Journal of Research in Pharmacy

Research Article

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Antimicrobial activity of three *Scutellaria* L. species from Turkey

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Received: 02 October 2018 / Revised: 20 December 2018 / Accepted: 28 December 2018

ABSTRACT: Plant-sourced antimicrobials are known for their therapeutic potency against multi-drug-resistant pathogens. The members of *Scutellaria* L. have been used to cure several diseases in East Asia, Europe, and North America. The genus *Scutellaria* belonging to Lamiaceae family is composed of around 360 species worldwide and 18 species in Turkey. In this study, 36 extracts prepared with different solvents from aerial parts and roots of *S. salviifolia* Benth., *S. diffusa* Benth. and *S. pontica* C. Koch were investigated for their antimicrobial activity against four bacteria (*Escherichia coli* ATCC 25922, *Enterococcus faecalis* ATCC 29212, *Pseudomonas aeruginosa* ATCC 27853, *Staphylococcus aureus* ATCC 29213) and three yeasts (*Candida albicans* ATCC 90028, *C. krusei* ATCC 6258, *C. parapsilosis* ATCC 90018) by using the broth microdilution method. Gentamicin, vancomycin and fluconazole were used as positive control. According to our results, all of the tested extracts showed stronger antimicrobial activity against yeasts than bacteria. The chloroform extract of *S. salviifolia* root showed the highest antifungal effect against *C. krusei* with 32 µg/ml MIC value compared with all the tested extracts and the positive control fluconazole (64 µg/ml MIC value).

KEYWORDS: *Scutellaria*; Lamiaceae; plant extract; antimicrobial activity; minimum inhibitory concentration.

1. INTRODUCTION

Indiscriminate use of antibiotics has led to the development of multidrug-resistant pathogens causing various infectious diseases. Currently, plant-based antimicrobials are considered as an important source of novel therapeutics against multi-drug-resistant pathogens. Plant extracts and their secondary metabolites such as quinones, alkaloids, lectins, polypeptides, flavonoids, terpenoids, essential oils and tannins have significant potential to cope with infectious diseases by bacteria, viruses, parasites and fungi without any known side effects [1, 2].

The genus *Scutellaria* L. (Lamiaceae) is composed of around 360 species distributed temperate climate and tropical mountains including East Asia, North America, and Europe [3]. The members of genus *Scutellaria* have been utilized traditionally to cure several diseases because of their anti-inflammatory, sedative, antioxidant, antiviral and antithrombotic activities more often in China, Japan and Korea. From the genus *Scutellaria*, numerous compounds were isolated including flavonoids, phenylethanoid glycosides, iridoid glycosides, diterpenes, triterpenoids, alkaloids, phytosterols and polysaccharides, which are responsible for their biological activities such as antitumor, hepatoprotective, antioxidant, anti-inflammatory, anticonvulsant, antibacterial and antiviral [4]. Radix Scutellariae baicalensis known as "Huang-qin" and Herba Scutellariae barbatae known as "Ban-zhi-lian" are commonly used in traditional Chinese medicine and recorded in the Chinese and Japanese Pharmacopoeias. *S. galericulata* L. and *S. lateriflora* L. are the mainly used species in Europe and North America for epilepsy, neuralgia and anxiety [4, 5].

In Turkey, the genus *Scutellaria* (known as "kaside, sancı otu, şimşek otu, korku otu") is represented by 18 species or 39 taxa including subspecies and varieties and 17 of those are endemic [6-8]. In East Anatolia, aerial parts and leaves of *Scutellaria orientalis* L. are used internally as carminative, astringent and against abdominal pain and externally for wound healing [9-11]. Aerial parts of *S. salviifolia* Benth. is used for gastrointestinal system diseases [8].

How to cite this article: Arıtuluk ZC, Özkul Koçak C, Renda G, Ekizoğlu M, Ezer, N. Antimicrobial activity of three *Scutellaria* L. species from Turkey. J Res Pharm. 2019; 23(3): 552-558.

ISSN: 2630-6344

https://doi.org/10.12991/jrp.2019.162

S. salviifolia, *S. diffusa* Benth. and *S. pontica* C. Koch belong to the Section Salviifoliae (Boiss.) Edmondson. Among them, *S. salviifolia* is an endemic species of Turkish flora [12]. Although biological activities of many *Scutellaria* species have been reported, there are only a few reports concerning phytochemical properties and biological activities of these species. In previous studies, phenolic compounds and diterpenoids were isolated from the species *S. pontica* [13, 14]. The essential oil compositions of *S. diffusa* and *S. salviifolia* were also investigated [15]. Saracoğlu et al. [16] revealed the cytotoxic and cytostatic activities of phenylethanoid glycosides which were isolated from the species *S. salviifolia*. Şenol et al. [17] screened the acetylcholinesterase, butyrylcholinesterase, and tyrosinase inhibitory activities of the methanol extracts prepared from the aerial parts of the 33 *Scutellaria* taxa including *S. diffusa* and *S. salviifolia*. The antioxidant activity of the methanol and ethyl acetate extracts of these taxa by using DPPH and FRAP assays was also determined in the same study [17]. Antibacterial effects of methanol extracts prepared from the leaves, stems and flowers of *S. salviifolia* were also investigated [18].

The aim of this study was to assess antibacterial and antifungal effects of methanol, *n*-hexane, chloroform, ethyl acetate, *n*-butanol and water extracts of aerial parts and roots of *S. salviifolia*, *S. diffusa* and *S. pontica* by using broth microdilution method identified as minimum inhibitory concentration (MIC) values [19, 20].

2. RESULTS AND DISCUSSION

Antimicrobial activity of 36 extracts of the aerial parts and roots of *S. salviifolia*, *S. diffusa* and *S. pontica* has been evaluated *in vitro* against two Gram-positive bacteria *Staphylococcus aureus* ATCC 29213, *Enterococcus faecalis* ATCC 29212, two Gram-negative bacteria *Escherichia coli* ATCC 25922, *Pseudomonas aeruginosa* ATCC 27853 and three yeasts *Candida albicans* ATCC 90028, *C. krusei* ATCC 6258, *C. parapsilosis* ATCC 90018 that are known to cause infections in humans. The percentage yields of extracts are given in Table 1. Table 2 shows the antibacterial activity results of the tested extracts while Table 3 presents the obtained results of the antifungal activity.

Table 1. The percentage yields of the tested extracts.

Extract[a]	Yields (%)					
	***S. salviifolia* Root**	***S. salviifolia* Herb**	***S. diffusa* Root**	***S. diffusa* Herb**	***S. pontica* Root**	***S. pontica* Herb**
MeOH	17.4	24.6	12	27.2	20.1	33.6
n-Hexane	5.1	1.7	3.4	3.1	2.1	3.2
$CHCl_3$	8.2	18	13	5.5	5.8	5.3
EtoAc	15.7	9.8	12.1	8.8	12.9	9.6
n-BuOH	25.9	31.9	19.5	40.1	23.7	36.1
H_2O	45	37.8	51.6	40.2	54.8	45.7

[a] MeOH: Methanol extract; $CHCl_3$: Chloroform extract; EtoAC: Ethyl acetate extract; *n*-BuOH: *n*-Butanol extract; H_2O: remaining aqueous extract.

In general, crude methanol extracts prepared from roots and aerial parts of plants exhibited low or no antimicrobial activity with ≥1024 µg/ml MIC values in the tested range of concentrations while, the tested extracts prepared from the crude methanol extracts by using a partition with different solvents of increasing polarity such as *n*-hexane, chloroform and ethyl acetate exhibited higher activity. All tested *n*-butanol extracts from roots and aerial parts and aqueous extracts from roots of plants showed low or no activity similar to the methanol extracts. But aqueous extracts from aerial parts of plants exhibited antimicrobial activity against some bacteria and yeasts with the range of 512-64 µg/ml MIC values (Table 2-3).

The antibacterial activity results revealed that chloroform extract of *S. salviifolia* root showed against *E. faecalis*, *E. coli* and *P. aeruginosa* while *S. pontica* root showed against *E. coli* and *P. aeruginosa* the highest activity both with 128 µg/ml MIC value. Besides chloroform extract of *S. salviifolia* root, *n*-hexane and chloroform extracts of *S. pontica* herb exhibited the highest activity against *S. aureus* with 256 µg/ml MIC value. *n*-Hexane extract of roots of *S. salviifolia*, *n*-hexane and ethyl acetate extracts of aerial parts of *S. salviifolia*, ethyl acetate extracts of roots and aerial parts of *S. diffusa* and chloroform extracts of roots and aerial parts of *S. pontica* showed growth inhibitory effect against *E. faecalis* with 256 µg/ml MIC value. *n*-Hexane extract of roots of *S.*

salviifolia and chloroform extract of aerial parts of *S. pontica* possessed antibacterial activity against *P. aeruginosa* with 256 µg/ml MIC value. However, the effectivenesses of all tested extracts were lower compared with vancomycin (0.125 and 0.5 µg/ml MIC values) and gentamicin (1 and 16 µg/ml MIC values) as the positive controls (Table 2).

Table 2. Antibacterial activity of tested extracts against tested microorganism.

			MIC (µg/ml) values against the tested bacteria strains			
			S. aureus	*E. faecalis*	*E. coli*	*P. aeruginosa*
Plant name	**Plant part**	**Extract[a]**	**ATCC 29213**	**ATCC 29212**	**ATCC 25922**	**ATCC 27853**
S. salviifolia	Root	MeOH	>1024	1024	>1024	>1024
		n-Hexane	512	256	512	256
		$CHCl_3$	256	128	128	128
		EtoAc	512	512	512	512
		n-BuOH	>1024	1024	>1024	>1024
		H_2O	>1024	>1024	>1024	>1024
S. salviifolia	Herb	MeOH	1024	1024	1024	1024
		n-Hexane	1024	256	512	512
		$CHCl_3$	1024	1024	512	512
		EtoAc	512	256	512	512
		n-BuOH	>1024	>1024	>1024	>1024
		H_2O	1024	512	512	512
S. diffusa	Root	MeOH	512	1024	>1024	1024
		n-Hexane	>1024	>1024	>1024	>1024
		$CHCl_3$	512	512	512	512
		EtoAc	1024	256	512	512
		n-BuOH	1024	>1024	>1024	>1024
		H_2O	>1024	>1024	>1024	>1024
S. diffusa	Herb	MeOH	>1024	>1024	>1024	>1024
		n-Hexane	1024	512	512	512
		$CHCl_3$	512	512	512	512
		EtoAc	1024	256	512	512
		n-BuOH	>1024	1024	>1024	>1024
		H_2O	1024	512	1024	512
S. pontica	Root	MeOH	1024	>1024	>1024	>1024
		n-Hexane	512	512	512	512
		$CHCl_3$	512	256	128	128
		EtoAc	512	512	512	512
		n-BuOH	1024	>1024	>1024	>1024
		H_2O	>1024	>1024	>1024	>1024
S. pontica	Herb	MeOH	512	>1024	512	1024
		n-Hexane	256	512	1024	512
		$CHCl_3$	256	256	512	256
		EtoAc	512	512	512	512
		n-BuOH	512	>1024	>1024	>1024
		H_2O	512	512	512	512
Vancomycin[b]			0.5	0.125	-	-
Gentamicin[c]			1	16	1	1

[a] MeOH: Methanol extract; $CHCl_3$: Chloroform extract; EtoAC: Ethyl acetate extract; *n*-BuOH: *n*-Butanol extract; H_2O: remaining aqueous extract.
[b] Positive control-Vancomycin (only used for Gram positive standard bacteria. Quality control ranges are as follows: *S. aureus* ATCC 29213: 0.5-2 µg/ml; *E. faecalis* ATCC 29212: 1-4 µg/ml.
[c] Positive control-Gentamicin. Quality control ranges are as follows: *S. aureus* ATCC 29213: 0.12-1 µg/ml; *E. faecalis* ATCC 29212: 4-16 µg/ml, *E. coli* ATCC 25922 0.25-1 µg/ml, P. aeruginosa ATCC 27853 0.5-2 µg/ml.

According to our results, all of the tested extracts showed stronger antimicrobial activity against yeasts than bacteria. Especially, the *n*-hexane, chloroform and ethyl acetate extracts of roots and aerial parts exhibited antifungal activity with a range of 256-32 µg/ml MIC value. The chloroform extract of *S. salviifolia* root showed the highest antifungal activity against *C. krusei* with 32 µg/ml MIC value compared with all the tested extracts and the positive control fluconazole (64 µg/ml MIC value). Chloroform extract of the aerial parts of *S. pontica* also exhibited high antifungal activity against *C. krusei* as well as fluconazole with 64 µg/ml MIC value. The chloroform and ethyl acetate extracts from roots of *S. salviifolia*, *n*-hexane extracts from aerial parts of *S. salviifolia* and the aqueous extract from aerial parts of *S. pontica* showed antifungal activity against at least one of *C. albicans* and *C. parapsilosis* yeasts with 64 µg/ml MIC value. Nevertheless, all tested extracts exhibited lower antifungal activity against *C. albicans* and *C. parapsilosis* compared with fluconazole (1 and 0.5 µg/ml MIC values, respectively) as the positive control (Table 3).

Table 3. Antifungal activity of tested extracts against tested microorganism.

			MIC (µg/ml) values against the tested fungal strains		
			C. albicans	***C. krusei***	***C. parapsilosis***
Plant name	**Plant part**	**Extract[a]**	**ATCC 90028**	**ATCC 6258**	**ATCC 90018**
S. salviifolia	Root	MeOH	1024	1024	1024
		n-Hexane	128	128	128
		$CHCl_3$	64	32	64
		EtoAc	256	128	64
		n-BuOH	1024	1024	1024
		H_2O	>1024	1024	1024
S. salviifolia	Herb	MeOH	512	256	256
		n-Hexane	256	128	64
		$CHCl_3$	128	128	1024
		EtoAc	256	128	256
		n-BuOH	1024	1024	1024
		H_2O	256	256	128
S. diffusa	Root	MeOH	1024	512	1024
		n-Hexane	>1024	512	512
		$CHCl_3$	256	128	128
		EtoAc	256	128	128
		n-BuOH	>1024	1024	1024
		H_2O	>1024	1024	1024
S. diffusa	Herb	MeOH	>1024	1024	1024
		n-Hexane	256	128	256
		$CHCl_3$	256	128	256
		EtoAc	256	128	256
		n-BuOH	1024	1024	1024
		H_2O	128	128	256
S. pontica	Root	MeOH	>1024	1024	1024
		n-Hexane	256	128	128
		$CHCl_3$	128	128	128
		EtoAc	256	128	128
		n-BuOH	>1024	1024	1024
		H_2O	>1024	1024	512
S. pontica	Herb	MeOH	1024	1024	1024
		n-Hexane	256	128	128
		$CHCl_3$	128	64	128
		EtoAc	256	128	128
		n-BuOH	>1024	>1024	1024
		H_2O	256	256	64
Fluconazole[b]			1	64	0.5

[a]MeOH: Methanol extract; $CHCl_3$: Chloroform extract; EtoAC: Ethyl acetate extract; *n*-BuOH: *n*-Butanol extract; H_2O: remaining aqueous extract

[b]Positive control- Quality control ranges are as follows: *C. albicans* ATCC 90028: 0.25-1.0 µg/ml; *C. krusei* ATCC 6528: 16-64 µg/ml; *C. parapsilosis* ATCC 90018: 0.25-1.0 µg/ml.

There are a few studies about the antimicrobial activity of *Scutellaria* species, especially on *S. baicalensis* Georgi which is used commonly in traditional Chinese medicine. Improvement of antimicrobial effectiveness

of penicillin G, ceftriaxone, ciprofloxacin and gentamicin against *S. aureus* resistance when concurrently used with ethanol extract of *S. baicalensis* have been reported by Yang et al. [21]. Another study assessed the antimicrobial activity of 70% ethanol extracts of *Artemisia apiacea* Hance and *S. baicalensis* by broth microdilution, modified-disc diffusion and agar dilution methods. The results of the study indicated that *A. apiacea* and *S. baicalensis* were effective against *Aspergillus niger*, *C. albicans*, *Bacillus subtilis* and *S. aureus* with a range of 0.03125 to 4 mg/ml MIC values. Interestingly, 3:5 ratio mixture of *A. apiacea* and *S. baicalensis* were found to be more effective than *A. apiacea* or *S. baicalensis* used individually [22]. Extraction method can change the chemical composition, so the biological activity of plants. The chemical composition associated with its biological activity of the extract varies with the extraction process and solvent composition. There is a study investigated the antibacterial activity and total phenolic constituents of 46 extracts of dietary spices and medicinal herbs including *S. baicalensis* by using agar-well diffusion method counter to five foodborne bacteria (*B. cereus*, *S. aureus*, *E. coli*, *Listeria monocytogenes* and *Salmonella anatum*). The results indicated a close association between the antimicrobial activity and phenolic components of the tested extracts [23]. The influence of the method of extraction on both phytochemical constitution and antimicrobial activity of *S. baicalensis* root have been evaluated by Lu et al. [24]. The results of the study indicated that different ethanol concentrations (60, 80 and 100%) used for extraction of *S. baicalensis* had an effect on the major flavonoid and phenolic acid contents in the extracts. 80% ethanol extract contained the highest amounts of seven determined bioactive components (baicalein, baicalin, chrysin, wogonoside, wogonin, chlorogenic acid and ferulic acid) showed the lowest MIC values against six foodborne pathogens [24].

On the other hand, there is only one study reported antimicrobial activity of the examined species previously. In that study, the antibacterial activity of methanol extract obtained from aerial parts of *S. salviifolia* along with some species from Lamiaceae family was investigated against *S. aureus*, *E. coli*, *Klebsiella pneumoniae*, *P. aeruginosa* and *S. enteritidis* by using microdilution method in concentrations between 6.25 mg/ml-50 mg/ml. According to the results of that study, among the tested extracts, *S. salviifolia* was found to possess the highest antibacterial activity with 12.5 mg/ml MIC value against *S. aureus*, *S. enteritidis* and *E. coli* and with 25 mg/ml MIC value against *K. pneumoniae* and *P. aeruginosa* [18]. In our study, we have found that *S. salviifolia* exhibited antibacterial activity against *S. aureus, E. faecalis*, *E. coli and*, *P. aeruginosa* with a 1024 µg/ml MIC value.

3. CONCLUSION

Antibacterial and antifungal activities of three *Scutellaria* species growing in Turkey were evaluated by this study for the first time. The results of the study showed that the species had more promising results in terms of antifungal activity than antibacterial activity. The chloroform extract of the roots of *S. salviifolia* was found to possess the highest antifungal activity among the tested extracts. Previous studies on this species have reported the isolation of flavonoids, iridoid glucosides, phenylethanoid glycosides, diterpenoids, triterpenoids, alkaloids and essential oils. The results of this study showed the importance and therapeutic potential of the species. But further detailed studies may be helpful to explore the compound(s) responsible for the activity.

4. MATERIALS AND METHODS

4.1. Chemicals

Dimethyl sulfoxide (DMSO), Fluconazole, Vancomycin, Gentamicin and all solvents using for extraction including Methanol, *n*-Hexane, Chloroform, Ethyl acetate and *n*-Butanol were purchased from Sigma Aldrich (St. Louis, MO, USA). All control antibiotics were prepared with sterile distilled water on the day of study. Tryptic Soy Broth (Oxoid, CM0129), Mueller Hinton Broth (Merck 110293), RPMI 1640 Medium (Gibco Laboratories 11875101) were freshly prepared with distilled water and sterilized.

4.2. Plant Materials

Plant materials were collected in flowering times from different sites of Turkey. *S. salviifolia* was collected from Amasya in June 2004. *S. diffusa* was collected from Karaman in June 2004. *S. pontica* was collected from Rize in August 2003. Voucher specimens have been deposited in the Herbarium of Hacettepe University Faculty of Pharmacy, Ankara, Turkey under related HUEF codes (HUEF 04158, HUEF 04160, HUEF 03040 respectively).

4.3. Extraction

The air-dried and powdered aerial parts (5 g) and roots (2 g) of plants were extracted with 150 ml methanol (MeOH) in water-bath at 50°C for two times. The obtained extracts were filtered, concentrated to dryness using a rotary evaporator and lyophilized in vacuo. The residues were stored at room temperature until use. The methanolic extracts of aerial parts (600 mg) and roots (200 mg) were separately dissolved in 100 ml distilled water and partitioned by successive solvent extraction with *n*-hexane (3x 100 ml), chloroform ($CHCl_3$) (3x 100 ml), ethyl acetate (EtOAc) (3x 100 ml) and *n*-butanol (*n*-BuOH) (3x 100 ml) respectively. All extracts, as well as remaining aqueous phase (H_2O), were concentrated to dryness.

4.4. Antimicrobial screening

4.4.1. Test organisms

Antimicrobial activity of the plant extracts was determined against four bacteria (*Escherichia coli* ATCC 25922, *Enterococcus faecalis* ATCC 29212, *Pseudomonas aeruginosa* ATCC 27853, *Staphylococcus aureus* ATCC 29213) and three yeasts (*Candida albicans* ATCC 90028, *C. krusei* ATCC 6258, *C. parapsilosis* ATCC 90018). All ATCC strains were obtained from the American Type Culture Collection (Rockville, Maryland, USA).

4.4.2. Antimicrobial activity test

Antimicrobial activity of the plant extracts was identified as minimum inhibitory concentration (MIC) values which were determined by broth microdilution method reported by the Clinical and Laboratory Standards Institute (CLSI) [19, 20]. The test was performed in sterile 96-well microplates. The plant extracts were dissolved in dimethyl sulphoxide (DMSO) in order to make 1024 µg/ml stock concentration and transferred into each microplate well in order to obtain two-fold serial dilutions ranging from 1 to 1024 µg/ml. The overnight cultures of each bacterium were suspended in Tryptic Soy Broth. After 4 hours of incubation at 35°C, the inocula were prepared by adjusting the turbidity of the suspension to match the 0.5 McFarland standard. The inoculum (50 µl) containing 106 CFU of each bacterium was added to each well containing 50 µl Mueller Hinton Broth. Overnight cultures of yeasts on Sabouraud Dextrose Agar (SDA) were inoculated on MHB. Standard suspensions of each yeast were added to each well containing 50 µl RPMI medium. A number of wells were reserved in each plate for sterility control (no inocula added), inocula viability (no compounds added) and solvent effect (DMSO). Gentamicin, vancomycin and fluconazole were used as positive controls. Plates were aerobically incubated at 35°C. After incubation for 16-20 h, microbial growth was evaluated by observing the presence of turbidity. MIC was defined as the lowest concentration of the plant extracts that had restricted microbial growth.

Author contributions: Concept – Z.C.A., N.E.; Design – Z.C.A., N.E.; Supervision - Z.C.A., C.Ö.K., G.R., N.E.; Materials – Z.C.A., C.Ö.K., G.R., M.E., N.E.; Data Collection and/or Processing – Z.C.A., C.Ö.K., M.E., N.E.; Analysis and/or Interpretation – Z.C.A., C.Ö.K., G.R.; Literature Search – Z.C.A., G.R.; Writing – Z.C.A., C.Ö.K., G.R.; Critical Reviews – Z.C.A., C.Ö.K., G.R., M.E., N.E.

Conflict of interest statement: The authors declared no conflict of interest.

REFERENCES

[1] Subramani R, Narayanasamy M, Feussner K-D. Plant-derived antimicrobials to fight against multi-drug-resistant human pathogens. 3 Biotech. 2017; 7(3): 172. [CrossRef]

[2] Rios J, Recio M. Medicinal plants and antimicrobial activity. J Ethnopharmacol. 2005; 100(1-2): 80-84. [CrossRef]

[3] Paton A. A global taxonomic investigation of *Scutellaria* (Labiatae). Kew Bull. 1990; 45(3): 399-450. [CrossRef]

[4] Shang X, He X, He X, Li M, Zhang R, Fan P, Zhang Q, Jia Z. The genus *Scutellaria* an ethnopharmacological and phytochemical review. J Ethnopharmacol. 2010; 128(2): 279-313. [CrossRef]

[5] Joshee N, Patrick TS, Mentreddy RS, Yadav AK. Skullcap: Potential medicinal crop. In: Janick J, Whipkey A (Eds). Trends in New Crops and New Uses. ASHS Press, Alexandria, VA, 2002, pp.580-586.

[6] Çiçek M, Yaprak AE. *Scutellaria yildirimlii* (Lamiaceae), a new species from Turkey. Phytotaxa. 2013; 132(1): 53-58. [CrossRef]

[7] Güner A, Aslan S, Ekim T, Vural M, Babaç M, Türkiye Bitkileri Listesi (Damarlı Bitkiler), Flora Dizisi 1., ANG Vakfi, Nezahat Gökyiğit Botanik Bahçesi Yayınları, İstanbul, 2012.

[8] Tuzlacı E, Türkiye Bitkileri Geleneksel İlaç Rehberi, İstanbul Tıp Kitabevi, İstanbul, 2016.

[9] Altundag E, Ozturk M. Ethnomedicinal studies on the plant resources of east Anatolia, Turkey. Procedia Soc Behav Sci. 2011; 19: 756-777. [CrossRef]

[10] Cakilcioglu U, Turkoglu I. An ethnobotanical survey of medicinal plants in Sivrice (Elazığ-Turkey). J Ethnopharmacol. 2010; 132(1): 165-175. [CrossRef]

[11] Mükemre M, Behçet L, Çakılcıoğlu U. Ethnobotanical study on medicinal plants in villages of Çatak (Van-Turkey). J Ethnopharmacol. 2015; 166: 361-374. [CrossRef]

[12] Edmondson JR. *Scutellaria* L. In: Davis PH. (Eds). Flora of Turkey and the East Aegean Islands, Vol. 7, Edinburgh University Press, Edinburgh, 1982, pp. 78.

[13] Ersöz T, Harput ÜŞ, Saracoğlu İ, Çalış İ, Ogihara Y. Phenolic compounds from *Scutellaria pontica.* Turk J Chem. 2002; 26(4): 581-588.

[14] Rodríguez B, de la Torre MC, Jimeno M-L, Bruno M, Vassallo N, Bondì M, Piozzi F, Servettaz O. Neoclerodane diterpenoids from *Scutellaria pontica.* J Nat Prod. 1997; 60(4): 348-355.

[15] Cicek M, Demirci B, Yilmaz G, Baser KHC. Essential oil composition of three species of *Scutellaria* from Turkey. Nat Prod Res. 2011; 25(18): 1720-1726. [CrossRef]

[16] Saracoglu I, Inoue M, Calıs I, Ogihara Y. Studies on constituents with cytotoxic and cytostatic activity of two Turkish medicinal plants *Phlomis armeniaca* and *Scutellaria salviifolia.* Biol Pharm Bull. 1995; 18(10): 1396-1400. [CrossRef]

[17] Şenol FS, Orhan I, Yilmaz G, Cicek M, Şener B. Acetylcholinesterase, butyrylcholinesterase, and tyrosinase inhibition studies and antioxidant activities of 33 *Scutellaria* L. taxa from Turkey. Food Chem Toxicol. 2010; 48(3): 781-788. [CrossRef]

[18] Yavuz C, Dereli Kılıç DD, Ayar A, Yıldırım T. Antibacterial effects of methanol extracts of some plant species belonging to Lamiaceae family. Int J Sec Metabolite. 2017; 4(3): 429-433. [CrossRef]

[19] Clinical and Laboratory Standards Institute, Methods for dilution antimicrobial susceptibility tests for bacteria that grow aerobically, Approved Standard 8th ed., M 07-A8, Clinical and Laboratory Standards Institute, Wayne, PA, 2008.

[20] Clinical and Laboratory Standards Institute, Reference method for broth dilution antifungal susceptibility testing of yeasts: approved Standard 3rd ed., M 27-A3, Clinical and Laboratory Standards Institute, Wayne, PA, 2008.

[21] Yang Z-C, Wang B-C, Yang X-S, Wang Q, Ran L. The synergistic activity of antibiotics combined with eight traditional Chinese medicines against two different strains of *Staphylococcus aureus.* Colloids Surf B Biointerfaces. 2005; 41(2-3): 79-81. [CrossRef]

[22] Trinh H, Yoo Y, Won K-H, Ngo HT, Yang J-E, Cho J-G, Lee S-W, Kim K-Y, Yi T-H. Evaluation of *in-vitro* antimicrobial activity of *Artemisia apiacea* H. and *Scutellaria baicalensis* G. extracts. J Med Microbiol. 2018; 67(4): 489-495. [CrossRef]

[23] Shan B, Cai Y-Z, Brooks JD, Corke H. The *in vitro* antibacterial activity of dietary spice and medicinal herb extracts. Int J Food Microbiol. 2007; 117(1): 112-119. [CrossRef]

[24] Lu Y, Joerger R, Wu C. Study of the chemical composition and antimicrobial activities of ethanolic extracts from roots of *Scutellaria baicalensis* Georgi. J Agric Food Chem. 2011; 59(20): 10934-10942. [CrossRef]