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Nutraceutical extracts from some endemic *Onosma* (*O. circinnata*, *O. bornmuelleri*, and *O. angustissima*) species: LC–ESI-MS/MS–based polyphenol profile, antioxidant and enzyme inhibition activities

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Abstract

This study aimed to determine the chemical composition of methanol extracts from *Onosma circinnata*, *Onosma bornmuelleri*, and *Onosma angustissima* and to investigate their antioxidant and enzyme inhibitory activities. Spectrophotometric analysis showed that the extracts were found to be rich in chlorogenic acid, luteolin 7-glucoside, rosmarinic acid, and apigenin 7-glucoside. While *O. bornmuelleri* showed the highest activity in DPPH, ABTS, and FRAP tests, *O. circinnata* was more effective in CUPRAC, phosphomolybdenum, and ferrous ion chelating tests. While *O. angustissima* showed significant inhibitory activities on AChE, BChE, and tyrosinase, *O. bornmuelleri* and *O. circinnata* showed the highest inhibitory activities on α-amylase and α-glucosidase. It was concluded that *O. circinnata* and *O. bornmuelleri* are effective antioxidant agents and *O. angustissima* can be considered as an alternative agent in the medical and cosmetic industries due to its ChE and tyrosinase inhibitory activities.

Novelty impact statement: Biological activities of *Onosma* species were brought to the literature for the first time with this study. *O. circinnata* showed remarkable antioxidant activity. *O. angustissima* exhibited the highest AChE, BChE and tyrosinase inhibitory activity.

1 | INTRODUCTION

Scientists agree that oxidative stress plays a major role in the pathology of many diseases. Natural antioxidants (especially polyphenols) from foods help to alleviate the negative effects of oxidizing agents on metabolism (Aruoma, 1998). In addition to vegetables and fruits, several hundred milligrams of vitamin E, vitamin C, β-carotene can be taken daily with consumption of wine, green tea, beer, chocolate, etc. (Pulido et al., 2003; Scalbert & Williamson, 2000). Researchers claim that consuming foods rich in polyphenols for a

Abbreviations: AAIA, α-Amylase inhibitory activity; ABTS, ABTS radical scavenging activity; ACEs, acarbose equivalent; AChEIA, acetyl cholinesterase inhibitory activity; AGIA, α-glucosidase inhibitory activity; BChEIA, butyryl cholinesterase inhibitory activity; BHA, butylated hydroxy anisole; BHT, butylated hydroxy toluene; CUPRAC, CUPRAC reducing power potential; DPPH, DPPH radical scavenging activity; EC50 (mg/ml), effective concentration at which the absorbance was 0.5 for phosphomolybdenum, CUPRAC and FRAP reducing assays; EDTA, Ethylenediaminetetraacetic acid (disodium salt); EDTAEs, ethylenediaminetetraacetic acid (disodium salt) equivalent; FRAP, FRAP reducing power potential; FICA, ferrous ion chelating activity; GAEs, gallic acid equivalent; GALAEs, galantamine equivalent; IC_{50} (mg/ml), the concentration at which 50% of the enzyme exhibits radical scavenging activity and inhibits the ferrous ion-ferrozine complex; KAEs, kojic acid equivalent; QEs, quercetin equivalent; RACI, relative antioxidant capacity index; TEs, trolox equivalent; TIA, tyrosinase inhibitory activity.

long time provides protection against the development of many diseases (Aruoma, 1998; Del Rio et al., 2013; Grosso et al., 2017; Rienks et al., 2017).

Some cholinesterase (ChEs) inhibitors, such as donepezil, galantamine, and rivastigmine, are used in the treatment of neurodegenerative diseases such as Alzheimer's (Mendiola-Precoma et al., 2016). However, in the treatment of Alzheimer's disease, inhibition of ChEs alone is not sufficient, oxidative stress should also be prevented (Aliev et al., 2008; Bonda et al., 2010). The synthetic ChE inhibitors mentioned above can effectively inhibit ChEs, but they are insufficient to exhibit antioxidant activity. Thus, the discovery of phytochemicals with strong antioxidant activity as well as acetylcholinesterase (AChE) and butyrylcholinesterase (BChE) inhibitory activity is needed (Olasehinde et al., 2020).

In the skin, which protects the human body against many external factors, the production of reactive oxygen species (ROS) that contribute to aging increases when exposed to excessive UV radiation (Rittié & Fisher, 2015). UV rays cause excessive activity of tyrosinase and therefore melanocytes in the basal layer of the skin to synthesize more melanin than necessary. Normal function of melanin is to protect DNA in skin cells from harmful effects of UV (Brenner & Hearing, 2008). However, excessive melanin synthesis and accumulation (hyperpigmentation) can lead to the formation of ageing spots on the skin, inflammation and skin cancer. The discovery of new and effective compounds with tyrosinase inhibitory activity is needed to suppress melanogenesis (Pillaiyar et al., 2017).

Diabetes is a chronic metabolic disease that develops due to hyperglycemia and its prevalence is increasing worldwide (King et al., 1998). The chronic course of the disease can sometimes lead to inadequate medical treatment methods (Kameswararao et al., 2003). One of the important strategies used in the treatment of the disease is to reduce postprandial hyperglycemia. The most important way to prevent hyperglycemia is to inhibit carbohydrate-hydrolyzing enzymes, such as α-amylase and α-glucosidase, thereby reducing the absorption of carbohydrate digestion products (Balan et al., 2017). Phytochemicals have the promising potential to reduce postprandial hyperglycemia by inhibiting these enzymes as well as their biological activities mentioned above (Chokki et al., 2020).

Onosma, the largest genus of the Boraginaceae, is represented by over 100 species in Turkey. The number of *Onosma* species spreading in the world is over 150. However, it is known that this number has exceeded 200 in studies conducted in recent years. Approximately, 50% of *Onosma* species in Turkey are endemic to this country. The vast majority of *Onosma* species are spread in Asia and Europe (Binzet, 2016; El-Shazly et al., 2003). The members of *Onosma* are used in food and medical industries due to the chemicals they contain. These species are also used as coloring agent in many foodstuffs, especially powdered pepper, due to their distinctive red color (Chakraborti et al., 2001). These species have also been used as anthelmintic and laxative agents by the people for many years. It has been determined that the flowers and leaves of the plants have cardiotonic properties (Mašković et al., 2015).

Highlights

- The chemistry and biological activities of three *Onosma* species were studied.
- Flavonoid glucosides and rosmarinic and chlorogenics acids were major compounds.
- *Onosma circinnata* showed remarkable antioxidant activity.
- *Onosma angustissima* exhibited the highest AChE, BChE, and tyrosinase inhibitory activities.
- A significant correlation was determined between chemical composition and activity.

The aim of this study was to determine the chemical composition and biological activities (antioxidant and enzyme inhibitory activities) of methanol (MeOH) extracts obtained from three different *Onosma* species (*O. circinnata*, *O. bornmuelleri*, and *O. angustissima*) collected from Turkey.

2 | MATERIAL AND METHOD

2.1 | Plant material and extract preparation

Onosma circinnata was collected from Demirozu-Bayburt highway, Demirozu, Bayburt-Turkey (1,679 m., 40° 12′ 09″N 40° 00′ 42″E) (Herbarium number: OC.5049). Additionally, *O. bornmuelleri* and *O. angustissima* were collected from Aras valley, Sogukpinar village, Uludag-Bursa-Turkey (1,403 m., 40° 03′ 53″N 29° 10′ 09″E) (Herbarium number: OC.5050) and Gulek castle, Tarsus-Mersin-Turkey (1,520 m., 37° 16′ 04″N 34° 47′ 01″E) (Herbarium number: OC.5051), respectively. Dr. Olcay Ceylan (Mugla Sitki Kocman University) performed the identification of the plant material. Aerial parts of the plants were used as the study material to obtain methanol (MeOH) extracts [extract yields: 9.53%, 4.96%, and 6.88% (w/w), respectively]. Details of the extraction procedure can be found in Supplementary information.

2.2 | Determination of the phenolic compositions of the extracts

Details of the spectrophotometric and chromatographic analyses are given in Supplementary information (Cittan & Çelik, 2018; Zengin et al., 2017).

2.3 | Biological activity

Details of the antioxidant (Apak et al., 2006; Kocak et al., 2016; Sarikurkcu et al., 2020; Tepe et al., 2011; Zengin et al., 2017) and

enzyme inhibitory activities (Ozer et al., 2018) tests are given in supplementary file.

2.4 | Statistical analysis

Details of the relative antioxidant capacity index (RACI) (Sun & Tanumihardjo, 2007) and statistical analysis can be found in the supplementary file.

3 | RESULTS AND DISCUSSION

3.1 | Chemical composition

Before proceeding with the biological activity tests of *O. circinnata*, *O. bornmuelleri*, and *O. angustissima*, the chemical compositions of the MeOH extracts obtained from these samples were determined. Total flavonoid and phenolic contents of the extracts are given in Figure 1. According to the data in the figure, *O. bornmuelleri* was far ahead of other *Onosma* species in terms of its flavonoid content (52.87 mg QEs/g). It was followed by *O. circinnata* and *O. angustissima*. On the other hand, *O. circinnata* and *O. bornmuelleri* were almost similar in terms of their total phenolic contents. The phenolic contents of these extracts were 25.91 and 25.52 mg GAEs/g, respectively.

In addition to the results of spectrophotometric analysis given above, the quantities of some selected phytochemicals in the extracts were determined chromatographically (Table 1). According to chromatographic analysis, the extracts were found to contain high amounts of chlorogenic acid, luteolin 7-glucoside and apigenin 7-glucoside. Additionally, the extracts were found to contain significant amounts of 4-hydroxybenzoic acid, vanillic acid, ferulic acid, pinoresinol, and luteolin. Considering the ratio of the main components in the extracts, it was understood that the data obtained by the spectrophotometric method were highly correlated with those obtained from the chromatographic method.

There are no reports in the literature regarding the chemical composition of the *Onosma* species. However, the chemical composition analyses performed by our research group on other *Onosma* species showed that the phytochemicals determined as major compounds in the current study (chlorogenic acid, luteolin 7-glucoside, apigenin 7-glucoside, 4-hydroxybenzoic acid, vanillic acid, ferulic acid, pinoresinol, and luteolin) were also common in other *Onosma* species (Kirkan et al., 2018; Ozer et al., 2018; Saravanakumar et al., 2019; Sarikurkcu, Sahinler, & Tepe, 2020).

3.2 | Antioxidant activity

Data on antioxidant activities of *Onosma* species are given in Table 2. The RACI values of the extracts and the coefficients showing the correlation between these values and antioxidant activity results are presented in Figures 2 and 3, respectively. Antioxidant activities of the extracts, calculated as positive control equivalent, are given in Figure 4.

According to the data presented in Figure 2, when all antioxidant activity tests were evaluated together, the sample with the highest antioxidant activity was *O. circinnata* (RACI: 0.67). In addition, the RACI value of *O. bornmuelleri* was determined to be 0.45. However, the RACI value of *O. angustissima* was negative (−1.12). On the other hand, it was determined that the correlation between RACI values of the extracts and antioxidant activities was quite high (Figure 3).

Onosma bornmuelleri was more effective than other *Onosma* species in radical scavenging assays. DPPH and ABTS radical scavenging activities of this extract were 2.46 and 2.05 mg/ml, respectively. *O. bornmuelleri* also showed the highest activity in FRAP test (0.78 mg/ml). However, the sample with the highest activity in the CUPRAC

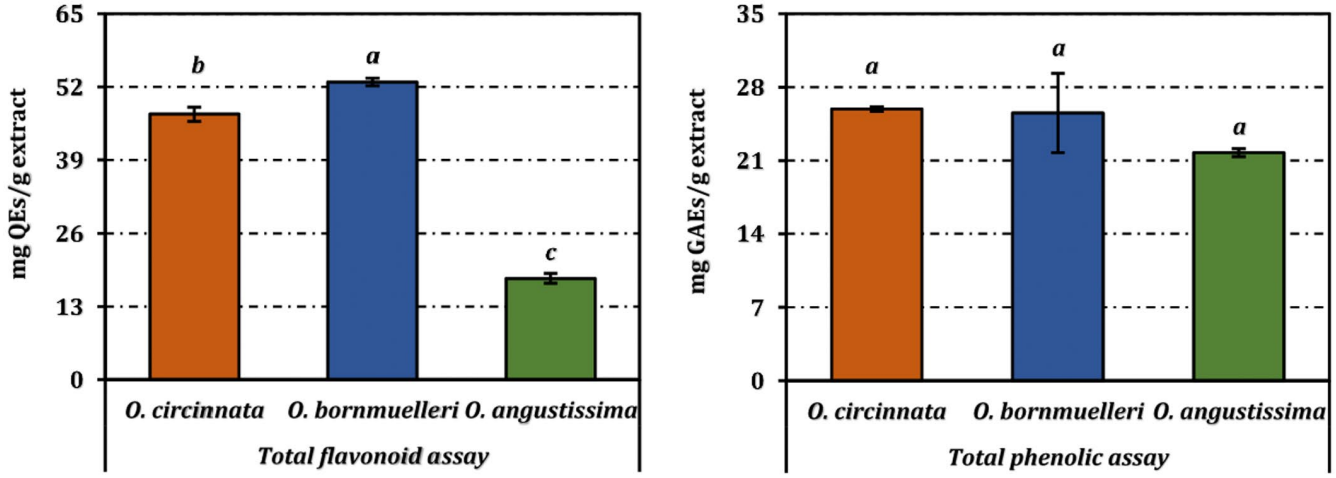

FIGURE 1 Amounts of total flavonoids and phenolics in the methanolic extracts of *Onosma* species. GAEs and QEs, gallic acid and quercetin equivalents, respectively. Different letters (a, b, c) on the bars show that the relevant data are statistically different from each other ($p < .05$)

TABLE 1 Concentrations of selected phenolic compounds in the methanolic extracts of *Onosma* species (μg/g extract)

Compound	*O. circinnata*	*O. bornmuelleri*	*O. angustissimum*
Gallic acid	4.6 ± 0.1^{b}	9.6 ± 0.1^{a}	4.2 ± 0.1^{c}
Protocatechuic acid	86.8 ± 2.9^{c}	195.6 ± 0.2^{a}	98.5 ± 2.3^{b}
3,4-Dihydroxyphenylacetic acid	nd	nd	6.43 ± 0.37
(+)-Catechin	nd	nd	nd
Pyrocatechol	nd	nd	nd
Chlorogenic acid	$38{,}142.2 \pm 499.7^{b}$	$47{,}560.2 \pm 132.8^{a}$	$3{,}494.6 \pm 146.3^{c}$
2,5-Dihydroxybenzoic acid	287.8 ± 1.7^{b}	333.1 ± 12.7^{a}	137.2 ± 8.6^{c}
4-Hydroxybenzoic acid	845.5 ± 10.6^{c}	$1{,}062.2 \pm 20.8^{a}$	979.1 ± 2.4^{b}
(-)-Epicatechin	nd	nd	nd
Caffeic acid	177.0 ± 1.5	175.9 ± 2.6^{b}	403.7 ± 0.4^{a}
Vanillic acid	790.8 ± 42.1^{a}	964.7 ± 105.7^{a}	407.1 ± 1.8^{b}
Syringic acid	37.0 ± 0.1^{b}	79.1 ± 3.4^{a}	36.3 ± 1.9^{b}
3-Hydroxybenzoic acid	5.2 ± 0.1^{c}	14.0 ± 0.2^{a}	10.8 ± 0.6^{b}
Vanillin	49.4 ± 0.5^{b}	73.4 ± 0.4^{a}	51.1 ± 2.1^{b}
Verbascoside	nd	nd	nd
Taxifolin	nd	nd	nd
Sinapic acid	122.3 ± 2.2^{a}	39.5 ± 0.6^{c}	67.8 ± 4.1^{b}
p-Coumaric acid	188.0 ± 1.1^{b}	474.8 ± 0.3^{a}	161.8 ± 7.1^{c}
Ferulic acid	637.8 ± 16.4^{b}	475.8 ± 67.0^{c}	959.4 ± 6.8^{a}
Luteolin 7-glucoside	$14{,}721.0 \pm 173.5^{b}$	$53{,}754.2 \pm 102.2^{a}$	$10{,}451.4 \pm 128.2^{c}$
Hesperidin	$2{,}128.1 \pm 0.9^{a}$	81.1 ± 21.4^{b}	67.8 ± 3.2^{b}
Hyperoside	$7{,}747.4 \pm 88.4^{a}$	641.3 ± 6.6^{b}	170.5 ± 3.4^{c}
Rosmarinic acid	$4{,}584.3 \pm 24.0^{b}$	$4{,}587.0 \pm 109.0^{b}$	$17{,}359.2 \pm 9.7^{a}$
Apigenin 7-glucoside	$15{,}735.7 \pm 194.0^{b}$	$28{,}843.8 \pm 1.9^{a}$	$16{,}171.1 \pm 209.9^{b}$
2-Hydroxycinnamic acid	nd	nd	nd
Pinoresinol	$1{,}356.7 \pm 24.3^{b}$	$1{,}472.6 \pm 20.4^{a}$	421.5 ± 27.0^{c}
Eriodictyol	nd	1.4 ± 0.1	1.8 ± 0.1
Quercetin	10.9 ± 0.1^{b}	10.2 ± 0.1^{b}	13.7 ± 0.8^{a}
Luteolin	748.7 ± 4.0^{c}	$3{,}171.0 \pm 191.3^{a}$	$1{,}785.5 \pm 12.9^{b}$
Kaempferol	24.4 ± 0.9^{b}	17.9 ± 2.8^{b}	43.5 ± 0.6^{a}
Apigenin	486.6 ± 11.6^{b}	571.3 ± 26.7^{a}	630.6 ± 6.5^{a}

Abbreviation: nd, not detected.

TABLE 2 Antioxidant activities (IC_{50}: mg/ml) of the methanolic extracts of *Onosma* species

Samples	DPPH scavenging	ABTS scavenging	CUPRAC reducing	FRAP reducing	Phosphomolybdenum	Ferrous ion chelating
O. circinnata	2.99 ± 0.02^{d}	2.12 ± 0.10^{b}	1.21 ± 0.02^{b}	0.87 ± 0.02^{d}	1.84 ± 0.06^{c}	1.51 ± 0.02^{b}
O. bornmuelleri	2.46 ± 0.06^{c}	2.05 ± 0.11^{b}	1.29 ± 0.06^{b}	0.78 ± 0.02^{c}	2.27 ± 0.12^{d}	2.00 ± 0.01^{c}
O. angustissima	4.72 ± 0.04^{e}	3.47 ± 0.08^{c}	1.96 ± 0.08^{c}	1.25 ± 0.02^{e}	2.40 ± 0.07^{d}	2.28 ± 0.01^{d}
Trolox	0.26 ± 0.02^{a}	0.31 ± 0.02^{a}	0.28 ± 0.02^{a}	0.11 ± 0.01^{a}	1.05 ± 0.08^{b}	nd
BHA	0.21 ± 0.01^{a}	0.20 ± 0.02^{a}	0.14 ± 0.01^{a}	0.09 ± 0.01^{a}	0.31 ± 0.02^{a}	nd
BHT	0.99 ± 0.02^{b}	0.29 ± 0.02^{a}	0.17 ± 0.01^{a}	0.19 ± 0.02^{b}	0.39 ± 0.01^{a}	nd
EDTA	nd	nd	nd	nd	nd	0.050 ± 0.002^{a}

Abbreviation: nd, not determined.

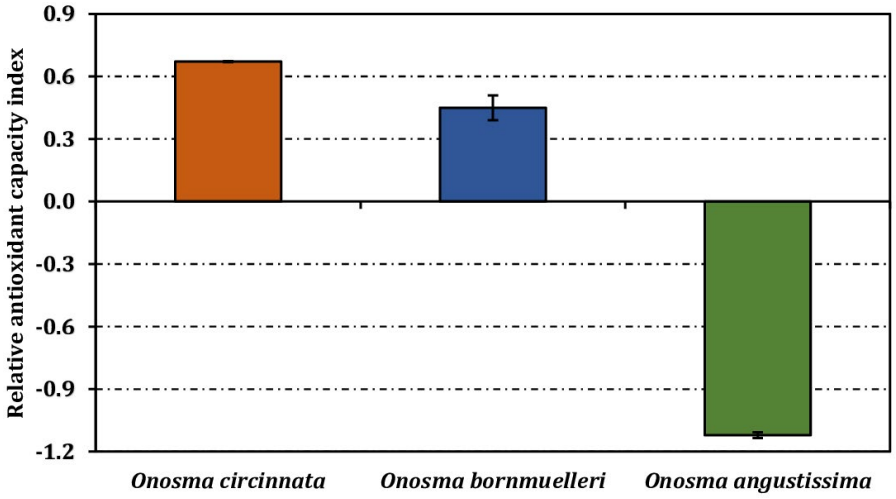

FIGURE 2 RACI of the methanolic extracts of *Onosma* species

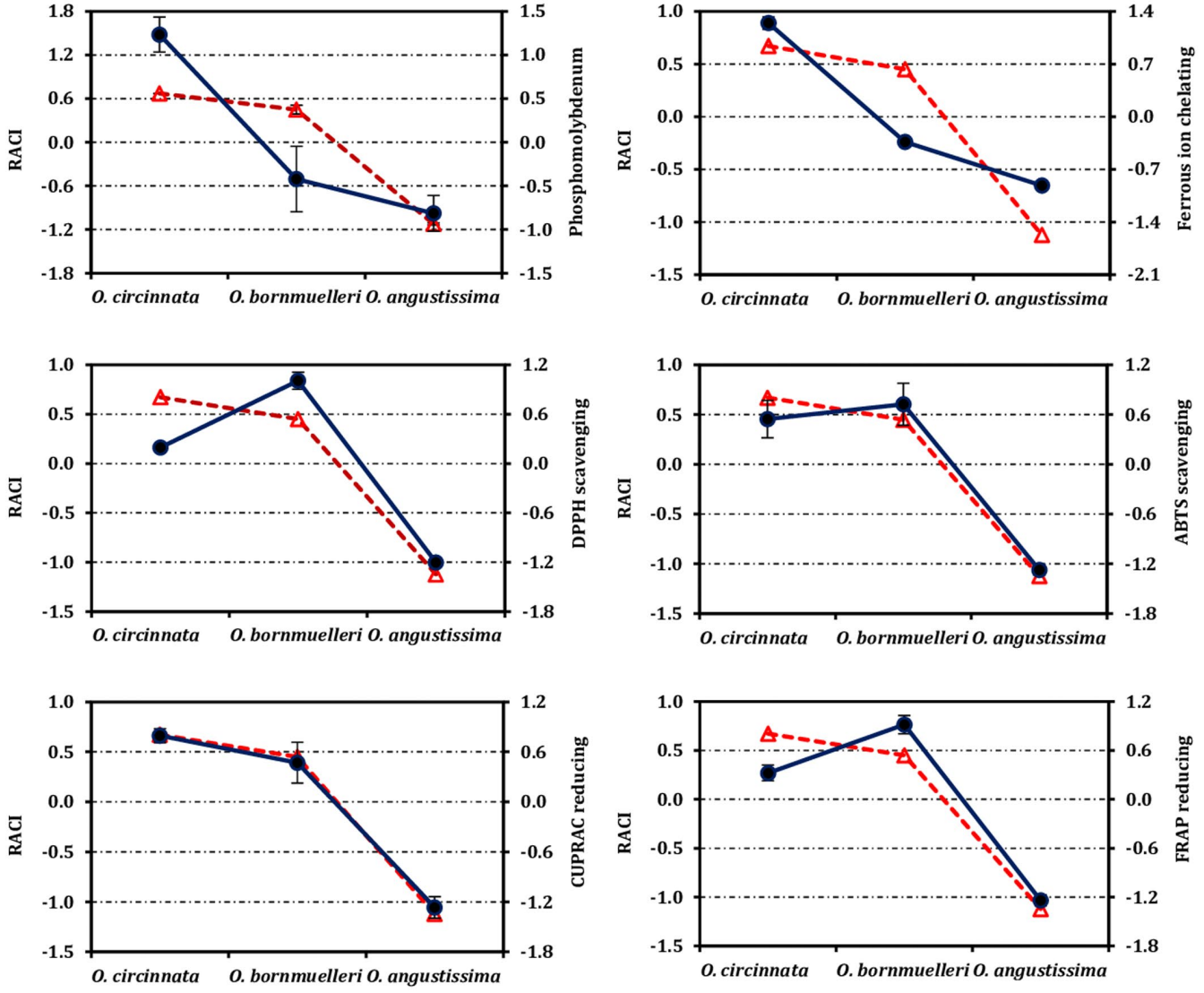

FIGURE 3 Antioxidant activity (solid dark blue line with circle) and RACI (dashed red line with triangle) of methanolic extracts of *Onosma* species

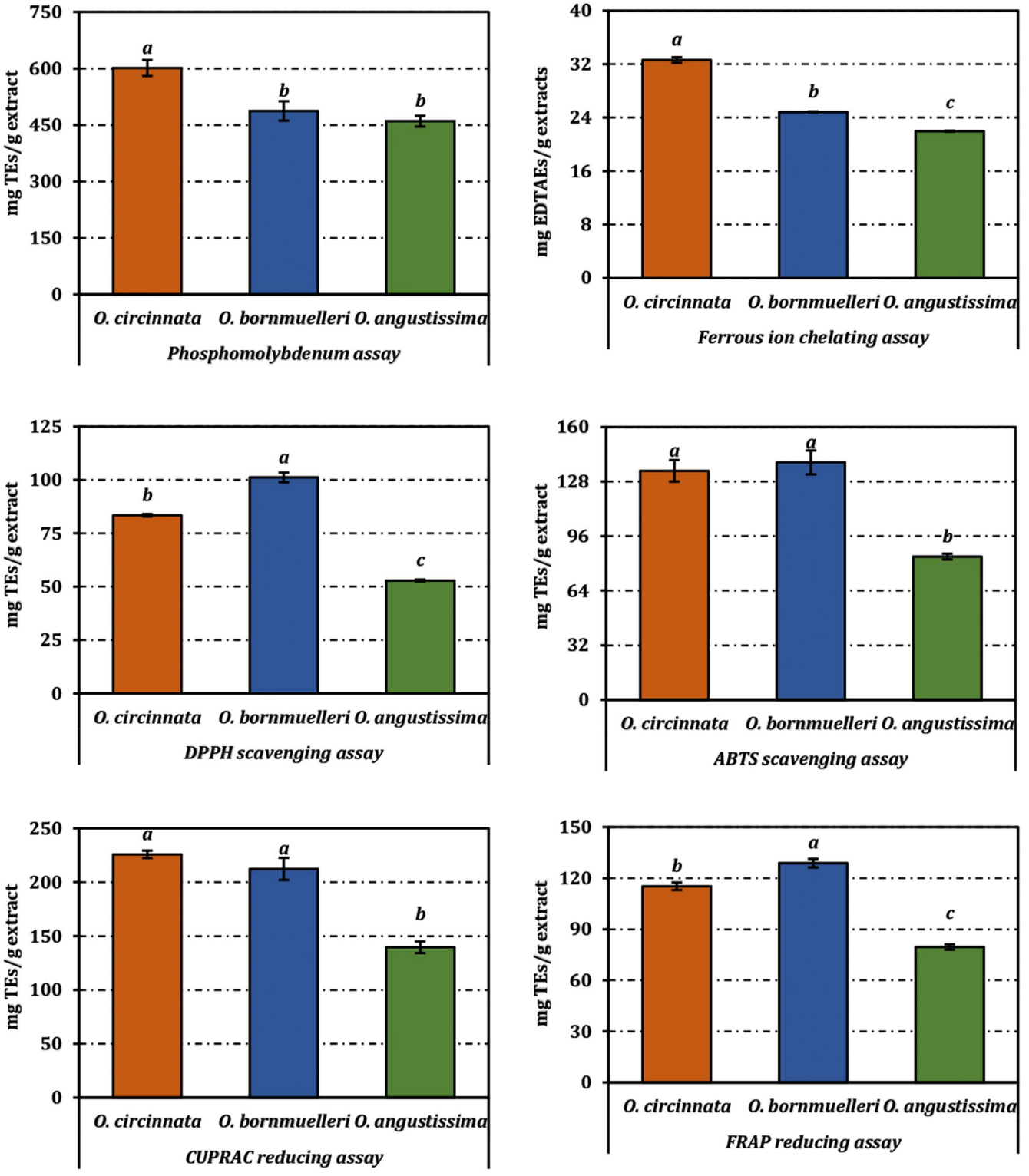

FIGURE 4 Antioxidative capacity of methanolic extracts of *Onosma* species

assay was *O. circinnata* (1.21 mg/ml). In addition to its performance in the CUPRAC assay, *O. circinnata* showed the best activity in phosphomolybdenum and ferrous ion chelating assays. The activity values of this extract in these tests were 1.84 and 1.51 mg/ml, respectively. *O. angustissima* exhibited the lowest activity compared to other *Onosma* species in all antioxidant activity tests. These data were found to be consistent with the chemical composition data presented in Table 1 and Figure 1.

There are no reports in the literature regarding the antioxidant activities of *Onosma* species analyzed in this study. However, there are some studies conducted by our research group on the antioxidant activity potential of other *Onosma* species (Kirkan et al., 2018;

Ozer et al., 2018; Saravanakumar et al., 2019; Sarikurkcu et al., 2018; Sarikurkcu, Sahinler, Ceylan, & Tepe, 2020; Sarikurkcu, Sahinler, Ceylan, & Tepe, 2020; Sarikurkcu, Sahinler, Husunet, et al., 2020; Sarikurkcu, Sahinler, & Tepe, 2020). Data from these studies show that members of the *Onosma* genus have significant antioxidant activity potential. Therefore, the data obtained from the present study showed a high correlation with the antioxidant activity data of other *Onosma* species. In addition, when the chemical compositions of *Onosma* species in the literature and the data obtained in the present study were compared, it was found that similar phytochemicals were found in high amounts (luteolin 7-glucoside, apigenin 7-glucoside, chlorogenic acid, 4-hydroxybenzoic acid, vanillic acid, ferulic acid, and luteolin). This explains the reason for the correlation between the antioxidant activities of *Onosma* species in the literature and those obtained from this study.

3.3 | Enzyme inhibitory activity

The enzyme inhibitory activities of the extracts are given in Table 3. In addition, the data obtained in positive control equivalent are presented in Figure 5.

The MeOH extract obtained from *O. angustissima* exhibited higher AChE and BChE inhibitory activities than other *Onosma* species. The AChE and BChE inhibitory activities of this extract were 1.11 and 2.74 mg/ml, respectively. The extracts exhibited higher AChE inhibitory activity than BChE. *O. angustissima* was also showed the highest activity in the tyrosinase inhibitory activity test (2.13 mg/ml). However, in the tests evaluating the inhibitory activities of the extracts on digestive enzymes, a different activity profile was detected from those obtained for ChE and tyrosinase inhibitory activity assays. While *O. bornmuelleri* showed the highest activity in α-amylase inhibitory activity test (2.75 mg/ml), *O. circinnata* showed the superior acitivity in α-glucosidase inhibitory activity test (2.69 mg/ml).

The data in Table 1 and Figure 1 showed that *O. circinnata* and *O. bornmuelleri* had richer amounts of phenolics/flavonoids than *O. angustissima*. However, these species exhibited weaker inhibitory activity on ChEs and tyrosinase than *O. angustissima*. Although *O. angustissima* appears to be poorer in terms of phytochemical composition data compared to other *Onosma* species, it was thought that the main reason underlying the high inhibitory activity of this extract on the enzymes in question may be the compounds in Table 1 in low amounts. Additionally, it should be kept in mind that some other components not included in Table 1 may have contributed to the activity. It was thought that *O. angustissima* extract should be subjected to bioactivity-guided fractionation in order to make a healthier evaluation on this issue.

On the other hand, it is possible to discuss the studies in the literature based on the main compounds of *O. bornmuelleri* and *O. circinnata*, which showed significant inhibitory activity on α-amylase and α-glucosidase. As stated before, according to the data in Table 1, chlorogenic acid and luteolin 7-glucoside were found in high amounts in both *Onosma* species. In addition to these compounds, a high amount of apigenin 7-glucoside was also found in *O. circinnata*.

In a study investigating the inhibitory activities of the aqueous MeOH extract obtained from the flowers, aerial parts and roots of *Tanacetum macrophyllum* on digestive enzymes, it was determined that chlorogenic acid was one of the major metabolites together with some other phytochemicals (Gevrenova et al., 2020). The α-amylase and α-glucosidase inhibitory activity of the extract were reported to be 0.65 and 1.45 mmol ACAE/g, respectively. Therefore, it was claimed that the aforementioned major compounds may be responsible for this activity and can be used to alleviate carbohydrate metabolism problems.

In some previous studies by our research group, some plant species rich in flavonoid glycosides, apigenin 7-glucoside and luteolin 7-glucoside, have been reported to exhibit significant inhibitory activity on α-amylase and α-glucosidase (Sarikurkcu et al., 2020; Sarikurkcu, Sahinler, Ceylan, & Tepe, 2020). These data are also supported by studies reported by other researchers. In a study by Witkowska-Banaszczak et al. (2020), it was reported that *Succisa pratensis* extract, which is rich in flavonoid glycosides, exhibited activity comparable to the activity of apigenin 7-glucoside and luteolin 7-glucoside on pancreatic α-amylase. In addition, the extracts obtained from *Sphallerocarpus gracilis* stems and leaves were found to be rich in luteolin 7-glucoside and determined to exhibit significant inhibitory activity on α-glucosidase (Ma et al., 2015). Therefore, it was concluded that the data obtained from the present study were compatible with the literature data.

TABLE 3 Enzyme inhibitory activities (IC_{50}: mg/ml) of the methanolic extracts of *Onosma* species

Assays	AChE inhibition	BChE inhibition	Tyrosinase inhibition	α-Amylase inhibition	α- Glucosidase inhibition
O. circinnata	1.27 ± 0.02^{c}	9.33 ± 0.56^{c}	2.32 ± 0.07^{c}	3.33 ± 0.08^{c}	2.69 ± 0.04^{a}
O. bornmuelleri	1.65 ± 0.02^{d}	na	2.29 ± 0.04^{bc}	2.75 ± 0.15^{b}	2.75 ± 0.08^{a}
O. angustissima	1.11 ± 0.01^{b}	2.74 ± 0.15^{b}	2.13 ± 0.01^{b}	3.48 ± 0.08^{c}	7.39 ± 0.75^{b}
Galantamine	0.0033 ± 0.0003^{a}	0.0053 ± 0.0004^{a}	nd	nd	nd
Kojic acid	nd	nd	0.33 ± 0.03^{a}	nd	nd
Acarbose	nd	nd	nd	0.96 ± 0.05^{a}	1.77 ± 0.04^{a}

Abbreviations: na, not active; nd, not determined.

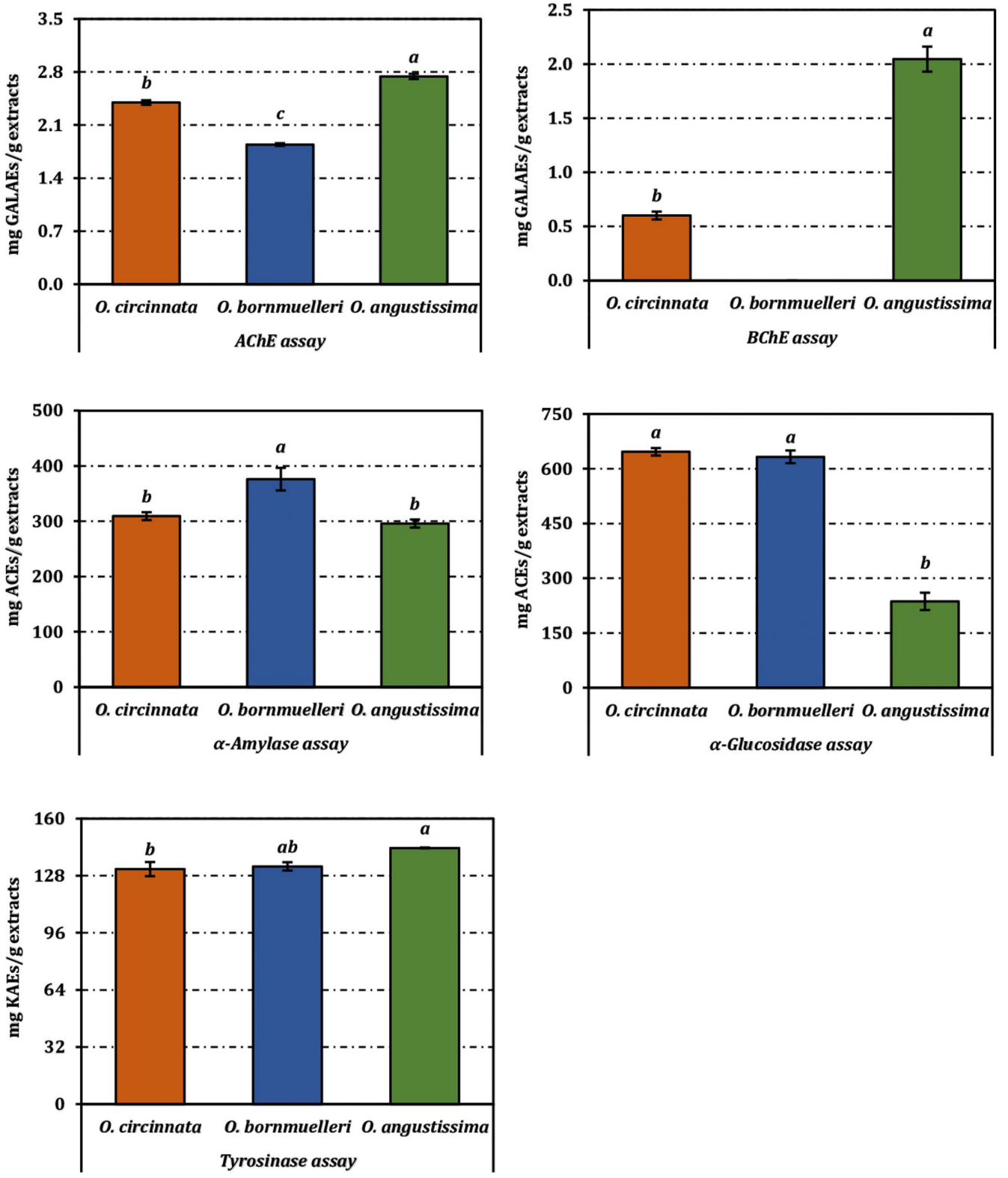

FIGURE 5 The capacity of methanolic extracts of *Onosma* species to inhibit some enzymes

3.4 | Correlation coefficients between the parameters

Correlation coefficients between parameters are given in Table 4. According to the data in the table, it was understood that phenolics/flavonoids contributed significantly to antioxidant and α-glucosidase inhibitory activities. It was determined that compounds showing high correlation with antioxidant activity were chlorogenic acid, luteolin 7-glucoside, hesperidin, hyperoside and pinoresinol. 4-Hydroxybenzoic and ferulic acids were found to contribute to the

TABLE 4 Correlations among chemical composition and assays

	TAP	DPPH	ABTS	CUPRAC	FRAP	FICA	AChEIA	BChEIA	TIA	AAIA	AGIA
RACI	0.985	0.999	0.992	0.997	0.997	0.999					
Total flavonoid	0.992	0.997	0.986	0.992	0.999	0.996	−0.997	−0.996	−0.960	0.760	0.997
Total phenolic	0.962	0.997	0.990	0.999	0.985	0.995	−0.972	−0.985	−0.928	0.850	0.989
Chlorogenic acid	0.987	0.999	0.990	0.996	0.998	0.999	−0.993	−0.996	−0.953	0.785	0.998
4-Hydroxybenzoic acid	−0.967	−0.998	−0.998	−0.998	−0.988	−0.999	0.979	0.994	0.920	−0.832	−0.996
Ferulic acid	−0.973	−0.999	−0.996	−0.999	−0.992	−0.999	0.983	0.995	0.931	−0.823	−0.997
Luteolin 7-glucoside	0.986	0.998	0.984	0.996	0.997	0.996	−0.991	−0.992	−0.961	0.787	0.994
Hesperidin	0.984	0.999	0.992	0.997	0.997	0.999	−0.991	−0.997	−0.948	0.792	0.998
Hyperoside	0.986	0.999	0.990	0.997	0.998	0.999	−0.992	−0.996	−0.952	0.788	0.998
Rosmarinic acid	−0.984	−0.999	−0.992	−0.997	−0.997	−0.999	0.991	0.997	0.948	−0.793	−0.998
Apigenin 7-glucoside	−0.807	−0.837	−0.889	−0.823	−0.828	−0.852	0.835	0.874	0.668	−0.648	−0.867
Pinoresinol	0.977	0.999	0.993	0.999	0.994	0.999	−0.985	−0.994	−0.94	0.816	0.996
Luteolin	−0.983	−0.999	−0.991	−0.998	−0.997	−0.999	0.990	0.995	0.95	−0.797	−0.997

inhibitory activity on ChEs and tyrosinase. In addition, according to the data in the table, luteolin 7-glucoside, hesperidin, hyperoside, and pinoresinol were major compounds contributing to α-glucosidase inhibitory activity of the extracts. The correlation coefficients given here are of course hypothetical values calculated based on the amounts of the compounds in question in the extracts. Therefore, it is possible to find situations that conflict with the activity findings. However, these correlation coefficients provide important clues in predicting the compounds contributing to activity. In order to document the actual activities of these compounds, it would be better to determine their activities by performing in vitro experiments.

4 | CONCLUSIONS

In this study, the relationship between the phytochemical compositions of three different *Onosma* species and their biological activity potentials were investigated and the correlation between these compounds and activities was documented. The data showed that *O. circinnata* and *O. bornmuelleri* could be effective antioxidant agents. On the other hand, it was concluded that *O. angustissima* can be considered as an alternative agent in the medical and cosmetic industries due to its ChE and tyrosinase inhibitory activites. Chromatographic analysis showed that all three extracts contained high amounts of chlorogenic acid, flavonoid glycosides (apigenin 7-glucoside and luteolin 7-glycoside) and rosmarinic acid. Correlation analysis showed that these compounds contributed particularly to antioxidant activity at a high rate. However, it was concluded that biological activity-guided fractionation should be performed to determine the compounds that contribute to the enzyme inhibitory activities of the extracts.

CONFLICT OF INTEREST

The authors have declared no conflicts of interest for this article.

AUTHOR CONTRIBUTIONS

Cengiz Sarikurkcu: Investigation; Methodology; Supervision; Writing-original draft. **Saliha Seyma Sahinler:** Data curation; Formal analysis. **Mehmet Sabih Ozer:** Conceptualization; Formal analysis; Investigation; Resources. **Arzuhan Sihoglu Tepe:** Data curation; Investigation; Writing-review & editing.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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SUPPORTING INFORMATION

Additional Supporting Information may be found online in the Supporting Information section.

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