PHYTOCHEMICAL ANALYSIS OF ACTIVE PHENOLIC COMPOUNDS IN SOME PLANTS USED AS TRADITIONAL FOLK DRUGS FOR CANCER AND LITERATURE REVIEW OF THEIR ANTI-CANCER EFFECTS

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Abstract. In this study, the composition of the phenolic compounds for *Malva neglecta*, *Nerium oleander*, *Quercus brantii* and *Vitis vinifera*, that are registered as traditional folk remedy used for cancer during the ethnobotanical surveys conducted in Türkiye, were analyzed in phytochemical terms. Such analysis revealed very significant ($p < 0.01$) content of the phenolic compounds in the chemical composition of the plants, and then the effect sizes (η^2) thereof were determined. Thus, the anticancer effect potentials of the plants were established in line with the chemotherapeutic activities of the phenolic compounds, the probable efficacy of which has been demonstrated in the content of the plants, as confirmed by the literature review. The plants, that presented the highest anti-carcinogenic activity potential on 12 established types of cancer, were: *Q. brantii* in bladder cancer*; M. neglecta*, *N. oleander*, *Q. brantii* and *V. vinifera* in breast cancer; *Q. brantii*, and *V. vinifera* in cervical cancer; *Q. brantii* and *V. vinifera* in colorectal cancer; *N. oleander* in chronic myeloid leukemia; *Q. brantii* in glioblastoma multiforme; *M. neglecta* and *V. vinifera* in liver cancer; *M. neglecta, Q. brantii*, and *V. vinifera* in lung cancer; *Q. brantii* in mesothelioma; *V. vinifera* in ovarian cancer; *M. neglecta,* and *Q. brantii* in prostate cancer; *M. neglecta* in skin cancer.
Keywords: *cancer, chemotherapeutic agent, ethnobotany, folk medicine, medicinal plants*

Abbreviations: gr = Gram; HCC = hepatocellular carcinoma; LC-MS/MS = Liquid chromatography-mass spectrometry; LOD = limit of detection; LOQ = limit of quantification; MANOVA = multivariate analysis of variance; m/z = mass/load; mL = milliliter; µg/L = microgram/liter; PhC = phenolic compound; Ppb = parts per billion (microgram (phenolic compound)/liter (extract + solvent)); Ppm = parts per million (milligram (phenolic compound)/liter (extract + solvent)); Fl = flower; Fr = fuit; Lf = leaf

Introduction

Cancer is a type of disease that has extremely high rate of mortality with increasing worldwide incidence also, it is ranked second amongst the leading causes of death in the world closely following heart diseases (Arı et al., 2017; Ayaz et al., 2019). There are more than 100 types of cancer known to take effect in the human body. Nowadays, majority (more than 60%) of the cancer drugs are produced from natural compounds. Therefore, plant secondary metabolites are of paramount importance in cancer treatment.

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Of the phytochemicals available in the plants, particularly the phenolic compounds represent the plant secondary metabolites that feature anticancer effects on different cancer cells as anticancer agents and that have been studied most extensively (Baykara, 2016; Ülger and Ayhan, 2020). With approximately 200,000 isolated so far, the phenolic compounds are contemplated to be the natural sources of the antioxidant demand by the human metabolism, and constitute one of the core groups of the pharmacologically active compounds in the content of the plants. In addition to the antioxidant properties thereof, the phenolic compounds further feature anticarcinogenic and antimutagenic properties, and find application in the pharmaceutical industry (Demir and Akpınar, 2020).

In this study, the anticancer potentials of several plants used as traditional folk remedy for cancer in Türkiye were investigated by determining active compounds that feature chemotherapeutic properties on various types of cancer. This study is expected to act as reference for any future experimental studies (in vitro and in vivo) and for advanced pharmacological studies in the field of cancer while revealing the abundance of the phenolic compounds at such plants in phytochemical terms.

Materials and methods

Plant material

Malva neglecta, Nerium oleander, Quercus brantii and *Vitis vinifera* constitute the material of this study. Öztürk et al. (2018) reported that *M. neglecta, N. oleander, V. vinifera*, and some *Quercus* species are officially took part as medicinal plants and drugs in Turkish pharmacopoeia. When establishing the plant materials, the species registered during the ethnobotanical surveys in Türkiye and most frequently used as anticancer agents by the folk were picked. Plants were collected from the region where it was recorded that they were used as folk medicine against cancer from the ethnobotanical studies conducted in the Southeastern Anatolia Region (Türkiye). *Malva neglecta, Quercus brantii*, and *Vitis vinifera* were collected from the Mardin region and *Nerium oleander* from the Adıyaman region in 2022 during their flowering and fruit periods. It was elaborated to pick plants from distinct families in order ensure differentiate the chemical compositions as far as possible. The laboratory studies conducted were based on the parts of the plants (flower, fruit and leaf) used as anticancer agents in ethnobotanical terms and the usage patterns thereof. The publication named the Flora of Turkey (Davis et al., 1967, 1978, 1982) was used as reference for identifying the plants.

Solvents and preparation of plant extracts

Extraction process was performed in 3 distinct solvents for each plant part. Approximately 99% ethanol, 99% methanol and distilled water were used as solvent. The ethanolic, methanolic and distilled water extracts (1 g (plant part)/100 mL (solvent)) obtained through the infusion method were subjected to phytochemical analyses.

LC-MS/MS characterization, profile and analytical parameters of the method

The analysis was performed at the ppb level, and Shimadzu model LC-MS/MS-8030 was used for the analysis. The key analytical parameters of the phenolic compounds profiled using the LC-MS/MS method as determined by the said device are provided in *Table 1*.

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Table 1. *Analytical parameters of LC-MS/MS method*

Compounds	Regression equation	R2	RT (min)	Parent ion (m/z)	LOD (µg/L)	LOQ (µg/L)	RSD (%)
Caffeic acid	y = 1216.32x- 5693.93	0.9877	2.83	179.0> 135.00	2.57	9.58	0.14
Catechin hydrate	y=1699.08x+1652.81	0.9992	2.53	291.00> 139.10	2.05	6.84	0.04
Ellagic acid	y=18.8408x+911.550	0.9967	3.68	301.10> 228.90	237.42	791.40	0.23
Fumaric acid	y=100.917x- 1701.62	0.9989	0.80	115.20> 71.10	7.91	26.38	0.13
Gallic acid	y=302.567x- 1984.34	0.9951	1.57	169.10> 124.90	3.92	13.06	0.21
Hydroxycinnamic acid	y=328.527x- 10764.7	0.9995	3.48	162.90> 119.00	7.33	24.44	0.40
Naringenin	y=700.801x-26469.0	0.9997	3.95	271.00> 150.90	68.43	228.12	0.07
Quercetin	y=150.003x- 391.549	0.9997	3.89	301.10> 150.90	7.79	25.98	0.19

Data analysis

The data were analyzed using SPSS 27 packaged software according to the statistical methods. The population of the study used in determining the statistical methodology consists of 36 extracts obtained from 3 plant parts (flower, fruit and leaf) from 4 plants using 3 solvents (ethanol, methanol and distilled water). The analysis represents a parametric statistical study based on numerical data from the chromatography. The data were analyzed using MANOVA and LSD tests, and described and interpreted using the tables. Distribution of the data indicates that some variables fail to satisfy the assumption on homogeneous distribution. Normality was assumed for the data wherein the factor group failed to present normal distribution over the dependent group, and the data were analyzed accordingly. The analyses revealed the degree of differentiation for the chemical contents of plant parts in terms of phenolic compounds, and the clinical significance was established. It was assumed that the level $p < 0.01$ refers to very significant difference, and the level $p < 0.05$ refers to significant difference.

Results

Use of the plants as a traditional folk remedy for cancer

The ethnobotanical surveys conducted in Türkiye formed the basis for identifying the plants used as a traditional folk remedy for cancer. Ultimately, the 4 species registered in 16 ethnobotanical surveys for their use as traditional folk remedy were identified for this study (*Table 2*).

Phytochemical analysis

In this study, ethanolic, methanolic and distilled water extracts of the plant parts (flower, fruit and leaf) were analyzed for phenolic compounds at the level of milligrams (ppm). Eight phenolic compounds were identified in the plant extracts. The quantities of said phenolic compounds and the plant parts containing thereof are indicated in *Table 3* with the corresponding solvent.

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Table 2. *Four selected plants used as a traditional folk remedy for cancer*

Scientific names	Family	Common names	Region	References
Malva neglecta	Malvaceae	Mallow	Mediterranean	Yeşilada et al., 1995
			Eastern Anatolia	Nadiroğlu et al., 2019
			Central Anatolia	Günbatan et al., 2016
			Black Sea	Karcı et al., 2017
			Marmara	Yeşilyurt et al., 2017
			Southeastern Anatolia	Kılıç, 2019
Nerium oleander	Apocynaceae	Oleander	Mediterranean	Akaydın et al., 2013
			Aegean	Gürdal and Kültür, 2013; Sargın et al., 2013; Sargın et al., 2015
			Black Sea	Karcı et al., 2017
			Southeastern Anatolia	Gençay, 2007; Gelse, 2012
Quercus brantii	Fagaceae	Black oak	Southeastern Anatolia	Kılıç, 2019
Vitis vinifera	Vitaceae	Vitis	Aegean	Deniz et al., 2010; Sargın et al., 2015
			Central Anatolia	Günbatan et al., 2016
			Marmara	Güneş, 2017
			Southeastern Anatolia	Yiğit, 2014; Kılıç, 2019

Statistical analysis

The plants were statistically evaluated in terms of their phenolic compound content. When the effect value is considered in general, the fact that the difference in chemical composition of the plants presents significant effect ($0.01 \leq \eta^2$) in all assumptions of the MANOVA test according to the phenolic compound variations determined at the plants under the study is shown in *Table 4*.

The effect size value (Partial Eta Squared) indicates the extent of the effect that the factor group has on the dependent variable. The effect size value (η^2) is considered as small effect if $0.01 \leq \eta^2 \leq 0.06$, as medium effect if $0.06 \leq \eta^2 \leq 0.14$, and as large effect if $0.14 \leq \eta^2$ (Cohen, 1988; Pallant, 2005). Considering the effect size for the clinical trials reveals that the value $\eta^2 \geq 0.5$ refers to clinical significance (Kirby et al., 2002; Süt, 2011). The review on whether the phenolic compounds variations determined in the plants in the study induce any significant difference on the content of the plants indicated that the ellagic acid presented large effect size at the level of $\eta^2 \geq 0.5$, thus expressing clinical significance; while catechin hydrate, fumaric acid, gallic acid and quercetin presented large effect size ($0.14 \leq \eta^2$) (*Table 5*).

It is observed that the data fail to satisfy the multi-normality distribution, one of the core assumptions of the LSD test. However, the assumption most widely recognized in this respect is the assumption proposed by George and Mallery (2010), which states that the variables actually have normal distribution if the Kurtosis and Skewness values of the variables are in the range of + 2 to -2. In this study, the Kurtosis and Skewness values of the variables are observed to be in the range of + 2 to -2; thus, it is assumed that the data actually present normal distribution. The analysis of the data using the LSD test indicated that the plants presented significant difference ($p < 0.05$) from each other in terms of the phenolic compounds. The relationship between the plant with the highest content concentration in terms of respective phenolic compound and the other plants, as revealed by the LSD test, is shown in *Table 6*.

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Table 3. *Amounts of phenolic compounds determined in plants*

Phenolic compound	Scientific name of plant	Part of plant	Solvent	Quantity (ppm)
Caffeic acid	*Malva neglecta*	Flower	Water	1.02
Catechin hydrate	*Quercus brantii*	Leaf	Methanol	1.01
	Vitis vinifera	Flower	Ethanol	1.07
			Methanol	1.81
			Water	3.45
		Fruit	Ethanol	14.13
			Methanol	20.33
			Water	12.64
Ellagic acid	*Quercus brantii*	Flower	Ethanol	10.71
			Methanol	20.49
		Fruit	Ethanol	12.89
			Methanol	26.60
			Water	43.30
		Leaf	Ethanol	3.46
			Methanol	8.94
			Water	6.34
	Vitis vinifera	Flower	Ethanol	8.53
			Methanol	8.84
			Water	30.05
		Fruit	Methanol	1.59
Fumaric acid	*Malva neglecta*	Flower	Ethanol	1.07
			Methanol	2.95
			Water	3.45
		Fruit	Ethanol	2.71
			Methanol	4.15
			Water	6.99
		Leaf	Methanol	1.37
			Water	1.48
	Nerium oleander	Flower	Methanol	1.16
	Quercus brantii	Flower	Methanol	2.48
			Water	1.23
	Vitis vinifera	Flower	Methanol	1.01
		Fruit	Ethanol	1.28
			Methanol	2.46
			Water	1.15
Gallic acid	*Quercus brantii*	Flower	Water	1.19
		Fruit	Methanol	5.78
			Water	18.57
		Leaf	Water	2.85
	Vitis vinifera	Flower	Water	1.41
Hydroxycinnamic acid	*Malva neglecta*	Flower	Water	1.85
Naringenin	*Nerium oleander*	Leaf	Ethanol	1.79
			Methanol	1.93
Quercetin	*Quercus brantii*	Flower	Methanol	2.45
			Water	1.64
		Leaf	Water	1.03
	Vitis vinifera	Flower	Ethanol	4.61
			Methanol	2.87
			Water	6.68
		Leaf	Water	1.21

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Table 4. *Results of the MANOVA test (general)*

Multivariate tests[a]							
Effect		Value	F	Hypothesis df	Error df	Sig.	Partial eta squared (η^2)
Parts of the plants	Pillai's trace	1.77	4.91	24	81	.000	.59
	Wilks' lambda	.05	5.14	24	73.10	.000	.61
	Hotelling's trace	5.22	5.15	24	71.00	.000	.63
	Roy's largest root	2.63	8.89[c]	8	27.00	.000	.72

[a]Design: Intercept + Plants
[c]The statistic is an upper bound on F that yields a lower bound on the significance level

Table 5. *Results of the MANOVA test (according to the dependent groups)*

Tests of between-subjects effects							
Source	Dependent variable	Type III sum of squares	df	Mean square	F	Sig.	Partial eta squared (η^2)
Plants	Caffeic_acid	.08	3	.02	1	.40	.08
	Catechin_hydrate	46.75	3	15.58	8.46	.00	.44
	Ellagic_acid	151.33	3	50.44	15.39	.00	.59
	Fumaric_acid	24.55	3	8.18	7.18	.00	.40
	Gallic_acid	15.63	3	5.21	3.69	.02	.25
	Hydroxycinnamic_acid	.11	3	.03	.66	.57	.05
	Naringenin	.33	3	.11	2.28	.09	.17
	Quercetin	16.66	3	5.55	3.54	.02	.24

Table 6. *Results of the LSD test*

LSD dependent variable	(I) Plant	(J) Plant	Mean difference (I-J)	Std. error	Sig.	95% confidence interval	
						Lower bound	Upper bound
Catechin hydrate	*Vitis vinifera*	*Malva neglecta*	2.66	.63	.00	1.36	3.96
		Nerium oleander	2.66	.63	.00	1.36	3.96
		Quercus branti	2.55	.63	.00	1.25	3.85
Ellagic acid	*Quercus branti*	*Malva neglecta*	5	.85	.00	3.26	6.73
		Nerium oleander	5	.85	.00	3.26	6.73
		Vitis vinifera	2.88	.85	.00	1.15	4.62
Fumaric acid	*Malva neglecta*	*Nerium oleander*	2.11	.50	.00	1.08	3.13
		Quercus branti	1.88	.50	.00	.86	2.91
		Vitis vinifera	1.55	.50	.00	.53	2.58
Gallic acid	*Quercus branti*	*Malva neglecta*	1.55	.55	.00	.41	2.69
		Nerium oleander	1.55	.55	.00	.41	2.69
		Vitis vinifera	1.44	.55	.01	.30	2.58
Quercetin	*Vitis vinifera*	*Malva neglecta*	1.66	.59	.00	.46	2.86
		Nerium oleander	1.66	.59	.00	.46	2.86
		Quercus branti	1.11	.59	.06	-.09	2.31

Literature review of anticancer effects of active phenolic compounds in the plants

A literature review was conducted so as to determine whether the phenolic compounds identified from the phytochemical analysis are active compounds in terms of anticancer effects, and the anticarcinogenic activities of said compounds on the types of cancer are shown in *Table 7*.

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Table 7. *Anticarcinogenic activities of the phenolic compounds on cancer types*

Phenolic compound	Cell/animal model	Cancer type	Anticarcinogenic activity	Reference
Caffeic acid	Primary tumors (Mice)	Lung cancer	Antiproliferative effect	Rocha et al., 2012; Pavlíková, 2023
	AH109A cell line	Liver cancer	Antiproliferative effect	
	T47D cell line	Breast cancer	Apoptotic effect	
	A431, CAL27, SKMEL5, SKMEL28 cell lines	Skin cancer	Apoptotic effect, antitumorigenic effect	Pavlíková, 2023
	PC3 cell line	Prostate cancer	Antiproliferative effect	Rocha et al., 2012
Catechin hydrate	MCF7 cell line	Breast cancer	Apoptotic effect	Alshatwi, 2010
	SiHa cell line	Cervical cancer	Antiproliferative effect, cytotoxic effect	Hazzani and Alshatwi, 2011
Ellagic acid	T24 cell line	Bladder cancer	Apoptotic effect	Li et al., 2005
	HCT116 cell line	Colorectal cancer	Antiproliferative effect	Yakobov et al., 2023
	MCF7 cell line	Breast cancer	Antiproliferative effect	
Fumaric acid	ICR mice	Liver cancer (HCC)	Anticarcinogenic effect	Akao and Kuroda, 1990
Gallic acid	A549 cell line	Lung cancer	Antiproliferative effect	Maurya et al., 2011; Wianowska and Olszowy-Tomczyk, 2023
	MCF-7 cell line	Breast cancer	Antiproliferative effect, apoptotic effect	Wang et al., 2014; Wianowska and Olszowy-Tomczyk, 2023
	H2452 cell line	Mesothelioma	Antiproliferative effect	Abotaleb et al., 2020
	U87 cell line	Glioblastoma multiforme	Apoptotic effect	
	SiHa cell line	Cervical cancer	Apoptotic effect	Abotaleb et al., 2020; Wianowska and Olszowy-Tomczyk, 2023
	DU145 cell line	Prostate cancer	Apoptotic effect	Abotaleb et al., 2020; Wianowska and Olszowy-Tomczyk, 2023
	HCT116 cell line	Colorectal cancer	Apoptotic effect	Abotaleb et al., 2020; Wianowska and Olszowy-Tomczyk, 2023
Hydroxycinnamic acid	DU145 cell line	Prostate cancer	Cytotoxic effect, apoptotic effect	Rocha et al., 2012
Naringenin	K562 cell line	Chronic myeloid leukemia	Antiproliferative effect	Li et al., 2015
	MCF7 cell line	Breast cancer	Antiproliferative effect	Madureira et al., 2023
Quercetin	MCF7, MDAMB231 cell lines	Breast cancer	Antiproliferative effect	Maugeri et al., 2023
	Caco2, HT29, HCT116, HCT15, CO115, SW480 cell lines	Colorectal cancer	Apoptotic effect, antiproliferative effect	Maugeri et al., 2023
	HepG2, Huh7 cell lines	Liver cancer	Apoptotic effect, antiproliferative effect	Maugeri et al., 2023
	A549 cell line	Lung cancer	Apoptotic effect	Zheng et al., 2012
	A2780S cell line	Ovarian cancer	Antiproliferative effect	Gao et al., 2012

Anticancer potential of the plants

The anticancer potentials of the plants identified by considering the phenolic compounds that the plant parts contain (*Table 3*) and the anticancer effects thereof (*Table 7*) are shown in *Table 8*.

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***Table 8.** Anticancer potentials of the plants on cancer types*

Cancer types	**Anticancer potential**											
	Malva neglecta			***Nerium oleander***			***Quercus brantii***			***Vitis vinifera***		
	Fl	**Fr**	**Lf**	**Fl**	**Fr**	**Lf**	**Fl**	**Fr**	**Lf**	**Fl**	**Fr**	**Lf**
Bladder cancer	---	---	---	---	---	---	+	$+^{*}$	+	+	+	---
Breast cancer	$+^{*}$	---	---	---	---	$+^{*}$	+,+,+	$+^{*},+^{*}$	+,+,+,+	$+,+,+,+^{*}$	$+^{*},+$	+
Cervical cancer	---	---	---	---	---	---	+	$+^{*}$	+,+	+,+	$+^{*}$	---
Colorectal cancer	---	---	---	---	---	---	+,+,+	$+^{*},+^{*}$	+,+,+	$+,+,+^{*}$	+	+
Chronic myeloid leukemia	---	---	---	---	---	$+^{*}$	---	---	---	---	---	---
Glioblastoma multiforme	---	---	---	---	---	---	+	$+^{*}$	+	+	---	---
Liver cancer	$+^{*},+$	$+^{*}$	+	+	---	---	+,+	---	+	$+,+^{*}$	+	+
Lung cancer	$+^{*}$	---	---	---	---	---	+,+	$+^{*}$	+,+	$+,+^{*}$	---	+
Mesothelioma	---	---	---	---	---	---	+	$+^{*}$	+	+	---	---
Ovarian cancer	---	---	---	---	---	---	+	---	+	$+^{*}$	---	+
Prostate cancer	$+^{*},+^{*}$	---	---	---	---	---	+	$+^{*}$	+	+	---	---
Skin cancer	$+^{*}$	---	---	---	---	---	---	---	---	---	---	---

+Indicates each active compound the plants contain
[*] Indicates high anticancer potential (High anticancer potential of the plants on the types of cancer was determined according to the anticarcinogenic activities of the active compound of the part of the plant with the highest concentration of active compound)

As can be seen in *Table 8,* the types of cancer that the plants studied herein and determined to have high anticancer potential may be effective can be listed as follows: The plants, that presented the highest anti-carcinogenic activity potential on 12 established types of cancer, were: *Q. brantii* in bladder cancer*; M. neglecta, N. oleander, Q. brantii* and *V. vinifera* in breast cancer; *Q. brantii*, and *V. vinifera* in cervical cancer; *Q. brantii* and *V. vinifera* in colorectal cancer; *N. oleander* in chronic myeloid leukemia; *Q. brantii* in glioblastoma multiforme; *M. neglecta* and *V. vinifera* in liver cancer; *M. neglecta, Q. brantii,* and *V. vinifera* in lung cancer; *Q. brantii* in mesothelioma; *V. vinifera* in ovarian cancer; *M. neglecta,* and *Q. brantii* in prostate cancer; *M. neglecta* in skin cancer.

Discussion

We may discuss the following in the light of *Tables 3, 7* and *8* compiled on the basis of the findings obtained in the study;

As is the case for many members of the Malvaceae family, *Malva neglecta* is also reported to present robust antioxidant activity and have high quantities of total phenolic and total flavonoid contents (Gençalp et al., 2020; Günbatan et al., 2023). With respect to the anticancer activity, on the other hand, increased extract concentrations of some *Malva* species have been demonstrated to exert significant antiproliferative effects in breast cancer cell lines (Gençalp et al., 2020). One may contemplate that said anticancer effect is attributable to the caffeic acid as the study revealed that the flower of the plant *M. neglecta* contains caffeic acid having anticancer effect on the breast cancer.

A member of the Apocynaceae family, *Nerium oleander* comes from the family that present very broad bioactivity properties. Presenting numerous biological and pharmacological activities, this poisonous plant is used frequently in the traditional medicine (Turan et al., 2006; Ayouaz et al., 2023). The cytotoxic effects of the leaf, stem and root extracts of *N. oleander* on chronic myeloid leukemia cell lines are studied by means of the MTT test. All three extracts are observed to have pronounced

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antileukemic effects on the leukemia cells (Turan et al., 2006). Naringenin is found to exert a significant inhibitory effect on the cell growth in the chronic myeloid leukemia cell line (Li et al., 2015). One may contemplate that said antileukemic effect is attributable to naringenin as the study revealed that the leaves of the plant *N. oleander* contains naringenin having anticancer effect on the chronic myeloid leukemia cell line.

A member of the Fagaceae family, *Quercus* species are reported to have antioxidant, antimateriel and antiviral activities (Moradi et al., 2016; Konovalova et al., 2023). The extracts of *Quercus brantii* fruit are shown to suppress proliferation of the cervical cancer cell lines through early induction of apoptosis (Moradi et al., 2016). One may contemplate that said anticancer effect is attributable to gallic acid as the study revealed that *Q. brantii* contains gallic acid having anticancer effect on the cervical cancer, and that the fruit of the plant has highest concentration of gallic acid when compared to other plants.

Various experimental studies have been conducted on the by-products of *V. vinifera*, a climbing shrub from the *Vitaceae* family, and reported to have antitumor activity (Loizzo et al., 2019; Sharafan et al., 2023). The leaf of the plant has been demonstrated to have antiproliferative effect on the human lung cancer cell line and the lung large carcinoma cell line (Loizzo et al., 2019). One may contemplate that said anticancer effect is attributable to quercetin as the study revealed that the leaf of *V. vinifera* contains quercetin, a phenolic compound with anticarcinogenic effect on the lung cancer.

Discovery of caffeic acid in the content of *M. neglecta* (Haşimi et al., 2017) and ellagic acid in the content of *V. vinifera* (Duran, 2014) also in other studies where the phenolic compounds of the plants are assayed further confirms the results of the phytochemical analysis of this study.

Conclusion

This study is a 3-step study consisting of phytochemical research, statistical analysis, and anticancer examination. With this study, the phenolic compound composition of the examined plants, which has an anticancer effect on different cancer cells, is revealed from a phytochemical perspective, and the anticancer effect potential of the plants on specific types of cancer are determined. In our study, after determining the phytochemical structure of the plants and proving their statistical effectiveness, the evaluation of the plants in terms of anticancer reveals the new aspect of our study contributing to the literature. In this way, the potential effects of plants that are recorded in ethnobotanical studies to be used for medicinal purposes against cancer without scientific knowledge can be scientifically determined and cancer-specific plant material can be scientifically identified.

Four plants mentioned in this study are determined to have anticancer effect potentials on 12 types of cancer. In folk medicine, said plants are applied arbitrarily rather than targeted use depending on the specific type of cancer. The results from this study may contribute to the more rational use of said plants depending on the specific cancer types in folk medicine and the development of plant-derived drugs in pharmacology for these 12 cancer types.

Q. brantii and *V. vinifera* are identified as the plants most abundant in phytochemical terms as they contain 5 distinct phenolic compounds characterized as chemotherapeutic

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agents on the types of cancer, followed by *Malva neglecta* with 3 distinct phenolic compounds and *N. oleander* raking last with 2 distinct phenolic compounds.

In the light of this study, said 4 plant species are considered to worth further research for the experimental cancer researches planned for the future as the variation quantity of the phenolic compounds with chemotherapeutic activity on types of cancer present large effect size on these plants. More accurate experimental research can be conducted on the breast cancer, bladder cancer and colorectal cancer, taking into consideration the plant parts identified to vary significantly from each other, particularly in terms of ellagic acid expressing clinical significance on the plants.

Based on the data acquired from this study, one may stipulate further experimental studies conducted on breast, liver, lung, prostate, and skin cancers using *M. neglecta*; on breast and chronic myeloid leukemia cancers using *N. oleander*; on bladder, breast, cervical, colorectal, glioblastoma multiforme, lung, mesothelioma, and prostate cancers using *Q. brantii*; and on breast, cervical, colorectal, liver, lung, and ovarian cancers using *V. vinifera*.

Moreover, further experimental studies and herbal medicine studies can be carried out on the respective types of cancer using the plants *Q. brantii* and *V. vinifera*, determined to have 4 distinct phenolic compounds effective on breast cancer and 3 distinct phenolic compounds effective on colorectal cancer.

Furthermore, the cancer research studies can be further intensified on *Q. brantii* determined to have active phenolic compounds on 10 distinct types of cancer with high anticancer potential on 8 types of cancer.

Detected active compounds found in the four species

1. Caffeic acid
2. Catechin hydrate
3. Ellagic acid
4. Fumaric acid
5. Gallic acid
6. Hydroxycinnamic acid
7. Naringenin
8. Quercetin

Author contributions. İ.H.A.: Laboratory studies, Statistics, Writing-original draft and Writing-reviewing draft; Ö.F.K.: Plant collection, Plant Identification and Writing-reviewing draft; H.T.Ç.: Writing-reviewing draft, Proofreading, Statistics, and Translation.

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