



Identification of the major phenolic compounds in *Alcea setosa* (Boiss.) Alef. and a systematic review of their chemotherapeutic activities

İbrahim Hakki ARSLAN^{ID}

Harran University, Hilvan Vocational School, Dept. of Property Protection and Security, Şanlıurfa, Türkiye
*iha@harran.edu.tr

Received : 11.05.2026
Accepted : 09.07.2026
Online : 17.08.2026

Alcea setosa (Boiss.) Alef.'teki başlıca fenolik bileşiklerin tanımlanması ve kemoterapötik aktivitelerinin sistematik bir incelemesi

Abstract: In this study, the aim was to determine potential chemotherapeutic agents with a phenolic structure in *Alcea setosa* (Boiss.) Alef. plant. In this context, solutions were obtained from various parts of the plant (flowers, leaves, seeds, and stems) using the infusion method with multiple solvents. These solutions were analyzed for phenolic compounds by LC-MS/MS. The major compounds in the plant parts were statistically determined ($0.14 \leq \eta^2$) according to the amount of identified phenolic compounds. As a result of the phytochemical analysis, 12 phenolic compounds were detected in the plant. The major phenolic compounds found in the plant parts were determined as follows: caffeic acid, fumaric acid, 4-hydroxybenzoic acid, hydroxycinnamic acid, kaempferol, luteolin, myricetin, naringenin, quercetin, syringic acid, and vanillic acid in the flower part; hydroxycinnamic acid, luteolin, resveratrol, and syringic acid in the leaf part; fumaric acid in the seed part; luteolin in the stem part. In the literature, it was seen that these compounds exhibit chemotherapeutic activity against 19 cancer types (bladder cancer, breast cancer, colorectal cancer, chronic myeloid leukemia, endometrial cancer, erythroleukemia, gastric cancer, glioblastoma multiforme, liver cancer, lung cancer, melanoma, neuroblastoma, oral cancer, ovarian cancer, pancreatic cancer, promyelocytic leukemia, prostate cancer, skin cancer, thyroid cancer). It can be suggested that, due to the potential chemotherapeutic agents found in the plant's flower, leaf, stem, and seed parts, these parts may serve as good material for future experimental research and drug development studies.

Key words: *Alcea setosa*, anticancer, chemotherapeutic agent, phenolic compound, phytochemistry

Özet: Bu çalışmada, *Alcea setosa* (Boiss.) Alef. bitkisinde fenolik yapıya sahip potansiyel kemoterapötik ajanların belirlenmesi amaçlanmıştır. Bu bağlamda, bitkinin çeşitli kısımlarından (çiçek, yaprak, tohum ve gövde) çoklu çözücüler kullanılarak infüzyon yöntemiyle çözeltiler elde edilmiştir. Bu çözeltiler, LC-MS/MS yöntemiyle fenolik bileşikler açısından analiz edilmiştir. Bitki kısımlarındaki başlıca bileşikler, tanımlanan fenolik bileşiklerin miktarına göre istatistiksel olarak ($0.14 \leq \eta^2$) belirlenmiştir. Fitokimyasal analiz sonucunda bitkide 12 fenolik bileşik tespit edilmiştir. Bitki kısımlarında bulunan başlıca fenolik bileşikler şu şekilde belirlenmiştir: çiçek kısmında kafeik asit, fumarik asit, 4-hidroksibenzoik asit, hidroksisinnamik asit, kaempferol, luteolin, mirisetin, naringenin, kuersetin, siringik asit ve vanilik asit; yaprak kısmında hidroksisinnamik asit, luteolin, resveratrol ve siringik asit; tohum kısmında fumarik asit; gövde kısmında ise luteolin. Literatürde, bu bileşiklerin 19 kanser türüne (mesane kanseri, meme kanseri, kolorektal kanser, kronik miyeloid lösemi, endometriyal kanser, eritrolösemi, mide kanseri, glioblastoma multiforme, karaciğer kanseri, akciğer kanseri, melanom, nöroblastoma, ağız kanseri, yumurtalık kanseri, pankreas kanseri, promyelositik lösemi, prostat kanseri, cilt kanseri, tiroid kanseri) karşı kemoterapötik aktivite gösterdiği görülmüştür. Bitkinin çiçek, yaprak, gövde ve tohum kısımlarında bulunan potansiyel kemoterapötik ajanlar nedeniyle, bu kısımların gelecekteki deneysel araştırmalar ve ilaç geliştirme çalışmaları için iyi birer materyal olarak kullanılabileceği öne sürülebilir.

Anahtar Kelimeler: *Alcea setosa*, antikanser, fenolik bileşik, fitokimya, kemoterapötik ajan

Citation: Arslan İH (2026). Identification of the major phenolic compounds in *Alcea setosa* (Boiss.) Alef. and a systematic review of their chemotherapeutic activities. *Anatolian Journal of Botany* 10: 144-155.

1. Introduction

Cancer is a dynamic process resulting from a multi-stage and complex disruption of the cell's biochemical processes (Bulut-Atalay & Küpeli, 2025). Cancer is the second leading cause of death worldwide after cardiovascular disease and is influenced by many factors (environmental, genetic, lifestyle, etc.). With the increasing global population, changing environmental factors, and the growing elderly population, the number of cancer cases is steadily increasing. This increase is expected to continue (Cömert & Gençtürk, 2025; Dogan & Doğan, 2025; Ziyank, 2025). In 2020, it is estimated that there were 19.3 million new cancer cases and 10 million cancer-related deaths worldwide (Kurhan & Ekici, 2021). It is predicted that by 2030, there will be 21.7 million new cancer cases

and 13 million cancer-related deaths (Szymaszek et al., 2024). According to projections, the number of new cancer cases is reported to increase by 47% from 2020 to 2040, reaching 28.4 million (Kurhan & Ekici, 2021).

The primary goal of cancer treatment is to destroy cancer cells that reduce a patient's quality of life and cause death. In this way, it aims to improve the patient's quality of life and life expectancy. However, there will always be a need to develop treatment protocols that minimize negative impacts on patients' quality of life from treatment and/or develop more effective treatment protocols (Alshabi et al., 2022).

Phenolic compounds, which are one secondary metabolite of plants, have pro-oxidative potential and possess

anticancer properties that can sensitize tumor cells to oxidative stress (Acquaviva et al., 2021). In recent years, the increase in cancer-related deaths and the fact that plants exhibit certain anticancer effects have led to a rise in demand for natural herbal products. Furthermore, because plants possess antioxidant properties and compounds with anticancer effects (phenolic compounds, flavonoids, alkaloids, terpenoids, isoprenoids, etc.), their anticancer effects have attracted attention in the scientific field and have become a frequently studied topic (Şengün & Özenoğlu, 2023; Çukurovalı-Soykurt et al., 2024; Demirbağ & Aykaç, 2025). Herbal therapy is a treatment that falls outside modern medical methods yet comes closest to them. Among all therapies called complementary medicine, phytotherapy is the therapy that receives the most scientific support (Kurhan & Ekici, 2021). Further, when examining the medications used by cancer patients to cope with some side effects of chemotherapy, it was found that phytotherapy was the most common method used by patients among the participants, at 97.1% (Toygar et al., 2020). Natural products have a wide range of therapeutic effects in cancer treatment. Because of these properties, they are of vital importance in the discovery of cancer drugs. The 20th century saw significant progress in extracting active compounds from natural sources, leading to the discovery of various active compounds with significant potential in treating challenging types of cancer (Chunarkar-Patil et al., 2024). Today, more than 60% of cancer drugs are produced from natural compounds. Therefore, plant secondary metabolites, which are active compounds of plants that can exhibit anticancer effects, are of great importance in cancer treatment (Arslan et al., 2023; Ülger & Ayhan, 2020).

Malvaceae is a family of flowering plants comprising approximately 244 genera and 4225 species, distributed in tropical and temperate regions worldwide (Sameh et al., 2024). *Alcea setosa* (Boiss.) Alef. is a member of the Malvaceae family and is distributed in the Istanca, Çatalca-Kocaeli, and Southern Marmara Sections; Main Aegean Section; Upper Kızılırmak Section; Hakkari Section; Adana Section; Southeastern Anatolia Region of Türkiye. *Alcea setosa* (Boiss.) Alef. belongs to the *Alcea* genus, of which there are 20 species in Türkiye (Uzunhisarcıklı, 2012). Otherwise, ethnobotanical studies conducted in the Şanlıurfa (Türkiye) region have documented that the local people used the plant for medicinal purposes in the treatment of various diseases (Fidan & Akan, 2019).

In this study, the aim was to determine potential chemotherapeutic agents with a phenolic structure found in the chemical composition of the flower, leaf, stem, and seed parts of *Alcea setosa* (Boiss.) Alef. plant, which grows naturally in Türkiye. In this context, the major compounds of the plant parts were determined by phytochemical and statistical analyses, and the chemotherapeutic activities of these compounds were demonstrated in the literature.

2. Materials and Method

2.1. Plant Material

The material of this study consists of *Alcea setosa* (Boiss.) Alef. plant (Fig. 1). The work titled Flora of Turkey and the East Aegean Islands was used as the primary basis for plant identification. The botanical characteristics of the plant are

as follows: Tall perennial stems are hispid-setose with an indumentum of long, stellate, fascicled or simple hairs, without smaller, adpressed stellate hairs, rarely glabrescent. Leaves usually lobed, the upper leaves often deeply so, crenate, with an indumentum of stellate hairs. Epicalyx segments are 1/2 as long as the calyx or longer. Calyx clearly to obscurely striate. Petals white or pink. Mericarps pilose, not conspicuously rugose (Cullen, 1967). *A. setosa* was collected during the flowering and fruiting periods in the Şanlıurfa region of Türkiye (Rural area of Karaköprü central district/Şanlıurfa) in May and July 2025. Dried plant samples were prepared as laboratory material. The aerial parts (flowers, leaves, seeds, and stems) of the plant were separated, and the plant parts were extracted using the infusion method.

2.2. Preparation of plant extracts

Extraction procedures were performed using three different solvents for each plant part: pure ethanol (>99%), pure methanol (>99%), and distilled water. Ethanolic ($\approx 78^\circ\text{C}$), methanolic ($\approx 65^\circ\text{C}$), and aqueous ($\approx 100^\circ\text{C}$) mixtures prepared at a ratio of 1 g of plant material to 100 mL of solvent were boiled for 5 minutes under atmospheric pressure. Ethanolic, methanolic, and aqueous extracts obtained via infusion were subjected to phytochemical analyses.

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

Phenolic compound analysis was conducted using a Shimadzu LC-MS/MS-8030 instrument, with detection sensitivity at the micrograms (ppb) level. Liquid chromatography is equipped with an LC-20ADXR dual pump, DGU-20A3R degaser, CTO-10ASvp column furnace and SIL-20ACXR auto sampler. Chromatographic separation was carried out using a C18 reversed-phase analytical column from Supelco Discovery (5 cm $\times$ 2.1 mm, 5 μm). The column temperature was maintained at 40°C , and the maximum pressure was 400 bar. The elution gradient was created using mobile phase A (0.1% formic acid + 20% water + 80% methanol) and mobile phase B (0.1% formic acid + 20% methanol + 80% water). The solvent flow rate was 0.4 mL/minute, and the injection volume was set at 4 μL (Table 1). In this context, the diagram in Figure 2 shows the peaks corresponding to the detected phenolic compounds.

2.4. Data analysis

The data obtained from the chromatography device was analyzed using statistical methods in the SPSS 27 software.

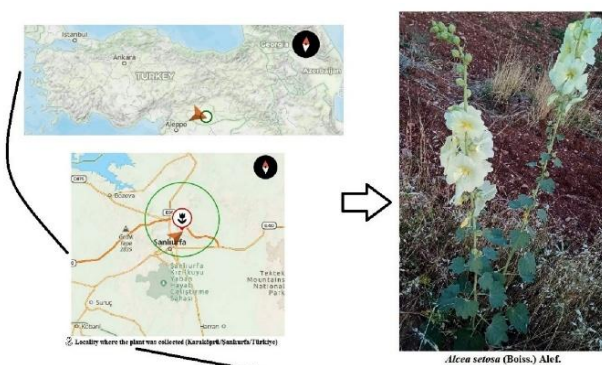
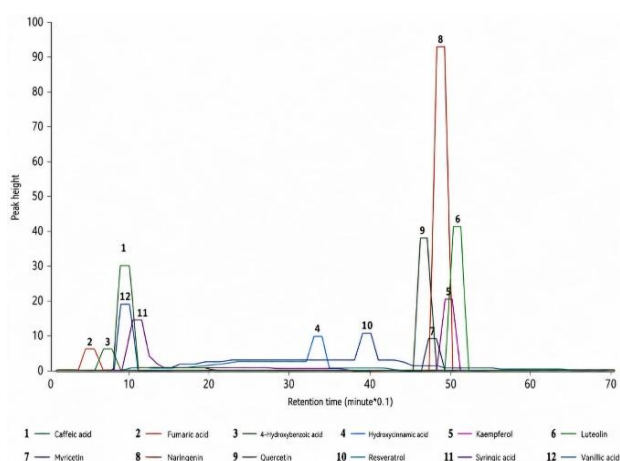


Fig. 1. *Alcea setosa* (Boiss.) Alef.

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

Compounds	Regression equation	R ²	Retention time (minute)	Parent ion (m/z)	LOD/LOQ (µg/L)	RSD (%)
Caffeic acid	y=2262.47x+1134.37	0.9990	0.822	178.90>135.10	81.80/272.67	0.116
Fumaric acid	y=106.939x+2043.28	0.9965	0.469	115.00>70.90	2.76/9.20	0.091
4-Hydroxybenzoic acid	y=949.592x+9749.84	0.9999	0.687	137.20>92.90	15.34/51.14	0.127
Hydroxycinnamic acid	y=1583.68x-11323.90	0.9990	3.107	163.00>119.10	7.79/25.98	0.169
Kaempferol	y=1377.89x-2580.82	0.9999	4.940	286.90>153.00	3.92/13.06	0.030
Luteolin	y=1339.10x+9914.84	0.9998	4.956	284.80>133.00	6.4/21.4	0.09
Myricetin	y=35.5199x+151.557	0.9991	4.817	316.80>151.00	237.42/791.40	0.183
Naringenin	y=2360.80x-7366.23	0.9985	4.872	270.90>151.00	38.50/128.20	0.07
Quercetin	y=1345.53x-52402.80	0.9989	4.768	300.80>151.00	68.40/228.10	0.28
Resveratrol	y=1702.87x-29121.10	0.9985	3.815	229.00>135.00	7.91/ 26.38	0.06
Syringic acid	y=930.371x-1928.99	0.9998	0.926	198.90>140.10	41.83/ 139.43	0.11
Vanillic acid	y=124.688x+1362.73	0.9995	0.860	168.95>65.20	84.78/282.61	0.201

**Figure 2.** Peaks of the detected phenolic compounds

The study sample consisted of 12 extracts from flowers, leaves, seeds and stems of the plant, prepared using ethanol, methanol, and distilled water as solvents. The statistical analysis involved MANOVA and LSD tests to compare the phenolic compound content across the different plant parts. The results were presented and interpreted using tables to demonstrate the extent of change in phenolic compounds and the clinical significance value (η^2) of these variations. The $p < 0.01$ level was considered highly significant, and the $p < 0.05$ level was considered significant.

3. Results

3.1. Phytochemical Analysis

In this study, 12 phenolic compounds were identified in extracts obtained from the plant parts. The amount of phenolic compounds determined in 1 gram of dried plant material (in the extract obtained from 1 gram of dried plant material with 100 mL of solvent) was expressed in ppb ($\mu\text{g} \cdot \text{L}^{-1}$). The amounts of phenolic compounds detected, the plant parts containing these compounds, and the solvents used to obtain the plant extracts are shown in Table 2.

3.2. Statistical analysis

When the effect value is examined in general with the MANOVA test, it is shown in Table 4 that, according to all

assumptions of the MANOVA test, the chemical composition in the phenolic structure in the plant parts explains the differentiation of the plant parts from each other at an extremely high level ($89\% < \eta^2$).

The Partial Eta Squared value serves as a measure of the strength of the association between a group factor and the dependent variable. It quantifies the extent of impact that the factor has on the outcome, providing insight into the degree of influence that the group factor exerts on the dependent variable. The effect size value (η^2) is considered small if $0.01 \leq \eta^2 \leq 0.06$, medium if $0.06 \leq \eta^2 \leq 0.14$, and large if $0.14 \leq \eta^2$ (Arslan et al., 2023). When the effect size is examined for clinical studies, it is reported that a value of $\eta^2 \geq 0.5$ indicates clinical significance (Kilic, 2014). When it is examined whether the amount of each phenolic compound in the plant parts creates a significant difference in the phenolic compound profile of the plant parts, it is seen that all of the phenolic compounds detected are active compounds with a statistically significant ($p < 0.05$) large effect size ($0.14 \leq \eta^2$) in terms of differentiating the chemical content of the plant parts. Furthermore, it was determined that all analyzed polyphenols exhibited a highly significant ($p < 0.01$) effect size, with $\eta^2 \geq 0.5$, indicating statistical clinical significance (Table 5).

Upon analyzing with the Least Significant Difference (LSD) test, it was established that there were significant differences ($p < 0.05$) among the plant parts concerning their phenolic compound concentrations. The outcomes of the LSD test are presented in Table 6, illustrating the relationships between the plant part exhibiting the highest concentration of each specific phenolic compound and the other plant parts analyzed.

It has been statistically determined that flower part of the plant in terms of the amount of caffeic acid, flower and seed parts of the plant in terms of the amount of fumaric acid, flower part of the plant in terms of the amount of 4-hydroxybenzoic acid, flower and leaf parts of the plant in terms of the amount of hydroxycinnamic acid, flower part of the plant in terms of the amount of kaempferol, flower, leaf and stem parts of the plant in terms of the amount of luteolin, flower part of the plant in terms of the amount of myricetin, flower part of the plant in terms of the amount of

Table 2. Amounts of phenolic compounds determined in the plants

Phenolic compound	Part of the plant	Solvent	Quantity (ppb)
Coffeic acid	Flower	Ethanol	1548.26
		Methanol	1447.83
		Water	2439.48
	Leaf	Ethanol	369.72
		Methanol	86.47
		Water	813.90
Fumaric acid	Flower	Ethanol	81478.83
		Methanol	80481.27
		Water	109937.26
	Leaf	Ethanol	15348.11
		Methanol	13769.94
		Water	23970.58
	Seed	Ethanol	63560.36
		Methanol	55147.69
		Water	84456.09
	Stem	Ethanol	13058.42
		Methanol	9014.57
		Water	27294.90
4-Hydroxybenzoic acid	Flower	Ethanol	4217.05
		Methanol	3881.17
		Water	4514.16
Hydroxycinnamic acid	Flower	Ethanol	1426.68
		Methanol	1216.57
		Water	2268.48
	Leaf	Ethanol	1376.25
		Methanol	1337.51
		Water	2598.24
Kaempferol	Flower	Ethanol	8315.81
		Methanol	10679.29
		Water	2047.42
	Stem	Ethanol	180.68
		Methanol	441.95
		Water	36.73
Luteolin	Flower	Ethanol	328.44
		Methanol	380.79
		Water	128.09
	Leaf	Ethanol	50.13
		Methanol	73.89
		Water	8.35
Myricetin	Flower	Ethanol	190.53
		Methanol	475.08
		Water	26.64
Naringenin	Flower	Ethanol	2563.57
		Methanol	4083.99
		Water	1841.46
Quercetin	Flower	Ethanol	4326.68
		Methanol	4518.47
		Water	1644.79
Resveratrol	Leaf	Ethanol	330.02
		Methanol	475.72
		Water	162.63
Syringic acid	Flower	Ethanol	557.85
		Methanol	830.62
		Water	49.31
	Leaf	Ethanol	84.37
		Methanol	51.96
		Water	247.64
Vanillic acid	Flower	Ethanol	81.77
		Methanol	64.15
		Water	251.06
	Leaf	Ethanol	842.39
		Methanol	742.43
		Water	1374.70
	Leaf	Ethanol	368.29
		Methanol	171.40
		Water	441.75

Table 3. Phenolic compounds that the plant parts contain

Phenolic compound	The Plant Parts			
	Flower	Leaf	Seed	Stem
Caffeic acid	+	+	---	---
Fumaric acid	+	+	+	+
4-Hydroxybenzoic acid	+	---	---	---
Hydroxycinnamic acid	+	+	---	---
Kaempferol	+	---	---	+
Luteolin	+	+	---	+
Myricetin	+	---	---	---
Naringenin	+	---	---	---
Quercetin	+	---	---	---
Resveratrol	---	+	---	---
Syringic acid	+	+	---	---
Vanillic acid	+	+	---	---

+ Indicates the presence of the phenolic compound.

* Indicates the highest concentration.

--- Not detected

naringenin, flower part of the plant in terms of the amount of quercetin, leaf part of the plant in terms of the amount of resveratrol, flower and leaf parts of the plant in terms of the amount of syringic acid, flower part of the plant in terms of the amount of vanillic acid; has a significantly higher ratio ($p < 0.05$) than other parts of the plant, and this ratio represents a statistically significant effect size at the clinical significance level ($\eta^2 \geq 0.5$) (Table 5 and Table 6). Accordingly, the major compounds in the plant parts (compounds that are statistically significantly higher than those in other plant parts, based on their concentrations in the plant part) have been determined as follows: caffeic acid, fumaric acid, 4-hydroxybenzoic acid, hydroxycinnamic acid, kaempferol, luteolin, myricetin, naringenin, quercetin, syringic acid, and vanillic acid in the flower part; hydroxycinnamic acid, luteolin, resveratrol, and syringic acid in the leaf part; fumaric acid in the seed part; luteolin in the stem part.

3.3. Systematic analysis of chemotherapeutic activities of phenolic compounds in the plant

In this study, phenolic compounds, which were identified through phytochemical analyses and whose major compounds have been statistically determined, are reported in the literature to possess chemotherapeutic activity against numerous cancer types. A systematic literature search (content analysis method) was conducted to find studies that may include the chemotherapeutic activity of the relevant phenolic compound. Literature searches were performed in the Web of Science (WOS), PubMed (MEDLINE), WILEY, Taylor & Francis Online, ScienceDirect, and Google Scholar databases using the keywords 'cancer', 'anticancer', 'cancer cell line', and 'name of the relevant phenolic compound'. Within the scope of the study, a literature review was conducted between February and March 2026, and it was repeated in June 2026. It has been determined that the first anticancer study using compounds identified in the plant was published in 1982 (Kuroda et al., 1982). In this context, studies conducted between 1982 and 2026 have been reviewed in the literature. In literature, the chemotherapeutic activities of these phenolic compounds against cancer types are shown in Table 7.

Table 4. Results of the MANOVA test (general)

Multivariate Tests ^a							
Effect	Value	F	Hypothesis df	Error df	Sig.	Partial Eta Squared	Effect
Plant Parts	Pillai's Trace	2.669	6.714	18.000	15.000	.000	.890
	Wilks' Lambda	.000	62.981	18.000	8.971	.000	.990
	Hotelling's Trace	1218.000	112.778	18.000	5.000	.000	.998
	Roy's Largest Root	884.681	737.234 ^c	6.000	5.000	.000	.999

a. Design: Intercept + Plant Parts, 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
Plant Parts	Caffeic acid	85.667	3	28.556	42.833	.000	.941
	Fumaric acid	12.333	3	4.111	9.867	.005	.787
	4-Hydroxybenzoic acid	169.000	3	56.333	676.000	.000	.996
	Hydroxycinnamic acid	120.333	3	40.111	240.667	.000	.989
	Kaempferol	174.667	3	58.222	34.933	.000	.929
	Luteolin	22.000	3	7.333	9.778	.005	.786
	Myricetin	121.000	3	40.333	69.143	.000	.963
	Naringenin	144.000	3	48.000	64.000	.000	.960
	Quercetin	30.250	3	10.083	121.000	.000	.978
	Resveratrol	30.250	3	10.083	7.562	.010	.739
	Syringic acid	16.333	3	5.444	32.667	.000	.925
	Vanillic acid	64.917	3	21.639	129.833	.000	.980

Table 6. Results of the LSD test

LSD Dependent Variable	(I) Plant	(J) Plant	Mean Difference	Std Error	Sig.	95% Confidence Interval	
						Lower Bound	Upper
Caffeic acid	Flower	Leaf	2.6667*	.66667	.004	1.1293	4.2040
		Seed	6.3333*	.66667	.000	4.7960	7.8707
		Stem	6.3333*	.66667	.000	4.7960	7.8707
Fumaric acid	Flower	Leaf	2.0000*	.52705	.005	.7846	3.2154
		Seed	.3333	.52705	.545	-.8820	1.5487
		Stem	2.3333*	.52705	.002	1.1180	3.5487
4-Hydroxybenzoic acid	Flower	Leaf	8.6667*	.23570	.000	8.1231	9.2102
		Seed	8.6667*	.23570	.000	8.1231	9.2102
		Stem	8.6667*	.23570	.000	8.1231	9.2102
Hydroxycinnamic acid	Leaf	Flower	.0000	.33333	1.000	-.7687	.7687
		Seed	6.3333*	.33333	.000	5.5647	7.1020
		Stem	6.3333*	.33333	.000	5.5647	7.1020
Kaempferol	Flower	Leaf	9.3333*	1.05409	.000	6.9026	11.7641
		Seed	9.3333*	1.05409	.000	6.9026	11.7641
		Stem	6.6667*	1.05409	.000	4.2359	9.0974
Luteolin	Stem	Flower	-1.0000	.70711	.195	-2.6306	.6306
		Leaf	1.0000	.70711	.195	-.6306	2.6306
		Seed	2.6667*	.70711	.005	1.0361	4.2973
Myricetin	Flower	Leaf	7.3333*	.62361	.000	5.8953	8.7714
		Seed	7.3333*	.62361	.000	5.8953	8.7714
		Stem	7.3333*	.62361	.000	5.8953	8.7714
Naringenin	Flower	Leaf	8.0000*	.70711	.000	6.3694	9.6306
		Seed	8.0000*	.70711	.000	6.3694	9.6306
		Stem	8.0000*	.70711	.000	6.3694	9.6306
Quercetin	Flower	Leaf	3.6667*	.23570	.000	3.1231	4.2102
		Seed	3.6667*	.23570	.000	3.1231	4.2102
		Stem	3.6667*	.23570	.000	3.1231	4.2102
Resveratrol	Leaf	Flower	3.6667*	.94281	.005	1.4925	5.8408
		Seed	3.6667*	.94281	.005	1.4925	5.8408
		Stem	3.6667*	.94281	.005	1.4925	5.8408
Syringic acid	Leaf	Flower	.0000	.33333	1.000	-.7687	.7687
		Seed	2.3333*	.33333	.000	1.5647	3.1020
		Stem	2.3333*	.33333	.000	1.5647	3.1020
Vanillic acid	Flower	Leaf	1.6667*	.33333	.001	.8980	2.4353
		Seed	5.3333*	.33333	.000	4.5647	6.1020
		Stem	5.3333*	.33333	.000	4.5647	6.1020

Table 7. Chemotherapeutic activities of the phenolic compounds in cancer types

Phenolic Compound	Cell/Animal Model	Cancer Type	Chemotherapeutic Activity	Reference
Caffeic acid	Primary tumors (Mice)	Lung cancer	Antiproliferative effect	(Pavlikova, 2022; Rocha et al., 2012)
	AH109A cell line	Liver cancer	Antiproliferative effect	(Pavlikova, 2022; Rocha et al., 2012)
	T47D cell line	Breast cancer	Apoptotic effect	(Pavlikova, 2022; Rocha et al., 2012)
	A431, CAL27, SKMEL5, SKMEL28 cell lines	Skin cancer	Apoptotic effect, Antitumorigenic effect	(Pavlikova, 2022)
	CAL-27 cell line	Oral cancer	Apoptotic effect	(Pavlikova, 2022)
	PC3 cell line	Prostate cancer	Antiproliferative effect	(Rocha et al., 2012)
Fumaric acid	ICR mice	Liver cancer (HCC)	Anticarcinogenic effect	(Akao & Kuroda, 1990)
	ICRIJCL mice	Lung cancer	Anticarcinogenic effect	(Kuroda et al., 1982)
	ICRIJCL mice	Gastric cancer	Anticarcinogenic effect	
4-Hydroxybenzoic acid	MCF7 cell line	Breast cancer	Apoptotic effect	(Wang et al., 2018)
	A549 cell line	Lung cancer	Antiproliferative effect	(Sannino et al., 2018)
	K-562 cell line	Erythroleukemia	Antiproliferative effect	(Myint et al., 2021)
Hydroxycinnamic acid	DU145 cell line	Prostate cancer	Cytotoxic effect, Apoptotic effect	(Rocha et al., 2012)
Kaempferol	HT-29, HCT116, DLD1 cell lines	Colorectal cancer	Cytotoxic, Apoptotic and, Antitumorigenic effect	(Nejabati & Roshangar, 2022)
	MKN28, SGC7901 cell lines	Gastric cancer	Antiproliferative effect	(Song et al., 2015)
	MDA-MB-231 cell line	Breast cancer	Antiproliferative and Apoptotic effect	(Zhu & Xue, 2019)
	Mouse models	Bladder cancer	Antitumorigenic effect	(Dang et al., 2015)
	A549 cell line	Lung cancer	Antiproliferative effect, Apoptotic effect	(Nguyen et al., 2003)
	PANC-1, Mia PaCa-2 cell lines	Pancreatic cancer	Apoptotic effect	(Wang et al., 2021)
	PC-3 cell line	Prostate cancer	Apoptotic effect	(Karakurt et al., 2024)
Luteolin	HCT-15, HT-29, SNU-407, LoVo cell lines	Colorectal cancer	Antiproliferative effect, Apoptotic effect	(Çetinkaya & Baran, 2023; Kang et al., 2019)
	A549, H460 cell lines	Lung cancer	Antiproliferative effect, Apoptotic effect	(Çetinkaya & Baran, 2023; Park et al., 2013)
	PC-3, LNCaP cell lines	Prostate cancer	Antiproliferative effect, Apoptotic effect	(Çetinkaya & Baran, 2023; Han et al., 2016)
	Hs-746T, MKN28, BGC-823, SGC-7901 cell lines	Gastric cancer	Antiproliferative effect, Apoptotic effect	(Çetinkaya & Baran, 2023; Wu et al., 2015)
	U87MG, T98G, U251MG cell lines	Glioblastoma multiforme	Antiproliferative effect	(Çetinkaya & Baran, 2023; Wang et al., 2017)
	HepG2, SK-Hep-1, SMMC-7721 cell lines	Liver	Apoptotic effect	(Cao et al., 2018; Çetinkaya & Baran, 2023)
	MCF-7, MDA-MB-231, BT-20 cell lines	Breast	Antiproliferative effect, Apoptotic effect	(Çetinkaya & Baran, 2023; Sun et al., 2015)
Myricetin	PC-3, DU-145, C4-2, RWPE1 cell lines	Prostate cancer	Antiproliferative effect	(Crocetto et al., 2021)
	SV-HUC, SW-780, T24 cell lines	Bladder cancer	Antiproliferative effect, Apoptotic effect	(Crocetto et al., 2021; Sun et al., 2012)
	HCT15 cell line	Colorectal cancer	Apoptotic effect	(Kim et al., 2014)
	Primary tumors (Mice)	Skin cancer	Antiproliferative effect	(Jung et al., 2008)
Naringenin	K562 cell line	Chronic myeloid leukemia	Antiproliferative effect	(Li et al., 2015)
	MCF-7 cell line	Breast cancer	Antiproliferative effect	(Madureira et al., 2023)
Quercetin	MCF7, MDAMB231 cell lines	Breast cancer	Antiproliferative effect	(Maugeri et al., 2023)
	SCC-25 cell line	Oral cancer	Antiproliferative effect	(ElAttar & Virji, 1999)
	Caco2, HT-29, HCT116, HCT15, CO115, SW480 cell lines	Colorectal cancer	Apoptotic effect, Antiproliferative effect	(Maugeri et al., 2023)
	HepG2, HuH-7 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)
Resveratrol	A2780, CaOV3, ES-2, TOV-112D, A1947 cell lines	Ovarian cancer	Autophagocytosis	(Opipari Jr et al., 2004)
	MCF-7, MCF-10F, MDAMB-231 cell lines	Breast cancer	Antiproliferative effect	(Mgbonyebi et al., 1998)
	SH-SY5Y cell line	Neuroblastoma	Antiproliferative effect	(Miloso et al., 1999)
	FTC, PTC cell lines	Thyroid cancer	Apoptotic effect	(Shih et al., 2002)
	A549 cell line	Lung cancer	Apoptotic effect	(Kim et al., 2003)
	SCC-25 cell line	Oral cancer	Antiproliferative effect	(ElAttar & Virji, 1999)
	LnCaP, DU145, PC-3 cell lines	Prostate cancer	Antiproliferative effect	(Kampa et al., 2000)
	A375, SK-mel28 cell lines	Melanoma	Apoptotic effect	(Niles et al., 2003)
	SNU-1 cell line	Gastric cancer	Antiproliferative effect	(Holian et al., 2002)

	HCT116, Caco-2, SW480 cell lines	Colorectal cancer	Antiproliferative effect,	(Mahyar-Roemer et al., 2001)
	PANC-1, AsPC-1 cell lines	Pancreatic cancer	Apoptotic effect	(Ding & Adrian, 2002)
	HL-60 cell line	Promyelocytic	Apoptotic effect	(Clément et al., 1998)
Syringic acid	SW480	Colorectal cancer	Antiproliferative effect	(Mihanfar et al., 2021)
	HepG2 cell line	Liver cancer	Cytotoxic effect	(Gheena & Ezhilarasan, 2019)
	HaCaT cell line	Skin cancer	Anticarcinogenesis	(Ha et al., 2018)
	AGS cell line	Gastric cancer	Antiproliferative effect, Apoptotic effect	(Pei et al., 2021)
Vanillic acid	HCT116	Colorectal cancer	Antiproliferative effect	(Gong et al., 2019)
	Rat model	Endometrial cancer	Apoptotic effect	(Abotaleb et al., 2020)

The potential chemotherapeutic agents contained in plant parts are defined according to the chemotherapeutic activities in cancer types in the literature of the phenolic compounds found in the plant parts (Table 2; Table 3; Table 7). Potential chemotherapeutic agents in plant parts in terms of cancer types are shown in Table 8 and Figure 3 (The representative images of phenolic compounds and cancer types in Figure 3 were created using the ChatGPT artificial intelligence program).

The plant parts containing these compounds with potential chemotherapeutic activity may have anticancer effects against the following 19 cancer types: flower and stem in bladder cancer; flower, leaf and stem in breast cancer; flower, leaf and stem in colorectal cancer; flower in chronic myeloid leukemia; flower and leaf in endometrial cancer; flower in erythroleukemia; flower, leaf, seed and stem in gastric cancer; flower, leaf and stem in glioblastoma multiforme; flower, leaf, seed and stem in liver cancer; flower, leaf, seed and stem in lung cancer; leaf in melanoma; leaf in neuroblastoma; flower and leaf in oral cancer; flower and leaf in ovarian cancer; flower, leaf and

stem in pancreatic cancer; leaf in promyelocytic leukemia; flower, leaf and stem in prostate cancer; flower and leaf in skin cancer; leaf in thyroid cancer (Table 8).

Phytochemically, the plant's flowers were found to be the richest part, containing 11 different phenolic compounds. The leaves and stems ranked second and third with 7 and 3 different phenolic compounds, respectively, while the seeds were the least phenolic compound-rich part with only 1 phenolic compound (Table 3, Table 7).

It has been determined that the plant's flower contains 6 different phenolic compounds with anticancer effects in breast, colorectal, and lung cancer; 5 different phenolic compounds with anticancer effects in liver and prostate cancer; 4 different phenolic compounds with anticancer effects in stomach cancer; 3 different phenolic compounds with anticancer effects in skin cancer; and 2 different phenolic compounds with anticancer effects in bladder and oral cancer. It has also been determined that the plant's leaves contain potential chemotherapeutic agents against 16 different types of cancer, followed by its flowers against 15 different types of cancer, its stem against 9 different types of cancer, and finally its seeds against 3 different types of cancer (Table 8).

Table 8. Potential chemotherapeutic agents in plant parts in terms of cancer types

Potential chemotherapeutic agents				
Cancer types	The Plant Parts			
	Flower	Leaf	Seed	Stem
Bladder cancer	+,+			+
Breast cancer	+,+,+,+,+,+	+,+,+		+,+
Colorectal cancer	+,+,+,+,+,+	+,+,+,+		+,+
Chronic myeloid leukemia	+			
Endometrial cancer	+	+		
Erythroleukemia	+			
Gastric cancer	+,+,+,+	+,+,+,+	+	+,+,+
Glioblastoma multiforme	+	+		+
Liver cancer	+,+,+,+,+	+,+,+,+	+	+,+
Lung cancer	+,+,+,+,+,+	+,+,+,+	+	+,+,+
Melanoma		+		
Neuroblastoma		+		
Oral cancer	+,+	+,+		
Ovarian cancer	+	+		
Pancreatic cancer	+	+		+
Promyelocytic leukemia		+		
Prostate cancer	+,+,+,+,+	+,+,+,+		+,+
Skin cancer	+,+,+	+,+		
Thyroid cancer		+		

+ Indicates each phenolic compound (potential chemotherapeutic agent) that has been identified in the literature as having chemotherapeutic activity against the relevant cancer type

4. Discussions

Natural products are well-known for their numerous activities, including enhancing the effectiveness of chemotherapy drugs and reducing side effects (Atanasov et al., 2021). The compounds found in natural products are used as potential precursor compounds for drug development (Ahmadi et al., 2015). The vast majority of drugs developed in the field of cancer are naturally derived drugs (Shokoohinia et al., 2018; Ülger & Ayhan, 2020). In this study, *A. setosa* was investigated as a potential natural source material for drug development research in the field of cancer.

Plants develop biochemical defense mechanisms in response to stress conditions. They accumulate different phenolic compounds in response to various stress conditions. The type of phenolic compounds accumulated can vary depending on the type of stress condition (Atak & Uslu, 2018; Salunke & Koche, 2023). This study determined that the flower part of the plant contains a greater number and quantity of phenolic compounds compared to other parts of the plant. These results indicate that the flower part of the plant has a more advanced biochemical defense mechanism than other parts of the plant in terms of phenolic compounds. The plant's flower part is followed by the leaf, the stem, and the seed. (Table 2 and Table 6). Furthermore, research indicates that phenolic compounds possess biological activity such as anti-inflammatory, antidiabetic, antiallergic, antimicrobial,

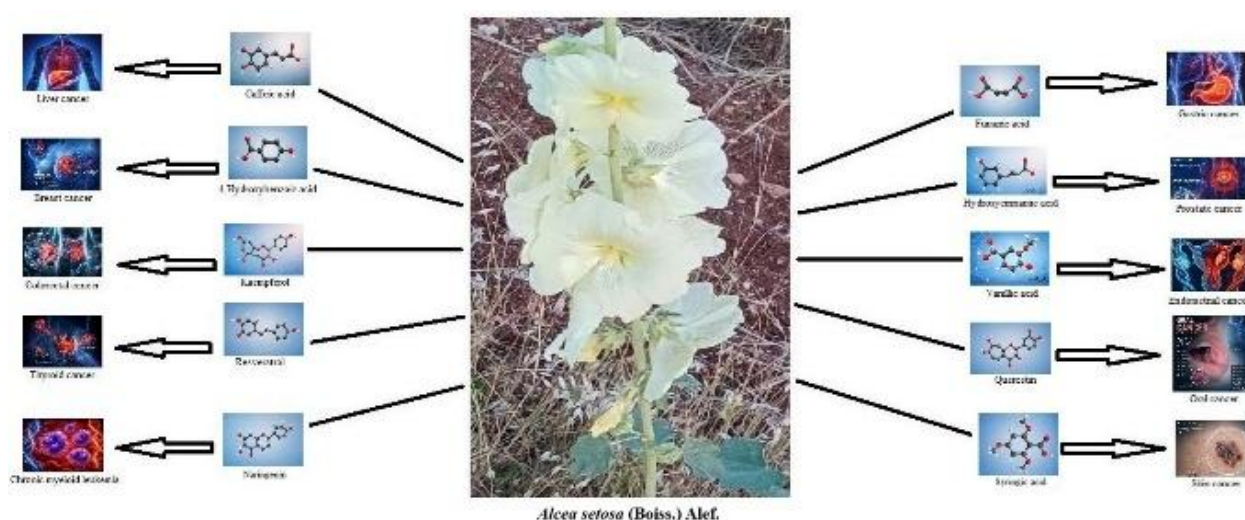


Figure 3. Potential chemotherapeutic agents of the plant in some cancer types

antiviral, antipathogenic, antithrombotic, and anticancer properties (Atak & Uslu, 2018; Arslan et al., 2023). In this context, the results of this study primarily highlight the biological significance of the flower part of the plant, followed by the leaf, stem, and seed parts.

In the study conducted by Bajes et al. (2021), *A. setosa* has been reported to exhibit antiproliferative effects against human breast cancer cells (T47D) and colorectal adenocarcinoma cells (Caco-2) (Bajes et al., 2021). In this study, it was determined that the chemical composition of the *A. setosa* plant contains caffeic acid with antiproliferative effects on the T47D cell line, and quercetin and resveratrol phenolic compounds with antiproliferative effects on the Caco-2 cell line (Table 2 and Table 7). The antiproliferative effect of *A. setosa* may be due to the aforementioned phenolic compounds, which exhibit antiproliferative effects against relevant cancer cell lines.

In the study conducted by Parry et al. (2025), *Alcea rosea* has been reported to exhibit potent cytotoxic effects against HCT116 (IC₅₀=30.94 µg/mL), HT-29 (IC₅₀=46.89 µg/mL) and SW480 (IC₅₀=63.40 µg/mL) colorectal cancer cell lines (Parry et al., 2025). In the study conducted by Abutaha et al. (2024), *A. rosea* extract was found to exhibit dose-dependent cytotoxic effects against liver cancer cell line HuH-7 (IC₅₀=2.39 µg/mL) and breast cancer cell line MDA-MB-231 (IC₅₀=5.67 µg/mL). Additionally, *A. rosea* extract was determined to inhibit HuH-7 cell migration in a time-dependent manner (Abutaha et al., 2024). In this study, it was determined that the chemical composition of *A. setosa* plant contains vanillic acid, resveratrol, quercetin, and kaempferol phenolic compounds with anticancer effects on the HCT116 cell line; kaempferol, luteolin, and quercetin phenolic compounds with anticancer effects on the HT-29 cell line; quercetin, resveratrol, and syringic acid phenolic compounds with anticancer effects on the SW480 cell line; quercetin phenolic compound with anticancer effects on the HuH-7 cell line; and kaempferol and luteolin phenolic compounds with anticancer effects on the MDA-MB-231 cell line (Table 2 and Table 7). It is quite possible that the chemical composition of *A. rosea*, a plant belonging to the genus *Alcea*, is very similar to that of *A. setosa*, another plant in the same genus. It is possible that *A. setosa*

may exhibit anticancer effects in future experimental studies on HCT116, HT-29, SW480, HuH-7, and MDA-MB-231 cell lines.

Despite the inclusion of some plants belonging to the genus *Alcea* as medicinal plants in the Turkish Pharmacopoeia and their numerous recorded benefits in traditional medicine, scientific studies on them are limited in many areas (Öztürk et al., 2018; Ozkol & Karatas, 2024). Most existing studies have focused on other members of the Malvaceae family, such as *Althaea officinalis* (Ozkol & Karatas, 2024). When looking at the literature, it seems that there are limited biochemical, experimental and clinical studies in the field of cancer research related to *A. setosa*.

Conclusion

Based on the results of this study, experimental research may focus on cancer types for which the plant has been identified as containing potential chemotherapeutic agents and for which there are no existing studies in the literature. It can be suggested that, due to the potential chemotherapeutic agents found in the plant's flower, leaf, stem and seed parts, these parts may serve as good material for future experimental research and drug development studies.

Abbreviations

g = Gram

LC-MS/MS = Liquid chromatography-mass spectrometry

LOD = Limit of Detection

LOQ = Limit of Quantification

MANOVA = Multivariate Analysis of Variance

mL = Milliliter

µg= Microgram

Ppb = Parts Per Billion [Microgram (Phenolic Compound) / Liter (Extract + Solvent)]

Conflict of Interest

Author has declared no conflict of interest.

Acknowledgments

This research did not receive support from any funding agency.

References

- Abotaleb M, Liskova A, Kubatka P, Büsselberg D (2020). Therapeutic potential of plant phenolic acids in the treatment of cancer. *Biomolecules* 10(221): 1-23. <https://doi.org/10.3390/biom10020221>.
- Abutaha N, Wadaan MA, Alghamdi RA, Al-Mekhlafi FA (2024). Potential anticancer activity of alcea rosea and molecular docking of selected target proteins in liver cancer cells. *International Journal of Morphology* 42(6): 1746-1754.
- Acquaviva R, Tomasello B, Di Giacomo C, Santangelo R, La Mantia A, Naletova I, Sarpietro MG, Castelli F, Malfa GA (2021). Protocatechuic acid, a simple plant secondary metabolite, induced apoptosis by promoting oxidative stress through HO-1 downregulation and p21 upregulation in colon cancer cells. *Biomolecules* 11(10): 1485. <https://doi.org/10.3390/biom11101485>.
- Ahmadi F, Derakhshandeh K, Jalalizadeh A, Mostafaie A, Hosseinzadeh L (2015). Encapsulation in PLGA-PEG enhances 9-nitro-camptothecin cytotoxicity to human ovarian carcinoma cell line through apoptosis pathway. *Research in Pharmaceutical Sciences* 10(2): 161-168.
- Akao M, Kuroda K (1990). Inhibitory effect of fumaric acid on hepatocarcinogenesis by thioacetamide in mice. *Chemical and Pharmaceutical Bulletin* 38(7): 2012-2014.
- Alshabi AM, Alkahtani SA, Shaikh IA, Orabi MAA, Abdel-Wahab BA, Walbi IA, Habeeb MS, Khateeb MM, Shettar AK, Hoskeri JH (2022). *Tribulus terrestris* cytotoxicity against breast cancer MCF-7 and lung cancer A549 cell lines is mediated via activation of apoptosis, caspase-3, DNA degradation, and suppressing Bcl-2 activity. *Separations* 9(11): 383. <https://doi.org/10.3390/separations9110383>.
- Arslan İH, Kaya ÖF, Tosiyağülü Çelik H (2023). Phytochemical analysis of active phenolic compounds in some plants used as traditional folk drugs for cancer and literature review of their anti-cancer effects. *Applied Ecology & Environmental Research* 21(6): 5901-5914. http://dx.doi.org/10.15666/aecer/2106_59015914.
- Atak E, Uslu ME (2018). Phenolic compounds: extraction methods and analysis methods. *Soma Vocational School Technical Sciences Journal* 3(27): 39-48.
- Atanasov AG, Zotchev SB, Dirsch VM, Supuran CT (2021). International natural product sciences taskforce. *Nature Reviews Drug Discovery* 20(3): 200-216. <https://doi.org/10.1038/s41573-020-00114-z>.
- Bajes HR, Oran SA, Bustanji YK (2021). Chemical composition and antiproliferative and antioxidant activities of methanolic extract of *Alcea setosa* A. Malvaceae. *Research Journal of Pharmacy and Technology* 14(12): 6447-6454. <http://dx.doi.org/10.52711/0974-360X.2021.01115>
- Bulut-Atalay E, Küpeli C (2025). Biochemical events occurring during the cancer process, In: Current approaches in biochemistry. Koçyiğit ÜM (Ed.), BİDGE Publications, 1st Edition, pp. 102-132 ISBN: 978-625-372-886-1.
- Cao Z, Zhang H, Cai X, Fang W, Chai D, Wen Y, Chen H, Chu F, Zhang Y (2018). Luteolin promotes cell apoptosis by inducing autophagy in hepatocellular carcinoma. *Cellular Physiology and Biochemistry* 43(5): 1803-1812. <https://doi.org/10.1159/000484066>.
- Çelik Ş, Çoşkun F, Yılmaz O (2015). A study of body measurements of Turkish spotted horses in different ages. *Journal of Agricultural Faculty of Gaziosmanpaşa University* 32(1): 10-16. doi.org/10.13002/jafag816.
- Çetinkaya M, Baran Y (2023). Therapeutic potential of luteolin on cancer. *Vaccines* 11(3): 554. <https://doi.org/10.3390/vaccines11030554>.
- Chunarkar-Patil P, Kaleem M, Mishra R, Ray S, Ahmad A, Verma D, Bhayye S, Dubey R, Singh HN, Kumar S (2024). Anticancer drug discovery based on natural products: from computational approaches to clinical studies. *Biomedicines* 12(1): 201. <https://doi.org/10.3390/biomedicines12010201>.
- Clément MV, Hirpara JL, Chawdhury SH, Pervaiz, S (1998). Chemopreventive agent resveratrol, a natural product derived from grapes, triggers CD95 signaling-dependent apoptosis in human tumor cells. *Blood, The Journal of the American Society of Hematology* 92(3): 996-1002. <https://doi.org/10.1182/blood.V92.3.996>.
- Cömert D, Gençtürk N (2025). Prevention from cervical cancer. *Gümüşhane University Journal of Health Sciences* 14(3): 1253-1261. <https://doi.org/10.37989/gumussagbil.1411960>.
- Crocetto F, Di Zazzo E, Buonerba C, Aveta A, Pandolfo SD, Barone B, Trama F, Caputo VF, Scafuri L, Ferro M (2021). Kaempferol, myricetin and fisetin in prostate and bladder cancer: a systematic review of the literature. *Nutrients* 13(11): 3750. <https://doi.org/10.3390/nu13113750>.
- Çukurovalı-Soykurt S, Çavdar M, Güler S (2024). Effect of antioxidant fruits on cancer. *International Journal of Interdisciplinary Interaction in Health Sciences* 3(3): 8-15.
- Cullen J (1967). *Alcea* L., In: Flora of Turkey and the East Aegean Islands. Davis PH (Ed.), Edinburgh: Edinburgh University Press, Volume 2, 414 pp.
- Dang Q, Song W, Xu D, Ma Y, Li F, Zeng J, Zhu G, Wang X, Chang LS, He D (2015). Kaempferol suppresses bladder cancer tumor growth by inhibiting cell proliferation and inducing apoptosis. *Molecular Carcinogenesis* 54(9): 831-840. <https://doi.org/10.1002/mc.22154>.
- Demirbağ A, Aykaç MC (2025). Multitarget mechanisms of action of plant-derived compounds in cancer cells: cell cycle regulation, apoptosis, and signaling pathways, In: Current Studies in Biology II. Kılıç DD (Ed.), Lyon: Livre de Lyon publications, 1st Edition, 1-27 pp. <https://doi.org/10.5281/zenodo.18051255>.

- Ding XZ, Adrian TE (2002). Resveratrol inhibits proliferation and induces apoptosis in human pancreatic cancer cells. *Pancreas* 25(4): e71-e76.
- Doğan N, Doğan İ (2025). Regional differences in colorectal cancer mortality, Türkiye. *Kocatepe Medical Journal* 26(2): 162-167. <https://doi.org/10.18229/kocatepetip.1545816>
- ElAttar TMA, Virji AS (1999). Modulating effect of resveratrol and quercetin on oral cancer cell growth and proliferation. *Anti-Cancer Drugs* 10(2): 187-194.
- Fidan EŞ, Akan H (2019). An ethnobotanical study in some villages around the Tek Tek Mountains National Park, Şanlıurfa (Turkey). *Bağbahçe Science Journal* 6(2): 64-94.
- Gao X, Wang B, Wei X, Men K, Zheng F, Zhou Y, Zheng Y, Gou M, Huang M, Guo G (2012). Anticancer effect and mechanism of polymer micelle-encapsulated quercetin on ovarian cancer. *Nanoscale* 4(22): 7021-7030.
- Gheena S, Ezhilarasan D (2019). Syringic acid triggers reactive oxygen species-mediated cytotoxicity in HepG2 cells. *Human & Experimental Toxicology* 38(6): 694–702. <https://doi.org/10.1177/0960327119839173>.
- Gong J, Zhou S, Yang S. (2019). Vanillic acid suppresses HIF-1 α expression via inhibition of mTOR/p70S6K/4E-BP1 and Raf/MEK/ERK pathways in human colon cancer HCT116 cells. *International Journal of Molecular Sciences* 20(3): 465. <https://doi.org/10.3390/ijms20030465>.
- Ha SJ, Lee J, Park J, Kim YH, Lee NH, Kim YE, Song KM, Chang PS, Jeong CH, Jung SK (2018). Syringic acid prevents skin carcinogenesis via regulation of NoX and EGFR signaling. *Biochemical Pharmacology* 154: 435-445. <https://doi.org/10.1016/j.bcp.2018.06.007>.
- Han K, Meng W, Zhang J, Zhou Y, Wang Y, Su Y, Lin S, Gan Z, Sun Y, Min D (2016). Luteolin inhibited proliferation and induced apoptosis of prostate cancer cells through miR-301. *OncoTargets and Therapy*. 9: 3085-3094. <https://doi.org/10.2147/OTT.S102862>.
- Holian O, Wahid S, Atten MJ, Attar BM (2002). Inhibition of gastric cancer cell proliferation by resveratrol: role of nitric oxide. *American Journal of Physiology-Gastrointestinal and Liver Physiology* 282(5): G809-G816. <https://doi.org/10.1152/ajpgi.00193.2001>.
- Jung SK, Lee KW, Byun S, Kang NJ, Lim SH, Heo YS, Bode AM, Bowden GT, Lee HJ, Dong Z (2008). Myricetin suppresses UVB-induced skin cancer by targeting Fyn. *Cancer Research* 68(14): 6021–6029. <https://doi.org/10.1158/0008-5472.CAN-08-0899>.
- Kampa M, Hatzoglou A, Notas G, Damianaki A, Bakogeorgou E, Gemetzi C, Kouroumalis E, Martin PM, Castanas E (2000). Wine antioxidant polyphenols inhibit the proliferation of human prostate cancer cell lines. *Nutrition and Cancer* 37(2): 223-233. https://doi.org/10.1207/S15327914NC372_16.
- Kang KA, Piao MJ, Hyun YJ, Zhen AX, Cho SJ, Ahn MJ, Yi JM, Hyun, JW (2019). Luteolin promotes apoptotic cell death via upregulation of Nrf2 expression by DNA demethylase and the interaction of Nrf2 with p53 in human colon cancer cells. *Experimental & Molecular Medicine* 51(4): 1-14. <https://doi.org/10.1038/s12276-019-0238-y>.
- Karakurt S, Batur HG, Bilgiseven İM, Karakurt S (2024). Dietary edible flavonoid kaempferol induces apoptosis and inhibits cell migration in prostate cancer cells. *Food in Health and Disease: Scientific and Professional Journal of Nutrition and Dietetics* 13(1): 16-27.
- Kılıç S (2014). Effect size. *Journal of Mood Disorders* 4(1): 44-46. <https://doi.org/10.5455/jmood.20140228012836>.
- Kim ME, Ha TK, Yoon JH, Lee JS (2014). Myricetin induces cell death of human colon cancer cells via BAX/BCL2-dependent pathway. *Anticancer Research* 34(2): 701-706.
- Kim Y, Lee WH, Choi TH, Rhee SH, Park KY, Choi YH (2003). Involvement of p21WAF1/CIP1, pRB, Bax and NF- κ B in induction of growth arrest and apoptosis by resveratrol in human lung carcinoma A549 cells. *International Journal of Oncology* 23(4): 1143-1149. <https://doi.org/10.3892/ijo.23.4.1143>.
- Kurhan İ, Ekici H (2021). Phytotherapy and cancer approach in complementary traditional medicine. *Bulletin of Veterinary Pharmacology and Toxicology Association* 12(1): 15-20. <https://doi.org/10.38137/vftd.900797>.
- Kuroda K, Kanisawa M, Akao M (1982). Inhibitory effect of fumaric acid on forestomach and lung carcinogenesis by a 5-nitrofur naphthyridine derivative in mice. *Journal of the National Cancer Institute* 69(6): 1317-1320. <https://doi.org/10.1093/jnci/69.6.1317>.
- Li RF, Feng YQ, Chen JH, Ge LT, Xiao SY, Zuo XL (2015). Naringenin suppresses K562 human leukemia cell proliferation and ameliorates Adriamycin-induced oxidative damage in polymorphonuclear leukocytes. *Experimental and Therapeutic Medicine* 9(3): 697-706. <https://doi.org/10.3892/etm.2015.2185>.
- Madureira MB, Concato VM, Cruz EMS, Bitencourt de Morais JM, Inoue FSR, Concimo Santos N, Gonçalves MD, Cremer de Souza M, Basso Scandolara T, Fontana Mezonzi M (2023). Naringenin and hesperidin as promising alternatives for prevention and co-adjuvant therapy for breast cancer. *Antioxidants* 12(3): 586. <https://doi.org/10.3390/antiox12030586>.
- Mahyar-Roemer M, Katsen A, Mestres P, Roemer K (2001). Resveratrol induces colon tumor cell apoptosis independently of p53 and precede by epithelial differentiation, mitochondrial proliferation and membrane potential collapse. *International Journal of Cancer* 94(5): 615-622. <https://doi.org/10.1002/ijc.1516>.
- Maugeri A, Calderaro A, Patanè GT, Navarra M, Barreca D, Cirmi S, Felice MR (2023). Targets involved in the anti-cancer activity of quercetin in breast, colorectal and liver neoplasms. *International Journal of Molecular Sciences* 24(3): 2952. <https://doi.org/10.3390/ijms24032952>.

- Mgbonyebi OP, Russo J, Russo IH (1998). Antiproliferative effect of synthetic resveratrol on human breast epithelial cells. *International Journal of Oncology* 12(4): 865-874. <https://doi.org/10.3892/ijo.12.4.865>.
- Mihanfar A, Darband SG, Sadighparvar S, Kaviani M, Mirza-Aghazadeh-Attari M, Yousefi B, Majidinia M (2021). In vitro and in vivo anticancer effects of syringic acid on colorectal cancer: Possible mechanistic view. *Chemico-Biological Interactions* 337: 109337. <https://doi.org/10.1016/j.cbi.2020.109337>.
- Miloso M, Bertelli AAE, Nicolini G, Tredici G (1999). Resveratrol-induced activation of the mitogen-activated protein kinases, ERK1 and ERK2, in human neuroblastoma SH-SY5Y cells. *Neuroscience Letters* 264 (1999): 141-144. [https://doi.org/10.1016/S0304-3940\(99\)00194-9](https://doi.org/10.1016/S0304-3940(99)00194-9).
- Myint O, Wattanapongpitak S, Supawat B, Kothan S, Udomtanakunchai C, Tima S, Tungjai M (2021). Protein binding of 4-hydroxybenzoic acid and 4-hydroxy-3-methoxybenzoic acid to human serum albumin and their anti-proliferation on doxorubicin-sensitive and doxorubicin-resistant leukemia cells. *Toxicology Reports* 8: 1381-1388. <https://doi.org/10.1016/j.toxrep.2021.07.001>.
- Nejabati HR, Roshangar L (2022). Kaempferol: A potential agent in the prevention of colorectal cancer. *Physiological Reports* 10(20): e15488. <https://doi.org/10.14814/phy2.15488>.
- Nguyen TTT, Tran E, Ong CK, Lee SK, Do PT, Huynh T T, Nguyen TH, Lee JJ, Tan Y, Ong CS (2003). Kaempferol-induced growth inhibition and apoptosis in A549 lung cancer cells is mediated by activation of MEK-MAPK. *Journal of Cellular Physiology* 197(1): 110-121. <https://doi.org/10.1002/jcp.10340>
- Niles RM, McFarland M, Weimer MB, Redkar A, Fu YM, Meadows GG (2003). Resveratrol is a potent inducer of apoptosis in human melanoma cells. *Cancer Letters* 190(2): 157-163. [https://doi.org/10.1016/S0304-3835\(02\)00676-6](https://doi.org/10.1016/S0304-3835(02)00676-6).
- Opipari Jr AW, Tan L, Boitano AE, Sorenson DR, Aurora A, Liu JR (2004). Resveratrol-induced autophagocytosis in ovarian cancer cells. *Cancer Research* 64(2): 696-703. <https://doi.org/10.1158/0008-5472.CAN-03-2404>.
- Ozkol R, Karatas E (2024). In vitro evaluation of *Alcea rosea* leaf extract on human dermal fibroblast cells and its wound healing potential. *International Biotechnology And Nanotechnology Congress, Ardahan University (Türkiye)*, pp. 552-561. <https://doi.org/10.5281/zenodo.14242863>.
- Öztürk B, Demiröz T, Özdemir S, & Karaalp C. (2018). The place and importance of medicinal plants of Turkey in pharmacopoeia and herbal monographs. *Journal of Turkish Pharmacopoeia* 3(2): 10-30.
- Park SH, Park HS, Lee JH, Chi GY, Kim GY, Moon SK, Chang YC, Hyun JW, Kim WJ, Choi YH (2013). Induction of endoplasmic reticulum stress-mediated apoptosis and non-canonical autophagy by luteolin in NCI-H460 lung carcinoma cells. *Food and Chemical Toxicology* 56: 100-109. <https://doi.org/10.1016/j.fct.2013.02.022>.
- Parry RA, Wani SH, Mir IA, Bhat BA, Hussain MU, Mir MA, Bashir N, Fadul AN, Jangra S, Vats S (2025). Anti-inflammatory and anticancer properties of *Alcea rosea* extracts: Insights from in vitro and in vivo studies. *Frontiers in Pharmacology* 16: 1595604. <https://doi.org/10.3389/fphar.2025.1595604>.
- Pavlikova N (2022). Caffeic acid and diseases-Mechanisms of action. *International Journal of Molecular Sciences* 24(1): 588. <https://doi.org/10.3390/ijms24010588>.
- Pei J, Velu P, Zareian M, Feng Z, Vijayalakshmi A (2021). Effects of syringic acid on apoptosis, inflammation, and AKT/mTOR signaling pathway in gastric cancer cells. *Frontiers in Nutrition* 8: 788929. <https://doi.org/10.3389/fnut.2021.788929>.
- Rocha LD, Monteiro MC, Teodoro AJ (2012). Anticancer properties of hydroxycinnamic acids-a review. *Cancer and Clinical Oncology* 1(2): 109-121. <http://dx.doi.org/10.5539/cco.v1n2p109>.
- Salunke P, Koche D (2023). Role of phenolic compounds in plant defense mechanism: an updated review. *Indian Journal of Applied & Pure Biology* 38(3): 1199-1215.
- Sameh S, Elissawy AM, Al-Sayed E, Labib RM, Chang HW, Yu SY, Chang FR, Yang SC, Singab ANB (2024). Family Malvaceae: a potential source of secondary metabolites with chemopreventive and anticancer activities supported with in silico pharmacokinetic and pharmacodynamic profiles. *Frontiers in Pharmacology* 15: 1465055. <https://doi.org/10.3389/fphar.2024.1465055>.
- Sannino F, Sansone C, Galasso C, Kildgaard S, Tedesco P, Fani R, Marino G, De Pascale D, Ianora A, Parrilli E (2018). *Pseudoalteromonas haloplanktis* TAC125 produces 4-hydroxybenzoic acid that induces pyroptosis in human A459 lung adenocarcinoma cells. *Scientific Reports* 8(1): 1190. <http://dx.doi.org/10.1038/s41598-018-19536-2>
- Şengün FŞ, Özenoğlu A (2023). The effects of flavonoids on the development and progression of cancer. *Eurasian Journal of Health Sciences* 6(1): 57-65. <https://doi.org/10.53493/avasyasbd.1164133>.
- Shih A, Davis FB, Lin HY, Davis PJ (2002). Resveratrol induces apoptosis in thyroid cancer cell lines via a MAPK-and p53-dependent mechanism. *The Journal of Clinical Endocrinology & Metabolism* 87(3): 1223-1232. <https://doi.org/10.1210/jcem.87.3.8345>.
- Shokoohinia Y, Jafari F, Mohammadi Z, Bazvandi L, Hosseinzadeh L, Chow N, Bhattacharyya P, Farzaei MH, Farooqi AA, Nabavi SM (2018). Potential anticancer properties of osthol: A comprehensive mechanistic review. *Nutrients* 10(1): 36. <https://doi.org/10.3390/nu10010036>.
- Song H, Bao J, Wei Y, Chen Y, Mao X, Li J, Yang Z, Xue Y (2015). Kaempferol inhibits gastric cancer tumor growth: An in vitro and in vivo study. *Oncology Reports* 33(2): 868-874. <https://doi.org/10.3892/or.2014.3662>.
- Sun DW, Zhang HD, Mao L, Mao CF, Chen W, Cui M, Ma R, Cao HX, Jing CW, Wang Z (2015). Luteolin inhibits breast cancer development and progression in vitro and in vivo by suppressing notch signaling and regulating MiRNAs. *Cellular Physiology and Biochemistry* 37(5): 1693-1711. <https://doi.org/10.1159/000438535>.

- Sun F, Zheng XY, Ye J, Wu TT, Wang J li, Chen W (2012). Potential anticancer activity of myricetin in human T24 bladder cancer cells both in vitro and in vivo. *Nutrition and Cancer* 64(4): 599-606. <https://doi.org/10.1080/01635581.2012.665564>.
- Szymaszek P, Tyska-Czochara M, Ortyl J (2024). Application of photoactive compounds in cancer theranostics: review on recent trends from photoactive chemistry to artificial intelligence. *Molecules* 29(13): 3164. <https://doi.org/10.3390/molecules29133164>.
- Toygar I, Yeşilbalkan ÖU, Kürkütü M, Aslan A (2020). Complementary and alternative medicines used by cancer patients to cope with chemotherapy-induced constipation. *Complementary Therapies in Clinical Practice* 39: 101108. <https://doi.org/10.1016/j.ctcp.2020.101108>.
- Ülger TG, Ayhan NY (2020). Functional effects of plant secondary metabolites on health. *Journal of Acıbadem University Health Sciences* 11(3): 384-390. <https://doi.org/10.31067/0.2020.288>.
- Uzunhisarcıklı ME (2012). *Alcea* L., In: A Checklist of the Flora of Turkey (Vascular Plants). Güner, A. (Ed.), İstanbul: Nezahat Gökyiğit Botanical Garden Press, 1st Edition, 618 pp.
- Wang F, Wang L, Qu C, Chen L, Geng Y, Cheng C, Yu S, Wang D, Yang L, Meng Z (2021). Kaempferol induces ROS-dependent apoptosis in pancreatic cancer cells via TGM2-mediated Akt/mTOR signaling. *BMC Cancer* 21(1): 396. <https://doi.org/10.1186/s12885-021-08158-z>.
- Wang Q, Wang H, Jia Y, Ding H, Zhang L, Pan H (2017). Luteolin reduces migration of human glioblastoma cell lines via inhibition of the p-IGF-1R/PI3K/AKT/mTOR signaling pathway. *Oncology Letters* 14(3): 3545-3551. <https://doi.org/10.3892/ol.2017.6643>.
- Wang XN, Wang KY, Zhang XS, Yang C, Li XY (2018). 4-Hydroxybenzoic acid (4-HBA) enhances the sensitivity of human breast cancer cells to adriamycin as a specific HDAC6 inhibitor by promoting HIPK2/p53 pathway. *Biochemical and Biophysical Research Communications* 504(4): 812-819. <https://doi.org/10.1016/j.bbrc.2018.08.043>.
- Wu H, Huang M, Liu Y, Shu Y, Liu P (2015). Luteolin induces apoptosis by up-regulating miR-34a in human gastric cancer cells. *Technology in Cancer Research & Treatment* 14(6): 747-755. <https://doi.org/10.7785/tcrt.2012.500434>.
- Zheng SY, Li Y, Jiang D, Zhao J, Ge JF (2012). Anticancer effect and apoptosis induction by quercetin in the human lung cancer cell line A-549. *Molecular Medicine Reports* 5(3): 822–826. <https://doi.org/10.3892/mmr.2011.726>.
- Zhu L, Xue L (2019). Kaempferol suppresses proliferation and induces cell cycle arrest, apoptosis, and DNA damage in breast cancer cells. *Oncology Research* 27(6): 629. <https://doi.org/10.3727/096504018X15228018559434>.
- Ziyanok S (2025). Diabet and cancer. *East Black Sea Journal of Health Sciences* 4(3): 280-293. <https://doi.org/10.59312/ebshealth.1765591>