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Bioactive constituents, antioxidant effects and enzyme inhibitory properties of two *Onosma* species (*Onosma trapezuntea* and *O. rigidum*)

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ABSTRACT

The genus *Onosma* is the biggest genus in the family Boraginaceae and its members are widely used for traditional purposes in several countries folk medicine. In the current work, two *Onosma* (*O. trapezuntea* and *O. rigidum*) species were examined for biological properties and chemical characterization. To evaluate biological properties, antioxidant and enzyme inhibitory assays were performed. Antioxidant assays included free radical scavenging (2,2′-azino-bis(3-ethylbenzothiazoline-6-sulphonic acid (ABTS) and 1,1-diphenyl-2-picrylhydrazyl (DPPH)), reducing power (cupric reducing antioxidant capacity (CUPRAC) and ferric reducing antioxidant power (FRAP)), metal chelating and phosphomolybdenum. Enzyme inhibitory were assessed against cholinesterase, tyrosinase, α-amylase and α-glucosidase. Total phenolic and flavonoid contents in *O. trapezuntea* were higher than those of *O. rigidum*. Liquid chromatography-mass spectrometry (LC-MS) analysis revealed that chlorogenic acid, rosmarinic acid and hyperoside were dominant compounds in the chemical profiles of the tested *Onosma* extracts. Generally, *O. trapezuntea* exhibited stronger antioxidant abilities than *O. rigidum*. However, the best chelating ability was recorded in *O. rigidum*. In addition, *O. rigidum* was more active on cholinesterase and α-glucosidase when compared with *O. trapezuntea*. The tested extracts exhibited similar tyrosinase inhibitory potentials. Consequently, our findings suggested that the tested *Onosma* species could be presented as valuable sources of natural ingredients such as antioxidant and enzyme inhibitors.

1. Introduction

In the last few years, consumers have become increasingly concerned about the side effects of synthetic compounds in the food and pharmaceutical industries. For example, recent reports have indicated that many additives used in food processing exhibit negative side effects such as toxicity. These concerns have led to the search of different sources as raw materials for pharmaceuticals and drugs. In this sense, plants are unique treasures (Elkordy et al., 2021). Plants produce some non-nutritious compounds called secondary metabolites and they have been exhibited a wide range of health-valuable biological activities including antimicrobial, antioxidant, anticancer, and enzyme inhibitory effects (Adetunji et al., 2021). Considering the growing world population, human beings constantly need new and safe sources from nature. On that note, research activities have been focused on the uninvestigated wild plants for finding novel compounds (Majolo et al., 2019).

The family Boraginaceae contains important genera and *Onosma* L. is the largest one among the genera of this family. The genus contains more than 100 species in Turkey and has a high rate of endemism ratio (50%) (Sarikurkcu et al., 2018). The members of the *Onosma* genus have been widely used in the traditional medicinal systems. For example, some of them have been used as laxative, stimulant, tonic and to treat bronchitis, abdominal pain, fever, and burns (Altundag and Ozturk, 2011; Dalar et al., 2018; Hayta et al., 2014; Rinner et al., 2010; Safavi et al., 2019; Sut et al., 2017; Tetik et al., 2013; Tosun et al., 2008). In another sight, the members of the genus *Onosma* are widely used as food and food stuffs. For example, *O. tauricum* var. *brevifolium* has been widely used in the preparation of omelet (Simsek et al., 2004). In addition, *O. hispidum* has been reported to be the source of food colouring in food preparation (Kumar et al., 2013).

This ethnobotanical database has been caused to many chemical and biological studies on the members of the genus *Onosma*. In these studies, remarkable biological activities including antioxidant (Kirkan et al., 2018; Sarikurkcu et al., 2020a, b; Sarikurkcu et al., 2020c), antimicrobial (Katanić Stanković et al., 2020; Özgen et al., 2003), anticancer (Mašković et al., 2015; Ozgen et al., 2006;

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Rinner et al., 2010), wound healing (Safavi et al., 2019) and anti-inflammatory (Kundakovic et al., 2006) as well as new isolated compounds such as uplandicine, leptanthine, isobutyrylshikonin, isovalerylshikonin ferulic and vanillic acids (El-Shazly et al., 2003; Mroczek et al., 2004; Naz et al., 2006; Sut et al., 2017).

Given this information, researchers are very willing to conduct further studies on the genus *Onosma*. To the best of our knowledge, no information was observed on biological and chemical properties of *O. trapezuntea* and *O. rigidum* in the literature. Thus, we aimed to determine biological properties of the *Onosma* species by using antioxidant and enzyme inhibitory assays. To determine antioxidant properties, free radical scavenging (ABTS and DPPH), reducing power (FRAP and CUPRAC), metal chelating and total antioxidant (phosphomolybdenum) assays were used. Enzyme inhibitory properties were investigated against cholinesterase, tyrosinase, α-amylase and α-glucosidase. In order to establish a connection between chemical composition and biological properties, the tested extracts were examined with the LC-MS technique. Obtained observations could provide a new scientific starting point on the *Onosma* genus.

2. Materials and methods

2.1. Plant material and solvent extraction

The aerial parts of *Onosma trapezuntea* Boiss. & A.Huet ex Hand.-Mazz. (58 m., 50°59′01″N 39°33′05″E, Herbarium number: OC.5047) and *Onosma rigidum* Ledeb. (1160 m., 41°15′19″N 42°21′13″E, Herbarium number: OC.5048) were collected from Akcaabat-Trabzon and Savsat-Artvin, Turkey on 22 May 2019. They were authenticated by Dr. Olcay Ceylan, and deposited at the Department of Biology, Mugla Sıtkı Koçman University (Mugla-Turkey). The plants were firstly air-dried in the shade for several weeks, and then ground using a laboratory mill.

The methanol extracts from the aerial parts of *O. trapezuntea* and *O. rigidum* were prepared by maceration for 24 h. Five grams of the plant materials were mixed with 100 mL of solvent (1:20) and agitation was set to 150 rpm. All of the extracts were stored at +4 °C until analyzed after concentrating the methanol extracts under reduced pressure. Extraction yields are given in Table 1.

2.2. Total flavonoid and phenolic contents

Aluminum chloride method was used for total flavonoid content (TFC) while total phenolic content (TPC) was determined with FCR reagent and the results were calculated as equivalents of quercetin and gallic acid, respectively (Sarikurkcu et al., 2013). Please see the supplementary file for the details.

2.3. Liquid chromatography–electrospray tandem mass spectrometry (LC–ESI–MS/MS) analysis

Analysis of the selected phytochemicals in the extracts was carried out by an Agilent Technologies 1260 Infinity liquid chromatography system hyphenated to a 6420 Triple Quad mass spectrometer on which a chromatographic separation on a Poroshell 120 EC—C18 (100 mm × 4.6 mm I.D., 2.7 μm) column was performed by using the analytical conditions reported in an earlier paper conducted by (Cittan and Çelik, 2018). Please see the supplementary file for the details.

Table 1
Extraction yield, total phenolic and flavonoid contents of the methanol extracts from *O. trapezuntea* and *O. rigidum*[x].

Samples	*Onosma trapezuntea*	*Onosma rigidum*
Yield (%)	7.90	11.80
Total flavonoids (mg QE/g extract)	14.51±1.04[b]	7.42±0.52[a]
Total phenolics (mg GAE/g extract)	24.08±0.63[b]	10.63±0.07[a]

[x] Within each row, means sharing the different superscripts show comparison between the extracts by Tukey's test at $p<0.05$. GAEs and QEs, gallic acid and quercetin equivalents, respectively.

2.4. Biological activity

The antioxidant properties were determined using the following assays: total antioxidant capacity by phosphomolybdenum method (Zengin et al., 2015a), cupric ion (CUPRAC) and ferric ion (FRAP) reducing power (Apak et al., 2006; Kocak et al., 2016), scavenging ability towards DPPH radical (Odabas Kose et al., 2010) $ABTS^{+}$ free radical scavenging (Zengin et al., 2015b) and ferrous ion chelating (Tepe et al., 2011). The antioxidant activity is expressed both as IC_{50} values (the sample concentration providing 50% of radical scavenging and ferrous ion chelating or 0.500 absorbance for the reducing power and phosphomolybdenum assays, respectively) and as mg standard equivalent/g extract. Trolox and Ethylenediaminetetraacetic acid (disodium salt) (EDTA) were used as positive controls. Inhibitory activities of the extracts were determined by following the analysis conditions specified by

For enzyme inhibitory activities, the extracts were analyzed against AChE, BChE, tyrosinase, α-amylase, and α-glucosidase by using previously reported experimental conditions (Zengin et al., 2015c). The enzyme inhibitory activity is expressed both as IC_{50} values (the sample concentration providing 50% of enzyme inhibition) and as mg standard equivalent/g extract. Kojic acid, Galanthamine and Acarbose were used as positive controls. Please see the supplementary file for the details.

2.5. Statistical analysis

All tests were repeated three times to increase the scientific consistency of the results. The results were presented as the mean and standard deviation (mean ± SD). ANOVA (one-way analysis of variance) by Tukey's honestly significant difference post hoc test and Student's *t*-test with α = 0.05 (SPSS v. 22.0) was applied to detect the statistical similarities/differences between the data. Pearson's correlation was determined between chemical components and the biological activities. Then, partial least square (PLS) analysis was also done to determine the contribution of the phytochemical compounds to the biological activities. The analysis was carried out with SIMCA version 14.0.

3. Results and discussion

Recently, polyphenols have been implicated in the control of some chronic and degenerative diseases, particularly those related to oxidative stress. Several clinical studies have indicated that an increase in the intake of phenolics in the diet may reduce the risk of global health problems. (de Carvalho et al., 2020; Santhakumar et al., 2018; Singh et al., 2020) Thus, safe sources of polyphenols are one of the most attractive subjects in scientific research studies. In the current study, total phenolic and flavonoids content in the tested extracts were detected by colorimetric methods and the results are tabulated in Table 1. *Onosma trapezuntea* contained higher total levels of phenolics (24.08 mg GAE/g extract) and flavonoid (14.51 mg QE/g) when compared to *O. rigidum* (10.63 mg GAE/g and 7.42 mg QE/g). In both species, the levels of total flavonoids accounted for more than 50% of total phenolics. In the literature, various observations for total phenolic and flavonoid contents in extracts of the members of the genus *Onosma* (Kirkan et al., 2018; Mašković et al., 2015; Zengin et al., 2019). However, the results obtained by spectrophotometric assays could not reflect accurate levels of phenolics in the extracts. Recent studies have shown that the reagents used in the spectrophotometric assays cannot be reduced by just certain compounds. For example,

Folin-Ciocalteu reagent could be reduced by both phenolics and non-phenolics such as peptides (Sánchez-Rangel et al., 2013). This fact led to the need to determine exact phenol levels in the plant extracts using advanced chromatographic techniques. In the light of these informations, we detected chemical profiles of two *Onosma* extracts by using LC-MS technique. Table 2 shows that the main components were chlorogenic acids, hesperidin and rosmarinic acids. In accordance with our results, it has been reported by several authors that rosmarinic and chlorogenic acids are major compounds in the members of the family Boraginaceae, including the genus *Onosma* (Bedane et al., 2020; Kirkan et al., 2018; Trifan et al., 2020; Varvouni et al., 2020; Yildirim, 2020). Many papers have indicated the compounds exhibited significant biological properties including antioxidant, antimicrobial and cytotoxic properties (Devi et al., 2015; Imran et al., 2019; Marchev et al., 2021; Roohbakhsh et al., 2014; Tian et al., 2021). In this context, observed activities of the tested *Onosma* species can be attributed to the presence of these compounds. For this purpose, we performed correlation and PLS analysis between chemical components and observed biological activities. Fig. 1 indicates the Pearson's correlation values and more compounds exhibited positive correlation with the biological activities tested. Most of the chemical components including rosmarinic and chlorogenic acids indicate the positive correlation ($R>0.9$) between and free radical scavenging and reducing power assays. PLS analysis is useful tool two matrices, and it is widely used to evaluate the relation between chemical components and biological activities of plant extracts (Ak et al., 2021; Gevrenova et al., 2021). With this in mind, a PLS analysis were performed in this study and most of the biological activities were clearly correlated with the chemical components in the tested extracts (Fig. 2).

Antioxidants are the main players in inactivating free radicals especially reactive oxygen species and this process is important to alleviate the harmful effects of these radicals. This concept has emerged in the production of several synthetic compounds as antioxidants. However, the synthetic compounds exhibited unpleasant side effects such as toxicity and carcinogenic (Pisoschi et al., 2021; Yan et al., 2020). Thus, we are searching to answer the question: "which compounds could be replaced by synthetic ones" (Fierascu et al., 2018; Neha et al., 2019). Plant secondary metabolites meet the answer to the question. In this sense, some studies have indicated that many secondary metabolites exhibit stronger antioxidant properties than synthetic compounds mentioned (Ahangarpour et al., 2019). Based on the above information, we determined antioxidant profiles of two *Onosma* extracts, and the results are presented in Table 3.

DPPH and ABTS were used to determine the radical scavenging ability of the *Onosma* extracts. In both assays, *O. trapezuntea* exhibited stronger radical scavenging ability than that of *O. rigidum*. Regarding reducing abilities of the tested extracts, *O. trapezuntea* possessed a 2-fold reducing ability than *O. rigidum* in FRAP and CUPRAC assays. Overall, these findings were consistent with the total phenolic content in the extracts. Thus, we concluded that phenolics were main players in free radical scavenging and reducing power assays. Obtained results are corroborated with several researchers, who reported a strong correlation between total phenolics and radical scavenging and reducing power abilities (İnan et al., 2020; Mwamatope et al., 2020; Wu et al., 2020). In contrast to radical scavenging and reducing power assays, *O. rigidum* was more effective than *O. trapezuntea* in phosphomolybdenum and metal chelating assays. However, no statistical differences were observed among the tested species in the test systems. The different results in phosphomolybdenum and metal chelating assays can be attributed to the presence of non-phenolic compounds such as peptides or sulfates in the extracts. This fact was also confirmed by correlation analysis (Fig. 1). Previous studies on the antioxidant properties of the members of the genus *Onosma* (Katanić Stanković et al., 2020; Kirkan et al., 2018; Mašković et al., 2015; Özgen et al., 2003; Sarikurkcu et al., 2018, 2020a, b; Sarikurkcu et al., 2020c).

In the past few decades, humankind has needed urgent therapeutic precautions to control several diseases that have been termed global health problems. The prevalence of these diseases is increasing day by day and this fact is reaching the alert level. In this scenario, enzymes are effective players to manage these diseases and their inhibition can be linked to alleviating the symptoms of these diseases mentioned. For example, acetylcholine (ACh) is an important neurotransmitter in the synaptic cleavage and plays the main role in neurotransmission. In Alzheimer's patients, the level of ACh is lower than that of healthy persons. In this sense, the increasing of ACh level is an effective way to manage the cognitive functions of AD patients. This fact is known as the cholinergic hypothesis and it is one of the most acceptable approaches in the management of AD (Karakaya et al., 2019). As another example, α-amylase and α-glucosidase inhibition are effective tools in the management of blood glucose levels in diabetes patients. To this end, synthetic compounds have been manufactured as inhibitors in order to manage the symptoms of these diseases (Papoutsis et al., 2021; Sun et al., 2020). Though considerable effects of these compounds, most of them have negative side effects on human health (Bernardo et al., 2021; Ogundajo et al., 2018; Spínola and Castilho, 2017; Suliman et al., 2021). At this point, natural enzyme inhibitors are of particular interest in the pharmaceutical industry due to their safe, easily accessible and more effective action compared to synthetic ones.

Hence, we investigated the enzyme inhibitory properties of two *Onosma* species and the results are given in Table 4. Both cholinesterase, *O. rigidum* exhibited stronger ability when compared with *O. trapezuntea*. However, galanthamine was an excellent inhibitor against these enzymes. In tyrosinase inhibitory assay, the tested extracts exhibited similar effects with values of 2.16 and 2.19 mg/ml.

Table 2
Concentration (μg/g extract) of selected phytochemicals in the methanol extracts from *O. trapezuntea* and *O. rigidum*[x].

Compounds	*Onosma trapezuntea*	*Onosma rigidum*
Gallic acid	11.01±0.26^{b}	3.88±0.17^{a}
Protocatechuic acid	248.54±0.04^{b}	118.30±0.26^{a}
3,4-Dihydroxyphenylacetic acid	Nd	3.60±0.34
(+)-Catechin	Nd	39.74±0.96
Pyrocatechol	Nd	nd
Chlorogenic acid	53,782.56±510.11^{b}	17,076.64±18.37^{a}
2,5-Dihydroxybenzoic acid	142.04±0.80^{b}	32.85±0.78^{a}
4-Hydroxybenzoic acid	777.43±0.25^{b}	444.98±0.40^{a}
(-)-Epicatechin	nd	nd
Caffeic acid	255.58±8.39^{b}	152.20±1.68^{a}
Vanillic acid	734.26±16.24^{b}	450.62±35.31^{a}
Syringic acid	62.97±2.26^{b}	28.17±2.08^{a}
3-Hydroxybenzoic acid	6.09±0.51	nd
Vanillin	98.43±0.99^{b}	50.69±1.59^{a}
Verbascoside	nd	nd
Taxifolin	nd	1.25±0.06
Sinapic acid	130.98±0.87^{b}	44.85±2.50^{a}
p-Coumaric acid	351.37±6.03^{b}	79.23±1.46^{a}
Ferulic acid	362.11±24.35^{a}	339.71±13.75^{a}
Luteolin 7-glucoside	3251.52±56.54^{b}	769.39±2.28^{a}
Hesperidin	30,074.97±871.05^{b}	20,920.92±19.53^{a}
Hyperoside	946.36±29.06^{a}	6068.43±96.01^{b}
Rosmarinic acid	9091.26±149.17^{b}	3745.61±91.97^{a}
Apigenin 7-glucoside	669.88±6.99^{b}	620.63±3.23^{a}
2-Hydroxycinnamic acid	nd	nd
Pinoresinol	434.14±18.67^{b}	356.42±6.26^{a}
Eriodictyol	2.73±0.15^{b}	1.01±0.01^{a}
Quercetin	8.85±0.17^{a}	27.26±0.65^{b}
Luteolin	143.25±3.78^{a}	284.03±8.02^{b}
Kaempferol	5.57±1.01^{a}	16.45±1.27^{b}
Apigenin	84.80±0.46^{b}	68.90±0.93^{a}

[x] Within each row, means sharing the different superscripts show comparison between the samples by Tukey's test at $p < 0.05$. nd, not detected.

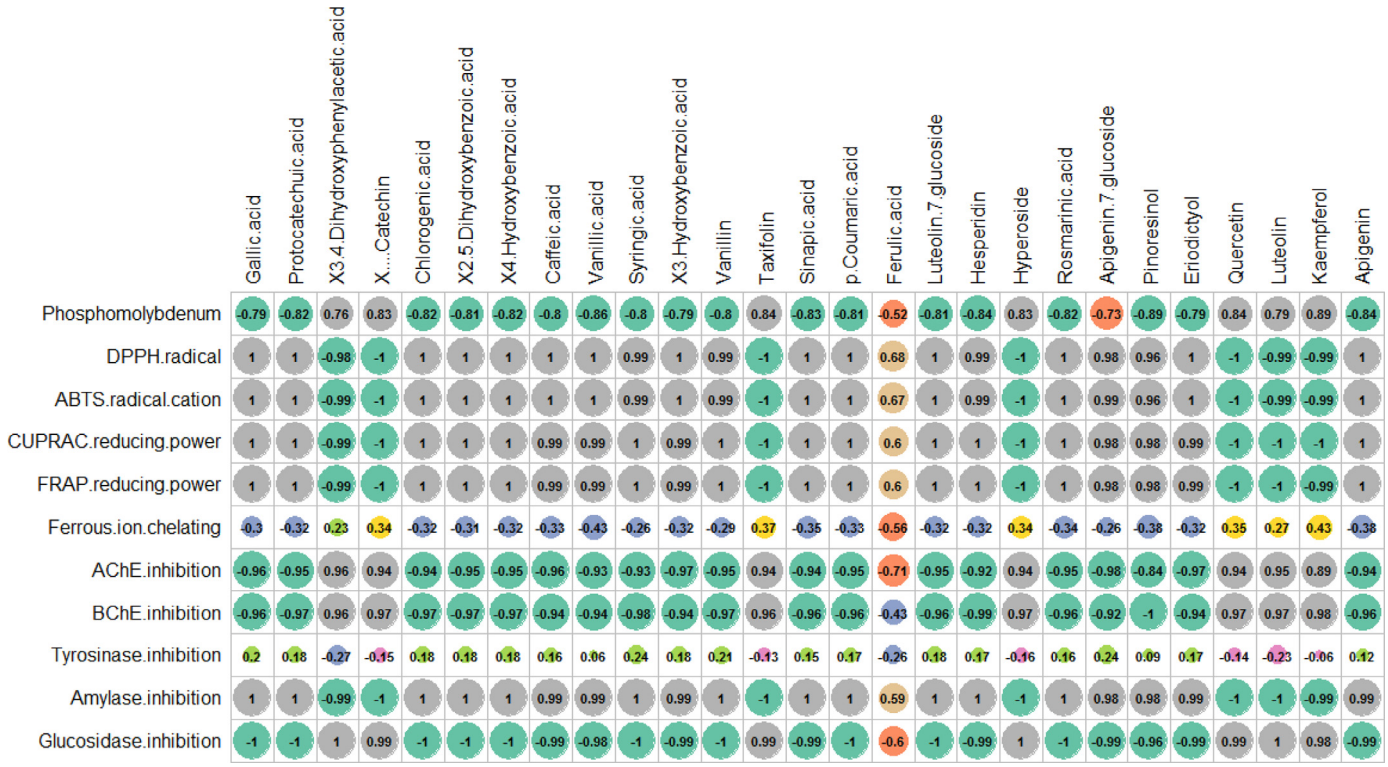

Fig. 1. Pearson correlation analysis between the chemical components and biological activities ($p<0.05$).

Regarding α-amylase and α-glucosidase inhibitory effects, *O. trapezuntea* was more active on α-amylase in comparison with *O. rigidum*. However, *O. rigidum* was the best on α-glucosidase. The observed enzyme inhibitory ability could be attributed to the presence of phenolic compounds listed in Table 2. In Fig. 1, some phenolic components were correlated with the observed enzyme inhibitory abilities. For example, the cholinesterases inhibition abilities were strongly linked to the presence of hyperoside and luteolin. In

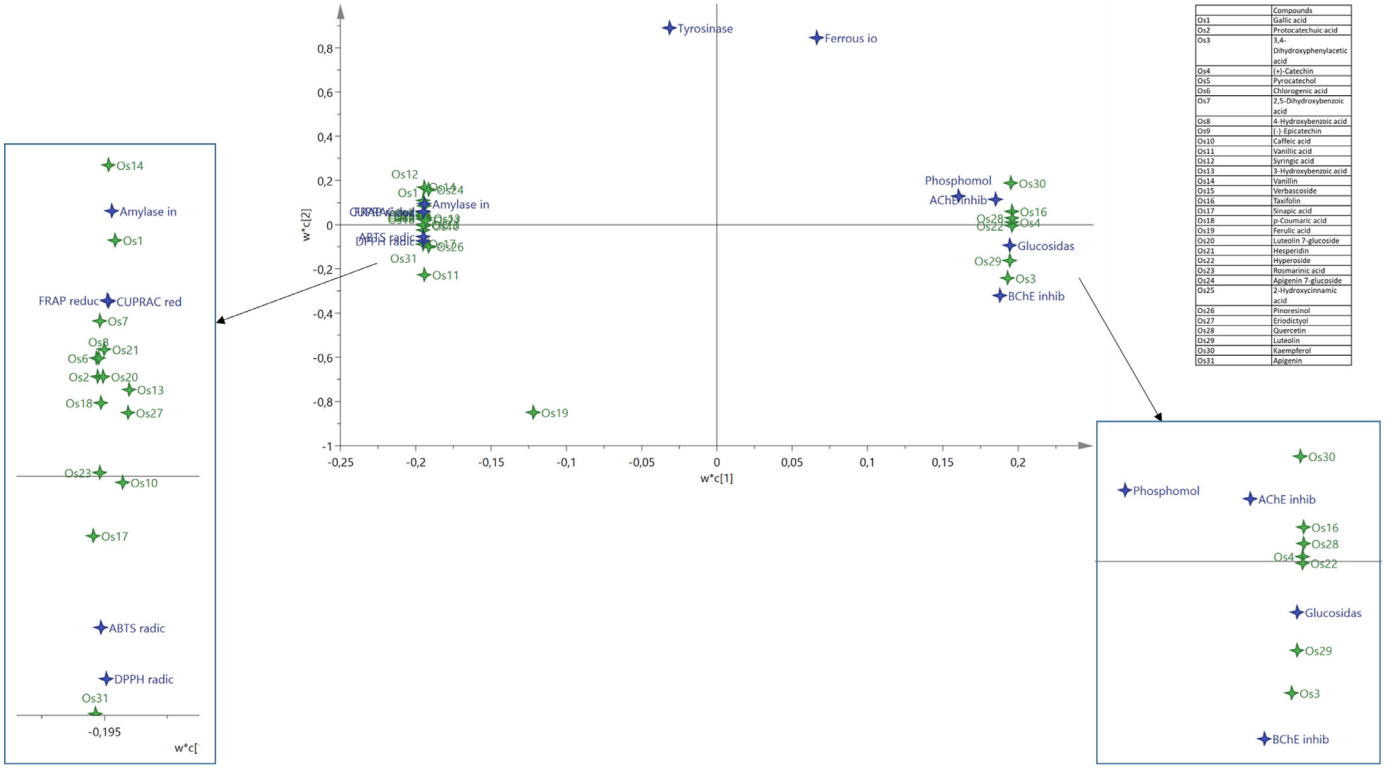

Fig. 2. Partial least squared (PLS) analysis for indicating chemical components and observed biological activities. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

Table 3
Antioxidant activities of standards and the methanol extracts from *O. trapezuntea* and *O. rigidum*[x].

Assays	*O. trapezuntea*	*O. rigidum*	Trolox	EDTA
Effective concentration (EC_{50}: *mg/mL)*				
Phosphomolybdenum	2.14±0.02[a]	2.09±0.03[a]	1.13±0.03[b]	-
DPPH radical	3.05±0.06[b]	7.19±0.74[a]	0.26±0.03[c]	-
ABTS radical cation	2.63±0.05[b]	5.23±0.29[a]	0.32±0.04[c]	-
CUPRAC reducing power	1.31±0.03[b]	2.56±0.07[a]	0.28±0.02[c]	-
FRAP reducing power	0.90±0.02[b]	1.78±0.04[a]	0.11±0.02[c]	-
Ferrous ion chelating	4.36±0.01[a]	4.27±0.29[a]	-	0.052±0.001[b]
Antioxidant activity				
Phosphomolybdenum (mg TEs/g extract)	516.75±4.70[a]	530.60±8.62[a]	-	-
DPPH radical (mg TEs/g extract)	81.84±1.71[b]	34.96±3.56[a]	-	-
ABTS radical cation (mg TEs/g extract)	109.47±1.88[b]	57.57±2.88[a]	-	-
CUPRAC reducing power (mg TEs/g extract)	209.12±5.03[b]	107.16±2.90[a]	-	-
FRAP reducing power (mg TEs/g extract)	111.08±2.56[b]	55.65±1.35[a]	-	-
Ferrous ion chelating (mg EDTAEs/g extract)	11.84±0.01[a]	12.10±0.78[a]	-	-

[x] Within each row, means sharing the different superscripts show comparison between the samples by Tukey's test at $p < 0.05$. EC_{50} (mg/mL), effective concentration at which the absorbance was 0.5 for reducing power and phosphomolybdenum assays and at which 50% of the DPPH (1,1-diphenyl-2-picrylhydrazyl) and ABTS (2,2′-azino-bis (3-ethylbenzothiazoline-6-sulphonic acid) radicals were scavenged and the ferrous ion-ferrozine complex were inhibited. CUPRAC: Cupric reducing power antioxidant capacity; FRAP: Ferric reducing antioxidant power. EDTA, ethylenediaminetetraacetic acid (disodium salt). "-", not determined. TEs and EDTAEs, trolox and ethylenediaminetetraacetic acid (disodium salt) equivalents, respectively.

Table 4
Enzyme inhibition activities of standards and the methanol extracts from *O. trapezuntea* and *O. rigidum* [x].

Assays	*O. trapezuntea*	*O. rigidum*	Galanthamine	Acarbose	Kojic acid
Effective concentration (EC_{50}: *mg/mL)*					
AChE inhibition	1.27±0.03[b]	1.18±0.02[a]	0.0039±0.0004[c]	-	-
BChE inhibition	2.55±0.16[a]	2.06±0.01[b]	0.0056±0.0006[c]	-	-
α-Amylase inhibition	3.35±0.07[b]	5.38±0.01[a]	-	1.10±0.15[c]	-
α- Glucosidase inhibition	3.08±0.06[a]	1.11±0.05[c]	-	1.80±0.07[b]	-
Tyrosinase inhibition	2.16±0.01[a]	2.19±0.11[a]	-	-	0.32±0.03[b]
Enzyme inhibition activity					
AChE inhibition (mg GALAEs/g extracts)	2.40±0.05[a]	2.59±0.03[a]			
BChE inhibition (mg GALAEs/g extracts)	2.20±0.14[a]	2.72±0.01[b]			
α-Amylase inhibition (mg ACEs/g extracts)	307.24±6.91[b]	190.57±0.53[a]			
α- Glucosidase inhibition (mg ACEs/g extracts)	565.67±11.20[a]	1567.83±75.87[b]			
Tyrosinase inhibition (mg KAEs/g extracts)	141.09±0.06[a]	139.79±7.20[a]			

[x] Within each row, means sharing the different subscripts show comparison between the samples by Tukey's test at $p < 0.05$. IC_{50} (mg/mL), inhibition concentration at which 50% of the enzyme activities were inhibited. "-", not determined. AChE: Acetylcholinesterase; BChE. Butyrylcholinesterase. GALAEs, KAEs, and ACEs mean galanthamine, kojic acid, and acarbose equivalents, respectively.

addition, these components showed a positive relationship with the observed glucosidase inhibitory effects. In the amylase inhibition assay, several compounds including rosmarinic and chlorogenic acids were linked to the abilities. In contrast to other enzymes, tyrosinase did not correlate with the phenolic components listed in Table 2. This fact also was confirmed by PLS analysis, and any compounds were not the same line with tyrosinase (Fig. 2). In accordance with our findings, chlorogenic acid, luteolin, rosmarinic acid and hyperoside have been reported significant enzyme inhibitors in earlier reports (Khan et al., 2018; Martinez-Gonzalez et al., 2019; Oboh et al., 2015, 2013; Şöhretoğlu et al., 2018). These findings were suggested that the tested *Onosma* species were promoted to combat Alzheimer's disease, diabetes mellitus and skin disorders. In addition, the observations were provided valuable scientific contributions to the pool of knowledge on pharmaceutical properties of the genus *Onosma*.

4. Conclusion

The present study is the first in-depth report on the biological properties and chemical profiles of the methanol extracts from *O. trapezuntea* and *O. rigidum*. In chemical characterization, chlorogenic acid, rosmarinic acid, hyperoside were the main constituents in the tested extracts. In antioxidant capacity assays, generally, *O. trapezuntea* exhibited stronger effects than *O. rigidum*. These results are in agreement with the total phenol and flavonoid content of the extracts tested. Both extracts exhibited inhibitory effects on the tested enzymes and these findings could prove that the tested *Onosma* species might be significant sources of natural enzyme inhibitor agents. Taken together, the tested *Onosma* species could be suggested as natural ingredients in the preparation of food and pharmaceutical formulations in order to replace with synthetic compounds. This finding will make a major contribution to the underutilized wild plant species. However, more studies are suggested to understand the toxic profiles of the *Onosma* species tested.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Supplementary materials

Supplementary material associated with this article can be found in the online version at doi:10.1016/j.sajb.2021.09.036.

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