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Chemical Composition, Antioxidant and Enzyme Inhibitory Activity of *Onopordum caricum*

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Abstract: Plants are rich sources of biologically and/or pharmacologically active phytochemicals. This study aimed to determine the chemical composition, antioxidant, tyrosinase, anti-cholinesterase, and anti-diabetic activities of ethyl acetate (EtOAc), methanol (MeOH), and water extracts obtained from the aerial parts of *Onopordum caricum* (Hub.-Mor.), which is an endemic plant species to Turkish flora. As a result of spectrophotometric analysis, the MeOH extract was the richest in total phenolics and flavonoids (46.26 mg GAEs/g and 20.97 mg QEs/g, respectively). In quantitative chromatographic analysis, the MeOH extracts contained considerable amounts of chlorogenic acid, eriodictyol, luteolin 7-O-glucoside, vanillic acid, syringic acid, 4-hydroxybenzoic acid, and pinoresinol. Except for the ferrous ion chelating activity assay, MeOH extract showed higher activity than others in all test systems. The activity data exhibited by the MeOH extract in phosphomolybdenum, DPPH and ABTS radical scavenging, CUPRAC, and FRAP tests were 1.46, 1.10, 1.30, 0.87, and 0.76 mg/mL, respectively. The EtOAc extract showed higher activity in all enzyme inhibition assays. The AChE, BChE, α-amylase, α-glucosidase and tyrosinase inhibitory activities of this extract were 0.95, 1.20, 2.37, 1.18 and 1.77 mg/mL, respectively. There was a very high correlation between the extracts' total phenolic and flavonoid contents and their antioxidant activities (phosphomolybdenum, radical scavenging, and reducing power). Since the antioxidant and enzyme inhibitory activity data presented in the current study were found to be higher than the activities of some other *Onopordum* species in the literature, it was concluded that the plant species in question could be used in the treatment of Alzheimer's, diabetes, hyperpigmentation, and disorders occurred as a result of oxidative stress pressure.

Keywords: *Onopordum caricum*; antioxidant activity; chemical composition; enzyme inhibitory activity.

1. Introduction

Tyrosinase, which is common in both plants and mammals, is an important enzyme that plays a role in the melanin biosynthesis of organisms. Tyrosinase synthesizes melanin via *o*-quinone as a result of a series of metabolic reactions [1]. This process, also called melanogenesis, is a normal physiological process that creates a filter that protects the skin against the sun's harmful rays [2]. However, excessive expression (hyperpigmentation) causes darkening of the skin in humans and browning in vegetables and fruits [3-5]. In recent years, interest in the use of tyrosinase inhibitory agents for skin whitening and preventing browning has increased [6]. Phytochemicals are among the most inexpensive and rich sources for new and alternative tyrosinase inhibitors [7].

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As UV rays increase the oxidative pressure on the skin, they cause the melanogenesis process to accelerate. UV rays cause an increase in the amount of reactive oxygen species that contribute to the melanogenesis process by activating tyrosinase [8]. Reactive oxygen species can also trigger the proliferation of pigment-producing skin cells by causing DNA damage [9]. Exogenous antioxidant supplementation may effectively reduce oxidative stress and thus hyperpigmentation in the organism [10]. Many studies have found a strong correlation between plants' phenolic/flavonoid content and their antioxidant activity [11].

Alzheimer's disease, one of the most common types of dementia, is a chronic neurodegenerative disease. This disease, which is generally seen more frequently in the elderly population, is considered a significant health problem worldwide [12]. Researchers refer to two primary hypotheses while developing treatment strategies for this disease. These are the cholinergic and amyloid hypotheses [13-15]. Today, the use of cholinesterase (ChE) inhibitors is the most effective strategy for treating Alzheimer's disease. For this purpose, some cholinesterase inhibitors such as memantine, donepezil, rivastigmine, and galantamine are used [16-18]. Acetylcholine (ACh) and butyrylcholine (BCh), which are neurotransmitters, are degraded by acetylcholinesterase (AChE) and butyrylcholinesterase (BCh), respectively. Since the amount of these neurotransmitters decreases in the brain of Alzheimer's patients, AChE and BChE activity accelerate degeneration even more [19,20]. Scientists are skeptical of using the ChE as mentioned earlier inhibitors because of some of their side effects. Therefore, there is a need to find new molecules with more vital ChE inhibitory activity and fewer side effects [21]. In addition to the activity patterns given above, plants are also rich sources of compounds with cholinesterase inhibitory activity.

Plants are rich sources for antioxidant, tyrosinase inhibitory, anti-Alzheimer's activities, and the treatment of diabetes, another global health problem. In non-insulin-dependent diabetes (type 2 diabetes), glycemic control is considered one of the essential treatment strategies [22,23]. The most basic way to achieve glycemic control is to extend the carbohydrate digestion time [24,25]. α-Amylase and α-glucosidase are enzymes that break down the starch by breaking the α-1-4-glycoside bond. Inhibiting these enzymes is of great importance in glycemic control [22,23]. Today, some anti-hyperglycemic drugs such as voglibose, miglitol, or acarbose are used for this purpose [26]. However, these agents, liver failure, abdominal pain, diarrhea, etc., cause undesirable side effects [27,28]. In recent years, researchers have determined that some phytochemicals have a significant inhibitory effect on these enzymes. In addition to reducing hyperglycemia, these phytochemicals also exhibit fewer side effects than currently used anti-diabetic drugs [28,29].

The genus *Onopordum* includes about 50 species spread throughout Europe and Asia. Roots, shoots, and inflorescences of some members of this genus are consumed in Europe [30]. Some of its members are also used as a source of honey in beekeeping. It is known that some types are used in the treatment of cancer in folk medicine. Its tea is used as a diuretic and sedative. It is also known to contain cardiotonic and hemostatic phytochemicals [31]. It is suggested that the infusion obtained from leaves and inflorescences has an edema-reducing effect [32].

This study aimed to determine the chemical composition, antioxidant, anti-tyrosinase, anti-cholinesterase, and anti-diabetic activities of ethyl acetate (EtOAc), methanol (MeOH), and water extracts obtained from the aerial parts of *Onopordum caricum* (Hub.- Mor.), which is an endemic plant species to Turkish flora.

2. Materials and Methods

2.1. Plant Material and Extract Preparation

Aerial parts of *O. caricum* was collected from Emirbeyazit, Mugla, Mentese-Turkey on May 19, 2018 (620 m., N 37o10’ 24”’ E 28o 22’ 56’’). Dr. Olcay Ceylan (Mugla Sitki Kocman University) identified the species. A sample of the collected plant material was deposited at the Herbarium of Mugla Sitki Kocman University, Department of Biology. (Herbarium number: OC.2110).

Aerial parts of the plants were 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 [33].

2.3. Biological Activity

Details of the methods used to reveal biological activities were given in the supplementary file [33].

2.4. Statistical Analysis

Details of the statistical analysis were presented in the supplementary file. The percentage measurement uncertainties (%) of the obtained data were also given in Tables S3, S4, S5 and S6 in the supplementary file.

3. Results and Discussion

3.1. Chemical Composition of the Extracts

The yields of EtOAc, MeOH, and water extracts obtained from the aerial parts of O. caricum were given in Table 1. According to the data in the table, the highest yield was obtained as a result of extraction with water (11.17%). It was followed by MeOH (7.79%) and EtOAc (3.58%), respectively.

Table 1. Extraction yield, total flavonoid and phenolic contents of *O. caricum* extracts

Assays	EtOAc extract	MeOH extract	Water extract
Yield (%)	3.58	7.79	10.17
Total flavonoids (mg REs/g extract)	5.62 ± 0.01^{b}	20.97 ± 0.03^{a}	2.74 ± 0.20^{c}
Total phenolics (mg GAEs/g extract)	18.55 ± 0.18^{c}	46.26 ± 0.37^{a}	28.55 ± 0.18^{b}

REs and GAEs: Rutin and gallic acid equivalents, respectively. Values indicated by the same superscripts within the same row are not different from the honestly significant difference after Tukey's hoc test at a 5% significance level.

Table 1 also presents the results obtained from the total phenolic and flavonoid compound analysis of the extracts. It has been determined that the amount of phenolic compounds in the extracts was higher than those of flavonoids. MeOH extract was the richest in total phenolics and flavonoids (46.26 mg GAEs/g and 20.97 mg QEs/g, respectively). EtOAc and water extracts were the poorest in phenolics and flavonoids (18.55 mg GAEs/g and 2.74 mg REs/g, respectively).

Table 2 shows the results of the chromatographic analysis in which the amounts of certain phytochemicals in the extracts were determined. It should be underlined that there was a significant correlation between the results of the total phenolic/flavonoid compound analysis given in Table 1 and those obtained from the chromatographic analysis. Most of the phytochemicals in Table 2 were found in the MeOH extract at a higher concentration than the other extracts. Chlorogenic acid, eriodictyol, luteolin 7-O-glucoside, vanillic acid, syringic acid, 4-hydroxybenzoic acid, and pinoresinol were found in MeOH extract at a concentration above 1000 mg/g. In addition, the MeOH extract was found to contain significant amounts of kaempferol (951.1 mg/g), apigenin 7-O-glucoside (918.29 mg/g), protocatechuic acid (663.8 mg/g) and apigenin (592.41 mg/g). On the other hand, 2,5-dihydroxybenzoic acid was found in higher concentrations in water extract than other phytochemicals (525.52 mg/g, respectively) (Figures S1 and S2). Compared to the others, the EtOAc extract was the poorest in terms of phytochemicals screened. Apigenin in this extract stood out with its concentration (707.91 mg/g) compared to other phytochemicals.

According to the literature search results, no data were found in the literature regarding the chemical composition of the plant species analyzed in the current study. Therefore, the chemical composition data presented here were brought to the literature for the first time by the present study.

Table 2. Concentration (µg/g extract) of selected phenolic compounds in *O. caricum* extracts.

Compound	EtOAc extract	MeOH extract	Water extract
Gallic acid	nd	16.59±0.43^{a}	7.59±0.40^{b}
Protocatechuic acid	9.61±0.24^{c}	663.80±0.73^{a}	651.56±3.39^{b}
Pyrocatechol	8.40±0.15^{b}	33.77±0.39^{a}	36.56±4.07^{a}
3,4-Dihydroxyphenylacetic acid	1.81±0.08^{c}	18.17±0.02^{a}	13.27±0.15^{b}
(+)-Catechin	nd	10.31±0.09	nd
Chlorogenic acid	29.05±1.19^{b}	6180.97±13.23^{a}	23.04±0.02^{b}
2,5-Dihydroxybenzoic acid	6.26±0.01^{c}	37.70±2.35^{b}	525.52±3.81^{a}
4-Hydroxybenzoic acid	49.12±1.06^{c}	1213.04±10.70^{a}	471.83±0.14^{b}
(-)-Epicatechin	2.11±0.08^{b}	2.36±0.04^{a}	2.18±0.03^{ab}
Vanillic acid	nd	1560.14±51.64^{a}	223.24±2.36^{b}
Caffeic acid	3.04±0.03^{c}	322.93±0.30^{a}	245.96±1.04^{b}
Syringic acid	16.80±1.68^{c}	1318.26±0.96^{a}	457.48±18.13^{b}
3-Hydroxybenzoic acid	3.84±0.01^{c}	20.05±0.52^{a}	13.57±1.43^{b}
Vanillin	11.97±0.12^{b}	202.51±2.06^{a}	12.61±0.21^{b}
Verbascoside	nd	6.22±0.10^{a}	6.14±0.05^{a}
Taxifolin	nd	227.74±0.34^{a}	8.82±0.55^{b}
Sinapic acid	5.68±0.15^{b}	9.71±1.57^{ab}	14.57±1.54^{a}
p-Coumaric acid	10.55±0.52^{c}	419.61±1.44^{a}	86.65±0.41^{b}
Ferulic acid	12.06±0.63^{c}	386.47±6.53^{a}	88.97±2.77^{b}
Luteolin 7-O-glucoside	13.35±0.37^{b}	2411.03±3.31^{a}	nd
Hesperidin	nd	68.92±1.24^{a}	0.47±0.01^{b}
Hyperoside	2.25±0.04^{b}	110.93±0.17^{a}	1.45±0.12^{c}
Rosmarinic acid	3.64±0.21^{c}	14.30±0.52^{a}	11.09±0.10^{b}
Apigenin 7-O-glucoside	59.22±0.53^{b}	918.29±4.64^{a}	nd
2-Hydroxycinnamic acid	3.49±0.11^{b}	3.05±0.24^{b}	7.71±0.31^{a}
Pinoresinol	59.09±1.60^{b}	1203.99±5.19^{a}	nd
Eriodictyol	19.02±0.78^{b}	2833.91±3.16^{a}	11.33±0.74^{b}
Quercetin	nd	25.50±0.47^{a}	8.83±1.38^{b}
Luteolin	26.80±0.76^{c}	128.25±0.16^{a}	42.49±0.65^{b}
Kaempferol	66.01±1.09^{c}	951.10±0.11^{a}	69.25±0.78^{b}
Apigenin	707.91±20.69^{a}	592.41±4.45^{b}	177.98±0.49^{c}

According to Tukey's honestly significant difference post hoc test at a 5% significance level, the values indicated by the same superscripts within the same row are not different. nd: Not detected

3.2. Antioxidant Activity Potential of the Extracts

Data on the antioxidant activities of the extracts are given in Table 3. The data in the table were given in terms of both EC_{50}/IC_{50} and positive control equivalents. Except for the ferrous ion chelating activity assay, MeOH extract showed higher activity than others in all test systems. This finding showed a positive correlation between the antioxidant activity potential of the MeOH extract and the chemical composition data given in Tables 1 and 2. The activity data exhibited by the MeOH extract in phosphomolybdenum, DPPH and ABTS radical scavenging, CUPRAC, and FRAP tests were 1.46, 1.10, 1.30, 0.87and 0.76 mg/mL, respectively. MeOH extract was found to have higher scavenging activity on DPPH than on ABTS. In addition, the FRAP reducing activity of the MeOH extract was higher than the CUPRAC reducing activity. The EtOAc extract exhibited higher activity in the ferrous ion chelating activity test than other extracts (1.07 mg/mL). It was followed by water and MeOH extracts, respectively (1.18 and 2.53 mg/mL, respectively).

Results from the RACI test confirmed the high antioxidant activity of the MeOH extract. According to Figure 1, the RACI coefficient of the MeOH extract was found to be 0.80. It was followed by water (-0.12) and EtOAc extracts (-0.68), respectively.

To the best of our knowledge, the antioxidant activity of *O. caricum* has not previously been reported elsewhere. Therefore, it is not possible to compare the antioxidant activity of the plant species in question with any literature data. However, there are some data on the antioxidant activities of some

other species belonging to the same genus in the literature. These include *O. arenarium* [34], *O. acanthium* [35], *O. illyricum* [36] and *O. leptolepis* [37].

Identifying the phytochemicals responsible for antioxidant activity in the extracts analyzed here is impossible with the current study design. However, based on the data presented in Table 2, it is possible to reach some literature data on the extent to which phytochemicals in high amounts in MeOH extract can contribute to antioxidant activity. As can be seen from the data in Table 2, MeOH extract contains high amounts of chlorogenic acid, eriodictyol, luteolin 7-O-glucoside, vanillic acid, syringic acid, 4-hydroxybenzoic acid, and pinoresinol. There are some reports in the literature that these compounds themselves or the extracts in which they are present in high amounts exhibit remarkable antioxidant activity [38-50]. Therefore, it was understood that the literature data supported the data obtained from the present study.

Table 3. Antioxidant activity of *O. caricum* extracts

Antioxidant activity	EtOAc	MeOH	Water	Trolox	EDTA
Phosphomolybdenum (EC_{50}: mg/mL)	1.97 ± 0.02^{c}	1.46 ± 0.11^{b}	2.62 ± 0.08^{d}	0.59 ± 0.02^{a}	
DPPH scavenging (IC_{50}: mg/mL)	5.55 ± 0.11^{d}	1.10 ± 0.01^{b}	1.55 ± 0.05^{c}	0.053 ± 0.001^{a}	
ABTS scavenging (IC_{50}: mg/mL)	15.31 ± 0.92^{b}	1.30 ± 0.01^{a}	1.42 ± 0.01^{a}	0.10 ± 0.01^{a}	
CUPRAC reducing (EC_{50}: mg/mL)	2.30 ± 0.03^{d}	0.87 ± 0.01^{b}	1.43 ± 0.01^{c}	0.10 ± 0.01^{a}	
FRAP reducing (EC_{50}: mg/mL)	2.42 ± 0.01^{d}	0.76 ± 0.01^{b}	1.14 ± 0.01^{c}	0.05 ± 0.003^{a}	
Ferrous ion chelating (IC_{50}: mg/mL)	1.07 ± 0.01^{b}	2.53 ± 0.02^{d}	1.18 ± 0.01^{c}		0.026 ± 0.001^{a}
Activity in positive control equivalent					
Phosphomolybdenum (mg TEs/g)	303.90 ± 2.97^{b}	412.50 ± 30.97^{a}	229.50 ± 7.21^{b}		
DPPH scavenging (mg TEs/g)	9.73 ± 0.20^{c}	48.88 ± 0.07^{a}	34.94 ± 1.23^{b}		
ABTS scavenging (mg TEs/g)	6.55 ± 0.39^{c}	76.91 ± 0.85^{a}	70.63 ± 0.60^{b}		
CUPRAC reducing (mg TEs/g)	45.23 ± 0.53^{c}	119.55 ± 1.20^{a}	72.67 ± 0.42^{b}		
FRAP reducing (mg TEs/g)	19.14 ± 0.05^{c}	61.02 ± 0.57^{a}	40.45 ± 0.32^{b}		
Ferrous ion chelating (mg EDTAEs/g)	24.82 ± 0.16^{a}	10.48 ± 0.07^{c}	22.49 ± 0.03^{b}		

TEs and EDTAEs mean trolox and ethylenediaminetetraacetic acid (disodium salt) equivalents, respectively. Values indicated by the same superscripts within the same row are not different from the honestly significant difference after Tukey's hoc test at a 5% significance level.

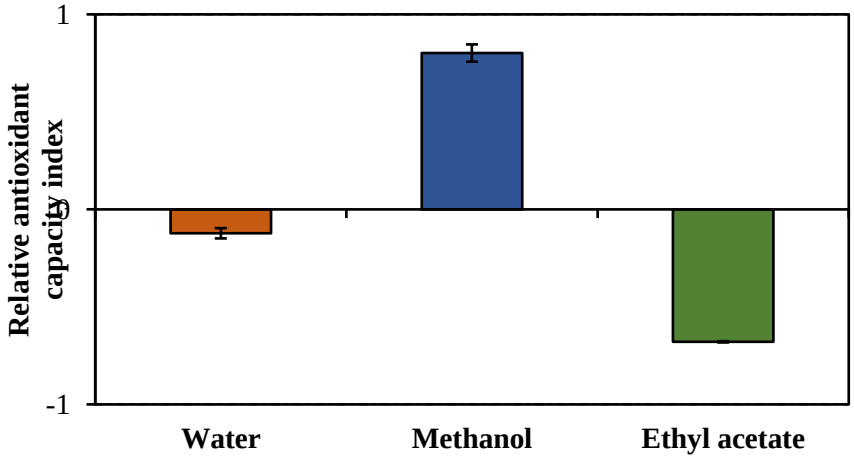

Figure 1. Relative antioxidant capacity index of *O. caricum* extracts

3.3. Enzyme Inhibitory Activity of the Extracts

The data obtained on the AChE, BChE, tyrosinase, a-amylase and a-glucosidase inhibitory activities of the extracts were given in Table 4. As in Table 3, the results were given in terms of both the IC_{50} and the equivalent of the positive control (galanthamine, kojic acid, and acarbose).

EtOAc extract showed higher activity in all enzyme inhibition assays. The AChE, BChE, α-amylase, α-glucosidase and tyrosinase inhibitory activities of this extract were 0.95, 1.20, 2.37, 1.18 and 1.77 mg/mL, respectively. The MeOH extract exhibited moderate enzyme inhibitory activity. However, the water extract showed no activity on ChEs, while it showed weak inhibitory activity on digestive enzymes and tyrosinase.

As in the sections where both phytochemical composition and antioxidant activity data are evaluated, the enzyme inhibitory activity of the plant material in question has not been reported before. Therefore, AChE, BChE, tyrosinase, a-amylase and a-glucosidase inhibitory activities of *O. caricum* were brought to the literature for the first time with this study.

The EtOAc extract, which showed the highest inhibitory activity in all test systems, contained a high amount of apigenin (707.91 mg/g), according to the data in Table 2. There are some reports in the literature that apigenin, a common flavonoid, may contribute to cholinesterase [44], α-amylase, α-glucosidase [51,52] and tyrosinase [44,53] inhibitory activity of the extract. Thus, apigenin is thought to contribute significantly to the enzyme inhibitory activity of the EtOAc extract of *O. caricum*.

3.4. Correlation Coefficients Between the Parameters

The correlation between the data obtained from total phenolic/flavonoid assays and activity tests was given in Table 5. The same table also presents the correlation coefficients between biological activity parameters and phytochemicals found in high amounts in the extracts. There was a very high correlation between the extracts' total phenolic and flavonoid contents and their antioxidant activities (phosphomolybdenum, radical scavenging, and reducing power). In addition, the correlation coefficients between free radical scavenging activity with protocatechuic acid and 4-hydroxybenzoic acid and phosphomolybdenum and reducing power with chlorogenic acid, vanillic acid, luteolin 7-O-glucoside, apigenin 7-O-glucoside, pinoresinol, eriodictyol, and kaempferol was over 0.9. According to the data in Table 5, the correlation coefficients between kaempferol and AChE, tyrosinase, and α-amylase were also relatively high.

Table 4. Enzyme inhibition activity of *O. caricum* extracts

Enzyme inhibitory activity	EtOAc	MeOH	Water	Galanthamine	Acarbose	Kojic acid
1	0.95±0.01^{b}	1.18±0.01^{c}	na	0.0036±0.0003^{a}		
2	1.20±0.20^{b}	5.45±0.47^{c}	na	0.0034±0.0003^{a}		
3	2.37±0.02^{b}	3.18±0.01^{c}	8.66±0.01^{d}		0.95±0.02^{a}	
4	1.18±0.01^{a}	4.43±0.02^{b}	>20^{c}		1.67±0.02^{a}	
5	1.77±0.04^{b}	1.99±0.05^{b}	7.65±0.13^{c}			0.08±0.002^{a}
	Activity in positive control equivalent					
1	3.90±0.01^{a}	3.14±0.02^{b}	na			
2	2.96±0.50^{a}	0.64±0.06^{b}	na			
3	401.60±4.08^{a}	298.99±0.37^{b}	109.66±0.04^{c}			
4	1420.02±5.07^{a}	376.62±1.68^{b}	56.48±1.50^{c}			
5	43.22±0.98^{a}	38.36±0.96^{b}	10.00±0.17^{c}			

GALAEs, KAEs, and ACEs mean galanthamine, kojic acid, and acarbose equivalents, respectively. Values indicated by the same superscripts within the same row are not different from the honestly significant difference after Tukey's hoc test at a 5% significance level. Na, not active. **1**: AChE inhibition (IC_{50}: mg/mL, mg GALAEs/g), **2**: BChE inhibition (IC_{50}: mg/mL, mg GALAEs/g), **3**: α-Amylase inhibition (IC_{50}: mg/mL, mg ACEs/g), **4**: α-Glucosidase inhibition (IC_{50}: mg/mL, mg ACEs/g), **5:** Tyrosinase inhibition (IC_{50}: mg/mL, mg KAEs/g)

Table 5. Pearson correlation coefficients among phenolic compounds and assays

	26	**1**	**2**	**3**	**4**	**5**	**7**	**8**	**9**	**10**	**11**
1	0.444										
2	0.186	0.961									
3	0.696	0.950	0.829								
4	0.571	0.988	0.908	0.987							
5	-0.831	-0.859	-0.686	-0.975	-0.928						
6	0.694	0.953	0.833	0.999	0.987						
7	0.674	-0.340	-0.588	-0.036	-0.195	-0.184					
8	0.097	-0.832	-0.947	-0.629	-0.741	0.447	0.785				
9	0.705	-0.300	-0.547	0.013	-0.145	-0.233	0.998	0.758			
10	0.545	-0.500	-0.715	-0.202	-0.356	-0.017	0.986	0.876	0.976		
11	0.117	-0.833	-0.953	-0.622	-0.738	0.434	0.805	0.988	0.774	0.893	
12	0.950	0.670	0.441	0.867	0.777	-0.955	0.466	-0.165	0.509	0.312	-0.149
13	0.698	0.948	0.824	0.999	0.986	-0.977	-0.026	-0.621	0.024	-0.193	-0.614
14	0.122	0.942	0.998	0.792	0.879	-0.638	-0.639	-0.963	-0.599	-0.758	-0.971
15	0.901	0.770	0.567	0.930	0.860	-0.988	0.332	-0.305	0.379	0.170	-0.292
16	-0.764	0.220	0.477	-0.096	0.064	0.312	-0.991	-0.698	-0.996	-0.955	-0.720
17	0.700	0.948	0.826	1.000	0.986	-0.977	-0.029	-0.623	0.021	-0.196	-0.616
18	0.845	0.849	0.672	0.971	0.920	-0.999	0.204	-0.428	0.251	0.037	-0.417
19	-0.455	0.580	0.768	0.302	0.452	-0.096	-0.931	-0.894	-0.911	-0.964	-0.911
20	0.903	0.770	0.564	0.929	0.858	-0.988	0.336	-0.302	0.382	0.174	-0.288
21	0.922	0.730	0.520	0.908	0.830	-0.978	0.385	-0.252	0.431	0.225	-0.237
22	0,917	0,740	0,532	0,914	0,838	-0,981	0,372	-0,265	0,418	0,212	-0,251
23	0,902	0,770	0,566	0,930	0,860	-0,988	0,334	-0,304	0,380	0,171	-0,291
24	0,900	0,774	0,571	0,932	0,862	-0,989	0,329	-0,309	0,375	0,166	-0,296
25	0,659	-0,364	-0,606	-0,059	-0,217	-0,161	0,999	0,803	0,997	0,989	0,818

1: DPPH, 2: ABTS, 3: CUPRAC, 4: FRAP, 5: Ferrous ion chelating activity, 6: RACI, 7: Acetylcholinesterase inhibitory activity, 8: Butyrylcholinesterase inhibitory activity, 9: Tyrosinase inhibitory activity, 10: α-Amylase inhibitory activity, 11: α-Glucosidase inhibitory activity, 12: Total flavonoid content, 13: Total phenolic content, 14: Protocatechuic acid, 15: Chlorogenic acid, 16: 2,5-Dihydroxybenzoic acid, 17: 4-Hydroxybenzoic acid, 18: Vanillic acid, 19: Sinapic acid, 20: Luteolin 7-O-glucoside, 21: Apigenin 7-O-glucoside, 22: Pinoresinol, 23: Eriodictyol, 24: Kaempferol, 25: Apigenin, 26: Total antioxidant activity,

4. Conclusions

In this study, the in vitro antioxidant and enzyme inhibitory activities of the extracts obtained from the aerial parts of *O. caricum* were analyzed. It was understood that the extracts have antioxidant activity comparable to positive control agents. In addition, EtOAc extract exhibited remarkable enzyme inhibitory activity. Since the antioxidant and enzyme inhibitory activity data presented in the current study were found to be higher than the activities of some other *Onopordum* species in the literature (for example, *O. acanthium*) [54], it was concluded that the plant species in question could be used in the treatment of Alzheimer's, diabetes, hyperpigmentation, and disorders occurred as a result of oxidative stress pressure. However, it is thought that more detailed analyzes should be carried out to determine the phytochemicals responsible for the activity in these extracts.

Supporting Information

Supporting information accompanies this paper on http://www.acgpubs.org/journal/records-of-natural-products

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