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Original Article

An investigation and comparison of concentration change in simulated body fluid medium conditions of the Calcium element in 27 different *Salvia* species

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ABSTRACT

Background and Aims: In this study, calcium (Ca) element concentration changes of *Salvia* species in simulated body fluid (SBF) medium conditions were investigated and the results in these medium conditions were compared with each other.
Methods: *Salvia* species samples were air-dried and ground into powder. *Salvia* species was prepared as a herbal tea. Prepared teas were left in three different SBF medium conditions. The samples were analyzed using Flame Atomic Absorption Spectroscopy (FAAS) method to determine the Ca absorptions. Also, a correlation analysis of the results obtained in three different SBF medium conditions and the species in simulated gastric fluid (SGF) medium conditions was performed.
Results: When the SBF medium conditions were compared, it was determined that the highest Ca absorption of all *Salvia* species occurred in the SGF conditions. Thus, it can be said that the Ca in plants and foods occurs in the gastric fluid medium and its absorption occurs there. When the result of the correlation analysis was evaluated, it was determined that there was a stronger correlation between the SGF and simulated intestinal fluid (SIF) mediums compared to other mediums.
Conclusion: The Ca absorption was determined according to what remained in the SGF the most. Based on the results obtained from SBF medium conditions, it can be said which element is taken in which body fluid medium. Information on the differences between samples belonging to different SBF medium conditions was not obtained. However, when the simulated fluid medium conditions were evaluated individually, information was obtained for two or more samples.

Keywords: Calcium, FAAS, *Salvia*, SBF

INTRODUCTION

The Lamiaceae family, also known as Labiatae, is represented by more than 245 genera and 7886 species worldwide (Celep & Dirmenci, 2017). Members of this family include medicinal and aromatic species of commercial importance. These species are *Salvia* L., *Satureja* L., *Origanum* L., *Thymus* L., etc. (Kaya, Başer, Satil, & Tümen, 2000; Kurkcuoglu, Turnen, & Baser, 2001; Satıl, Ünal, & Hopa, 2007). In the flora of Turkey, this family is represented by 45 genera, 558 species, and 742 taxa (Yılar, Bayar, & Onaran, 2019).

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The genus *Salvia* belongs to the *Lamiaceae* family and is represented by more than 1000 species worldwide (Al Jaber, 2016; Gedik, Kiran, Emre, & Kursat, 2016; Nickavar, Rezaee, & Nickavar, 2016; Asadi-Samani, Khaledi, Khaledi, Samarghandian, & Gholipour, 2019; Coşge Şenkal, 2019; Güzel et al., 2019; Moridi Farimani, Miran, & Ebrahimi, 2019). This genus is distributed across Central and South America (500 species), West Asia (200 species), and East Asia (100 species) (Kahraman & Doğan, 2010; Büyükkartal, Kahraman, Çölgeçen, Doğan, & Karabacak, 2011; Kahraman, Doğan, & Celep, 2011). It is represented by 101 species in the flora of Turkey and 53 of them are endemic (Firat, 2020).

The species of this genus and the essential oils obtained from them are used in herbal tea, culinary herb, food preservatives, food flavorings, cosmetics, perfumery, and the pharmaceutical industry (Senatore, Formisano, Arnold, & Piozzi, 2005; Tosun et al., 2009; Kahraman, Celep, & Doğan, 2010; Nickavar et al., 2016; Güzel et al., 2019; Kahnamoei et al., 2019). Species of this genus are used to treat various diseases in traditional medicine in various parts of the world for wound healing, stomach ailments, alleviation of abdominal pain, liver and rheumatic pains, analgesic, antirheumatic, antioxidant, antibacterial, antimicrobial, antitumor, antidementia, cytotoxic, antiviral, carminative, diuretic, hemostatic, spasmolytic, sedative, as an antiseptic, in the treatment of hepatitis, menstrual disorders, in the treatment of colds, sedatives, stimulants, tonics, in the treatment of fever, bronchitis, tuberculosis, obesity, diabetes, depression, dementia, and menstrual disorders (Altun, Ünal, Kocagöz, & Gören, 2007; Kahraman, Celep, Doğan, & Bagherpour, 2010; Öztekin, Başkan, Kepekçi, Erim, & Topçu, 2010; Al-Qudah, Al-Jaber, Abu Zarga, & Abu Orabi, 2014; Al Jaber, 2016; Hegazy et al., 2018; Bağcı, Akbaba, Maniu, Ungureanu, & Hritcu, 2019; Bakir et al., 2020). Also, in folk medicine, *Salvia* species have been used since ancient times as memory-enhancing and neuroprotective agents (Çulhaoğlu, Hatipoğlu, Dönmez, & Topçu, 2015). The *Salvia* species in Turkey are known as "Adaçayı", "Çalba", "Şalba" and "Dağ çayı" and these species are used as herbal tea in folk medicine (Erdogan-Orhan, Baki, Şenol, & Yilmaz, 2010; Bağcı et al., 2019; Utsukarci et al., 2019). In Turkish folk medicine, *Salvia* species are used as antibacterials, antiseptics, diuretics, carminatives, spasmolytics, stimulants, and in treatment of wounds, colds, and coughs (Güzel et al., 2019).

For determination of element contents and concentrations of samples in the fields of chemistry, biology, medicine, pharmacy, food, environment, and agriculture various methods are used such as Atomic Absorption Spectrometry (AAS), FAAS, Graphite Furnace Atomic Absorption Spectrometry (GF-AAS), Inductively Coupled Plasma Atomic Emission Spectrometry (ICP-AES), Inductively Coupled Plasma Optical Emission Spectrometry (ICP-OES), Inductively Coupled Plasma Mass Spectrometry (ICP-MS), Instrumental Neutron Activation Analysis (INAA), and X-ray Fluorescence Spectrometry (XRF) (Pytlakowska, Kita, Janoska, Połowniak, & Kozik, 2012; Szymczycha-Madeja, Welna, & Zyrnicki, 2013; Zhang et al., 2015; Targan, Yelboğa, & Cittan, 2018; Tunay et al., 2020).

Mineral elements are of unique and versatile importance to both plants and humans. Minerals are found in plants as ions, inorganic and organic salts. Mineral elements are grouped into macro, micro, and ultra-micro elements. Macro-elements are generally considered as minerals of which the body needs more than 100 mg per day. These elements are C, H, O, N, P, K, Ca, Mg, Na, and S (Umaz, 2021). Ca is responsible for bone formation and metabolism, vascular contraction and vasodilation, muscle function, nerve conduction, intracellular signaling, and hormonal secretion. It also provides strength to bones and teeth with phosphate (Ross, Taylor, Yaktine, & Del Valle, 2011; Lippert, 2020; Shkembi & Huppertz, 2022).

Ca is absorbed in the ionized form (Ca^{2+}) in the gastrointestinal tract (a long tubular structure between the mouth and anus and a system that includes many organs associated with this structure and whose main task is digestion) (Shkembi & Huppertz, 2022). Ca is absorbed by active transport (intercellular) and passive diffusion (extracellular) across the intestinal mucosa. Active transport of the Ca is dependent on the action of calcitriol and the intestinal vitamin D receptor (VDR). Passive diffusion involves the movement of calcium between mucosal cells. this diffusion is dependent on luminal: serosal electrochemical gradients (Ross et al., 2011).

This study has the distinction of being the first in terms of examining where the Ca element in the species is absorbed under body fluid medium conditions and the concentration change. In this study, 27 different *Salvia* species used for herbal tea, medicinal, and various purposes were prepared as herbal tea and left in three different SBF mediums. The concentration variation of the Ca element, which is important for plants and humans, was investigated and compared in SBF medium conditions. Correlation analysis between the species of Ca in SGF medium conditions was performed. In addition, in order to determine whether the correlation coefficients between the obtained results were the same or not, the correlation coefficients on the basis of Ca in different SBF medium conditions were calculated and compared.

MATERIALS AND METHODS

Herbal materials

Herbarium samples of 27 *Salvia* species collected from different parts of Turkey were prepared to be placed in the herbarium and dried in accordance with the purpose of the study. Dried species were identified and preserved by Mehmet Fırat to be placed in Van Yüzüncü Yıl University, Faculty of Science Herbarium (VANF) (Table 1).

Chemicals and reagents

In the study, analytical grade chemicals were used for the preparation of three different SBF medium conditions. NaCl (EMSURE, for Analysis), $MgCl_2.6H_2O$ (for Analysis), CH_3COOK (EMSURE, for Analysis), Lactic acid (EMPROVE), NaBr (EMPROVE), $CaCl_2$ (EMSURE ACS reagent), Pepsin (Biochemistry) for Analysis), KH_2PO_4 (for EMSURE Analysis), D(+)-Fructose (for Biochemistry), and NH_4OH (EMSURE for Analysis) were purchased from Merck (Germany). D(+)-Glucose (anhydrous), NaOH (ACS reactive pellet), HNO_3 (70%), H_2O_2 (34.5-36.5%), $CuCl_2.2H_2O$ (Reactive), Urea (ACS reactive), HCl (≥ 37% ACS reagent) was purchased from Sigma Aldrich (Germany). $CaCl_2.2H_2O$ (ACS reagent), H_3PO_4 (≥

Table 1. Herbarium number, collection places, and collection times of plants belonging to 27 different *Salvia* species.

Plant species	Species Codes	Gathering Places	Harvesting Times	Herbarium Number
Salvia blepharochlaena Hedge & Hub.-Mor.	**S1**	Nevşehir	2014	M. FIRAT 32102 (VANF)
Salvia brachyantha (Bordz.) Pobed. subsp. *brachyantha*	**S2**	Van	2015	M. FIRAT 32469 (VANF)
Salvia candidissima Vahl subsp. *candidissima*	**S3**	Van-Gürpınar	2015	M. FIRAT 32092 (VANF)
Salvia ceratophylla L.	**S4**	Nevşehir	2015	M. FIRAT 32174 (VANF)
Salvia cerino-pruinosa Rech.f. var. *cerino-pruinosa*	**S5**	Elazığ	2015	M. FIRAT 32539 (VANF)
Salvia cerino-pruinosa Rech.f. var. *elazigensis* Kahraman, F.Celep & Dogan	**S6**	Elazığ	2015	M. FIRAT 32539 (VANF)
Salvia divaricata Montbret & Aucher ex Benth.	**S7**	Erzincan-Kemah	2017	M. FIRAT 33829 (VANF)
Salvia hydrangea DC. ex Benth.	**S8**	Kars-Kagızman	2014	M. FIRAT 30696 (VANF)
Salvia hypargeia Fisch. & C.A.Mey.	**S9**	Van	2015	M. FIRAT 31173 (VANF)
Salvia indica L.	**S10**	Hakkari	2015	M. FIRAT 32455 (VANF)
Salvia kronenburgii Rech. f.	**S11**	Van-Gürpınar	2014	M. FIRAT 30650 (VANF)
Salvia kurdica Boiss. & Hohen. ex Benth.	**S12**	Şırnak	2014	M. FIRAT 32614 (VANF)
Salvia limbata C.A.Mey.	**S13**	Van	2014	M. FIRAT 30660 (VANF)
Salvia macrochlamys Boiss. & Kotschy	**S14**	Van	2014	M. FIRAT 30907 (VANF)
Salvia microstegia Boiss. & Balansa	**S15**	Hakkari	2015	M. FIRAT 32472 (VANF)
Salvia montbretii Benth.	**S16**	Diyarbakır	2015	M. FIRAT 32463 (VANF)
Salvia multicaulis Vahl.	**S17**	Van	2014	M. FIRAT 30656 (VANF)
Salvia pachystachys Trautv.	**S18**	Van	2015	M. FIRAT 30878 (VANF)
Salvia pinnata L.	**S19**	Diyarbakır	2014	M. FIRAT 31318 (VANF)
Salvia pseudeuphratica Rech.f.	**S20**	Elazığ	2015	M. FIRAT 32584 (VANF)
Salvia sclarea L.	**S21**	Van-Bahçesaray	2014	M. FIRAT 30921 (VANF)
Salvia siirtica Kahraman, Celep & Doğan	**S22**	Hakkari	2014	M. FIRAT 30755 (VANF)
Salvia spinosa L.	**S23**	Mardin	2016	M. FIRAT 30908 (VANF)
Salvia suffruticosa Montbret & Aucher ex Benth.	**S24**	Van	2014	M. FIRAT 30657 (VANF)
Salvia trichoclada Benth.	**S25**	Van-Çatak	2014	M. FIRAT 30658 (VANF)
Salvia viridis L.	**S26**	Adana	2015	M. FIRAT 32461 (VANF)
Salvia xanthocheila Boiss. ex Benth.	**S27**	Van	2014	M. FIRAT 30668 (VANF)

99%), NaF (98.5-100.5%) were purchased from Honeywell/Fluka (USA). Uric acid (≥99% for Biochemistry, Roth Germany), and $K_3PO_4.3H_2O$ (97%) were purchased from abcr Gmbh (Germany). The Ca standard (1000 mg/L, Plasma CAL Calibration solution SCP28AES) in FAAS measurements was used. Linearity was evaluated using the least 6-point 3-parallel matrix calibration. Calibration curves were determined with six concentrations (5, 10, 25, 50, 75, and 100 mg/L). Calibration standard solutions (5-100 mg/L) were prepared by appropriate dilution of stock Ca standard (1000 mg/L). LOD and LOQ values of the Ca element were calculated using 10 independent blank solutions.

Preparation of SBF

Preparation of simulated saliva fluid (SSF)

1.28 g NaCl was put into 1 L flask and dissolved in 500 mL ultrapure water. Then, 0.125 g $MgCl.6H_2O$, 0.095 g KCl, 1.508 g CH_3COOK, 0.167 g $CaCl_2$, 0.386 g $K_3PO_4.3H_2O$, 0.0042 g NaF, and 0.05 mL H_3PO_4 were added to the solution and mixed. The residue and turbidity formed in the solution were clarified by adding 1 drop of H_3PO_4. Then, ultrapure water was added and mixed so that the final volume of the solution was 1 L. The solution was mixed by adding lactic acid according to the desired pH. The pH of the solution was adjusted to 6.3 (Shannon, 1982).

Preparation of SGF

0.265 g $CaCl_2.2H_2O$ was put into a 1 L flask and dissolved in 500 mL of ultrapure water. Then, the solution was mixed by adding 0.153 g $MgCl.6H_2O$, 0.865 g KCl, 2.856 g NaCl, 0.0008 g NaBr, 0.0009 g NaF, 0.0003 g $CuCl_2.2H_2O$, 0.138 g D(+)-fructose, 0.350 g D(+)-glucose, 0.084 g Urea, 0.0084 g uric acid and 3.20 g pepsin. Then, ultrapure water was added and mixed so that the final volume of the solution was 1 L. The solution was mixed by adding 0.04 M HCl and 0.1 M NH_4OH according to the desired pH. The pH of the solution was adjusted to 1.54 (Stefaniak et. al., 2010).

Preparation of SIF

6.80 g KH_2PO_4 was put into a 1 L flask and dissolved in 500 mL of ultrapure water. Then, 0.90 g of NaOH was added to the solution and mixed. Then, ultrapure water was added and mixed so that the final volume of the solution was 1 L. The solution was mixed by adding 2 M HCl according to the desired pH. The pH of the solution was adjusted to 6.80 (Stippler et. al., 2004).

Preparation of *Salvia* species as herbal tea

0.5 g *Salvia* species was put into a 100 mL beaker and washed two times with ultrapure water to remove dust and residues. Then, 50 mL boiled ultrapure water was added to the beaker and was left to brew for 10 min. Then, the tea in the beaker was filtered with blue banded filter paper. The resulting filtrate was used in experimental studies.

Experimental designs in SBF medium of prepared herbal tea

50 mL SBF was placed in a 250 mL beaker and 50 mL of prepared herbal tea was added to it. The mixture was put on a mixer and mixed to rotate at 50 rpm. The stirring times designed for the simulated mediums were as follows: 30 seconds for SSF medium, 180 minutes for SGF medium, and 300 minutes for SIF medium. Then the mixture was filtered with filter paper and the samples were placed in screw-capped tubes to be read in the FAAS device. The above-mentioned procedures were performed separately for each SBF medium. Analysis was performed in three replicates for simulated saliva, gastric and intestinal fluid medium. In the study, 27 *Salvia* species were used and three different SBF mediums were studied based on the duration of food intake.

Table 2. FAAS instrument operating analytical conditions

Measured Element	Ca
Wavelength	422.7 nm
Slit Width	0.7 nm
Lamp Current	10 mA
Gas Flow Rate	2 L/min
Flame Height	7 mm
Flame Type	Air-Acetylene

FAAS analysis

The Ca analysis in SBF medium of species samples and prepared herbal tea was performed using FAAS (AA-7000, Shimadzu, Japan) (Table 2).

The linear range, calibration equation, correlation coefficient (R^2), limit of detection (LOD), and limit of measurement (LOQ) values are shown in Table 3. The sensitivity of the method was evaluated by determining the limits of detection (LOD) and limits of quantification (LOQ). The LOD and LOQ values were determined under FAAS conditions from 3S/m and 10S/m respectively. The S was the standard deviation of the blank and m was the slope of the calibration equation. The LOD and LOQ values in SSF, SGF, and SIF medium conditions were found as 1.440 and 4.751 mg/L; 1.309 and 4.320 mg/L; 2.524 and 8.328 mg/L, respectively. The correlation coefficients (R^2) in SSF, SGF, and SIF medium conditions were determined as 0.990, 0.995, and 0.998, respectively (Table 3).

Statistical analysis

The analysis of the species was replicated three times and the mean values of the data were used in the statistical analysis. The correlation of Ca elements in 27 *Salvia* species structures between three different SBF medium conditions was determined using linear correlation with SSPS 21 statistical package program (2012).

RESULTS AND DISCUSSION

Variation in SBF medium conditions of Ca concentration

Ca is known to be an important mineral element for plants and humans. For this reason, regarding the Ca element in the species which is used for medicinal and various purposes, it is important to know what ratio is absorbed especially in humans. This study was carried out to estimate the amount that can be taken up by the organism of an element found in the digestible materials (herbal tea, food, and medicines). When the Ca absorption in SBF medium conditions of *Salvia* species was examined, it was determined that the Ca absorption of the species varied between 118-373 mg/kg in SSF medium conditions. The Ca absorption of the S22 sample was determined to be higher than other species in SSF medium conditions. In addition, the Ca absorptions of almost all species were detected

Table 3. FAAS instrument operating analytical conditions.

		SSF			
Element	**Linear Range (mg/L)**	**Calibration Equation**	**R^2**	**LOD (mg/L)**	**LOQ (mg/L)**
Ca	25-100	y= 0.0028104x - 0.19540	0.990	1.440	4.751
		SGF			
Element	**Linear Range (mg/L)**	**Calibration Equation**	**R^2**	**LOD (mg/L)**	**LOQ (mg/L)**
Ca	5-75	y= 0.0038165x - 0.25492	0.995	1.309	4.320
		SIF			
Element	**Linear Range (mg/L)**	**Calibration Equation**	**R^2**	**LOD (mg/L)**	**LOQ (mg/L)**
Ca	10-100	y= 0.0025610x - 0.20674	0.998	2.524	8.328

to be close to each other. As a result, it was determined that the Ca element was taken into the SSF medium in all 27 *Salvia* species (Table 4). When the Ca absorption between the species is compared under SSF medium conditions, it can be said that higher absorption in the S22 species gives more Ca^{2+} ions to the medium.

Table 4. Ca contents in simulated body fluid medium conditions of the species (n=3.

	SSF	SGF	SIF
Samples	**Ca (mg/kg)**	**Ca (mg/kg)**	**Ca (mg/kg)**
S1	230±27	18300±421	11096±844
S2	263±22	27511±109	**13119±123**
S3	308±19	33740±344	11352±164
S4	237±12	31838±810	11322±219
S5	275±4	37184±149	9398±65
S6	213±21	37723±166	11644±95
S7	195±22	31521±566	11256±633
S8	294±16	39783±151	12287±128
S9	214±46	37445±501	11494±678
S10	288±19	42316±184	12290±431
S11	267±19	27030±787	9307±304
S12	271±6	36991±113	9521±272
S13	296±20	40034±120	10182±438
S14	147±13	39442±513	10012±650
S15	283±18	38128±470	10302±755
S16	211±19	**62374±159**	10023±465
S17	187±14	55063±241	8415±112
S18	251±24	38177±150	8715±169
S19	330±17	38881±411	9104±120
S20	219±17	37626±405	8904±207
S21	263±21	37981±817	8976±490
S22	**373±10**	37746±766	8521±223
S23	292±19	36990±247	8521±406
S24	118±7	37668±626	9307±172
S25	210±14	37210±672	9458±209
S26	240±6	37131±158	12628±272
S27	262±6	38923±268	9120±82

The Ca absorption in the species was determined that varied between 18300-62374 mg/kg in SGF medium conditions. The Ca absorption of the S16 sample was determined to be higher than the other species in SGF medium conditions. It was determined that in all *Salvia* species, the Ca was taken into the SGF medium (Table 4).

The Ca absorption of the species was determined as varying between 8415-13119 mg/kg in SIF medium conditions. The Ca absorption of the S2 sample was determined to be higher than the other species in SIF medium conditions. It was determined that the Ca was taken into SIF medium in all *Salvia* species (Table 4).

Schwedt, Tawali, & Koch, (1998) the total content of zinc in the extraction with simulated gastric and intestinal fluid of foodstuffs has beendetermined. In simulated gastric juice, the total zinc content in Buckwheat flour, Rye flour, Potato, Pea, and Beef products was reported as 3.628, 1.222, 0.362, 0.751, and 4.654 mg/kg, respectively. In simulated intestinal juice, the total zinc content in the products was determined as 1.023, 0.130, 0.256, 0.371, and 3.562 mg/kg, respectively. It has been stated that the zinc element is mostly absorbed from the gastric juice (Schwedt et. al., 1998).

Giacomino et. al., (2014) the metal bioaccessibility of three drugs purchased in India has been investigated by extraction with solutions simulating gastric and intestinal fluids. The concentrations of the elements extracted upon contact between gastric and intestinal juices of the samples of drug C, D and F were reported as 1740 and 2170, 7640 and 5091, 1893 and 2490 mg/kg, respectively. Generally, it has been specified that the release of most of the analytes in the gastric medium was lower than that in the intestinal one (Giacomino et. al., 2014).

Wang et. al., (2019) the uptake of Fe, Zn, Ca, and Mg in gastric and intestinal fluids of acidic heteropolysaccharide (LP) from *Lycium barbarum* L. leaves have been determined. The Ca intakes in the gastric and intestinal fluids of the crude LP (LPC) have been reported as 0.19 and 0.54 mg, respectively. It has been stated that the Ca element is mostly absorbed from the intestinal juice (Wang et. al., 2019).

When Table 4 was examined, the ranking of Ca absorption of *Salvia* species in SBF medium conditions was determined as SGF > SIF > SSF. Thus, it was determined that the Ca element was absorbed most in gastric fluid and least in saliva fluid (Table 4). It can be said that the absorption of Ca in the saliva fluid being less than in other body fluids is due to the fact that the pH of the saliva is close to neutral. It has been reported in the literature that saliva has only a negligible effect on the level of mobilization of metal contaminants, as the pH of saliva is close to neutral (Giacomino et. al., 2014). When the SGF and SIF medium conditions were compared, the Ca absorption of *Salvia* species was determined as being higher in SGF medium conditions. It can be said that the most absorption of Ca in the gastric fluid medium is due to the acid pH of the gastric juice permiting a greater dissolution of the hydroxides, oxides, other salts, and organic species of the elements contained in the plant. Although the pH of the intestinal fluid was close to neutral, the Ca absorption in the species was determined as being high. Thus, it reveals that the Ca found in food, medicine, and herbal teas is absorbed in the intestine. Consequently, the Ca element, its carbonates, oxides, sulfites, and salts in plants and foods are mostly absorbed in gastric and intestinal fluid. It can be said that in human and animal bodies, Ca passes through the gastric and intestinal medium. When the Ca is evaluated in general, it can be said that it is absorbed in the gastric medium and is taken into the living body. The findings of this study showed that the Ca element in *Salvia* species was absorbed from the SGF and SIF fluid medium and was similar to the results in the literature.

Correlation analysis of SGF

It was aimed to determine whether there were differences between species according to SGF of the correlation coefficient and direction with correlation analysis. Correlation analysis for species in SGF medium conditions was used to provide information in determining whether there is a relationship in terms of Ca absorption between species that are related to each other and the relationship between species in the same region or close locations. Therefore, correlation analyses were performed for species in SGF medium conditions (Table 5 and 6). According to the results of the bivariate analysis of the samples belonging to SGF, the Pearson correlation coefficient (r) was at $p < 0.01$ confidence level; it was determined that there was a strong negative relationship in terms of Ca absorption between S5 with S4, S16 with S7, and S19 with S8 (r = -0.999). In addition, it was determined that there was a strong positive relationship (r = 0.999) in terms of Ca absorption between S26 with S21 species in the same medium conditions. When the Pearson correlation coefficients of the samples belonging to these simulated medium conditions were compared, it was determined that the strongest correlation at $p < 0.01$ confidence level was between S5 with S4, S16 with S7, S19 with S8, and S26 with S21 (Table 5).

When the $p < 0.05$ confidence level of the Pearson correlation coefficient (r) of the samples belonging to SGF was examined, it was determined that there was a strong negative relationship in terms of Ca absorption between S12 with S2, S12 with S9, S15 with S11, S17 with S12, S17 with S16, S23 with S20 and S24 with S3 (r = -0.999). It was determined that there was a strong negative relationship in terms of Ca absorption between S23 with S1 (r = -0.998), S26 with S9, and S19 with S11 (r = -0.997). In addition, it was determined that there was a strong positive relationship in terms of Ca absorption between S9 with S2, S17 with S7, S25 with S6 (r = 0.999), S17 with S2, S27 with S6, S11 with S8, S15 with S13 (r = 0.998) (Table 5).

Davis has been examined the close kinship of *Salvia* species with each other. He assigned a number to each *Salvia* species. According to these numbers, he said that the species between 1-7, 8-14, 15-31, 32-41, 42-47, 48-83, and 84-86 showed close kinship relationships (Table 6) (Davis, 1982). The relatedness of *Salvia* species to each other is defined by the closeness to each other of the numbers given to them. In this context, when the correlation coefficient and effect were examined, according to the results of the correlation analysis at $p < 0.01$ confidence level, a strong relationship between the species in terms of calcium absorption was determined. However, it was determined that there is no relationship between consanguinity and Ca absorption within these species (Table 6).

At the $p < 0.05$ confidence level, it was determined that there was a relationship in terms of calcium absorption between S26 (Species Kinship Code: 43) with S9 (44), S11 (38) with S8 (36), and S15 (57) with S.13 (71) which only have kinship to each other from the species which has a strong relationship with each other. As a result, it was determined that although there was a strong relationship between species in terms of calcium absorption at both $p < 0.01$ and $p < 0.05$ confidence levels, there was generally no relationship between the closely related species with each other (Table 6).

When the correlation coefficient and relationship between species collected from in the same region were evaluated, it was determined that there was only a relationship in terms of Ca absorption between S15 with S11, S24 with S3, S9 with S2, S17 with S7, S17 with S2, S27 with S6, S11 with S8, and S15 with S13 (Eastern Anatolia Region) from the species with a strong relationship with each other in the $p < 0.05$ confidence level. Dogan et. al., (2008) *Salvia* made the intra-genus classification. They divided the species into seven different sections. These sections are *Hymenosphace* Benth., *Aethiopis* Benth., *Plethiosphace* Benth., *Horminum* Benth., *Drymosphace* Benth., *Hemisphace* Benth., and *Salvia* Hedge. They grouped the species based on these sections (Table 6) (Dogan et. al., 2008). When the results of correlation analysis at $p < 0.01$ confidence level were examined at the intra-genus classification level, it was determined that there was no relationship between species in terms of Ca absorption. At the $p < 0.05$ confidence level, it was determined that there was a relationship in terms of Ca absorption only between S8 with S11 (*Hymenosphace-Hymenosphace*), S13 with S15 (*Aethiopis-Aethiopis*), and S9 with S2 (*Aethiopis-Aethiopis*) from the species with a relationship with each other (Table 6). Thus, the significant correlation between Ca element concentrations in species indicates a similar ability or presence of the same source for the *Salvia* species. The dependence between the species with the strongest correlation above can be explained by their common origin.

Correlation analysis of simulated body fluid medium conditions

It was aimed to determine whether the correlation coefficient and its direction differ in three different SBF medium conditions. For this reason, correlation analysis were performed for three different SBF medium conditions (Table 7) (Figure 1).

According to the correlation matrix of the Ca element in three different SBF medium conditions, negative correlations were detected between SGF with SIF (r= -0.276), SGF with SSF (r= -0.132)

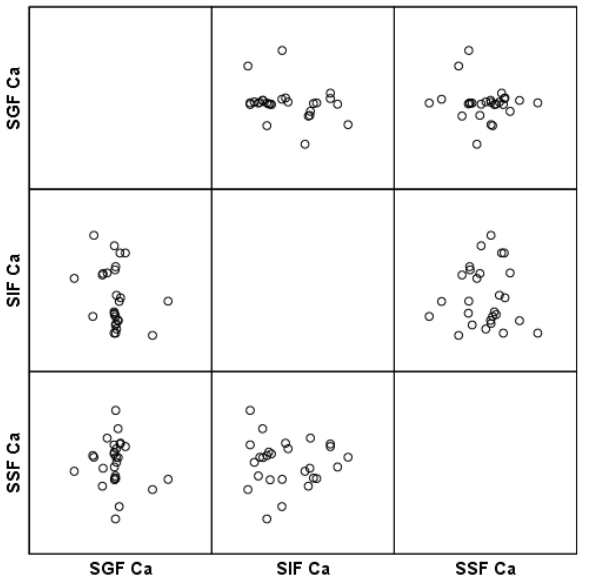

Figure 1. Scatter/Dot plot of Ca in simulated body medium conditions of the species.

Table 5. Correlation matrix for the Ca concentration of species in SGF medium conditions.

	S1	S2	S3	S4	S5	S6	S7	S8	S9	S10	S11	S12	S13	S14	S15	S16	S17	S18	S19	S20	S21	S22	S23	S24	S25	S26	S27
S1	1																										
S2	0,725	1																									
S3	0,988	0,822	1																								
S4	0,977	0,561	0,932	1																							
S5	-0,978	-0,566	-0,935	**-0,999**[a]	1																						
S6	-0,925	-0,408	-0,855	-0,985	0,984	1																					
S7	0,794	0,994	0,878	0,646	-0,650	-0,503	1																				
S8	0,900	0,953	0,956	0,786	-0,790	-0,667	0,98	1																			
S9	0,702	0**,999**[b]	0,803	0,533	-0,538	-0,378	0,99	0,942	1																		
S10	-0,855	-0,262	-0,765	-0,946	0,944	0,988	-0,363	-0,543	-0,230	1																	
S11	0,926	0,932	0,973	0,823	-0,827	-0,712	0,965	**0,998**[b]	0,919	-0,595	1																
S12	-0,739	**-0,999**[b]	-0,834	-0,578	0,583	0,427	-0,996	-0,959	**-0,999**[b]	0,282	-0,939	1															
S13	-0,961	-0,886	-0,992	-0,880	0,883	0,784	-0,931	-0,985	-0,871	0,679	-0,994	0,896	1														
S14	0,254	-0,482	0,103	0,455	-0,450	-0,603	-0,386	-0,193	-0,511	-0,719	-0,131	0,463	0,022	1													
S15	-0,944	-0,912	-0,983	-0,852	0,855	0,747	-0,950	-0,993	-0,898	0,635	**-0,999**[b]	0,920	**0,998**[b]	0,079	1												
S16	-0,793	-0,994	-0,877	-0,644	0,649	0,502	**-0,999**[a]	-0,979	-0,990	0,361	-0,965	0,996	0,930	0,388	0,950	1											
S17	0,769	**0,998**[b]	0,858	0,615	-0,619	-0,468	**0,999**[b]	0,971	0,995	-0,325	0,954	**-0,999**[b]	-0,915	-0,423	-0,937	**-0,999**[b]	1										
S18	0,175	0,805	0,324	-0,040	0,034	0,213	0,737	0,586	0,824	0,362	0,534	-0,792	-0,439	-0,908	-0,490	-0,739	0,764	1									
S19	-0,895	-0,956	-0,953	-0,779	0,782	0,658	-0,982	**-0,999**[a]	-0,946	0,533	**-0,997**[b]	0,962	0,983	0,204	0,992	0,982	-0,973	-0,596	1								
S20	0,995	0,652	0,968	0,993	-0,994	-0,958	0,729	0,852	0,627	-0,902	0,883	-0,668	-0,929	0,349	-0,906	-0,728	0,701	0,076	-0,846	1							
S21	-0,638	-0,993	-0,748	-0,458	0,463	0,297	-0,975	-0,910	-0,996	0,145	-0,882	0,990	0,825	0,583	0,856	0,975	-0,983	-0,870	0,914	-0,558	1						
S22	-0,705	-0,023	-0,588	-0,840	0,837	0,922	-0,129	-0,326	0,011	0,971	-0,385	0,044	0,483	-0,865	0,431	0,127	-0,089	0,575	0,315	-0,772	-0,097	1					
S23	**-0,998**[b]	-0,679	-0,976	-0,989	0,989	0,947	-0,753	-0,870	-0,654	0,886	-0,900	0,694	0,942	-0,316	0,921	0,752	-0,726	-0,111	0,864	**-0,999**[b]	0,587	0,749	1				
S24	-0,991	-0,811	**-0,999**[b]	-0,939	0,941	0,865	-0,868	-0,950	-0,791	0,777	-0,968	0,823	0,990	-0,122	0,980	0,868	-0,848	-0,305	0,947	-0,973	0,735	0,604	0,980	1			
S25	-0,916	-0,388	-0,844	-0,981	0,979	**0,999**[b]	-0,484	-0,650	-0,357	0,991	-0,696	0,407	0,770	-0,621	0,732	0,482	-0,448	0,234	0,641	-0,952	0,275	0,930	0,940	0,854	1		
S26	-0,647	-0,994	-0,756	-0,469	0,474	0,308	-0,977	-0,915	**-0,997**[b]	0,157	-0,887	0,992	0,832	0,573	0,862	0,978	-0,985	-0,864	0,919	-0,568	**0,999**[a]	-0,080	0,597	0,743	0,287	1	
S27	-0,948	-0,468	-0,888	-0,994	0,993	**0,998**[b]	-0,559	-0,715	-0,438	0,975	-0,757	0,487	0,824	-0,549	0,790	0,558	-0,526	0,147	0,706	-0,975	0,359	0,894	0,967	0,897	0,996	0,371	1

[a] Correlation is significant at the 0.01 level, [b] Correlation is significant at the 0.05 level.

Table 6. The relatedness of *Salvia* species to each other and the in-genus classification.

Species	Species Codes	Species Kinship Code	Sections
Salvia blepharochlaena	S1	34	*Hymenosphace* Benth.,
Salvia brachyantha subsp. *brachyantha*	S2	49	*Aethiopis* Benth.,
Salvia candidissima subsp. *candidissima*	S3	66	*Aethiopis* Benth.,
Salvia ceratophylla L.	S4	53	*Aethiopis* Benth.,
Salvia cerino-pruinosa var. *cerino-pruinosa*	S5	-	*Hymenosphace* Benth.,
Salvia cerino-pruinosa var. *elazigensis*	S6	-	*Hymenosphace* Benth.,
Salvia divaricata	S7	1	*Salvia* Hedge (*Eusphace* Benth.,)
Salvia hydrangea	S8	36	*Hymenosphace* Benth.,
Salvia hypargeia	S9	44	*Aethiopis* Benth.,
Salvia indica L.	S10	72	*Aethiopis* Benth.,
Salvia kronenburgii	S11	38	*Hymenosphace* Benth.,
Salvia kurdica	S12	6	*Salvia* Hedge (*Eusphace* Benth.,)
Salvia limbata	S13	71	*Aethiopis* Benth.,
Salvia macrochlamys	S14	7	*Salvia* Hedge (*Eusphace* Benth.,)
Salvia microstegia	S15	57	*Aethiopis* Benth.,
Salvia montbretii	S16	45	*Aethiopis* Benth.,
Salvia multicaulis	S17	40	*Hymenosphace* Benth.,
Salvia pachystachys	S18	27	*Salvia* Hedge (*Eusphace* Benth.,)
Salvia pinnata L.	S19	11	*Salvia* Hedge (*Eusphace* Benth.,)
Salvia pseudeuphratica	S20	-	*Hymenosphace* Benth.,
Salvia sclarea L.	S21	50	*Aethiopis* Benth.,
Salvia siirtica	S22	-	-
Salvia spinosa L.	S23	46	*Aethiopis* Benth.,
Salvia suffruticosa	S24	29	*Salvia* Hedge (*Eusphace* Benth.,)
Salvia trichoclada	S25	14	*Salvia* Hedge (*Eusphace* Benth.,)
Salvia viridis L.	S26	43	*Horminum* Benth.,
Salvia xanthocheila	S27	58	*Aethiopis* Benth.,

Species kinship between 1-7, 8-14, 15-31, 32-41, 42-47, 48-83 and 84-86.

Table 7. Correlation matrix of species in simulated body fluid medium conditions.

	SGF	SIF	SSF
SGF	1		
SIF	-0.276	1	
SSF	-0.132	-0.027	1

and SSF with SIF (r= -0.027). When the correlations in SBF medium conditions were evaluated together, they were determined that SGF-SIF > SGF-SSF > SSF-SIF. When all the correlation coefficients were evaluated in general, it was determined that all SBF medium conditions were weakly correlated with each other. In addition, considering all correlation coefficients, SGF and SIF medium were detected to have stronger negative correlations than other mediums. The fact that these correlations were different from the specified SBF mediums can be explained as the result of taking other elements such as the Ca element into the medium.

CONCLUSION

Plants have medical benefits because they contain various bioactive compounds as well as mineral elements. For this reason, it is important to know the contents of mineral elements in plants and how much these elements are absorbed. In this context, this study has determined the Ca content and absorption of 27 *Salvia* species in three different SBF conditions. In addition, the correlation analysis of the obtained results has been performed.

According to the analysis results in different SBF medium conditions of the samples belonging to *Salvia* species, it has been determined that the Ca absorption in the SGF the most. Based on the results obtained from SBF medium conditions, it can be said which element is taken in which body fluid medium. In ad-

dition, it can be said that element-based synthesized drugs are a guide in the selection of the target region they want to affect.

According to the results of the bivariate analysis in SBF medium conditions, information on the differences between the samples belonging to different SBF medium conditions could not be obtained. However, when SBF medium conditions are evaluated alone, the only information that may indicate the same source or behavior is obtained for two or more items. Thus, it was determined that more complex analysis systems should be used to determine the difference in terms of the medium conditions.

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REFERENCES

- Al-Qudah, M. A., Al-Jaber, H. I., Abu Zarga, M. H., & Abu Orabi, S. T. (2014). Flavonoid and phenolic compounds from *Salvia palaestina* L. growing wild in Jordan and their antioxidant activities. *Phytochemistry*, *99*, 115–120. https://doi.org/10.1016/j.phytochem.2014.01.001
- Al Jaber, H. (2016). *Salvia ceratophylla* from Jordan : Volatile organic compounds, essential oil composition and antioxidant activity. *Jordan Journal of Chemistry*, *11*, 108–119.
- Altun, M., Ünal, M., Kocagöz, T., & Gören, A. C. (2007). Essential oil compositions and antimicrobial activity of *Salvia* species. *Journal of Essential Oil-Bearing Plants*, *10*, 251–258. https://doi.org/10.1080/0972060X.2007.10643550
- Asadi-Samani, M., Khaledi, M., Khaledi, F., Samarghandian, S., & Gholipour, A. (2019). Phytochemical properties and antibacterial effects of *Salvia multicaulis* vahl., *euphorbia microsciadia* boiss., and reseda lutea on staphylococcus aureus and acinetobacter baumanii. *Jundishapur Journal of Natural Pharmaceutical Products*, *14*, 63640. https://doi.org/10.5812/jjnpp.63640
- Bağcı, E., Akbaba, E., Maniu, C., Ungureanu, E., & Hritcu, L. (2019). Evaluation of antiamnesic activity of *Salvia multicaulis* essential oil on scopolamine-induced amnesia in rats: in vivo and in silico approaches. *Heliyon*, *5*, e02223. https://doi.org/10.1016/j.heliyon.2019.e02223
- Bakir, D., Akdeniz, M., Ertas, 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
- Büyükkartal, H. N., Kahraman, A., Çölgeçen, H., Doğan, M., & Karabacak, E. (2011). Mericarp micromorphology and anatomy of *Salvia hedgeana* Dönmez, *S. Huberi* Hedge and *S. rosifolia* Sm. (section *Salvia* Hedge, Lamiaceae). *Acta Botanica Croatica*, *70*, 65–80. https://doi.org/10.2478/v10184-010-0011-8
- Celep, F., & Dirmenci, T. (2017). Systematic and biogeographic overview of Lamiaceae in Turkey. *Natural Volatiles & Essential Oils*, *4*, 14–27.
- Coşge Şenkal, B. (2019). The effect of cuttings stages on components and content of essential oils from *Salvia viridis* L. *Kahramanmaraş Sütçü İmam Üniversitesi Tarım ve Doğa Dergisi*, *22*, 71–77. https://doi.org/10.18016/ksutarimdoga.vi.428853
- Çulhaoğlu, B., Hatipoğlu, S. D., Dönmez, A. A., & Topçu, G. (2015). Antioxidant and anticholinesterase activities of lupane triterpenoids and other constituents of *Salvia trichoclada*. *Medicinal Chemistry Research*, *24*, 3831–3837. https://doi.org/10.1007/s00044-015-1424-7
- Davis P.H. (1982). *Flora of Turkey and the East Aegean Islands*. Edinburgh, E: British Library Cataloguing in Publication Data.
- Dogan, M., Pehlivan, S., Akaydin, G., Bagci, E., Uysal, I., & Dogan, H. M. 'Salvia species in Turkey L. (Labiatae) taxonomic revision of the genus', The Scientific and Technological Research Council of Turkey (TUBITAK) Project number: 104T450. Ankara, Turkey, 2008.
- Erdogan-Orhan, I., Baki, E., Şenol, S., & Yilmaz, G. (2010). Sage-called plant species sold in Turkey and their antioxidant activities. *Journal of the Serbian Chemical Society*, *75*, 1491–1501. https://doi.org/10.2298/JSC100322115E
- Firat, M. (2020). An addition to the flora of Turkey : *Salvia reuteriana* (Lamiaceae), with contributions to its taxonomy. *Iranian Journal of Botany*, *26*, 137–140. https://doi.org/10.22092/ijb.2020.343177.1288
- Gedik, O., Kiran, Y., Emre, I., & Kursat, M. (2016). Karyological notes for seven *Salvia* L. taxa grown in Turkey. *Cytologia*, *81*, 395–402. https://doi.org/10.1508/cytologia.81.395
- Giacomino, A., Abollino, O., Casanova, C., Gioia, C. La, Magi, E., & Malandrino, M. (2014). Determination of the total and bioaccessible contents of essential and potentially toxic elements in ayurvedic formulations purchased from different commercial channels. *Microchemical Journal*, *12*, 1–36. https://doi.org/10.1016/j.microc.2014.12.005
- Güzel, S., Özay, Y., Kumaş, M., Uzun, C., Özkorkmaz, E. G., Yıldırım, Z., … Kahraman, A. (2019). Wound healing properties, antimicrobial and antioxidant activities of *Salvia kronenburgii* Rech. f. and *Salvia euphratica* Montbret, Aucher & Rech. f. var. *euphratica* on excision and incision wound models in diabetic rats. *Biomedicine and Pharmacotherapy*, *111*, 1260–1276. https://doi.org/10.1016/j.biopha.2019.01.038
- Hegazy, M. E. F., Hamed, A. R., El-Halawany, A. M., Hussien, T. A., Abdelfatah, S., Ohta, S., Efferth, T. (2018). Cytotoxicity of abietane diterpenoids from *Salvia multicaulis* towards multidrug-resistant cancer cells. *Fitoterapia*, *130*, 54–60. https://doi.org/10.1016/j.fitote.2018.08.002
- Kahnamoei, M. B., Tabefam, M., Ebrahimi, S. N., Danton, O., Hamburger, M., & Farimani, M. M. (2019). Chemical constituents from the ethyl acetate extract of *Salvia hydrangea*. *Natural Product Communications*, *14*, 1–4. https://doi.org/10.1177/1934578X19848852
- Kahraman, A., Celep, F., & Doğan, M. (2010). Morphology, anatomy, palynology and nutlet micromorphology of *Salvia macrochlamys* (Labiatae) in Turkey. *Biologia*, *65*, 219–227. https://doi.org/10.2478/s11756-010-0013-y
- Kahraman, A., Celep, F., Doğan, M., & Bagherpour, S. (2010). A taxonomic revision of *Salvia euphratica* sensu lato and its closely related species (sect. Hymenosphace, Lamiaceae) using multivariate analysis. *Turkish Journal of Botany*, *34*, 261–276. https://doi.org/10.3906/bot-0910-194
- Kahraman, A., Doğan, 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
- Kahraman, A., & Doğan, M. (2010). Comparative study of *Salvia limbata* C.A. and *S. palaestina* Bentham (sect. Aethiopis Bentham, Labiatae) from East Anatolia, Turkey. *Acta Botanica Croatica*, *69*, 47–64.
- Kaya, A., Başer, K. H. C., Satil, F., & Tümen, G. (2000). Morphological and anatomical studies on *Cyclotrichium origanifolium* (Labill.) Manden. & Scheng. (Labiatae). *Turkish Journal of Botany*, *24*, 273–278.

- Kurkcuoglu, M., Turnen, G., & Baser, K. H. C. (2001). Essential oil constituents of *Satureja boissieri* from Turkey. *Chemistry of Natural Compounds*, *37*, 329–331.
- Lippert, F. (2020). Macroelements : Ca, Na, K, P, Cl. In F.V. Zohoori, & R.M. Duckworth (Eds.), *The Impact of Nutrition and Diet on Oral Health* (pp. 22–31). Basel, Karger: Monogr Oral Sci.
- Moridi Farimani, M., Miran, M., & Ebrahimi, S. N. (2019). New diterpenoids from the aerial parts of *Salvia reuterana*. *Iranian Journal of Pharmaceutical Research*, *18*, 406–411. https://doi.org/10.22037/ijpr.2019.2314
- Nickavar, B., Rezaee, J., & Nickavar, A. (2016). Effect-directed analysis for the antioxidant compound in *Salvia verticillata*. *Iranian Journal of Pharmaceutical Research*, *15*, 241–246. https://doi.org/10.22037/ijpr.2016.1793
- Öztekin, N., Başkan, S., Kepekçi, E. S., Erim, F. B., & Topçu, G. (2010). Isolation and analysis of bioactive diterpenoids in *Salvia* species (*Salvia chionantha* and *Salvia kronenburgiii*) by micellar electrokinetic capillary chromatography. *Journal of Pharmaceutical and Biomedical Analysis*, *51*, 439–442. https://doi.org/10.1016/j.jpba.2009.04.012
- Pytlakowska, K., Kita, A., Janoska, P., Połowniak, M., & Kozik, V. (2012). Multi-element analysis of mineral and trace elements in medicinal herbs and their infusions. *Food Chemistry*, *135*, 494–501. https://doi.org/10.1016/j.foodchem.2012.05.002
- Ross, A. C., Taylor, C. L., Yaktine, A. L., & Del Valle, H.B. (2011). Overview of calcium. *In Dietary Reference Intakes for Calcium and Vitamin D* (pp. 35–74). Washington, DC: The National Academies Press.
- Satıl, F., Ünal, M., & Hopa, E. (2007). Comparative morphological and anatomical studies of *Hymenocrater bituminosus* Fisch. & C.A.Mey. (Lamiaceae) in Turkey. *Turkish Journal of Botany*, *31*, 269–275.
- Schwedt, G., Tawali, A. B., & Koch, K. (1998). Strategy of analysis for the estimation of the bioavailability of zinc in foodstuffs. *Fresenius Journal of Analytical Chemistry*, *360*, 589–594.
- Senatore, F., Formisano, C., Arnold, N. A., & Piozzi, F. (2005). Essential oils from *Salvia* sp. (Lamiaceae). III. composition and antimicrobial activity of the essential oil of *Salvia palaestina* Benth. growing wild in Lebanon. *Journal of Essential Oil Research*, *17*, 419–421. https://doi.org/10.1080/10412905.2005.9698949
- Shannon I.L. (1982). Fluoride treatmentprograms for high-caries-risk patients. *Clin Prevent Dent 4*, 11-20.
- Shkembi, B., & Huppertz, T. (2022). Calcium absorption from food products : Food matrix effects. *Nutrients*, *14*, 180–211. https://doi.org/https://doi.org/10.3390/nu14010180
- Stefaniak A. B., Abbas Virji M., Harvey C. J., Sbarra D. C., Day G. A., Hoover M. D. (2010). Influence of artificial gastric juice composition on bioaccessibility of cobalt-and tungsten-containing powders. *International Journal of Hygiene and Environmental Health*, *213*, 107-115.
- Stippler E., Kopp S., Dressman J. B. (2004). Comparison of US pharmacopeia simulated intestinal fluid TS (without pancreatin) and phosphate standard buffer pH 6.8, TS of the international pharmacopeia with respect to their use in in vitro dissolution testing. *Dissolution Technologies*, *11*, 6-10.
- Szymczycha-Madeja, A., Welna, M., & Zyrnicki, W. (2013). Multi-element analysis, bioavailability and fractionation of herbal tea products. *J. Braz. Chem. Soc.*, *24*, 777–787.
- Targan, Ş., Yelboğa, E. G., & Cittan, M. (2018). Macro and trace element contents of some wild plants consumed as vegetable in Manisa District, Turkey. *Journal of the Turkish Chemical Society, Section A: Chemistry*, *5*, 751–762. https://doi.org/10.18596/jotcsa.363151
- Tosun, M., Ercisli, S., Sengul, M., Ozer, H., Polat, T., & Ozturk, E. (2009). Antioxidant properties and total phenolic content of eight *Salvia* species from Turkey. *Biological Research*, *42*, 175–181. https://doi.org/10.4067/S0716-97602009000200005
- Tunay, Z., Yener, İ., Varhan Oral, E., Barla Demirkoz, A., Tokul-Ölmez, Ö., Firat, M., Ertaş, A. (2020). Trace element analysis in some *Salvia* species by inductively coupled plasma-mass spectrometry (ICP-MS) and chemometric approach. *Journal of Research in Pharmacy*, *24*, 297–309. https://doi.org/10.35333/jrp.2020.146
- Utsukarci, B. Sen, Gurdal, B., Bilgin, M., Satana, D., Demirci, B., Tan, N., & Mat, A. (2019). Biological activities of various extracts from *Salvia cassia* Sam. Ex rech.f. and chemical composition of its most active extract. *Records of Natural Products*, *13*, 24–36. https://doi.org/10.25135/rnp.68.18.02.090
- Umaz, A. (2021). Evaluation chemometric and metal analysis of 200 medicinal and aromatic plant species growing in the eastern region of our country by spectroscopic methods (Doctoral dissertation). Retrieved from https://tez.yok.gov.tr/UlusalTezMerkezi/tezSorguSonucYeni.jsp
- Wang, M., Wang, J., Fu, L., Al-wraikat, M., Lu, P., Shan, L., & Zhang, B. (2019). Degradation of polysaccharides from *Lycium barbarum* L. leaves improves bioaccessibility and gastrointestinal transport of endogenous minerals. *International Journal of Biological Macromolecules*, *11*, 243–281. https://doi.org/10.1016/j.ijbiomac.2019.11.243
- Yılar, M., Bayar, Y., & Onaran, A. (2019). Chemical composition and allelopathic effect of *Origanum onites* L. essential oil. *Plant Protection Bulletin*, *59*, 71–78. https://doi.org/10.16955/bitkorb.542301
- Zhang, X., Ding, W., Li, J., Liu, F., Zhou, X., & Tian, S. (2015). Multi-elemental analysis of *Ziziphora clinopodioides* from different regions, periods and parts using atomic absorption spectrometry and chemometric approaches. *Brazilian Journal of Pharmacognosy*, *25*, 465–472. https://doi.org/10.1016/j.bjp.2015.07.021