid in the water extract (5287 µg/g). The water extract additionally contained significant amounts of rosmarinic acid (4248 µg/g), ferulic acid (803 µg/g), vanillic acid (634 µg/g), and protocatechuic acid (202 µg/g). According to the results of LC–ESI–MS/MS analysis, the ethyl acetate extract was poorer than the other extracts in terms of phytochemicals in Table 1. As with the MeOH and water extracts, the compound with highest amount in the ethyl acetate extract was 4-hydroxybenzoic acid (125 µg/g).

There are no previously published data in the literature regarding the chemical composition of the *Onosma* species reported in the present study. However, as stated above, in many articles previously published by our research group, it has been determined that different *Onosma* species show a high similarity to each other in terms of their phytochemical compositions. In particular, 4-hydroxybenzoic acid and rosmarinic acid, which were found to be found in high amounts in the current study, are found in significant amounts in many *Onosma* species in the literature (Kirkan et al., 2018; Sarikurkcu et al., 2018; Sarikurkcu et al., 2020a, b; Sarikurkcu et al., 2020c; Sarikurkcu et al., 2020d; Tlili et al., 2021). For this reason, it was concluded that the data obtained from the present study are compatible with those in the literature.

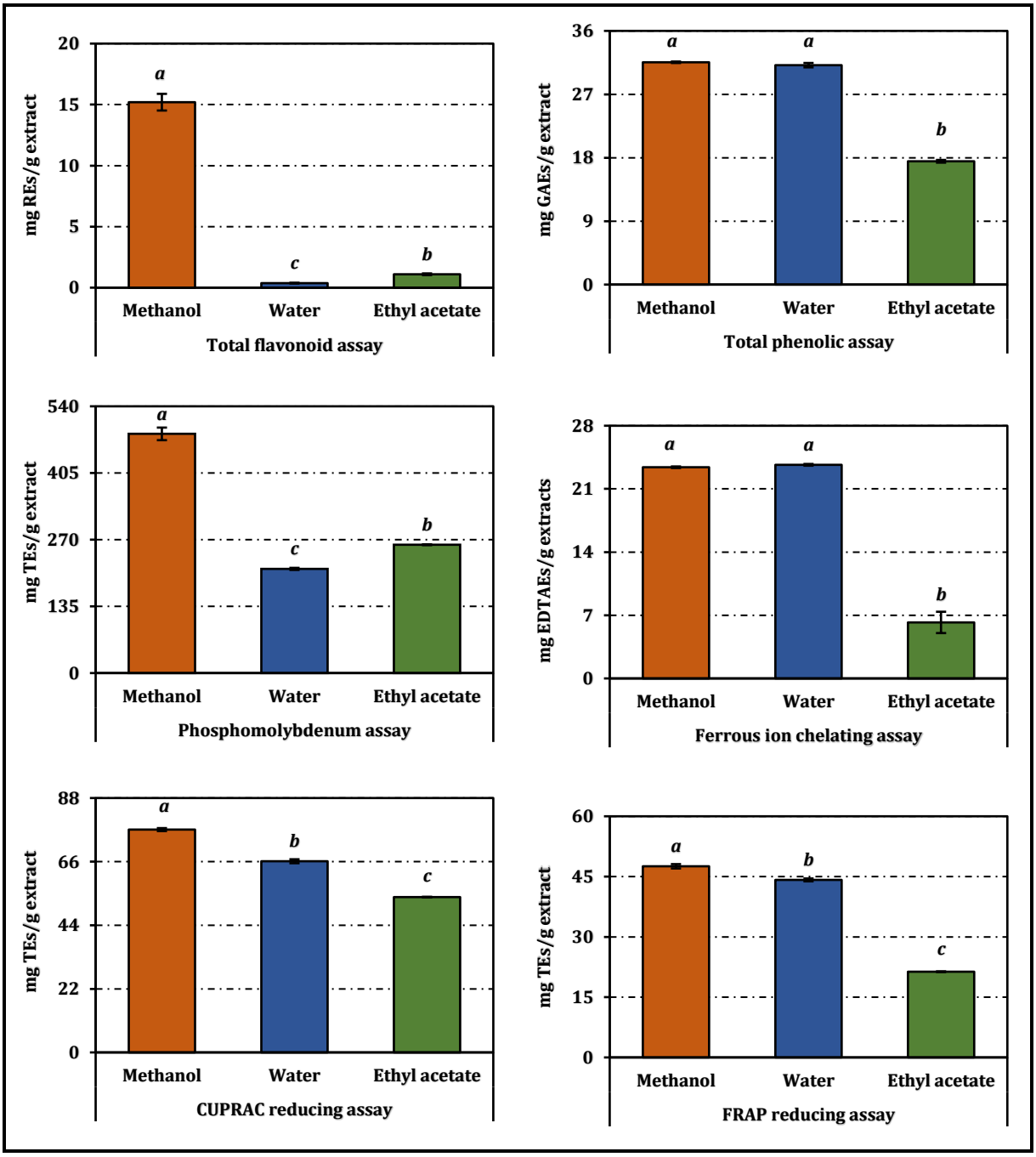
3.2. Antioxidant activity

In order to determine the antioxidant activities of the extracts, antioxidant activity tests, the details of which are given in the supplementary file, were applied (Figure 1).

MeOH extract exhibited the highest activity in the phosphomolybdenum test where total antioxidant activity was

analyzed (484.20 mg TEs/g). It was followed by ethyl acetate (259.80 mg TEs/g) and water extracts (210.90 mg TEs/g), respectively.

In the ferrous ion chelating assay, the activities of MeOH and water extracts were almost equal (23.40 and 23.67 mg EDTAEs/g, respectively). In this test system, the activity of the ethyl acetate extract was determined as 6.21 mg EDTAEs/g.



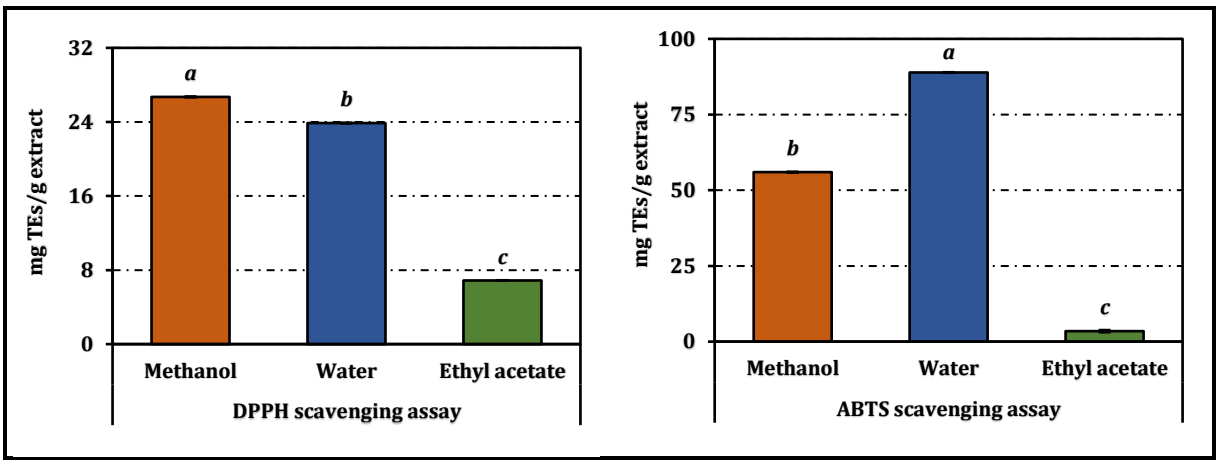


Figure 1. Antioxidant activity, total flavonoid and phenolic contents of *O. rascheyana* extracts
[REs, GAEs, TEs and EDTAEs mean rutin, gallic acid trolox and ethylenediaminetetraacetic acid (disodium salt) equivalents, respectively].
Values indicated by the same superscripts are not different from the honestly significant difference after Tukey's hoc test at 5% significance level.

Table 1. Concentration (µg/g extract) of selected phenolic compounds in *O. rascheyana* extracts[1]

Compound	MeOH	Water	Ethyl acetate
Gallic acid	6.23 ± 0.04^{b}	10.8 ± 0.5^{a}	3.94 ± 0.09^{c}
Protocatechuic acid	289 ± 1^{a}	202 ± 2^{b}	13.6 ± 0.5^{c}
3,4-Dihydroxyphenylacetic acid	16.8 ± 0.3^{b}	37.9 ± 0.1^{a}	14.2 ± 0.3^{c}
Pyrocatechol	27.9 ± 0.6^{c}	32.5 ± 0.6^{b}	158 ± 1^{a}
(+)-Catechin	18.0 ± 1.9	nd	nd
Chlorogenic acid	2.97 ± 0.10^{b}	102 ± 1^{a}	4.67 ± 0.06^{b}
2,5-Dihydroxybenzoic acid	15.2 ± 1.1^{b}	63.8 ± 2.8^{a}	10.4 ± 0.1^{b}
4-Hydroxybenzoic acid	4002 ± 7^{b}	5287 ± 69^{a}	125 ± 1^{c}
(-)-Epicatechin	2.22 ± 0.12^{a}	2.31 ± 0.19^{a}	2.20 ± 0.02^{a}
Vanillic acid	154 ± 2^{b}	634 ± 12^{a}	168 ± 5^{b}
Caffeic acid	14.1 ± 0.5^{b}	111 ± 4^{a}	17.8 ± 1.2^{b}
Syringic acid	81.7 ± 2.4^{b}	173 ± 9^{a}	4.20 ± 0.25^{c}
3-Hydroxybenzoic acid	34.5 ± 0.3^{b}	40.0 ± 1.9^{a}	12.3 ± 1.2^{c}
Vanillin	13.3 ± 0.8^{c}	155 ± 1^{a}	19.31 ± 0.49^{b}
Verbascoside	5.67 ± 0.04^{a}	6.17 ± 0.26^{a}	6.11 ± 0.04^{a}
Taxifolin	7.40 ± 0.09^{b}	10.3 ± 0.5^{a}	7.77 ± 0.31^{b}
Sinapic acid	9.41 ± 0.18^{b}	46.7 ± 1.0^{a}	5.15 ± 0.26^{c}
p-Coumaric acid	349 ± 7^{b}	2377 ± 8^{a}	27.0 ± 0.1^{c}
Ferulic acid	84.1 ± 0.1^{b}	803 ± 40^{a}	19.1 ± 0.8^{b}
Luteolin 7-glucoside	nd	38.0 ± 0.4	nd
Hesperidin	1.91 ± 0.02^{b}	2941 ± 5^{a}	6.78 ± 0.14^{b}
Rosmarinic acid	7.65 ± 0.13^{b}	4248 ± 11^{a}	15.7 ± 1.4^{b}
Hyperoside	1.40 ± 0.06^{b}	76.5 ± 1.2^{a}	1.21 ± 0.14^{b}
Apigenin 7-glucoside	nd	7.24 ± 0.07	nd
2-Hydroxycinnamic acid	4.16 ± 0.10^{a}	2.73 ± 0.10^{b}	3.86 ± 0.18^{a}
Eriodictyol	9.59 ± 0.07^{a}	10.0 ± 0.4^{a}	9.73 ± 0.07^{a}
Pinoresinol	nd	nd	164 ± 8
Quercetin	1.62 ± 0.06^{b}	6.65 ± 0.61^{a}	1.55 ± 0.05^{b}
Luteolin	nd	4.86 ± 0.10	nd
Kaempferol	nd	13.1 ± 1.4	nd
Apigenin	nd	82.0 ± 0.5^{a}	6.11 ± 0.07^{b}

[1]The values indicated by the same superscripts within the same row are not different according to the Tukey's honestly significant difference post hoc test at 5% significance level.
nd: Not detected

The reducing power potentials of the extracts were determined by CUPRAC and FRAP tests. The activities exhibited by the extracts in the CUPRAC test were higher than those in the FRAP test. In both test systems, the MeOH extract exhibited the highest activity (77.09 and 47.56 mg TEs/g, respectively). The ethyl acetate extract exhibited the lowest activity in both the CUPRAC and FRAP test (53.74 and 21.33 mg TEs/g, respectively).

DPPH and ABTS radical scavenging tests were applied to determine the scavenging activity of the extracts on free radicals. While MeOH extract showed high activity in DPPH radical scavenging assay (26.70 mg TEs/g), water extract showed the highest activity in ABTS radical scavenging test (88.90 mg TEs/g).

Relative antioxidant capacity index (RACI) data of extracts are given in Figure 2. The RACI value of the MeOH extract was calculated as 0.84, according to the data obtained as a result of the evaluation of the data obtained from all antioxidant activity tests together. It was followed by water and ethyl acetate extracts (0.23 and -1.06, respectively).

The correlation values between the RACI values of the extracts and their antioxidant activities are given in Figure 3. According to the data in the figure, the antioxidant activities of the extracts in all test systems, except the phosphomolybdenum test, were correlated with their RACI values.

According to literature data, the antioxidant activity of *O. rascheyana* has not been studied before. However, it is possible to

compare the data obtained from the current study with the antioxidant activities of other *Onosma* species previously published by our research group. Antioxidant activity data from the present study are generally consistent with antioxidant activity data from other *Onosma* species in the literature. (Kirkan et al., 2018; Ozer et al., 2018; Saravanakumar et al., 2019; Sarikurkcu et al., 2018; Sarikurkcu et al., 2020a, b; Sarikurkcu et al., 2020c; Sarikurkcu et al., 2020d; Tlili et al., 2021). There are also some data in the literature showing that 4-hydroxybenzoic acid and rosmarinic acids, which are the main components of MeOH extract with high antioxidant activity, can exhibit strong antioxidant activity (Babaei et al., 2020; Kim et al., 2014; Park et al., 2008; Ying et al., 2009).

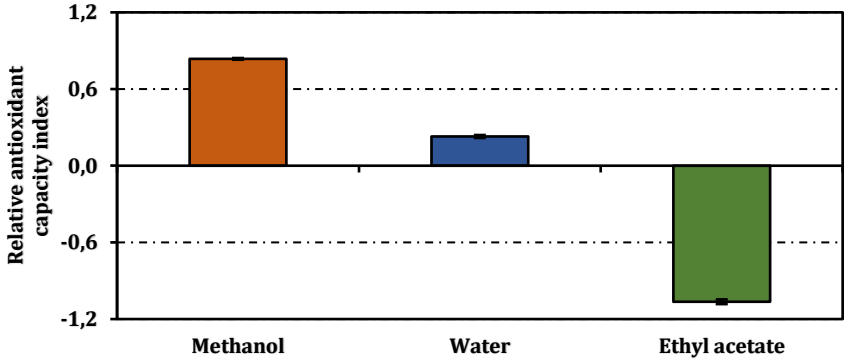


Figure 2. RACI of *O. rascheyana* extracts

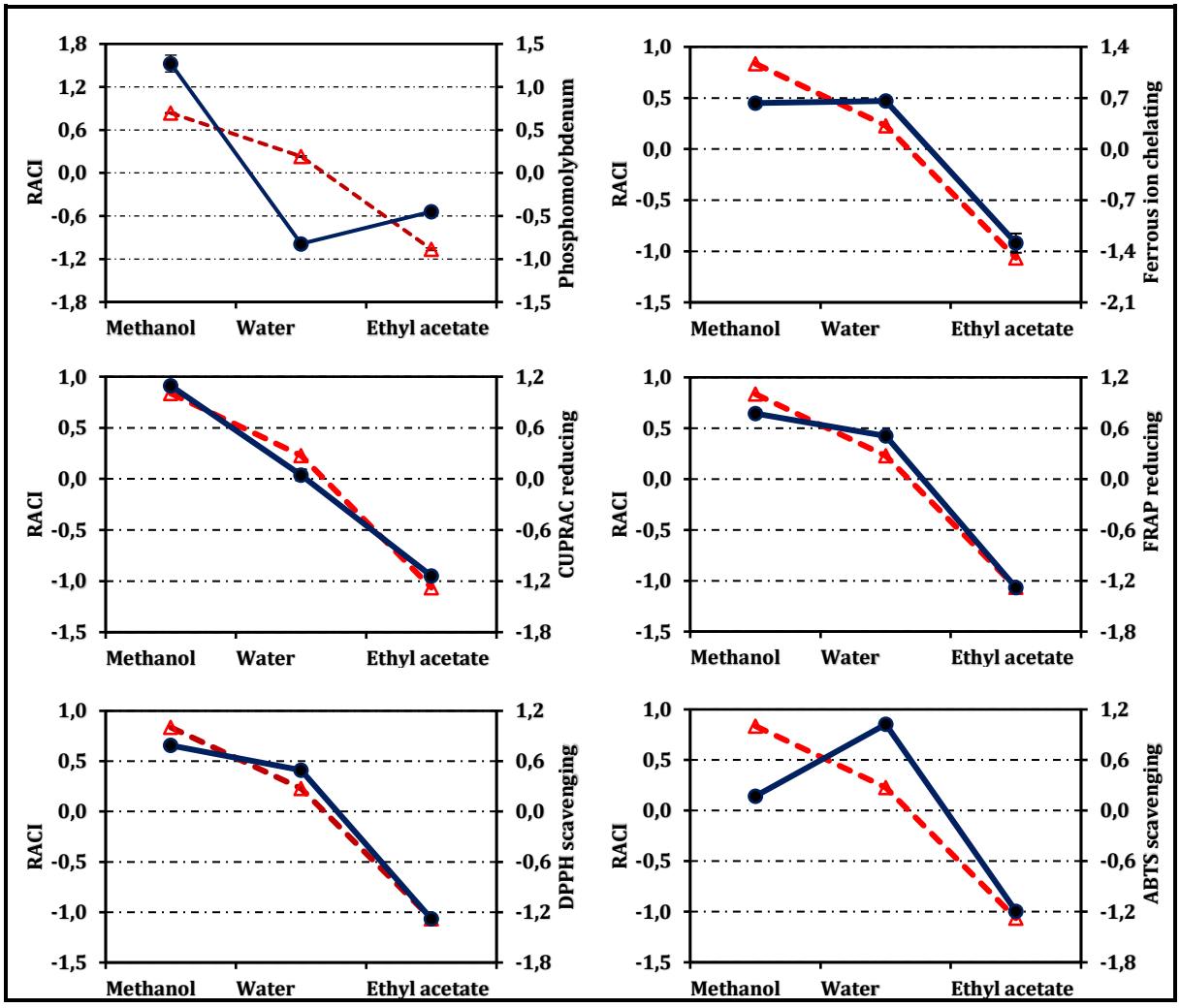


Figure 3. Correlation between RACI (dashed red line with triangle) and antioxidant activity (solid dark blue line with circle) of *O. rascheyana* extracts

3.3. Enzyme inhibitory activity

The inhibitory activities of the extracts of *O. rascheyana* on AChE, BChE, tyrosinase, α-amylase and α-glucosidase are given in Figure 4.

In the inhibitory activity tests on digestive enzymes, the ethyl acetate extract exhibited the highest activity. The inhibitory activity of this extract on α-amylase and α-glucosidase was determined as 421.93 and 1568.92 mg ACEs/g, respectively. On the other hand, the water extract exhibited the weakest activity on both enzymes (44.68 and 122.46 mg ACEs/g, respectively).

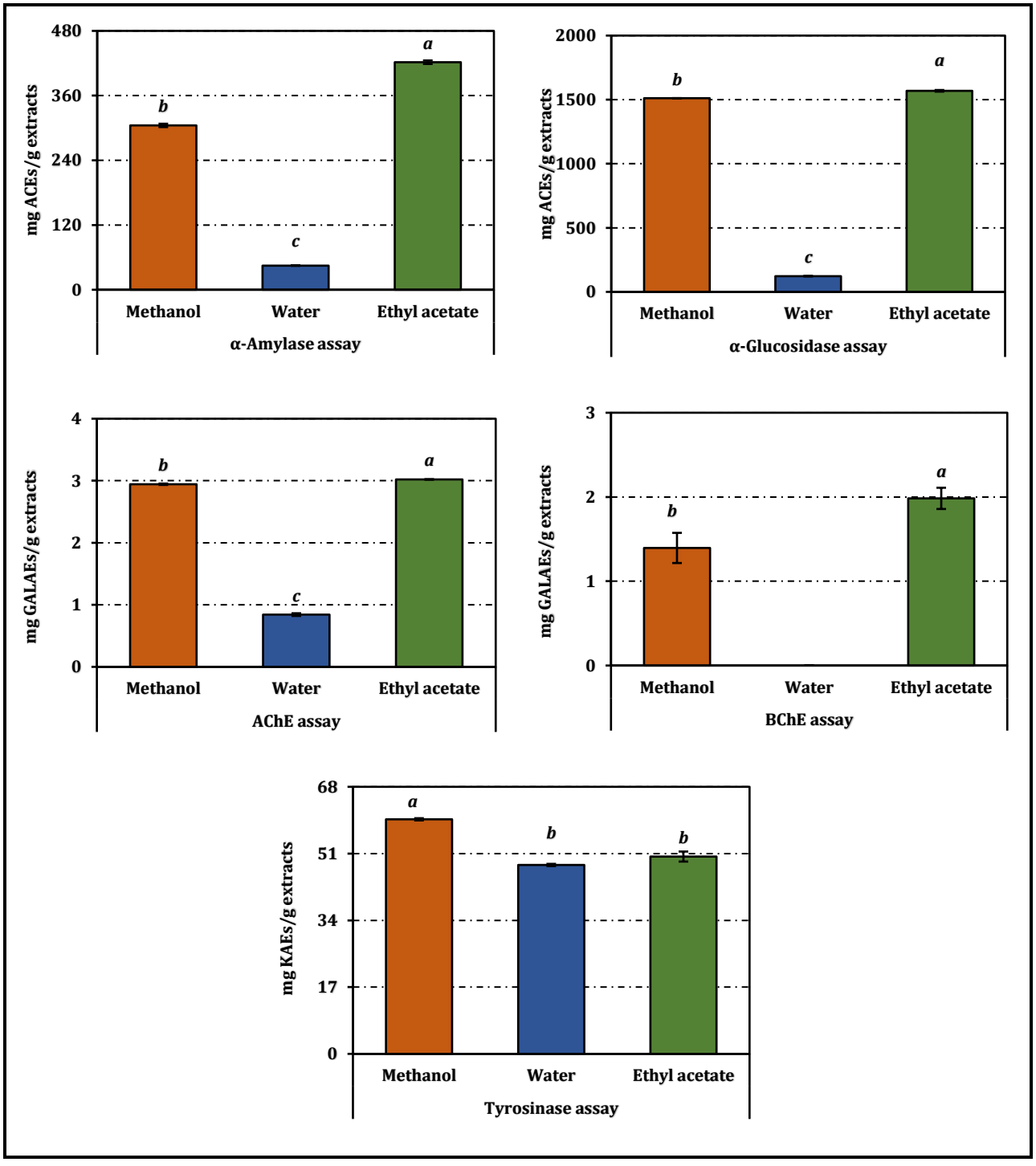


Figure 4. Enzyme inhibition activity of *O. rascheyana* extracts

ACEs, GALAEs and KAEs mean acarbose, galanthamine and kojic acid equivalents, respectively.

Values indicated by the same superscripts are not different from the honestly significant difference after Tukey's hoc test at 5% significance level.

The ethyl acetate extract also showed higher activity on cholinesterases than the others. The inhibitory activity of this extract on AChE and BChE was 3.02 and 1.98 mg GALAEs/g, respectively. Just as in the test system where digestive enzymes were inhibited, the MeOH extract ranked second after the ethyl acetate extract. The water extract, on the other hand, provided an

inhibition of 0.84 mg GALAEs/g on AChE, but was ineffective on BChE.

A different activity profile was detected in the tyrosinase inhibitory activity test than those obtained from the test systems detailed above. In this test system, the inhibitory activity of the MeOH extract was higher than the other extracts (59.72 KAEs/g). It was followed by ethyl acetate and water extracts, whose inhibitory activity values were quite close to each other (50.24 and 48.10 mg KAEs/g, respectively).

No data on the inhibitory activities of *O. rascheyana* on the enzymes discussed in the current study could be found in the literature. The literature data on the enzyme inhibitory activities of *Onosma* species generally consists of the articles published as a result of the researches of our study group (Kirkan et al., 2018; Ozer et al., 2018; Saravanakumar et al., 2019; Sarikurkcu et al., 2018; Sarikurkcu et al., 2020a, b; Sarikurkcu et al., 2020c; Sarikurkcu et al., 2020d; Tlili et al., 2021). Data from the present study indicate that *O. rascheyana* has similar enzyme inhibitory activity potential as other *Onosma* species.

3.4. Correlations among phenolics and assays

Since the determination of the compounds responsible for the activity via bioassay-guided fractionation could not be performed in the current study, correlation analysis was applied to determine to what extent the main components of the extracts contribute to the activities (Table 2).

Table 2. Correlations among phenolic compounds and assays

	TAP	DPPH	ABTS	CUPRAC	FRAP	FICA	AChEIA	BChEIA	TIA	AAIA	AGIA
RACI	0.998	0.999	0.999	0.999	0.999	0.998					
Total phenolic	0.999	0.999	0.999	0.999	0.999	0.998	-0.989	-0.938	0.993	-0.999	-0.996
Total flavonoid	0.994	0.999	0.999	0.999	0.999	0.996	-0.995	-0.949	0.987	-0.999	-0.992
Protocatechuic acid	0.998	0.999	0.999	0.999	0.999	0.998	-0.989	-0.937	0.990	-0.999	-0.994
Pyrocatechol	-0.998	-0.999	-0.999	-0.999	-0.999	-0.998	0.990	0.941	-0.992	0.999	0.995
Chlorogenic acid	-0.998	-0.999	-0.999	-0.999	-0.999	-0.999	0.990	0.943	-0.995	0.998	0.997
4-Hydroxybenzoic acid	0.998	0.999	0.999	0.999	0.999	0.998	-0.990	-0.938	0.991	-0.999	-0.994
Vanillic acid	-0.932	-0.900	-0.900	-0.940	-0.940	-0.960	0.959	0.980	-0.971	0.935	0.969
Caffeic acid	-0.935	-0.950	-0.950	-0.950	-0.950	-0.963	0.965	0.985	-0.972	0.941	0.971
p-Coumaric acid	0.997	0.999	0.999	0.999	0.999	0.997	-0.992	-0.943	0.990	-0.999	-0.994
Ferulic acid	0.998	0.999	0.999	0.999	0.999	0.998	-0.989	-0.939	0.992	-0.999	-0.995
Hesperidin	-0.998	-0.999	-0.999	-0.999	-0.999	-0.995	0.988	0.932	-0.986	0.999	0.990
Rosmarinic acid	-0.984	-0.986	-0.985	-0.987	-0.986	-0.972	0.972	0.895	-0.954	0.990	0.962

Data show the Pearson Correlation Coefficients between the parameters. TAP: total antioxidant activity by phosphomolybdenum method. AAIA. AChEIA. BChEIA. AGIA. and TIA: α-amylase. acetyl cholinesterase. butyryl cholinesterase. α-glucosidase. and tyrosinase inhibition activities. respectively. ABTS and DPPH: ABTS and DPPH radical scavenging activities. respectively. CUPRAC and FRAP: CUPRAC and FRAP reducing power potential; respectively. RACI: relative antioxidant capacity index. FICA: Ferrous ion chelating activity

According to the data in the table, it was determined that there was a high correlation between the phenolic and flavonoid compound contents of the extracts and their antioxidant activities. In addition, protocatechuic, ferulic, *p*-coumaric and 4-hydroxybenzoic acids also appear to contribute significantly to antioxidant activity. According to the correlation coefficients in the table, it is thought that some phenolic compounds (pyrocatechol, chlorogenic acid, vanillic acid, caffeic acid, hesperidin and rosmarinic acid) contribute significantly to the enzyme inhibitory activities of the extracts.

4. Conclusions

In this study, the chemical compositions, antioxidant and enzyme inhibitory activities of MeOH, water and ethyl acetate extracts obtained from the aerial parts of *O. rascheyana* were analyzed. It was concluded that MeOH and water extracts exhibited considerably higher antioxidant activity than ethyl acetate extract. It is thought that this situation may be caused by the highly polar phenolic compounds or flavonoids in the extracts in question. Correlation analyzes confirm this idea. On the other hand, as in many previous studies carried out by our research group, it was concluded that the enzyme inhibitory activity of ethyl acetate extract was higher than that of other extracts. It is anticipated that the remarkable enzyme inhibitory activity of the extract may be due to low polarity compounds. However, in all test systems presented here, it is thought that fractionation studies accompanied by quantitative chromatographic techniques should be performed to determine the phytochemicals responsible for the extracts activities.

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Conflict of interest

The authors confirm that there are no known conflicts of interest.

CRediT authorship contribution statement

Cengiz Sarikurkcu: Conceptualization, Investigation, Data curation, Writing - original draft, Supervision
Ersin Demir: Resources, Conceptualization, Visualization, Formal analysis, Investigation, Methodology
Mehmet Sabih Ozer: Resources, Formal analysis, Investigation, Writing - original draft
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Supplementary File

The supplementary file accompanying this article is available at https://dergipark.org.tr/en/download/journal-file/25005.

References

Abesundara, K.J., Matsui, T., Matsumoto, K., 2004. α-Glucosidase inhibitory activity of some Sri Lanka plant extracts, one of which, *Cassia auriculata*, exerts a strong antihyperglycemic effect in rats comparable to the therapeutic drug acarbose. *Journal of Agricultural and Food Chemistry*, 52, 2541-2545.

Apak, R., Güçlü, K., Özyürek, M., Esin Karademir, S., Erçağ, E., 2006. The cupric ion reducing antioxidant capacity and polyphenolic content of some herbal teas. *International Journal of Food Sciences and Nutrition*, 57, 292-304.

Asanuma, M., Miyazaki, I., Ogawa, N., 2003. Dopamine-or L-DOPA-induced neurotoxicity: the role of dopamine quinone formation and tyrosinase in a model of Parkinson's disease. *Neurotoxicity Research*, 5, 165-176.

Babaei, M., Zamfir, G.M.B., Chen, X., Christensen, H.B., Kristensen, M., Nielsen, J., Borodina, I., 2020. Metabolic Engineering of *Saccharomyces cerevisiae* for Rosmarinic Acid Production. *ACS Synthetic Biology*, 9, 1978-1988.

Cittan, M., Çelik, A., 2018. Development and validation of an analytical methodology based on Liquid Chromatography–Electrospray Tandem Mass Spectrometry for the simultaneous determination of phenolic compounds in olive leaf extract. *Journal of Chromatographic Science*, 56, 336-343.

El-Sayed, S.T., Al-Azzouny, R.A., Ali, O.S., 2019. Purification and functional characterization of a novel tyrosinase (diphenolase) inhibitory peptides prepared from *Solunum tuberosum* peels protein via enzymatic hydrolysis. *Biocatalysis and Agricultural Biotechnology*, 17, 331-338.

Fan, M., Zhang, G., Hu, X., Xu, X., Gong, D., 2017. Quercetin as a tyrosinase inhibitor: Inhibitory activity, conformational change and mechanism. *Food Research International*, 100, 226-233.

Funke, I., Melzig, M.F., 2006. Traditionally used plants in diabetes therapy: phytotherapeutics as inhibitors of alpha-amylase activity. *Revista Brasileira de Farmacognosia*, 16, 1-5.

Gheibi, N., Taherkhani, N., Ahmadi, A., Haghbeen, K., Ilghari, D., 2015. Characterization of inhibitory effects of the potential therapeutic inhibitors, benzoic acid and pyridine derivatives, on the monophenolase and diphenolase activities of tyrosinase. *Iranian Journal of Basic Medical Sciences*, 18, 122-129.

Kamkaen, N., Mulsri, N., Treesak, C., 2007. Screening of some tropical vegetables for anti-tyrosinase activity. *Thai Pharmaceutical and Health Science Journal*, 2, 15-19.

Kim, D.K., Jeon, H., Cha, D.S., 2014. 4-Hydroxybenzoic acid-mediated lifespan extension in Caenorhabditis elegans. *Journal of Functional Foods*, 7, 630-640.

Kim, Y.M., Jeong, Y.K., Wang, M.H., Lee, W.Y., Rhee, H.I., 2005. Inhibitory effect of pine extract on α-glucosidase activity and postprandial hyperglycemia. *Nutrition*, 21, 756-761.

Kirkan, B., Sarikurkcu, C., Ozer, M.S., Cengiz, M., Atilgan, N., Ceylan, O., Tepe, B., 2018. Phenolic profile, antioxidant and enzyme inhibitory potential of *Onosma tauricum* var. *tauricum*. *Industrial Crops and Products*, 125, 549-555.

Kocak, M.S., Sarikurkcu, C., Cengiz, M., Kocak, S., Uren, M.C., Tepe, B., 2016. *Salvia cadmica*: Phenolic composition and biological activity. *Industrial Crops and Products*, 85, 204-212.

Kubo, I., Kinst-Hori, I., Chaudhuri, S.K., Kubo, Y., Sánchez, Y., Ogura, T., 2000. Flavonols from *Heterotheca inuloides*: tyrosinase inhibitory activity and structural criteria. *Bioorganic & Medicinal Chemistry*, 8, 1749-1755.

Loizzo, M., Tundis, R., Menichini, F., 2012. Natural and synthetic tyrosinase inhibitors as antibrowning agents: an update. Comprehensive *Reviews in Food Science and Food Safety*, 11, 378-398.

Madsen, H.L., Bertelsen, G., 1995. Spices as antioxidants. *Trends in Food Science & Technology*, 6, 271-277.

Ozer, M.S., Kirkan, B., Sarikurkcu, C., Cengiz, M., Ceylan, O., Atilgan, N., Tepe, B., 2018. *Onosma heterophyllum*: Phenolic composition, enzyme inhibitory and antioxidant activities. *Industrial Crops and Products*, 111, 179-184.

Park, S.U., Uddin, M.R., Xu, H., Kim, Y.K., Lee, S.Y., 2008. Biotechnological applications for rosmarinic acid production in plant. *African Journal of Biotechnology*, 7, 4959-4965.

Saghaie, L., Pourfarzam, M., Fassihi, A., Sartippour, B., 2013. Synthesis and tyrosinase inhibitory properties of some novel derivatives of kojic acid. *Research in Pharmaceutical Sciences*, 8, 233-242.

Saravanakumar, K., Sarikurkcu, C., Sarikurkcu, R.T., Wang, M.H., 2019. A comparative study on the phenolic composition, antioxidant and enzyme inhibition activities of two endemic *Onosma* species. *Industrial Crops and Products*, 142, 111878.

Sarikurkcu, C., Kirkan, B., Ozer, M.S., Ceylan, O., Atilgan, N., Cengiz, M., Tepe, B., 2018. Chemical characterization and biological activity of *Onosma gigantea* extracts. *Industrial Crops and Products*, 115, 323-329.

Sarikurkcu, C., Kocak, M.S., Tepe, B., Uren, M.C., 2015. An alternative antioxidative and enzyme inhibitory agent from Turkey: *Robinia pseudoacacia* L. *Industrial Crops and Products*, 78, 110-115.

Sarikurkcu, C., Sahinler, S.S., Ceylan, O., Tepe, B., 2020a. *Onosma ambigens*: Phytochemical composition, antioxidant and enzyme inhibitory activity. *Industrial Crops and Products*, 154, 112651.

Sarikurkcu, C., Sahinler, S.S., Ceylan, O., Tepe, B., 2020b. *Onosma pulchra*: Phytochemical composition, antioxidant, skin-whitening and anti-diabetic activity. *Industrial Crops and Products*, 154, 112632.

Sarikurkcu, C., Sahinler, S.S., Husunet, M.T., Istifli, E.S., Tepe, B., 2020c. Two endemic *Onosma* species (*O. sieheana* and *O. stenoloba*): A comparative study including docking data on biological activity and phenolic composition. *Industrial Crops and Products*, 154, 112656.

Sarikurkcu, C., Sahinler, S.S., Tepe, B., 2020d. *Onosma aucheriana*, *O. frutescens*, and *O. sericea*: Phytochemical profiling and biological activity. *Industrial Crops and Products*, 154, 112633.

Sasaki, Y.F., Kawaguchi, S., Kamaya, A., Ohshita, M., Kabasawa, K., Iwama, K., Taniguchi, K., Tsuda, S., 2002. The comet assay with 8 mouse organs: results with 39 currently used food additives. *Mutation Research/Genetic Toxicology and Environmental Mutagenesis*, 519, 103-119.

Schwarz, K., Bertelsen, G., Nissen, L.R., Gardner, P.T., Heinonen, M.I., Hopia, A., Huynh-Ba, T., Lambelet, P., McPhail, D., Skibsted, L.H., 2001. Investigation of plant extracts for the protection of processed foods against lipid oxidation. Comparison of antioxidant assays based on radical scavenging, lipid oxidation and analysis of the principal antioxidant compounds. *European Food Research and Technology*, 212, 319-328.

Tanabe, H., Yoshida, M., Tomita, N., 2002. Comparison of the antioxidant activities of 22 commonly used culinary herbs and spices on the lipid oxidation of pork meat. *Animal Science Journal*, 73, 389-393.

Tepe, B., Sarikurkcu, C., Berk, S., Alim, A., Akpulat, H.A., 2011. Chemical composition, radical scavenging and antimicrobial activity of the essential oils of *Thymus boveii* and *Thymus hyemalis*. *Records of Natural Products*, 5, 208-220.

Tlili, N., Sarikurkcu, R.T., Ceylan, O., Sarikurkcu, C., 2021. *Onosma polyantha* vs. *Onosma mollis*: Analysis of Phenolic Compounds Using Liquid Chromatography–Electrospray Ionization Tandem Mass Spectrometry (LC-ESI-MS/MS) and Assessment of the Antioxidant Activity. *Analytical Letters*, 54, 1389-1400.

Ying, W., Calas-Blanchard, C., Cortina-Puig, M., Liu, B.H., Marty, J.L., 2009. An Electrochemical Method for Sensitive Determination of Antioxidant Capacity. *Electroanalysis*, 21, 1395-1400.

Zengin, G., Sarikurkcu, C., Gunes, E., Uysal, A., Ceylan, R., Uysal, S., Gungor, H., Aktumsek, A., 2015. Two *Ganoderma* species: Profiling of phenolic compounds by HPLC-DAD, antioxidant, antimicrobial and inhibitory activities on key enzymes linked to diabetes mellitus, Alzheimer's disease and skin disorders. *Food and Function*, 6, 2794-2802.

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