

# Ethnopharmacology, Phytoconstituents, Essential Oil Composition and Biological Activities of the genus *scutellaria*

Raju Sripathi and Subban Ravi\*

Department of Chemistry,  
Karpagam University, Coimbatore-641021, Tamil Nadu, India

## Abstract

Plants are used in different traditional systems of Indian medicine. *Scutellaria* (Lamiaceae) includes about 350 species commonly known as skullcaps is widespread in Europe, the United States and East Asia with a long history of traditional uses in many countries in the world. Phytochemical investigations have revealed that the plant contain flavonoids and diterpene compounds known to possess multiple health beneficial effects. This review presents the comprehensive overview of traditional uses, phytochemical constituents and pharmacological properties of *Scutellaria* genus such that the potential use of this plant in various traditional medicines can be systematically evaluated.

**Key Words:** *Scutellaria* genus, Essential oil, Structure, Biological activity

## INTRODUCTION

*Scutellaria* (Lamiaceae) includes about 350 species commonly known as skullcaps [1] is widespread in Europe, the United States and East Asia. Have already been reviewed the ethnopharmacology, the biological activities and the correlated chemical compounds of *Scutellaria* species. More than 295 compounds have been isolated, among them predominantly flavonoids and diterpenes has been reported. Studies show that *Scutellaria* and its active principles possess wide pharmacological actions, such as antitumor, anti-angiogenesis, hepatoprotective, antioxidant, anticonvulsant, antibacterial and antiviral activities [1,2]. Individual compounds have been screened for pharmacological activity from *Scutellaria* and *in vitro*. Currently many more compounds, biological activities, essential oils from *Scutellaria* have been reported.

To our knowledge, till date, no particular review is available with an updated information on *Scutellaria* genus. Therefore, the present review is aimed to compile an up-to-date and comprehensive review of *Scutellaria* that covers its ethnomedicinal uses, phytochemical contents and scientifically proven pharmacological properties. Hopefully the information provided in this review will be useful and applicable for future research works aiming towards exploiting the plants nutraceutical potentials. Increasing data supports application and exploitation for new drug development.

The genus is widespread in temperate regions and tropical mountains including Europe, North America and East Asia [3]. Plants of this genus have been widely used in local medicine for thousands of years [4]. Modern pharmacology research has confirmed that the extracts or monomeric compounds of the genus *Scutellaria* possess antitumor, hepatoprotective, antioxidant, anti-

inflammatory, anticonvulsant, antibacterial and antiviral effects [1].

The chemical compounds of the genus *Scutellaria* have been studied since 1889 more than 295 compounds have been obtained from 35 species. Phenolic compounds (Flavonoids, Phenylethanoid glycosides) and terpenes (Iridoid glycosides, Diterpenes and Triterpenoids) are the two main groups of constituents, and the plants also contain alkaloids, phytosterols and polysaccharides among others. The main compounds of flavonoids, baicalin, baicalein, wogonin and ganhuangenin possess anti-cancer, anti-HIV, anti-bacterial, anti-viral, anti-inflammatory and anticonvulsant effects. Jodrellin A, jodrellin B, scutalbin A and scutecyprol B, which are the main compounds of diterpenes have antifeedant effects, etc. In this review, the advances in ethnopharmacology, phytochemistry, biological and pharmacological activities of the genus *Scutellaria* are already reported.

## BIOLOGY AND ETHNOPHARMACOLOGY

Most *Scutellaria* species are annual or perennial herbaceous plants from 5 cm to 1 m tall, but a few are subshrubs and some are aquatic. They have four-angled stems and opposite leaves. The flowers have upper and lower lips. The genus is most easily recognized by the typical shield on the calyx [4].

In East Asia, some *Scutellaria* species are widely used as traditional medicine, especially in China, Korea and Japan due to its anti-inflammatory, antiviral, sedative, antithrombotic and antioxidant effects. The traditional uses of genus *scutellaria* is reported in **Table 1**.

The genus *scutellaria* is also used to activate blood circulation, intestinal catarrh, digestive system cancer and nerve tonics. In Canada, the skullcap herbs is generally sold as tea in health food stores [5,6].

Table-1. Traditional uses of *Scutellaria* genus

Name of the plants	Traditional uses	Reference
<i>S. barbata</i>	Traditional Chinese medicinal herb, used in treatment of digestive system cancer, hepatomalungs cancer, breast cancer and inflammatory.	[1,7]
<i>S. viscidulà</i>	Traditional Chinese medicinal herb widely used to treat inflammatory and bacterial diseases.	[8,9]
<i>S. lateriflora</i>	American traditional medicinal herb, used for treating nervous disorders as well as antispasmodic used to treat anxiety, neuralgia and epilepsy.	[10]
<i>S. discolor</i>	Used as folk medicine common cold, cuts and insect strings.	[11]
<i>S. amoena</i>	Traditional Chinese medicinal herb used for clinical treatment of hyperlipemia, atherosclerosis, hypertension, dysentery, common cold and inflammatory diseases such as atopic dermatitis.	[1,12]
<i>S. flavescene</i>	Traditional Chinese medicinal herb used for antiviral and Anti-RSV effect.	[13]
<i>S. galericulata</i>	American traditional medicinal herb used to cure nervine, sore. cold and fever.	[10]
<i>S. parvula</i>	America traditional medicinal herbs used to treat inflammatory and bacterial diseases.	[6]
<i>S. polydon</i>	American traditional medicinal herb used for curing viral diseases	[15]
<i>S. ovata</i>	American traditional medicine.	[15]
<i>S. alpine</i>	European traditional medicinal herb used as antispasmodic, diaphortic and local medicine.	[2,5]
<i>S. alpinesubsp.javalanbrensis</i>	Traditional Chinese medicine	[14]
<i>S. rubicundasubsp.rubicunda</i>	Used to cure fungal diseases and also used as feeding agent.	[3]
<i>S. hypericifollia</i>	Traditional Chinese medicinal herb and well known ancient drug in China.	[16]
<i>S. rehderiana</i>	Traditional Chinese medicinal herb, used as a key ingredient combination with other Chinese herbs to cure diabetes, hyphoidl fever and its complications.	[1]
<i>S. likiangensis</i>	Traditional Chinese medicinal herb, used as a ingredient combination with other Chinese herbs for number of prescriptions.	[8]
<i>S. tenax</i>	Traditional Chinese medicinal herb, used as an ancient drug for inflammation.	[1]
<i>S. scandens</i>	Nepalese crude drug used to treat wounds and swelling by insects.	[15]
<i>S. indica</i>	Used as analgesin, detoxification and promoting blood circulation effect.	[17]
<i>S. postrata</i>	Asian traditional medicinal herb. It has long been used traditional medicine in Asia, Europe and America.	[18]
<i>S. linearis</i>	Used as traditional medicine by peoples in Asia, Europe and America.	[8,9]
<i>S. grossa</i>	It as long been used traditional medicine in Asia, Europe and America.	[18]
<i>S. strigillosa</i>	Used as traditional medicines in Asia and Europe.	[17]
<i>S. seleriana</i>	Used as traditional medicine by peoples in Asia , Europe and America	[19]
<i>S. altissima</i>	Traditional Chinese medicinel herb used for treatment of cancer, bronchitis and hepatitis.	[20,21]
<i>S. albida</i>	Anti-spasmodic, diaphortic and febrifugal.	[4]
<i>S. rubicunda</i>	Anti-feedent and Anti - fungal	[22]
<i>S. baicalensis</i>	Pneumonia, Hypertension, Jaundice, dysentery, intestinal catarrch and Pyogenic infection.	[1]
<i>S. rivularis</i>	It is a folk medicine of Taiwan, used for the treatment of tumors, hepatitis, liver cirrhosis, jaundice	[23]
<i>S. litwinowii</i>	Used as traditional Indian medicinal herbs for the anti-cancer activity.	[24]
<i>S. pinnatifida A</i>	Used as a traditional Chinese medicinal plant that has utilised in folk medicine for its antioxidant and antimicrobial effects.	[10]
<i>S. sieberibenth</i>	Used as a herbal medicine as diaphortic, febrifugae, tonic, etc....	[25]
<i>S. immaculata and S. ramosissima</i>	Used as Uzbek traditional medicines to treat epilepsy, inflammation, allergies, chorea, nervous tension status and high blood pressure.	[26]
<i>S. rivularis</i>	It is used as a folk medicine in Taiwan for the treatment of tumours, hepatitis, liver cirrhosis, Jaundice and other diseases	[1]
<i>S. volubilis</i>	They are traditionally used for nervous system treatment, as well as to cure heart and kidney affections.	[57,1]
<i>S. repens</i>	Used as a traditional Chinese medicine and herbal medicine to treat various diseases in human and veterinary ailments.	[4]

## COMPOUNDS

The medicinal value of plants lies in some chemical substrates that produce a definitive physiological action on the human body.

From the genus *scutellaria* already about 295 compounds was reported including flavanoides, phenyl ethanoid glycosides, Iridoidglycosides, diterpenoid, triterpenes, alkaloids and other compounds. Some of the compounds displayed May bioactivities *in vivo* or *in vitro*. In addition to the compounds already reported [25] the following 52 compounds from the *scutellarian* species has been reported (Table 2) in the present review CHART 1.

Bioassay-guided fractionation was conducted on an EtOAc-soluble extract of the whole plants of *S. barbata*, monitored by inhibition of Epstein-Barr virus (EBV) lytic replication. Twenty six neo-clerodan diterpenoids were reported out of which 13 compounds are new (scutolides A→L) and 13 previously known. The configuration of new compounds Scutolides A and Scutolide K were confirmed by single-crystal X-ray diffraction. All the 26 compounds were evaluated for inhibitory effects against EBV lytic replication. Eleven compounds exhibited moderate to potent inhibition, EC<sub>50</sub> values from 3.2 to 23.6 μM and selective index (SI) values from 2.1 to 109.2. More specifically the new compound showed most potent activity, which EC<sub>50</sub> and SI values of 3.2 μM and 46.1, respectively, while compound barbatin D (EC<sub>50</sub>=16.4 μM) exhibited the highest SI of 109.2. This study is first to report that neo-clerodan diterpenoids demonstrate significant effect against EBV lytic replication [28].

LC-MS investigation of *S. immaculata* and *S. ramosissima* plants allowed the identification, for the first time, of an additional 9 and 16 flavanoids respectively. The methanol, chloroform and water extracts from those plants and six flavanoids (scutellarian, chrysin, apigenin, apigenin-7-O-glucoside, cynaroside and pinocembrine) exhibited significant inhibition of cell growth against HeLa, HepG-2 and MCF-7 cells. The chloroform extract of *S. ramosissima* showed potent cytotoxic effects with IC<sub>50</sub> value 9.25±1.07 mg/12.83±1.49 μg/ml and 17.29±1.27 μg/ml, respectively. The highest anti-trypanosomal effect against *T. b. brucei* was shown by the chloroform extract of *S. ramosissima* with an IC<sub>50</sub> value of 61 μg/ml. The pure flavanoids showed IC<sub>50</sub> range between 3 and 29 μM, with cynaroside as the most active compounds with an IC<sub>50</sub> value of 3.961±0.133 μg/ml. The chloroform extract of *S. ramosissima* showed potent antimicrobial activity against *Streptococcus pyogenes* (minimum inhibitory concentration, MIC = 0.03 mg/ml). Pinocembrine exhibited a strong activity against all bacteria except *Escherichia coli* and yeast. Water extracts of *S. ramosissima* and *S. immaculata* exhibited potent antioxidant activity with IC<sub>50</sub> value of 5.62±0.51 μg/ml and 3.48±0.02 μg/ml respectively. *Scutellarin* exerted stronger anti-oxidant activity than other flavonoids [26]. Those compounds show almost no or minor toxicity to normal epithelial and normal peripheral blood and myeloid cells. The Anti-tumor functions of those flavones are

largely due to the ability to scavenging oxygen radicals, attenuate NF-κB activity, suppress COX-2 gene expression, inhibit several genes important for regulations of the cell cycle, and to prevent viral infection [26,1]. Baicalein and baicin were shown to protect several types of tissue against damages from reactive oxygen species (ROS) and these flavanoids are reported largely responsible for the antimicrobial effects. Baicalein has also been shown to inhibit HIV-1 reverse transcriptase [26].

Investigation of *S. immaculata* and *S. ramosissima* allowed the identification of the following additional flavanoids, chrysin-6-arabinosyl-8-C-glucoside, isorhamnetin-7-O-rhamnosyl-glucoside, rhamnetin-7-O-rhamnosyl-glucoside, Scutellarin, baicalin, 5,7,2',5'-tetrahydroxy-8,6'-dimethoxyflavanone, Oroxylin A-7-O-glucoside, 5,6,7-trihydroxyflavanone (dihydroxybaicalein)-7-O-glucoside, Norwogonin-7-O-glucuronide, Oroxylin-7-O-glucuronide, wogonin-7-O-glucuronide, Norwogonin, 5,7,3-trihydroxy-4-methoxyflavone, baicalein, 5,7,4-trihydroxy-8-methoxyflavone, wogonin, Chrysin and 5,2-dihydroxy-6,7,8-methoxyflavone [1].

Anti-feedent activity of neo-clerodan diterpenoids against Colorado potato beetle larvae we can conclude that the presence in the clerodane structure of a spiroepoxide substituent at C-4 and two ester groups at C-6 and C-19, together with hexahydro- or tetrahydrofurofuran moiety at C-9, is condition for development of activity. Such dependence was reported in previously investigated on other insects [29].

All tested eleven neo-clerodan diterpenoids displayed a 2α, 19-hemiacetal or acetal functionality in the decalin ring, C-4-C-18 spiroepoxide and an acetate group at C-6 position. At the C11-C6 substructure there is a very common, for clerodane isolated from *Scutellaria* species, hexahydrofuro[2,3b]furan moiety with the exception of compound scutalbin A with tetrahydrofurofuran ring and scutegalerin C, scutegalerin D, scutegalin D, in which C-15 and C-16 are involved in the concentration of a single ring hemiacetal (scutegalin D) or acetal (scutegalerin C and scutegalerin D) [2].

The ethanol extract of the aerial part of *Scutellaria barbata* eluted a white slice crystal which was identified purely as (6S, 9R)-6-Hydroxy-4,4,7a-trimethyl-5,6,7,7a-tetrahydro-1-benzofuran-2(4H)-one [28]. The aerial part of *Scutellaria barbata* resulted in the isolation of ethyl-4-hydroxy-3,5-dimethoxybenzoate. The crystal belonged to the monoclinic space group P(1)/c with a=11.5521(6) Å, b=13.5055(7) Å, c=16.4171(7) Å, β=117.240(3)° and Z=8. [28].

Even though various types of chemical compounds have been identified from *Scutellaria*, research reports on isolated compound and the bioactivity and the mechanism of action of the isolated compounds are limited. Additionally the effects of these compounds on the ailments like cancer, HIV, blood pressure, cardio-vascular disease and others, need to be investigated in detail.

Table 2. Compound isolated from *Scutellaria* genus

Plant	Compounds	Reference
<i>S. barbata</i>	Scutolide A	[27]
	Scutolide B	
	Scutolide C	
	Scutolide D	
	Scutolide E	
	Scutolide F	
	Scutolide G	
	Scutolide H	
	Scutolide I	
	Scutolide J	
	Scutolide K	
	Scutolide L	
	Barbatellari ne B	
	Scutebarbatine Y	
	Barbatin D	
	Scutebarbatine L	
	6 - 7-di-O-acetoxbarbatin A	
	Scutebarbatine A	
	Scutebata J	
	Scutebarbatine K	
	Scutebata D	
	Scutebata F	
	Barbatine D	
Barbatine A		
Barbatine B		
<i>S. litwinowii</i>	2 (S)-2', 7-Dihydroxy-5, 8 - dimethoxyflavanone	[28]
	(S)-2-(4-hydroxyphenyl)-6-methyl-2, 3-dihydro-4H-pyran-4-one.	
	(6S,9R)6-Hydroxy-4, 4, 7a-trimethyl-5, 6, 7, 7a-tetrahydro-1-benzouran-2 (H)-one	
	Ethyl-4 - hydroxy-3, 5-dimethoxy-benzo atherosclerosis	
	Wogonin	
<i>S. galericulata</i>	Neobaicalein	[24]
	Baicalein	
	6-hydroxyfavone	
	Scutegalerin A	
<i>S. galericulata</i>	Scutegalerin B	[22]
	Scutegalerin C	
	Scutegalerin D	
	Scutegalerin E	
	Scutegalerin E	
	Scutalbin A	
	neoajugapyrin A	
14,15-dihydrojodrelli-T		
<i>S. immaculata</i>	Wogonin	[26]
	Scutellariàn	
	Baicalin	
	Baicalein	
<i>S. immaculata</i>	Chrysin	[26]
	Wogonin	
	Norwogonin	
	Baicalin	
<i>S. ramosissima</i>	Baicalein	[26]
	Chrysin	
	Scutellarian	
	Oroxylin A-7 - glucoside	
	Oroxylin A-7 - glucucuronide	
	Norwogonin-7-O-glucuronide	
	Wogonin-7-O-glucuronide	
	5,7,3-trihydroxy-4'-methoxyflavone	
	5,6,7-trihydroxyflavanone(dihydroxybaicalein)-7-O-glucuronide	
	5,7,4'-trihydroxy-8-methoxyflavone	
	5,7,2',5'-tetrahydroxy-8-6'-dimethoxyflavone	
	5,2'-dihydroxy-6-7-8-trimethoxyflavone	
	Chrysin-6-arabinosyl-8-C-glucoside	
	Rhamnetin-7-O-rha-glu	
	Isorhamnetin-7-O-rha-glu	

<i>S. ramosissima</i>	Norwogonin	[26]
	Oroxylin A-7 - glucoside	
	Norwogonin-7-O-glucuronide	
	Wogonin-7-O-glucuronide	
	Chrysin-7-O-glucuronide	
	5,6,7-trihydroxyflavanone(dihydroxybaicalein)-7-O-glucuronide	
	5,7,3-trihydroxy-4'-methoxyflavone	
	Wogonin	
	Norwogonin	
	Baicalin	
	Baicalein	
	Chrysin	
	Scutellarian	
	Oroxylin A-7 - glucoside	
	Oroxylin A-7 - glucucuronide	
	Norwogonin-7-O-glucuronide	
Wogonin-7-O-glucuronide		
5,7,3-trihydroxy-4'-methoxyflavone		
5,6,7-trihydroxyflavanone(dihydroxybaicalein)-7-O-glucuronide		
5,7,4'-trihydroxy-8-methoxyflavone		
5,7,2',5'-tetrahydroxy-8-6'-dimethoxyflavone		
5,2'-dihydroxy-6-7-8-trimethoxyflavone		
Chrysin-6-arabinosyl-8-C-glucoside		
Rhamnetin-7-O-rha-glu		
Isorhamnetin-7-O-rha-glu		

#### ESSENTIAL OIL

Essential oil has been isolated and their composition was reported for 16 species (Table 3). Among them from *S. barbata*, *S. Orientalis* and *S. baicalensis* Essential oil has been isolated from different species and from different places. The essential oil of only a few species of *Scutellaria* has been investigated and reported [29-31]. Recently some more species have been added to the list and presented in the Table 3. Caryophyllene, Linalool and Germacrene D appears to be major compounds, Except *S. Orientalis*, *S. laterfolia* and *S. parvula* where Hexadecanoic acid, aromadendrone, hexahydrofarnesylacetone, Cadinene and  $\alpha$ -bisabolol are the main compounds, respectively germacrene D and  $\beta$ -caryophyllene occurs together and Linalool and  $\alpha$ -terpineol present together. However, additional works are warranted to search for possible biological activities of these volatile compounds including oils and also the possibilities for their commercial exploitation.

**Table-3. Essential Oil isolated from *Scutellaria* genus**

Plants	Major compounds	References
<i>S. barbata</i>	Hexadecanoic acid , 1-Octan-3-ol, 2,6-dimethylocta-2,7-diene-3-ol.	[1]
(Southern China )	Hexahydrofarnesylacetone(11%) 3, 7, 11, 15-tetramethyl-8-hexadecen-1ol (7.8%) Menthol (7.7%) 1-Octan-3-ol,(7.1%)	[25]
<i>S. Orientalis</i> ssp. <i>alpina</i>	Hexadecanoicacid (7.6%) Caryophyllene (7.4%) Caryophyllene oxide (6.8%)	[1]
<i>S. utriculata</i>	Linalool (20.1%) 4-Vinyl guaiacol (15.5%) $\alpha$ -Terpineol (8.9%)	[7]
<i>S. grossa</i> (India )	Linalool (37%) 1-octen-3-ol (32%)	[32]
<i>S. albida</i> Ssp. <i>albida</i> (Turkey )	Linalool (52.63%) trans-nerolid (9.08%) Nonanal (6.73%)	[25]
<i>S. baicalensis</i> (India )	Caryophyllene (22.3-41.5%) GermacreneD(12.4-27.5%) Cadinene (3.1-5.4%)	[33]
	Acetophenone (E)-4 - phenyl-3-buton-2-ene Pelmeher Olic acid	[1]
<i>S. diffusa</i> (Turkey )	Hexadecanoic acid (29.9%) Caryophyllene oxide (8.5%) $\beta$ -Caryophyllene (3.2%)	[34]
<i>S. heterophylla</i> (Turkey )..	Germacrene D (21%) Hexadecanoic acid (16.4%) $\beta$ -Caryophyllene (13%)	[34]
<i>S. salviifolia</i> (Ecuador )	Germacrene D (40%) Bicyclogermacrene (14%) $\beta$ -Caryophyllene (11%)	[34]
<i>S. rupestris</i> ssp. <i>adenotricha</i> (Greece )	Linalool (38.8%) Geraniol (8.1%) $\alpha$ -Terpineol (7.1%)	[25]
<i>S. pinnatifida</i> A (Iran)	Germacrene D (9.5%) $\alpha$ -pinene (5.37%) Cinnamate Born (4.09%)	[10]
<i>S. laeteviolacea</i>	1-octen-3-ol (27.2%) Germacrene D (21.7%) $\beta$ -Caryophyllene (9.6%)	[17]
<i>S. repens</i> Buch-Harm. <i>ex D</i> (India )	Aromadendrene (30.7%) $\beta$ -Funebrene (15%) Gurjuene (8%)	[10]
<i>S. volubilis</i> (Ecuador )	Germacrene D (20.4%) $\beta$ -Caryophyllene (17.5%) $\alpha$ -humulene (14.7%)	[22]
<i>S. brevibracteata</i> (Italy)	Caryophyllene (14.4%) Hexadecanoic acid (12.6%) (E)-phytol (10.7%)	[1]
<i>S. hastifolia</i> (Italy)	Caryophyllene (12.9%) Germacrene D (7.7%) Caryophyllene oxide (6.9%)	[1]
<i>S. havanensis</i> (Cuba)	$\beta$ -Caryophyllene ( 75.6 % ) $\alpha$ - humulene( 11.6^% ) Caryophyllene oxide ( 2.6%)	[35]
<i>S. Orientalis</i> ssp. <i>alpina</i> (Italy)	Hexahydrofarnesylacetone (11.7%) Hexadecanoic acid (7.6%) Caryophyllene oxide (6.8%)	[1]
<i>S. lateriflora</i> ( Iran )	$\beta$ -Cadinene ( 27.0 % ) Calamenene ( 15.2 % ) $\beta$ - elemene ( 9.2 % )	[1]
<i>S. porvula</i>	Caryophyllene ( 29.4 % ) trans- $\beta$ -Farnesene ( 17.0 % )	[1]
<i>S. wightianabenth</i> (India)	Beta-Farnesene ( 22.07% ) 1, 4 - benzenediol -2,5-dimethyl (21.58%) Pipertone oxide (16.133%)	[25]
<i>S. rubicunda</i> subsp. <i>linneana</i> (Sicily )	Caryophyllene ( 28.7 % ) Linalool ( 27.8% )	[1]

### BIOLOGICAL ACTIVITIES

Even though several traditional uses of *Scutellaria* are recognized, a scientific validity and supporting evidence is a pre-essential for commercial exploitation. In the preceding text some of the available reports pertaining towards the pharmacological potential of the plant extracts are being discussed. **Table 4** provide an overview of some important works on the isolated chemical compounds and their activity undertaken on the *Scutellaria* plant.

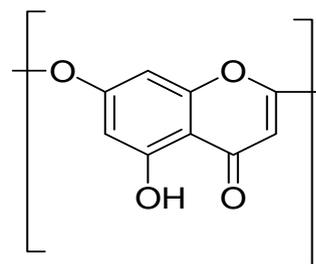
Anti-tumor activity has been exhibited by *S.barbata* and *S.baicalensis*. Anti-RSV, Anti-HIV, anti-inflammatory, Hepatoprotective, Neuro protective, Anti-mutegen, Anti-HBV, Anti-convulsant activities has been reported from the compounds isolated from *S.baicalensis*. Anti-feedent activity was exhibited by *S.rubicunda* and *S.galericulata*. Anti-oxidant activity has been reported from the compounds isolated from *S.baicalensis*, *S.barbata*, *S.immaculata* and *S.wightiana*. Anxiolytic activity was exhibited by Wogonin isolated *S.remosissima*, *S.barbata* and the essential oil of *S.sieberi*, *S.rupestris* and *S.grossa*. from *S.baicalensis* and Baicalin isolated from *S.laterfolia*. Anti-microbial activity was exhibited by *S.immaculata*,

Anti-feedent activity of neo-clerodane diterpenoids against colorado potato breedle larvae we can conclude that the presence in the clerodane structure of a spiroepoxide substituent at C-4 and two ester groups at C- 6 and C-19, together with hexahydro- or tetrahydrofurofuran moiety at C-9, is condition for development of activity. Such dependenc was reported in previously investigated on other insects [36].

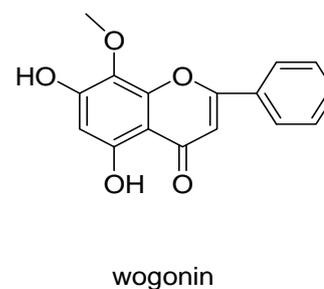
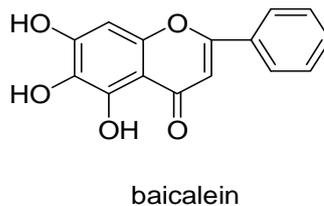
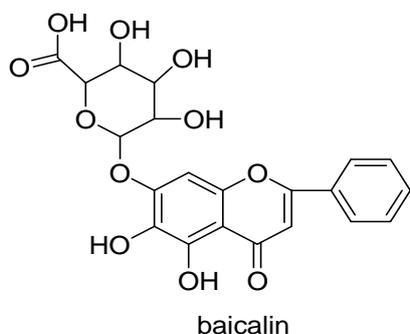
From the **Table-2** it was observed that most of the biological activities are due to wogonin, baicalin and baicalein. Baicalin is a flavone glycoside. It is the glucuronide of baicalein. Baicalein is a trihydroxyflavone with the hydroxy groups at positions C-5, -6 and -7. It is the aglycone of baicalin. Wogonin is 5,7-Dihydroxy-8-methoxyflavone

As individual compounds the reports showed that wogonin, baicalein along with its analog baicalin, is a positive

allosteric modulator of the benzodiazepine site and/or a non-benzodiazepine site of the GABA<sub>A</sub> receptor [37-42]. It displayed subtype selectivity for  $\alpha_2$  and  $\alpha_3$  subunit - containing GABA<sub>A</sub> receptors [34]. Accordingly baicalein has showed anxiolytic effects in mice without incidence of sedation or myorelaxation [40, 41, 43, 44]. Baicalein is also an antagonist of the estrogen receptor, or an antiestrogen [45] inhibit certain types of lipoxygenases [46] and act as an anti-inflammatory agent [47]. It has antiproliferative effects on ET-1-induced proliferation of pulmonary artery smooth muscle cell proliferation via inhibition of TRPC1 channel expression [48]. Possible antidepressant effects have also been attributed to baicalein in animal research [49]. Baicalein is an inhibitor of CYP2C9, an enzyme of the cytochrome P450 system that metabolises drugs in the body. Baicalein has been shown to inhibit *Staphylococcus aureus* biofilm formation and the quorum sensing system *in vitro* [50,51]. If we critically view all the above three molecules in addition to the other compounds like luteolin, oroxylin A, apigenin, 5,7,4'-trihydroxy-8-methoxy flavone and 3,5,7,2',6'-pentahydroxy flavanone reported in the **Table-4** suggest that the ring B and C of the flavanoid moiety may or may not have any substitutions, but the ring A should have oxygen functions in the 5 and 7 position. In addition to this preferably there should be an oxygen function either in the 6<sup>th</sup> position or in the 8<sup>th</sup> position. This moiety may be considered as the pharmacophore which may be responsible for all the activities represented in the **Table-4**.



However, based on the availability of the reports, there is still a wide gap in looking for the biological activities. Hence, further studies in this view are deserved.



**Table-4. Biological activity in *Scutellaria* genus**

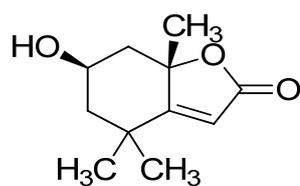
Name of Effect	Species	Compounds	References	
Anti-tumor	<i>S. barbata</i>	Barbatins A-C	[5,32]	
		Scutebarnatine B	[5,32]	
		2',3',5,7-tetrahydroxy flavone apigenin	[32,6]	
		Viscidula III	[32,6]	
		Luteolin	[32,6]	
		<i>S. baicalensis</i>	Wogonin	[8]
		Baicalin	[52]	
		Baicalein	[52]	
Anti-RSV	<i>S. baicalensis</i>	Scutellariàn	[13]	
		5,7,4'-trihydroxy-8-methoxy flavone	[53]	
		Oroxylin A	[13]	
		Wogonin	[13]	
		Ganhuangenin	[13]	
		Baicalein	[14]	
Antifeedant	<i>S. rubicunda</i>	Scuteocyprol B	[3,54]	
		Jodrellin A	[3]	
		Jodrellin B	[3]	
		Scutalbin A	[3]	
		<i>S. galericuleta</i>	Scutalbin A Neo-clerodanedieterpenoids	[27]
Anti-inflammatory	<i>S. baicalensis</i>	Wogonin	[1]	
		Baicalein	[55]	
Hepatoprotective	<i>S. baicalensis</i>	Wogonin	[21]	
		Baicalin	[21]	
		Baicalein	[33]	
Neuroprotective and memory improvement	<i>S. baicalensis</i>	Wogonin	[21,1]	
		Baicalin	[1]	
		Baicalein	[1]	
Antimutagenic	<i>S. baicalensis</i>	Baicalein	[27]	
		Baicalin	[56]	
Anti-oxidant	<i>S. baicalensis</i>	Ganhuangenin	[21]	
		3,5,7,2',6'-pentahydroxy flavanoneflavanone	[21]	
		Baicalein	[1]	
		<i>S. barbata</i>		[57]
		<i>S. immaculata</i> & <i>S. ramosissima</i>	Neo-clerodanedieterpenoids	[26,58] [22]
Anti-oxidative	<i>S. baicalensis</i>	Baicalin	[59]	
Anxiolytic	<i>S. baicalensis</i>	Wogonin	[60]	
	<i>S. laterfolia</i>	Baicalin	[61]	
Anti-HIV	<i>S. baicalensis</i>	Baicalin	[62]	
Anti-HIV-1	<i>S. baicalensis</i>	Baicalin	[62]	
Anti-HBV	<i>S. baicalensis</i>	Wogonin	[27]	
Anticonvulsant	<i>S. baicalensis</i>	Wogonin	[33]	
Anti-microbial	<i>S. immaculata</i>	Essential oil	[26,58]	
	<i>S. ramosissima</i>	Essential oil	[26]	
	<i>S. barbata</i>	Essential oil	[18]	
	<i>S. albida</i> <i>Ssp. albida</i>	Essential oil	[6]	
	<i>S. sieberibenth</i>	Essential oil	[6]	
	<i>S. rupestris</i> <i>spadenotricha</i>	Essential oil	[6]	
Antibacterial	<i>S. grossa</i>	Essential oil	[1]	
Larvicidal activity	<i>S. wightianabenth</i>	Essential oil	[23]	
Antioxidant	<i>S. wightianabenth</i>	Essential oil	[23]	

### CONCLUSION

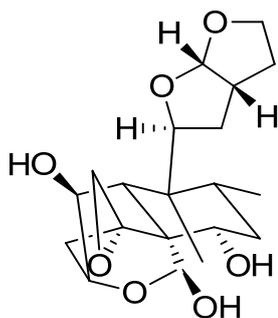
India is a country with an enormous wealth of medicinal plants. But most of these plants are not properly exploited. If these plants were properly exploited, we could have a large number of natural remedies for digits of ailments. The above study is meant to reveal some of the most available shrubs in the genus *Scutellaria*.

In this paper, we briefly summarized the ethnobotanical information, new compounds isolated, essential oil composition and biological activities of *Scutellaria* plant. Various literatures related to these areas were reviewed to gather all information related to the ethnobotanical, phytochemical, pharmacological properties of *Scutellaria* plant. A significant number of studies have provided important evidences that *Scutellaria* plants possesses adequate therapeutic potential and could be explored further for commercial purposes.

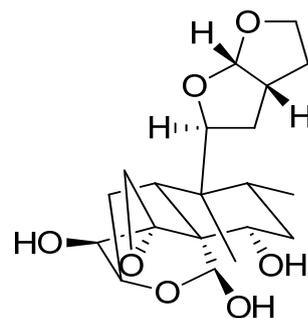
Even though there are various types of bioactive compounds isolated and identified from *Scutellaria* plant as highlighted in the phytochemical section, their contribution towards the plant claimed medicinal uses or demonstrated pharmacological activities were also not fully studied. Thus, the quest for new compounds from *Scutellaria* plant with specific pharmacological activity remains unsolved. It is suggested that researches should be increased to isolate, identify, and collect the compounds from *Scutellaria* species so that their pharmacological potential could be investigated thoroughly. In conclusion, it is hoped that this paper will serve as an encouragement for others to further explore the pharmacological potentials of the genus *Scutellaria* with hope of developing it as a new therapeutic agents, nutraceuticals and functional foods as it is considered as one of the important herbs, particularly in the Indian folk medicine. Most of the plants in this species have a tremendous medicinal value. But still there is a need to reveal more number of plants in this genus. Also the phytochemical and pharmacological evaluation should be done on these plants.



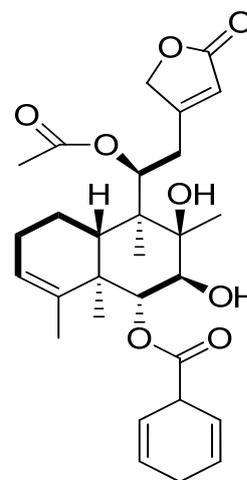
(6S,9R) 6-hydroxy-4,4',7a-trimethyl--5,6,7,7a-tetrahydro-1-benzofuran-2(4H)-one



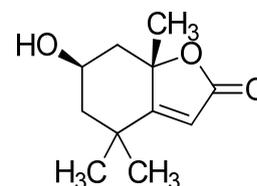
14,15-dihydrojodrellin T



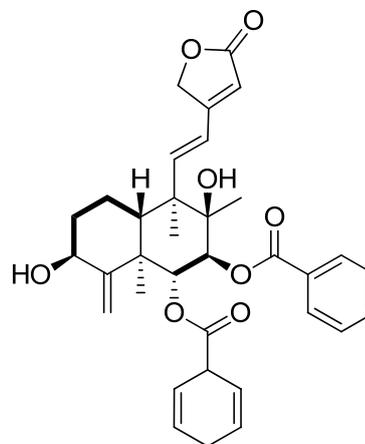
Scutegalerin A



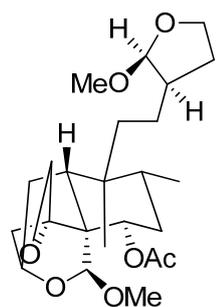
Scutolide F



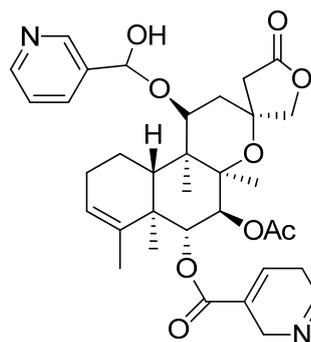
(6S,9R) 6-hydroxy-4,4,7a-trimethyl-5,6,7,7a-tetrahydro-1-benzofuran-2(4H)-one



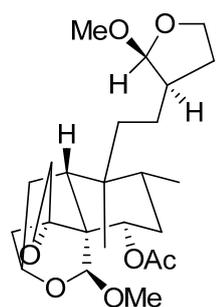
Scutolide L



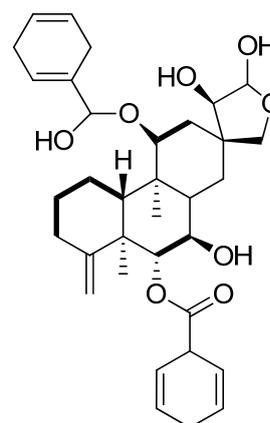
scutegalerin D



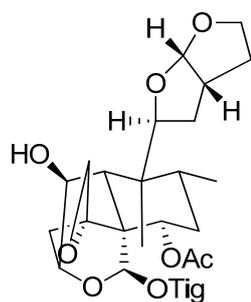
barbatined



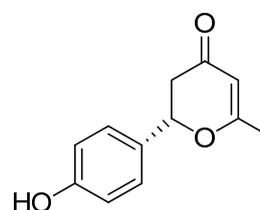
Scutegalerin C



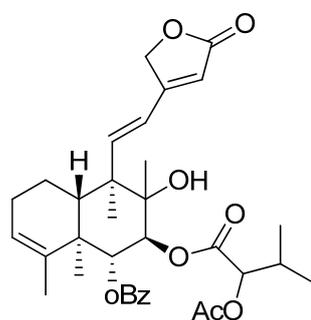
(14R)-14beta-hydroxyscutolide K



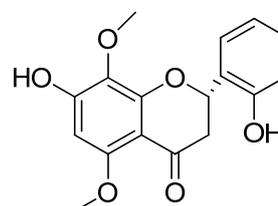
Scutegalerin A



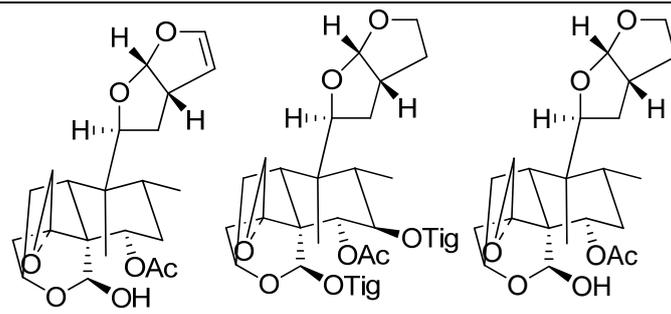
(S)-2-(4-hydroxyphenyl)-6-methyl-2,3-dihydro-4H-pyran-4-one



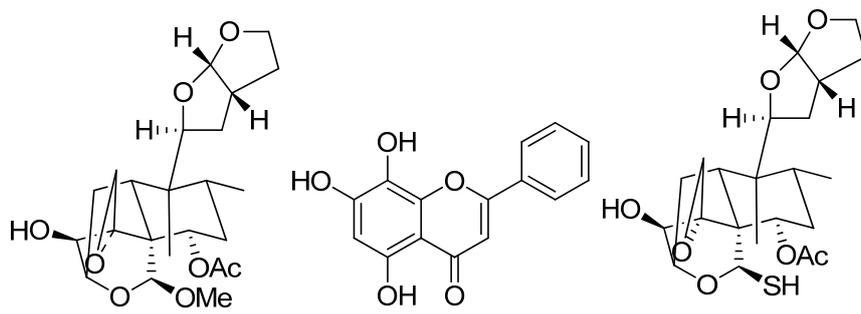
Scutolide D



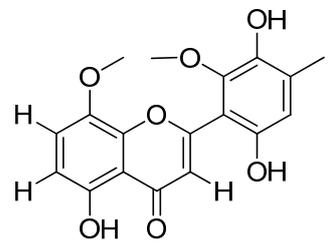
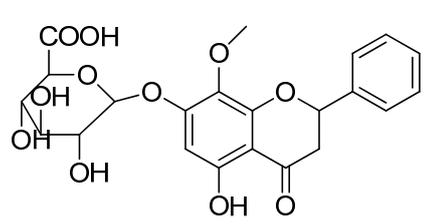
2(S)-2',7-dihydroxy-5,8-dimethoxyflavanone



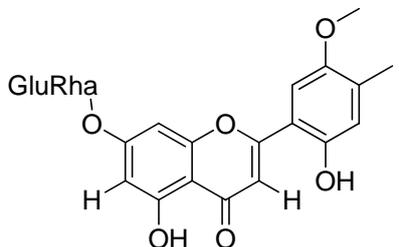
Scutalbin A      Scutegalin A      Scutecolumnin C



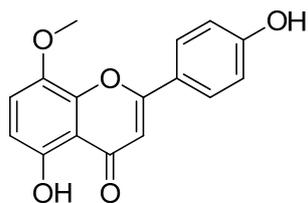
Scutegalerin E      Norwogonin      Neoajugapyrin A



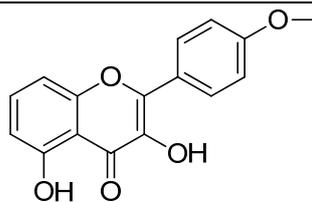
Wogonin-7-O-glucuronide      5,7,2',5'-tetrahydroxy-8,6'-dimethoxyflavones



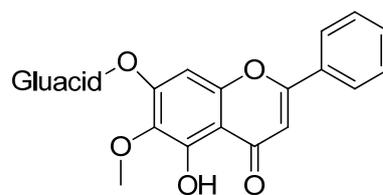
Isorhammetin-7-O-rha-glu



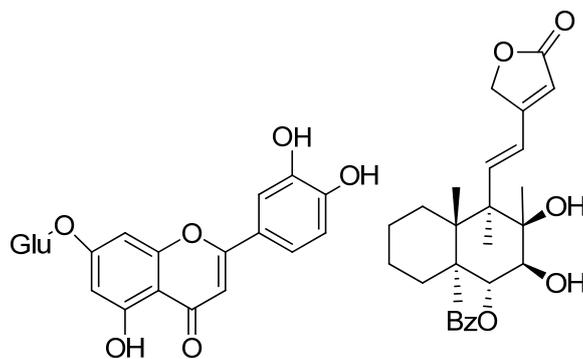
5,7,4'-Trihydroxy-8-methoxyflavone



5,7,3'-Trihydroxy-4'-methoxyflavone

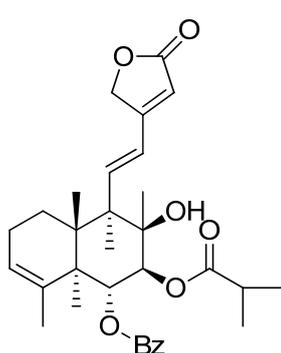


Oroxylin A-7-O-glucuronide

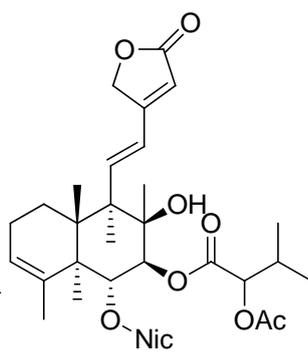


Cynaroside

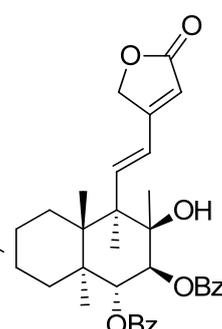
Scutebata J



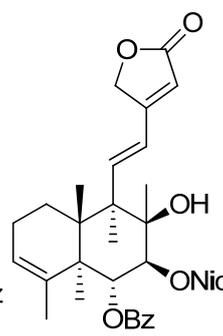
Scutolide C



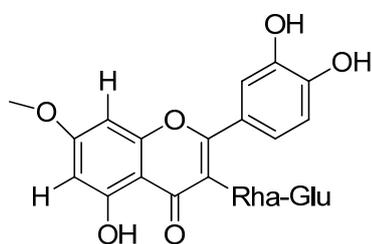
Scutebarbatine L



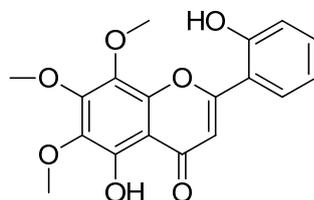
Barbatin D



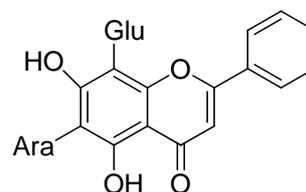
Scutebarbatine Y



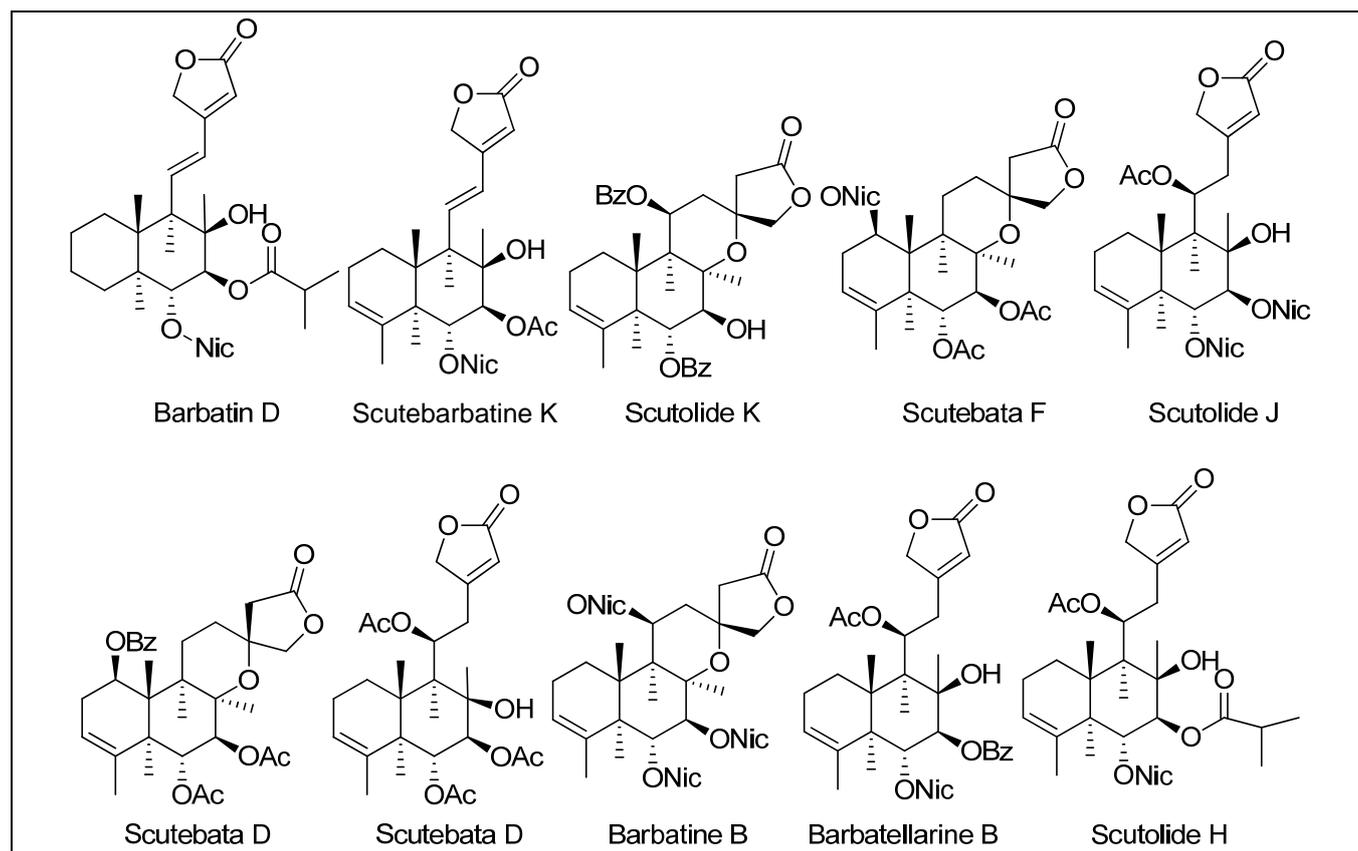
Rhammetin-7-O-rha-glu



5,2'-Dihydroxy-6,7,8-trimethoxyflavone



Chrysin-6-arabinosyl-8-C-glucoside

CHART 1. Compounds from the *scutellarian* species

## REFERENCES

- Xiong Z, Jiang B, Wu PF, Antidepressant effects of a plant-derived flavonoid baicalin involving extracellular signal-regulated kinases cascade, *Biol. Pharm. Bull.*, 2011, 34: 253.
- Bother R, Differential patterns in the *scutellarianalbida* group (Lamiaceae) in the Aegean area, *Nordic. j. Botany*, 1985, 5: 421.
- Bruno M, Piozzi F, Maggio AM, Simmonds MSJ, Antifeedant activity of neo-clerodan diterpenoids from two Sicilian species of *Scutellaria*, *Biochemical Systematics and Ecology*, 2002, 30: 793.
- Duke AD, *Handbook of medicinal herb*, CRC Press Boca Raton, FL, 1986, 440.
- Dai SJ, Tao JY, Liu K, Jiang YT, Shen L, Neo-Clerodan diterpenoids from *Scutellaria barbata* with cytotoxic activities, *Phytochemistry*, 2006b, 67, 1326.
- Skaltsa HH, Lazari DM, Kyriazopoulos P, Golegou S, Triantaphyllidis S, Sokovic M, Kypriotakis Z. *J. Essential Oil Resec.*, 2005, 17: 232.
- Qian B, *Clinical-Effects of Anticancer Chinese Medicine*, Shanghai Translation Publishing House, 1987.
- Wang F, Xu Z, Ren L, Tsang SY, Xue H, "GABA A receptor subtype selectivity underlying selective anxiolytic effect of baicalin", *Neuropharmacology*, 2008, 55.
- Zhang CZ, Zhang YF, Chen JP, Liang XM, Purification and characterisation of baicalin --glucuronidase hydrolyzing baicalin to baicalin from fresh roots of *Scutellaria viscidula* Bge, *Process Biochemistry*, 2005, 40: 1911.
- Ali M, The essential oil composition of *Scutellaria pinnatifida* A. Hanilt. Subsp. *Mucida* (stapt) Rech. f. and comparison with two other subspecies in Iran, *International Journal of plant, animal and environmental science*, 2014, 374.
- Sonoda M, Nishiyama T, Matsukawa Y, Moriyasu M, Cytotoxic activities of flavonoids from two *Scutellaria* plants in Chinese medicine, *Journal of Ethnopharmacology*, 2004, 91: 65.
- Xiao LH, Wang HY, Song SJ, Zhang GP, Song HX, Xu SX, Isolation and identification of the chemical constituents of roots of *Scutellaria amoena* C. H. Wrigth, *Journal of Shenyang Pharmaceutical University (in Chinese)*, 2003, 20: 181.
- Ma SC, Du J, But PPH, Deng XL, Zhang YW, Ooi VEC, Xu HX, Lee SHS, Lee SF, Antiviral Chinese medicinal herb against respiratory syncytial virus, *Journal of Ethnopharmacology*, 2002, 79: 205.
- MuNoz DM, Torre MCD, Rodrfeuez B, Simmons MSJ, Blaney WM, Neo-clerodane Insect antifeedants from *Scutellaria alpinasubsp. Jawalambrenensis*, *Phytochemistry*, 1997, 44: 590.
- Li BQ, Fu T, Yao DY, Mikovits JA, Ruscetti FW, Wang JM, Flavonoid baicalin inhibits HIV-1 infection at the level of viral entry, *Biochemical and Biophysical Research Communications*, 200b, 276: 534.
- Dai SJ, Chen M, Liu K, Jiang YT, Shen L, Four new neo-clerodan diterpenoid alkaloids from *Scutellaria barbata* with cytotoxic activities, *Chemical Pharmaceutical Bulletin*, 2006a, 54: 869.
- Miyaichi Y, Morimoto T, Yaguchi K, Kizu H, Studies on the constituents of *scutellaria* species (XXI) constituents of the leaves of *Scutellaria strigillosa* Hemsley, *Journal of Natural Medicine*, 2006, 60: 157.
- Kikuchi, Miyaichi Y, Yamaguchi Y, Kizu Y, Tomimori T, Studies on the nepalese crude drugs XIV, on the phenolic compounds from the roots of *Scutellaria postrata*, *exBenth*, *Chemicals and pharmaceutical Bulletin*, 1991a, 39: 1047.
- Esquivel B, Flores E, Hernandez-Ortega C, Toscano, RA, Neo-clerodan diterpenoids from *Scutellaria drummondii*, *Phytochemistry*, 1995, 38: 175.
- Li ZP, Wei HQ, Chemical compounds of the genus *Scutellaria* World, *Phytomedicines*, 1994, 9: 47.
- Malakov PY, Papanov GY, A clerodan diterpenoids from *Scutellaria altissima*, *Phytochemistry*, 1996, 41: 855.
- Bruno M, Vassallo N, Simmonds MSJ, A diterpenoid with antifeedant activity from *scutellaria rubicunda*, *Phytochemistry*, 1999, 50: 973.
- Lin YL, Lin RJ, Kimm Shen KP, Dai ZK, Chen IJ, Wu JR, Wu BN, Baicalin, isolated from *Scutellaria baicalensis*, protects against endothelin-1-induced pulmonary artery smooth muscle cell proliferation via inhibition of TRPC1 channel expression, *Journal of Ethnopharmacology*, 2011, 138: 373.

- [24] Zhang SQ, Obregon D, Ehrhart J, Deng J, Tian J, Hou H, Giunta B, Sawmiller D, Tan J, Baicalein reduces  $\beta$ -amyloid and promotes nonamyloidogenic amyloid precursor protein processing in an Alzheimer's disease transgenic mouse model", *Journal of Neuroscience Research*, 2013, 91: 1239 .
- [25] Sripathi S, Ravi S, A study of the essential oil of *Scutellaria wightiana* benth and its antioxidant and Larvicidal activity, *Indo American Journal of Pharm Research*, 2014, 111: 5478.
- [26] Nilufar Z, Mamadaliyeva FH, Mahmoud Z, Read EL, Ahmed T, Razan H, Dilduza RES, Shahniz A, Micheal W, Flavonoids in *scutellariaimmaculata* and *Scutellaria romosissima* (Lamiaceae ) and their biological activity, *Journal of pharmacy and pharmacology*, 2011.
- [27] Awad RA, Arnason JT, Trudeau V, Bergeron C, Budzinski JW, Foster BC, Merali Z, Phytochemical and biological analysis of skullcap ( *Scutellaria lateriflora* L ) a medicinal plant with anxiolytic properties, *Phytomedicine*, 2003, 10:640 .
- [28] Shan K, Zhaoyu W, Lijing C, Shengtan Z, Jingming L, Isolation and characterization of (6S,9R)-6-Hydroxy -4, 4 , 7a-trimethyl-5 , 6 , 7 , 7a-tetrahydro -1-benzofuran-2 (4H)-one from *scutellariabarbata* , *Journal of Medicinal plants Research*, 2011, 5, 613.
- [29] Zahra T N, Javad A, Heydar P, Seyed HM, Naser MV, Alireza M, Seyed , A Wogonin and neobaicalein from *Scutellaria litwinowii* roots are apoptotic for HeLa cells., *Brazilian Journal of Pharmacognosia*, 2012, 22:268 .
- [30] Wang H, Hui KM, Xu S, Chen Y, Wong JT, Xue H , Two flavones from *Scutellaria baicalensis* Georgian and their binding affinities to the benzodiazepine site of the GABAA receptor complex, *Pharmazie*, 2012, 57, (12): 857 .
- [32] Hui KM, Wang XH, Xue H, Interaction of flavones from the roots of *Scutellaria baicalensis* with the benzodiazepine site, *Planta Med*, 2000, 66:91.
- [32] Zhang SQ, Obregon D, Ehrhart J, Deng J, Tian J, Hou J, Giunta B, Sawmiller D, Tan J, Baicalein reduces  $\beta$ -amyloid and promotes nonamyloidogenic amyloid precursor protein processing in an Alzheimer's disease transgenic mouse model, *Journal of Neuroscience Research*, 2013, 91: 1239 .
- [33] Liao JF, H. Wang HI, Che MC, Chen CC, Chen CF, Benzodiazepine binding site-interactive flavones from *Scutellaria baicalensis* root, *Planta Med*, 1998, 64, 571.
- [34] Edwin LC, Nobuo Y, Complementary and Alternative Approaches to Biomedicine, Springer Science & Business Media, 2004, pp. 18.
- [35] Carvalho RS, Duarte FS, De Lima TS, Involvement of GABAergic non-benzodiazepine sites in the anxiolytic-like and sedative effects of the flavonoid baicalein in mice, *Behav. Brain Res*; 2011, 221:75.
- [36] Bozov PJ, Katia HN, Veselin PB, Tonka A, Vasileva. 24 Antifeedant activity of neo-clerodan diterpenoids from *Scutellaria galericulata* against Colorado potato beetle larvae, *J. BioSci Biotech*, 2011, 15:161.
- [37] Wang F, Xu Z, Ren L, Tsang SY, Xue H , "GABA A receptor subtype selectivity underlying selective anxiolytic effect of baicalin", *Neuropharmacology*, 2008, 55 (7): 1231-1237.
- [38] Constable F, Medicinal plant biotechnology, *Planta Med*, 1990, 56:421.
- [39] Stefanie S, *Psychoactive Herbs in Veterinary Behavior Medicine*. John Wiley & Sons. 2008, pp. 139.
- [40] Deschamps JD, Kenyon VA, Holman TR, Baicalein is a potent in vitro inhibitor against both reticulocyte 15-human and platelet 12-human lipoygenases, *Bioorganic and Medicinal Chemistry*, 2006, 14:4295.
- [41] Hsieh CJ, Hall K, Hat T, Li C, Krishnaswamy G, Chi DS, Baicalein inhibits IL-1 $\beta$ - and TNF- $\alpha$ -induced inflammatory cytokine production from human mast cells via regulation of the NF- $\kappa$ B pathway, *Clin Mol Allergy*, 2007, 5: 5.
- [42] Lin YL, Lin RJ, Shen KP, . Dai ZK, Chen JJ, Wu JR, Wu BN, Baicalein, isolated from *Scutellaria baicalensis*, protects against endothelin-1-induced pulmonary artery smooth muscle cell proliferation via inhibition of TRPC1 channel expression, *Journal of Ethnopharmacology* , 2011, 138: 373.
- [43] Wang F, Ren FC, Li YJ, Liu J, . *Chem. Pharm. Bull*, 2010, 58:1267 .
- [44] Si D, Wang Y, Zhou YH, Guo Y, Wang J, Zhou H, Li ZS, JFawcett JP, Mechanism of CYP2C9 inhibition by flavones and flavonols, *Drug Metabolism and Disposition*, 2009, 37: 629 .
- [45] Chan HX, Chen ZY, Tsang DSC, Leung LK, Baicalein adduct formation by modulating CYP1A1 and CYP1B1 activities, *Biomedicine Pharmacotherapy*, 2002, 56:269 - 275.
- [46] Dai SJ, Wang GF, Chen M, Liu, Five new neo-clerodan diterpenoid alkaloids
- [47] Tan Y, Lv ZP, Bai XC, Liu XY, Zhang XF, Traditional Chinese medicine Baoganning increases phosphorylation of CREB in liver fibrosis *in vivo* and *in vitro*, *Journal of Ethnopharmacology*, 2006, 105:69.
- [48] Mehmet C , Betul D, Gulderen Y, Kemal HCB, Essential oil compositions of three species of *Scutellaria* from Turkey, *Natural product research*, 2011, 25:1720 .
- [49] David MD, Carmen LWR, Victor GC, Amando C, Eva SO, Selective and high yield isolation of pure Wogonin from aerial parts of *Scutellaria havanensis* Jacq., *Int. J. Pharm. Sci. Rev. Res*, 2006, 30:104.
- [50] Chan HX, Chen ZY, Tsang DSC, Leung LK, Baicalein adduct formation by modulating CYP1A1 and CYP1B1 activities, *Biomedicine Pharmacotherapy*, 2005, 56:269.
- [51] Nagai T, Moriguchi R, Suzuki Y, Tomimori T, Yamada H. Mode of action of the anti-influenza virus activity of plant flavonoid, 5,7,4 -trihydroxy-8-methoxyflavone, from the roots of *Scutellaria baicalensis*, *Antiviral Research*, 1995, 26:11.
- [52] Brun M, Rossell S, Maggio A, Piozzi F, Scaglioni L, Servetta O, Scuteparvin , a new neo-clerodan diterpenoids from *Scutellaria parvula*, *Biochemical Systematics and Ecology*, 2004, 32: 75.
- [53] Dai SJ, Liang DD, Ren Y, Liu K, Shen L, *Planta Med*, 2007, 73: 1217.
- [54] Woo KJ, Lim JH, Suh SI, Kwon YK, Shin SW, Kim SC, Choi YH, Park JW, Kwon TK, Differential inhibitory effects of baicalein and baicalin on LPS-induced cyclooxygenase-2 expression through inhibition of C/EBP DNA binding activity, *Immunobiology*, 2006, 211: 359.
- [55] Johan G, de Boer B, Quiney PB, Walter C, Thomas, Protection against aflatoxin-B1-induced liver mutagenesis by *Scutellaria baicalensis*, *Mutation Research*, 2005, 15:578.
- [56] Zhang CZ, Zhang YF, Chen JP, Liang XM, Purification and characterization of baicalin --glucuronidase hydrolyzing baicalin to baicalein from fresh roots of *Scutellaria viscidula* Bge, *Process Biochemistry*, 2005, 40:1911- 1915.
- [57] Cunningham AB, African medicinal plants: setting priorities at the interface between conservation and primary health care. People and plant initiative working paper 1. Nairobi: UNESCO, 1993, [rbgkew.org.uk/peopleplant/wp/wp1/index.htm](http://rbgkew.org.uk/peopleplant/wp/wp1/index.htm).
- [58] Hu BH, Liu YL, Study on the structure of the new flavonoids from *Scutellaria amoena* C.H. Wright, *Acta Pharmaceutica Sinica*, 1988, 24:200.
- [59] Hu BH, Liu YL, Zhang T, Study on the structure of scuteamoenin from *Scutellaria amoena* C. H, Wright, *Acta Pharmaceutica Sinica*, 1990, 25:302 .
- [60] Cook NC, Samman S, Flavonoids chemistry, metabolism, cardioprotective effects and dietary sources, *Nutritional Biochem*, 1996, 7:66.
- [61] Cozar O, Carmen G, Monica C, Comparative analysis of some active principles of herb plants by GC - MS, *Talanta*, 2000, 53:253.
- [62] Li ZP, Wei HQ, 1994. Chemical compounds of the genus *Scutellaria* World, *Phytomedicine*, 1994, 47 .