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Comparison of The Antimicrobial Activity of Some *Scutellaria orientalis* L. Taxa Growing in Turkey

Gülderen Yılmaz[1], **Duygu Şimşek**[2], **Nurten Altanlar**[2], **Mehmet Çiçek**[3,*]

[1]Department of Pharmaceutical Botany, Faculty of Pharmacy, Ankara University, Ankara, Turkey
[2]Department of Pharmaceutical Microbiology, Faculty of Pharmacy, Ankara University, Ankara, Turkey
[3]Department of Molecular Biology and Genetics, Faculty of Science and Art, Pamukkale University, Denizli, Turkey

Abstract: *Scutellaria* species are commonly used in the treatment of various diseases in traditional medicine. One of the members of Lamiaceae, the genus *Scutellaria* L. has approximately 471 species on earth. The genus is represented by 39 taxa in Turkey which 17 of them are endemics. In this study, plant samples of 15 *S. orientalis* subspecies from different regions of our country were collected and methanol extracts were prepared from aerial parts. *In vitro* antimicrobial activity of these extracts against three gram positive and three gram negative bacteria and against a yeast using broth microdilution method. Methanol extracts of *S. orientalis* taxa were found to have moderate to low antimicrobial activity compared to the literature.

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1. INTRODUCTION

Due to increasing resistance to antimicrobials and slowdown in the exploration of new ones, combating with infectious diseases is getting harder nowadays. Studies on extracts or compounds from plants remain important to discover new sources as antimicrobial agents. The genus *Scutellaria* L. (Lamiaceae) contains 471 species throughout the world [1]. *Scutellaria* species are generally subcosmopolitan plants and are distributed especially in the central Iran-Turanian region of Asia [2]. In Turkey, the genus includes about 39 taxa and 17 of these are endemics (43.6%) [3-9].

Scutellaria orientalis L. consists 16 subspecies and 2 varieties in Turkey and most of them are endemic [3,7]. The plants have been dispersed among the East-West Anatolia and Iran-Turanian regions of Turkey. Many *Scutellaria* species have been used in traditional medicine for centuries. The genus has numerous biological activities such as anti-convulsant, anti-cancer, anti-diarrheal, anti-feedant, anti-hypertensive, anti-inflammatory, anti-microbial, anti-oxidant, anti-thrombotic, hepatoprotective and sedative activities [10-11]. *Scutellaria* species are known as “kaside, korku otu, sancı otu, şimşek otu” in Turkish. There are various uses in traditional medicine and the most common of them are as sedative in the form of

CONTACT: Mehmet Çiçek ✉ mcicek@pau.edu.tr Department of Molecular Biology and Genetics, Faculty of Science and Art, Pamukkale University, Denizli, Turkey

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hemostatic, wound healing agent and tonic in Turkey [7,12-13]. According to ethnobotanical studies in Anatolian traditional medicine, leaves of some subspecies of *S. orientalis* L. (subsp. *orientalis*, subsp. *sosnowskyi* (Takht.) Fed., subsp. *bicolor* (Hochst.) J.R.Edm., subsp. *pichleri* (Stapf) J.R.Edm. and subsp. *virens* (Boiss. & Kotschy) J.R.Edm.) were also used as wound healer, externally, as carminative, abdominal pain relief and also used for its astringent effects [14-21].

There are many studies on the phytochemical properties of *Scutellaria* species. Phenolic compounds, diterpenoids were isolated by Ersöz et al. and Rodríguez et al. from *S. pontica* K.Koch [16, 19]. Essential oil compositions of *S. albida* L., *S. diffusa* Benth., *S. heterophylla* Montbret & Aucher ex Benth, *S. salviifolia* Benth., *S. brevibracteata* Stapf, *S. galericulata* L. and *S. tortumensis* (Kit Tan & Sorger) A.P.Khokhr. were also investigated [20-23]. Cytotoxic activity of phenylethanoid glycosides isolated from *S. salviifolia* was determined [24]. The acetylcholinesterase, butyrylcholinesterase and tyrosinase inhibitory activities of methanol extracts and the antioxidant activity of methanol and ethyl acetate extracts were investigated by DPPH and FRAP experiments in a study by Şenol et al. [25]. In recent years, İçen et al. investigated the chemical composition of *S. orientalis* subsp. *virens* essential oil [26]; Yavuz et al. examined antibacterial effects of *S. salviifolia* [27]; Zengin et al. (2018) studied antioxidant activity, enzyme inhibitory activity and phenolic components of *S. orientalis* and *S. salviifolia* [28]; Arıtuluk et al. examined antibacterial and antifungal activity of *S. diffusa, S. pontica* K. Koch and *S. salviifolia* [11]; Bardakçı et al. performed flavonoid quantification of *S. albida, S. albida* L. subsp. *velenovskyi* (Rech.f.) Greuter & Burdet, *S. hastifolia* L. and *S. orientalis* from Turkey [29]. In this study, we planned to investigate the antibacterial and antifungal activity of methanol extracts of 15 subspecies of *S. orientalis* using broth microdilution method.

2. MATERIAL and METHODS

2.1. Plant Material

Aerial parts of fifteen subspecies of *S. orientalis* taxa (*S. orientalis* L. subsp. *virens* (Boiss. & Kotschy) J.R.Edm, *S. orientalis* L. subsp. *orientalis*, *S. orientalis* L. subsp. *sosnowskyi* (Takht.) Fed., *S. orientalis* L. subsp. *bicolor* (Hochst.) J.R.Edm., *S. orientalis* L. subsp. *macrostegia* (Hausskn. ex Bornm.) J.R.Edm., *S. orientalis* L. subsp. *cretacea* (Boiss. & Hausskn.) J.R.Edm., *S. orientalis* L. subsp. *pectinata* (Benth.) J.R.Edm., *S. orientalis* L. subsp. *pinnatifida* J.R.Edm., *S. orientalis* L. subsp. *alpina* (Boiss.) O.Schwarz var. *alpina*, *S. orientalis* L. subsp. *porphyrostegia* J.R.Edm., *S. orientalis* L. subsp. *carica* J.R.Edm., *S. orientalis* L. subsp. *santolinoides* (Hausskn. ex Bornm.) J.R.Edm., *S. orientalis* L. subsp. *sintenisii* (Hausskn. ex Bornm.) J.R.Edm., *S. orientalis* L. subsp. *haussknechtii* (Boiss.) J.R.Edm., *S. orientalis* L. subsp. *bornmuelleri* (Hausskn. ex Bornm.) J.R.Edm.) were collected from common territories of diverse localities in Turkey. All taxa were identified according to "*Flora of Turkey and the East Aegean Islands*" [3] by Mehmet Çiçek. The voucher specimen are kept in the Herbarium of Ankara University Faculty of Pharmacy, Ankara, Turkey (AEF). The species names, collection localities, dates and herbarium numbers of 15 taxa are given in Table 1.

2.2. Preparation of Extracts

Aerial parts of *S. orientalis* taxa were dried and then powdered. About 5 g powdered samples were extracted with methanol (2x200 ml) in a rotary shaker for 24 h. Extracts were filtered and further concentrated to dryness under reduced pressure at 37ºC using a rotary evaporator (Büchi, Switzerland). Methanol extracts were obtained and kept in the freezer +4°C until the experimental practices.

2.3. Antimicrobial Activity

2.3.1. Preparation of Bacterial and Fungal Suspensions

Microorganisms used in the experiment were gram negative bacteria (*Klebsiella pneumoniae* ATCC 13883, *Pseudomonas aeruginosa* ATCC 27853, *Escherichia coli* ATCC 25922; gram positive bacteria *Bacillus subtilis* ATCC 6633, *Staphylococcus aureus* ATCC 29213, *Enterococcus faecalis* ATCC 29212 and yeast *Candida albicans* ATCC 10231). Microorganisms were obtained from the culture collection of the Ankara University, Faculty of Pharmacy, Pharmaceutical Microbiology Department.

Antibacterial and antifungal activity tests proceeded similarly with CLSI recommendations by broth microdilution method with some modifications [30,31]. Glycerol stocks kept at -80°C were inoculated to Sabouraud Dextrose Agar (SDA, Oxoid) medium for yeast and Mueller-Hinton Agar (MHA, Merck) medium for bacteria, incubated for 20 h at 35±2°C. Isolated colonies from the second passage of overnight cultures transferred into 0.85% NaCl to obtain turbidity of 0.5 McFarland standards. Sabouraud Dextrose Broth (SDB) medium for yeast and Mueller-Hinton Broth (MHB, Merck) medium for bacteria were used to dilute these suspensions to give a final concentration 2.5×10^3 CFU/ml for yeast and 5×10^5 CFU/ml for bacteria.

2.3.2. Broth Microdilution Method

Firstly, two-fold 8 serial dilutions of *S. orientalis* methanol extracts (1000 to 7.81 µg/ml) were prepared in 96-well microplates using SDB media for yeast and MHB media for bacteria in 100 µl volume. After serial dilution, 100 µl concentration-adjusted microorganism suspensions were transferred to each well and microplates were left for incubation (24 h for yeast and 20 h for bacteria) at 35±2°C. Sterility and growth control wells were included. Ciprofloxacin and miconazole were used as positive controls. The well of lowest concentration with no growth was recorded as MIC (µg/ml) value, at the end of incubation time. All experiments conducted in two parallels.

3. RESULTS and DISCUSSION

3.1. Antimicrobial Activity Results

In this study, *in vitro* antibacterial and anti yeast activity of methanol extracts of fifteen *S. orientalis* taxa was evaluated using broth microdilution assay against the above mentioned panel of human pathogenic strains of three gram positive bacteria, three gram negative bacteria and a yeast. The results are given in Table 2 as Minimum Inhibitory Concentrations (MIC).

To the best of our knowledge and according to the literature survey, there is no report on comparative antimicrobial activity of *S. orientalis* subspecies growing naturally in Turkey. This study is the first to demonstrate that 15 subspecies of *S. orientalis* possessed *in vitro* antibacterial activity.

According to the results of our study, antibacterial activity values of all methanol extract of *S. orientalis* taxa were found to be between 250-62.5 µg/ml. Antimicrobial activity scale of MIC values 500 to 100 µg/ml were evaluated as moderate, and MIC values less than 100 µg/ml were considered to be good according to the concentration ranges stated by Morales et al. (2008) [32]. As seen in Table 2, it was found that methanolic extracts obtained from the aerial parts of *S. orientalis* taxa have moderate to good antimicrobial activity. All of the species (except *S. orientalis* subsp. *virens* (125 µg/ml MIC value) showed stronger activity (62.5 µg/ml MIC value) against Gram negative *P. aeruginosa* ATCC 27853. Other gram negative bacteria, *K. pneumoniae* ATCC 13883 and *E. coli* ATCC 25922 were affected more than gram positive bacteria. Least affected bacteria were *S. aureus* ATCC 29213 and *E. faecalis* ATCC 29212.

Among the extracts, *S. orientalis* subsp. *orientalis*, *S. orientalis* subsp. *santolinoides* and *S. orientalis* subsp. *haussknechtii* were the most effective ones.

Table 1. The localities of studied the subspecies of *S. orientalis*

Scutellaria ssp.	Locality	Altitude	Collection Date
S. orientalis subsp. *alpina* var. *alpina*	Isparta: Yalvaç, between Akşehir and Isparta	1470 m	19.05.2005
S. orientalis subsp. *bicolor*	Elazığ: Maden to Elazığ	986 m	20.05.2006
S. orientalis subsp. *bornmuelleri*	Van: Hakkari to Van	1383 m	13.06.2006
S. orientalis subsp. *carica*	Aydın: Aydın to Karacasu	321 m	02.05.2006
S. orientalis subsp. *cretacea*	Malatya: Kayseri between Malatya	895 m	28.05.2005
S. orientalis subsp. *haussknechtii*	Mardin: south of Mardin, near Deyrulzafaran Monastery	927 m	30.05.2005
S. orientalis subsp. *macrostegia*	Malatya: 34 km from Kemaliye to Arapgir	1200 m	22.05.2007
S. orientalis subsp. *orientalis*	Erzincan: 45 km from Tercan to Erzincan	1291 m	28.06.2006
S. orientalis subsp. *pectinata*	Malatya: 2 km northwest of Darende	1214 m	28.05.2005
S. orientalis subsp. *pinnatifida*	Ankara: Gölbaşı, Beynam forest	1515 m	11.06.2006
S. orientalis subsp. *porphyrostegia*	Siirt: near Botan Çayı	530 m	19.05.2006
S. orientalis subsp. *santolinoides*	Erzincan: İliç, near Boyalık village	1160 m	23.05.2007
S. orientalis subsp. *sintenisii*	Sivas: Divriği to Gedikbaşı	1177 m	25.06.2006
S. orientalis subsp. *sosnowskyi*	Van: Güzelsu between Başkale, Güzeldere	2757 m	13.06.2006
S. orientalis subsp. *virens*	Van: 66 km from Tatvan to Van, Kuskunkıran pass	2245 m	22.06.2007

Also, all of the extracts showed good activity with a value of 62.5 µg/ml against *C. albicans* ATCC 10231, except for *S. orientalis* subsp. *virens, S. orientalis* subsp. *santolinoides* and *S. orientalis* subsp. *bornmuelleri* since their activities were moderate with a value of 125 µg/ml. According to these results, all methanol extracts of *S. orientalis* taxa showed higher antimicrobial activity against yeasts than bacteria.

Dereboylu et al. (2012) investigated antimicrobial activity of *Scutellaria cypria* var. *cypria, S. cypria* var. *elatior* and *S. sibthorpii* essential oils against *B. subtilis* ATCC 6633, *S. aureus* ATCC6538-P, *E. faecalis* ATCC 29212, *Salmonella typhimurium* CCM 5445, *K. pneumoniae* CCM 2318, *E. coli* ATCC 12228, *P. aeruginosa* ATCC 27853 and *C. albicans* ATCC 10239. They reported the antibacterial activity in the range of ≥20-10 mg/ml and antifungal activity ≥20 mg/ml. [33].

In a study conducted in 2017, antimicrobial activity of *S. salviifolia* methanol extract was tested with the disc diffusion and microdilution methods. MIC results of methanol extract varied between 12,5-25 mg/ml against *E. coli, K. pneumoniae, S. enteritidis P. aeruginosa, S. aureus* [27].

Table 2. Minimum inhibitory concentration results of methanol extracts of samples (in µg/ml)

Methanol extracts	Microorganisms						
	S. aureus ATCC 29213	*E. faecalis* ATCC 29212	*B. subtilis* ATCC 6633	*E. coli* ATCC 25922	*P. aeruginosa* ATCC 27853	*K.pneumoniae* ATCC 13883	*C. albicans* ATCC 10231
S. orientalis subsp. *virens*	250	250	250	250	125	125	125
S. orientalis subsp. *orientalis*	125	250	125	125	62,5	125	62,5
S. orientalis subsp. *sosnowskyi*	250	250	250	250	62,5	125	62,5
S. orientalis subsp. *bicolor*	250	250	250	125	62,5	125	62,5
S. orientalis subsp. *macrostegia*	250	250	125	125	62,5	125	62,5
S. orientalis subsp. *cretacea*	250	250	250	125	62,5	125	62,5
S. orientalis subsp. *pectinata*	250	250	125	125	62,5	125	62,5
S. orientalis subsp. *pinnatifida*	250	250	125	250	62,5	125	62,5
S. orientalis subsp. *alpina* var. *alpina*	250	250	250	125	62,5	125	62,5
S. orientalis subsp. *porphyrostegia*	250	125	250	250	62,5	125	62,5
S. orientalis subsp. *carica*	250	250	125	125	62,5	125	62,5
S. orientalis subsp. *santolinoides*	250	125	125	125	62,5	125	125
S. orientalis subsp. *sintenisii*	250	125	125	250	62,5	125	62.5
S. orientalis subsp. *haussknechtii*	125	250	125	125	62,5	125	62,5
S. orientalis subsp. *bornmuelleri*	250	250	250	250	62,5	125	125
Ciprofloxacin	0,312	0,156	0,078	0,0097	0,625	0,039	-
Miconazole	-	-	-	-	-	-	1,56

Arıtuluk et al. (2019) found that aqueous, methanol and n-butanol extracts from roots and methanol and n-butanol extracts from aerial parts of *S. salviifolia, S. diffusa* and *S. pontica* and n-hexane extracts from root parts of *S. diffusa* showed low or no antibacterial activity (≥1024 µg/ml). Aqueous extracts from the aerial parts showed moderate activity with the values of 1024-512 µg/ml; chloroform, ethylacetate and n-hexane extracts of roots and aerial parts showed low to moderate or no activity with the values of ≥1024-256 µg/ml, ≥1024-256 µg/ml, ≥1024-256 µg/ml, respectively. Their anti yeast fungal activity results ranged between ≥1024-32 µg/ml. Chloroform extracts from roots and *n-hexane* extracts from aerial parts of *S. salviifolia* and chloroform and aqueous extracts from the aerial parts of *S. pontica* had good antifungal activity against some *Candida* spp. with values between 64-32 µg/ml. And totally they found higher antifungal activity than antibacterial, in accordance with our results [11].

4. CONCLUSION

This study is the first report on comparative antimicrobial activity of *S. orientalis* taxa from Turkey with methanol extracts by microdilution method to the best of our knowledge. It was determined that the methanol extracts of these 15 taxa had similar levels of activity with slightly different values, which ranged between 250-62.5 µg/ml against all microorganisms. In the future, we plan to investigate antibacterial and anti yeast tests of different *Scutellaria* species and compare their results.

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Declaration of Conflicting Interests and Ethics

The authors declare no conflict of interest. This research study complies with research publishing ethics. The scientific and legal responsibility for manuscripts published in IJSM belongs to the author(s).

Orcid

Gülderen Yılmaz https://orcid.org/0000-0002-6569-4766
Duygu Şimşek https://orcid.org/0000-0003-1027-4139
Nurten Altanlar https://orcid.org/0000-0003-2977-2269
Mehmet Çiçek https://orcid.org/0000-0003-4058-3717

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