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Research Article

Determination of phenolic compounds in *Nasturtium Officinale* by LC-MS / MS using different extraction methods and different solvents

Leyla ERCAN[1]* Mehmet DOĞRU[2]

[1]*Mardin Artuklu University Central Research Laboratory Application and Research Center, 47000, Mardin, Türkiye*

[2]*Dicle University, Faculty of Ziya Gökalp Education, Dicle University, 21280, Diyarbakır, Türkiye*

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*****Corresponding author e-mail: leylaercan@artuklu.edu.tr

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ABSTRACT

This study aimed to determine the phenolic compound contents of *Nasturtium officinale (N. officinale)* extracts prepared with water, methanol, ethanol, and chloroform, as well as extracts prepared by evaporation and lyophilization, and parts of *N. officinale* by LC-MS/MS (Liquid Chromatography-Mass spectrometry/Mass spectrometry). The results obtained not only contribute to knowledge about the benefits of *N. officinale* but also show the effect of different solvents and different extraction methods on the determination of phenolic compounds. In addition to these results, the importance of the cold chain in the determination of some phenolic compounds has also been demonstrated. While it is observed that the number of phenolic components obtained from the extracts prepared with methanol and ethanol is high; It is observed that some phenolic compounds such as quinic acid, fumaric acid, aconitic acid, and p-coumaric acid dissolve very well in water and temperature is important.

Keywords: Phenolic components, LC-MS/MS, *Nasturtium officinale*, quinic acid, extraction

1. INTRODUCTION

N. officinale (watercress) is a plant from the Brassicaceae family.[1] The Brassicaceae family includes edible plant species rich in phenolic compounds that may benefit health.[2,3]. There are many studies on the health benefits of watercress.[4] *N. officinale* is considered a valuable traditional medicinal plant due to its many health-beneficial components such as vitamins, carotenoids, and glucosinolates.[5,6] In addition, *N. officinale* is popularly used as an anti-inflammatory, and low-dose hydrophilic extract has been reported to prevent kidney stone formation in rats.[7,8] Such studies on plants have led to research that allows to reveal of the bioactive components of plants and the factors that affect them.[9] It has become necessary to investigate the phenolic component content of *N. officinale*, whose benefit has been proven in all these studies. Numerous studies have been carried out showing that plant-derived phenolic compounds may have antiallergic, anti-inflammatory, antidiabetic, antimicrobial, and antiviral properties and may have protective effects on cancer, diabetes mellitus, osteoporosis, and neurodegenerative diseases.[10–16] However, the most appropriate methods for determining these phenolic compounds in plants are being investigated.

Chromatographic methods are mostly used to determine the phenolic component content.[17,18] Recently, research has been carried out to simultaneously reveal more phenolic compound content and develop more efficient analysis methods.[17,19] In these studies, it is aimed to find more efficient analytical methods and extraction methods. Especially with devices such as HPLC, and LC-MS/MS, the effect of solvents on phenolic component analysis is being investigated.[18,20].Due to the health benefits of phenolic compounds and their wide range of uses, phenolic compound analyses in plants and fruits are intensively carried out.[12,13,21,22].

The goal of this study is to analyze the phenolic components of *N. officinale* utilizing various extraction techniques and solvents. Thus the phenolic components of *N. officinale* have been identified, and the effects of

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the extraction process and various solvents on the phenolic component analysis of *N. officinale* were examined, aiming to guide future research in this field.

2. MATERIALS AND METHODS

2.1. Materials

Herbal material was collected from its natural environment in Kayseri province in the spring season. The dried *N. officinale* was used by grinding. The plant samples were authenticated by Prof. Dr. Hasan AKAN. It is stored in herbarium number 6363 at Harran University. Of the chemicals used in the analysis, methanol and ethanol were purchased from Merck KGaA EMD Millipore Corporation (analytical purity, Germany), and chloroform (99 %, France) was purchased from Carlo Erba Reagents. In addition, ultrapure water was used in the experiments.

2.2. Methods

For each extract, 200 mL of solvent was added to 20 g of sample. Then stirred for 12 h at room temperature by a magnetic stirrer. The suspension was filtered with filter paper. The solids were extracted under the same conditions with 100 mL of the same solvent and filtered through a filter paper. The filtered extracts were filtered through filter paper after both extracts were combined. The aqueous extract was divided into two parts and the first extract was frozen by balloon in a deep freezer (-80 °C). Thus, with cold extraction, material loss due to temperature increase is prevented, and at the same time the sample is made suitable for drying in the lyophilizer. Since the drying process in the lyophilizer takes place by sublimation, the sample should be left in the lyophilizer in the frozen state. Frozen extracts were lyophilized to dryness at a pressure of 50 mbar pressure. The other half was evaporated in the evaporator at 40 °C and 1 mbar pressure. The methanol, ethanol, and chloroform extracts were prepared by the same method, and the solvents were removed in the rotary evaporator at 35 °C, 150 mbar pressure. 10 mg of each extract was dissolved in 10 mL of solvent for analysis.[23] In LC-MS/MS, the phenolic components of *N. officinale* extracts prepared with different extraction methods and different solvents were determined using a method developed by M. Abdullah Yilmaz, which allows simultaneous analysis of 53 phenolic compounds. [18] In this method, a reverse phase C18 analytical column was used in the UHPLC (Nexera model, Shimadzu brand). Gradient elution used two solutions: A (water + 0.1 % formic acid + 5 mM ammonium formate) and B (methanol + 0.1 % formic acid + 5 mM ammonium formate). The gradient profile was: 20-100 % B (0-25 min), 100 % B (25-35 min), and 20 % B (35-45 min).[18]

3. RESULTS AND DISCUSSION

In total ion chromatograms, *N. officinale* extracts gave signals for numerous identifiable compounds. As can be seen from the chromatograms given below, different solvents are; chloroform extract (Figure 1), ethanol extract (Figure 2), methanol extract (Figure 3), and different methods; As a result of the analyses using evaporated extract (Figure 4), lyophilized extract (Figure 5), lyophilized plant stem extract (Figure 6), lyophilized plant leaf extract (Figure 7), the number and amount of phenolic compounds showed significant differences. A quantitative comparison of phenolic components in *N. officinale* extracts and parts of *N. officinale* is given in Table 1. When the results were examined, it was seen that alcoholic extracts gave better results than water and chloroform in terms of the number of phenolic components, as seen in Figure 8. Methanol preferably extracted protocatechuic acid, caffeic acid, rosmarinic acid, naringenin, and luteolin phenolic compounds (Table 1). In contrast, ethanol was superior at extracting the phenolic compounds rutin, hesperidin, and nicotiflorin. Although chloroform extract gave better results in terms of vanillin, coumarin, and chrysin phenolic compounds, it did not give very efficient results considering the number of phenolic components.

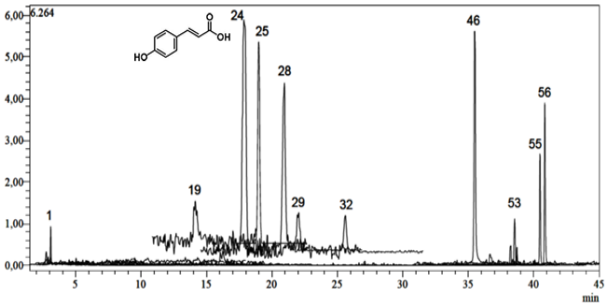

Figure 1. Total ion chromatogram (TIC) of the plant extract prepared with chloroform.

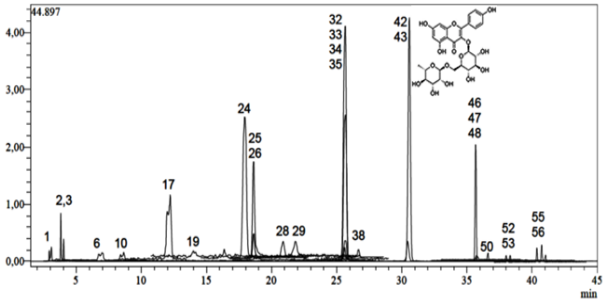

Figure 2. Total ion chromatogram of the plant extract prepared with ethanol.

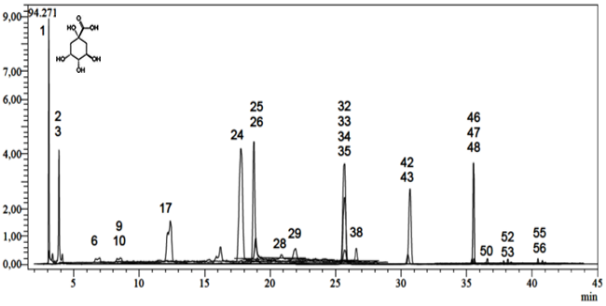

Figure 3. Total ion chromatogram of the plant extract prepared with methanol.

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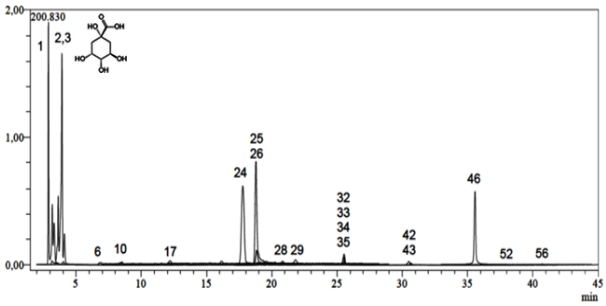

Figure 4. Total ion chromatogram of the evaporated extract of the plant prepared with water.

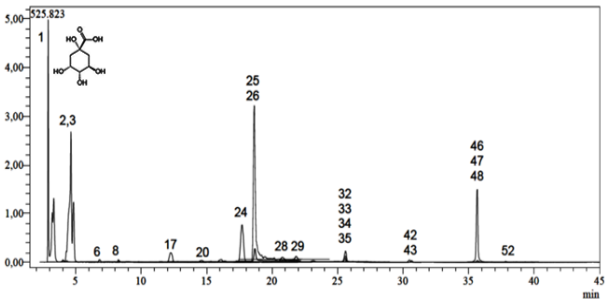

Figure 5. Total ion chromatogram of the lyophilized extract of the plant prepared with water.

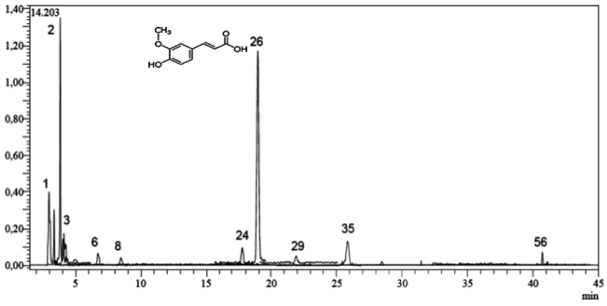

Figure 6. Total ion chromatogram of the lyophilized extract of the plant stem prepared with water.

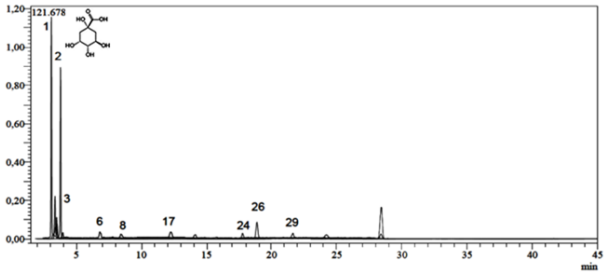

Figure 7. Total ion chromatogram of the lyophilized extract of the leaf of the plant prepared with water.

When the results were examined, it was seen that alcoholic extracts gave better results than water and chloroform in terms of the number of phenolic components, as seen in Figure 8. Methanol preferably extracted protocatechuic acid, caffeic acid, rosmarinic acid, naringenin, and luteolin phenolic compounds (Table 1). In contrast, ethanol was superior at extracting the phenolic compounds rutin, hesperidin, and nicotiflorin. Although chloroform extract gave better results in terms of vanillin, coumarin, and chrysin phenolic compounds, it did not give very efficient results considering the number of phenolic components.

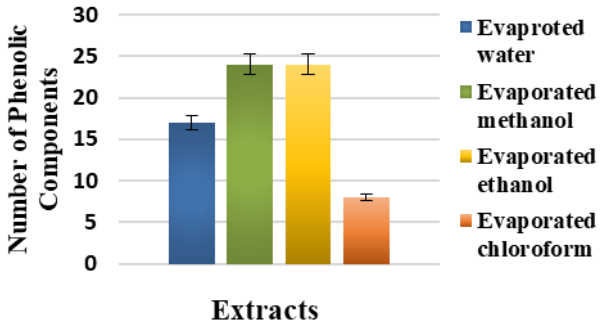

Figure 8. Comparison of different extracts of N. officinale in terms of the number of phenolic compounds.

According to the comparison of the four most abundant compounds (quinic acid, fumaric acid, p-coumaric acid, aconitic acid) in the leaf and stem parts of N. officinale, the leaf part gave more productive results (Figure 9).

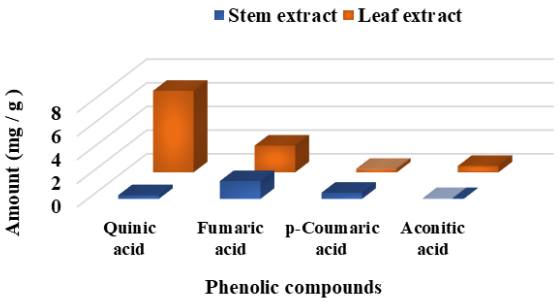

Figure 9. Comparison of leaf and stem extracts in terms of the four most abundant phenolic compounds in N. Officinale.

When the results were examined in terms of the amount of phenolic compounds it was seen that some phenolic compounds were obtained more than others in the water. Quinic acid, aconitic acid, fumaric acid, p-coumaric acid, ferulic acid, astragalin, kaempferol, isoquercitrin, and syringic aldehyde were better recovered in water extracts (Table 1). When the lyophilized and evaporated extracts were examined, it was concluded that cold extraction was much more efficient (Figure 10).

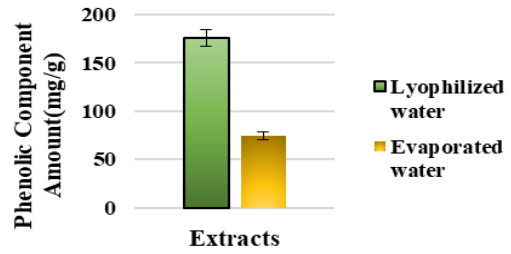

Figure 10. The effect of temperature on the amount of phenolic compounds according to phenolic content results.

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Table 1. Quantitative comparison of phenolic compounds in different extracts of *N. Officinale*.

				Analyte concentration (mg / g extract)						
No	**Ref. No**	**Analyte**	**RT[a]**	**Lyophilized Water**	**Evaporated Water**	**Evaporated Methanol**	**Evaporated Ethanol**	**Evaporated Chloroform**	**Lyophilized Stem Extract**	**Lyophilized Leaf Extract**
1	1	Quinic acid	3.0	149.917	58.748	8.429	0.834	0.040	0.314	6.892
2	2	Fumaric acid	3.9	7.776	5.714	5.299	2.049	---	1.504	2.261
3	3	Aconitic acid	4.0	4.439	1.693	0.793	0.068	---	0.066	0.539
4	6	Protocatechuic acid	6.8	0.125	0.192	0.247	0.173	---	0.023	0.035
5	8	Gentisic acid	8.3	0.106	---	---	---	---	0.033	0.065
6	9	Chlorogenic acid	8.4	---	---	0.044	---	---	---	---
7	10	Protocatechuic aldehyde	8.5	---	0.029	0.037	0.036	---	---	---
8	17	Caffeic acid	12.1	0.350	0.046	0.372	0.275	---	---	0.017
9	19	Vanillin	13.9	---	---	---	0.071	0.072	---	---
10	20	Syringic aldehyde	14.6	0.034	---	---	---	---	---	---
11	24	p-Coumaric acid	17.8	6.832	5.198	4.418	2.722	0.617	0.517	0.297
12	26	Ferulic acid	18.8	2.998	1.390	2.890	0.773	---	0.155	1.024
13	28	Coumarin	20.9	0.011	0.010	0.020	0.040	0.055	---	---
14	29	Salicylic acid	21.8	0.037	0.026	0.051	0.033	0.011	0.009	0.009
15	33	Rutin	25.6	0.541	0.273	3.686	4.063	---	---	---
16	34	Isoquercitrin	25.6	1.117	0.699	0.510	0.400	---	---	---
17	35	Hesperidin	25.8	0.396	0.200	2.115	2.438	---	0.043	0.400
18	38	Rosmarinic acid	26.6	---	---	0.162	0.087	---	---	---
19	42	Astragalin	30.4	0.403	0.242	0.348	0.363	---	---	---
20	43	Nicotiflorin	30.6	0.318	0.124	3.025	4.566	---	---	---
21	47	Quercetin	35.7	0.089	---	0.026	0.020	---	---	---
22	48	Naringenin	35.9	0.004		0.025	0.011	---	---	---
23	50	Luteolin	36.7	---	---	0.010	0.007	---	---	---
24	52	Kaempferol	37.9	0.041	0.014	0.021	0.035	---	---	---
25	53	Apigenin	38.2	---	---	0.003	0.004	0.001	---	---
26	55	Chrysin	40.5	---	---	0.003	0.006	0.006	---	---
27	56	Acacetin	40.7	---	0.006	0.017	0.023	0.025	0.003	-----

The No is sequential according to the retention time and the Ref No is related to the data peak number in chromatograms.

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When the lyophilized and evaporated extracts were compared, the lyophilized extract gave much better results than the evaporated extract in terms of the number of phenolic components and the amounts of phenolic compounds (Figure 11). Leaves were richer in phenolic content than stems, except for p-coumaric acid. The lyophilized sample of the aqueous extract was richer in phenolic compounds than the others.

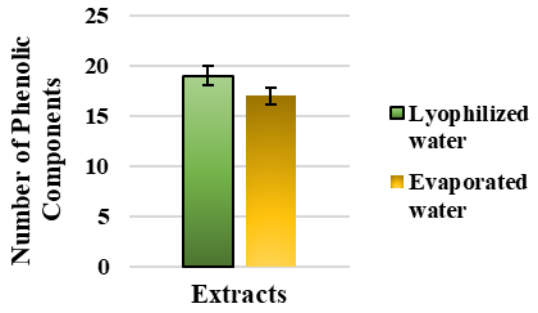

Figure 11. Effect of temperature on the number of components.

Both cold extraction methods and hot extraction methods can affect the analysis of phenolic compounds. In addition, the choice of solvents used in the extraction may affect the phenolic component analysis differently depending on the chemical structure of the phenolic components contained in the plant. In this study, low-temperature evaporation compared to freeze-drying reduced the recovery of phenols such as gentisic acid, syringic aldehyde, quercetin, and naringenin. Even at low temperatures, these phenolic compounds are damaged by heat and move away from the environment. In other words, the cold chain gains importance in the determination of these phenolic compounds.

Quinic acid, fumaric acid, aconitic acid, and p-cumaric acid, on the other hand, were found to be significantly greater in aqueous solution compared to other extractions using water, methanol, ethanol, and chloroform as solvents. Although the solutions prepared with methanol and ethanol had similar results, a higher amount of phenolic content was observed in methanol compared to ethanol. It was concluded that chloroform is not a suitable solvent for determining phenolic content. Although chloroform extract gave good results in terms of phenolic compounds such as vanillin, coumarin, and chrysin, it was not suitable for the recovery of many phenolic compounds. While alcoholic solvents provide a higher number of phenolic compounds in the determination of phenolic compounds, the recovery of phenolic compounds such as quinic acid and aconitic acid in an aqueous solution is twice as high. It has been revealed that *N. officinale* is particularly rich in quinic acid. *N. officinale* is also rich in aconitic acid, fumaric acid, p-coumaric acid, ferulic acid and isoquercitin. It is clear from a comparison of the plant's leaves and stems that the leaf contains a greater proportion of phenolic compounds than the stem. But p- coumaric acid was found more in the stem part of the plant. Low temperature is an important factor for the recovery of quinic acid, fumaric acid, aconitic acid, p-coumaric acid, ferulic acid, isoquercitrin, astragalin, nicotiflorin, quercetin, gentisic acid, syringic aldehyde, naringenin, kaempferol, caffeic acid. Caffeic acid and ferulic acid are also affected by the type of solvent. The polarity of the solvent also plays a role in increasing the solubility of phenolic compounds and antioxidant compounds. [24,25]

The amount of coumarin increased from a polar to a non-polar solvent. Quinic acid, fumaric acid, aconitic acid, p-coumaric acid, isoquercitrin, astragalin, quercetin are better recovered in polar solvent. In particular, low temperature is very important for the recovery of gentisic acid, syringic aldehyde phenolic components. According to these results, *N. officinale* can be described as a plant rich in phenolic compounds. Previously, 14 phenolic compounds, including proanthocynidin B1, sinapic acid, caftaric acid, and quinic acid derivatives, were detected in the 60% methanol extract of *N. officinale* leaves, and 20 phenolic compounds were detected in the 60% methanol extract of the root part. [26] Another study detected 12 phenolic compounds in *N. officinale* leaves during frying in sunflower oil. [27] In this study, 27 phenolic compounds were detected in different extracts. The freshness of the sample utilized, the extraction technique, the habitat in which the plant grows, as well as differences in the standard phenolic chemicals used, may all have an impact on these results. However, all these studies are important to reveal the use and properties of *N. officinale*. There are many publications regarding the benefits of these phenolic compounds. We can summarize some of them as follows. Ouinic acid esters exhibited anti-inflammatory activity.[10]

Chlorogenic acid, quinic acid, and caffeic acid have been experimented with to evaluate anti-HBV activities in hepatitis B virus infection, and three compounds have been found to inhibit HBsAg production as well as HBV-DNA replication. [28] The effects of quercetin and quinic acid on the liver, kidney, and pancreatic tissues were analyzed in mice with diabetes mellitus, and these results reported that quercetin and quinic acid have synergistic effects on hyperglycemia, hyperlipidemia, and insulin resistance. [29] Aconitic acid can be used to synthesize biodegradable polyesters for tissue engineering applications. [30] Fumaric acid is a dicarbonic acid. [31] Initially used therapeutically in psoriasis, fumaric acid has immunomodulatory and neuroprotective effects. [32] In addition, fumaric acid is one of the drugs approved for MS patients. [33] The antioxidant activity of p-coumaric acid in reducing oxidative stress and inflammatory reactions has been reported.[34] It has been reported that hesperidin has a lot of benefits such as antioxidant, antimicrobial, anticancer, anti-inflammatory, and antidiabetic properties, and also limits the proliferation of various cancer cells such as pancreatic, skin, breast, liver, colon, and lung. [35–37]

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Analyzing different solvents may be beneficial for the detection of different phenolic compounds. However, the disadvantage of this method is that it is time-consuming. For this reason, it is advisable to experiment with emulsions that combine several solvents. When we evaluated all these results, it was found that *N. officinale* contains many valuable phenolic compounds. It has been revealed that the extraction method and the properties of the solvent used are important in revealing phenolic compounds. The results of this research can be a guide for the method and solvent in phenolic compound analysis, as well as for research that can be done with quinic acid or *N. officinale*.

3.1. Statistical analysis

In the one-way ANOVA statistical analysis test between evaporated water, evaporated methanol, evaporated ethanol, and chloroform there was a significant difference between groups between the evaporated water extract and the methanol, ethanol, and chloroform extracts. That is, the significance was found to be 0.05>p. Also, there is a significant difference between the lyophilized sample and the evaporated sample (0.05>p).

4. CONCLUSIONS

In this study, *N. officinale* was examined in terms of phenolic component, 27 phenolic compounds were detected in different extracts, and it was found that the main phenolic component was quinic acid. Thus, it has been shown that *N. officinale* is an important source in studies that can be done with quinic acid. In addition, as a result of the experiments, the importance of the cold chain in extraction was also revealed. It was determined that the aqueous extract, the solvent of which was evaporated at low temperature, lost some phenolic compounds such as gentisic acid, syringic aldehyde, quercetin, and naringenin. In addition to all these, it has been revealed that the polarity of the solvent used is very important in the analysis of phenolic compounds.It has been emphasized that the method and solvent used in the analysis are very important in determining the phenolic component content, which can vary according to the environment in which the plant is grown, the freshness of the plant, the drying method, and storage conditions.

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Conflict of interest

The authors declare that there is no conflict of interest.

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