

Skullcap: Potential Medicinal Crop

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INTRODUCTION

Scutellaria species, Lamiaceae, popularly known as skullcaps have been extensively used in traditional medical systems of China, India, Korea, Japan, European countries, and North America. The most extensively used and documented species is baical skullcap (*Scutellaria baicalensis*) although other species such as *S. amoena*, *S. hypericifolia*, *S. tenax*, *S. rehderiana*, and *S. viscidula* have been substituted (Song 1981). Baicalin, baicalein, and wogonin are major ingredients and have been studied in *S. rivularis* (Chou 1978; Tomimori et al. 1984, 1986a, 1990), *S. discolor* (Tomimori et al. 1985, 1986b), *S. indica* (Chou and Lee 1986; Miyaichi et al. 1987, 1989), and *S. scadens* (Miyaichi et al. 1988a,b).

The English name “skullcap” describes the shape of the calyx at the base of the flowers, which resemble miniature medieval helmets. During the 19th century, the common name used in America was “mad dog.” Other popular names include scullcap, hoodwort, quaker bonnet, helmet flower, European skullcap, greater skullcap, American skullcap, blue skullcap, blue pimpernel, hoodwart, hooded willow herb, side-flowering skullcap, mad dog weed, and mad weed.

Scutellaria is a large genus, about 300 species, growing from Siberia to Sri Lanka. It is well adapted to the North American climate where it has over 90 species. Plants are herbaceous, slender, rarely shrubby, scattered over temperate regions and tropical mountains around the globe. They flourish under full sunlight, limited feeding, and well-drained soil.

BOTANY

The skullcap (scullcap) is a North American perennial. It grows in wet places in Canada and the northern and the eastern United States. Its generic name is derived from the Latin scutella (little dish), from the lid of the calyx. The fibrous, yellow root system supports a branching stem 30 to 90 cm tall, with opposite, ovate, and serrate leaves. The root is a short creeper which supports hairy, square, and branched stems from 15 to 45 cm tall, or in small plants, nearly simple, with opposite leaves, heart-shaped at the base, 1 to 6 cm long with scalloped or toothed margins. The blue to lavender flowers are in racemes and grow from the leaf axils. The flowers are tube shaped, hooded, with two lips, the upper lip being the hood and the lower lip having two shallow lobes. Flowering generally occurs from May to August. Above ground plant parts are collected during summer around bloom time, dried in shade and stored for later use as medicinal herb. Skullcaps are now becoming popular in southern gardens owing to their drought tolerance as well as bright and showy blooms (Fig. 1) (E. McDowell, pers. commun.).

FOLKLORE AND USES IN ALTERNATIVE MEDICINE

Skullcap is a powerful medicinal herb and it is used in alternative medicine as an anti-inflammatory, abortifacient, antispasmodic, slightly astringent, emmenagogue, febrifuge, nervine, sedative, and a strong tonic. Skullcap is

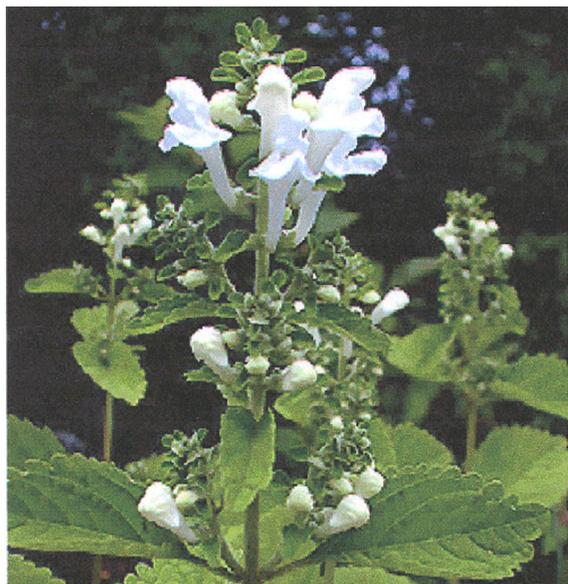


Fig. 1. *Scutellaria ocmulgee*.

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also utilized in treating a wide range of nervous conditions including epilepsy, insomnia, hysteria, anxiety, delirium tremens, and withdrawal from barbiturates and tranquilizers. A medicinal infusion of this plant is used to promote menstruation. It should not be given to a pregnant woman since it can induce miscarriage. *Scutellaria* infusion is also used for treating neuralgia, headaches in general as well as those arising from incessant coughing, without any unpleasant side effects. Normally, it should be used with extra caution since an overdose of this medicinal herb can cause giddiness, stupor, confusion, and twitching.

Skullcap is well known among the Cherokee and other Native American tribes, as a strong emmenagogue and medicinal herb for females. It is used in some tribes as a ceremonial plant to induct young girls into womanhood. Native Americans used skullcap to promote menstruation, and it was reputed to be effective against rabies, hence some of its common names. Cherokee women use skullcap to maintain healthy menstrual cycles, and a root decoction is taken after the birth of a child to stimulate the reproductive system. Skullcap is also used in purification ceremonies if menstrual taboos are broken. The Iroquois use an infusion of the root to keep the throat clear. Other Native American tribes use closely related species as bitter tonics for the kidneys. The herb is used to induce visions and as a ceremonial plant to be smoked as tobacco by some Native Indians.

Wogon Scutellariae Radix, a well known ancient drug in the traditional Chinese medicine, is prepared from *S. baicalensis* roots (dry and without exodermis), which is conventionally collected in spring and fall (Tang and Eisenbrand 1992). It is officially listed in the Japanese Pharmacopeia JPXIII and Chinese Pharmacopeia. It is one of the most widely used crude drugs for the treatment of bronchitis, hepatitis, diarrhea, and tumors. Chinese physicians use the root of *S. baicalensis* or "huang qin," as an antibacterial, diuretic, antispasmodic, and promoter of bile flow. In Nepal, *S. discolor* leaves are used as a folk remedy for common cold, cuts, and insect stings (Sinha et al. 1999).

Scutellaria is a traditional treatment for epilepsy in European countries. Homeopaths have reported some success in the use of this plant to treat chronic fatigue syndrome. It is helpful for skin and urinary tract infections and is also used where hypertension is related to over-heated conditions. Note that serious health problems could arise from incomplete and/or misleading information on the use of traditional medicines. For example, misidentification of a Chinese herb resulted in the loss of renal function in more than 100 patients (Betz 1998). Potential problems with herbal preparations are: (a) contamination with bacteria, fungi, insects, and pollutants, (b) seasonal variation in bioactive compounds, (c) degradation of active ingredients in processing and storage of plant materials, and (d) a lack of understanding of the unique physiology of medicinal plants (Li et al. 2000).

BIOACTIVE COMPOUNDS

Hattori (1930) was first to isolate wogonin from *S. baicalensis* roots and determined its chemical structure (Fig. 2). Wogonin is present only in small amounts in roots while baicalin, a flavone glycoside, pervades the entire plant (Shibata et al. 1923). Upon acid hydrolysis, baicalin from roots yields glucuronic acid plus baicalein (Fig. 2), a flavone aglycone. There are over 50 flavones isolated from *S. baicalensis* (Tang and Eisenbrand 1992; Miyaichi and Tomimori 1994, 1995; Zhang et al. 1994; Ishimaru et al. 1995; Zhou et al. 1997). Other *Scutellaria* phytochemicals include flavones, flavonoids, chrysin, iridoids, neo-clerodanes, scutapins, and isoscutellarein. Shin and Lee (1995), successfully produced baicalin in callus cultures of *S. baicalensis*. Using the hairy root culture system, Hirotsu (1999), isolated a brand new flavone glucoside, along with 15 known flavones and five

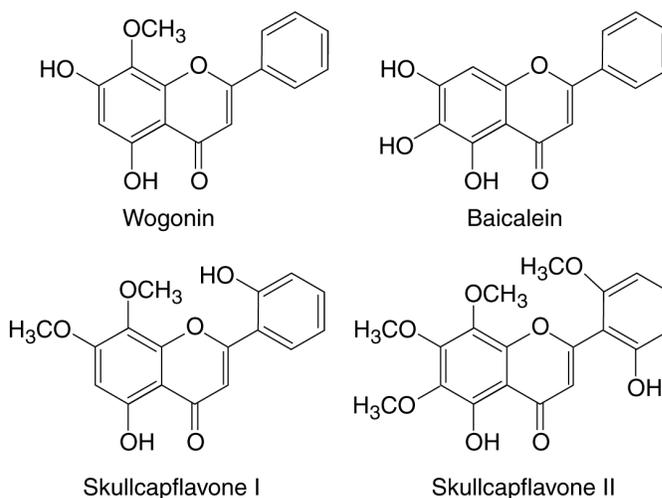


Fig. 2. Structure of compounds isolated from *S. baicalensis* Georgi roots.

phenylethanoids from *S. baicalensis*. Thus it is suggested that hairy root cultures could possibly be used in herbal medicine as a substitute for *Scutellaria Radix* (Zhou et al. 1997; Hirotsu 1999).

MEDICAL STUDIES

Sato et al. (2000) showed antibacterial properties of apigenin and luteolin in the crude extracts of *S. barbata*. Constituents were selectively toxic to *Staphylococcus aureus*, including both methicillin-resistant and sensitive strains. Flavones isolated from *S. baicalensis* roots were found inhibitory to HIV-1 (human immunodeficiency virus) by Li et al. (1993), to HTLV-I (human T cell leukemia virus type I) by Baylor et al. (1992), and to mouse skin tumor promotion (Konoshima et al. 1992). Plant extracts of *S. rivularis* have shown anti-inflammatory and hepatoprotective activity in test animals (Ching and Den 1996). Akishiro et al. (1992) were awarded a patent for therapeutic use of a flavone from *S. baicalensis*, as sialidase enzyme inhibitor of the influenza virus. It has been suggested that baicalin may play a significant role in lipid metabolism through lipogenic and lipolytic pathways of adipose cells (Eun et al. 1994; Chung et al. 1995). Scutalpin C, one of the diterpenoids from *Scutellaria*, has shown strong insect antifeedant bioactivity against the *Spodoptera littoralis* larvae (Munoz et al. 1997). Studies have shown that reactive oxygen species (ROS) including superoxide, hydrogen peroxide, and hydroxyl radicals, contribute to myocardial ischemia-reperfusion injury (Halpern et al. 1995). In vitro studies revealed that baicalein can directly scavenge ROS (Shieh et al. 2000; Shao et al. 1999) protecting cells from lethal damage.

CULTIVATION

Major species of medicinal *Scutellaria* grow in the wild, and systematic cultivation methods for crop production have not been worked out. Skullcaps used for ornamental purposes are established by seeds or cuttings in sunny garden locations with good drainage. Seeds are sown in early spring when there is no more danger of late frosts. Although there are no major insect-pests or diseases reported for *Scutellaria*, it is susceptible to two virus pathogens: tomato spotted wilt virus (TSWV) and impatiens necrotic spot virus (INSV).

PROPAGATION

Efforts in *Scutellaria* propagation have been underway at Fort Valley State University. Mature seeds of *S. montana* and *S. integrifolia* were collected in late summer from the Wildlife Resources Division of the Georgia Department of Natural Resources, Social Circles, Georgia. Seeds of two species were planted for germination in the greenhouse but only *S. integrifolia* germinated. Some success in micropropagation of *Scutellaria* has been reported (Sinha et al. 1999; Stojakowska et al. 1999; Li et al. 2000). Shoot growth from the *S. montana* and *S. integrifolia* plants were cultured in vitro in basal MS (Murashige and Skoog 1962) medium supplemented with 0.5 mg L⁻¹ BA (6-benzylamino purine) and 0.1 mg L⁻¹ NAA (naphthaleneacetic acid). Multiple shoot clumps were allowed to elongate in the basal MS medium to reach 4–6 cm length. Microshoots rooted when cultured in MS basal, rooting medium (M527) from Phytotechnology Laboratories (Shawnee Mission, Kansas), or MS + 1 mg L⁻¹ IBA (Joshee and Yadav 2002).

FUTURE PROSPECTS AND CONCLUSION

Numerous herbal formulations including PC SPES from BotanicLab, Brea, California, Zyflamend PM and Zyflamend Creme from New Chapter, and Migra-Profen from Gaia Herbs, all of which contain *Scutellaria* as an ingredient, are currently available in the market. In recent years, *Scutellaria*-based herbal formulations have been employed to establish its medical/scientific value using in vitro cell culture systems (Li et al. 1993; Shao et al. 1999; Sato et al. 2000; Chen 2001). *Scutellaria baicalensis* and *S. lateriflora* are the two species which have been used in most of the herbal formulations. Since there are over 300 *Scutellaria* species distributed all over the world other *Scutellaria* species need to be evaluated. Our current research here at FVSU focuses on the *Scutellaria* species found in and around the state of Georgia (Table 1). Some of these species are becoming rare or threatened because of population pressure, environmental pollution, and destruction of their natural habitat (Patrick et al. 1995). Future studies are planned to include propagation, cultivation, and conservation of native *Scutellaria* germplasm. Many of the skullcaps have showy, beautiful blooms and there is a great potential for these species as ornamentals.

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Table 1. Different species of *Scutellaria* that are native to and growing in and around the state of Georgia.

<i>Scutellaria</i> species	Flower color	Flower size (mm)	Bloom period	Plant description and habitat	Distribution and status
<i>S. alabamensis</i> Alexander	Violet blue	20–22	June–July	Hairy leaves averaging 50 mm long and 20 mm wide.	Georgia, Florida, South Carolina
<i>S. arenicola</i> Small	Violet blue	25	June–July	Bracts under the flowers are as long as the calyx. Thrives in sandy woods.	N Florida, Georgia, South Carolina
<i>S. arguta</i> Buckley	Violet and white	15–20	June–Aug.	Weak stemmed plant that spreads by runners. Flowers on 5–15 cm long racemes. Near mountain woods.	Delaware to Indiana and southward to South Carolina and Tennessee.
<i>S. australis</i> (Fassett) Epling	Blue	8–10	May–July	Gland tipped hairy stems, narrow ovate hairy leaves. Thrives in dry woods and on prairies.	Texas to Nebraska and most regions further east.
<i>S. elliptica</i> Muhl. ex Spreng.	Light violet	15–21	May–Aug.	Soft hairy stems. Leaves 4–7 cm long by 2–3.5 cm wide. Flowers in 3–10 cm racemes. Thrives in dry woods and thickets.	Southern New York to Missouri and southward to Florida and Texas.
<i>S. floridana</i> Chapm.	Pale violet, blue, white	--	April–July	Leaves up to 3 mm wide and 26 mm long. Thrives in pineland swamps.	A threatened species in Florida
<i>S. glabriuscula</i> Fernald	Pale blue to white	18–27	April–July	Slender hairy stems, ovate to elliptical leaves on petioles 5 mm long. Thrives in sandy soils.	Florida
<i>S. incana</i> Biehler	Blue	18–25	June–Sept.	Ovate leaves. Flowers are in racemes at or near the tip in a branched inflorescence. Found in dry woods, thickets and clearings.	New Jersey, W New York to Iowa, south to Florida, Alabama, Arkansas, Kansas
<i>S. integrifolia</i> L.	Violet blue white or pale pink streaked lower lip	23	May–June	Densely hairy, slender stems bearing narrow lanceolate to oblong leaves with almost no petiole. Flowers in 5–10 cm long racemes. Grows on edges of woods and fields on coastal plains.	New York to Missouri and southward from Texas to Florida
<i>S. lateriflora</i> L.	Violet pink to white	7–8	June–Sept.	Smooth, often glossy leaves vary from ovate to lanceolate. Flowers are in one sided racemes. Found in swampy woods, thickets and meadows.	Widespread in US and parts of western Canada
<i>S. leonardi</i> Epling	Blue	8–10	May–July	Square stems bear lanceolate hairless leaves. Flowers arise from pedicels, and thrives in dry woods and prairies.	North Dakota to Oklahoma.

<i>S. mellichampii</i> Small	Violet blue	25	June–July	Inflorescence 5–15 cm long. Grows in sandy woods.	Georgia, South Carolina
<i>S. montana</i> Chapm.	Blue and white	26–35	May–June	10–15 cm racemes, habitat is dry soil on rocky slopes in undisturbed mature oak and hickory woodlands where trees range from 70–200+ years old.	Endangered species found in Georgia and Tennessee
<i>S. multiglandulosa</i> (Kearn.) Small	Pale blue to white	20–23	April–July	One or two capitate glandular stems Wide lanceolate leaves grows in dry pine lands, bog type fields, and peat laden terrain or shores.	Florida, Georgia
<i>S. nervosa</i> Pursh.	Pale blue	10	May–July	Weak slender stems bear deltoid to ovate leaves, sessile except for some lower leaves. Flowers arise singularly from pedicel. Found in moist woods and thickets.	New Jersey to Ontario and Iowa southward to North Carolina and Tennessee
<i>S. ocmulgee</i> Small	Violet blue	23	June–Oct.	Stem clothed throughout with capitate glands and curled hairs in upper parts. Leaves round to ovate, crenate, hairy.	Threatened species in Georgia
<i>S. ovata</i> Hill	Blue violet with whitish lip	13–25	May–July	10 cm racemes, hairy stems and ovate leaves up to 10 cm long. Grows more abundant on westward facing terrain and often associated with limestone or calcium bearing rocks.	Maryland to Minnesota to Texas, South Carolina, ssp. <i>pseudoarguta</i> threatened in West Virginia
<i>S. parvula</i> Michx.	Blue with darker spots on lower lip	8–10	May–July	Slim horizontal square stems swollen at intervals into tubers. Ovate leaves on short petioles. Found in dry woods and prairies associated with mainly calcareous soils. Perhaps a natural hybrid of <i>S. serrata</i> , <i>S. montana</i> , and/or <i>S. ovalifolia</i> . Most similar to <i>S. montana</i> but has glabrous foliage and elongated internodes. Found in Mesic hardwood forests.	North Dakota to Oklahoma
<i>S. pseudoserrata</i>	--	--	--		Alabama, North Carolina, Tennessee
<i>S. saxatilis</i> Riddell	Violet and white	14–19	June–Aug.	5–15 cm racemes, weak stemmed plant spreads by runners, stem is nearly smooth but glands in the inflorescence. Leaf triangular, sparsely hairy. Found along rocky woods, talus slopes, bluffs.	Delaware to Indiana and southward to South Carolina and Tennessee
<i>S. serrata</i> Andrews	Blue	23–26	May–June	Glabrous plant with smooth ovate leaves. Flowers in racemes 8–10 cm long. Likes rich woods and bluffs.	New York to West Virginia, to Missouri South Carolina, Alabama

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