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An Important Euroasian Genus: *Scutellaria* L.

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Abstract: *Scutellaria* is found on every continent except for Antarctica. Especially it is found in Eurasia which has rich areas with the most species. The objective of this study is to focus on the importance of this genus. *Scutellaria* species need to be set a value upon and evaluated. Because the genus *Scutellaria* is rich in flavonoids and diterpenoids and has a wide range of pharmacological effects such as antitumor, anti-angiogenesis, hepatoprotective, antioxidant, anticonvulsant, antibacterial, antiviral activities and cancer cell inhibition. Furthermore *Scutellaria* species have very beautiful blooms. Some countries such as the US and China achieved cultivation of this genus and they grow some species of *Scutellaria* as a crop production and ornamentals. But in Turkey, cultivation for crop production hasn't been worked on yet. *Scutellaria* species can be cultivated so as to gain economic and ecological benefits. Even though the wild populations of *Scutellaria* is widely distributed in the world, some of these species are becoming rare or threatened with population pressure, environmental pollution, and destruction of their natural habitat. Conservation by cultivation is an effective means for protecting genetic resources.

***Key words*:** Lamiaceae, *Scutellaria*, conservation, Turkey

1. INTRODUCTION

Scutellaria L. (skullcap) is a cosmopolitan genus of Lamiaceae with approximately 350 species [1-2]. This species is found mainly in temperate regions and tropical mountains. *Scutellaria* is found on every continent except for Antarctica. Especially it is found in Eurasia which has rich areas with the most species. *Scutellaria* is represented by 34 taxa of which 15 species are endemic to Turkey in the flora of Turkey [3].

"Skullcap" describes the shape of the calyx at the base of the flower. This structure called scutellum is formed from a fold in the upper calyx lip that stands erect and enlarges during fruiting [1].

Scutellaria have been used in herb spices, fragrances, traditional and folk medicines in different parts of the world for centuries. They are well known among people as powerful medicinal herbs which are mild relaxants that affect the neural and muscular-skeletal systems [4-11]. Nowadays, many of *Scutelaria* species have been studied in the fields of health,chemistry and phytochemistry, and their therapeutic activities have been tested, such as

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spasmolytic, antidiarrhea, antifungal, antipyretic, antioxidant, anticancer, anti-HIV, antibacterial, antiviral, anti-inflammatory, anticonvulsant [12-14].

Our goal in this study is to emphasize the importance of the genus *Scutellaria*.

1.1. Diversity

Scutellaria spreads out almost all over the world, except for the Amazon basin, the lower parts of tropical Africa, South Africa, Pacific Islands, northern parts of Central Asia and the deserts of the North Pole (Figure 1). The genus has maximum diversity at the Irano-Turanian region, particularly Central Asia and Afghanistan. Eastern Mediterranean and the Andes are the second center of its speciation [1]. *Scutellaria* is well adapted to Eurasian climate. There are about 300 species of the genus in Asia [15-23].The comparison of genus *Scutellaria* with the number of taxa in Turkey and surrounding flora, the number of endemic taxa and the rate of endemism are given at Table 1. It is seen obviously, the rate of endemism in countries close to the gene center is higher than the other countries.

In Turkey, *Scutellaria* species diversity is very high and the members of the genus are distributed all over the country. Within Flora of Turkey the genus is represented by 24 species, 1 hybrid species and 13 subspecies, totally 34 taxa. 15 species of them are endemic [3]. But for some species, there exists a very high risk of extinction due to small or fragmented populations (Table 2).

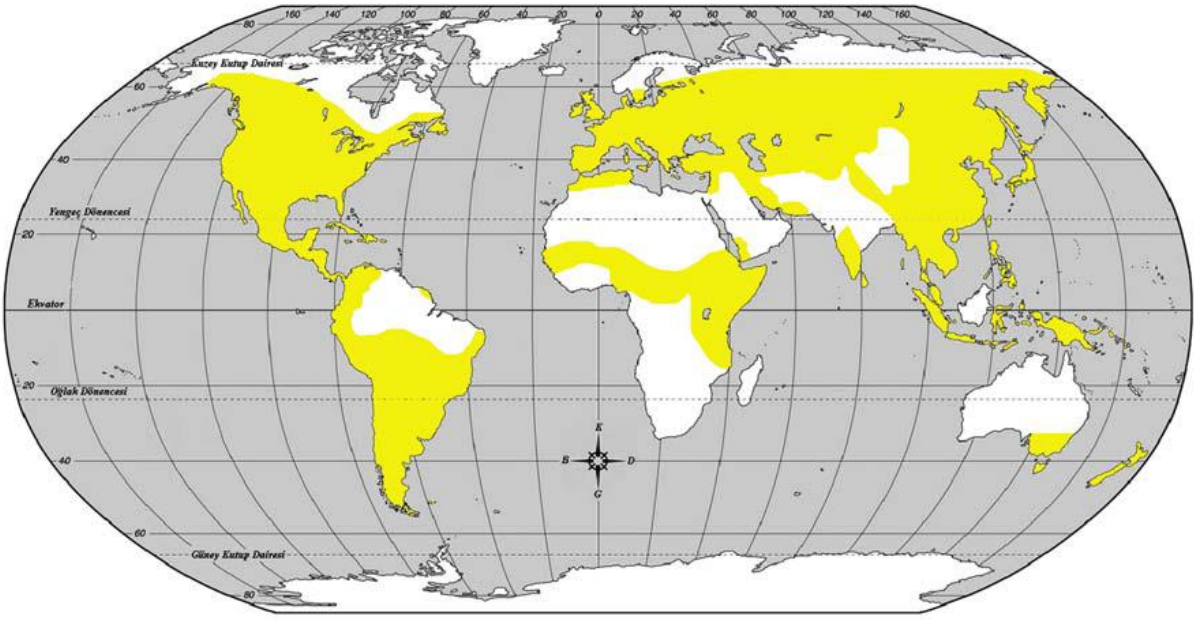

Figure1. The yellow area shows the world distribution map of *Scutellaria* species [24].

Table 1. The comparison of genus *Scutellaria* with the number of taxa in Turkey and surrounding flora, the number of endemic taxa and the rate of endemism

Countries or Regions	The number of taxa	The number of endemic taxa	The rate of endemism (%)
Flora of Turkey [3]	34	15	44
Flora of the Soviet Union [25]	148	109	74
Flora of Syria, Palestine, the Sinai Desert [26]	12	1	8
Flora of Palestine [27]	3	0	0
Flora of Iranica area [18]	54	39	72
Flora of Europe [28]	19	12	63
Flora of Cyprus [29]	3	3	100

2. ECOLOGY AND MORPHOLOGY

Scutellaria has a wide wild population and is found in very different environmental types, from xerophytic areas to flooded areas [1]. Even though *Scutellaria* can grow in very different environments on variety of continents, it is often found in disturbed areas [31-32]. Turkish species live on volcanic or calcareous rocky and stony hillside, step, hardpan and marl, alpine pasture, lake, river and water carrier bank, woodlands (from sea level to 3500 m) (Table 2). American species live in xerophytic environments [24] or low woodlands and along roadsides in moist habitats [31]. Species native to Northern China often appears in grassland, sunny grassy slopes and shrubbery or forest habitats (from 12 to 2000 m) with a cold-dry climate [33]. In New Zealand and Australia *Scutellaria* is found in frequently flooded and somewhat disturbed areas [24, 34].

Scutellaria is a perennial plant often sufirutescent at base, ± lacking aromatic odour. Its stem base prostrates on the ground or grows upward, height 30 to 120 cm. The taproot is stout and slightly conical. The stems shape is four prism and branches grow out at base. Inflorescence a raceme or a spike; flowers arising singly in axils of bracts or floral leaves, on very short pedicels, *Scutellaria* species are typically characterized by the shape of calyx with two undivided lips and the presence of a scutellum on the upper lip. Its blue-purple or white flowers bloom from June to September. Its opposite leaves, heart-shaped at the base, 1 to 6 cm long with scalloped or toothed margins. The flowers are tube shaped, hooded, with two lips, the upper lip being the hood and the lower lip having two shallow lobes. Stamens 4, anthers included under hood, ciliate, lower pair longer, monothecous, upper pair with 2 divergent thecae. Style unequally bifid. Nutlets depressed-globose to broadly ellipsoid, often tuberculate, pubescent with stellate hairs.

Table 2. Inflorescence, habitat features, threat categories, Turkey and World Distribution of Turkish *Scutellaria* species

	Taxa	Inflorescence	Habitat and Height	Threat Categorie*	Spread in Turkey	World Distribution	Phytogeographic Region
SECT. *SCUTELLARIA*	*S. galericulata* L.	June-September	lakes, rivers and waterways edges,sea-level -2500 m	LC	northern, western and eastern Anatolia	Temperate northern hemisphere;	Cosmopolitan
	S. hastifolia L.	May-June	Lake, river and stream edges 80-800 m	VU	Northwest (Ankara, Bursa, Sakarya) and W. Anatolia (İzmir)	from Europe to the Caucasus	Euro-Siberian
	S. altissima L.	June-August	*Carpinus* forest, 75-1800 m	VU	North and northeast Anatolia (İstanbul, Kars, Kastamonu Zonguldak)	from Middle East Europe to the Caucasus	Euro-Siberian
	S. porphyrantha Rech.f.	June-August	volcanic rock slopes, rocky slopes, *Quercus forest* 1800-2059 m	EN	Eastern Anatolia (Hakkari, Şırnak)	Turkey, Northern Iraq	Iran-Turan
	S. albida L. subsp. *albida*	May-July	*Quercus*, *PinusForest*, stony slopes, scrub, 50-1500 m	LC	Northwest and Western Anatolia	from southeast Europe to Transcaucasia	East Mediterranean
	S. albida subsp. *velenovskyi* (Rech.f.) Greuter & Burdet	May-July	Limestone cliffs, streams and rivers edge, the subalpine regions 200-1950 m	LC	Northwest and Western Anatolia	Bulgaria, Greece, Romania, Yugoslavia, East Aegean Islands, Turkey	East Mediterranean
	S. albida subsp. *colchica* (Rech.f.) J.R.Edm	June-August	Rocky, rocky slopes and shrubs, 445-1800 m	NT	Northeast Anatolia	From the Crimea, the northeast of Turkey to Transcaucasia	Euro-Siberian (Auxin element)
	S. albida subsp. *condensata* (Rech.f.) J.R.Edm	June-August	calcareous rocks, bushes and rocky slopes, granite cliffs, 445-1800 m	NT	Northeast Anatolia	Crimea, Turkey, Transcaucasia	Euro-Siberian (Auxin element)
	S. brevibracteata Stapf. subsp. *brevibracteata*	May-August	scrub, limestone cliffs and rocky slopes, sea level - 1830 m	LC	Southwestern Anatolia	Turkey (endemic)	Mediterranean
	S. brevibracteata subsp. *subvelutina* (Rech.f.) Greuter & Burdet	May-June	limestone cliffs and rocky slopes and shades, 400-1660 m	LC	Southern Anatolia, Central Anatolia, the North Anatolian	Turkey, Lebanon, Syria, Palestine, Saudi Arabia	East Mediterranean

	S. brevibracteata subsp. *pannosula* (Rech.f.) Greuter & Burdet	July-August	rocky limestone slopes 1113- 1123 m	CR	Southern Anatolia (Mersin)	Turkey (endemic)	Mediterranean
	S. glaphyrostachys Rech.f.	June-August	limestone cliffs and rocky slope, scrub, 305-2135 m	NT	South and southwest Anatolia	Turkey (endemic)	East Mediterranean
SECT. *SALVIIFOLIAE*	*S. salviifolia* Benth.	April-August	stony and rocky slopes, steppe, scrub, 400-2200 m	LC	North, South, Central and Western Anatolia	Turkey (endemic)	not clear
	S. diffusa Benth.	July-August	Subalpine regions 700-2200 m	NT	Southern Anatolia	Turkey (endemic)	East Mediterranean
	S. pontica K.Koch.	July-August	alpine and sub-alpine meadows, steppe and shrubs, granite and stony-rocky volcanic slopes, 1600-3100 m	LC	Northeast Anatolia; Artvin, Bayburt, Rize, Trabzon	Turkey, Transcaucasia	Euro-Siberian (Auxin element)
	S. heterophylla Montbret et Aucher ex Benth.	May-June	stony slopes, scrub, clay hills 150-800 m	NT	Southern Anatolia (Adıyaman, Kilis, Gaziantep, Hatay, Mersin, Osmaniye)	Turkey, Syria, Lebanon	East Mediterranean
SECT. *LUPULINARIA*	*S. virens* Boiss. & Kotschy	June-September	Limestone rocky slopes 1690-3000 m	LC	Eastern Anatolia (Van, Bitlis, Muş)	Turkey, the Caucasus	Iran-Turan
	S. orientalis L.	May-June	volcanic rock slopes, clay slopes, granite and metamorphic hills 300-1750 m	LC	Northeast Anatolia	Crimea, Central Russia, Turkey, Transcaucasia	not clear
	S. sosnowskyi Takht. subsp. *sosnowskyi*	May-July	rocky, stony and clay slopes, dry steppes, volcanic rock slopes 1520-2700 m	LC	Eastern Anatolia	From Turkey's eastern to Transcaucasia	Iran-Turan
	S. bicolor Hochst., J.A.Lorent	May-July	limestone cliffs and rocky slopes 530-2000 m	LC	Eastern Anatolia	Turkey (endemic)	Iran-Turan
	S. macrostegia Hausskn. ex Bornm.	May-June	rocky slopes, rocky cliffs and eroded slopes 930-1650 m	LC	Eastern Anatolia, western Anatolia	Turkey (endemic)	Iran-Turan
	S. pectinata subsp.	May-September	arid steep slopes, calcareous soils,	LC	Central, Northeast and East Anatolia (Ankara,	Turkey, Iraq, Syria (Sinai Desert)	Iran-Turan

	pectinata Montbret & Aucher ex Benth.		limestone slopes 870-2160 m		Erzincan Sivas and Trabzon)		
	S. sosnowskyi subsp. *pinnatifida* M.Cicek et O.Ketenoglu	April-August	limestone cliffs and rocky slopes, gypsum, clay and lime lands 300-2700 m	LC	West, South, Southwest, North, Northwest and Central Anatolia	from Southeast Europe to Turkey	not clear
	S. pichleri (Stapf) Rech.f.	May-August	dry rocky hills and slopes, steppe, metamorphic areas 1690-2590 m	VU	Eastern Anatolia (Erzurum/Bayburt, Hakkari, Van)	Turkey, Iraq and Iran	Iran-Turan
	S. sintenisii Hausskn. ex Bornm.	May-July	rocky limestone slopes, calcareous soils 880-1700 m	LC	West Central Anatolia and Eastern Anatolia (Ankara, Elazığ, Erzincan)	Turkey (endemic)	Iran-Turan
	S. haussknechtii Boiss.	May-July	rocky limestone slopes 680-1150 m	VU	Southeast Anatolia (Batman, Mardin)	Turkey (endemic)	Iran-Turan
	S. bornmuelleri Hausskn. ex Bornm. subsp. *bornmuelleri*	June- July	dry stony and rocky limestone slopes,	LC	Southeast Anatolia (Hakkari, Van)	Turkey, Iraq	Iran-Turan
	S. tomentosa Bertol.	May-July	lime-stony soils and slopes, stony dry areas 380-1200 m	LC	Southeast Anatolia	Turkey, the Sinai desert of Syria, Palestine, Iraq and Iran	Iran-Turan
	S. tortumensis (Kit Tan & Sorger) A.P.Khokhr.	June-July	eroded cliffs and rocky slopes 1200-1330 m	NT	Northeast Anatolia (Erzurum)	Turkey (endemic)	Iran-Turan
	S. anatolica M.Cicek & O.Ketenoglu	June	volcanic rocky-stony slopes 1540-1610 m	CR	South Anatolia (Adana, Niğde)	Turkey (endemic)	Iran-Turan

*Critically endangered (CR), Endangered (EN), Vulnerable (VU), Nearly Threatened (NT), Least Concern (LC) [30].

3. USES IN ALTERNATIVE MEDICINE

Some species of *Scutellaria* used in alternative medicine for at least a few hundred years [10]. The dry root of *Scutellaria* is one of the most popular and multi-purpose herb used in China and in several oriental countries. Some *Scutellaria* species used in the traditional Chinese medicines are *Scutellaria baicalensis* Georgi, *Scutellaria viscidula* Bge, *Scutellaria amoena* C.H., *Scutellaria rehderiana* Diels, *Scutellaria ikonnikovi* Juz., *Scutellaria likiangensis* Diels, and *Scutellaria hypericifolia* Levl [35]. It has been widely used in the treatment of hepatitis, jaundice, tumour, leukaemia, arteriosclerosis, diarrhea, and inflammatory diseases [36].

Scutellaria is not widely used in Turkey; however it has been used as styptic, wound for healing and strengthening in Anatolian folk medicine [37].

4. BIOACTIVE COMPOUNDS

Phytochemicals of *Scutellaria* are flavones, flavonoids, chrysin, iridoids, neo-clerodanes, scutapins, and isoscutellarein. Flavonoids work as antitumor. *Scutellaria baicalensis* has high flavonoids includings: Wogonin (5,7-dihydroxy-8-methoxyflavone), Wogonoside (Wogonin-7-glucuronic acid), Baicalin (7-glucuronic acid, 5,6-dihydroxy-flavone), and Baicalein (5,6,7-trihydroxyfavone) [38-40].

Shin and Lee (1995) produced successfully baicalin in callus cultures of *S. baicalensis* using the hairy root culture system [41]. Thus it is suggested that hairy root cultures could possibly be used in herbal medicine as a substitute for *Scutellaria* radix [42, 43].

Hirotani (1999) isolated 16 flavones and five phenylethanoids from *S. baicalensis* [43]. Saraçoğlu et al. (1995) isolated 10 glycoside compounds from *Scutellaria salviifolia* Benth. and determined that some phenylpropanoid glycoside exhibit antitumor activities [44]. Gousiadou et al. (2013) isolated irioid glycoside from *Scutellaria albida* L. subsp. *albida*. It shows antioksidant properties [45].

Iridoidglucosides were isolated from *S. albida* subsp. *colchica*, phenylethanoidglycosides were isolated from *Scutellaria albida* subsp. *colchica* (Rech. f.) J.R.Edm, *S. orientalis* L. subsp. *pinnatifida* and *S. salviifolia* Benth. several neo-clerodane diterpenoids with insect antifeedant activity have been reported from *S. galericulata* L. [46-48].

5. MEDICAL STUDIES

The components of *Scutellaria* have a wide range of pharmacological actions, such as antitumor, anti-angiogenesis, hepatoprotective, antioxidant, anticonvulsant, antibacterial and antiviral activities [14].

The flavones isolated from the roots of *Scutellaria* were showed to exert antioxidant [49], anti-viral [50-54], anti-thrombotic [55-56], anti-inflammatory [57] and anti-cardiovascular illness [58]. The bioactive phytochemical flavones of *Scutellaria* have anti-inflammatory effect. This activity of the *Scutellaria* flavones are at least in part due to their ability to suppress expression of monocyte chemotactic protein-1, a crucial factor for early inflammatory responses, and to down-regulate several inflammation-associated genes such as inducible nitric oxide synthase, cyclooxygenases, and lipoxygenases and, consequently, inhibit production of nitric oxide (NO) and prostaglandin [59-65]. It has also been recognized as a muscle relaxant.

Besides the anti-inflammatory activities, the flavones obtained from *Scutellaria* have been also shown cytostatic and cytotoxic activities against many human cancer cells. Importantly, they have no (or very little) toxicity against normal epithelial and normal peripheral blood and myeloid cells. Xiao-Chai-Hu-Tang showed that *S. baicalensis* alone could inhibit proliferation of several human myeloma cell lines in vitro [66] and stopped tumour

growth in vivo in bladder, head/neck squamous and sarcoma mouse tumour models [67-69]. In contrast, *S. baicalensis* has not growth inhibitory effects on non-tumorigenic oral squamous cells [68]. Because of this point *S. baicalensis* is a very attractive as a new anticancer drug.

6. CULTIVATION

Not only *Scutellaria* species grow in the wild, but also some *Scutellaria* species like *S. baicalensis*, *S. agrestis* A. St.-Hil. ex Benth, *S. incana*, *S. lateriflora*, and *S. floridana* were cultivated in China, US and Central Europe [70-71]. In Turkey any systematic cultivation methods for crop production have not been worked out yet.

7. CONCLUSION

Because of having a wide range of pharmacological actions, numerous members of *Scutellaria* genus are very important as medicinal plants. Especially having cytostatic and cytotoxic activities against many human cancer cells are very noteworthy.

In recent years, *Scutellaria* based herbal formulations have been employed to establish its medical/scientific value using in vitro cell culture systems. *Scutellaria baicalensis* and *S. lateriflora* are the two species which have been used in most of the herbal formulations. They are currently available in the market in some countries like US, China, etc. Our current research here focuses on *Scutellaria* species found in and around Turkey. Few studies have been carried out on Turkish *Scutellaria* species and further work is needed on these species. Despite the fact that there are the numbers of *Scutellaria* taxa in Turkey, very few studies on their phytochemicals were conducted. If the work to be done on this matter is increased, maybe there will be a chance to find new bioactive compounds and more *Scutellaria* species can be used as drugs containing.

Some of these species are becoming rare or threatened because of population pressure, environmental pollution, and destruction of their natural habitat. But, there is not any regulation for the protection of the endangered *Scutellaria* species. It is very important that it must be taken preventive measures to conserve this species. It is also necessary that we should initiate preservation of endangered seeds of these taxa in gene banks.

Conservation by cultivation is an effective means for protecting genetic resources. We suggest that these species should be cultivated thus gaining economic and ecological benefits. Actually some countries such as the US and China achieved cultivation of this genus and they grow some species of *Scutellaria* as a crop production.

Scutellaria is not only medicinal plant but also it has brilliant beautiful blooms. For this reason there is a great potential for these species as ornamentals.

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