KSÜ Tarım ve Doğa Derg 29 (4), 849-862, 2026
KSU J. Agric Nat 29 (4), 849-862, 2026
DOI:10.18016/ksutarimdoga.vi.1804808

Chemical and biological evaluation of five endemic *Salvia* species: Rich source of rosmarinic, caffeic, fumaric and malic acids

Serkan YIĞITKAN[1], Leyla BALUR ADSIZ[2], Mustafa Abdullah YILMAZ[3], Evin AYGUN[4]
Hilal Saruhan FIDAN[5], Esra YARIS[6], Mehmet AKDENIZ[7], Mehmet Veysi ÇAĞLAYAN[8], Ismail YENER[9]
Mehmet BOGA[10], Mehmet FIRAT[11], Ufuk KOLAK[12], Abdulselam ERTAS[13]✍

[1]Dicle University, Faculty of Pharmacy, Department of Pharmacognosy, 21280, Diyarbakir, Türkiye, [2,3,4,6,8,9,10,13]Dicle University, Faculty of Pharmacy, Department of Analytical Chemistry, 21280, Diyarbakir, Türkiye, [5]Dicle University, Faculty of Pharmacy, Department of Biochemistry, 21280 Diyarbakir, Türkiye, [7]The Council of Forensic Medicine, Diyarbakir Group Chairmanship, 21070, Diyarbakir, Türkiye
[11]Yüzüncü Yıl University, Faculty of Education, Department of Biology, 65080 Van, Türkiye, [12]Istanbul University, Faculty of Pharmacy, Department of Analytical Chemistry, 34116 Istanbul, Türkiye
[1]https://orcid.org/0000-0002-6202-1515, [2]https://orcid.org/0009-0001-9276-6892, [3]https://orcid.org/0000-0002-4090-7227
[4]https://orcid.org/0009-0004-9680-6654, [5]https://orcid.org/0000-0002-5790-9915, [6]https://orcid.org/0009-0003-8575-0520
[7]https://orcid.org/0000-0002-4435-4826, [8]https://orcid.org/0000-0002-9803-6444, [9]https://orcid.org/0000-0002-0988-9462
[10]https://orcid.org/0000-0003-4163-9962, [11]https://orcid.org/0000-0001-5814-614X,[12]https://orcid.org/0000-0002-0339-635X
[13]https://orcid.org/0000-0002-2193-8386
✉: abdulselamertas@hotmail.com

ABSTRACT

Medicinal plants have been used to treat many diseases since ancient times, and treatment with herbs is becoming more and more preferred in society due to their synergistic effects and the serious side effects of synthetic drugs. In this study, the phenolic contents of 5 endemic species (*Salvia cerino-pruinosa* var. *elazigensis*, *S. cerino-pruinosa* var. *cerino-pruinosa*, *S. rosifolia, S. pseudeuphratica* and *S. kurdica*) belonging to the genus *Salvia*, which are widely used among the public, were determined by LC-MS/MS and their antioxidant, cytotoxic, anti-Alzheimer, urease, tyrosinase, elastase and collegenase activities were investigated. Petroleum ether extracts prepared from mixed parts of the species were found to be the poorest in terms of phenolic content, while ethanol extracts were the richest. Therefore, as the polarity of the solvent increased during the preparation of the sample extracts, it was observed that the extracts became richer in terms of phenolic component diversity. In general, all ethanol extracts were found to be rich in rosmarinic acid, caffeic acid, fumaric acid and malic acid. Especially *S. cerino-pruinosa* var. *elazigensis* was found to be richer in terms of component diversity and amounts compared to other species. Especially the rosmarinic acid (34638.45 µg analyte/g extract) content of the leaf part of this species is remarkable. In general, antioxidant activities of all species were found to be high or moderate, while enzyme activities were low. This is the first detailed study in the literature on the chemical contents and biological activities of extracts of various parts of 5 endemic species prepared using different solvents (petroleum ether, chloroform and ethanol). The ethanol extract of the leaf of *S. cerino-pruinosa* var. elazigensis has high total phenolic, rosmarinic acid content and antioxidant potential and the cytotoxic activity of *S. rosifolia* has potential for use in food supplement, food preservative and pharmaceutical industries.

Biochemistry

Research Article

Article History
Received : 20.10.2025
Accepted : 29.12.2025

Keywords
Salvia
LC-MS/MS
Rosmarinic acid
Biological activities
Antiaging

Beş endemik *Salvia* türünün kimyasal ve biyolojik değerlendirmesi: Rosmarinik, kafeik, fumarik ve malik asitlerin zengin kaynağı

ÖZET

Tıbbi bitkiler eski çağlardan beri birçok hastalığın tedavisinde kullanılmış olup, sinerjik etkileri ve sentetik ilaçların ciddi yan etkileri nedeniyle toplumda bitkilerle tedavi giderek daha fazla tercih edilmektedir. Bu çalışmada, halk arasında yaygın olarak kullanılan *Salvia* cinsine ait 5 endemik türün (*Salvia cerino-*

Biyokimya

Araştırma Makalesi

Makale Tarihçesi
Geliş Tarihi : 20.10.2025
Kabul Tarihi : 29.12.2025

pruinosa var. *elazigensis*, *S. cerino-pruinosa* var. *cerino*-pruinosa, *S. rosifolia, S. pseudeuphratica* ve *S. kurdica*) fenolik içerikleri LC-MS/MS yöntemi ile belirlenmiş ve antioksidan, sitotoksik, anti-Alzheimer, antiüreaz, antitirozinaz, antielastaz ve antikolejenaz aktiviteleri araştırılmıştır. Türün karışık kısımlarından hazırlanan petrol eteri özütleri fenolik içerik bakımından en fakir, etanol özütleri ise en zengin olarak bulunmuştur. Dolayısıyla örnek özütlerin hazırlanması sırasında çözücünün polaritesi arttıkça, özütlerin fenolik bileşen çeşitliliği bakımından daha zengin hale geldiği gözlenmiştir. Genel olarak tüm etanol özütlerinin rosmarinik asit, kafeik asit, fumarik asit ve malik asit açısından zengin olduğu bulunmuştur. Özellikle *S. cerino-pruinosa* var. *elazigensis* diğer türlere kıyasla bileşen çeşitliliği ve miktarları bakımından daha zengin bulunmuştur. Özellikle bu türün yaprak kısmının rosmarinik asit (34638,45 µg analit/g özüt) içeriği dikkat çekicidir. Genel olarak tüm türlerin antioksidan aktiviteleri yüksek veya orta düzeyde, enzim aktiviteleri ise düşük bulunmuştur. Bu çalışma, 5 endemik türün çeşitli kısımlarının farklı çözücüler (petrol eteri, kloroform ve etanol) kullanılarak hazırlanan ekstraktlarının kimyasal içerikleri ve biyolojik aktiviteleri üzerine literatürde yapılan ilk detaylı çalışmadır. *S. cerino-pruinosa* var. *elazigensis* yaprağının etanol ekstraktı yüksek toplam fenolik ve rosmarinik asit içeriğine ve antioksidan potansiyele sahiptir ve *S. rosifolia*'nın sitotoksik aktivitesi, gıda takviyesi, gıda koruyucu ve ilaç endüstrilerinde kullanım potansiyeline sahiptir.

Anahtar Kelimeler
Salvia
LC-MS/MS
Rosmarinik asit
Biyolojik aktivite
Antiaging

To Cite: Yigitkan, S., Adsiz, L. B., Yilmaz, M. A., Aygun, E., Fidan, H. S., Yaris, E., Akdeniz, M., Çağlayan, M. V., Yener, İ., Boga, M., Firat, M., Kolak, U., Ertaş, A. (2025). *Chemical and biological evaluation of five endemic Salvia species: Rich source of rosmarinic, caffeic, fumaric and malic acids. KSU J. Agric Nat 29* (4), 849-862. DOI: 10.18016/ksutarimdoga.vi.1804808.

Atıf İçin: Yigitkan, S., Adsiz, L. B., Yilmaz, M. A., Aygun, E., Fidan, H. S., Yaris, E., Akdeniz, M., Çağlayan, M. V., Yener, İ., Boga, M., Firat, M., Kolak, U., Ertaş, A. (2025). *Beş endemik Salvia türünün kimyasal ve biyolojik değerlendirmesi: Rosmarinik, kafeik, fumarik ve malik asitlerin zengin kaynağı. KSÜ Tarım ve Doğa Derg 29* (4), 849-862. DOI: 10.18016/ksutarimdoga.vi.1804808.

INTRODUCTION

Medicinal plants are biologically active materials that have been used by the people since ancient times to treat many diseases (Yigitkan et al., 2021; Yigitkan et al., 2024; Cavusoglu et al., 2024; Yildirim et al., 2025) The genus *Salvia* in the Labiatae family is represented by about 100 species, 50% of which are endemic in Turkey (Kahraman et al., 2011). Many *Salvia* species are more or less active in terms of essential oil (0.1-1.0%). The genus *Salvia* has been used for therapeutic purposes for many years (Delamare et al., 2007). Since ancient times, *Salvia* species have been used to treat various diseases and are also consumed as tea and spices. The diterpenes and triterpenes they contain are primarily responsible for their anti-inflammatory, antiviral, cytotoxic, and hepatotoxic properties, while the flavones they carry are known to have a variety of properties including antibacterial, antioxidant, cytotoxic, etc (Son et al., 2005; Topcu et al., 2017; Yener et al., 2020).

Extracts made from *Salvia* species are known to have a strong antioxidant capacity and to be active against a variety of malignant cells (Tayarani-Najaran et al., 2013; Ozer et al., 2013). Since 1968, researchers have studied the phytochemistry and biology of Turkish *Salvia* species, isolating numerous novel and well-known secondary metabolites from their roots and aerial parts (Kolak, 2007; Topcu et al., 2017).

Turkey is a globally significant center for the genus *Salvia*, hosting numerous species, approximately 50% of which are endemic. This high endemism rate makes *Salvia* species in the Turkish flora extremely valuable not only from a botanical perspective but also in terms of phytochemical diversity and biological activity potential. Despite this, a large portion of Turkey's endemic Salvia species remain insufficiently characterized in terms of chemical content and biological activity.

Five endemic species (*Salvia cerino-pruinosa* Rech. f. var. *elazigensis*, *S. cerino-pruinosa* Rech. f. var. *cerino-pruinosa, S. rosifolia* Sm., *S. pseudeuphratica* Rech. and *S. kurdica* Boiss & Hohen. Ex Bentham) have been the subject of few studies in the literature (Yaris et al., 2021; Ertas et al., 2022). When the previous studies are examined, essential oil, aroma and terpenoid content analyses and isolation studies are observed. Studies that comprehensively evaluate the phenolic profiles of endemic species through LC-MS/MS analysis and their

multifaceted biological activities are quite limited. Research on endemic species such as *Salvia cerino-pruinosa*, *S. rosifolia*, *S. pseudeuphratica*, and *S. kurdica* is scarce, and their biological potential remains largely unexplored.

In the present study, three different solvents (ethanol, chloroform and petroleum ether) were used to prepare extracts from different parts of the species (root, leaf, flower, branch and whole plant). The prepared extracts were screened in detail for the first time in the current study in terms of phenolics and flavanoids by LC-MS/MS and their antioxidant (*β*-carotene, ABTS, DPPH, CUPRAC), cytotoxicity (PDF (Healthy primary dermal fibroblast cell line), HT-29 (colon cancer cell line), MCF-7 (breast cancer cell line)), and enzyme (anti-Alzheimer (against acetyl- and butyryl cholinesterase enzymes), antiurease, antityrosinase, antielastase and antichollegenase) activities were determined. While there are numerous studies in the literature on *Salvia* species, this study aims to reveal both the chemical content and biological activities of five endemic species together and with numerous parameters.

MATERIAL and METHOD

Plant material

The whole plant materials of *Salvia* species were collected from the east and southeast parts of Turkey in 2015, and determined by Dr. Mehmet Firat. The voucher specimens were kept in Van Yüzüncü Yıl University's Herbarium (VANF). Table 1 provides comprehensive details about the samples. The plant materials were air-dried in the dark at room temperature kept at +4°C until used for analysis.

Table 1. Information about *Salvia* species
Çizelge 1. *Salvia* türleri hakkında bilgi

Name of the Species	Part/Extraction solvent	Abbreviations	Collection location	Collection time	Herbarium number	Extraction yield (% w/w)
Salvia cerino-pruinosa Rech var. *elazigensis* Kahraman, Celep & Dogan	Root/Ethanol	SCERE	Elâzığ, Turkey	May-2015	VANF-32539	1.47
	Branch/Ethanol	SCEBE				0.40
	Leaf/Ethanol	SCELE				6.60
	Flower/Ethanol	SCEFE				9.36
	Whole/Ethanol	SCEWE				3.11
	Whole/Petroleum ether	SCEWP				0.43
	Whole/Chloroform	SCEWC				0.72
Salvia cerino-pruinosa Rech var. *cerino-pruinosa*	Root/Ethanol	SCCRE	Elâzığ, Turkey	May-2015	VANF-32538	1.78
	Branch/Ethanol	SCCBE				1.74
	Leaf/Ethanol	SCCLE				8.75
	Flower/Ethanol	SCCFE				7.43
	Whole/Ethanol	SCCWE				3.24
	Whole/Petroleum ether	SCCWP				0.47
	Whole/Chloroform	SCCWC				1.04
Salvia rosifolia Sm	Root/Ethanol	SRRE	Kars, Turkey	July-2015	VANF-32536	3.18
	Branch/Ethanol	SRBE				2.87
	Leaf/Ethanol	SRLE				13.63
	Flower/Ethanol	SRFE				9.32
	Whole/Ethanol	SRWE				5.29
	Whole/Petroleum ether	SRWP				0.80
	Whole/Chloroform	SRWC				1.82
Salvia pseudeuphratica Rech	Root/Ethanol	SPRE	Elâzığ, Turkey	July-2015	VANF-32584	2.35
	Branch/Ethanol	SPBE				1.10
	Leaf/Ethanol	SPLE				11.90
	Flower/Ethanol	SPFE				3.18
	Whole/Ethanol	SPWE				4.54
	Whole/Petroleum ether	SPWP				0.85
	Whole/Chloroform	SPWC				4.08
Salvia kurdica Boiss. and Hohen. ex Bentham	Root/Ethanol	SKRE	Şırnak, Turkey	September-2015	VANF-32614	2.60
	Branch/Ethanol	SKBE				5.08
	Leaf/Ethanol	SKLE				17.29
	Whole/Ethanol	SKWE				10.08
	Whole/Petroleum ether	SKWP				3.99
	Whole/Chloroform	SKWC				6.98

Extraction and chemical content analyses

In the extraction study, shade-dried roots and aerial parts of the species (3x8h) were macerated with ethanol, chloroform, and petroleum ether. Stock solutions (4000 µg/mL) of the extracts obtained were prepared and used in the analyses by making the necessary dilutions (Bakir et al. 2020). Thirty-seven phenolic-and flavonoid-derivative compounds were determined in five endemic *Salvia* species extracts using an LC-MS/MS method

previously developed and validated by our research group (Yilmaz et al., 2018). The liquid chromatograph was equipped with LC-30AD binary pumps, CTO-10ASvp column oven, DGU- 20A3R degasser and SIL-30AC autosampler. The chromatographic separation was performed on an RP-C18 Inertsil ODS-4 (100 mm × 2,1 mm, 2 µm) analytical column. Reversed-phase ultrahigh performance liquid chromatography was optimized to achieve optimum separation for 37 phytochemical compounds and to overcome the suppression effects. LOD (limit of detection) was between 0.05 and 25.8 µg/L, while LOQ (limit of quantification) was between 0.17 and 85.9 µg/L. The recoveries of phenolic compounds varied between 96.9−106.2%.

Biological activities of the extracts

In the supplemental material, full biological activity study details were provided. The extracts' total flavonoid and phenolic contents were determined to be equal to quercetin and pyrocatechol, respectively (Moreno et al., 2000; Slinkard & Singleton, 1977). The antioxidant ability of *Salvia* species's extracts was assessed using lipid peroxidation, DPPH free radical, ABTS cation radical scavenging, and cupric reducing antioxidant capabilities (CUPRAC) techniques (Blois, 1958; Miller, 1971; Re et al., 1999; Apak et al., 2004). Furthermore, the inhibitory activities of anticholinesterase, urease, tyrosinase, elastase and collagenase enzyme activities of their extracts were investigated (Ellman et al., 1961; Hearing & Jimenez, 1987; Kraunsoe et al., 1996; Thring et al., 2009; Hina et al., 2015). Additionally, the MTT method was taken into consideration while determining the cytotoxic effects of their extracts (Mojarraba et al., 2013).

Statistical analysis

The activity assay findings were displayed as means±SD. An unpaired test and a one-way analysis of variance (ANOVA) were used to assess the findings. At $p<0.05$, the differences were considered statistically significant.

Supplementary Materials

Detailed information about all testing methods used in the manuscript is provided as a supplementary material.

RESULTS and DISCUSSION

The results of LC-MS/MS

In this study, phenolic contents of the extracts of 5 endemic *Salvia* species prepared with different solvents (ethanol, chloroform, and petroleum ether) were determined by LC-MS/MS (Table 2). Considering the toxicity and content richness of the solvents, ethanol extracts of roots, branches, leaves and flowers of each species were prepared and analyzed by LC-MS/MS. All petroleum ether extracts were found to have extremely low phenolic content when the LC-MS/MS results of the mixed portions of the samples made with various solvents were examined. In terms of component diversity among the analyzed species, the SKWP sample was determined to be rather richer than the other samples. Examining the LC-MS/MS data of the chloroform extracts made from the combined portions of the species under study, it can be observed that all samples have a phenolic content that is typically lower than that of ethanol extracts but higher than that of petroleum ether extracts. Different amounts of hesperidin, *p*-coumaric acid, caffeic acid, salicylic acid, malic acid and apigenin were detected in all chloroform extracts. In addition, rosmarinic acid, fumaric acid, vanillin and apigetrin were in many species. When the results are evaluated in general, it is seen that SCCWC and SKWC samples are richer in terms of component diversity and amounts compared to other samples.

Looking at the LC-MS/MS results of the ethanol extracts prepared from the mixed parts of the species in this study; in general, all samples found to be in phenolic content than petroleum ether and chloroform extracts. All of the ethanol extracts included varying concentrations of hesperidin, *p*-coumaric acid, caffeic acid, salicylic acid, rosmarinic acid, fumaric acid, vanillin, malic acid, naringenin, apigenin, isoquercitrin, apigetrin, and rhoifolin. In addition, chlorogenic acid, protocatechuic acid and hesperetin were found in all samples except SKWE sample (Table 2). Especially rosmarinic acid, fumaric acid and malic acid contents of the species were found to be quite high compared to other components. SCEWE sample was richer in fumaric acid, apigetrin, rhoifolin and nicotiflorin (2068.33, 1549.17, 422.96 and 1430.38 µg analytes/g extract, respectively) and SCCWE sample was richer in caffeic acid, vanillic acid, rosmarinic acid and protocatechuic acid (520. 42, 1094.10, 18969.95 and 289.09 µg analytes/g extract, respectively. In addition, SRWE sample was found to be richer in hesperidin, quinic acid, chlorogenic acid, and malic acid (744.93, 308.62, 215.48, and 4553.55 µg analytes/g extract, respectively). SCEWE and SCCWE samples were found to be richer than the other samples in terms of component diversity and quantities when the results were taken as a whole.

According to the LC-MS/MS results of the ethanol extracts prepared from various parts of the studied species, it was observed that the root and the branch parts close to the root of the SCE species were close to each other in terms of content, and the aerial parts, leaves and flowers of the SCE species were close to each other and

Table 2. Identification and quantification of phenolic compounds of extracts of *Salvia species* by LC-MS/MS (µg analyte/g extract)[a]
Çizelge 2. Salvia türlerinin ekstraktlarındaki fenolik bileşiklerin LC-MS/MS ile tanımlanması ve miktar tayini (µg analit/g ekstrakt)[a]

Sample	1	2	3	4	5	7	8	9	10	11	12	13	14	15	18	19	20	21	23	24	25	31	33	34	35	36
SCERE	ND	2908.19	578.29	ND[b]	694.85	ND	112.98	929.47	463.82	ND	247.38	12.61	15.39	ND	22.54	6.64	7107.27	ND	32.59	ND	33.85	ND	ND	2.78	ND	ND
SCEBE	ND	1453.65	1656.57	ND	156.44	ND	ND	575.19	147.63	ND	50.8	30.67	10.57	ND	77.69	11.08	1701.59	1453.96	93.1	ND	63.19	ND	3.31	27.27	5.7	ND
SCELE	208.17	3004.02	738.3	ND	626.7	ND	ND	691.71	879.52	ND	24.32	100.35	121.3	ND	44.15	165.93	34638.45	ND	940.47	ND	1599.2	ND	3.28	131.79	ND	ND
SCEFE	318.44	5743.01	1214.7	ND	130.61	ND	ND	ND	267.87	ND	ND	36.77	33.95	ND	1047.65	262.4	14898.05	3573.88	481.94	ND	6902.16	5.84	4.58	225.77	25.98	ND
SCEWE	291.87	4482.51	2068.33	ND	214.34	62.88	ND	142.06	320.7	ND	68.04	41.81	45.18	ND	285.31	135	15666.13	1430.38	422.96	ND	1549.17	3.98	5.05	85.14	19.18	ND
SCEWP	ND	ND	77.03	ND	ND	ND	ND	ND	ND	ND	ND	ND	0.24	ND	10.55	4.99	11.1	ND	ND	ND	3.5	ND	ND	0.45	ND	ND
SCEWC	ND	135.56	269.82	ND	ND	ND	ND	ND	2.33	ND	83.12	4.01	5.01	ND	13.48	ND	9.3	ND	ND	ND	10.73	ND	5.18	104.97	7.91	ND
SCCRE	351.04	1093.84	561.75	ND	307.55	145.11	54.75	1582.52	282.53	ND	257.46	12.77	16.34	ND	52.45	ND	4419.28	ND	10.66	ND	28.21	ND	8.05	4.22	31.36	ND
SCCBE	ND	1795.09	2474.45	54.46	280.75	13.25	ND	1344.15	259.38	ND	152.7	31.72	18.85	ND	274.75	17.96	5397.2	ND	97.46	ND	71.36	11.45	3.52	32.54	9.6	ND
SCCLE	ND	1989.32	717.99	ND	166.89	ND	ND	697.48	772.43	ND	ND	34.11	39.67	ND	22.72	45.36	29611.71	ND	127.17	ND	299.88	ND	ND	14.49	ND	ND
SCCFE	133.87	5249.16	1398.46	ND	111.31	ND	ND	ND	263.69	ND	ND	51.21	14.08	ND	131.58	143.77	12895.8	1291.35	60.17	ND	455.6	3.68	5.82	70.64	65.99	ND
SCCWE	ND	3047.52	1115.93	ND	289.09	152.98	41.41	1094.1	520.42	ND	89.37	33.95	31.38	39.28	157.16	75.83	18969.95	ND	254.95	ND	303.19	6.46	6.65	32.9	15.38	ND
SCCWP	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	0.18	ND	18.87	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
SCCWC	ND	833.93	255.98	ND	ND	ND	ND	ND	11.54	ND	110.7	4.63	0.38	ND	24.18	5.87	131.62	ND	ND	ND	7.14	ND	1.28	4.61	10.82	ND
SRRE	ND	2927.62	163.06	ND	81.82	30.04	ND	205.73	303.42	ND	17.45	8.24	0.33	ND	133.78	16.36	3202.34	ND	11.03	ND	ND	ND	ND	4.5	10.49	ND
SRBE	106.02	3035.61	412.98	ND	479.97	271.94	55.1	469.4	876.32	ND	55.88	28.72	13.27	ND	1678.23	8.43	3786.9	ND	60.22	ND	7.37	ND	5.2	52.34	183.48	ND
SRLE	228.32	4923.36	775.58	ND	41.39	117.87	ND	ND	293.79	ND	ND	42.12	18.65	ND	226.64	11.92	19379.81	892.43	89.19	ND	140.96	ND	1.29	57.38	ND	ND
SRFE	936.01	4485.48	2660.71	ND	365.69	350.48	ND	ND	237.69	88.93	25.96	92.23	25.15	ND	152.05	228.94	6864.59	1668.32	556.55	ND	257.77	14.71	3.09	659	4.4	ND
SRWE	308.62	4553.55	755.65	ND	152.74	215.48	ND	ND	510.1	ND	57.48	56.11	31.45	6.91	744.93	57.17	7410.93	391.48	260.13	69.14	78.35	ND	2.89	112.32	17.83	ND
SRWP	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	0.17	ND	16.45	ND	ND	ND	ND	ND	ND	ND	ND	1.25	ND	ND
SRWC	ND	74.41	ND	ND	ND	ND	ND	ND	27.95	ND	70.19	3.99	4.65	ND	17.37	ND	20.97	ND	ND	ND	ND	ND	5.14	61.66	26.54	ND
SPRE	ND	1185.55	146.56	ND	151.04	ND	53.21	ND	225.37	ND	100.84	5.28	13.54	ND	73.57	6.53	3604.27	ND	ND	ND	9.21	ND	0.76	3.55	13.34	ND
SPBE	ND	47.04	361.48	ND	272.18	ND	89.32	1058.98	225.72	ND	149.27	13.3	16.91	ND	109.15	ND	785.35	ND	ND	ND	45.95	ND	3.07	17.65	82.09	ND
SPLE	ND	4406.81	740.24	ND	123.89	ND	163.94	ND	328.83	ND	ND	109.25	87.28	ND	97.54	57.8	11256.23	ND	404.69	ND	2259.09	6.44	3.18	212.05	9.86	ND
SPFE	387.85	11130.09	2247.18	ND	77.28	ND	ND	ND	421.75	ND	ND	114.82	59.56	ND	269.87	26.8	14088.73	455.24	33.88	ND	1106.67	ND	2.37	124.18	80.27	ND
SPWE	ND	1677.3	399.72	ND	172.39	45.41	90.28	125.18	263.81	ND	43.73	54.04	53.07	174.76	120.32	43.73	5510.05	ND	164.07	91.93	1071.96	ND	4.05	184.73	27.34	ND
SPWP	ND	ND	223.18	ND	ND	ND	ND	ND	ND	ND	ND	ND	0.23	ND	31.82	ND	ND	ND	ND	ND	3.83	ND	ND	1.62	ND	ND
SPWC	ND	241.37	248.86	ND	ND	ND	ND	ND	1.86	ND	32.72	2.09	2.65	ND	46.76	ND	11.84	ND	ND	ND	8.89	ND	ND	33.93	ND	ND
SKRE	ND	3410.89	328.88	ND	801.46	ND	123.98	501.24	648.64	ND	151.01	114.44	51.39	ND	204.7	12.58	10536.04	194.59	ND	ND	19.71	ND	3.05	30.08	20.25	ND
SKBE	ND	6713.1	5312.29	ND	433.27	10.63	108.36	ND	337.69	ND	44.47	163.78	30.61	ND	162.31	175.33	4269.35	ND	190.07	ND	309.91	12.88	5.7	193.9	4.58	109.83
SKLE	ND	2722.03	844.5	ND	61.29	ND	88.73	ND	205.32	ND	ND	47	33.86	16.39	0.42	163.27	3727.6	ND	110.03	ND	878.08	4.87	8.37	536.66	ND	55.65
SKWE	ND	2313.73	893.02	ND	ND	ND	105.83	ND	166.02	ND	20.73	48.21	33.04	ND	42.51	120.13	7585.25	131.82	99.21	ND	528.49	ND	5.27	366.39	ND	46.28
SKWP	ND	265.47	578.49	ND	ND	ND	ND	ND	ND	ND	ND	6.71	0.31	ND	5.02	7.01	ND	ND	ND	ND	ND	ND	0.97	27.12	ND	ND
SKWC	ND	335.94	422.36	ND	ND	ND	ND	ND	1.37	ND	ND	14.03	7.39	ND	9.47	ND	ND	ND	ND	ND	12.19	ND	9.14	233.06	ND	ND

[a]Values in *µ*g/g (w/w) of plant ethanol extract, [b]ND: not detected, 1: Quinic acid, 2: Malic acid, 3: Fumaric acid, 4: Gallic acid, 5: Protocatechuic acid, 6: Pyrocatechol, 7: Chlorogenic acid, 8: 4-OH-Benzoic acid, 9: Vanillic acid, 10: Caffeic acid, 11: Syringic acid, 12:Vanillin, 13: Salicylic acid, 14: p-Coumaric acid, 15: Rutin, 16: tr-Ferulic acid, 17: Sinapinic acid, 18: Hesperidin, 19: Isoquercitrin, 20: Rosmarinic acid, 21: Nicotiflorin, 22: o-Coumaric acid, 23: Rhoifolin, 24: Quercitrin, 25: Cosmosiin, 26: Coumarin, 27: Myricetin, 28: Fisetin, 29: Cinnamic acid, 30: Liquiritigenin, 31: Quercetin, 32: Luteolin, 33: Naringenin, 34: Apigenin, 35: Hesperetin, 36: Kaempferol, 37: Chrysin. The U values (relative uncertainty at a 95% confidence level (k = 2)), which include the standard deviation and repeatability measurements for the LC-MS/MS method used, are included in the method validation study (Yilmaz et al., 2018).

contained similar components (Figure 1). The SCEFE sample was found to be richer in hesperidin, malic acid, apigenin, isoquercitrin, apigetrin and nicotiflorin (1047.65, 5743.01, 225.77, 262.40, 6902.16 and 3573.88 µg analytes/g extract, respectively). It is noteworthy that the amounts of hesperidin, apigetrin and nicotiflorin in the SCEFE sample are considerably higher than the other parts. SCELE sample was found to be richer in caffeic acid, rosmarinic acid and rhoifolin (879.52, 34638.45 and 940.47 µg analytes/g extract, respectively) compared to other samples. In addition, SCERE sample was found to be richer in vanillic acid, protocatechuic acid and vanillin (929.47, 694.85 and 247.38 µg analytes/g extract, respectively) than the other samples.

Evaluating the studied parts of the SCC species within themselves, it was found that the SCCFE sample was richer in malic acid, apigetrin and nicotiflorin (5249.16, 455.60 and 1291.35 µg analytes/g extract, respectively) compared to the other parts. Nicotiflorin's identification in the SCCFE sample, without detection in the other parts, is particularly unexpected. In addition, SCCLE sample contained caffeic acid and rosmarinic acid (772.43 and 29611.71 µg analytes/g extract, respectively), SCCBE sample contained hesperidin and fumaric acid (274.75 and 2474. 45 µg analytes/g extract) and SCCRE sample was richer in vanillic acid, protocatechuic acid and vanillin (1582.52, 307.55 and 257.46 µg analytes/g extract, respectively). The other components detected were close to each other and in low amounts in all parts.

According to the evaluation of the studied parts of the SR species, it was realized that the contents of rosmarinic acid, malic acid and fumaric acid were considerably higher than the other components in all parts of the species. The results showed that SRFE sample was richer in quinic acid, chlorogenic acid, fumaric acid, isoquercitrin, apigetrin, rhoifolin and nicotiflorin (936.01, 350.48, 2660.71, 228.94, 257.77, 556.55 and 1668.32 µg analytes/g extract, respectively). In addition, SRLE sample was richer in rosmarinic acid and malic acid (19379.81 and 4923.36 µg analytes/g extract, respectively), and SRBE sample was richer in hesperidin, caffeic acid and protocatechuic acid (1678.23, 876.32 and 479.97 µg analytes/g extract, respectively). In addition, the other components detected were close to each other and in low amounts in all parts.

When the examined portions of the SP species were assessed among themselves, the SPFE sample was discovered to be richer than the other samples in terms of component variety and quantities. The SPFE sample was found to be richer in hesperidin, caffeic acid, salicylic acid, rosmarinic acid, fumaric acid, malic acid and nicotiflorin (269.87, 421.75, 114.82, 14088.73, 2247.18, 11130.09 and 455.24 µg analytes/g extract, respectively). It is interesting to note that nicotiflorin and quinic acid were found only in the SPFE sample but not in the other parts. In addition, SPLE sample was richer in 4-OH-benzoic acid, apigenin, apigetrin and rhoifolin (163.94, 212.05, 2259.09 and 404.69 µg analytes/g extract, respectively), while SPBE sample was richer in vanillic acid, protocatechuic acid and vanillin (1058.98, 272.18, and 149.27 µg analytes/g extract).

After analyzing the examined portions of the SK species, it was determined that the SKRE sample had higher component variety and quantities than the other samples. SKRE sample was found to be richer in hesperidin, Caffeic acid, 4-OH-benzoic acid, rosmarinic acid, protocatechuic acid, malic acid and nicotiflorin (204.70, 648.64, 123.98, 10536.04, 801.46, 3410.89 and 194.59 µg analytes/g extract, respectively). In addition, vanillic acid (501.24 µg analyte/g extract) was detected only in SKRE sample. In addition, SKBE sample was richer in salicylic acid, fumaric acid, isoquercitrin, rhoifolin and kaemferol (163.78, 5312.29, 175.33, 190.07 and 109.83 µg analytes/g extract, respectively) and SKLE sample was richer in apigenin and apigetrin (536.66 and 878.08 µg analytes/g extract, respectively).

The polyphenol-structured, physiologically active ingredient in *Rosmarinus officinalis* is rosmarinic acid. As phytochemicals, polyphenol compounds are thought to be an effective substitute for anticancer medications, which are hazardous when used in chemotherapy and have a lot of adverse effects. Numerous bioactive characteristics of rosmarinic acid have been demonstrated by studies, and these characteristics have gained attention as antioxidant, antidepressant, hepatoprotective, anti-inflammatory, anti-angiogenic, anti-tumor, and anti-HIV activities (Takeda et al., 2002; Dubois et al., 2008). Furthermore, rosmarinic acid is a potent antioxidant that inhibits lipid peroxidation and scavenges reactive species (Yener et al., 2020). This antioxidant feature of rosmarinic acid might be explained by the presence of the 4-hydroxyl group in its structure. These groups ensure that this compound with phenolic structure has a high therapeutic effect against oxidative stress. Rosmarinic acid has a wide range of applications in the industry with this feature. It is used in food products to increase shelf life and to prevent degradation. Furthermore, it has found quite extensive application areas in the cosmetics and pharmaceutical industry (Kosar et al., 2008).

The literature has reports on a variety of bioactive components that have been found or isolated from *Salvia* species. According to the literature, *Salvia* species are abundant in rosmarinic acid in relation to this study (Halfon et al., 2019; Zengin et al., 2019). High concentrations of rosmarinic acid are found in the following species: *S. blepharochlaena* (22 mg/g), *S. euphratica* var. *leiocalycina* (10.3 mg/g), *S. verticillata* subsp. *amasiaca* (67 mg/g), *S. hispanica* (0.74 mg/g), and *S. officinalis* (8.4-10.8 mg/g DW). The findings of the current investigation are consistent with the literature when viewed within this context.

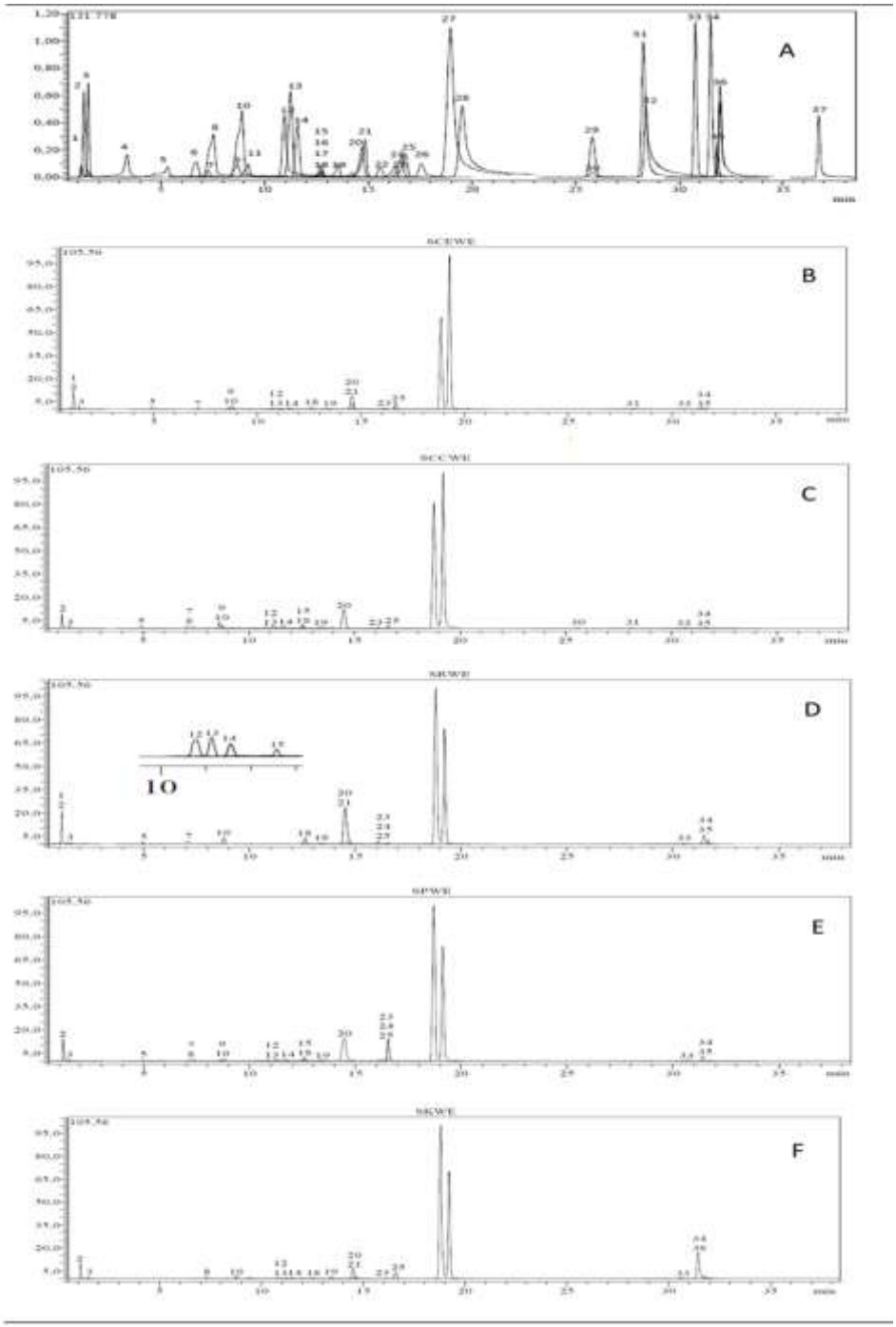

Figure 1. LC-MS/MS chromatograms A: TIC chromatogram of standard chemicals analyzed by LC-MS/MS method. 1: Quinic acid, 2: Malic acid, 3: Fumaric acid, 4: Gallic acid, 5: Protocatechuic acid, 6: Pyrocatechol, 7: Chlorogenic acid, 8: 4-OH-Benzoic acid, 9: Vanillic acid, 10: Caffeic acid, 11: Syringic acid, 12:Vanillin, 13: Salicylic acid, 14: p-Coumaric acid, 15: Rutin, 16: tr-Ferulic acid, 17: Sinapinic acid, 18: Hesperidin, 19: Isoquercitrin, 20: Rosmarinic acid, 21: Nicotiflorin, 22: o-Coumaric acid, 23: Rhoifolin, 24: Quercitrin, 25: Cosmosiin, 26: Coumarin, 27: Myricetin, 28: Fisetin, 29: Cinnamic acid, 30: Liquiritigenin, 31: Quercetin, 32: Luteolin, 33: Naringenin, 34: Apigenin, 35: Hesperetin, 36: Kaempferol, 37: Chrysin, B: LC-MS/MS chromatogram of ethanol extract of *Salvia cerino-pruinosa* var. *elazigensis* C: LC-MS/MS chromatogram of ethanol extract of *Salvia cerino-pruinosa* var. *cerino-pruinosa*, D: LC-MS/MS chromatogram of ethanol extract of *Salvia rosifolia*, E: LC-MS/MS chromatogram of ethanol extract of *Salvia pseudeuphratica*, F: LC-MS/MS chromatogram of ethanol extract of *Salvia kurdica*.

Şekil 1. LC-MS/MS kromatogramları A: LC-MS/MS yöntemiyle analiz edilen standart kimyasalların TİK kromatogramı. 1: Kinik asit, 2: Malik asit, 3: Fumarik asit, 4: Gallik asit, 5: Protokateşuik asit, 6: Pirokatekol, 7: Klorojenik asit, 8: 4-OH-Benzoik asit, 9: Vanilik asit, 10: Kafeik asit, 11: Şırınga asidi, 12: Vanilin, 13: Salisilik asit, 14: p-Kumarik asit, 15: Rutin, 16: tr-Ferulik asit, 17: Sinapinik asit, 18: Hesperidin, 19: İzokersitrin, 20: Rosmarinik asit, 21: Nikotiflorin, 22: o-Kumarik asit, 23: Rhoifolin, 24: Quercitrin, 25: Kozmosin, 26: Kumarin, 27: Mirisetin, 28: Fisetin, 29: Sinnamik asit, 30: Liquiritigenin, 31: Kuersetin, 32: Luteolin, 33: Naringenin, 34: Apigenin, 35: Hesperetin, 36: Kaempferol, 37: Krizin, B: Salvia cerino-pruinosa var. elazigensis'in etanol özütünün LC-MS/MS kromatogramı C: Salvia cerino-pruinosa var. cerino-pruinosa'nın etanol özütünün LC-MS/MS kromatogramı, D: Salvia rosifolia'nın etanol özütünün LC-MS/MS kromatogramı, E: Salvia pseudeuphratica'nın etanol özütünün LC-MS/MS kromatogramı, F: Salvia kurdica'nın etanol özütünün LC-MS/MS kromatogramı.

Across all species, rosmarinic acid emerged as the dominant compound, accompanied by relatively high levels of malic acid and fumaric acid, particularly in ethanol extracts. This compositional pattern is consistent with previous reports on *Salvia* species and highlights the strong affinity of these phenolic acids for polar solvents. Among the investigated taxa, *Salvia cerino-pruinosa* var. *elazigensis* displayed the richest phenolic profile in both diversity and concentration. Notably, the leaf and flower extracts of this species showed pronounced enrichment in rosmarinic acid and flavonoid glycosides, suggesting tissue-specific accumulation of bioactive metabolites. Similar organ-dependent variations were observed in other species, with aerial parts generally exhibiting higher phenolic content than roots and branches. As a result, the study suggests that five endemic *Salvia* species could be a natural source of rosmarinic acid and, due to their rich bioactive content, could have potential applications in the food and pharmaceutical industries.

Total phenolic and flavonoid content

The present investigation revealed that the total flavonoid and phenolic contents of ethanol extracts made from different sections of five endemic *Salvia* species were equivalent to quercetin and pyrocatechol, respectively (Table 3). In ethanol, chloroform and petroleum ether extracts, ethanol extracts≥chloroform extracts≥petroleum ether extracts in terms of total phenolic content in SCE, SCC and SK species. In SR and SP extracts, the opposite order was observed. It is seen that there is a similar order in flavonoid content. It can be concluded that SR and SP species are nonpolar, while SCE, SCC and SK species are richer in more polar phenolic compounds.

Taking into account the total amounts of flavonoids and phenolics in the ethanol extracts of the species' combined portions, SCEWE sample was found to be richer in both phenolic (212.99±5.99 µg PEs/mg extract) and flavonoid (52.60±1.96 µg QEs/mg extract) contents than the other species. The SPWE sample was the poorest in terms of both phenolic (38.02±1.40 µg PEs/mg extract) and flavonoid (24.87±0.78 µg QEs/mg extract) contents.

In SCE species, SCELE sample was richer than the other samples in terms of both phenolic and flavonoid (229.94±2.00 µg PEs/mg extract and 65.95±0.90 µg QEs/mg extract, respectively) contents. In SCC species, SCCLE sample was richer than the other samples in terms of both phenolic and flavonoid (92.01±3.42 µg PEs/mg extract and 39.31±0.20 µg QEs/mg extract, respectively) contents. In SR species, SRLE sample was richer than the other samples in terms of both phenolic and flavonoid (196.05±2.00 µg PEs/mg extract and 37.41±1.28 µg QEs/mg extract, respectively) contents. In SP species, SPFE sample was richer in phenolic content (48.43±2.00 µg PEs/mg extract) and SPLE sample was richer in flavonoid content (30.33±0.78 µg QEs/mg extract). The flower part of the SK species could not be studied because it could not be obtained sufficiently. Apart from this, when the species' studied parts are evaluated within themselves; SKRE sample is richer than the other samples in terms of phenolic content (125.42±5.99 µg PEs/mg extract) and SKLE sample is richer than the other samples in terms of flavonoid content (42.80±1.26 µg QEs/mg extract).

When the results were assessed as a whole, the SCE species was found to be richer than other species in terms of total phenolic and flavonoid content, parallel to the LC-MS/MS results.

Antioxidant and toxic-cytotoxic activities

Ethanol extracts were found to be more active in ABTS, DPPH, and CUPRAC techniques than extracts made with petroleum ether and chloroform, when the extracts made with different solvents were tested. It is noteworthy that only nonpolar chloroform and petroleum ether extracts showed high activity in *β*-carotene method. Among the ethanol, chloroform and petroleum ether extracts prepared with different solvents, SCEWE extract was found to be the most active extract in all 4 methods tested. Examining the antioxidant outcomes of the ethanol extracts made from the species' various components; SCEWE sample was found to have higher antioxidant potential than the other samples in *β*-carotene (IC_{50}: 28.95±0.11 µg/mL), DPPH (IC_{50}: 10.51±0.56 µg/mL), ABTS (IC_{50}: 24.09±0.62 µg/mL) and CUPRAC ($A_{0.5}$: 16.67±0.54 µg/mL) in all 4 methods (Table 3).

In the SCE species, in parallel with the total phenolic and flavonoid contents, the SCELE sample had higher antioxidant potential in DPPH (IC_{50}: 5.72±0.71 µg/mL), ABTS (IC_{50}: 2. 43±0.21 µg/mL) and CUPRAC ($A_{0.5}$: 11.67±0.07 µg/mL), while the SCEWE sample was found to have the highest antioxidant potential in the ß-carotene (IC_{50}: 28.95±0.11 µg/mL) method. It is quite remarkable that SCELE and SCEFE samples have higher antioxidant potential than *α*-TOC and BHT used as standard reference in DPPH and ABTS methods. In addition, it was determined that SCELE and SCEFE samples showed almost the same level of antioxidant properties as the standard *α*-TOC in the CUPRAC method.

In parallel with the total phenolic and flavonoid contents in SCC species, SCCFE sample had higher antioxidant potential in *β*-carotene (IC_{50}: 48.55±0.52 µg/mL) and DPPH (IC_{50}: 14. 17±0.71 µg/mL), while the SCCLE sample was found to have the highest antioxidant potential in ABTS (IC_{50}: 11.48±0.95 µg/mL) and CUPRAC ($A_{0.5}$: 29.53±0.78 µg/mL) methods. It is quite remarkable that SCCFE sample showed antioxidant properties at the level of *α*-TOC used as a standard in DPPH and SCCLE sample showed higher antioxidant potential than BHT in ABTS method.

Table 3. Biological activities of *Salvia* species
Çizelge 3. Salvia türlerinin biyolojik aktiviteleri

Samples	Antioxidant activity[1]						Cytotoxic activity[1]		
	IC_{50} (µg/mL)			$A_{0.5}$(µg/mL)			IC_{50} (µg/mL)		
	β-Carotene-linoleic acid	DPPH Free Radical	ABTS Cation Radical	CUPRAC	Phenolic content (µg PEs/mg extract)[2]	Flavonoid content (µg QEs/mg extract)[3]	HT-29	MCF-7	PDF
SCERE	35.87±0.04^{a}	39.85±0.39^{a}	46.08±0.02^{a}	34.75±1.24^{a}	119.77±9.99^{a}	23.08±0.36^{a}	-	-	-
SCEBE	193.52±4.30^{b}	89.35±0.53^{b}	75.92±0.56^{b}	73.00±2.56^{b}	81.64±3.99^{b}	17.99±0.3b^{b}	-	-	-
SCELE	69.04±0.98^{c}	5.72±0.01^{c}	2.43±0.21^{c}	11.67±0.07^{c}	229.94±2.00^{c}	65.95±0.90^{c}	-	-	-
SCEFE	99.96±0.74^{d}	10.58±0.69^{d}	6.25±0.49^{d}	22.29±0.34^{d}	187.57±1.89^{d}	41.02±0.18^{d}	-	-	-
SCEWE	28.95±0.11^{e}	10.51±0.56^{d}	24.09±0.62^{e}	16.67±0.54^{e}	212.99±5.99^{e}	52.60±1.96^{e}	238.05±0.90^{a}	336.50±4.04^{a}	≥1000^{a}
SCEWP	98.02±3.56^{f}	>1000^{e}	>1000^{f}	110.77±3.21^{f}	97.18±2.00^{f}	16.46±0.51^{b}	≥1000^{b}	≥1000^{b}	≥1000^{a}
SCEWC	102.68±0.03^{f}	>1000 ^{e}	503.91±2.46^{g}	184.09±3.45^{g}	152.26±2.92^{g}	30.08±1.62^{f}	65.89±0.40^{c}	85.93±1.49c	173.79±2.53^{b}
SCCRE	62.35±0.66^{g}	67.71±0.37^{f}	38.10±0.79^{h}	47.15±1.06^{h}	44.19±0.86^{h}	22.60±0.83^{g}	-	-	-
SCCBE	302.29±6.03^{h}	43.91±1.30^{g}	31.58±0.22^{i}	47.68±1.26^{h}	43.58±1.71^{h}	23.56±0.59^{g}	-	-	-
SCCLE	94.88±1.31^{i}	15.81±0.06^{h}	12.48±0.95^{i}	29.53±0.78^{i}	92.01±3.42^{i}	39.31±0.20^{d}	-	-	-
SCCFE	48.55±0.52^{i}	14.17±0.55^{h}	22.11±0.35^{j}	30.95±1.03^{i}	75.06±1.71^{j}	27.15±0.93^{h}	-	-	-
SCCWE	82.82±0.10^{j}	25.26±0.10^{i}	28.50±0.24^{k}	36.89±1.06^{a}	72.03±2.57^{j}	35.99±0.59^{i}	347.49±2.84^{d}	≥1000^{b}	≥1000^{a}
SCCWP	70.88±1.15^{c}	>1000 ^{e}	>1000 ^{f}	213.00±3.56^{j}	32.28±0.70^{k}	18.73±0.78^{b}	≥1000^{b}	≥1000^{b}	≥1000^{a}
SCCWC	35.26±0.06^{a}	486.25±9.62^{i}	202.12±4.60^{l}	172.73±2.68^{k}	54.64±1.85^{l}	39.43±1.56^{d}	164.06±2.14^{e}	137.80±0.84^{d}	152.95±1.58^{c}
SRRE	127.79±0.96^{k}	150.75±0.50^{j}	83.09±0.49^{m}	45.85±1.34^{l}	87.29±2.82^{m}	21.04±0.72^{g}	-	-	-
SRBE	102.11±2.36^{f}	109.05±1.00^{k}	77.66±0.80^{n}	51.15±2.12^{m}	107.06±3.99^{n}	22.06±0.67^{g}	-	-	-
SRLE	85.34±1.65^{l}	25.79±0.85^{i}	24.15±0.54^{e}	13.88±0.06^{n}	196.05±2.00^{o}	37.41±1.28^{i}	-	-	-
SRFE	124.37±0.56^{m}	80.16±0.27^{l}	111.48±2.65^{o}	39.55±1.49^{o}	102.82±2.00^{p}	20.87±0.39^{g}	-	-	-
SRWE	105.27±3.77^{f}	50.91±0.90^{m}	36.52±0.03^{p}	32.00±1.05^{i}	115.54±4.89^{a}	36.48±1.40^{i}	512.93±9.61^{f}	803.58±4.20^{e}	561.36±7.93^{d}
SRWP	86.35±4.27^{l}	>1000 ^{e}	>1000 ^{f}	93.95±2.33^{p}	172.03±3.99^{q}	45.73±0.68^{j}	≥1000^{b}	≥1000^{b}	≥1000^{a}
SRWC	44.99±0.82^{n}	>1000 ^{e}	>1000 ^{f}	68.25±2.01^{q}	169.21±4.99^{q}	50.43±0.18^{e}	65.03±0.39^{c}	29.77±0.72^{f}	158.94±0.28^{e}
SPRE	22.15±0.72^{o}	31.95±0.59^{n}	34.15±0.59^{r}	42.16±1.06^{r}	43.99±0.70^{h}	29.50±0.73^{f}	-	-	-
SPBE	87.78±0.55^{l}	100.11±0.60^{o}	61.95±0.99^{s}	60.55±1.67^{s}	30.87±0.86^{k}	20.11±0.39^{g}	-	-	-
SPLE	137.31±11.90^{p}	50.36±1.12^{m}	58.79±1.03^{t}	70.68±2.07^{q}	38.74±1.71^{r}	30.33±0.78^{f}	-	-	-
SPFE	101.58±1.84^{f}	45.40±0.43^{p}	49.99±0.84^{u}	55.74±2.03^{m}	48.43±0.00^{s}	21.40±0.32^{g}	-	-	-
SPWE	157.50±3.20^{r}	103.49±0.30^{r}	68.93±0.53^{v}	79.04±2.44^{t}	38.02±1.40^{r}	24.87±0.78^{g}	95.93±2.30^{g}	112.04±3.19^{g}	180.40±2.10^{f}
SPWP	169.72±11.00^{s}	>1000 ^{e}	>1000 ^{f}	132.93±3.58^{u}	91.53±5.99^{m}	27.49±1.40^{h}	≥1000^{b}	≥1000^{b}	≥1000^{a}
SPWC	71.28±0.06^{c}	455.25±8.64^{s}	207.79±4.68^{y}	130.47±3.55^{u}	90.94±7.99^{m}	30.84±0.90^{f}	57.05±0.18^{i}	98.44±1.16^{h}	142.31±0.83^{g}
SKRE	103.26±0.51^{f}	51.59±2.59^{m}	50.75±0.87^{u}	31.01±1.02^{i}	125.42±5.99^{a}	20.11±0.64^{g}	-	-	-
SKBE	108.87±0.23^{f}	190.36±3.50^{t}	199.46±3.98^{l}	89.83±2.35^{v}	81.64±8.47^{b}	19.90±0.18^{g}	-	-	-
SKLE	44.05±0.15^{n}	229.60±1.75^{u}	48.32±1.58^{u}	70.69±2.03^{q}	68.93±2.00^{t}	42.80±1.26	-	-	-
SKWE	132.36±0.53^{t}	76.85±0.32^{v}	133.98±1.07^{z}	35.92±1.23^{a}	98.59±0.00^{f}	39.54±0.54^{d}	612.68±5.62^{j}	782.31±6.82^{i}	≥1000^{a}
SKWP	142.80±1.07^{u}	>1000 ^{e}	>1000 ^{f}	89.47±2.24^{v}	68.93±2.00^{t}	27.40±0.72^{h}	≥1000^{b}	≥1000^{b}	≥1000^{a}
SKWC	117.64±0.45^{v}	>1000 ^{e}	>1000 ^{f}	73.93±1.56^{q}	77.40±2.00^{j}	40.00±0.90^{d}	215.25±2.38^{k}	278.23±1.03^{j}	128.79±1.92^{h}
α-TOC[4]	3.1±0.11^{y}	15.30±0.89^{h}	10.74±0.65^{i}	15.57±0.67^{e}	-	-	-	-	-
BHT[4]	1.5±0.01^{z}	54.56±1.50^{y}	13.25±0.45^{i}	6.76±0.12^{w}	-	-	-	-	-

[1]Values expressed are means ± S.D. of three parallel measurements and values were calculated according to negative control, Values with different letters in the same column were significantly different ($p<0.05$), [2]PEs, pyrocatechol equivalents (y=0.0177+0.0341 pyrocatechol (µg) (r^2=0.9920), [3]QEs, quercetin equivalents (y=0.0393+0.00073 quercetin (µg) (r^2=0.9925), [4]Standard compound

In SR species, in parallel with the total phenolic and flavonoid contents, SRLE sample was found to have higher antioxidant potential than the other samples in *β*-carotene (IC_{50}: 85.34±1.65 µg/mL), DPPH (IC_{50}: 25.79±0.85 µg/mL), ABTS (IC_{50}: 24.15±0.54 µg/mL) and CUPRAC ($A_{0.5}$: 13.88±0.06 µg/mL) in all 4 methods. It is especially important that the SRLE sample showed higher antioxidant properties than *α*-TOC used as a standard in the CUPRAC method.

In parallel with the total phenolic and flavonoid contents in SP species, SPRE sample was found to have higher antioxidant potential than the other samples in all 4 methods, *β*-carotene (IC_{50}: 22.15±0.72 µg/mL), DPPH (IC_{50}: 31.95±0.59 µg/mL), ABTS (IC_{50}: 34.15±0.59 µg/mL) and CUPRAC ($A_{0.5}$: 42.16±1.06 µg/mL). In general, the other samples showed moderate antioxidant properties.

In general, all SKE samples showed moderate antioxidant properties. SKRE sample was found to have higher antioxidant potential in DPPH (IC_{50}: 51.59±2.59 µg/mL) and CUPRAC ($A_{0.5}$: 31.01±1.02 µg/mL) methods and SKLE sample was found to have higher antioxidant potential in *β*-carotene (IC_{50}: 44.05±0.15 µg/mL) and ABTS (IC_{50}: 48.32±1.58 µg/mL) methods. Because of the high concentration of rosmarinic acid in these species, it is known from the literature on the antioxidant potential of *Salvia* species that they exhibit very strong antioxidant activity (Halfon et al., 2019). Numerous research have also demonstrated that rosmarinic acid has a very high potential for antioxidants in the literature (Bakir et al., 2020).

Using the MTT method, the toxic-cytotoxic effects of petroleum ether, chloroform, and ethanol extracts were assessed against malignant (HT-29, MCF-7) and healthy (PDF) cell lines. In general, the toxic effects of chloroform extracts of all species were found to be high. These chloroforme extracts also showed high cytotoxic effect on breast and colon cancer cell lines. SPWC extract showed the highest cytotoxic effect on colon cancer cell line (HT-29) (IC_{50}: 57.05±0.18 µg/mL), while SRWC extract showed the highest cytotoxic effect against breast cancer cell line (MCF-7) (IC_{50}: 29.77±0.72 µg/mL). The literature indicates that the SPWC type is rich in abietane compounds such as ferruginol, cryptanol, and 6.7-dehydroroyleanone, while the SRWC extract is rich in triterpene compounds such as ursolic and oleanolic acid (Yaris et al., 2021; Akdeniz et al., 2022). It can be said that this cytotoxic effect originates from these components. Furthermore, it has been demonstrated that this effect can be explained by synergistic interactions between multiple secondary metabolites, including phenolic acids and flavonoids found in moderate amounts according to LC-MS/MS results. Similar synergistic cytotoxic effects have previously been reported for *Salvia* species and other Lamiaceae members (Yaris et al., 2021).
Extracts made from *Salvia* species have been shown to be effective against a variety of malignant cells (Taharani-Najaran et al., 2013; Ozer et al., 2013). *Salvia* species are known to produce secondary metabolites with a variety of properties, including hepatotoxic, anti-inflammatory, cytotoxic/antitumor, and antioxidant properties (Son et al., 2005; Topcu et al., 2017). Ferruginol, a diterpene containing phenol ring also derived from *Salvia* species, has been shown in a study by Son et al. (2005) to be beneficial against lung, breast, and colon cancer. In this framework, detailed studies should be carried out on which secondary metabolites are responsible for these high cytotoxic effects of SPWC and SRWC extracts.

Enzyme inhibitory activities

Anticholinesterase enzyme activities of the extracts were determined against acetyl and butyrylcholinesterase enzymes (Table 4). When the acetylcholinesterase enzyme results of the species were analyzed; SKWC sample showed moderate activity (inhibition %: 25.93±1.68) while all other samples did not show acetylcholinesterase enzyme activity. Again, it was determined that all species except SR and SK species showed medium-high activity against butyrylcholinesterase enzyme. It was observed that the BChE activities of all species were ranked as petroleum ether extracts≥cholorform extracts≥ethanol extracts. In addition, in general, all parts of the species showed close to each other and showed moderate butyrylcholinesterase enzyme activity. SCCWP (inhibition%: 78.81±0.18) showed the highest butyrylcholinesterase enzyme activity among all samples.
In the literature, there are many studies on the anticholinesterase enzyme activity of *Salvia* species growing in Turkey. Orhan et al. (2007), studied with 14 *Salvia* species and found that the anticholinesterase activity potential of *Salvia* species was very high. Demirezer et al. (2015), study with 3 *Salvia* species, also found that the anticholiesterase activity potential of the species was quite high (Demirezer et al., 2015). In addition, it is mentioned in Turkish history books that *Salvia* species were used against amnesia disease in the Ottoman period (Duru et al., 2012). In parallel with the literature, it was determined that 3 of the 5 *Salvia* species studied showed medium-high anticholinesterase enzyme activity.
In this study, urease and tyrosinase enzyme activities of ethanol extracts were also determined (Table 4). The results showed that none of the studied species showed urease activity. The results of tyrosinase activity showed that SPRE (inhibition %: 45.73±2.14) sample showed the highest activity, while all other samples showed low antityrosinase activity in general. Looking at the elastase activity results; it was observed that all samples showed medium and low levels of elastase enzyme activity in general. SPRE (inhibition %: 26.59±0.10) showed the highest elastase enzyme activity. When the collagenase activity results are analyzed; it is seen that all samples showed low level of anticollagenase enzyme activity in general. Among the samples, SCERE (inhibition %: 25.24±0.13) showed the highest anticollagenase activity.
The generally low enzyme inhibition activities observed in the present study are in good agreement with previous investigations on *Salvia* species, particularly those focusing on extracts. Several studies on Turkish *Salvia* taxa have demonstrated that urease inhibition is often weak or absent unless specific alkaloids or highly active isolated constituents are present (Orhan et al., 2010; Zengin et al., 2018).

Similarly, tyrosinase inhibition in *Salvia* species has been reported to be modest at the extract level, with stronger effects typically observed after fractionation or isolation of flavonoids and diterpenoids (Demirezer et al.,

2015; Zengin et al., 2019). Elastase and collagenase inhibition activities have also been shown to depend strongly on triterpenoid-rich fractions rather than unfractionated extracts, explaining the generally low inhibition percentages reported for crude *Salvia* extracts (Thring et al., 2009; Zengin et al., 2020).

Table 4. Enzyme activities of *Salvia* species
Çizelge 4. Salvia türlerinin enzim aktiviteleri

	Enzyme activity (inhibition % at 100 µg/mL)[1]					
Samples	AChE	BChE	Urease	Tyrosinase	Elastase	Collagenase
SCERE	NA[a]	57.28±1.36[a]	NA[a]	24.88±0.99[a]	12.63±0.03[a]	25.24±0.13[a]
SCEBE	NA	9.60±0.07[b]	NA	17.35±0.32[b]	10.94±0.21[b]	20.20±0.16[b]
SCELE	NA	45.36±1.52[c]	NA	27.40±1.40[a]	14.63±0.02[c]	18.93±0.01[c]
SCEFE	NA	40.67±0.19[d]	NA	9.69±0.24[c]	8.63±0.04[d]	11.41±0.08[d]
SCEWE	NA	40.67±1.28[d]	NA	10.36±0.92[c]	10.53±0.09[b]	11.18±0.09[d]
SCEWP	NA	58.44±0.95[a]	NA	5.26±0.05[d]	6.90±0.05[e]	10.54±0.02[d]
SCEWC	NA	55.67±0.95[a]	NA	21.61±1.28[a]	15.63±0.12[c]	17.94±0.14[c]
SCCRE	NA	50.00±2.66[e]	NA	22.81±0.46[a]	16.30±0.04[c]	12.98±0.12[d]
SCCBE	NA	32.46±1.24[f]	NA	27.47±0.65[a]	17.05±0.12[c]	10.28±0.10[d]
SCCLE	NA	42.73±3.01[g]	NA	NA[e]	5.78 ±0.03[e]	12.98±0.13[d]
SCCFE	NA	42.48±1.43[g]	NA	11.02±0.23[c]	6.83±0.08[e]	11.86±0.11[d]
SCCWE	NA	52.01±2.66[e]	NA	14.38±0.36[f]	12.18±0.08[a]	12.98±0.12[d]
SCCWP	NA	78.81±0.18[h]	NA	NA	6.73±0.05[e]	9.41±0.03[d]
SCCWC	NA	64.91±2.13[i]	NA	11.89±0.56[c]	10.43±0.07[b]	9.15±0.04[d]
SRRE	NA	NA[j]	NA	25.30±1.03[a]	18.59 ±0.05[f]	15.22±0.10[e]
SRBE	NA	NA	NA	19.69±0.61[g]	13.60±0.06[c]	11.86±0.03[d]
SRLE	NA	NA	NA	21.27±1.08[a]	15.68±0.13[c]	14.00±0.11[e]
SRFE	NA	NA	NA	29.16±0.14[h]	21.69±0.06[h]	12.40±0.04[d]
SRWE	NA	NA	NA	24.49±1.10[a]	15.73±0.10[c]	17.66±0.12[c]
SRWP	NA	NA	NA	NA	7.49±0.02[e]	9.19±0.01[d]
SRWC	NA	NA	NA	19.34±0.42[g]	NA[g]	NA[f]
SPRE	NA	53.38±0.35[e]	NA	45.73±2.14[i]	26.59±0.10[i]	16.97±0.12[e]
SPBE	NA	54.47±0.77[a]	NA	31.58±1.24[h]	22.38±0.08[h]	11.15±0.01[d]
SPLE	NA	74.69±3.19[k]	NA	28.73±1.86[h]	16.03±0.04[c]	11.25±0.02[d]
SPFE	NA	59.15±1.06[a]	NA	19.86±1.12[g]	14.31±0.11[c]	13.54±0.10[g]
SPWE	NA	59.96±2.46[a]	NA	27.52±1.56[a]	16.70±0.04[c]	9.60±0.03[d]
SPWP	NA	66.79±1.14[l]	NA	NA	6.40±0.03[e]	8.25±0.02[d]
SPWC	NA	62.08±0.19[l]	NA	16.77±0.51[h]	11.48±0.06[b]	7.35±0.01[h]
SKRE	NA	NA	NA	23.86±0.46[a]	15.79±0.02[c]	11.71±0.02[d]
SKBE	NA	NA	NA	11.58±0.23[c]	9.42±0.04[b]	10.80±0.01[d]
SKLE	NA	NA	NA	16.62±0.54[b]	11.48±0.06[b]	8.51±0.01[i]
SKWE	5.18±0.67[b]	18.97±1.22[m]	NA	15.60±0.97[b]	16.06±0.04[c]	11.02±0.02[d]
SKWP	19.65±0.23[c]	NA	NA	31.04±1.47[h]	29.59±0.05[j]	11.56±0.03[d]
SKWC	25.93±1.68[d]	25.80±0.68[n]	NA	12.34±0.89[c]	17.50±0.12[c]	11.02±0.02[d]
Galanthamine[2]	86.14±0.38[e]	80.18±0.46[h]			-	-
Thiourea[2]	-	-	83.62±1.28[b]		-	-
Kojic acid[2]	-	-		85.29±2.09[j]		
Oleanolic acid[2]	-	-	-	-	40.77±0.86[k]	-
Epicatechin gallate[2]	-	-	-	-	-	83.63±1.88[j]

[1]Values expressed are means ± S.D. of three parallel measurements and values were calculated according to negative control, Values with different letters in the same column were significantly different ($p<0.05$), [2]Standard compound, NA: Not active

CONCLUSIONS

In the present study, phenolic contents of five endemic *Salvia* (*S. cerino-pruinosa* var. *elazigensis*, *S. cerino-pruinosa* var. *cerino-pruinosa*, *S. rosifolia*, *S. pseudeuphratica* and *S. kurdica*) extracts prepared from various parts of the species with different solvents were determined and compared by LC-MS/MS. In addition, the biological activities of all the extracts were examined in detail.

When the LC-MS/MS results of the studied species are evaluated as a whole, it is seen that petroleum ether extracts prepared from the mixed parts of the species are the poorest in terms of phenolic content, while ethanol extracts are the richest. Therefore, as the polarity of the solvent increased during the preparation of the sample extracts, it was observed that the extracts became richer in terms of phenolic component diversity. In general, all ethanol extracts were found to be rich in rosmarinic acid, caffeic acid, fumaric acid and malic acid. Among the ethanol extracts prepared from the mixed parts of the species, SCEWE and SCCWE samples were found to be richer in terms of component diversity and amounts compared to the other samples. Among all the sample extracts studied, SCELE sample was found to be richer in caffeic acid, rosmarinic acid and rhoifolin (879.52, 34638.45 and 940.47 µg analytes/g extract, respectively) and SCEFE sample was found to be richer in apigetrin and nicotiflorin (6902.16 and 3573.88 µg analytes/g extract, respectively).

In parallel with the LC-MS/MS results, in terms of total phenolic and flavonoid contents, it was determined that the leaf part of SCE species was richer than the other samples in terms of both phenolic (229.94±2.00 µg PEs/mg extract) and flavonoid (65.95±0.90 µg QEs/mg extract) contents among all samples. Also, in parallel with the LC-MS/MS and total phenolic-flavonoid results, the fact that especially the leaf part of the SCE species has higher antioxidant potential than α-TOC and BHT used as standard in all 3 methods (DPPH (IC_{50}: 5.72±0.01 µg/mL), ABTS (IC_{50}: 2.43±0.21 µg/mL) and CUPRAC ($A_{0.5}$: 11.67±0.07 µg/mL) shows that the leaf part of this species is very important. It can be said that the high antioxidant potential of the SCELE sample is due to the rosmarinic acid content (34638.45 µg analyte/g extract). In general, the enzyme activity potentials of all species were found to be low. It was observed that ethanol extracts prepared from leaf parts of all species except SP were more active than extracts prepared from other parts. Only in the SP sample, it was observed that the root ethanol extract was more active than the extracts prepared from other parts. In addition, it was determined that ethanol extracts were more active than chloroform and petroleum ether extracts in ABTS, DPPH and CUPRAC methods in general. These results show that the chemical content and biological activities vary considerably according to the species, various parts of the species and different solvents.

Importantly, both SPWC and SRWC extracts displayed reduced cytotoxicity toward the healthy PDF cell line compared to their effects on cancer cells, indicating a favorable selectivity profile. This selective behavior is a critical criterion for identifying plant extracts with potential anticancer relevance and supports further investigation of these samples. Nevertheless, the present findings are limited to in vitro cytotoxicity screening and do not provide insight into the underlying mechanisms of action. Therefore, future studies should focus on elucidating the molecular mechanisms responsible for the observed cytotoxic effects, such as apoptosis induction, cell cycle arrest, and modulation of oxidative stress pathways. In addition, bioassay-guided fractionation and isolation of active constituents are required to identify the compounds responsible for selective anticancer activity and to evaluate their efficacy and safety in more advanced biological models.

In conclusion, due to the very strong antioxidant activity and high rosmarinic acid content of SCELE extract and the high cytotoxic effects of SRWC extract against cancer cell lines, it can be said that these two species have the potential to be used in food preservative and pharmaceutical industries.

ACKNOWLEDGMENTS

This work was supported by The Scientific and Technological Research Council of Turkey (TUBITAK-Project number: KBAG 114Z801), also this study was funded by Scientific Research Projects Coordination Unit of Istanbul University (Project numbers: 40327 and 40410) and Van Yüzüncü Yıl University Scientific Research Projects Coordination Unit Coordinatorship (Project Number: FYD-2024-11073).

Contribution Rate Statement Summary of Researchers

S.Y., I.Y, A.E. and U.K. developed the project idea. E.Y., H.S.F., M.V.C., M.A, O.C., M.F. and M.A.Y., performed the experimental analyses and data collection. L.B.A., M.B., A.E. and S.Y. described the data, S.Y., I.Y., A.E. and U.K. wrote the first draft, and all authors revised and amended the manuscript.

Conflict of Interest

The authors of the articles declare that they have no conflict of interest.

REFERENCES

Akdeniz, M., Yener, I., Dincel, D., Firat, M., Karatas Degirmenci, D., & Ertas, A. (2022). Determination of fingerprints contents of different extracts and parts of six endemic *Salvia* taxa by GC–MS: Source species for valuable compounds with drug or drug potential. *Biomedical Chromatography*, 36, e5263. https://doi.org/10.1002/bmc.5263

Apak, R., Guclu, K., Ozyurek, M., & Karademir, S. E. (2004). Novel total antioxidant capacity index for dietary polyphenols and vitamins C and E using their cupric ion reducing capability in the presence of neocuproine: CUPRAC method. *Journal of Agricultural and Food Chemistry, 52*, 7970-7981. https://doi.org/10.1021/jf048741x.

Bakir, D., Akdeniz, M., Ertas, A., Yilmaz, M. A., Yener, I., Firat, M., & Kolak, U. (2020). A GC-MS method validation for quantitative investigation of some chemical markers in *Salvia hypargeia* Fisch. & C.A. Mey. of Turkey: Enzyme inhibitory potential of ferruginol. *Journal of Food Biochemistry, 44*, e13350. https://doi.org/10.1111/jfbc.13350.

Blois, M. S. (1958). Antioxidant determinations by the use of a stable free radical. *Nature, 181*, 1199-1200. https://doi.org/10.1038/1811199a0

Cavusoğlu, M., Yigitkan, S., Yener, İ., Çağlayan, M. V., Reşitoğlu, B., Akdeniz, M., Çavuş Kaya, E., Tekin, F., Yılmaz, M. A., & Ertaş, A. (2024). Ziziphora clinopodioides Lam. türünün kültür ile doğal ortamlarda yetişen örneklerinin kimyasal ve biyolojik yönden detaylı incelenmesi. *KSÜ Tarım ve Doğa Dergisi*, *27*(Suppl 2), 316–

326. https://doi.org/10.18016/ksutarimdoga.vi.1585656

Delamare, A. P. L., Moschen-Pistorello, I. T., Artico, L., Atti-Serafini, L., & Echeverrigaray, S. (2007). Antibacterial activity of the essential oils of *Salvia officinalis* L. and *Salvia triloba* L. cultivated in South Brazil. *Food Chemistry, 100,* 603-608. https://doi.org/10.1016/j.foodchem.2005.09.078

Demirezer, L. O., Gurbuz, P., Kelicen-Ugur, E. P., Bodur, M., Ozenver, N., Uz, A., & Guvenalp, Z. (2015). Molecular docking and ex *vivo* and *in vitro* anticholinesterase activity studies of *Salvia* sp. and highlighted rosmarinic acid. *Turkish Journal of Medical Sciences, 45*, 1141-1148. https://doi:10.3906/sag-1404-42

Demirezer, L. O., Kuruüzüm-Uz, A., Güvenalp, Z., & Kazaz, C. (2015). Phenolic compounds from Salvia species and their tyrosinase inhibitory activities. *Journal of Enzyme Inhibition and Medicinal Chemistry*, *30*, 224–229. https://doi.org/10.3109/14756366.2014.917682

Dubois, M., Bailly, F., Mbemba, G., Mouscadet, J. F., Debyser, Z., Witvrouw, M., & Cotelle, P. (2008). Reaction of rosmarinic acid with nitrite ions in acidic conditions: discovery of nitro- and *in vitro* rosmarinic acids as new anti-HIV-1 agents. *Journal of Medicinal Chemistry, 51*, 2575-2579. https://doi.org/10.1021/jm7011134

Duru, M. E., Tel, G., Ozturk, M., & Harmandar, M. (2012). Chemical composition, antioxidant and anticholinesterase activities of the essential oil of *Salvia chrysophylla* Staph. *Records of Natural Products, 6*, 175-179.

Ellman, G. L., Courtney, K. D., Andres, V., & Featherstone, R. M. (1961). A new and rapid colorimetric determination of acetylcholinesterase activity. *Biochemical Pharmacology, 7*, 88-95. https://doi.org/ 10.1016/0006-2952(61)90145-9.

Ertas, A., Akdeniz, M., Yener, I., Ozturk, M., Tokul-Olmez, O., Firat, M., & Kolak, U. (2022). Essential oil, aroma, and fatty acid profiles of five endemic *Salvia* taxa from Turkey with chemometric analysis. *Chemistry & Biodiversity, 19*, e202100408. https://doi.org/10.1002/cbdv.202100408

Halfon, B., Cetin, O., Kokdil, G., & Topcu, G. (2019). Chemical investigation and bioactivity screening of *Salvia cassia* extracts. *Records of Natural Products, 13*, 156-166. http://doi.org/10.25135/rnp.99.18.05.291

Hearing, V.J., & Jiménez, M. (1987). Mammalian tyrosinase-the critical regulatory control point in melanocyte pigmentation. *International Journal of Biochemistry, 19*, 1141-7. https://doi.org/10.1016/0020-711X(87)90095-4

Hina, Z., Ghazala, H. R., Arfa K., Huma, S., Sabiha, T., & Ajmal, K. (2015). Anti-urease activity of *Mimusops elengi* Linn (Sapotaceae). *European Journal of Medicinal Plants, 6*, 223-230. https://doi.org/10.9734/ EJMP/2015/12240.

Kahraman, A., Dogan, M., & Celep, F. (2011). *Salvia siirtica* sp. nov. (Lamiaceae) from Turkey. *Nordic Journal of Botany, 29*, 397-401. https://doi.org/10.1111/j.1756-1051.2011.00916.x

Kolak, U. (2007). New diterpenoids from the aerial parts of *Salvia pilifera*. *Turkish Journal of Chemistry, 31*, 363-369. https://journals.tubitak.gov.tr/chem/vol31/iss3/12

Kosar, M., Goger, F., & Baser, K. H. C. (2008). *In vitro* antioxidant properties and phenolic composition of *Salvia virgate* Jacq. from Turkey. *Journal of Agricultural and Food Chemistry, 569*, 2369–2374. https://doi.org/10.1021/jf073516b

Kraunsoe, J. A. E., Claridge, T. D. W., & Lowe, G. (1996). Inhibition of human leukocyte and porcine pancreatic elastase by homologues of bovine pancreatic trypsin inhibitor. *Biochemistry, 35*, 9090-9096. https://doi.org/ 10.1021/bi953013b.

Miller, H. E. (1971). A simplified method for the evaluation of antioxidants. *Journal of the American Oil Chemists Society, 48*, 91. https://doi.org/10.1007/BF02635693

Mojarraba, M., Langzian, M. S., Emamic, S. A., Asilic, J., & Tayarani-Najaranb, Z. (2013). *In vitro* anti-proliferative and apoptotic activity of different fractions of *Artemisia armeniaca*. *Revista Brasileira de Farmacognosia, 23*, 783-7888. http://dx.doi.org/10.1590/S0102-695X2013000500010.

Moreno, M. I. N., Isla, M. I., Sampietro, A. R., & Vattuone, M. A. (2000). Comparison of the free radical-scavenging activity of propolis from several regions of Argentina. *Journal of Ethnopharmacology, 71*, 109-114. https://doi.org/10.1016/S0378-8741(99)00189-0.

Orhan, I., Kartal, M., Naz, Q., Ejaz, A., Yilmaz, G., Kan, Y., Konuklugil, B., Şener, B., & Choudhary, M. I. (2007). Antioxidant and anticholinesterase evaluation of selected Turkish *Salvia* species. *Food Chemistry, 103*, 1247-1254. https://doi.org/10.1016/j.foodchem.2006.10.030

Orhan, I. E., Senol, F. S., Gülpınar, A. R., Kartal, M., & Sener, B. (2010). Acetylcholinesterase and urease inhibitory activities of some Turkish *Salvia* species. *Food Chemistry*, 123, 709–715. https://doi.org/10.1016/ j.foodchem.2010.05.033

Ozer, H., Altun, A., Saraydin, S. U., Soylu, S., Goktas, S., Tuncer, E., Inan, D. S., Koksal, B., Temiz, T. K., Tepe, B., Sen, M., Karadayi, K., & Turan, M. (2013). Antitumoral effects of *Salvia absconditiflora* Greuter & Burdet syn. *Salvia cryptantha* Montbret & Aucher ex Benth. on breast cancer. *Indian Journal of Traditional Knowledge, 12*, 390-397.

Re, R., Pellegrini, N., Proteggente, A., Pannala, A., Yang, M., & Rice-Evans, C. (1999). Antioxidant activity applying an improved ABTS radical cation decolorization assay. *Free Radical Biology and Medicine, 26*, 1231-1237. https://doi.org/10.1016/S0891-5849(98)00315-3

Slinkard, K., & Singleton, V. L. (1977). Total phenol analyses: Automation and comparison with manual methods. *American Journal of Enology and Viticulture, 28*, 49-55.

Son, K. H., Oh, H. M., Choi, S. K., Han, D. C., & Kwon, B. M. (2005). Anti-tumor abietane diterpenes from the cones of *Sequoia sempervirens*. *Bioorganic & Medicinal Chemistry Letters, 15*, 2019-2021. https://doi.org/10.1016/j.bmcl.2005.02.057

Takeda, H., Tsuji, M., Inazu, M., Egashira, T., & Matsumiya, T. (2002). Rosmarinic acid and caffeic acid produce antidepressive-like effect in the forced swimming test in mice. *European Journal of Pharmacology, 449*, 261-267. https://doi.org/10.1016/S0014-2999(02)02037-X

Tayarani-Najaran, Z., Asili, J., Aioubi, E., & Emami, S. A. (2013). Growth inhibition and apoptosis induction *of Salvia chloroleuca* on MCF-7 breast cancer cell line. *Iranian Journal of Pharmaceutical Sciences, 12*, 789-799.

Thring, T. S. A., Hili, P., & Naughton, D.P. (2009). Anti-collagenase, anti-elastase and anti-oxidant activities of extracts from 21 plants. *BMC Complementary and Alternative Medicine, 9*, 27 (2009). https://doi.org/10.1186/1472-6882-9-27.

Topcu, G., Yucer, R., & Senol, H. (2017). Bioactive constituents of Anatolian *Salvia* species. In: Georgiev, V., Pavlov, A. (eds) *Salvia* Biotechnology. Springer, Cham. pp. https://doi.org/10.1007/978-3-319-73900-7_2

Uysal, S. (2019). A comparative study of three drying methods on the phenolic profile and biological activities of *Salvia absconditiflora*. *Journal of Food Measurement and Characterization, 13*, 162-168. https://doi.org/10.1007/s11694-018-9929-7

Yaris, E., Balur Adsız, L., Yener, I., Tuncay, E., Yilmaz, M. A., Akdeniz, M., Kaplaner, E., Firat, & M., Ertas, A., Kolak, U. (2021). Isolation of secondary metabolites of two endemic species: *Salvia rosifolia* Sm. and *Salvia cerino-pruinosa* Rech. f. var. *elazigensis* (Lamiaceae). *Journal of Food Measurement and Characterization, 15*, 4929-4938. https://doi.org/10.1007/s11694-021-01065-8

Yener, I., Ozhan Kocakaya, S., Ertas, A., Erhan, B., Kaplaner, E., Oral, E. V., Yilmaz-Ozden, T., & Yilmaz, M. A., Ozturk, M., Kolak, U. (2020). Selective *in vitro* and *in silico* enzymes inhibitory activities of phenolic acids and flavonoids of food plants: Relations with oxidative stress. *Food Chemistry, 327*, 127045. https://doi.org/10.1016/j.foodchem.2020.127045

Yigitkan, S., Akdeniz, M., Yener, İ., Firat, M., Senturk, K., Alkan, H., & Ertaş, A. (2021). Chemical composition and biological activity of *Ixiolirion tataricum* (Pall.) Schult. & Schult.f. var. *tataricum*. *Records of Agricultural and Food Chemistry, 1*(1–2), 27–34. https://doi.org/10.25135/rfac.5.2112.2301

Yiğitkan, S., Çavuşoğlu, M., Çağlayan, M. V., Yener, İ., Fırat, M., Çavuş Kaya, E., Yılmaz, M. A., & Ertaş, A. (2024). *LC-MS/MS analysis and biological activities of different parts of Ziziphora capitata* L. *KSÜ Tarım ve Doğa Dergisi, 27*(Suppl 2), 307–315. https://doi.org/10.18016/ksutarimdoga.vi.1585230

Yildirim, G. B., Gürer, Ç. Ü., Yener, I., Akdeniz, M., Yigitkan, S., Yılmaz, M. A., Tireki, S., Ertaş, A., & Demirkoz, A. B. (2025). *Comparative evaluation of antioxidant and enzyme inhibition activities of pomegranate vinegars and extracts*. Records of Agricultural and Food Chemistry, *37*, 1–10. https://doi.org/10.25135/rfac.37.2510.3654

Yilmaz, M. A., Ertas, A., Yener, I., Akdeniz, M., Cakir, O., Altun, M., Demirtas, I., Boga, M., & Temel, H. (2018). A comprehensive LC-MS/MS method validation for the quantitative investigation of 37 fingerprint phytochemicals in *Achillea* species: A detailed examination of *A. coarctata* and *A. monocephala*. *Journal of Pharmaceutical and Biomedical Analysis, 154*, 413-424. https://doi.org/10.1016/j.jpba.2018.02.059

Zengin, G., Atasagun, B., Aumeeruddy, M. Z., Saleem, H., Mollica, A., Bahadori, M. B., & Mahomoodally, M. F. (2019). Phenolic profiling and *in vitro* biological properties of two Lamiaceae species (*Salvia modesta* and *Thymus argaeus*): A comprehensive evaluation. *Industrial Crops and Products, 128*, 308-314. https://doi.org/10.1016/j.indcrop.2018.11.027

Zengin, G., Uysal, A., Gunes, E., & Aktumsek, A. (2019). Survey of phytochemical composition and biological effects of Salvia species: Tyrosinase and antioxidant perspectives. *Industrial Crops and Products, 128*, 365–373. https://doi.org/10.1016/j.indcrop.2018.11.034

Zengin, G., Aktumsek, A., Ceylan, R., & Picot-Allain, M. C. N. (2018). Enzyme inhibitory properties of different extracts obtained from Salvia species: Insights into urease and cholinesterase inhibition. *Journal of Enzyme Inhibition and Medicinal Chemistry, 33,* 1564–1572. https://doi.org/10.1080/14756366.2018.1514373

Zengin, G., Mahomoodally, M. F., Sinan, K. I., & Ak, G. (2020). Chemical composition and biological properties of Salvia species: Focus on elastase and collagenase inhibition. *Phytochemistry Reviews, 19*, 1315–1338. https://doi.org/10.1007/s11101-020-09670-4