



BIOACTIVE COMPOUND VARIATIONS BASED ON CULTIVAR AND SEASON IN GLOBE ARTICHOKE [*CYNARA CARDUNCULUS* VAR. *SCOLYMUS* (L.) FIORI]

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ABSTRACT. Bioactive substances such as polyphenols in agricultural wastes have been attempted to exploit because of rising market interest in natural food additives. Globe artichoke, a native perennial herbaceous plant in the Mediterranean basin, has been known to have therapeutic effects since ancient times due to its high level of bioactive components. The head part is used for fresh consumption, while leaves are considered waste material, although leaves are known to be rich in bioactive compounds. The present study was conducted to study qualitatively and quantitatively the polyphenol profile of globe artichoke waste material (leaves) from October to April to see the season variation by using two open-pollinated (Bayrampaşa OP and Sakız OP) and one F₁ hybrid (Olympus F₁) globe artichoke cultivars by HPLC–DAD analysis. Results revealed that the leaves' bioactive compound profile varied between cultivars and harvested months. Based on the cultivar, the Sakız OP cultivar came forward regarding the bioactive compound profile of globe artichoke leaves. At the same time, March has been identified as the important month with the highest level of bioactive compounds. The findings of this study also demonstrated that globe artichoke leaves could utilize the nutraceutical and pharmacological content of the artichoke plant and should not be considered waste plant material.

Keywords: artichoke, open-pollinated cultivar, F₁ hybrid cultivar, polyphenols, flavonoids

INTRODUCTION

The globe artichoke [*Cynara cardunculus* var. *scolymus* (L.) Fiori] is a significant member of the *Asteraceae* family and is believed to be an ancestor of the thistle. Globe artichokes are native to the Mediterranean, southern Europe, and northwest Africa.

It is known that the edible parts of artichokes, receptacles, and bracts have undeniable healthful effects on humans [1]. On the other hand, uneaten parts of artichoke plants, especially leaves, have been used in folk medicine from time immemorial [2, 3, 4]. Globe artichoke also has several powerful health protection effects such as hepatoprotective, anticarcinogenic, antioxidative, antibacterial, and anticholesterol [5, 6, 7, 8].

With its high nutritional value and polyphenol content, artichoke is crucial for human health and nutrition; it has risen to the top of the list of plants attracting attention in the face of growing interest in natural antioxidants and functional foods. Artichoke extracts and capsules have been gaining much interest in recent years.

Different polyphenol profiles in plants can be generated by genetics, harvest time, variations in plant parts, environmental conditions, cultivation practices, biotic or abiotic stress factors, and different extraction methods, according to several researchers [3, 6, 9].

Distinct plant sections are expected to have varied phenolic components in different amounts, which might lead to biochemical variances due to physiological changes in plant development processes [10]. However, regardless of cultivar, it has been reported

that a single polyphenol can preferentially accumulate in a particular plant region at a specific period. This is because polyphenol's function in the plant is closely related to the duty that polyphenol performs [3, 9, 10, 11, 12, 13].

The present study aimed to find the most appropriate leaf harvest time (month) from October to April by cultivar to highlight the possibility of using artichoke leaves in numerous fields, particularly pharmaceuticals, by studying 13 key bioactive components in artichoke.

MATERIALS AND METHODS

Plant Material, Experimental Field Conditions, and Leaf Sampling

Evaluated artichoke cultivars were: Bayrampaşa, a late, open-pollinated (OP) cultivar, native to Turkey; Sakız, an early, OP cultivar, native to Turkey too; Olympus, a mid-early, F₁ hybrid cultivar. All of them were planted as offshoots (ovoli) forms in the experimental field of the Department of Horticulture, Faculty of Agriculture, Akdeniz University, Antalya.

The experimental field features the typical Mediterranean, with mild winter and hot, rainless summer climate conditions. The planting distance was arranged with 1.0 x 1.0 m rows. The experimental field's soil texture was characterized by 46.56% clay, 22.00% silt, 31.44% sand, 5.93% organic matter, pH 7.34, and EC 469.1 mS/cm (Table 1). Climate conditions during the experimental growing season (October to April; seven months period) of the experimental field were given in Table 2. All standard cultivation techniques were applied throughout the growing period [14].

Table 1. Soil characteristics of the experimental field

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

Table 2. Climate conditions during the experimental growing season of the experimental field

Harvested Months	Maximum temperature (°C)	Minimum temperature (°C)	Mean temperature (°C)	Mean precipitation (mm) (in days)	Mean humidity (%)
October	27.2	18.9	22.6	3.2 (7 days)	47.9
November	22.9	14.9	18.1	8.2 (14 days)	54.5
December	16.8	9.5	12.8	17.8 (21 days)	63.9
January	14.2	8.1	10.5	18.2 (29 days)	72.6
February	16.9	9.7	12.9	5.02 (18 days)	61.9
March	18.7	10.8	14.7	9.1 (13 days)	60.7
April	20.5	13.5	16.5	2.4 (16 days)	60.7

At least five leaves for each cultivar per replicate were collected for seven months (October to April). Collected leaves were weighed and immediately dried at 65 °C till

they reached the constant weight (about four days), then ground and kept at -18 °C in airtight locked bags until bioactive components were analyzed.

Reagents and Solvents

Reagents and solvents purchased were; high purity ($\geq 99.5\%$) methanol, acetonitrile, acetic acid from Isolab; powder form of 3-*O*-caffeoylquinic acid ($>98\%$) and 1,5-*O*-dicaffeoylquinic acid (99%) from Toronto Research Chemicals; 4-*O*-caffeoylquinic acid (99%), 5-*O*-caffeoylquinic acid (99%), 1,3-*O*-dicaffeoylquinic acid (99%), narirutin (99%), luteolin (99%), apigenin (99%) and apigenin 7-*O*-glucuronide (99%) from Cayman Chemical; *p*-coumaric acid ($\geq 99\%$) and caffeic acid ($\geq 98\%$) from Sigma-Aldrich; ferulic acid (99%) from J&K Scientific; luteolin 7-*O*-glucuronide (87%) from Harbison Walker International. Millipore Mill-Q Direct Q-3 ultrapure water system was used for ultrapure water.

Extraction Procedure, Standard Preparation, HPLC Analysis

Leaf samples were put into 15 mL polypropylene tubes after being weighed at 1 ± 0.01 g, and then 10 mL extraction solvent (80% methanol: 20% water) was added. Firstly, the tubes were exposed to agitating for 24 hours at an orbital stirrer at room temperature and then centrifuged at 4000 rpm for 15 minutes.

After filtering the samples with a 0.45 micrometer PTFE syringe tip filter, an aliquot of the supernatant was passed onto a 2 mL Eppendorf tube and subjected to a 10000-rpm centrifuge for 10 minutes. The last stage of the sample extraction procedure was taking the 1 mL sample extract, transferring it to 2 mL vials, and injecting it into the HPLC-DAD instrument for analysis [15].

Phenolic compounds' standard solutions were prepared by dissolving standards in pure methanol at 1000 mg kg^{-1} weighed with 1 ± 0.01 g sensitivity. Because the solutions prepared in methanol have a longer shelf life, it is preferred instead of water. The prepared stock solutions were stored at -18 °C and then used for the required calibration curves for quantitative determination by diluting in various concentrations. Phenolic compounds' standard solutions' calibration curves were prepared by injected into HPLC at concentrations of 5, 10, 25, 50, 100, and 250 mg kg^{-1} .

Bioactive compound analyses of samples were conducted with an Agilent 1100 HPLC instrument. The HPLC system consisted of a quaternary HPLC pump (G1311A), column oven (G1316A), autosampler (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., $5\mu\text{m}$ particle size C18 column, operated at 28 °C.

For quantitative determination of bioactive compounds, the HPLC method was adapted from Pandino et al. [15]; mobile phases were 5% acetic acid in water (mobile phase A) and acetonitrile (mobile phase B) at a flow rate of 1.0 mL/min, the column oven temperature was 28 °C, and the injection volume was 20 μL . The gradient started with 10% mobile phase B to reach 20% percent at 5 minutes, 40% mobile phase B at 45 minutes, and 100% mobile phase B at 55 minutes. The spectrum data were collected at 310 nm, 330 nm, and 280 nm. For each standard, the limits of detection (LOD) and quantification (LOQ) values of phenolic compounds were determined, and HPLC-DAD chromatograms were given in Figure 1. Each assessed bioactive component standard was identified based on the three cultivars' retention time (RT) and λ_{max} wavelength (Table 3).

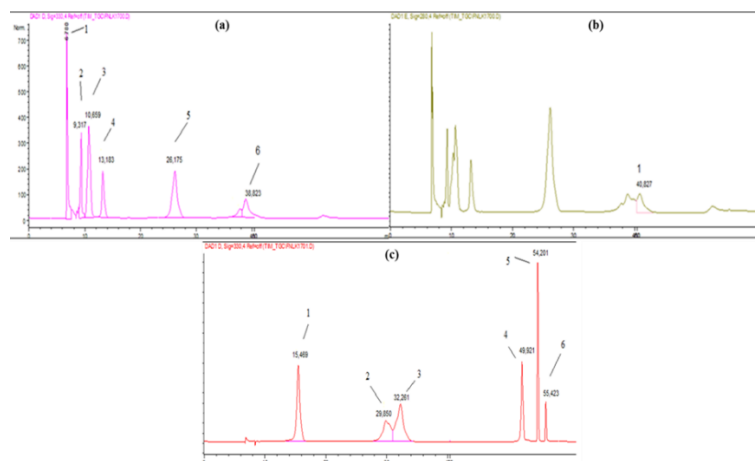


Fig. 1. (a) Spectrum of 50 ppm MIX1 standard mixture taken at 330 nm. (1) 3-*O*-caffeoylquinic acid, (2) 4-*O*-caffeoylquinic acid, (3) 5-*O*-caffeoylquinic acid, (4) 1,3-*O*-dicaffeoylquinic acid, (5) *p*-coumaric acid, (6) 1,5-*O*-dicaffeoylquinic acid; (b) Spectrum of 50 ppm MIX1 standard mixture taken at 280 nm. (1) Narirutin; (c) Spectrum of 50 ppm MIX2 standard mixture taken at 330 nm. (1) Caffeic acid, (2) Luteolin, (3) Ferulic acid, (4) Apigenin 7-*O*-glucuronide, (5) Luteolin, (6) Apigenin

Table 3. List of the retention time (RT), λ_{max} wavelength of assessed bioactive compounds in three cultivars

Compound Number	Compounds	Retention Time (min)	HPLC-DAD λ_{max} (nm)
1	3- <i>O</i> -caffeoylquinic acid	6.78	330
2	4- <i>O</i> -caffeoylquinic acid	9.31	330
3	5- <i>O</i> -caffeoylquinic acid	10.65	330
4	1,3- <i>O</i> -dicaffeoylquinic acid	13.18	330
5	<i>p</i> -coumaric acid	26.17	330
6	1,5- <i>O</i> -dicaffeoylquinic acid	38.82	330
7	Caffeic acid	15.46	330
8	Ferulic acid	32.26	280
9	Narirutin	40.82	330
10	Luteolin	54.20	330
11	Luteolin 7- <i>O</i> -glucuronide	29.85	330
12	Apigenin	55.42	330
13	Apigenin 7- <i>O</i> -glucuronide	49.92	330

Statistical Analysis

Experiments of the present study were carried out as a completely randomized factorial design with three replications. The statistical program JMP version 5.0.1 (SAS Institute Inc., Cary, NC, USA) was used for analyzing the data. ANOVA was performed to determine the effects of cultivars and months on certain bioactive components. Comparisons that obtained $P \leq 0.05$ were considered statistically significant. Additionally, correlation among all the obtained results was carried out through multivariate methods with the statistical program JMP version 5.0.1, with $P \leq 0.05$ as the threshold.

RESULTS AND DISCUSSION

3-*O*-caffeoylquinic Acid (Chlorogenic Acid)

The superiority of the Sakız OP cultivar (7576,62 mg kg⁻¹) was noticeable when considering the cultivars' 3-*O*-caffeoylquinic acid (chlorogenic acid) values in March. When the months were compared, the leaves harvested in March had greater 3-*O*-

caffeoylquinic acid values than those collected in other months (Figure 2). According to Nouraei et al. [16], 3-*O*-caffeoylquinic acid was the most common phenolic acid in their research. The amount of this bioactive component was 481 mg kg⁻¹ under normal settings but jumped to 1198 mg kg⁻¹ under stress, according to the researchers. Despite increased chlorogenic acid produced under stress conditions, the value of chlorogenic acid in the present study was higher. According to Lombardo et al. [3], chlorogenic acid is present in the receptacle and stem of the artichoke. Chlorogenic acid was present in leaves, too, at quite high amounts in the current study. Chlorogenic acid is one of the most important bioactive components with antioxidant and anticarcinogenic activities that is poorly absorbed in the small intestine [11, 17]. It's also responsible for artichoke's biological qualities, which are attributable to nutritionally related polyphenols [11, 17, 18]. This valuable component is found not only in the edible parts of the artichoke but also in the inedible parts, which expands the plant's potential use in several fields.

4-O-caffeoylquinic Acid

A similar trend was recorded when the values of 4-*O*-caffeoylquinic acid were assessed. When comparing cultivars, the Sakız OP cultivar was superior to other cultivars, with the maximum 4-*O*-caffeoylquinic acid value recorded in leaves harvested in March (1094,62 mg kg⁻¹) (Figure 2). Nonetheless, the lowest 4-*O*-caffeoylquinic acid value was also found in leaves of the Sakız OP cultivar harvested in January, clearly showing the seasonal effect on bioactive compounds. According to Lombardo et al. [3], the amount of 4-*O*-caffeoylquinic acid varies from 16 to 574 mg kg⁻¹, depending on cultivars and plant sections. The substance, detected at the highest concentration (574 mg kg⁻¹), was found on the flower stem and had a higher concentration than on the inner bracts, according to the same researchers. Similarly, the utility of this substance in the inedible section of the artichoke is considered outstanding in the current investigation.

5-O-caffeoylquinic Acid

The maximal amount of 5-*O*-caffeoylquinic acid was measured in Sakız in March (10269,63 mg kg⁻¹). In December, the lowest 5-*O*-caffeoylquinic acid value was found again in Sakız OP cultivar leaves (Fig.2). According to many types of research, the most prevalent bioactive components in artichokes are 1,5-*O*-dicaffeoylquinic acid and 5-*O*-caffeoylquinic acid. However, their amounts vary from one genotype to another. Using methanol extraction, Scavo et al. [19] identified 5-*O*-caffeoylquinic acid as the most prevalent component in artichoke, as found in the present study. Caffeoylquinic acids, among the natural antioxidants with health-promoting properties, show significant potential in preventing the development of cancers caused by reactive oxygen species [20]. These valuable bioactive chemicals offer great potential for the pharmaceutical and food industries and have a good effect on shelf life [4, 21].

Cynarin (1,3-O-dicaffeoylquinic Acid)

The highest value of cynarin (1,3-*O*-dicaffeoylquinic acid) was found in the Sakız OP cultivar harvested in March (560,21 mg kg⁻¹) (Figure 2). In their investigation, Lombardo et al. [3] discovered the largest level of cynarin (90 mg kg⁻¹) in the flower stalk. According to Nouraei et al. [16], the amount of cynarin measured in non-stress circumstances was 155 mg kg⁻¹, which increased to 498 mg kg⁻¹ under gradually increased stress conditions. Cynarin is a phenolic component found in artichokes with a

choleric action, increasing the amount of bile released by the liver [22]. According to numerous kinds of research, cynarin is the most prevalent dicaffeoylquinic acid in artichoke. Still, its presence and amount vary depending on various parameters such as genotype and plant sections [23, 24, 25].

1,5-*O*-dicaffeoylquinic Acid

There were statistically significant differences in 1,5-*O*-dicaffeoylquinic acid levels between cultivars and months in the present study (Figure 2). In March, the maximum amount of this important bioactive component was determined in Sakız OP (2597,82 mg kg⁻¹). Many researchers believe that 5-*O*-caffeoylquinic acid, as well as 1,5-*O*-dicaffeoylquinic acid, is the most abundant bioactive component in artichokes [4, 5, 26].

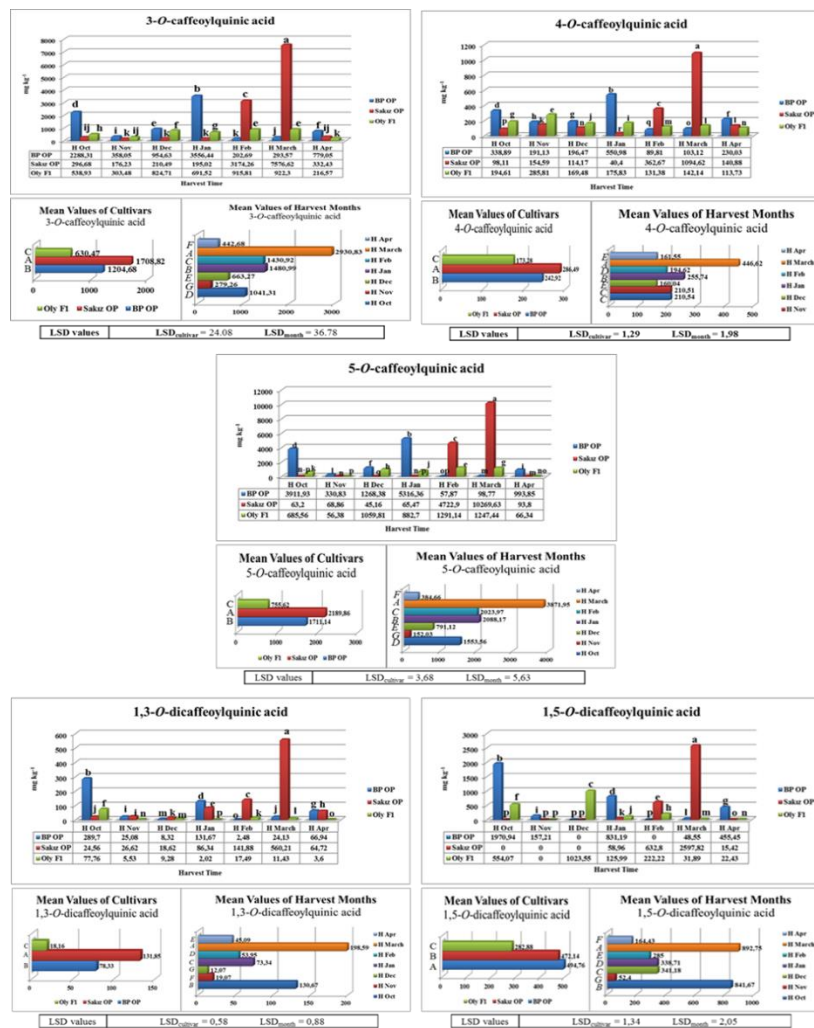


Fig. 2. Mono- and di-caffeoylquinic acid values for cultivars based on harvested months
 *H Oct: Harvest time on October; H Nov: Harvest time on November; H Dec: Harvest time on January; H Feb: Harvest time on February; H March: Harvest time on March; H Apr: April. **Different letters show that the mean difference is statistically significant at P<0.05.

Caffeic acid and *p*-coumaric Acid

Caffeic acid levels ranged from 4,55 mg kg⁻¹ in January to 107,83 mg kg⁻¹ in March, whereas *p*-coumaric acid levels ranged from 5,55 mg kg⁻¹ in December to 1629,40 mg

kg⁻¹ in March based on cultivar (Figure 3). Caffeic acid levels were found to be 172 mg kg⁻¹ under non-stress conditions and increase under stress conditions, according to Nouraei et al. [16]. The main reason for the difference regarding amounts is most likely due to cultivar differences used. *p*-coumaric acid was only found in leaves, according to the same researchers. *p*-coumaric acid, like chlorogenic acid, has essential health-promoting effects. Recently, it has become a noteworthy hydroxycinnamic acid due to its anti-inflammatory characteristics [11].

Ferulic Acid

Regarding leaf ferulic acid levels, the Sakiz OP cultivar was better in January (55,94 mg kg⁻¹) than other cultivars and other months (Figure 3). Ferulic acid and its derivatives are a biologically and structurally significant component of the plant cell wall that can inhibit some radical chain reactions, protecting the plant from UV radiation [27]. Various researchers have shown Ferulic acid to have antibacterial, anti-inflammatory, hepatoprotective, neuroprotective, anticarcinogenic, antidiabetic, anticholesterolemic, UV-protective, and radioprotective properties. It is also recognized that most of ferulic acid's pharmacological activities and capacity to disrupt free radical chain reactions are closely associated [27]. Lin et al. [28] revealed that ferulic acid can be utilized as an addition in sunscreen lotions on the market to boost the skin's and hair's protection from light and to prevent early and natural aging.

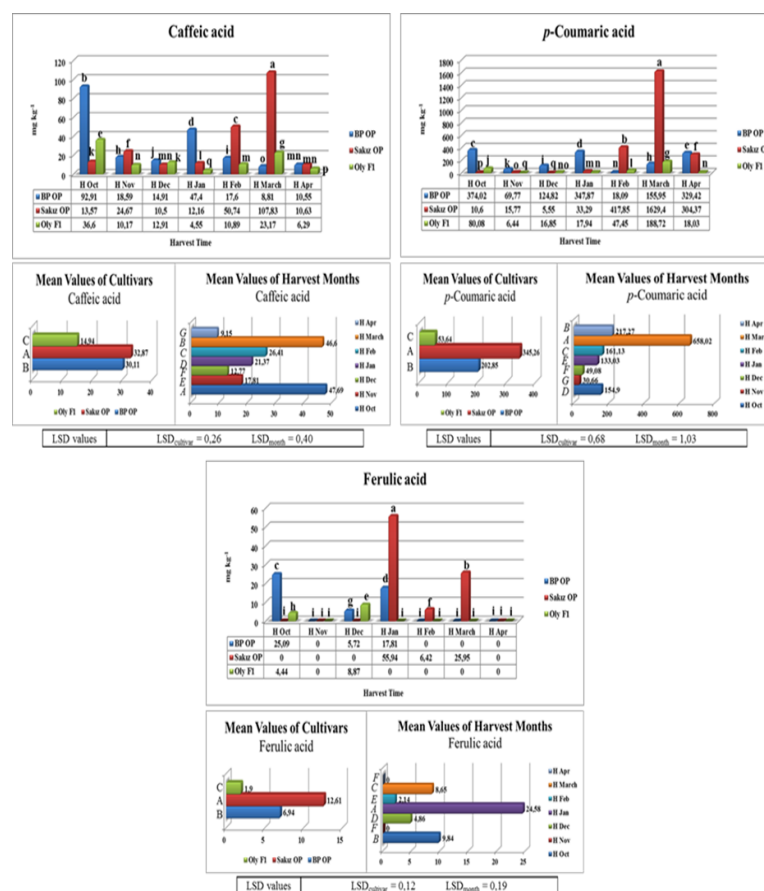


Fig. 3. Caffeic acid, *p*-coumaric acid, and ferulic acid values for cultivars based on harvested months *H Oct: Harvest time on October; H Nov: Harvest time on November; H Dec: Harvest time on January; H Feb: Harvest time on February; H March: Harvest time on March; H Apr: April. **Different letters show that the mean difference is statistically significant at P≤0.05.

Narirutin

The bioactive substance narirutin was also tested in the present research. Concerning cultivars and leaves harvest months, narirutin amounts ranged from 0 to 685,56 mg kg⁻¹. In March, the greatest level of narirutin was found in Sakız OP. According to Lombardo et al. [3], phenolic components accumulate in different parts of the artichoke depending on the genotype. The narirutin compound was not detected at all in the flowering phase, but it was detected at 586 mg kg⁻¹ in the leaves Lombardo et al. [3] was reported in the present research.

Luteolin and Luteolin 7-O-glucuronide

There were statistical differences in accumulated luteolin and luteolin 7-O-glucuronide levels between cultivars and months. As a result, the highest levels of luteolin and luteolin 7-O-glucuronide in Sakız OP were reported in March (200,33 mg kg⁻¹ and 3923,66 mg kg⁻¹, respectively). Among basic flavonoids, luteolin, apigenin, and glycosides are the most commonly found bioactive compounds in artichoke leaves and heads [13, 25]. According to Pandino et al. [4], luteolin in artichoke dominated more than other flavonoids. According to Nouraei et al. [16], the amount of luteolin was the lowest component in comparison to other components (53 mg kg⁻¹), excluding apigenin (13 mg kg⁻¹).

Apigenin and Apigenin 7-O-glucuronide

Regarding apigenin levels, the Sakız OP cultivar was also the best. Apigenin accumulation peaked in April with 1851,17 mg kg⁻¹, while apigenin 7-O-glucuronide accumulation peaked in March with 167,46 mg kg⁻¹. According to Nouraei et al. [16], apigenin levels were identified at a very low level (13 mg kg⁻¹), and this value dropped even more under stress conditions. On the other hand, Lombardo et al. [3] found that the level of apigenin 7-O-glucuronide in the leaves of the cultivars they studied was rather low (82 mg kg⁻¹). The researchers also stated that the genotype that demonstrated significant levels of apigenin and its derivatives accumulation (1207 mg kg⁻¹) might be employed as an apigenin donor in future studies and examined for this purpose in breeding programs. Apigenin and apigenin 7-O-glucuronide as flavonoids protect plants against UV light-induced photooxidative damage [29]. UV light with component B in the wavelength range of 280-320 nm can be quite harmful. Because leaves are the sections of the plant that are most exposed to the sun's rays, the plants activate enzymes that promote flavonoid biosynthesis rather than those that promote caffeoylquinic acid biosynthesis [13, 30]. As a result, flavonoids accumulating in plant tissues serve as a shield, helping to protect plants from harmful radiation [29]. Flavonoids, particularly luteolin and apigenin, have different pharmacological properties. In addition to its antibacterial properties, luteolin has recently gained attention for its ability to inhibit cholesterol production and bile secretion [4, 31, 32]. Apigenin is a compound found in several vegetables that could be useful in a variety of pharmacological purposes [4].

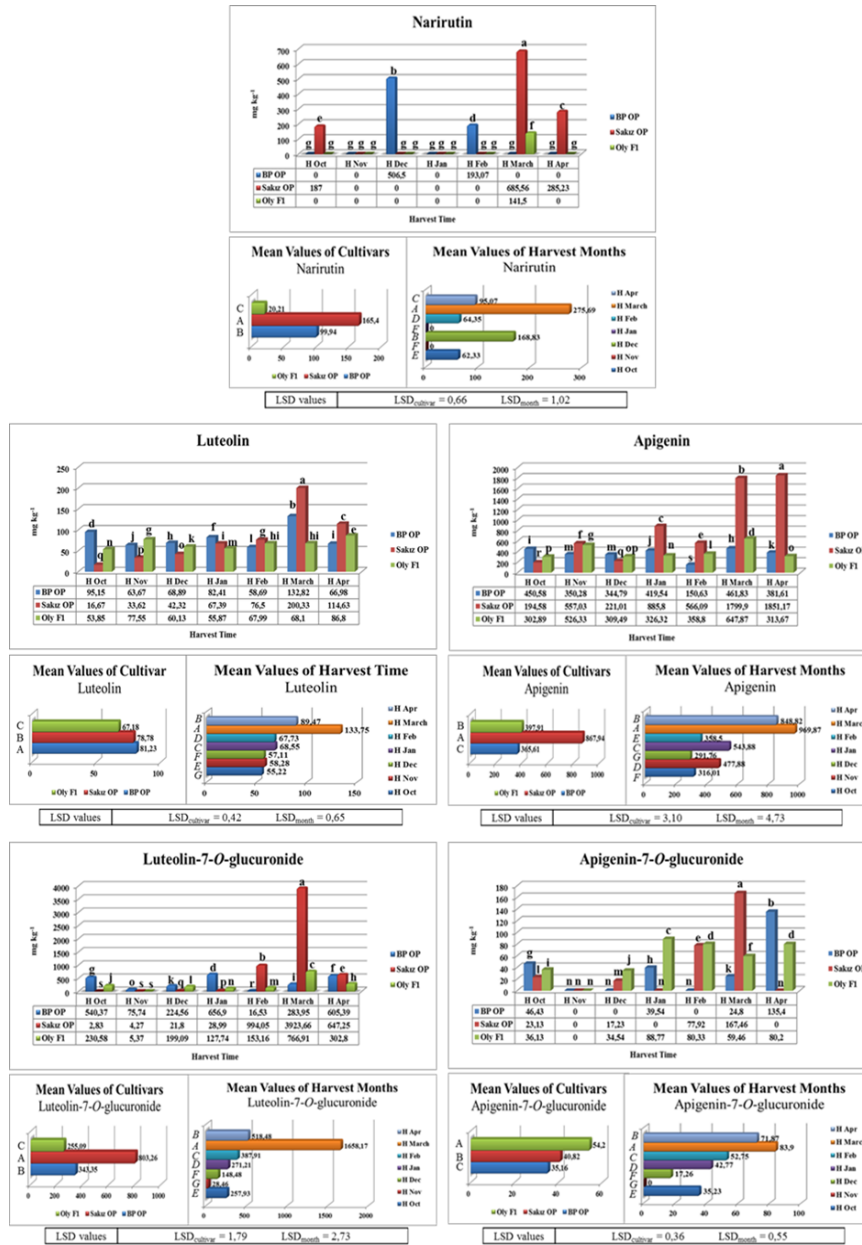


Fig. 4. Flavonoid values for cultivars based on harvested months

*H Oct: Harvest time on October; H Nov: Harvest time on November; H Dec: Harvest time on January; H Feb: Harvest time on February; H March: Harvest time on March; H Apr: April. **Different letters show that the mean difference is statistically significant at $P \leq 0.05$.

CONCLUSION

The current study demonstrated that bioactive compound accumulation levels vary depending on cultivars and months. Regarding assessed compounds, March was the most promising of the months, and Sakız OP cultivar took the lead over other cultivars regarding bioactive compounds examined. Except for ferulic acid (January) and apigenin (April), Sakız OP cultivar and March are the best choices for taking advantage of the current study's findings. Findings also clearly revealed that the leaves should not be considered as waste material and should not be discarded due to their potential for nutraceutical and pharmacological research and industries.

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