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# Central nervous system diseases and *Scutellaria*: a review of current mechanism studies

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ABSTRACT

*Scutellaria* comprises many species traditionally used for cognitive and neurological conditions. *In vitro* and *in vivo* studies have supported the value of bioactive compounds of the genus *Scutellaria* for CNS disorders such as Alzheimer, cerebral ischemia, depression and anxiety. In particular, the effects of plants belonging to the genus *Scutellaria* and their components are detailed on cognitive ability such as memory, attention and learning. In this review, the pharmacology of CNS effect and the related molecular mechanisms of the plants belonging to the genus *Scutellaria* and active constituents have been discussed.

## 1. Introduction

*Scutellaria* commonly known as skullcaps is a member of the Labiatae family which is an important perennial and annual herbs includes about 360–400 species [1,2]. The genus has widespread distribution in tropical mountains of North America, Europe and Asia and is found in Siberia to the tropics of South America [3]. *Scutellaria* been traditionally used in medicine as anti-allergic, anti-hepatitis, anti-inflammatory, antithrombotic, anti-bacterial, hepato-protective, anti-mutagenic and antioxidant [4,5].

Most plants of *Scutellaria* are annual or perennial herbs with 5 cm to 1 m height, but some are aquatic and a few are subshrubs. They have opposite leaves and four-angled stems. The flowers of this genus have upper and lower lips [6]. Up to now 300 compounds have been isolated from different species of the genus *Scutellaria*. Two main groups of component including terpenes (triterpenes, diterpenes and iridoid glycosides) and phenolic compounds (flavonoids and phenylethanoid glycosides) isolated from skullcaps. Alkaloids, phytosterols and polysaccharides are among other compounds presented in the genus *Scutellaria* [7–10]. Baicalin, baicalein and wogonin are flavonoids possess anti-HIV, anti-inflammatory, free radical scavenging, lipid peroxidation, antioxidant and anticancer activities [11–19]. Diterpenes such as scutalbin A, jodrellin A and jodrellin B, have anti-feedant effects.

In this review, neuro-psychologic activity of the plants belonging to the genus *Scutellaria* and active constituents, the related mechanism are summarized. In detail we have discussed the effect on cognitive ability such as memory, attention and learning. The potential effect of *Scutellaria* in dementia, including Alzheimer's disease is also reviewed. Finally, future researches are needed to increase our understanding of the potential health benefits of *Scutellaria* plants.

## 2. Main constituents in *Scutellaria* species

From the genus *Scutellaria*, 300 compounds including flavonoids, diterpenes, triterpenoids, phenylethanoid glycosides, iridoid glycosides, alkaloids, polysaccharides and phytosterols were isolated. *Scutellaria* plants are rich source of flavonoid and over 160 flavonoids have been identified from different species of the genus *Scutellaria*. Flavonoids include flavones and flavanonols, flavanones and flavonols, chalcones, flavonolignans and biflavonoids. The main flavonoids isolated from

*Abbreviation:* MMP-2 and MMP-9, matrix metalloproteinases; VEGF, vascular endothelial growth factor; NF-κB, nuclear factor-kappa B; HO-1, heme oxygenase-1; Nrf2, nuclear factor erythroid 2-related factor; INOS, inducible nitric oxide synthase; COX-2, cyclooxygenase-2; P-ERK, phospho extracellular signal–regulated kinases; P-JNK, phospho c-Jun N-terminal kinase; NO, nitric oxide; PGE2, prostaglandin E2; IL-6, interleukin 6; IL-8, interleukin 8; HMC-1, human mast cell line; IL-1β, interleukin-1β; IL-2, interleukin-2; IL-12, interleukin 12; TNF-α, tumor necrosis factor-alpha; MAPK, mitogen activated protein kinases; BHT, butylated hydroxytoluene; GI, gingival index; BDNF, brain-derived neurotrophic factor; PDE, phosphodiesterases; PCREB, phosphorylation of cyclic AMP response element binding; VaD, ventricular assist device; MAO A and B, L-Monoamine oxidases; NMDA, N-methyl-D-Aspartate receptor; BDS, benzodiazepine binding site; AAPH, 2,2′ Azobis (2-Amidinopropane) hydrochloride; ChAT, choline acetyltransferase; GABA, γ-aminobutyric acid; NSAIDs, non-steroidal anti-inflammatory drugs; MCAO, middle cerebral artery occlusion; AD, Alzheimer's disease; BCCAo, bilateral common carotid artery occlusion; LPS, lipopolysaccharide; T-PA, tissue-plasminogen activator; PGs, prostaglandins; NSAIDs, non-steroidal anti-inflammatory drugs; MS, multiple sclerosis

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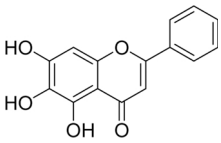
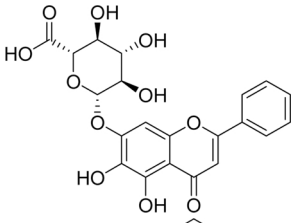
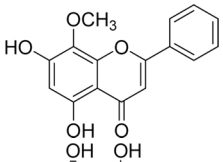
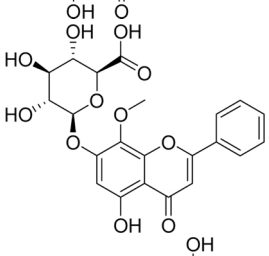
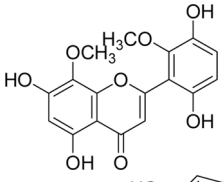
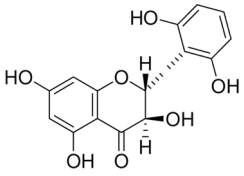
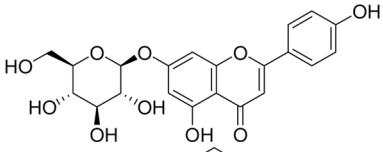
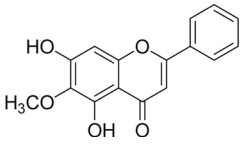
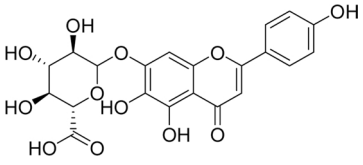
**Table 1**
Structure of main constituents from the genus *Scutellaria.*

| Species | Active component | structure | Ref |
|---|---|---|---|
| *S. baicalensis*<br>*S. litwindowii* | Baicalein |  | [14,55,57,68,73,89,92,99,106,108] |
| *S. baicalensis*<br>*S. litwindowii* | Baicalin |  | |
| *S. baicalensis*<br>*S. litwindowii* | Wogonin |  | |
| *S. baicalensis*<br>*S. litwindowii* | Wogonoside |  | |
| *S. baicalensis* | 5,7,2, 5 -tetrahydroxy-8,6 -dimethoxyflavone |  | [84] |
| *S. baicalensis* | 2(*R*), 3(*R*)-2′,3,5,6′,7-pentahydroxyflavanone |  | |
| *S. baicalensis* | Apigetrin |  | [112] |
| *S. baicalensis* | Oroxylin A |  | |
| *S. baicalensis*<br>*S. racemosa*<br>*S. lateriflora* | Scutellarin |  | [108] |

(*continued on next page*)

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