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EVALUATION OF PHENOLIC COMPOUNDS FROM SOME GLOBE ARTICHOKE [*Cynara cardunculus var. scolymus* (L.) Fiori] CULTIVARS BASED ON LEAF POSITION AND DIFFERENT PLANT DEVELOPMENT STAGE

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Abstract

In recent years, the use of globe artichoke [*Cynara cardunculus* var. *scolymus* (L.) Fiori] heads have increased in the pharmaceutical field and the active ingredient of many herbal medicines, especially globe artichoke leaves are considered as waste material, thrown away to nature, resulting with environmental pollution, in some countries. The present study is, thus, conducted to evaluate the phenolic compounds in the leaves of two globe artichoke cultivars as well as their change in different months. Globe artichoke leaves were harvested monthly, according to their positions as inner and outer (young and mature leaves, respectively). Leaf samples were dried and extracted using 70% methanolic extraction solvent and quantitatively analyzed at HPLC-DAD. Findings revealed that there were differences between cultivars and leaf positions as inner and outer and also among different plant development stage, in terms of content of bioactive components. Flavonoid levels in February were quite promising, while in terms of other phenolic compounds, December and January were prominent. Regarding the leaf positions, high flavonoid levels were dominant in inner leaves. The findings of the study can be beneficial for using globe artichoke leaf content in nutraceutical and pharmacological applications due to their high level of phenolics and should not be treated as waste material.

Keywords: Cynara cardunculus var. *scolymus*, globe artichoke, leaf, polyphenols, waste

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1. Introduction

Unlike maintaining the presence of an organism in its own ecosystem, surviving in a changing environment represents a hard period for living organisms. Plant secondary metabolites, a broad group of chemical compounds, are known to contribute to living species interactions in the ecosystem, being produced by the majority of plants to cope with several environmental stresses (Chomel et al., 2016; Isah, 2019). These secondary metabolites help plants to develop defense mechanisms against a number of biotic and abiotic stresses. Polyphenols, which constitute an important group of secondary metabolites, have the same role and also contribute to the growth and proliferation of plants. In the case of human being, the impact of polyphenols on the quality of life, when consumed regularly, is very important. In this regard, the importance of globe artichoke among vegetables is undeniable. Globe artichoke is a perennial herbaceous plant cultivated in a wide area in the Mediterranean region (Fratianni et al., 2007). It is mainly grown for receptacle and bracts, which are also called *capitula* and these parts of the plant plays an important role in Mediterranean style nutrition.

It is reported that not only the edible parts of this valuable plant but also the uneaten parts have beneficial effects on human health (Ceccarelli et al.,

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2010; Lattanzio et al., 2009; Maietta et al., 2017). Globe artichoke leaves have been used in herbal medicine since ancient times and are known for their healing effects on human health (Gebhardt, 2001; Lombardo et al., 2010; Pandino et al., 2013a). In addition to its antioxidant, anti-fungal, anti-bacterial, and hepatoprotective effects, it has many therapeutic effects such as accelerating blood flow, directing energy sources, initiating bile secretion from the liver, cholesterol biosynthesis and low-density lipoprotein oxidation (Kukić et al., 2008; Lattanzio et al., 2009; Romani et al., 2006; Ruiz-Aceituno et al., 2016).

The nutritional and therapeutic properties of the globe artichoke are due to high amounts of polyphenolic compounds such as mono- and di-caffeoylquinic acids and flavonoids (Farag et al., 2013; Pandino et al., 2011a; Schütz et al., 2004). Therefore, these broad therapeutic effects of artichoke leaf extracts should not be considered as the effect of a single bioactive component. It should be considered that the bioactive components are associated with each other to provide a strong and pronounced synergistic effect (Lattanzio et al., 2009; Schütz et al., 2004; Wang et al., 2003).

In addition, polyphenol compounds, which are considered to be the secondary metabolites, can act as herbicides, fungicides, bactericides, and thus have an important potential for weed, disease and, pest control (Scavo et al., 2019a). It is well understood that we should protect our planet and environmentally friendly trends need to fore fronted. It is thought that the extracts of precious bioactive compounds from some plant parts could be useful to be used in environmentally friendly strategies in order to combat weed, disease, and pest (Scavo et al., 2019b; 2020). Therefore, recently there is a great interest in these secondary metabolites, which are thought to serve as an adaptation to defense mechanisms of plants, particularly in those derived from extracts of by-product or non-food parts of plants (Scavo et al., 2019a).

In some foods, synthetic antioxidants are used to eliminate the changes in taste, texture, color and even nutritional values caused by oxidation (Dabbou et al., 2016; Shahidi, 1997) and to extend shelf life (Choi et al., 2000). Due to the safety problems associated with the use of synthetic antioxidants in the food field, the growing interest in high-quality bio-products, economic and environmentally friendly technologies in recent years has focused on bioactive components from natural sources rather than synthetic ones (Pandino et al., 2011a). Many researchers tested the potential use of natural antioxidants extracted from waste/residual parts of different food products (e.g. potato and mango peel, grape seed, apple pulp) (Berardini et al., 2005; Carle et al., 2001; Pandino et al., 2011a). In fact, these residues considered as waste also contain significant amounts of specific bioactive phytochemicals as well as lignin, cellulose, and sugar (Dabbou et al., 2016; Pandino et al., 2013a; Peschel et al., 2006; Ping et al., 2011). Another remarkable source of natural antioxidants is globe artichoke. Globe artichoke produces large amounts of agricultural and industrial waste, as leaves, and flower stem (Pandino et al., 2011a). But especially the leaves with high polyphenolic compounds content (Llorach et al., 2002; Lombardo et al., 2012; Pandino et al., 2013a; Pinelli et al., 2007; Romani et al., 2006; Wang et al., 2003) have high pharmaceutical potential, therefore, should not be treated as waste material.

Bearing in mind, the plant tissues have variable bioactive component profiles that are influenced by several internal and external factors (genotype, growing environmental conditions, growing management practices applied, and post-harvest processes) (Lombardo et al., 2018; Pandino et al., 2017). To our knowledge there are limited studies about the change of bioactive components in globe artichoke leaf based on leaf position (young and mature leaves) and different months. Therefore, the aim of the present study, was to evaluate and reveal the potential use of globe artichoke leaves, considered as waste, by determining some polyphenolic compounds of two cultivars' young and mature leaves.

2. Material and methods

Plants of Olympus F_1 and Madrigal F_1 were grown in the experimental fields of Department of Horticulture, Faculty of Agriculture, Akdeniz University, while polyphenol analyses were done in the laboratory of Department of Chemistry, Faculty of Science, Akdeniz University, Antalya.

2.1. Plant material and sample preparation

The experimental fields' soil in which the globe artichoke plants are grown is classified as clay soil in terms of texture characteristics. The local climate conditions are known as typical Mediterranean climate; winters are mild and wet, summers are dry and hot. The soil characteristics and the climate conditions of experimental field are given in Tables 1 and 2, respectively.

Experiments were conducted in these months beacuse it was reported that the quality of the heads with less browning reaction took place in these months beacuse of high level of polyphenolic compounds (Lombardo et al., 2018). The experiment was conducted with two cultivars of globe artichoke: 'Madrigal' is light green, conical shape and large head, suitable for autumn to spring production and for both fresh market and industry, while 'Olympus' is light green and light purple with less conical heads, suitable for mid-season production and for fresh consumption. All standard cultivation techniques were applied throughout the growing period (Pandino et al., 2013b). Ten fresh leaves from outer and inner positions were monthly collected from 4 different plants of two cultivars and weighed immediately. Leaves were dried in an oven at 65°C until they reached the constant weight. Dried inner and outer leaves were ground in a grinder with a sharp blade and ground leaf samples were stored at -20°C.

Table 1. Soil characteristics of the experimental field

Soil characteristics	
Clay (%)	46.56
Silt (%)	22.00
Sand (%)	31.44
Limestone (%)	42.90
Organic matter (%)	5.93
Conductivity (EC value) (mS/cm)	469.1
pH	7.34
Mineral substances	
K (ppm)	681.43
Na (ppm)	56.18
Ca (ppm)	5465.16
Mg (ppm)	432.70
Fe (ppm)	7.72
Mn (ppm)	28.04
Cu (ppm)	1.36
Zn (ppm)	3.52

Table 2. Climate conditions during the experimental growing season (December 2016 - February 2017) at the experimental field

Winter Months	***Maximum temperature (°C)***	***Minimum temperature (°C)***	***Mean temperature (°C)***	***Mean precipitation (mm) (in days)***	***Mean humidity (%)***
December	21.3	2.7	11.2	2.46 (11 days)	49.3
January	19.1	3.0	10.2	4.28 (12 days)	57.0
February	22.8	4.8	12.5	0.15 (4 days)	57.0

2.2. Standards and reagents

Standards and reagents (≥95% purity chlorogenic acid, caffeic acid, syringic acid, *ρ*-coumaric acid, ferulic acid, rosmarinic acid, quercetin, luteolin, apigenin and isorhamnetin) were purchased from Sigma-Aldrich and were of analytical or HPLC grade. Acetone (≥99.5%), methanol (≥99.9%), ethanol (≥99.8%) and ethyl acetate (≥99.8%) were also purchased from Sigma-Aldrich. Ultrapure water was obtained from Millipore Mill-Q Direct Q-3 ultrapure water system.

2.3. Extraction procedure for HPLC analysis

The dried outer and inner leaves of globe artichokes were well grinded separately, weighed as 1±0.01 g and put into the 15 mL polypropylene tubes. And then 10 mL of methanol: water (70:30) extraction solvent was added to the polypropylene tube, cover was closed and agitated for 6 hours at orbital stirrer at room temperature. The tubes were centrifuged at 4000 rpm for 10 minutes.

Samples were filtered using a filter with 0.45 micrometer PTFE syringe tip. Aliquot of supernatant sample was transferred to 2 mL Eppendorf tube and centrifuged again at 10000 rpm for another 10 minutes. Finally, 1 mL of sample extract was transferred to 2 mL vial and injected to the HPLC-DAD instrument.

2.4. Preparation of standards for HPLC analysis

A single standard of each phenolic compound was prepared in methanol at 1000 mg/L before storing at -18°C as stock solutions. By using stock solution of phenolic compounds, the points of calibration curve were done with proper dilutions. The calibration curves were prepared in a range 10-250 mg/L, except isorhamnetin (10-100 mg/L). The calibration curves showed good correlation with $R^2 \geq 0.995$.

2.5. HPLC analysis

An Agilent 1100 HPLC instrument was used for analysis of the samples. The system was consisted of quaternary HPLC pump (G1311A), column oven (G1316A), auto sampler (G1313A), degasser (G1379A) and diode array detector (DAD) (G1315A). The chromatographic separation of phenolic compounds was achieved on Agilent Hypersil ODS 250 mm x 4.6 mm I.D., 5µm particle size C18 column, operated at 28ºC. The HPLC method was adapted from Pandino et al. (2010). Mobile phases were 5% acetic acid in water (mobile phase A) and acetonitrile (mobile phase B). The gradient started with 10% mobile phase B to reach 20% at 5 minutes, 40% mobile phase B at 45-minute, 100% mobile phase B at 55 minutes.

The spectrum data were collected at 330nm, 280nm, 250nm, 310nm and 370 nm. The flow rate was 1.0 mL/min and the injection volume was 20 µL. The limit of detection (LOD) and limit of quantitation (LOQ) values of phenolic compounds and HPLC-DAD chromatograms are given in Table 3 and Fig. 1, respectively. Each assessed phenolic compound standard was identified based on the retention time (RT) and λ_{max} wavelength for two cultivars (Table 4).

Table 3. LOD and LOQ values of phenolic compounds in two cultivars

Compounds	***LOD (mg/L)***	***LOQ (mg/L)***
Chlorogenic acid	2.03	6.77
Caffeic acid	2.37	7.88
Syringic acid	1.53	5.09
p-coumaric acid	1.80	5.99
Ferulic acid	1.93	6.43
Rosmarinic acid	2.12	7.05
Quercetin	2.13	7.11
Luteolin	1.97	6.57
Apigenin	2.46	8.20
Isorhamnetin	2.32	7.74

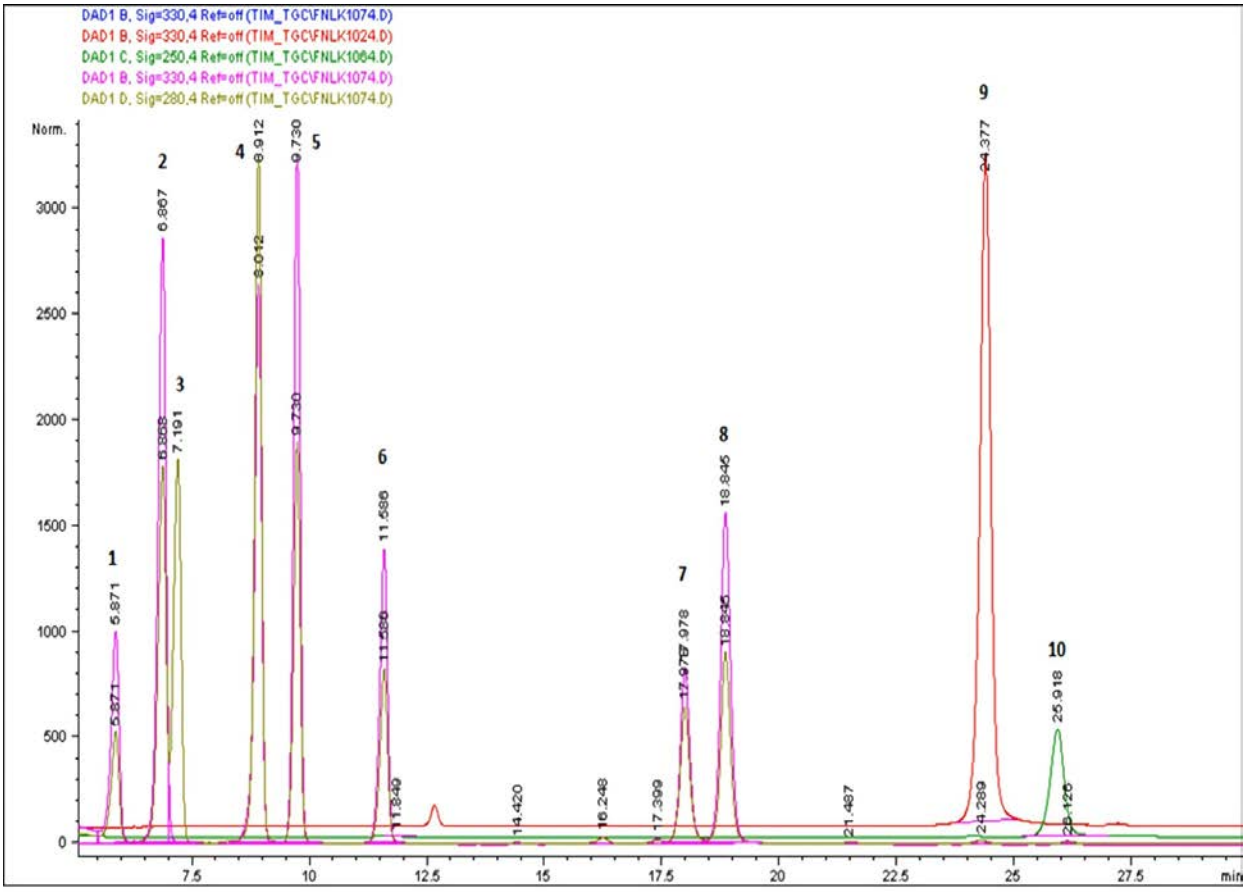

Fig. 1. The HPLC-DAD chromatograms: Chlorogenic acid (1), caffeic acid (2), syringic acid (3), *p*-coumaric acid (4), ferulic acid (5), rosmarinic acid (6), quercetin (7), luteolin (8), apigenin (9), isorhamnetin (10)

Table 4. List of the retention time (RT), λmax wavelength and molecular weight of assessed compounds in two cultivars

Peak Number	***Compounds***	***Retention Time (min)***	***HPLC-DAD λ_{max} (nm)***	***Molecular Weight (g mol^{-1})***
1	Chlorogenic acid	5.87	330	354.31
2	Caffeic acid	6.92	330	180.16
3	Syringic acid	7.19	280	198.17
4	*p*-coumaric acid	8.91	330	164.05
5	Ferulic acid	9.73	330	194.18
6	Rosmarinic acid	11.59	330	360.31
7	Quercetin	17.98	370	302.24
8	Luteolin	18.85	330	286.24
9	Apigenin	24.38	330	270.05
10	Isorhamnetin	25.92	250	316.26

2.6. Statistical analysis

The experiment was carried out in three replications, for cultivars, months and leaf positions. The data obtained from the study were subjected to variance analysis in the JMP package program and the differences between the averages were determined by LSD (least significant difference) test.

3. Results and discussion

The graphics of the fresh and dry weights of the leaves are shown in Fig. 2. The fresh weights of plant's leaves of both cultivars showed variation among months and between cultivars. As given in Table 2, the lowest mean temperatures and the highest precipitation days of the experimental field were in January, in Antalya. In addition, January had the lowest mean temperatures among the months of all year since 1930 according to meteorological data. On the other hand, February had 10.6°C mean temperatures among 1930 - 2019, while in 2017 mean temperature value increased to 12.5°C. In addition to temperature, it is known that the amount of precipitation and the number of rainy days as well as humidity level have important effects on plant development (Pandino et al., 2015). The variability and fluctuations of fresh weights of the leaves reported in present study are probably a reflection of differences in climate conditions as stated above.

In the present study, luteolin and apigenin were found to be high in February while the other polyphenolic compounds were found to be high in December and January. It is reported that significant differences in the content of phenolic compounds may occur in different growing seasons and different climate conditions (Lombardo et al., 2009; 2018). The differences recorded in present study among months, can be attributed to slightly high mean temperature in February. Pandino et al. (2013b) reported that, the most suitable harvest times for globe artichoke leaves and flower stem, considered as waste material but important in terms of polyphenol content, were between February and April. When the results obtained from present study were examined, it can be observed that the flavonoid levels in the leaves were the highest in February. The results of present study are, therefore, in agreement with previous findings of El Senousy et al. (2014) and Lombardo et al. (2010).

As stated in previous studies, besides different environmental conditions, plant's phenolic compositions present diversity based on genotypes and the position of plant parts during maturation. In this study, it was found that the genotype differences caused a difference in the bioactive components of globe artichoke (Tables 5-12). According to the results of present study among the polyphenols, chlorogenic acid, *p*-coumaric acid, rosmarinic acid, and apigenin were determined in high values in Olympus F_1 cultivar, while caffeic acid, syringic acid, ferulic acid, and luteolin were high in Madrigal F_1 cultivar. Pandino et al. (2011a) and Lombardo et al. (2009) reported that genetic background of genotypes affected phenolic compound contents. Similarly, in the present study, different results were found in terms of polyphenolic compounds of two globe artichoke cultivars.

With regards the leaf positions, among the polyphenols, chlorogenic acid, *p*-coumaric acid, luteolin, and apigenin were determined in high values in inner leaves, while caffeic acid, syringic acid, ferulic acid, were high in outer leaves. Many previous studies showed that certain phenolic compounds may be accumulated in different parts of plants (Fratianni et al., 2007; Lombardo et al., 2010; Lombardo et al., 2018; Lutz et al., 2011; Pandino et al., 2012; Wang et al., 2003). Therefore findings of the present study, regarding leaf positions were in agreement with previous studies. As many researchers reported, chlorogenic acid is the most common of all the different caffeoylquinic acids present in globe artichokes. Ciancolini et al. (2013) detected chlorogenic acid and 1,5-dicaffeoylquinic acid as main caffeic acid derivatives.

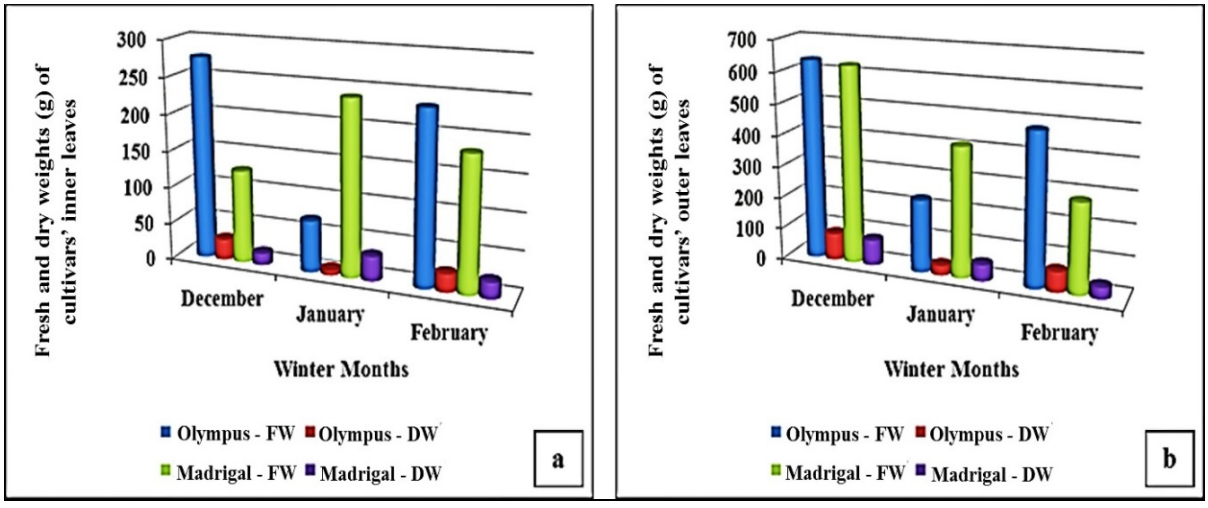

Fig. 2. Monthly fresh and dry leaf weight values (g) of the cultivars': (a) inner leaves, (b**)** outer leaves

In present study, high amounts of chlorogenic acid were also detected among polyphenols and flavonoids evaluated in globe artichoke leaves. When chlorogenic acid levels were evaluated, there were statistically significant differences between cultivars, different months and leaf positions (Table 5). While the highest amount of chlorogenic acid of inner leaves in Olympus globe artichoke cultivar was in January, it was the lowest in the inner leaves harvested in December for both cultivars. (Fig. 3a). As reported in previous studies, it is known that chlorogenic acid has important properties such as being an antioxidant and anticarcinogenic (Fratianni et al., 2007; Gonthier et al., 2003). Findings of the present study on chlorogenic acid content clearly reveal the value of artichoke's leaves on health properties.

Similar to chlorogenic acid, *ρ*-coumaric acid also shows important health improvement properties. In particular, due to its anti-inflammatory properties, it has emerged as a remarkable hydroxycinnamic acid in recent years (Fratianni et al., 2007). When *ρ*-coumaric acid levels were evaluated in present study, there were again statistically significant differences between cultivars, different months and leaf positions (Table 6). In this study, the highest levels of *ρ*-coumaric acid were determined in the inner leaves of Olympus plants collected in January. The lowest *ρ*-coumaric acid level was determined in the both leaf positions of Madrigal cultivar collected in February (Fig. 3e).

Table 5. Chlorogenic acid content of two globe artichoke cultivars

Chlorogenic acid		***Leaf Positions***						***Averages of Cultivars***
		Inner Leaves			***Outer Leaves***			
	Months	***Dec.***	***Jan.***	***Feb.***	***Dec.***	***Jan.***	***Feb.***	
Cultivars	**Olympus F_1**	189.84 g	12487.75 a	3686.74 c	3244.91 cd	2620.27 ef	5056.42 b	4547.65 *A*
	Madrigal F_1	87.09 g	2665.22 def	2745.79 def	3015.70 de	2957.91 de	2140.30 f	2268.67 *B*
Averages	**Leaf Positions x Months**	138.46 *D*	7576.48 *A*	3216.26 *BC*	3130.31 *C*	2789.08 *C*	3598.36 *B*	
	Leaf Positions	**Inner Leaves** = 3643.74 **A**			**Outer Leaves** = 3172.58 **B**			
	Months	**December** = 1634.39 C **January** = 5182.78 A **February** = 3407.31 B						
	Cultivars x Leaf Positions	**Olympus F_1 x inner leaves** = 5454.78 *A* **Olympus F_1 x outer leaves** = 3640.53 *B* **Madrigal F_1 x inner leaves** = 1832.70 *D* **Madrigal F_1 x outer leaves** = 2704.64 *C*						
	Cultivars x Months	**Olympus F_1 x Dec.** = 1717.38 ***D*** **Olympus F_1 x Jan.** = 7554.01 ***A*** **Olympus F_1 x Feb.** = 4371.58 ***B*** **Madrigal F_1 x Dec.** = 1551.39 ***D*** **Madrigal F_1 x Jan.** = 2811.56 ***C*** **Madrigal F_1 x Feb.** = 2443.05 ***C***						
LSD values		$LSD_{cultivar}$ = 242.63 $LSD_{leaf\ position}$ = 242.63 LSD_{month} = 297.16 $LSD_{cultivar\ x\ leaf\ position}$ = 343.13 $LSD_{cultivar\ x\ month}$ = 420.25 $LSD_{leaf\ position\ x\ month}$ = 420.25 $LSD_{cultivar\ x\ leaf\ position\ x\ month}$ = 594.33						

*Note: Different letters indicate a statistically significant difference at *** P ≤ 0.001; ** P ≤ 0.01; and * P ≤ 0.05, respectively. N.S. = not significant*

Table 6. *p*-coumaric acid content of two globe artichoke cultivars

p-coumaric acid		***Leaf Positions***						***Averages of Cultivars***
		Inner Leaves			***Outer Leaves***			
	Months	***Dec.***	***Jan.***	***Feb.***	***Dec.***	***Jan.***	***Feb.***	
Cultivars	**Olympus F_1**	23.10 c	30.14 a	7.93 e	6.16 f	4.39 g	6.56 f	13.05 *A*
	Madrigal F_1	27.69 b	1.50 i	1.18 i	2.56 h	10.35 d	0.97 i	7.37 *B*
Averages	**Leaf Positions x Months**	25.39 *A*	15.82 *B*	4.56 *D*	4.36 *D*	7.37 *C*	3.76 *E*	
	Leaf Positions	**Inner Leaves** = 15.26 **A**			**Outer Leaves** = 5.16 **B**			
	Months	**December** = 14.88 A **January** = 11.59 B **February** = 4.16 C						
	Cultivars x Leaf Positions	**Olympus F_1 x inner leaves** = 20.39 *A* **Olympus F_1 x outer leaves** = 5.70 *C* **Madrigal F_1 x inner leaves** = 10.12 *B* **Madrigal F_1 x outer leaves** = 4.62 *D*						
	Cultivars x Months	**Olympus F_1 x Dec.** = 14.63 ***C*** **Olympus F_1 x Jan.** = 17.26 ***A*** **Olympus F_1 x Feb.** = 7.24 ***D*** **Madrigal F_1 x Dec.** = 15.12 ***B*** **Madrigal F_1 x Jan.** = 5.92 ***E*** **Madrigal F_1 x Feb.** = 1.08 ***F***						
LSD values		$LSD_{cultivar}$ = 0.26 $LSD_{leaf\ position}$ = 0.26 LSD_{month} = 0.33 $LSD_{cultivar\ x\ leaf\ position}$ = 0.38 $LSD_{cultivar\ x\ month}$ = 0.47 $LSD_{leaf\ position\ x\ month}$ = 0.47 $LSD_{cultivar\ x\ leaf\ position\ x\ month}$ = 0.67						

*Note: Different letters indicate a statistically significant difference at *** P ≤ 0.001; ** P ≤ 0.01; and * P ≤ 0.05, respectively. N.S. = not significant*

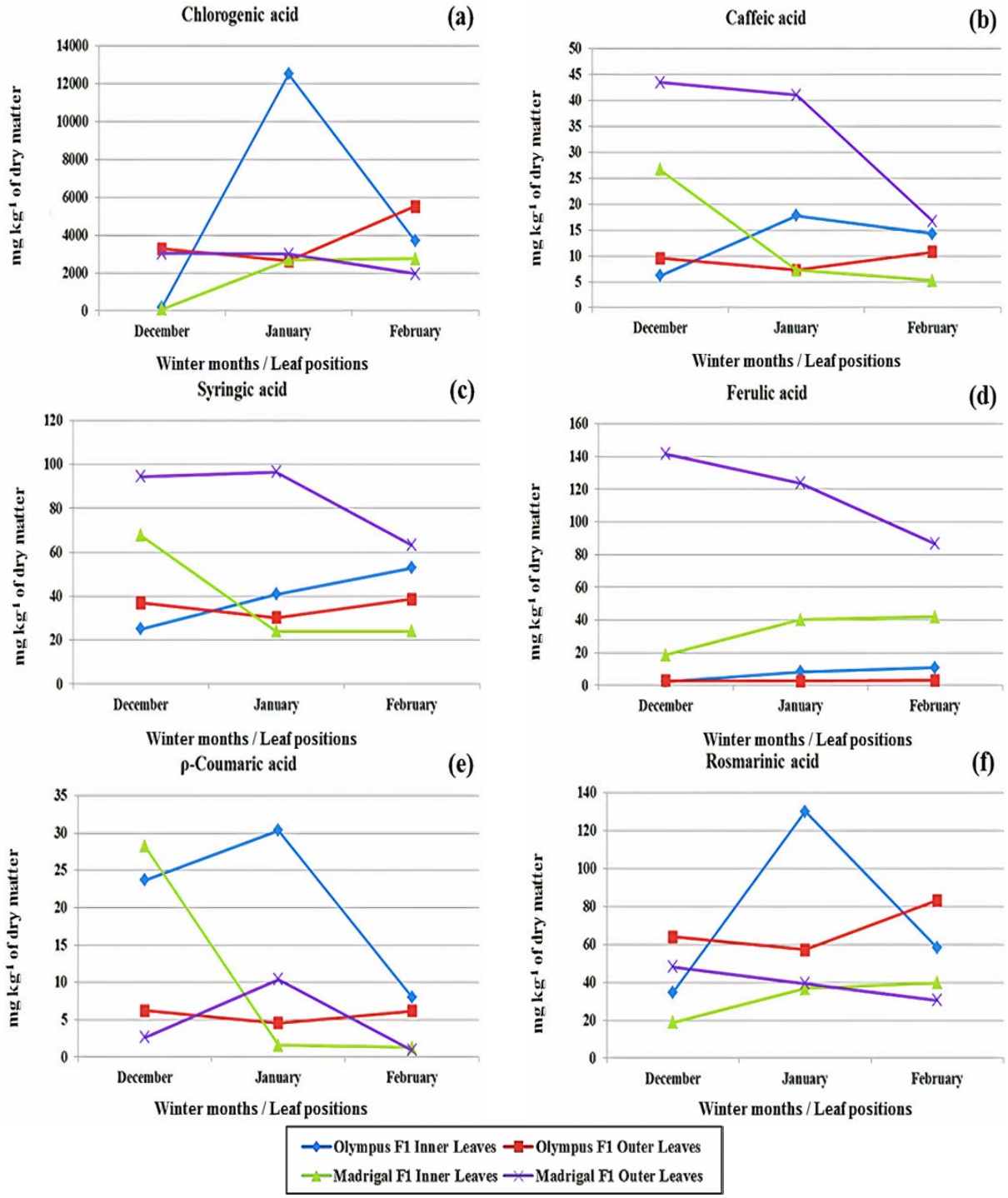

Fig. 3. Quantitative analysis of phenolic acids in two cultivars, according to different months and leaf positions: (a) Chlorogenic acid, (b) Caffeic acid, (c) Syringic acid, (d) Ferulic acid, (e) *ρ*-Coumaric acid, (f) Rosmarinic acid

There were also statistically significant differences between cultivars, different months and leaf positions with regards to caffeic acid and syringic acid levels (Tables 7 and 8). In the present study, the highest and lowest concentrations of caffeic acid were determined in Madrigal cultivar. The highest caffeic acid concentrations were detected in the outer leaves harvested in December and January, while the lowest concentration was found in the inner leaves harvested in February (Fig. 3b). Similarly, both the highest and the lowest concentrations of syringic acid were determined in the Madrigal cultivar. The highest syringic acid concentrations were detected in the outer leaves harvested in December and January, while the lowest concentration was determined in the inner leaves harvested in January (Fig. 3c).

Regarding to ferulic acid levels, there were also statistically significant differences between two globe artichoke cultivars, different months and leaf positions (Table 9). When cultivars evaluated for ferulic acid, it was found to be higher in Madrigal cultivar than Olympus. Ferulic acid, which was detected in higher

amounts in the outer leaves of cultivar Madrigal than in the inner leaves, was determined at the highest in December (Fig. 3d). Ferulic acid, a biologically and structurally important component of the plant cell wall, is capable of stopping radical chain reactions by resonance followed by polymerization, thereby providing protection against UV radiation (Brenelli de Paiva et al., 2013; Kroon et al., 1999). In many previous studies have been demonstrated that ferulic acid and some derivatives have antioxidant, antimicrobial, anti-inflammatory, hepatoprotective, neuroprotective, anticarcinogenic, antidiabetic, anti-cholesterolemic, UV-protective and radioprotective effects (Brenelli de Paiva et al., 2013). Again, with regard to ferulic acid, Lin et al. (2008) reported that it can be used as an additive in sunscreen creams available on the market to enhance skin and hair protection from light, and to combat premature and natural aging.

In terms of rosmarinic acid, statistically significant differences were observed between cultivars, different months and leaf positions (Table 10). In the present study, the highest and lowest concentrations of rosmarinic acid were determined in different cultivars. The highest rosmarinic acid concentration was determined in the inner leaves of Olympus cultivar harvested in January, while the lowest concentration was determined in the inner leaves of Madrigal cultivar harvested in December (Fig. 3f).

Table 7. Caffeic acid content of two globe artichoke cultivars

Caffeic acid		***Leaf Positions***						***Averages of Cultivars***
		Inner Leaves			***Outer Leaves***			
	Months	***Dec.***	***Jan.***	***Feb.***	***Dec.***	***Jan.***	***Feb.***	
Cultivars	**Olympus F_1**	6.06 fg	17.63 c	14.17 cd	9.52 ef	7.19 fg	11.59 de	11.03 *B*
	Madrigal F_1	26.52 b	7.17 fg	5.21 g	42.90 a	40.95 a	13.55 d	22.72 *A*
Averages	**Leaf Positions x Months**	16.29 *B*	12.40 *CD*	9.69 *D*	26.21 *A*	24.07 *A*	12.57 *C*	
	Leaf Positions	**Inner Leaves** = 12.79 **B**			**Outer Leaves** = 20.95 **A**			
	Months	**December** = 21.25 A			**January** = 18.23 B		**February** = 11.13 C	
	Cultivars x Leaf Positions	**Olympus F_1 x inner leaves** = 12.62 *B*			**Olympus F_1 x outer leaves** = 9.44 *C*			
		Madrigal F_1 x inner leaves = 12.97 *B*			**Madrigal F_1 x outer leaves** = 32.47 *A*			
	Cultivars x Months	**Olympus F_1 x Dec.** = 7.79 ***D*** **Olympus F_1 x Jan.** = 12.41 ***C*** **Olympus F_1 x Feb.** = 12.88 ***C*** **Madrigal F_1 x Dec.** = 34.71 ***A*** **Madrigal F_1 x Jan.** = 24.06 ***B*** **Madrigal F_1 x Feb.** = 9.38 ***D***						
LSD values		**$LSD_{cultivar}$** = 1.41 **$LSD_{leaf\ position}$** = 1.41 **LSD_{month}** = 1.73 **$LSD_{cultivar\ x\ leaf\ position}$** = 2.00 **$LSD_{cultivar\ x\ month}$** = 2.45 **$LSD_{leaf\ position\ x\ month}$** = 2.45 **$LSD_{cultivar\ x\ leaf\ position\ x\ month}$** = 3.47						

*Note: Different letters indicate a statistically significant difference at *** $P \leq 0.001$; ** $P \leq 0.01$; and * $P \leq 0.05$, respectively.*
N.S. = not significant

Table 8. Syringic acid content of two globe artichoke cultivars

Syringic acid		***Leaf Positions***						***Averages of Cultivars***
		Inner Leaves			***Outer Leaves***			
	Months	***Dec.***	***Jan.***	***Feb.***	***Dec.***	***Jan.***	***Feb.***	
Cultivars	**Olympus F_1**	24.84 gh	40.79 def	52.77 cd	36.93 efg	30.13 fgh	42.18 de	37.94 *B*
	Madrigal F_1	67.46 b	24.04 h	24.10 gh	94.24 a	96.33 a	53.27 c	59.91 *A*
Averages	**Leaf Positions x Months**	46.15 *BC*	32.42 *D*	38.43 *CD*	65.58 *A*	63.23 *A*	47.73 *B*	
	Leaf Positions	**Inner Leaves** = 39.00 **B**			**Outer Leaves** = 58.85 **A**			
	Months	**December** = 55.87 A			**January** = 47.82 B		**February** = 43.08 B	
	Cultivars x Leaf Positions	**Olympus F_1 x inner leaves** = 39.47 *B*			**Olympus F_1 x outer leaves** = 36.41 *B*			
		Madrigal F_1 x inner leaves = 38.53 *B*			**Madrigal F_1 x outer leaves** = 81.28 *A*			
	Cultivars x Months	**Olympus F_1 x Dec.** = 30.89 ***D*** **Olympus F_1 x Jan.** = 35.46 ***D*** **Olympus F_1 x Feb.** = 47.47 ***C*** **Madrigal F_1 x Dec.** = 80.85 ***A*** **Madrigal F_1 x Jan.** = 60.18 ***B*** **Madrigal F_1 x Feb.** = 38.69 ***CD***						
LSD values		**$LSD_{cultivar}$** = 5.02 **$LSD_{leaf\ position}$** = 5.02 **LSD_{month}** = 6.15 **$LSD_{cultivar\ x\ leaf\ position}$** = 7.10 **$LSD_{cultivar\ x\ month}$** = 8.70 **$LSD_{leaf\ position\ x\ month}$** = 8.70 **$LSD_{cultivar\ x\ leaf\ position\ x\ month}$** = 12.30						

*Note: Different letters indicate a statistically significant difference at *** $P \leq 0.001$; ** $P \leq 0.01$; and * $P \leq 0.05$, respectively.*
N.S. = not significant

Table 9. Ferulic acid content of two globe artichoke cultivars

Ferulic acid		*Leaf Positions*						*Averages of Cultivars*
		Inner Leaves			*Outer Leaves*			
	Months	*Dec.*	*Jan.*	*Feb.*	*Dec.*	*Jan.*	*Feb.*	
Cultivars	**Olympus F1**	2.29 f	8.28 ef	10.36 ef	2.85 f	2.48 f	4.81 f	5.18 *B*
	Madrigal F1	18.29 e	39.78 d	41.47 d	140.76 a	123.18 b	75.01 c	73.08 *A*
Averages	**Leaf Positions x Months**	10.29 *D*	24.03 *C*	25.92 *C*	71.81 *A*	62.83 *A*	39.91 *B*	
	Leaf Positions	**Inner Leaves** = 20.08 **B**			**Outer Leaves** = 58.18 **A**			
	Months	**December** = 41.05 A			**January** = 43.43 A		**February** = 32.91 B	
	Cultivars x Leaf Positions	**Olympus F1 x inner leaves** = 6.98 *C*			**Olympus F1 x outer leaves** = 3.38 *C*			
		Madrigal F1 x inner leaves = 33.18 *B*			**Madrigal F1 x outer leaves** = 112.98 *A*			
	Cultivars x Months	**Olympus F1 x Dec.** = 2.57 ***C*** **Olympus F1 x Jan.** = 5.38 ***C*** **Olympus F1 x Feb.** = 7.58 ***C*** **Madrigal F1 x Dec.** = 79.53 ***A*** **Madrigal F1 x Jan.** = 81.48 ***A*** **Madrigal F1 x Feb.** = 58.24 ***B***						
LSD values		**LSD$_{cultivar}$** = 5.50 **LSD$_{leaf\ position}$** = 5.50 **LSD$_{month}$** = 6.74 **LSD$_{cultivar\ x\ leaf\ position}$** = 7.78 **LSD$_{cultivar\ x\ month}$** = 9.53 **LSD$_{leaf\ position\ x\ month}$** = 9.53 **LSD$_{cultivar\ x\ leaf\ position\ x\ month}$** = 13.48						

*Note: Different letters indicate a statistically significant difference at *** P ≤ 0.001; ** P ≤ 0.01; and * P ≤ 0.05, respectively.*
N.S. = not significant

Table 10. Rosmarinic acid content of two globe artichoke cultivars

Rosmarinic acid		*Leaf Positions*						*Averages of Cultivars*
		Inner Leaves			*Outer Leaves*			
	Months	*Dec.*	*Jan.*	*Feb.*	*Dec.*	*Jan.*	*Feb.*	
Cultivars	**Olympus F1**	34.68 e	129.34 a	57.99 c	64.00 c	56.93 c	76.89 b	69.97 *A*
	Madrigal F1	18.82 f	36.69 e	39.00 e	47.89 d	39.17 e	32.63 e	35.70 *B*
Averages	**Leaf Positions x Months**	26.75 *D*	83.01 *A*	48.50 *C*	55.94 *B*	48.05 *C*	54.76 *B*	
	Leaf Positions	**Inner Leaves** = 52.75			**Outer Leaves** = 52.92			
	Months	**December** = 41.35 C			**January** = 65.53 A		**February** = 51.63 B	
	Cultivars x Leaf Positions	**Olympus F1 x inner leaves** = 74.00 *A*			**Olympus F1 x outer leaves** = 65.94 *B*			
		Madrigal F1 x inner leaves = 31.50 *D*			**Madrigal F1 x outer leaves** = 39.90 *C*			
	Cultivars x Months	**Olympus F1 x Dec.** = 49.34 ***C*** **Olympus F1 x Jan.** = 93.13 ***A*** **Olympus F1 x Feb.** = 67.44 ***B*** **Madrigal F1 x Dec.** = 33.35 ***D*** **Madrigal F1 x Jan.** = 37.93 ***D*** **Madrigal F1 x Feb.** = 35.81 ***D***						
	LSD values	**LSD$_{cultivar}$** = 3.23 **LSD$_{leaf\ position}$** = N.S. **LSD$_{month}$** = 3.96 **LSD$_{cultivar\ x\ leaf\ position}$** = 4.57 **LSD$_{cultivar\ x\ month}$** = 5.60 **LSD$_{leaf\ position\ x\ month}$** = 5.60 **LSD$_{cultivar\ x\ leaf\ position\ x\ month}$** = 7.92						

*Note: Different letters indicate a statistically significant difference at *** P ≤ 0.001; ** P ≤ 0.01; and * P ≤ 0.05, respectively.*
N.S. = not significant

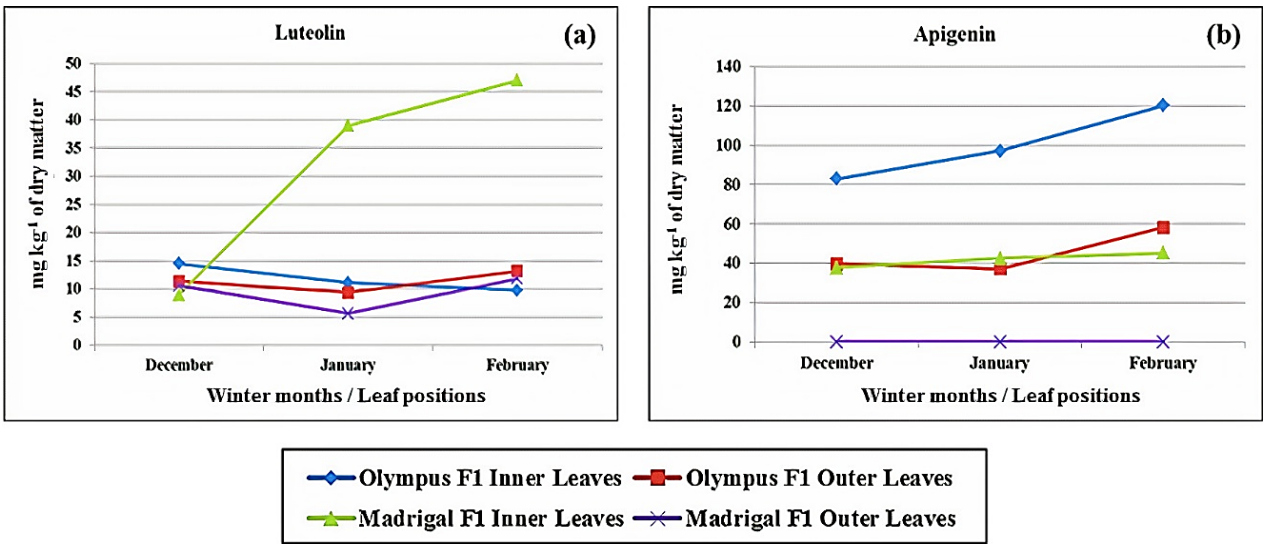

Fig. 4. Quantitative analysis of flavonoids in two cultivars, according to different months and leaf positions: (a) Luteolin, (b) Apigenin

Rosmarinic acid and its derivatives, which are widely studied in the pharmaceutical sense, have the potential to improve human health against neurodegenerative diseases, cancer, diabetes and allergic diseases due to their various biological activities such as anti-inflammatory, antioxidant, anti-angiogenic, anti-tumor and anti-microbial functions (Kim et al., 2015). The antioxidant effects of rosmarinic acid are mainly associated with membrane stabilization and free radical scavenger, which protects against oxidative damage, while the antioxidation and anti-inflammation effects protect the skin from injury caused by exposure to ultraviolet (UV) radiation (Kim et al., 2015).

Results regarding flavonoid content measurement of two cultivars were given in Tables 11 and 12. When the results of the study were evaluated, there were statistically significant differences between cultivars, different months and leaf positions with regards to luteolin levels, while there was no statistically significant difference regarding apigenin levels (Fig. 4). Luteolin and apigenin levels of the outer leaves showed fluctuations among the leaf collection months, while the highest amounts of apigenin in the Madrigal cultivar were obtained in January and February.

Bioactive compounds play different roles in plants (Pandino et al., 2011b). In particular, flavonoids mainly accumulate in epidermal cells of plant tissues (Pinelli et al., 2007) and have the task of protecting the leaf cells of plants from the photoxidative damage of UV light. The B component (280-320 nm) of UV light can be highly damaging. Since leaves are the most sun-exposed organ in plants, plants stimulate flavonoid biosynthetic enzymes rather than the enzymes involved in caffeoylquinic acid biosynthesis (Brosché and Strid, 2003; Pandino et al., 2011a). In this case, flavonoids accumulated in the tissues of plants can protect plants by acting as a shield against harmful radiation (Pinelli et al., 2007).

Flavonoids, especially luteolin and apigenin, are also known to have different pharmacological activities. It has been suggested that these two flavonoids are bioactive components of different plants (Fratianni et al., 2007; Perez-Garcia et al., 2000). Luteolin is thought to have an intermediate metabolite such as apigenin or eriodictiol, synthesized from naringenin along the two main metabolic pathways. The presence of luteolin appears to be important for the therapeutic effects of globe artichoke.

In addition to their antimicrobial activity, luteolin has attracted attention in recent years because it prevents cholesterol synthesis and bile secretion (Kukić et al., 2008; Pandino et al., 2013a; Zhu et al., 2004). Apigenin is found only in some plants and vegetables and is known to have the potential to be used in a variety of pharmaceutical applications (Pandino et al., 2013a). As stated in previous studies, luteolin at 30 µM concentration prevents new cholesterol biosynthesis up to 60%, while luteolin at higher concentrations can be increased to 80% (Fratianni et al., 2007; Gebhardt and Beck, 1996).

According to the Pandino et al. (2011a), while they determined the highest polyphenol content in the leaves and floral stems of the globe artichoke variety they studied, they found that the main components in the leaves were the luteolin derivatives. However, unlike Pandino et al. (2010), the Ciancolini et al. (2013) could not identify luteolin and apigenin from flavonoids in biomass extracts. Quercetin and isorhamnetin were found neither in the cultivars evaluated in their study. The reason for this may be due to different factors, genetic structure, harvest time, related to the plant parts analyzed (Lombardo et al., 2010; 2012), as well as to environmental factors, agricultural applications, and abiotic/biotic stresses (Ciancolini et al., 2013).

Table 11. Luteolin content of two globe artichoke cultivars

Luteolin		***Leaf Positions***						***Averages of Cultivars***
		Inner Leaves			***Outer Leaves***			
	Months	***Dec.***	***Jan.***	***Feb.***	***Dec.***	***Jan.***	***Feb.***	
Cultivars	**Olympus F1**	14.43 bc	10.94 bc	9.73 bc	11.29 bc	9.35 c	12.09 bc	11.31 *B*
	Madrigal F1	8.81 c	38.89 a	46.80 a	10.44 bc	5.54 c	20.38 b	21.81 *A*
Averages	**Leaf Positions x Months**	11.62 *BC*	24.91 *A*	28.26 *A*	10.87 *BC*	7.44 *C*	16.24 *B*	
	Leaf Positions	**Inner Leaves** = 21.60 **A**			**Outer Leaves** = 11.52 **B**			
	Months	**December** = 11.24 B			**January** = 16.18 B		**February** = 22.25 A	
	Cultivars x Leaf Positions	**Olympus F1 x inner leaves** = 11.70 *B*			**Olympus F1 x outer leaves** = 10.91 *B*			
		Madrigal F1 x inner leaves = 31.50 *A*			**Madrigal F1 x outer leaves** = 12.12 *B*			
	Cultivars x Months	**Olympus F1 x Dec.** = 12.86 ***C*** **Olympus F1 x Jan.** = 10.14 ***C*** **Olympus F1 x Feb.** = 10.91 ***C*** **Madrigal F1 x Dec.** = 9.63 ***C*** **Madrigal F1 x Jan.** = 22.21 ***B*** **Madrigal F1 x Feb.** = 33.59 ***A***						
LSD values		**LSDcultivar** = 4.29 **LSDleaf position** = 4.29 **LSDmonth** = 5.25 **LSDcultivar x leaf position** = 6.07 **LSDcultivar x month** = 7.43 **LSDleaf position x month** = 7.43 **LSDcultivar x leaf position x month** = 10.51						

*Note: Different letters indicate a statistically significant difference at *** P ≤ 0.001; ** P ≤ 0.01; and * P ≤ 0.05, respectively. N.S. = not significant*

Table 12. Apigenin content of two globe artichoke cultivars

Apigenin		*Leaf Positions*						*Averages of Cultivars*
		Inner Leaves			*Outer Leaves*			
	Months	*Dec.*	*Jan.*	*Feb.*	*Dec.*	*Jan.*	*Feb.*	
Cultivars	**Olympus F_1**	82.75	96.91	120.04	39.75	37.10	73.39	74.99 *A*
	Madrigal F_1	37.32	42.25	45.19	0	0	11.30	22.67 *B*
Averages	**Leaf Positions x Months**	60.03	69.58	82.62	19.87	18.55	42.34	
	Leaf Positions	**Inner Leaves** = 70.74 **A**			**Outer Leaves** = 26.92 **B**			
	Months	**December** = 39.95 B			**January** = 44.06 B		**February** = 62.48 A	
	Cultivars x Leaf Positions	**Olympus F_1 x inner leaves** = 99.90			**Olympus F_1 x outer leaves** = 50.08			
		Madrigal F_1 x inner leaves = 41.58			**Madrigal F_1 x outer leaves** = 3.76			
	Cultivars x Months	**Olympus F_1 x Dec.** = 61.25 **Olympus F_1 x Jan.** = 67.00 **Olympus F_1 x Feb.** = 96.72 **Madrigal F_1 x Dec.** = 18.66 **Madrigal F_1 x Jan.** = 21.12 **Madrigal F_1 x Feb.** = 28.24						
LSD values		**$LSD_{cultivar}$** = 9.33 **$LSD_{leaf\ position}$** = 9.33 **LSD_{month}** = 11.43 **$LSD_{cultivar\ x\ leaf\ position}$** = N.S. **$LSD_{cultivar\ x\ month}$** = N.S. **$LSD_{leaf\ position\ x\ month}$** = N.S. **$LSD_{cultivar\ x\ leaf\ position\ x\ month}$** = N.S.						

*Note: Different letters indicate a statistically significant difference at *** $P \leq 0.001$; ** $P \leq 0.01$; and * $P \leq 0.05$, respectively.*
N.S. = not significant

Studies carried out to date show that the quality and quantity of the chemical composition of globe artichoke leaves is known and used as raw material because of the biological properties (Coinu et al., 2007; Perez-Garcia et al., 2000). According to Fratianni et al. (2007), hydroxycinnamic acids and flavonoids contained in the leaves of the globe artichoke varieties used in their studies were extremely low.

These results differ from Wang et al. (2003) findings. In their study, they used three different cultivars and measured phenolic compounds and reported that phenolic content amount of leaves was higher than globe artichoke heads of three different cultivars. It will not be wrong to associate the differences in the results obtained in these two studies since Fratianni et al. (2007) used fairly young leaves, while Wang et al. (2003) evaluated mature, fully developed leaves. Present study also clearly shows the importance of leaf position in terms of polyphenols and flavonoids.

4. Conclusions

The findings of present study revealed that the amount of polyphenolic contents in the globe artichoke showed differences according to cultivar, leaf collection months and leaf position as inner and outer. Among the months, February was more promising in terms of flavonoids, while December and January were prominent in terms of other phenolic compounds.

When considering globe artichoke polyphenols for nutraceutical and pharmacological applications, regardless of cultivar differences, it should be taken into account that inner leaves have high flavonoid content in terms of leaf positions. Outer leaves collected in December and January had the highest phenolic compounds. Considering that there are several local and F_1 hybrids globe artichoke cultivars, similar studies should be conducted to reveal their nutraceutical and pharmacological potential. Last but not the least, the results clearly indicated that globe artichoke leaves are highly valuable in terms of polyphenolic compounds and should not be treated as waste material.

Studies for the protection of nature have gained importance against the main problems of the century we are in. In this study, it has been revealed that the leaves considered as waste material can be beneficial for humans. As a result, using globe artichoke leaves in nutraceutical and pharmacological applications, instead of considering waste material, will minimize the amount of waste and the protection of nature will be supported.

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References

Berardini N., Knödler M., Schieber A., Carle R., (2005), Utilization of mango peels as a source of pectin and polyphenolics, *Innovative Food Science and Emerging Technologies*, **6**, 442-452.

Brenelli de Paiva L., Goldbeck R., Dantas dos Santos W., Squina F.M., (2013), Ferulic acid and derivatives: molecules with potential application in the pharmaceutical field, *Brazilian Journal of Pharmaceutical Sciences*, **49**, 395-411.

Brosché M., Strid A., (2003), Molecular events following perception of ultraviolet-B radiation by plants, *Plant Physiology*, **117**, 1-10.

Carle R., Keller P., Schieber A., Rentschler C., Katzschner T., Rauch D., (2001), Method for obtaining useful materials from the by-products of fruit and vegetable processing. Patent Application, WO *01/78859 A1*.

Ceccarelli N., Curadi M., Picciarelli P., Martelloni L., Sbrana C., Giovannetti M., (2010), Globe artichoke as a functional food, *Mediterranean Journal of Nutrition and Metabolism*, **3**, 197-201.

Choi H.S., Song L.S., Ukeda L., Sawamura M., (2000), Radical-scavenging activities of citrus essential oils and their components: Detection using 1, 1-diphenyl-2-picrylhydrazyl, *Journal of Agricultural and Food Chemistry*, **48**, 4156-4161.

Chomel M., Guittonny-Larchevêque M., Fernandez C., Gallet C., DesRochers A., Paré D., Jackson B.G., Baldy V., (2016), Plant secondary metabolites: a key driver of litter decomposition and soil nutrient cycling, *Journal of Ecology*, **104**, 1527-1541.

Ciancolini A., Alignan M., Pagnotta M.A., Miquel J., Vilarem G., Crinò P., (2013), Morphological characterization, biomass and pharmaceutical compounds in Italian globe artichoke genotypes, *Industrial Crops and Products*, **49**, 326-333.

Coinu R., Stefania C., Urgeghe P.P., Mulinacci N., Pinelli P., Franconi F., Romani A., (2007), Dose-effect study on the antioxidant properties of leaves and outer bracts of extracts obtained from Violetto di Toscana artichoke, *Food Chemistry*, **101**, 524-531.

Dabbou S., Dabbou S., Flamini G., Pandino G., Gasco L., Helal A.N., (2016), Phytochemical compounds from the crop byproducts of Tunisian globe artichoke cultivars, *Chemistry and Biodiversity*, **13**, 1475-1483.

El Senousy A.S., Fara M.A., Al-Mahdy D.A., Wessjohann L.A., (2014), Developmental changes in leaf phenolics composition from three artichoke cvs. (*Cynara scolymus*) as determined via UHPLC–MS and chemometrics, *Phytochemistry*, **108**, 67-76.

Farag M.A., El-Ahmady S., Alian F., Wessjohann L.A., (2013), Metabolomics driven analysis of artichoke leaf and its commercial products via UHPLC–q-TOF-MS, *Phytochemistry*, **95**, 177-187.

Fratianni F., Tucci M., Palma M.D., Pepe R., Nazzaro F., (2007), Polyphenolic composition in different parts of some cultivars of globe artichoke (*Cynara cardunculus* L. var. *scolymus* (L.) Fiori), *Food Chemistry*, **104**, 1282-1286.

Gebhardt R., (2001), Anticholestatic activity of flavonoids from artichoke (*Cynara scolymus* L.) and of their metabolites, *Medical Science Monitor*, **7**, 316-320.

Gebhardt R., Beck H., (1996), Differential effects of garlic-derived organosulfides on cholesterol byosinthesis in primary rat hepatocyte cultures, *Lipids*, **31**, 1269-1276.

Gonthier M.P., Verny M.A., Besson C., Rémésy C., Scalbert A., (2003), Chlorogenic acid bioavailability largely depends on its metabolism by the gut microflora in rats, *Journal of Nutrition*, **133**, 1853-1859.

Isah T., (2019), Stress and defense responses in plant secondary metabolites production, *Biological Research*, **52**, 1-25.

Kim G.D., Park Y.S., Jin Y.H., Park C.S., (2015), Production and applications of rosmarinic acid and structurally related compounds, *Applied Microbiology and Biotechnology*, **99**, 2083-2092.

Kroon P.A., Garcia Cones M.T., Fillingham I.J., Williamson G., (1999), Release of ferulic acid dehydrodimers from plant cell walls by feruloyl esterases, *Journal of the Science of Food and Agriculture*, **79**, 428-434.

Kukić J., Popović V., Petrović S., Mucaji P., Ćirić A., Stojkovic D., Sokovic M., (2008), Antioxidant and antimicrobial activity of *Cynara cardunculus* extracts, *Food Chemistry*, **107**, 861-868.

Lattanzio V., Kroon P.A., Linsalata V., Cardinali A., (2009), Globe artichoke: a functional food and source of nutraceutical ingredients, *Journal of Functional Foods*, **1**, 131-144.

Lin J.K., Tournas J.A., Burch J.A., Monteiroriviere N.A., Zielinski J., (2008), Topical isoflavones provide effective photoprotection to skin, *Photodermatology, Photoimmunology and Photomedicine*, **24**, 61-66.

Llorach R., Espin J.C., Tomas-Barneran F.A., Ferreres F., (2002), Artichoke (*Cynara scolymus* L.) byproducts as a potential source of health-promoting antioxidant phenolics, *Journal of Agricultural and Food Chemistry*, **50**, 3458-3464.

Lombardo S., Pandino G., Mauro R., Mauromicale G., (2009), Variation of phenolic content in globe artichoke in relation to biological, technical and environmental factors, *Italian Journal of Agronomy*, **4**, 181-189.

Lombardo S., Pandino G., Mauromicale G., Knödler M., Carle R., Schieber A., (2010), Influence of genotype, harvest time and plant part on polyphenolic composition of globe artichoke [*Cynara cardunculus* L. var. *scolymus* (L.) Fiori], *Food Chemistry*, **119**, 1175-1181.

Lombardo S., Pandino G., Ierna A., Mauromicale G., (2012), Variation of polyphenols in a germplasm collection of globe artichoke, *Food Research International*, **46**, 544-551.

Lombardo S., Pandino G., Mauromicale G., (2018), The influence of pre-harvest factors on the quality of globe artichoke, *Scientia Horticulturae*, **233**, 479-490.

Lutz M., Henrıquez C., Escobar M., (2011), Chemical composition and antioxidant properties of mature and baby artichokes (*Cynara scolymus* L.), raw and cooked, *Journal of Food Composition and Analysis*, **24**, 49-54.

Maietta M., Colombo R., Lavecchia R., Sorrenti M., Zuorro A., Papetti A., (2017), Artichoke (*Cynara cardunculus* L. var. *scolymus*) waste as a natural source of carbonyl trapping and antiglycative agents, *Food Research International*, **100**, 780-790.

Pandino G., Courts F.L., Lombardo S., Mauromicale G., Williamson G., (2010), Caffeoylquinic acids and flavonoide in the immature inflorescence of globe artichoke, wild cardoon, and cultivated cardoon, *Journal of Agricultural and Food Chemistry*, **58**, 1026-1031.

Pandino G., Lombardo S., Mauromicale G., Williamson G., (2011a), Phenolic acids and flavonoids in leaf and floral stem of cultivated and wild *Cynara cardunculus* L. genotypes, *Food Chemistry*, **126**, 417-422.

Pandino G., Lombardo S., Mauromicale G., Williamson G., (2011b), Profile of polyphenols and phenolic acids in bracts and receptacles of globe artichoke (*Cynara cardunculus* var. *scolymus*) germplasm, *Journal of Food Composition and Analysis*, **24**, 148-153.

Pandino G., Lombardo S., Williamson G., Mauromicale G., (2012), Polyphenol profile and content in wild and cultivated *Cynara cardunculus* L., *Italian Journal of Agronomy*, **7**, 254-261.

Pandino G., Lombardo S., Mauromicale G., (2013a), Globe artichoke leaves and floral stems as a source of bioactive compounds, *Industrial Crops and Products*, **44**, 44-49.

Pandino G., Lombardo S., Lo Monaco A., Mauromicale G., (2013b), Choice of time of harvest influences the polyphenol profile of globe artichoke, *Journal of Functional Foods*, **5**, 1822-1828.

Pandino G., Lombardo S., Moglia A., Portis E., Lanteri S., Mauromicale G., (2015), Leaf polyphenol profile and SSR-based fingerprinting of new segregant *Cynara cardunculus* genotypes, *Frontiers in Plant Science*, **55**, 1-10.

Pandino G., Lombardo S., Antonino L.M., Ruta C., Mauromicale G., (2017), *In vitro* micropropagation and mycorrhizal treatment influences the polyphenols content profile of globe artichoke under field conditions, *Food Research International*, **99**, 385-392.

Perez-Garcia F., Adzet T., Canigueral S., (2000), Activity of artichoke leaf extract on reactive oxygen species in human leukocytes, *Free Radicals Research*, **33**, 661-665.

Peschel W., Sànchez-Rabaneda F., Diekmann W., Plescher A., Gartzìa I., Jiménez D., Lamuela-Raventós R., Buxaderas S., Codina C., (2006), An industrial approach in the search of natural antioxidants from vegetable and fruit wastes, *Food Chemistry*, **97**, 137-150.

Pinelli P., Agostini F., Comino C., Lanteri S., Portis E., Romani A., (2007), Simultaneous quantification of caffeoyl esters and flavonoids in wild and cultivated cardoon leaves, *Food Chemistry*, **105**, 1695-11701.

Ping L., Brosseb N., Sannigrahic P., Ragauskas A., (2011), Evaluation of grape stalks as a bioresource, *Industrial Crops and Products*, **33**, 200-204.

Romani A., Pinelli P., Cantini C., Cimato A., Heimler D., (2006), Characterization of Violetto di Toscana, a typical Italian variety of artichoke (*Cynara scolymus* L.), *Food Chemistry*, **95**, 221-225.

Ruiz-Aceituno L., García-Sarrió M.J., Alonso-Rodriguez B., Ramos L., Luz Sanz M., (2016), Extraction of bioactive carbohydrates from artichoke (*Cynara scolymus* L.) external bracts using microwave assisted extraction and pressurized liquid extraction, *Food Chemistry*, **196**, 1156-1162.

Scavo A., Pandino G., Restuccia C., Parafati L., Cirvilleri G., Mauromicale G., (2019a), Antimicrobial activity of cultivated cardoon (*Cynara cardunculus* L. var. *altilis* DC.) leaf extracts against bacterial species of agricultural and food interest, *Industrial Crops and Products*, **129**, 206-211.

Scavo A., Pandino G., Restuccia A., Lombardo S., Pesce G.R., Mauromicale G., (2019b), Allelopathic potential of leaf aqueous extracts from *Cynara cardunculus* L. on the seedling growth of two cosmopolitan weed species, *Italian Journal of Agronomy*, **14**, 78-83.

Scavo A., Pandino G., Restuccia A., Mauromicale G., (2020), Leaf extracts of cultivated cardoon as potential bioherbicide, *Scientia Horticulturae*, **261**, 109024, https://doi.org/10.1016/j.scienta.2019.109024.

Schütz K., Kammerer D., Carle R., Schieber A., (2004), Identification and quantification of caffeoylquinic acids and flavonoids from artichoke (*Cynara scolymus* L.) heads, juice, and pomace by HPLC–DAD-ESI/MS(n), *Journal of Agricultural and Food Chemistry*, **52**, 4090-4096.

Shahidi F., (1997), *Natural Antioxidants: An Overview*, In: *Natural Antioxidants: Chemistry, Health Effects and Applications*, Shahidi F. (Ed.), Champaign, IL, AOCS Press, 1-7.

Wang M., Simon J.E., Aviles I.F., He K., Zheng Q.Y., Tadmor Y., (2003), Analysis of antioxidative phenolic compounds in artichoke (*Cynara scolymus* L.), *Journal of Agricultural and Food Chemistry*, **51**, 601-608.

Zhu X., Zhang H., Lo R., (2004), Phenolic compounds from the leaf extract of artichoke (*Cynara scolymus* L.) and their antimicrobial activities, *Journal of Agricultural and Food Chemistry*, **52**, 7272-7278.