



Review

The genus *Scutellaria* an ethnopharmacological and phytochemical review

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ABSTRACT

Scutellaria (HUANG QIN) (Lamiaceae), which includes about **350** species commonly known as skullcaps, is widespread in Europe, the United States and East Asia. Some species are taken to clear away the heat-evil and expel superficial evils in traditional Chinese medicine (TCM). The present paper reviews the ethnopharmacology, the biological activities and the correlated chemical compounds of *Scutellaria* species. More than **295** compounds have been isolated, among them flavonoids and diterpenes. Studies show that *Scutellaria* and its active principles possess wide pharmacological actions, such as antitumor, anti-angiogenesis, hepatoprotective, antioxidant, anticonvulsant, antibacterial and antiviral activities. Currently, effective monomeric compounds or active parts have been screened for pharmacological activity from *Scutellaria in vivo* and *in vitro*. Increasing data supports application and exploitation for new drug development.

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Contents

1. Introduction	280
2. Biology and ethnopharmacology	280
3. Phytochemistry	289
3.1. Flavonoids	289
3.1.1. Flavones and flavonols	289
3.1.2. Flavanones and flavanonols	289
3.1.3. Biflavonoids	294
3.1.4. Flavonolignans	294
3.1.5. Chalcones	295
3.2. Phenylethanoid glycosides	295
3.3. Iridoid glycosides	295
3.4. Diterpenes	296
3.5. Triterpenoids	297
3.6. Neo-clerodane diterpenoid alkaloids	297
3.7. Alkaloids	298
3.8. Essential oils	298
3.9. Other compounds	299
4. Qualitative and quantitative analysis	300
5. Effects of crude extract	302
5.1. Antitumor	302
5.2. Anti-angiogenesis	305
5.3. Hepatoprotective	305

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5.4. Antioxidant	305
5.5. Anticonvulsant	307
5.6. Antibacterial and antiviral	307
5.7. Neuroprotective effects and memory improvement	308
6. Conclusion.....	310
References	311

1. Introduction

Scutellaria (Lamiaceae) includes about 350 species commonly known as skullcaps (Willis, 1966). The genus is widespread in temperate regions and tropical mountains including Europe, North America and East Asia (Bruno et al., 2002). Plants of this genus have been widely used in local medicine for thousands of years (Jiangsu New Medical College, 1977). 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.

The chemical compounds of the genus *Scutellaria* have been studied since 1889. In 1910, Goldschmiedt and Lerner isolated the first flavonoid scutellarein from *Scutellaria altissima* in Vietnam (Zeng and Chen, 1957). Since then, more than 295 compounds have been obtained from 35 species. Phenolic compounds (Flavonoids, Phenylethanoid glycosides) and Terpene compounds (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 presented.

2. 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 (Jiangsu New Medical College, 1977) (Fig. 1).

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. Radix *Scutellariae baicalensis* (HUANG QIN) and Herba *Scutellariae Barbatae* (BAN-ZHI-LIAN) have been listed in the Phar-

macopoeia of the People's Republic of China and Japan (MHWJ, 1996; PCMPH, 2000), and seven species have been listed in 'Zhong Yao Dictionary' in China (Jiangsu New Medical College, 1977).

Scutellaria baicalensis is indigenous to the Korean peninsula and to China, Japan, Mongolia and Russian Federation. In the Chinese medical classic "Shennong's Herba", it was thought as a "middle grade" herb. The general appearance of radix *Scutellariae* is conical, twisted or flattened root, 5–25 cm long, 0.5–3.0 cm in diameter. Externally it is yellow-brown, with coarse and marked longitudinal wrinkles and with scattered scars of lateral roots and remains of brown periderm; scars of stem or remains of stem at the crown; xylem rotted in old roots; hard in texture and easily broken; fibrous with a fractured surface and yellow in color, reddish-brown in the centre (FAPA, 1978; MHWJ, 1996; MHWK, 1998; PCMPH, 2000).

In China, *S. baicalensis* is widely distributed in Hebei, Shandong, Sichuan, Neimenggu, Gansu, Shannxi, Shanxi, Yunnan and other provinces. In local medicine, the roots have been used to clear away the heat-evil and expel superficial evils, eliminate stasis and activate blood circulation, induce diuresis and reduce edema in China. In the clinic, it is widely applied to cure pneumonia, hypertension, jaundice, dysentery and intestinal catarrh, pyogenic infection, etc. Recently, due to the marked decrease of wild resources, *S. baicalensis* has been listed as a nationally protected plant in China (Jiangsu New Medical College, 1977) (Fig. 1). Along with the development of pharmacology, chemistry and pharmaceuticals, *S. amoena*, *S. rehderiana*, *S. likiangensis*, *S. viscidula* have been studied systematically as substitutes for *S. baicalensis*. The roots of these plants are used as a key ingredient in combination with other Chinese herbs in a number of prescriptions such as *Huangqin Tang*, *Huangqin Qingfei Tang*, *Huangqin Lige Tang*, etc. (Table 1).

Scutellaria barbata, a plant native to southern China, is widely distributed in Anhui, Zhejiang, Henan, Jiangsu, Fujian, Guizhou, Yunnan, Shandong, Hebei and other provinces. This plant often grows in wet meadows and nearby pools and brooks. This herb was known in traditional Chinese medicine as *Ban-Zhi-Lian* and has been used to cure the pain and swelling of throat, edema and hemorrhoids. Moreover, it was thought to be an external agent for the treatment of snake bites (Jiangsu New Medical College, 1977). Extracts of *S. barbata* have shown *in vivo* growth inhibitory effects in a number of cancers. The herb has been used in the treatment of digestive system cancers, hepatoma, lung cancer, breast cancer and chorioepithelioma. In particular, sixty-two percent of patients suffering from hepatoma were completely cured when treated with *S. barbata* (Qian, 1987).

In Europe and North America, dried aerial parts of *S. galericulata* and *S. lateriflora* are mainly used as skullcap, and the latter plant grows in meadows and swampy woods in North America. In the Pharmacopoeia and National Formulary of the United States, the dried aerial parts of *S. lateriflora* were recorded as sedative/nerve tonics as well as an antispasmodic to treat epilepsy, anxiety, neuralgia and withdrawal from barbiturates and tranquilizers. In Canada, the skullcap herb is generally sold as a tea in health food stores, but can also be found as a tonic or in combination with other herbs such as valerian and passion flower in sleep-inducing tablets (Awad et al., 2003).

In addition, *S. indica* was employed for analgesia, detoxification, promoting blood circulation effects in China, Korea and India.



Fig. 1. The aerial parts and the roots of *Scutellaria baicalensis*.

Table 1The traditional use of *S. baicalensis* in China.

Name	Compositions	Traditional uses	References
Huangqin Tang I	Radix Scutellariae , Radix Platycodi Radix Paeoniae Alba, Radix Ophiopogonis, Radix Ginseng, Radix Rehmanniae, Radix Puerariae, Radix Trichosanthis, Radix Angelicae Sinensis, Fructus Mume, Fructus Gardeniae.	Removing heat to promote salivation, and curing the diabetes involving the upper warmer	'Wan Bing Hui Chun', Vol. 5
Huangqin Tang II	Radix Scutellariae	Hemostasis by clearing away heat, curing haemorrhagia nasalis	'Shang Han Zong Bing Lun', Vol. 3
Huangqin Tang III	Radix Scutellariae , Radix Peucedani, Cortex Cinnamomi, Rhizoma Pinelliae, Poria.	Curing typhoid fever and its complication	'Wai Tai Mi Yao', Vol. 'Sheng Shi Fang'
Huangqin Tang IV	Radix Scutellariae , Radix Paeoniae Alba, Radix Glycyrrhizae, Semen Ziziphi Spinosae.	Removing heat and alleviating pain	'Shang Han Lun'
Huangqin Shegan Tang	Radix Scutellariae , Radix Peucedani, Radix Glycyrrhizae, Rhizoma Belamcandae, Rhizoma Cimicifugae, Fructus Aurantii Immaturus, Cortex Cinnamomi.	Curing the diseases of gullet	'Shen Ji Zong Lu', Vol. 124
Huangqin Shaoyao Tang	Radix Scutellariae , Radix Paeoniae Alba, Radix Rehmanniae, Rhizoma Atractylodes Macrocephalae.	Curing women's typhoid fever and its complication	'Lei Zheng Huo Ren Book', Vol. 19
Huangqin Qingfei Tang	Radix scutellariae , Fructus Gardeniae.	Curing difficulty in micturition induced by pulmonary dryness	'Wei Sheng Bao Jian', Vol. 17
Huangqin Mudan Tang	Radix Scutellariae , Radix Paeoniae Alba, Radix et Rhizoma Rhei, Rhizoma Belamcandae, Fructus Aurantii Immaturus, Cortex Moutan, Semen Persicae, Sargassum, Tabanus, Hirudo, Larva holotrichiae.	Curing menstruation disease	'Bei Ji Qian Jin Yao Fang', Vol. 4
Huangqin Maohua Tang	Radix Scutellariae , Rhizoma Curculiginis, Radix Paeoniae Alba, Radix Glycyrrhizae.	Curing about vomiting immediately after intake of food	Xing Yuan Sheng Chun', Vol. 5
Huangqin Lige Tang	Radix Scutellariae , Radix Peucedani, Radix Coptidis, Rhizoma Alismatis, Rhizoma Arisaematis, Alumen. Fructus Aurantii, Pericarpium Citri Reticulatae, Rhizoma Atractylodes Macrocephalae.	Eliminating phlegm by cooling	'Lan Shi Mi Cang'
Huangqin Banxia Shengjiang Tang	Radix Scutellariae , Radix Paeoniae Alba, Radix Glycyrrhizae, Radix peucedani, Semen Ziziphi Spinosae.	Curing typhoid fever and its complication	'Shang Han Lun'
Huangqin Huashi Tang	Radix Scutellariae , Talcum, Fructus Amomi Rotundus, Pericarpium Arecae, Poria, Medulla Tetrapanacis, Polyporus.	Clearing away heat evil and promoting diuresis	'Wen Bing Tiao Bian', Vol. 2
Huangqin Houbu Tang	Radix Scutellariae , Radix Paeoniae Alba, Radix Puerariae, Radix Glycyrrhizae, Radix Bupleuri, Cortex Magnoliae Officinalis, Fructus Aurantii, Pericarpium Citri Reticulatae.	Curing diarrhea due to internal cold and superficial heat	'Gu Jin Yi Che', Vol. 1
Huangqin Beimu Tang	Radix Scutellariae , Radix Bupleuri, Radix Scrophulariae, Radix Platycodi, Radix Paeoniae Alba, Semen Armeniacae Amarum, Bulbus Fritillariae Cirrhosae, Fructus Schisandrae.	Curing the diseases of nostril	'Yi Xue Zhai Cui', Vol. 3
Huangqin Banxia Tang	Radix Scutellariae , Radix Peucedani Radix Glycyrrhizae, Radix Platycodi, Fructus Aurantii Immaturus, Folium Perillae, Herba Ephedrae, Semen Armeniacae Amarum.	Curing the syndrome of dyspnea	'Gu Jin Yi Tong', Vol. 44
Huangqin Shenma Tang	Radix Scutellariae , Radix Puerariae, Radix paeoniae Alba, Radix Glycyrrhizae, Rhizoma Cimicifugae.	Curing the body pain and headache of children.	'Pu Ji Fang', Vol. 369
Huangqin Siwu Tang	Radix Scutellariae , Radix Rehmanniae, Radix Angelicae Sinensis, Radix Paeoniae Alba, Rhizoma Chuanxiong, Rhizoma Atractylodes Macrocephalae.	Removing heat to cool blood, promoting blood flow and regulating menstruation	'Yi Zong Jin Jian', Vol. 44
Huangqin Renshen Tang	Radix Scutellariae , Radix Ginseng, Radix Glycyrrhizae, Cortex Cinnamomi, Semen Ziziphi Spinosae.	Curing typhoid fever and its complication	'Wai Tai Mi Fang', Vol. 2

Table 1 (Continued)

Name	Compositions	Traditional uses	References
Huangqin Jingjie Tang	Radix Scutellariae , Radix Bupleuri, Radix Glycyrrhizae, Radix Paeoniae Alba, Radix Angelicae Sinensis, Radix Saposhnikoviae, Herba Chenopodii Ambrosioidis, Fructus Arctii, Fructus Forsythiae, Semen Plantaginis, Perisotracum Cicadae, Fructus Gardeniae, Caulis Aristolochiae Manshuriensis, Talcum.	Curing common cold in children and its complication	'Liang Peng Hui Ji', Vol. 4
Huangqin Liuhe Tang	Radix Scutellariae , Radix Rehmanniae, Radix Angelicae Sinensis, Radix Paeoniae Alba, Rhizoma Chuanxiong, Rhizoma Atractylodes Macrocephalae.	Curing menstruation disease	'Yuan Rong'
Huangqin Jiegeng Tang	Radix Scutellariae , Radix Platycodi, Radix Paeoniae Alba, Bulbus Fritillariae Cirrhosae, Rhizoma Anemarrhenae, Herba Menthae.	Curing acute seasonal febrile disease and distention of head, pyrophobia	'Yi Fang Jian Yi', Vol. 2
Huangqin Jupi Tang	Radix Scutellariae , Radix Puerariae, Radix Glycyrrhizae, Semen Armeniacae Amarum, Fructus Aurantii Immaturus, Herba Ephedrae, Pericarpium Citri Reticulatae, Cortex Magnoliae Officinalis.	Curing the measles	'Ma Zhen Bei Yao Fang Lun'
Huangqin Lugen Tang	Radix Scutellariae , Radix Ginseng, Cortex Cinnamomi, Poria.	Curing typhoid fever and its complication	'Shen Ji Zong Lu', Vol. 23
Huangqin Qianhuo Tang	Radix Scutellariae , Radix Saposhnikoviae, Radix Glycyrrhizae, Rhizoma Seu Radix Notopterygii.	Curing the pain of supra-orbital bone and phlegmatic hygrosis	'Hui Yue', Vol. 6
Huangqin San	Radix Scutellariae , Radix Puerariae, Radix Glycyrrhizae, Radix et Rhizoma Rhei, Herba Ephedrae, Rhizoma Anemarrhenae,	Curing typhoid fever and its complication	'Shen Hui', Vol. 14
Huangqin Shigao Tang	Radix Scutellariae , Radix paeoniae Alba, Radix Glycyrrhizae, Radix peucedani, Rhizoma Cimicifugae, Gypsum Fibrosum.	Curing the toothache and uloncus	'Si Shen Xin Yuan', Vol. 8
Huangqin Wuwei San	Radix Scutellariae , Radix Coptidis, Radix Astragali, Cortex Phellodendri, Fossilia Ossis Mastodi.	Curing dysentery and abdominal pain	'Wai Tai Mi Fang', Vol. 25
Huangqin Xiebai Tang	Radix Scutellariae , Radix Glycyrrhizae, Cortex Mori, Cortex Lycii.	Curing the lung-heat and the difficulty in micturition	'Zheng Yin Mai Zhi', Vol. 4
Huangqin Zhimu Tang	Radix Scutellariae , Radix Glycyrrhizae, Rhizoma Anemarrhenae, Cortex Phellodendri.	Curing dysentery and abdominal pain of children.	'Shen Ji Zong Lu' Vol 178
Huangqin Yin	Radix Scutellariae , Radix Coptidis, Cortex Phellodendri,	Curing the diseases of intestine	'Shen Ji Zong Lu', Vol. 143
Huangqin Wuwu Tang	Radix Scutellariae , Radix Coptidis, Radix Astragali, Cortex Phellodendri, Fossilia Ossis Mastodi.	Curing dysentery and abdominal pain	'Wai Tai Mi Fang', Vol. 25
Huangqin Shaoyao San	Radix Scutellariae , Radix paeoniae Alba, Poria.	Nourishing yin and removing the heat	'Yi Fang Lei Ju', Vol. 215
Huangqin Huanglian Tang	Radix Scutellariae , Radix Coptidis, Radix Gentianae, Radix Rehmanniae.	Curing cataracta	'Lan Shi Mi Cang'
Huangqin Gao	Radix Scutellariae .	Curing non-traumatic hemorrhage, haematemesis, haematemesis of children	'Yong Le Da Dian', Vol. 133
Huangqin Dingluan Tang	Radix Scutellariae , Radix peucedani, Rhizoma Polygonati Odorati, Rhizoma Coptidis, Fructus Evodiae, Fructus Gardeniae, Pericarpium Citri Reticulatae.	Curing the cholera, hydrodipsia	'Huo Luan Lun', Vol. 4
Huangqin Baizhi San	Radix Scutellariae , Radix Angelicae Sinensis, Radix Stephaniae Tetrandrae, Radix Platycodi, Radix paeoniae Alba, Radix Angelicae Dahuricae, Radix Saposhnikoviae, Rhizoma Cassiae, Rhizoma Chuanxiong, Rhizoma Anemarrhenae, Fructus Atriplicis, Concha Haliotidis. Flos Chrysanthemi, Herba Ephedrae	Curing the diseases of eyes	'Yin Hai Jin Wei'
Huangqin Baizhi Tang	Radix Scutellariae , Radix Angelicae Dahuricae,	Clearing wind-heat pain	'Yi Bu Quan Lu', Vol. 165
Huangqin Beijia Tang	Radix Scutellariae , Radix Bupleuri, Radix Glycyrrhizae, Fructus Gardeniae, Fructus Mume, Carapax Trionycis	Curing typhoid fever and its complication	'Shen Ji Zong Lu', Vol. 33

The references in this table was cited from the Website: <http://www.39yao.cn> and <http://www.zysj.com.cn>.

Table 2The compounds isolated from the genus *Scutellaria*. (The structure of the compounds illustrated in Fig. 2.).

No.	Compounds	Species	References
<i>Flavonoids</i>			
1	Chrysin	<i>S. amoena</i> <i>S. baicalensis</i> <i>S. linearis</i> <i>S. viscidula</i> <i>S. strigillosa</i>	Zhou (1997) Takagi et al. (1980) Hussain et al. (2008) Zhang et al. (2005) Miyaichi et al. (2006)
2	Chrysin-7-O-D-glucuronopyranoside	<i>S. amoena</i> <i>S. prostrata</i> <i>S. grossas</i>	Zhou (1997) Kikuchi et al. (1991a) Kikuchi et al. (1991b)
3	Chrysin-6-C-D-glu-8-C-L-arabinopyranoside	<i>S. baicalensis</i> <i>S. amoena</i>	Takagi et al. (1981) Zhou and Yang (2000)
4	Chrysin-6-C-L-Ara-8-C-D-glucopyranside	<i>S. baicalensis</i>	Takagi et al. (1981) Miyaichi and Tomimori (1994)
5	Chrysin-8-C-D-glucopyranside	<i>S. amoena</i> <i>S. baicalensis</i>	Zhou and Yang (2000) Miyaichi and Tomimori (1995)
6	6-Hydroxyflavone	<i>S. baicalensis</i>	Miyaichi and Tomimori (1994)
7	Baicalin	<i>S. baicalensis</i> <i>S. amoena</i> <i>S. viscidula</i> <i>S. barbata</i> <i>S. lateriflora</i>	Tomimori et al. (1984a) Xiao et al. (2003) Zhang et al. (2005) Lin and Shieh (1996) Makino et al. (2008)
8	Baicalein	<i>S. baicalensis</i> <i>S. hypericifolia</i> <i>S. amoena</i> <i>S. viscidula</i> <i>S. barbata</i> <i>S. lateriflora</i>	Tomimori et al. (1984a) Dong and Chen (1992) Liu et al. (1980) Tomimori and Imoto (1984b) Zhang et al. (2005) Makino et al. (2008)
9	Baicalein-6-O-D-glucuronopyranoside	<i>S. grossas</i>	Kikuchi et al. (1991b)
10	Baicalein-7-O-D-glucopyranside	<i>S. baicalensis</i> . <i>S. amoena</i>	Tomimori et al. (1984a) Zhou (1997)
11	Baicalein-7-O-L-rhamnoside	<i>S. galericulata</i>	Li and Wei (1994)
12	Norwogonin	<i>S. amoena</i> <i>S. baicalensis</i> <i>S. viscidula</i> <i>S. strigillosa</i>	Xiao et al. (2003) Tomimori et al. (1983) Zhang et al. (2005) Miyaichi et al. (2006)
13	Norwogonin-7-O-D-glucuronopyranoside	<i>S. grossas</i> <i>S. prostrata</i>	Kikuchi et al. (1991b) Kikuchi et al. (1991a)
14	Norwogonin-8-O-D-glucuronopyranoside	<i>S. discolor</i>	Tomimori et al. (1988)
15	5-Hydroxy-7,8-dimethoxyflavone	<i>S. baicalensis</i> <i>S. barbata</i>	Tomimori et al. (1983) Zhang et al. (2005)
16	Oroxylin A	<i>S. hypericifolia</i> <i>S. amoena</i> <i>S. baicalensis</i> <i>S. rehderiana</i> <i>S. viscidula</i> <i>S. seleriana</i>	Dong and Chen (1992) Zhou (1997) Huen et al. (2003) Su et al. (2004) Zhang et al. (2005) Esquivel et al. (1998)
17	Oroxylin A-7-O-D-glucuronopyranoside	<i>S. prostrata</i> <i>S. baicalensis</i>	Kikuchi et al. (1991a) Tomimori et al. (1982)
18	Oroxylin A-7-O-D-glucopyranside	<i>S. ovata</i>	Li and Wei (1994)
19	Oroxylin A-7-O-D-glucuronopyranoside methyl ester	<i>S. amoena</i>	Zhou (1997)
20	Wogonin	<i>S. baicalensis</i> <i>S. amoena</i> <i>S. barbata</i> <i>S. viscidula</i> <i>S. rehderiana</i> <i>S. linearis</i> <i>S. lateriflora</i>	Takagi et al. (1980) Xiao et al. (2003) Tomimori et al. (1984a) Wang et al. (2003) Su et al. (2004) Hussain et al. (2008) Makino et al. (2008)
21	Wogonoside	<i>S. baicalensis</i> <i>S. amoena</i> <i>S. linearis</i> <i>S. viscidula</i>	Takagi et al. (1980) Liu et al. (1980) Wang et al. (2003) Zhang et al. (2005)
22	5,8-Dihydroxy-6,7-dimethoxyflavone	<i>S. baicalensis</i>	Tomimori et al. (1984a)
23	5,6-Dihydroxy-7-O-glucosideflavone	<i>S. baicalensis</i>	Tomimori et al. (1984a)
24	5,7,2'-Trihydroxyflavone	<i>S. baicalensis</i>	Tomimori et al. (1984a)

Table 2 (Continued)

No.	Compounds	Species	References
25	5,7,2'-Trihydroxyflavone-7-O-D-glucuronopyranoside	<i>S. likiangensis</i>	Wang et al. (1988)
26	5,7,2'-Trihydroxy-6-methoxyflavone	<i>S. amoena</i> <i>S. baicalensis</i> <i>S. viscidula</i>	Zhou (1997) Tomimori et al. (1984a) Zhang et al. (2005)
27	5,7,2'-Trihydroxy-6-methoxyflavone-7-O-D-glucuronopyranoside methyl ester	<i>S. amoena</i>	Zhou (1997)
28	5,7,2'-Trihydroxy-6-methoxyflavone-7-O-D-glucuronopyranoside	<i>S. amoena</i>	Zhou (1997)
29	5,7,2'-Trihydroxy-6-methoxyflavone-7-O-D-glucopyranside	<i>S. amoena</i>	Zhou (1997)
30	Tenaxin-I	<i>S. tenax</i> <i>S. baicalensis</i>	Liu et al. (1984) Tomimori et al. (1988)
31	Tenaxin-II	<i>S. viscidula</i> <i>S. baicalensis</i>	Liu et al. (1986) Tomimori et al. (1988)
32	Scutevurin	<i>S. indica</i> <i>S. barbata</i> <i>S. baicalensis</i>	Miyaichi et al. (1987) Tomimori et al. (1984a) Tomimori et al. (1988)
33	Scutevurin-7-O-D-glucuronide	<i>S. prostrata</i>	Kikuchi et al. (1991a)
34	Ikonnioside I	<i>S. likiangensis</i>	Wang et al. (1988)
35	5,2'-Dihydroxy-6,7,8-trimethoxyflavone	<i>S. baicalensis</i>	Tomimori et al. (1983)
36	Apigenin	<i>S. prostrata</i> <i>S. barbata</i> <i>S. linearis</i> <i>S. strigillosa</i>	Kikuchi et al. (1991a) Wang (1981) Hussain et al. (2008) Miyaichi et al. (2006)
37	Apigenin-7-O-D-glucopyranside	<i>S. cretica</i>	Li and Wei (1994)
38	Apigenin-7-O-D-glucuronopyranoside	<i>S. prostrata</i> <i>S. alpina</i>	Kikuchi et al. (1991a) Kikuchi et al. (1991c)
39	Scutellarein	<i>S. barbata</i> <i>S. baicalensis</i> <i>S. viscidula</i> <i>S. rehderiana</i>	Wang (1981) Huen et al. (2003) Wang et al. (2003) Su et al. (2004)
40	Scutellarin	<i>S. barbata</i>	Wang (1981)
41	Scutellarein-7-O-D-glucopyranside	<i>S. indica</i>	Miyaichi et al. (1989)
42	4'-Hydroxy wogonin	<i>S. barbata</i>	Liu (2005)
43	Hispidulin	<i>S. barbata</i>	Wang (1981)
44	Hispidulin-7-O-D-glucuronide	<i>S. cretica</i>	Li and Wei (1994)
45	5,7,4'-Trihydroxy-8-methoxyflavone	<i>S. baicalensis</i> <i>S. barbata</i> <i>S. viscidula</i>	Tomimori et al. (1984a) Liu (2005) Wang et al. (2003)
46	Luteloin	<i>S. discolor</i> <i>S. barbata</i> <i>S. linearis</i>	Miyaichi et al. (1987) Wang (1981) Hussain et al. (2008)
47	Luteloin-7-O-D-glucuronopyranoside	<i>S. prostrata</i>	Kikuchi et al. (1991a)
48	Luteloin-7-O-D-glucopyranside	<i>S. cretica</i>	Li and Wei (1994)
49	(2S)5,7,3',4'-Tetrahydroxyflavone (eriodictyol)	<i>S. barbata</i> <i>S. baicalensis</i>	Wang (1981) Takagi et al. (1980)
50	5,7,2'-Trihydroxy-8,6'-dimethoxyflavone	<i>S. baicalensis</i>	Li and Wei (1994)
51	5,8,2'-Trihydroxy-7-methoxyflavone	<i>S. baicalensis</i>	Li and Wei (1994)
52	5,8,2'-Trihydroxy-7-O-D-glucopyranoside	<i>S. barbata</i>	Wang (1981)
53	5,8,2'-Trihydroxy-6,7-dimethoxyflavone	<i>S. baicalensis</i>	Takagi et al. (1980)
54	5,6,2'-Trihydroxy-7,8-dimethoxyflavone	<i>S. grossa</i> <i>S. barbata</i>	Kikuchi et al. (1991b) Lin (1988a)
55	5,6,2'-Trihydroxy-7,8,6'-trimethoxyflavone	<i>S. prostrata</i>	Kikuchi et al. (1991a)
56	5,7,2'-Trihydroxy-6'-methoxyflavone	<i>S. baicalensis</i>	Xiao et al. (2003)
57	5,2'-Dihydroxy-6,7,8,6'-tetramethoxyflavone	<i>S. amoena</i>	Hu et al. (1990)
58	5,2'-Dihydroxy-7,8,6'-trimethoxyflavone	<i>S. barbata</i> <i>S. baicalensis</i> <i>S. indica</i>	Lin (1988a) Tomimori et al. (1984a) Miyaichi et al. (1989)
59	Skullcapflavone I	<i>S. baicalensis</i>	Takagi et al. (1980)
60	Rehderianin I	<i>S. rehderiana</i>	Su et al. (2004)
61	5,2',5'-Trihydroxy-6,7,8-trimethoxyflavone	<i>S. baicalensis</i>	Tomimori et al. (1984a)
62	Viscidulin II	<i>S. viscidula</i>	Yu et al. (1984)
63	Viscidulin II-2'-O-D-glucuronide	<i>S. barbata</i>	Liu (2005)
64	5,2',6'-Trihydroxy-6,7,8-trimethoxyflavone	<i>S. alpina</i>	Kikuchi et al. (1991c)
65	5,2',6'-Trihydroxy-6,7,8-trimethoxyflavone-2'-O-D-glucoside	<i>S. baicalensis</i>	Ishimaru et al. (1995)
66	5,6,2',6'-Tetrahydroxy-7,8-dimethoxyflavone	<i>S. prostrata</i>	Kikuchi et al. (1991d)

Table 2 (Continued)

No.	Compounds	Species	References
67	Skullcapflavone II	<i>S. amoena</i> <i>S. baicalensis</i> <i>S. viscidula</i>	Hu et al. (1990) Makino et al. (2008) Zhang et al. (2005)
68	5,2',6'-Trihydroxy-6,7-dimethoxyflavone-2'-O-D-glucoside	<i>S. baicalensis</i>	Ishimaru et al. (1995)
69	5,7,6'-Trihydroxy-8-methoxyflavone-2'-O-D-(2-caffeoyl)-glucoside	<i>S. discolor</i>	Tomimori et al. (1988)
70	Viscidulin III	<i>S. hypericifolia</i> <i>S. baicalensis</i> <i>S. viscidula</i>	Dong and Chen (1992) Tomimori et al. (1984a) Wang et al. (2003)
71	Viscidulin III-2'-O-D-glucopyranoside	<i>S. baicalensis</i>	Takagi et al. (1980)
72	5,7,8,2'-Tetraflavone-7-O-D-glucuronide	<i>S. barbata</i>	Tomimori et al. (1984a)
73	5,7-Dihydroxy-2'-methoxyflavone	<i>S. prostrata</i>	Kikuchi et al. (1991a)
74	5,7-Dihydroxy-2'-methoxyflavone-7-O-D-glucuronide	<i>S. prostrata</i>	Kikuchi et al. (1991a)
75	5,7-Dihydroxy-8,2'-dimethoxyflavone	<i>S. discolor</i> <i>S. barbata</i>	Miyaichi et al. (1987) Liu (2005)
76	5,7-Dihydroxy-8,2'-dimethoxyflavone-7-O-D-glucuronide	<i>S. indica</i>	Miyaichi et al. (1989)
77	Savlinenin	<i>S. baicalensis</i>	Li and Wei (1994)
78	Acacetin	<i>S. prostrata</i>	Kikuchi et al. (1991a)
79	Acacetin-7-O-D-glucoside (tilianin)	<i>S. polydon</i>	Li and Wei (1994)
80	Pectolinarigenin	<i>S. polydon</i>	Li and Wei (1994)
81	5,7,2',3'-Tetrahydroxyflavone	<i>S. baicalensis</i> <i>S. barbata</i>	Tomimori et al. (1984a) Sonoda et al. (2004)
82	5,7,2',6'-Tetrahydroxyflavone	<i>S. baicalensis</i> <i>S. amoena</i> <i>S. viscidula</i>	Tomimori et al. (1984a) Hu and Liu (1989) Zhang et al. (2005)
83	Altisin	<i>S. grossas</i> <i>S. altissima</i>	Kikuchi et al. (1991b) Li and Wei (1994)
84	5,7-Dihydroxy-8,2',6'-trimethoxyflavone	<i>S. discolor</i>	Miyaichi et al. (1987)
85	Ganhuangenin	<i>S. rehderiana</i> <i>S. baicalensis</i>	Su et al. (2004) Ma et al. (2002)
86	5,7,2',5'-Tetrahydroxyflavone	<i>S. baicalensis</i>	Takagi et al. (1980)
87	5,7,2',5'-Tetrahydroxy-8,6'-dimethoxyflavone	<i>S. baicalensis</i>	Tomimori et al. (1984a)
88	5,7-Dihydroxy-6,8,2',3'-tetramethoxyflavone	<i>S. baicalensis</i>	Tomimori et al. (1982)
89	5,2'-Dihydroxy-7,8,6'-trimethoxyflavone-2'-O-D-glucuronopyranoside	<i>S. barbata</i>	Liu (2005)
90	Ovatin	<i>S. ovata</i>	Li and Wei (1994)
91	5,8-dimethoxyflavone-7-O-D-glucuronopyranoside	<i>S. barbata</i>	Li et al. (2004)
92	6,2'-Dihydroxy-5,7,8,6'-tetramethoxyflavone	<i>S. baicalensis</i>	Tomimori et al. (1981)
93	7-Hydroxy-5,8,2'-trimethoxyflavone	<i>S. discolor</i>	Miyaichi et al. (1987)
94	Cirsilineol	<i>S. barbata</i>	Li et al. (2004)
95	Isoscutellarein	<i>S. prostrata</i> <i>S. indica</i>	Li and Wei (1994) Miyaichi et al. (1989)
96	Isoscutellarein-8-O-D-glucuronide	<i>S. indica</i> <i>S. baicalensis</i>	Miyaichi et al. (1989) Huen et al. (2003)
97	8-Methoxy-5-O-glucoside flavone	<i>S. baicalensis</i>	Tomimori et al. (1981)
98	Wogonin-5-O-D-glucoside	<i>S. baicalensis</i>	Tomimori et al. (1981)
99	3,5,7,2',6'-Pentahydroxyflavone	<i>S. baicalensis</i>	Tomimori et al. (1981)
100	5,7,2',6'-Tetrahydroxyflavonol (Viscidulin I)	<i>S. amoena</i> <i>S. hypericifolia</i> <i>S. baicalensis</i>	Hu et al. (1990) Dong and Chen (1992) Tomimori et al. (1984a)
101	5,7,2',6'-Tetrahydroxyflavonol-2'-O-D-glucopyranside	<i>S. amoena</i>	Zhou (1997)
102	(2R,3R)3,5,7,2'-Tetrahydroxyflavanone	<i>S. amoena</i> <i>S. viscidula</i>	Hu and Liu (1989) Wang et al. (2003)
103	Pinocembrin	<i>S. altissima</i>	Tomimori et al. (1986)
104	Dihydrobaicalin	<i>S. baicalensis</i> <i>S. amoena</i>	Tomimori et al. (1983) Zhou and Yang (2000)
105	Dihydrooroxylin A	<i>S. baicalensis</i>	Tomimori et al. (1983)
106	Dihydronorwogonin	<i>S. amoena</i>	Hu and Liu (1989)
107	Dihydroscutellarein	<i>S. scandens</i>	Miyaichi et al. (1989)
108	(2S)5,7,2'-Trihydroxyflavanone	<i>S. indica</i>	Miyaichi et al. (1987)
109	5,7,2'-Trihydroxy-6-methoxyflavanone-7-O-β-D-glucuronopyranoside	<i>S. amoena</i>	Zhou and Yang (2000)
110	Dihydroscuteverin	<i>S. indica</i>	Miyaichi et al. (1987)
111	Dihydrorehderianin I	<i>S. indica</i>	Miyaichi et al. (1987)
112	Carthamidin	<i>S. barbata</i> <i>S. baicalensis</i>	Xiang et al. (1982) Ishimaru et al. (1995)

Table 2 (Continued)

No.	Compounds	Species	References
113	Carthamidin-7-O-D-glucuronide	<i>S. baicalensis</i>	Tomimori et al. (1984a)
114	Isocarthamidin	<i>S. barbata</i> <i>S. baicalensis</i>	Xiang et al. (1982) Tomimori et al. (1984a)
115	Isocarthamidin-7-O-D-glucuronide	<i>S. baicalensis</i>	Tomimori et al. (1984a)
116	Dihydrohispidulin	<i>S. baicalensis</i>	Ishimaru et al. (1995)
117	(±)5,7,4'-Trihydroxy-8-methoxyflavanone	<i>S. barbata</i> <i>S. baicalensis</i> <i>S. amoena</i>	Liu (2005) Ishimaru et al. (1995) Xiao et al. (2003)
118	5,7,4'-Trihydroxy-6-methoxyflavanone	<i>S. baicalensis</i>	Tomimori et al. (1981)
119	(2S)5,7,2',6'-Tetrahydroxyflavanone	<i>S. baicalensis</i> <i>S. amoena</i> <i>S. viscidula</i>	Ishimaru et al. (1995) Hu and Liu (1989) Wang et al. (2003)
120	Scuteamoenin	<i>S. amoena</i>	Hu and Liu (1989)
121	(2S)-5,2',6'-Trihydroxy-7-methoxyflavanone	<i>S. amoena</i> <i>S. viscidula</i>	Hu and Liu (1989) Wang et al. (2003)
122	(±)5,2'-Dihydroxy-6,7,6'-trimethoxyflavanone	<i>S. discolor</i>	Tomimori et al. (1985)
123	Dihydrorevivularin	<i>S. discolor</i>	Tomimori et al. (1985)
124	Scuteamoenoside	<i>S. amoena</i>	Hu and Liu (1989)
125	(2S)5-Hydroxy-7,8,2',6'-tetramethoxyflavanone	<i>S. grossa</i>	Kikuchi et al. (1991b)
126	(2S)5,7-Dihydroxy-8,2'-dimethoxyflavanone	<i>S. discolor</i>	Tomimori et al. (1985)
127	(2S)5,2-Dihydroxy-7,8,6'-trimethoxyflavanone-2-O-D-glucuronide	<i>S. indica</i>	Miyaichi et al. (1987)
128	(2S)5,7,2',5'-Tetrahydroxy-6-methoxyflavanone	<i>S. scandens</i>	Miyaichi et al. (1988)
129	(2S)5,7,5',2'-Tetrahydroxy-6-methoxyflavanone-2'-O-D-glucoside	<i>S. scandens</i>	Miyaichi et al. (1988)
130	(2S)5,7,5',2'-Tetrahydroxy-6-methoxyflavanone-2'-O-D-(2-O-feruolyl)-glucoside	<i>S. scandens</i>	Miyaichi et al. (1988)
131	(2S)5,7,5',2'-Tetrahydroxy-6-methoxyflavanone-2'-O-D-(2-O-sinapyl)-glucoside	<i>S. scandens</i>	Miyaichi et al. (1988)
132	(2S)5,7,5',2'-Tetrahydroxy-6-methoxyflavanone-2'-O-D-(2-O-vanilloyl)-glucoside	<i>S. scandens</i>	Miyaichi et al. (1988)
133	(2S)7-Hydroxy-5,8,2'-trimethoxyflavanone	<i>S. discolor</i>	Tomimori et al. (1985)
134	(2S)7,2',6'-Trihydroxy-5-methoxyflavanone	<i>S. baicalensis</i>	Tomimori et al. (1984a)
135	Alpinetin	<i>S. barbata</i>	Xiang et al. (1982)
136	(2S)5,6,7,2',3',4',5'-Heptamethoxyflavanone	<i>S. indica</i>	Miyaichi et al. (1989)
137	(2R,3R)3,5,7-trihydroxyflavanone	<i>S. amoena</i>	Hu et al. (1990)
138	5,7,4'-trihydroxyflavanone (naringenin)	<i>S. barbata</i>	Xiang et al. (1982)
139	(2R,3R)-3,5,7,2',6'-Pentahydroxyflavanone	<i>S. baicalensis</i> <i>S. amoena</i> <i>S. viscidula</i> <i>S. linearis</i>	Takagi et al. (1980) Hu et al. (1990) Zhang et al. (2005) Hussain et al. (2008)
140	3,6,7,2',6'-Pentahydroxyflavanone	<i>S. baicalensis</i>	Tomimori et al. (1981)
141	(<i>trans</i>)-5,7,2',6'-Tetrahydroxyflavanonol	<i>S. baicalensis</i>	Takagi et al. (1980)
142	(<i>cis</i>)-5,7,2'-Trihydroxyflavanonol-3-O-β-D-glucopyranoside	<i>S. amoena</i>	Kikuchi et al. (1991b)
143	Amoenin D. [(<i>trans</i>)-5,7,2',6'-tetrahydroxy flavanone 3-O-β-D-glucopyranoside]	<i>S. amoena</i>	Zhou and Yang (2000)
144	Amoenin E. [(<i>cis</i>)-5,7,2',6'-tetrahydroxy flavanone 3-O-β-D-glucopyranoside]	<i>S. amoena</i>	Zhou and Yang (2000)
145	Amoenin B	<i>S. amoena</i>	Zhou and Yang (2000)
146	Amoenin C	<i>S. amoena</i>	Zhou and Yang (2000)
147	8,8'-Bibaiaclein	<i>S. discolor</i>	Tomimori et al. (1985)
148	Amentoflavone	<i>S. linearis</i>	Hussain et al. (2008)
149	Scutellaprostin A	<i>S. prostrata</i>	Kikuchi et al. (1991d)
150	Scutellaprostin B	<i>S. prostrata</i>	Kikuchi et al. (1991d)
151	Scutellaprostin C	<i>S. prostrata</i>	Kikuchi et al. (1991d)
152	Scutellaprostin D	<i>S. prostrata</i>	Kikuchi et al. (1991d)
153	Scutellaprostin E	<i>S. prostrata</i>	Kikuchi et al. (1991d)
154	Scutellaprostin F	<i>S. prostrata</i>	Kikuchi et al. (1991d)
155	2,2'-Dihydroxy-3,4,5,6'-tetramethoxy-4',5'-Methylenedioxychalcone	<i>S. indica</i>	Miyaichi et al. (1989)
156	2,3,4,5,2',4',5',6'-Octamethoxychalcone	<i>S. indica</i>	Miyaichi et al. (1989)
157	2,3,4,5,2',6'-Hexamethoxy-4',5'-Methylenedioxy	<i>S. indica</i>	Miyaichi et al. (1989)
158	2'-Hydroxy-2,3,4,5,4',5',6'-heptamethoxychalcone	<i>S. indica</i>	Miyaichi et al. (1989)
159	2'-Hydroxy-2,3,4,5,6'-pentamethoxy-4',5'-Methylenedioxy	<i>S. indica</i>	Miyaichi et al. (1989)
160	Amoenin A.	<i>S. amoena</i>	Zhou and Yang (2000)
161	2',4'-Dihydroxy-2,3,6'-trimethoxychalcone	<i>S. discolor</i>	Tomimori et al. (1985)
162	2,6,2',4'-Tetrahydroxy-6'-methoxychalcone	<i>S. baicalensis</i>	Li and Wei (1994) Tomimori et al. (1984a)
<i>Phenylethanoid glycosides</i>			
163	2-(3'-Hydroxy-4'-methoxyphenyl)-ethyl-1-O-β-D-glucoside	<i>S. prostrata</i>	Kikuchi et al. (1991a)
164	2-(3'-Hydroxy-4'-methoxyphenyl)-ethyl-1-O-β-D-(4-D-feruolyl)-glucoside	<i>S. prostrata</i>	Kikuchi et al. (1991a)
165	Acetoside	<i>S. prostrata</i> <i>S. albida</i> <i>S. baicalensis</i>	Kikuchi et al. (1991a) Gousiadou et al. (2007) Zhou et al. (1997)
166	Leucosceptoside A	<i>S. prostrata</i> <i>S. baicalensis</i>	Kikuchi et al. (1991a) Zhou et al. (1997)

Table 2 (Continued)

No.	Compounds	Species	References
167	Martynoside	<i>S. prostrata</i> <i>S. albida</i> <i>S. baicalensis</i>	Kikuchi et al. (1991a) Gousiadou et al. (2007) Zhou et al. (1997)
168	2-(3-Hydroxy-4-methoxyphenyl)-ethyl-1-O- α -L-rhamnosyl (1 \rightarrow 3)- β -(4-D-feruolyl)glucoside	<i>S. baicalensis</i>	Zhou et al. (1997)
169	Salidroside	<i>S. baicalensis</i>	Tomimori et al. (1982)
170	Darendoside A	<i>S. baicalensis</i>	Tomimori et al. (1983)
171	Darendoside B	<i>S. baicalensis</i>	Tomimori et al. (1983)
172	Isomartynoside	<i>S. albida</i>	Gousiadou et al. (2007)
173	4-Hydroxy- β -phenylethyl- β -D-glucopyranoside	<i>S. baicalensis</i>	Zhou et al. (1997)
<i>Iridoid glycosides</i>			
174	Catalpol	<i>S. albida</i> <i>S. subvelutina</i>	Gousiadou et al. (2007) Franzyk et al. (1998)
175	Dihydrocatalpol	<i>S. albida</i>	Gousiadou et al. (2007)
176	Scutellarioside I	<i>S. altissima</i>	Wang et al. (1988)
177	Scutellarioside II	<i>S. altissima</i>	Wang et al. (1988)
178	6'-O-E- <i>p</i> -coumaroylgardoside	<i>S. albida</i>	Gousiadou et al. (2007)
179	6'-O- <i>p</i> -E-coumaroyl-8- <i>epi</i> -loganic acid	<i>S. albida</i>	Gousiadou et al. (2007)
180	Antirrhinoside	<i>S. subvelutina</i>	Franzyk et al. (1998)
181	Picroside III	<i>S. albida</i>	Gousiadou et al. (2007)
182	10-Descinnamoylglobularinin	<i>S. albida</i>	Gousiadou et al. (2007)
183	Globularin (scutellaroside-I)	<i>S. albida</i>	Gousiadou et al. (2007)
184	Gardoside	<i>S. albida</i>	Gousiadou et al. (2007)
185	8- <i>Epi</i> -loganic acid	<i>S. albida</i>	Gousiadou et al. (2007)
186	Macfadienoside	<i>S. albida</i>	Gousiadou et al. (2007)
<i>Diterpenes</i>			
187	Scutaltisin	<i>S. columnae</i> var. <i>columnae</i> <i>S. altissima</i>	Malakov and Papanov (1998a) Malakov and Papanov (1996)
188	Ajugapitin	<i>S. lateriflora</i>	Bruno et al. (1998)
189	Scutellone D	<i>S. barbata</i>	Lin (1988a)
190	Scutellone E	<i>S. barbata</i>	Lin (1988a)
191	Scutellone F	<i>S. barbata</i>	Lin (1988b)
192	Scutellone H	<i>S. barbata</i>	Lin (1989)
193	Scutellone I	<i>S. barbata</i>	Lin (1989)
194	Scutellone A	<i>S. barbata</i>	Lin (1987a)
195	Scutellone B	<i>S. barbata</i>	Lin (1988a)
196	Scutellone C	<i>S. barbata</i>	Lin (1988b)
197	Scutellone G	<i>S. barbata</i>	Lin (1989)
198	Jodrellin A	<i>S. woronowii</i> <i>S. rubicunda</i> subsp. <i>rubicunda</i> <i>S. alpina</i> subsp. <i>javallambrensis</i>	Lin (1988a) Bruno et al. (2002) Muñoz et al. (1997)
199	Jodrellin B	<i>S. strigilloso</i> <i>S. rubicunda</i> subsp. <i>rubicunda</i> <i>S. alpina</i> subsp. <i>javallambrensis</i>	Miyaichi et al. (2006) Bruno et al. (1999) Muñoz et al. (1997)
200	Jodrellin T	<i>S. strigilloso</i>	Miyaichi et al. (2006)
201	14,15-Dihydrojodrellin T	<i>S. strigilloso</i>	Miyaichi et al. (2006)
202	Scutecolumnin A	<i>S. altissima</i> <i>S. albida</i>	Malakov and Papanov (1996) Bruno et al. (1996a)
203	Scutecolumnin B	<i>S. altissima</i> <i>S. albida</i>	Malakov and Papanov (1996) Bruno et al. (1996a)
204	Scutecolumnin C	<i>S. columnae</i> var. <i>columnae</i> <i>S. alpina</i> <i>S. alpina</i> subsp. <i>javallambrensis</i> <i>S. altissima</i> <i>S. albida</i>	Malakov and Papanov (1998a) María et al. (1995) Muñoz et al. (1997) Malakov and Papanov (1998a) Bruno et al. (1996a)
205	11-Episcutecolumnin C	<i>S. columnae</i> var. <i>columnae</i>	Malakov and Papanov (1998a)
206	Clerodin	<i>S. altissima</i> <i>S. albida</i>	Malakov and Papanov (1996) Bruno et al. (1996a)
207	Galericulin	<i>S. galericulata</i>	Rodríguez et al. (1996)
208	Scutenisin	<i>S. orientalis</i> subsp. <i>sintensisii</i>	Ezer et al. (1998)
209	Neoandrographolide	<i>S. barbata</i>	Zhu and Liu (1993)
210	Scutedrummonin	<i>S. drummondii</i>	Esquivel et al. (1995)
211	Barbatin A	<i>S. barbata</i>	Dai et al. (2006b)
212	Barbatin B	<i>S. barbata</i>	Dai et al. (2006b)
213	Barbatin C	<i>S. barbata</i>	Dai et al. (2006b)
214	Scuterivulactone A/D	<i>S. barbata</i>	Kizu et al. (1987)
215	Scuterivulactone C ₂	<i>S. barbata</i>	Dai et al. (2006b)
216	Scutelaterin A	<i>S. lateriflora</i>	Bruno et al. (1998)
217	Scutelaterin B	<i>S. lateriflora</i>	Bruno et al. (1998)

Table 2 (Continued)

No.	Compounds	Species	References
218	Scutelaterin C	<i>S. lateriflora</i>	Bruno et al. (1998)
219	Lupulin A	<i>S. linearis</i>	Hussain et al. (2008)
220	Lupulin B	<i>S. linearis</i>	Hussain et al. (2008)
221	Lupulin C	<i>S. linearis</i>	Hussain et al. (2008)
222	Lupulin D	<i>S. linearis</i>	Hussain et al. (2008)
223	11-Deacetylscutalpin	<i>S. alpina</i> subsp. <i>javalambrensis</i>	Muñoz et al. (1997)
224	Scutalsin	<i>S. rubicunda</i> subsp. <i>rubicunda</i> <i>S. altissima</i> <i>S. albida</i>	Bruno et al. (2002) Malakov and Papanov (1996) Bruno et al. (1996a)
225	Scutecyprol A	<i>S. rubicunda</i> subsp. <i>rubicunda</i> <i>S. columnae</i> subsp. <i>gussonei</i> <i>S. cypria</i> subsp. <i>cypria</i>	Bruno et al. (2002) Bruno et al. (2002) Bruno et al. (1996b)
226	Scutecyprol B	<i>S. rubicunda</i> subsp. <i>rubicunda</i> <i>S. rubicunda</i> subsp. <i>linneana</i> <i>S. columnae</i> var. <i>columnae</i> <i>S. cypria</i> subsp. <i>cypria</i>	Bruno et al. (2002) Bruno et al. (1999) Malakov and Papanov (1998a) Bruno et al. (1996b)
227	Scutegrossin A	<i>S. rubicunda</i> subsp. <i>rubicunda</i>	Bruno et al. (2002)
228	Scutalbin A	<i>S. rubicunda</i> subsp. <i>rubicunda</i> <i>S. altissima</i> <i>S. albida</i>	Bruno et al. (2002) Malakov and Papanov (1996) Bruno et al. (1996a)
229	Scutalbin C	<i>S. rubicunda</i> subsp. <i>linneana</i> <i>S. altissima</i> <i>S. albida</i>	Bruno et al. (2002) Malakov and Papanov (1996) Bruno et al. (1996a)
230	Scutalbin B	<i>S. altissima</i> <i>S. albida</i>	Malakov and Papanov (1996) Bruno et al. (1996a)
231	Ajugarin V	<i>S. parvula</i> <i>S. drummondii</i>	Bruno et al. (2004) Esquivel et al. (1995)
232	2 α -Hydroxyajugarin V	<i>S. drummondii</i>	Esquivel et al. (1995)
233	2 α -Hydroxy-deacetylajugarin V	<i>S. drummondii</i>	Esquivel et al. (1995)
234	Scuteparvin	<i>S. parvula</i>	Bruno et al. (2004)
235	11-Episcutecyprin,	<i>S. columnae</i> var. <i>columnae</i>	Malakov and Papanov (1997a)
236	Scuteselerin	<i>S. seleriana</i>	Esquivel et al. (1998)
237	Scutebaicalin	<i>S. baicalensis</i>	Ahmed et al. (1996)
238	Scutalpin L	<i>S. orientalis</i> subsp. <i>pinnatifida</i> <i>S. alpina</i> <i>S. baicalensis</i>	Malakov and Papanov (1997b) María et al. (1995) Ahmed et al. (1996)
239	Scutalpin B	<i>S. alpina</i> <i>S. alpina</i> subsp. <i>javalambrensis</i>	María et al. (1995) Muñoz et al. (1997)
240	Scutalpin D	<i>S. alpina</i> <i>S. alpina</i> subsp. <i>javalambrensis</i>	María et al. (1995) Muñoz et al. (1997)
241	Scutalpin G	<i>S. alpina</i> <i>S. alpina</i> subsp. <i>javalambrensis</i>	María et al. (1995) Muñoz et al. (1997)
242	Scutalpin H	<i>S. alpina</i>	María et al. (1995)
243	Scutalpin I,	<i>S. alpina</i> <i>S. alpina</i> subsp. <i>javalambrensis</i>	María et al. (1995) Muñoz et al. (1997)
244	Scutalpin J	<i>S. alpina</i> <i>S. alpina</i> subsp. <i>javalambrensis</i> <i>S. orientalis</i> subsp. <i>sintensisii</i>	María et al. (1995) Muñoz et al. (1997) Ezer et al. (1998)
245	Scutalpin K	<i>S. alpina</i>	María et al. (1995)
246	Scutalpin M	<i>S. alpina</i>	María et al. (1995)
247	Scutalpin O	<i>S. alpina</i>	Malakov and Papanov (1998b)
248	Scutalpin N	<i>S. alpina</i>	Malakov and Papanov (1998b)
249	Scutalpin E	<i>S. orientalis</i> subsp. <i>sintensisii</i>	Ezer et al. (1998)
250	Scutalpin C	<i>S. alpina</i> subsp. <i>javalambrensis</i>	Muñoz et al. (1997)
251	Scutorientalin A	<i>S. orientalis</i> subsp. <i>pinnatifida</i>	Malakov and Papanov (1997b)
252	Scutorientalin B	<i>S. orientalis</i> subsp. <i>pinnatifida</i>	Malakov and Papanov (1997c)
253	Scutorientalin C	<i>S. orientalis</i> subsp. <i>pinnatifida</i>	Malakov and Papanov (1997c)
254	Scutorientalin D	<i>S. orientalis</i> subsp. <i>pinnatifida</i>	Malakov and Papanov (1997c)
255	Scutorientalin E	<i>S. orientalis</i> subsp. <i>pinnatifida</i>	Malakov and Papanov (1997c)
256	Scutegalin B	<i>S. galericulata</i>	Rodríguez et al. (1996)
257	Scutegalin C	<i>S. galericulata</i>	Rodríguez et al. (1996)
258	Scutegalin D	<i>S. columnae</i> var. <i>columnae</i> <i>S. galericulata</i>	Rodríguez et al. (1996) Malakov and Papanov (1998a)

Table 2 (Continued)

No.	Compounds	Species	References
<i>Triterpenoids</i>			
259	Scutellaric acid	<i>S. barbata</i>	Zhu and Liu (1993)
260	Ursolic acid	<i>S. strigillosa</i>	Miyaichi et al. (2006)
<i>Neo-Clerodane Diterpenoid Alkaloids</i>			
261	Scutebarbatine A	<i>S. barbata</i>	Wang and Li (1996)
262	Scutebarbatine B	<i>S. barbata</i>	Dai et al. (2006a)
263	Scutebarbatine C	<i>S. barbata</i>	Dai et al. (2006a)
264	Scutebarbatine D	<i>S. barbata</i>	Dai et al. (2006a)
265	Scutebarbatine E	<i>S. barbata</i>	Dai et al. (2006a)
266	Scutebarbatine F	<i>S. barbata</i>	Dai et al. (2006a)
267	Scutebarbatine G	<i>S. barbata</i>	Dai et al. (2007)
268	6,7-Di-O-nicotinoylscutebarbatine G	<i>S. barbata</i>	Dai et al. (2007)
269	6-O-nicotinoyl-7-O-acetylscutebarbatine G	<i>S. barbata</i>	Dai et al. (2007)
270	Scutebarbatine H	<i>S. barbata</i>	Dai et al. (2007)
271	7-O-nicotinoylscutebarbatine H	<i>S. barbata</i>	Dai et al. (2007)
<i>Alkaloids</i>			
272	Sophoranol	<i>S. flavescens</i>	Ma et al. (2002)
273	Sophoridine	<i>S. flavescens</i>	Ma et al. (2002)
274	Allmatrine	<i>S. flavescens</i>	Ma et al. (2002)
275	Anagyrine;	<i>S. flavescens</i>	Ma et al. (2002)
276	Cytosine	<i>S. flavescens</i>	Ma et al. (2002)
277	Isomatrine	<i>S. flavescens</i>	Ma et al. (2002)
278	Matrine	<i>S. flavescens</i>	Ma et al. (2002)
279	N-methylcytisine	<i>S. flavescens</i>	Ma et al. (2002)
280	Oxymatrine	<i>S. flavescens</i>	Ma et al. (2002)
281	Osysophocarpine	<i>S. flavescens</i>	Ma et al. (2002)
282	Sophocarpine	<i>S. flavescens</i>	Ma et al. (2002)
<i>Others compounds</i>			
283	Aurantiamide acetate	<i>S. barbata</i>	Lin (1987b)
284	Daucosterol	<i>S. barbata</i>	Liu (2005)
<i>Phytosterols</i>			
285	6 β -Hydroxy-4-stigmasten-3-one	<i>S. strigillosa</i>	Miyaichi et al. (2006)
286	6- β -Hydroxy-4,22-stigmastadien-3-one	<i>S. strigillosa</i>	Miyaichi et al. (2006)
<i>Tocopherols</i>			
287	2 R, 4' R, 8' R- γ -tocopherol	<i>S. strigillosa</i>	Miyaichi et al. (2006)
288	(S)-5,5'-Bi- γ -tocopheryl	<i>S. strigillosa</i>	Miyaichi et al. (2006)
289	(R)-5,5'-Bi- γ -tocopheryl	<i>S. strigillosa</i>	Miyaichi et al. (2006)
290	Solanachromene	<i>S. strigillosa</i>	Miyaichi et al. (2006)
291	Tocopherylquinone	<i>S. strigillosa</i>	Miyaichi et al. (2006)
292	Pinosylvin	<i>S. scandens</i>	Li and Wei (1994)
293	Pinosylvin-2-carboxylic acid	<i>S. scandens</i>	Li and Wei (1994)
294	Pinosylvin-3-O- β -D-glucoside	<i>S. scandens</i>	Li and Wei (1994)
295	Gaylussacin	<i>S. scandens</i>	Li and Wei (1994)

The leaves of *S. scandens* are used to treat wounds and swelling by insects in Nepal (Li and Wei, 1994). *S. albida* ssp. *albida* is a herbaceous perennial plant and has a general distribution from N. Italy to the Balkan Peninsula and Crimea (Bothmer, 1985). It presents antispasmodic, diaphoretic and febrifuge properties and was used in local medicine (Duke, 1986). The aerial parts of *S. rubicunda* subsp. *Linneana* an endemic species growing in the central part of Sicily has antifeedant and anti-fungal activities (Bruno et al., 1999).

3. Phytochemistry

From the genus *Scutellaria*, 295 compounds were isolated, including flavonoids, phenylethanoid glycosides, iridoid glycosides, diterpenes, triterpenoids, alkaloids, phytosterols, polysaccharides and other compounds (Table 2). Some of them displayed many bioactivities *in vivo* or *in vitro* (Table 3).

3.1. Flavonoids

Flavonoids and their derivatives are the main components of the *Scutellaria* genus. More than 160 compounds, including flavones (1–99) and flavonols (100–101), flavanones (102–136) and flavanonols (137–146), biflavonoids (147–148), flavonolignans (149–154), chalcones (155–162), have been isolated. Most of them

have methoxyl or hydroxyl groups at various positions on their aromatic rings.

3.1.1. Flavones and flavonols

Compounds 1–101 isolated from the *Scutellaria* genus are flavones and flavonols. Among these compounds, baicalin (7), baicalein (8), oroxylin A (16), wogonin (20), wogonoside (21), apigenin (36), scutellarein (39), 5,7,4'-trihydroxy-8-methoxyflavone (45), luteolin (46), viscidulin III (70), 2',3',5,7-tetrahydroxyflavone (81) and ganhuangenin (85) from *S. baicalensis*, *S. barbata* or *S. laterifolia*, have been confirmed to have antitumor, hepatoprotective, antioxidant, anti-inflammatory, anti-RSV, antimutagenic, neuroprotective, anxiolytic, and other activities. The relationship between compound structures and their activities have been elucidated. For example, the methoxyl group on C(8), wogonin (20) and wogonoside (21) shows stronger inhibition toward histamine and IgE production than 3,5,7,2',6'-pentahydroxyflavanone (139). On the other hand, 3,5,7,2',6'-pentahydroxyflavanone (139) with two hydroxyl groups in the B ring shows stronger activity than wogonin (20) and wogonoside (21) against lipid peroxidation (Lim, 2003).

3.1.2. Flavanones and flavanonols

Flavanones and flavanonols 102–146 with various substitutions have been isolated from *S. baicalensis*, *S. amoena*, *S.*

Table 3The activities of some compounds from *S. baicalensis*, *S. barbata*, *S. laterifolia*, *S. rubicunda*.

Compounds	Species	Effects	<i>In vivo</i>	<i>In vitro</i>	Ref.
Baicalein	<i>S. baicalensis</i>	Antitumor		100 μ M Inhibited TGF- β 1-induced apoptosis via increase in cellular H2O2 formation and NF- κ B activation in human hepatoma Hep3B cells ($p < 0.01$)	Chou et al. (2003)
				12.5 μ M Prevented cisplatin-induced apoptosis through inhibition of the mitochondrial depolarization in human glioma cells	Lee et al. (2005)
				50 μ M Prevented carcinogen-DNA adduct formation ($p < 0.01$)	Chan et al. (2002)
		Hepatoprotective	Inhibited protein nitration and lipid peroxidation in liver homogenate and the oxidation of protein in liver microsome	Inhibited the decrease of cell viability and the contents of GSH in HepG2 cells, the inhibition order was baicalein > baicalin > wogonin	Tan et al. (2006)
		Antioxidant		400 μ M Scavenged hydroxyl radical, DPPH radical and alkyl radical in a dose-dependent manner	Gao et al. (1999)
		Anti-inflammatory effects		75 μ M Inhibited inflammation through inhibition of COX-2 gene expression through blockade of C/EBP β DNA binding activity	Woo et al. (2006)
				Bond a variety of chemokines and limit their biological function.	Li et al. (2000a)
		Anti-RSV		50% inhibition concentration (IC50) 20.8 μ g/ml	Ma et al. (2002)
		Antimutagenesis		Baicalin, baicalein, wogonin (at 250 μ g/plate) suppressed 47%, 93%, 41% of NQNO mutagenic activity with TA98 strain and 72%, 62%, 57% of NQNO mutagenic activity with TA100 strain, respectively. And suppressed 64%, 99%, 79%, 95% of the 2-aminofluorene mutagenic activity with TA98 and 94%, 100%, 85% and 100% at the same concentration with TA100, respectively. So they inhibited both direct and indirect the types of mutagens and clearly in the Ames test	Woz'niak et al. (2004)
				Possessed strong antiradical properties in the DPPH assay	Johan et al. (2005)
	<i>S. laterifolia</i>	Neuroprotective effect and memory improvement		Prevented neurotoxicity induced by both glutamate and glucose deprivation in primary cultured rat brain neurons by protecting PC12 cells from hydrogen peroxide-induced toxicity	Lee et al. (2003)
				Protected neurons from the deleterious effects of 6-hydroxydopamine via the attenuation of oxidative stress, mitochondrial dysfunction, caspase activity, and JNK activation	Lee et al. (2005)
		Anxiolytic	Displayed anxiolytic effect in rats through bind to the benzodiazepine site of the GABA _A receptor		Awad et al. (2003)

Baicalin	<i>S. baicalensis</i>	Antitumor		20 μ M Inhibited EROD activities and reduced CYP1A1/1B1 mRNA expression induced by DMBA. At the same time it could reduce DMBA–DNA adduct formation in MCF-7 cells. ($p < 0.01$). So it could inhibit the proliferation of prostate cancer cells	Chan et al. (2000)
		Hepatoprotective	Exhibited the best hepatoprotective effect on CC14-induced liver injuries at the 10 mg/kg concentration		Lin and Shieh (1996)
		Anti-oxidative	20 mg/kg Played the key role of the anti-oxidative properties in the regulation of age-related alterations ($p < 0.01$).		Kim et al. (2006)
		Anti-RSV		With 50% inhibition concentration 20.8 μ g/ml	Ma et al. (2002)
				Inhibited superantigenic staphylococcal exotoxins-stimulated T-cell proliferation, decreased the production of IL-1, IL-6, TNF, interferon γ , monocyte chemotactic protein 1, MIP-1 α , and MIP-1 β mRNA and protein by human peripheral blood mononuclear cells.	Krakauer et al. (2001)
				Mitigated the pathogenic effects of staphylococcal exotoxins by inhibiting the signaling pathways activated by superantigens.	Liu et al. (2000)
				Possessed strong antiradical properties in the DPPH assay	Johan et al. (2005)
		Neuroprotective effect and memory improvement		Prevented neurotoxicity induced by glutamate deprivation by protecting PC12 cells from hydrogen peroxide-induced toxicity	Lee et al. (2003)
		Anti-HIV-1		At the noncytotoxic concentrations, inhibited both T cell tropic (X4) and monocyte tropic (R5) HIV-1 Env protein mediated fusion with cells expressing CD4/CXCR4 or CD4/CCR5. and blocked the replication of HIV-1 early strong stop DNA in cells at the initial stage of HIV-1 viral adsorption	Li et al. (2000b)
				In the T cell strain CEM infected by HIV virus, it displayed the marked cytotoxic, made DNA damage, especially for the CEM-HIV cell which released massive HIV virus.	Wu et al. (2001)
	<i>S. laterifolia</i>	Anxiolytic	Performed anxiolytic effect in rats through bind to the benzodiazepine site of the GABAA receptor		Awad et al. (2003)

Table 3 (Continued)

Compounds	Species	Effects	<i>In vivo</i>	<i>In vitro</i>	Ref.
Wogonin	<i>S. baicalensi</i>	Antitumor		As a potential adjuvant therapy for drug-resistant human non-small lung cancer, especially for those with the aldo-keto reductases superfamily overexpression. 10 μ M inhibited IL-6-induced AKR1C1/1C2 expression and drug resistance	Wang et al. (2007)
				200 μ M 72 h Did not affect the proliferation of normal fetal lung diploid cells but did inhibit the proliferation of monocytic leukemia cells and osteogenic sarcoma cells. Had a cancer-specific apoptosis-inducing activity	Himeji et al. (2007)
	<i>S. barbata</i>			Inhibited the proliferation of HL-60, IC50 17.4 μ M	Sonoda et al. (2004)
	<i>S. baicalensis</i>	Hepatoprotective	5, 10 mg/kg Decreased the toxicity produced by D-GalN ($p < 0.01$) and APAP-induced hepatotoxicity		Lin and Shieh (1996)
		Anti-HBV	Inhibited the Duck hepatitis B virus DNA polymerase with an IC50 of 0.57 μ g/ml. wogonin dosed i.v. once a day for 10 days reduced plasma DHBV DNA level with an ED50 of 5mg/kg in DHBV-infected ducks and reduced plasma HBsAg level in human HBV-transgenic mice.	Suppressed the secretion of the HBV antigens with an IC50 of 4 μ g/ml at day 9 for both HBsAg and HbeAg and reduced HBV DNA level in a dose-dependent manner in the human HBV-transfected liver cell line HepG2.2.15.	Guo et al. (2007)
		Antioxidant	Inhibited histamine release in cells stimulated with calcium ionophore A23187 or compound 48/80, and alleviated the increase in the IgE content induced by concanavalin A		Lim et al. (1999), Lim, 2003
		Anti-inflammatory	As a direct COX-2 inhibitor. Cured skin inflammatory diseases by modulating of the expression of proinflammatory molecules. Wogonin (1000 mg/ear/3 days) slightly increased COX-1 and fibronectin mRNA. On the other hand, wogonin (250–1000 mg/ear/3 days) potentially lowered mRNA levels of COX-2 and TNF- α with less effect on intercellular adhesion molecule-1 and interleukin-1b in a sub-chronic skin inflammation model of tetradecanoylphorbol-13-acetate-induced ear edema		Chi et al. (2000) Chi et al. (2003)
			At 200 mg/site/treatment, wogonin caused a 55.3% reduction of prostaglandin E2 production on the dorsal skin compared with an increased production in the TPA-treated control group. And inhibited mouse ear edema induced by TPA in both preventive (58.1% inhibition) as well as curative treatment (31.3% inhibition). So it might be beneficial for COX-2-related skin disorders	Controlled the expression COX-2 down regulation of skin fibroblast from skin fibroblasts in culture against skin inflammation	Park et al. (2001) Chi and Kim (2005)

		Anticonvulsant	10 mg/kg Displayed the anticonvulsant by mediating the GABA ergic neuron ($p < 0.01$)		Park et al. (2007)
		Anti-RSV		With 50% inhibition concentration 7.4 $\mu\text{g/ml}$	Ma et al. (2002)
		Neuroprotective effect and memory improvement		Had a protective effect on neuronal cells damaged by oxygen and glucose deprivation in rat hippocampal slices in culture	Son et al. (2004)
				Might have a neurotoxic effect on the brain	Lee et al. (2003)
		Anxiolytic		Exerted the anxiolytic effect through positive allosteric modulation of the GABAA receptor complex via interaction at the BZD-S.	Hui et al. (2002)
Barbatins A-C, and Scutebarbtine B	<i>S. barbata</i>	Antitumor		Showed significant cytotoxic activities against HONE-1 nasopharyngeal, KB oral epidermoid carcinoma, and HT 29 colorectal carcinoma cells, with IC50 values in the range 3.5–8.1 μM	Dai et al. (2006a,b)
2',3',5,7-tetrahydroxy flavone	<i>S. barbata</i>	Antitumor		Inhibited the proliferation of HL-60, IC50 = 9.5 μM .	Sonoda et al. (2004)
Apigenin	<i>S. barbata</i>	Antitumor		Inhibited the proliferation of HL-60, IC50 = 15.0 μM	Sonoda et al. (2004)
Viscidulin III	<i>S. barbata</i>	Antitumor		Inhibited the proliferation of HL-60, IC50 = 17.4 μM	Sonoda et al. (2004)
Luteolin	<i>S. barbata</i>	Antitumor		Inhibited the proliferation of HL-60, IC50 = 18.4 μM .	Sonoda et al. (2004)
Ganhuangenin	<i>S. baicalensis</i>	Antioxidant	Inhibited histamine release in cells stimulated with calcium ionophore A23187 or compound 48/80, and alleviated the increase in the IgE content induced by concanavalin A in the amounts of 10 and 100 mM		Lim et al. (1999)
		Anti-RSV		With 50% inhibition concentration 83.3 $\mu\text{g/m}$	Ma et al. (2002)
3,5,7,2',6'-pentahydroxyl flavanone	<i>S. baicalensis</i>	Antioxidant	Inhibited histamine release in cells stimulated with calcium ionophore A23187 or compound 48/80 and inhibited LTB4 production and inhibited the release of lipid peroxidation induced by ConA was in order of PHF > WG > WGS		Lim, 2003
Oroxylin A	<i>S. baicalensis</i>	Anti-RSV		With 50% inhibition concentration 14.5 $\mu\text{g/m}$	Ma et al. (2002)
		Neuroprotective effect and memory improvement		Protected cognitive impairments induced by cholinergic dysfunction via the GABAergic nervous system.	Kim et al. (2007)
Scutellarein	<i>S. baicalensis</i>	Anti-RSV		With 50% inhibition concentration 20.8 $\mu\text{g/m}$	Ma et al. (2002)
5,7,4'-trihydroxy-8-methoxyflavone	<i>S. baicalensis</i>	Anti-RSV		Reduced the single-cycle replication of A/PR8 from 4 h to 12 h after incubation and the dose which decrease the virus titer one tenth was 11 μM .	Nagai et al. (1995)
Scutecepyrol B	<i>S. rubicunda</i>	Antifeedant		Showed significant activity against larvae from all the five species tested at 100 ppm.	Bruno et al. (1999)
Jodrellin A, Jodrellin B, Scutalbin A and Scutecepyrol B	<i>S. rubicunda</i>	Antifeedant		Had potent antifeedant activity against all five species of <i>Lepidoptera</i> .	Bruno et al. (2002)

indica, *S. barbata*, *S. scandens* and other species. 3,5,7,2',6'-Pentahydroxyflavanone (**139**) can markedly inhibit histamine release and inhibit LTB₄ production in cells stimulated with calcium ionophore A23187 or compound 48/80 at a concentration of 100 mM. At the same time, the inhibitory effects on the content of lipid peroxidation induced by ConA was in the order of 3,5,7,2',6'-pentahydroxyl flavanone > Wogonin > Wogonoside (Lim, 2003).

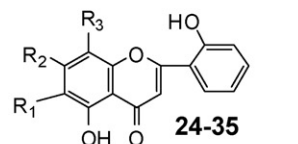
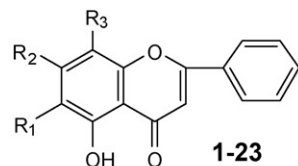
3.1.3. Biflavonoids

There are two biflavonoids (**147,148**) reported. 8,8'-Bibaiaclein (**147**) was reported from *S. discolor*, and compounds with this structure have two baicalein molecules connected at C (8) (Tomimori et

al., 1985). Amentoflavone (**148**) was obtained from *S. linearis*, and the structure was two different flavones connected by C (5')-C (8) (Hussain et al., 2008). The biflavonoids usually exist in Gymnosperms. In the *Scutellaria* genus, only these two compounds have been isolated.

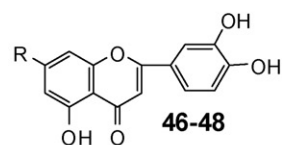
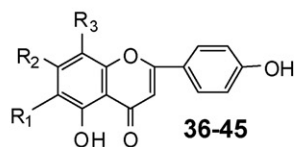
3.1.4. Flavonolignans

Up to now, only six flavonolignans have been isolated from the genus *Scutellaria*. In 1991, Kikuchi et al obtained scutellaprostins (A–F) (**149–154**) from *S. prostrata* for the first time, and the structure of these compounds were determined to be formed by the polymerization between the A ring of flavonoids and lignans (Kikuchi et al., 1991d).



No.	R ₁	R ₂	R ₃
24	H	OH	H
25	H	GluA	H
26	OCH ₃	OH	H
27	OCH ₃	O-Glu A Et ester	H
28	OCH ₃	O-Glu A	H
29	OCH ₃	O-Glu	H
30	OCH ₃	OCH ₃	OCH ₃
31	OCH ₃	OH	H
32	H	OH	OCH ₃
33	H	O-D-GluA	OCH ₃
34	OH	O-Glu A	H
35	OCH ₃	OCH ₃	OCH ₃

	R ₁	R ₂	R ₃
1	H	OH	H
2	H	O-GluA	H
3	Glu	OH	Ara
4	Ara	OH	Glu
5	H	OH	Glu
6	OH	H	H
7	OH	O-GluA	H
8	OH	OH	H
9	O-GluA	OH	H
10	OH	O-Glu	H
11	OH	O-rha	H
12	H	OH	OH
13	H	O-GluA	OH
14	H	OH	O-GluA
15	H	OCH ₃	OCH ₃
16	OCH ₃	OH	H
17	OCH ₃	O-GluA	H
18	OCH ₃	O-Glu	H
19	OCH ₃	O-GluA Et ester	H
20	H	OH	OCH ₃
21	H	O-GluA	OCH ₃
22	OCH ₃	OCH ₃	OH
23	OH	O-Glu	H



	R
46	OH
47	O-GluA
48	O-Glu

	R ₁	R ₂	R ₃
36	H	OH	H
37	H	O-Glu	H
38	H	O-GluA	H
39	OH	OH	H
40	OH	O-Glu	H
41	OH	O-GluA	H
42	H	OH	OCH ₃
43	OCH ₃	OH	H
44	OCH ₃	O-GluA	H
45	H	OH	OCH ₃

Fig. 2. The chemical structure of isolated compounds from the genus *Scutellaria* (the name of chemical compound listed in Table 2).

3.1.5. Chalcones

Due to the breakage of chemical bond between C1 and C2, compounds **155–162** belong to the Chalcones. **155–159** are five simple chalcones isolated from *S. indica* (Miyaichi et al., 1989). Amoenin A (**160**) was obtained from *S. amoena* in 2000 (Zhou and Yang, 2000). 2',4'-dihydroxy-2,3,6'-trimethoxy-chalcone (**161**), 2,6,2',4'-tetrahydroxy-6'-methoxychalcone (**162**) were isolated from *S. discolor* and *S. baicalensis* (Li and Wei, 1994; Tomimori et al., 1984a).

3.2. Phenylethanoid glycosides

10 Phenylethanoid glycosides identified from the genus *Scutellaria*. 2-(3'-hydroxy-4'-methoxyphenyl)-ethyl-1-O- α -L-rhamnosyl (1 \rightarrow 3)- β -(4-D-feruolyl)glucoside (**163**) and 2-(3'-hydroxy-4'-methoxyphenyl)-ethyl-1-O- β -D-(4-D-feruolyl)-glucoside (**164**) obtained from *S. prostrata* (Kikuchi et al., 1991a). Acetoside

(**165**), Leucosceptoside A (**166**), Martynoside (**167**) were isolated from *S. prostrata*, *S. albida* ssp. *albida*, *S. baicalensis*, respectively (Kikuchi et al., 1991a; Gousiadou et al., 2007; Zhou et al., 1997). Moreover, 2-(3-hydroxy-4-methoxyphenyl)-ethyl-1-O- α -L-rhamnosyl (1 \rightarrow 3)- β -(4-D-feruolyl)glucoside (**168**), salidroside (**169**), darendoside A (**170**), darendoside B (**171**), 4-hydroxy- β -phenylethyl- β -D-glucopyranoside (**173**) were isolated from *S. baicalensis* (Zhou, 1997; Tomimori et al., 1982, 1983). Gousiadou et al. (2007) isolated one known phenylethanoid glycosides from *S. albida*, isomartynoside (**172**).

3.3. Iridoid glycosides

After successful chromatography on silica gel columns and RP-HPLC, **13** iridoid glycosides were isolated from the methanol extract of the aerial parts of *S. albida* ssp. *albida* (Gousiadou et al., 2007).

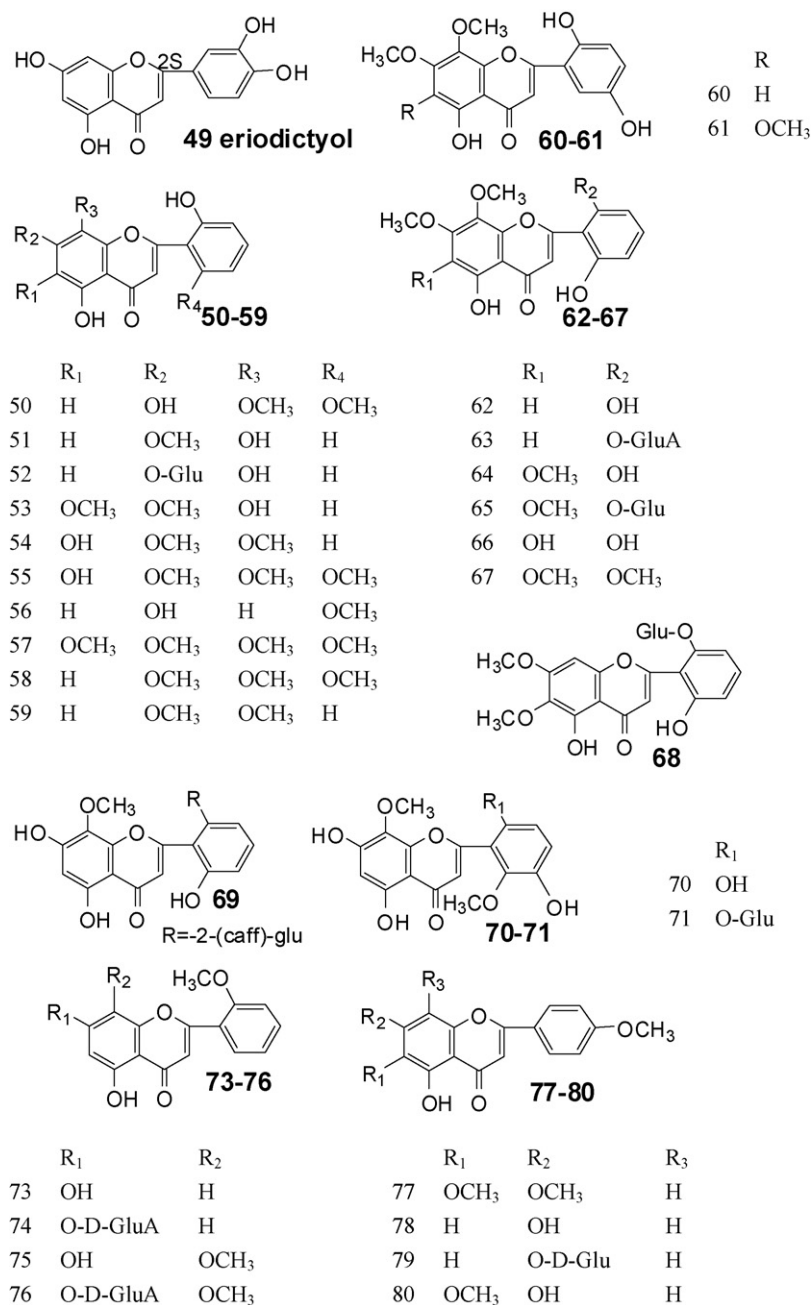


Fig. 2. (Continued)

Other iridoid glycosides were isolated from the aerial parts of *S. subvelutina* (Franzyk et al., 1998).

3.4. Diterpenes

The genus is rich in neoclerodane diterpenoids (187–258), which usually show some heterocyclic function. These include the epoxides, lactones, hydrofurans groups. Many of these prod-

ucts have remarkable antifeedant activity against pest insects. Especially, jodrellin A (198), jodrellin B (199), scutalbin A (228) and scutecypol B (230) from *S. rubicunda* subsp. *rubicunda* have been found to have potent antifeedant activity against all five species of *Lepidoptera* (Bruno et al., 1999). At the same time, barbatins A–C (211–213), show significant cytotoxic activity against HONE-1 nasopharyngeal (IC_{50} = 4.7 μ M, 5.0 μ M, 4.1 μ M), KB oral epidermoid carcinoma (IC_{50} = 7.7 μ M, 8.1 μ M, 7.1 μ M) and HT 29

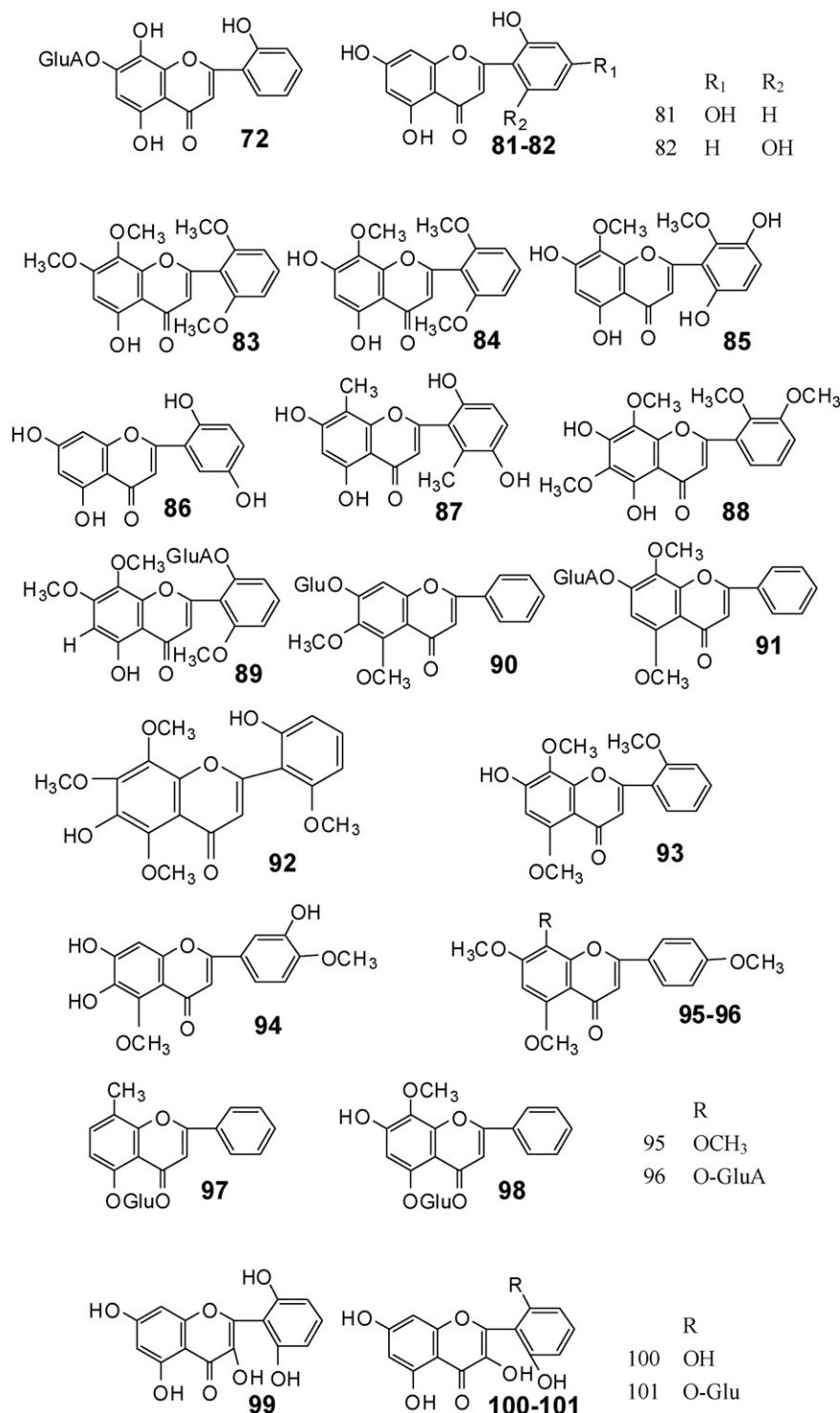


Fig. 2. (Continued)

colorectal carcinoma cells (IC_{50} = 5.9 μ M, 6.6 μ M, 4.3 μ M) (Dai et al., 2006a,b).

3.5. Triterpenoids

In 1993, Zhu et al. isolated an oleanane-type triterpenoid acid, scutellaric acid (**259**) from *S. barbata* for the first time (Zhu and Liu, 1993). In 2006, Miyaichi et al. isolated one known triterpenoid, ursolic acid (**260**) from the leaves of *S. strigillosa* (Miyaichi et al., 2006).

3.6. Neo-clerodane diterpenoid alkaloids

In 1996, scutebarbatine A (**261**), a new neoclerodane-type diterpenoid alkaloid was isolated from *S. barbata* for the first time (Wang and Li, 1996). In 2006, 2007, Dai et al. (2006a,b, 2007) obtained scutebarbatines and its derivatives (**262–2271**) from *S. barbata*. Scutebarbatine B (**262**) showed significant cytotoxic activities against HONE-1 nasopharyngeal (IC_{50} = 4.4 μ M), KB oral epidermoid carcinoma (IC_{50} = 6.1 μ M) and HT 29 colorectal carcinoma cells (IC_{50} = 3.5 μ M) (Dai et al., 2006a,b).

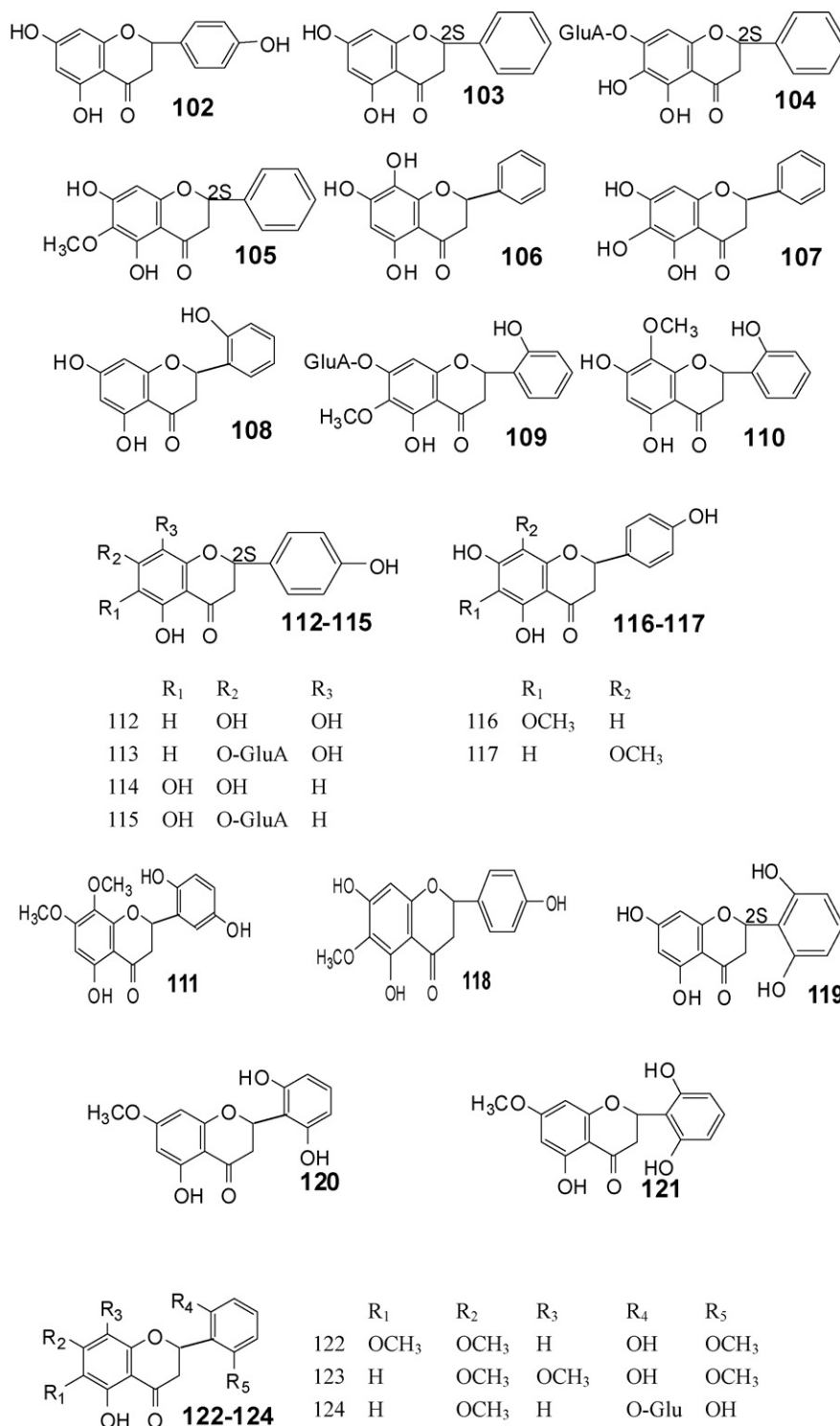


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3.7. Alkaloids

Only eleven alkaloids (**272–282**) were isolated from *S. flavescens* by column chromatography using silica gel and aluminum oxide in 2002 (Ma et al., 2002). Among these compounds, sophoranol (**272**), anagyrene (**275**), oxymatrine (**280**) showed potent antiviral activities against RSV with IC_{50} values of 10.4 μ g/ml and SI values of 24.0, 24.0 and 12.0.

3.8. Essential oils

The essential oils of only a few species of *Scutellaria* have been investigated. The oil of *S. albida* ssp. *albida* from Greece was characterized by the presence of high concentrations of linalool (52.6%) and *trans*-nerolidol (9.0%) (Skaltsa et al., 2000). Other species from Greece, *S. sieberi* and *S. rupestris* ssp. *adenotricha* also contain high amounts of linalool, 22.7% and 38.8%, respectively (Skaltsa et al., 2005). The main components in the oil from

aerial parts of *S. barbata* from China are hexahydrofarnesyl acetone (11.0%), 3,7,11,15-tetramethyl-2-hexadecen-1-ol (7.8%), menthol (7.7%) and 1-octen-3-ol (7.1%) (Yu et al., 2004). The oil of *S. lateriflora* from Iran is composed of sesquiterpenes (78.3%) of which β -cadinene (27.0%) and calamenene (15.2%) are major components along with β -elemene (9.2%), α -cubebene (4.1%) and α -humulene (4.2%) (Yaghmai, 1988). Lawrence et al. (1972) described sesquiterpenes in the oils of *S. galericulata* and *S. parvula*. The former was characterized by high content of sesquiterpene hydrocarbons with caryophyllene (29.4%) and *trans*- β -farnesene (17.0%) as the main components, while the latter showed α -bisabolol (20.6%) as the main compound accompanied by *trans*- α -bergamotene (13.4%). The main components of the oil from roots of *S. baicalensis* are acetophenone, (E)-4-phenyl-3-buten-2-one, 1-phenyl-1,3-butandione, palmitic and oleic acids (Katsuya et al., 1987). Linalool (27.8%), Caryophyllene (28.7%) are the main compounds from *S. rubicunda* subsp. *linnaeana* endemic in Sicily (Rosselli et al., 2007).

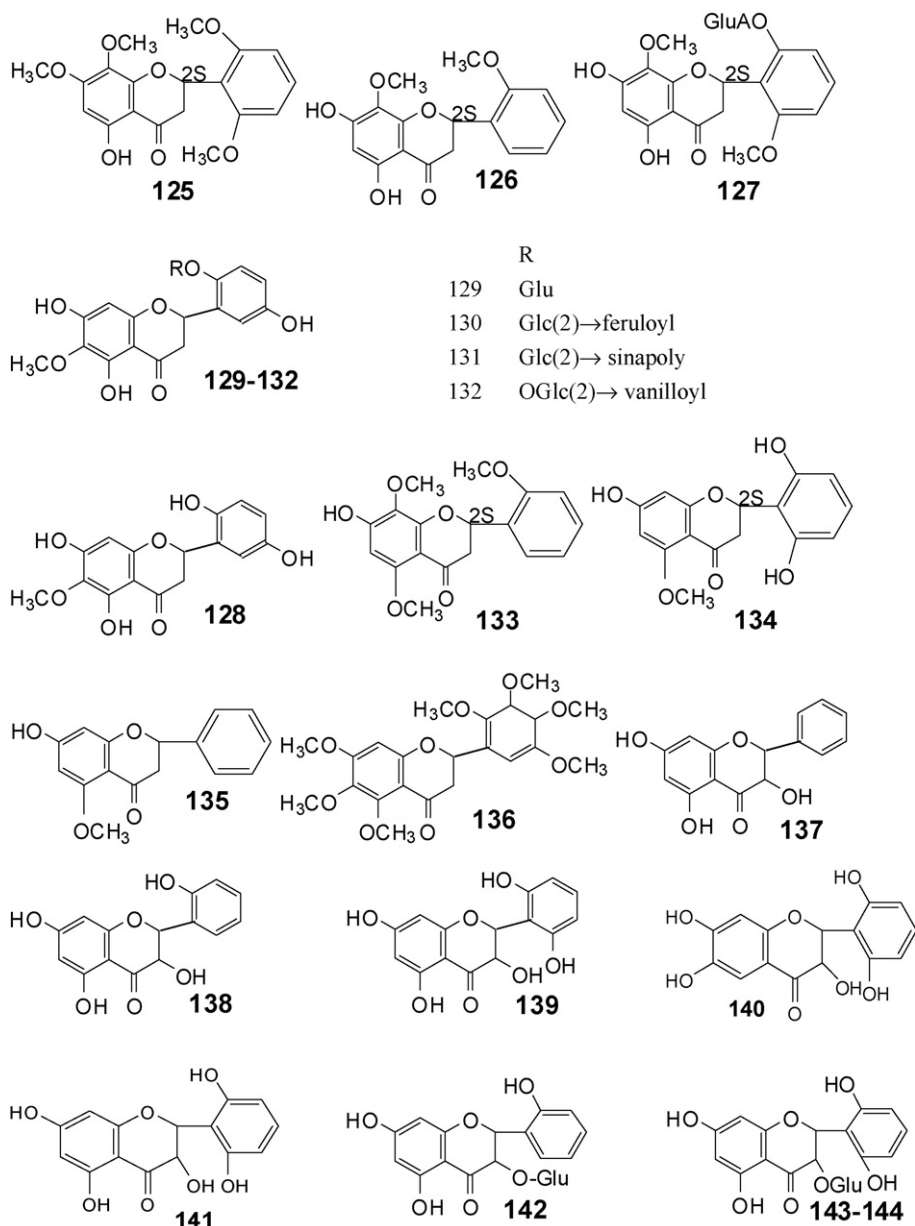


Fig. 2. (Continued)

3.9. Other compounds

Aurantiamide acetate (**283**) was isolated from *S. barbata* (Lin, 1987b). In 2007, from the *S. albida* ssp. *albida*, Gousiadou et al. (2007) isolated six known phenolic derivatives, E-*p*-coumaric acid, E-caffeic acid, E-ferulic acid, E-*p*-coumaroylglucoside, vanilloylglucoside and benzyl- β -glucopyranoside. Moreover, *p*-coumaric acid acetate, *p*-hydroxybenzaldehyde and *p*-hydroxybenzylacetone were

also obtained from *S. barbata* (Xiang et al., 1982). Miyaichi et al. (2006) obtained two phytosterols (**285**, **286**) and five tocopherols (**297–291**) from the leaves of *S. strigillosa*. From *S. linearis* β -sitosterol and β -sitosterol glucopyranoside were obtained (Hussain et al., 2008). Daucosterol (**284**) and dibutyl phthalate were isolated from the *S. amoena* (Zhou and Yang, 2000). In 1938, pinosylvin and its derivatives (**292–294**), galyussacin (**295**) were isolated from *S. scandens* endemic in Nepal (Li et al., 1994), and

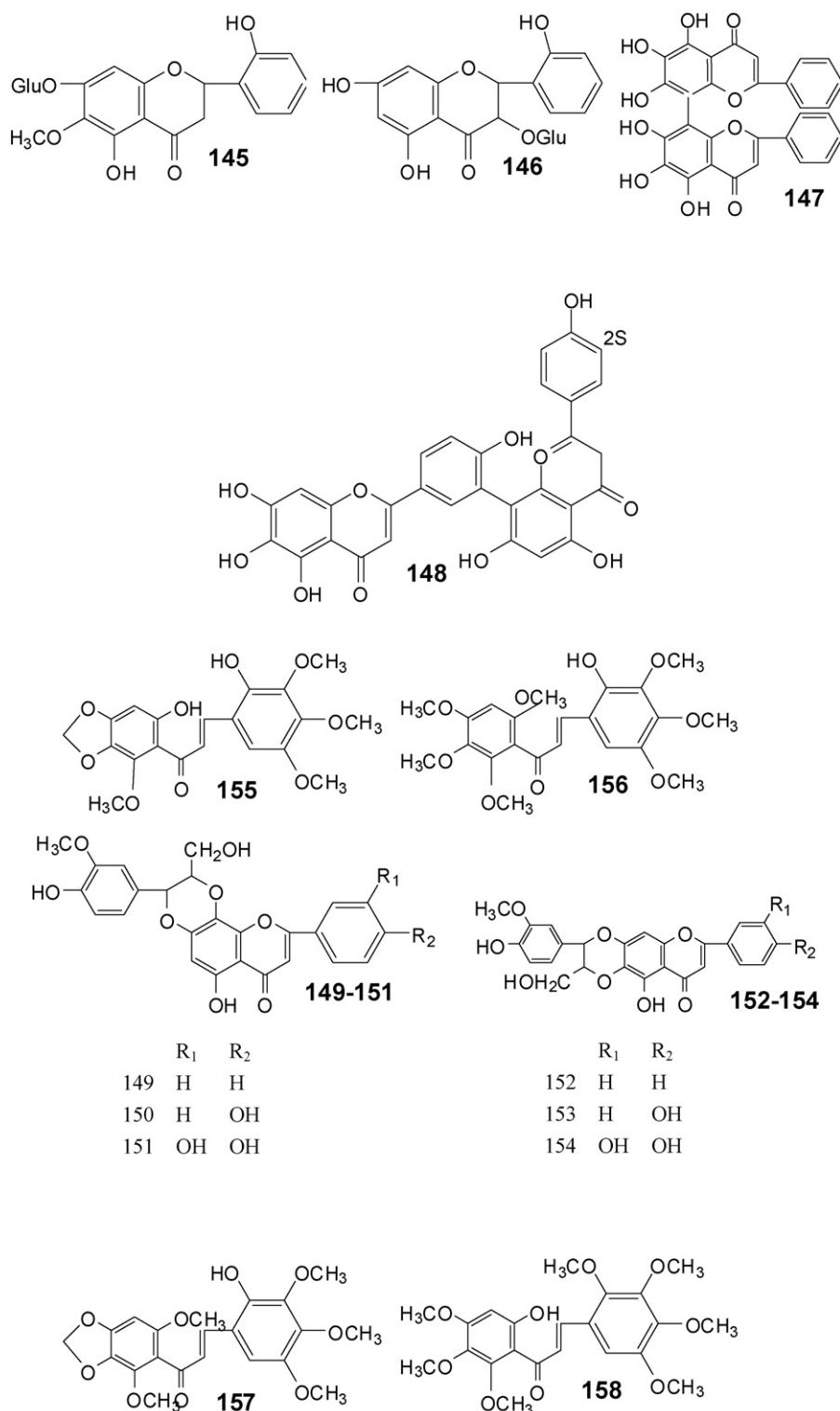


Fig. 2. (Continued)

polysaccharides, SBP, SPS4 obtained from *S. barbata* (Xu et al., 1992).

4. Qualitative and quantitative analysis

Obviously, flavonoids are the main and effective components of the genus *Scutellaria*. One or more flavonoids are usually adopted for qualitative and quantitative analysis for *Scutellaria*. Baicalin (**7**), the main flavonoid with the highest content, is employed by many countries and peoples to control the quality of medical materials

and preparations. For example, the pharmacopeia of China suggests that the content of baicalin in the Radix *Scutellaria* should more than 9%. Today, it is widely accepted that the quality cannot be measured by mono-content. In 2002, six flavones in twenty-five samples of *S. baicalensis*, from the southeast of Russia to the northeast of China, were analyzed by HPLC to describe the differences between native and no-native herbs (Yang et al., 2002). In this study, flavonoid glycosides and aglycones were determined with a mobile phase of MeOH-H₂O-CH₃COOH (41:59:0.2) and MeOH-H₂O-CH₃COOH (50:50:0.2), respectively. The detection wavelength was 275 nm.

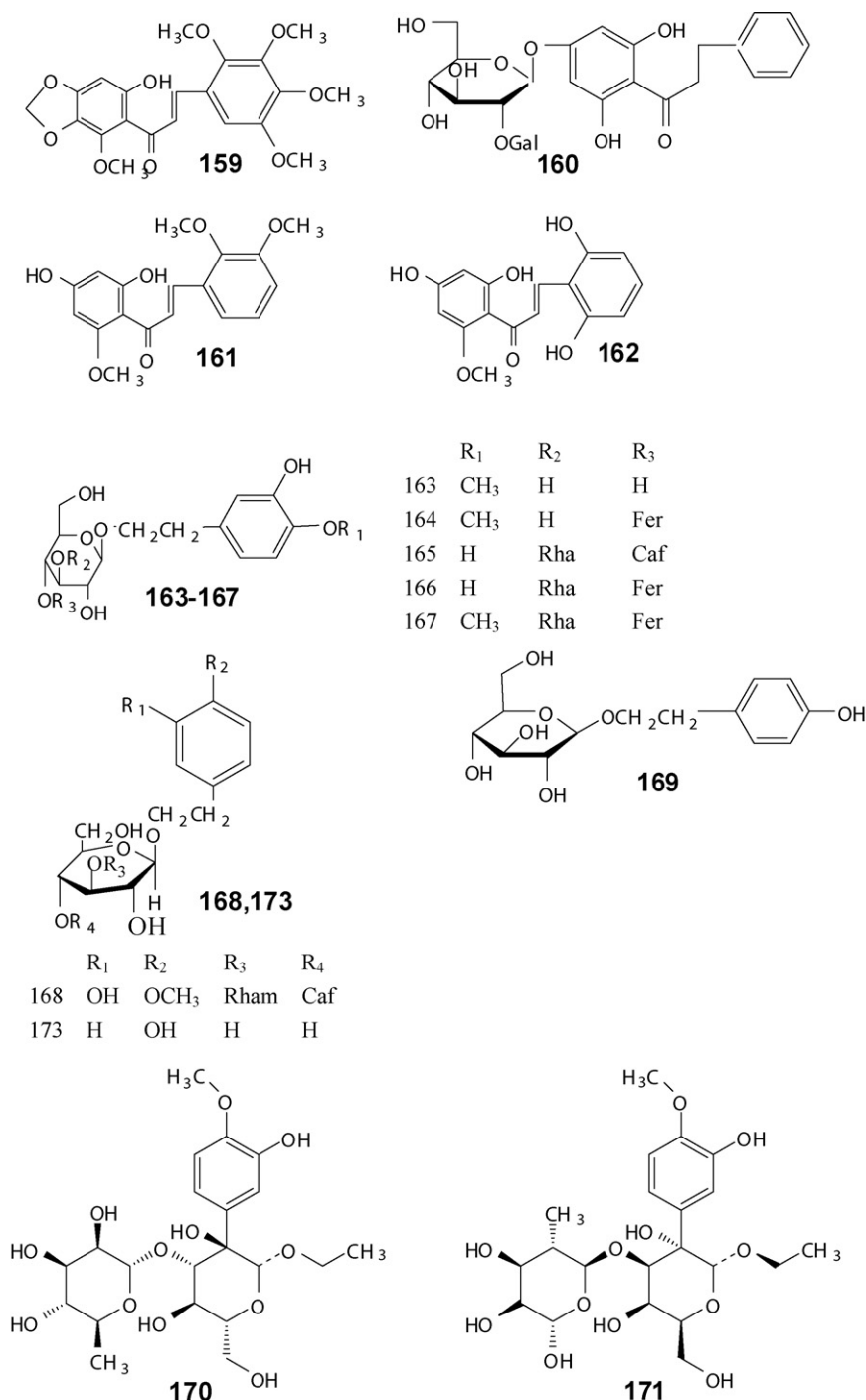


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The results showed that the contents of baicalin (**7**) are 6–9%, wogonin (**20**) are 2–8%, baicalein (**8**) are 0.1–1.6%, wogonoside (**21**) are 0.01–0.3%, viscidulin I (**100**) and trace amounts of oroxylin A (**16**). The native and non-native herbs had no distinct differences in absolute component ratios. The ratio of baicalin and wogonoside was under three. The ratio of baicalin and baicalein, baicalin and wogonin was between twenty and fifty. Finally, these ratios were suggested for the assessment of the quality of *S. baicalensis*.

Chemical fingerprint analysis has been introduced and accepted by WHO (1991), SFDAC (2000) and other authorities as a strategy for

quality assessment of herbal medicines. It has been recognized as a rapid and reliable means for the identification and qualification of herbal medicines (Liang et al., 2004). Song et al. (2006) applied the gradient mobile system to compare *S. baicalensis* from 30 different cultivating areas in China. The results showed that similarity is correlated with the habitat of the herb. All samples tested contained the same eight peaks, which was identified as the characteristic fingerprints. However, the content of each peak showed large differences among samples. Similar degrees of HPLC fingerprints could be used to compare crude drugs from different habitats.

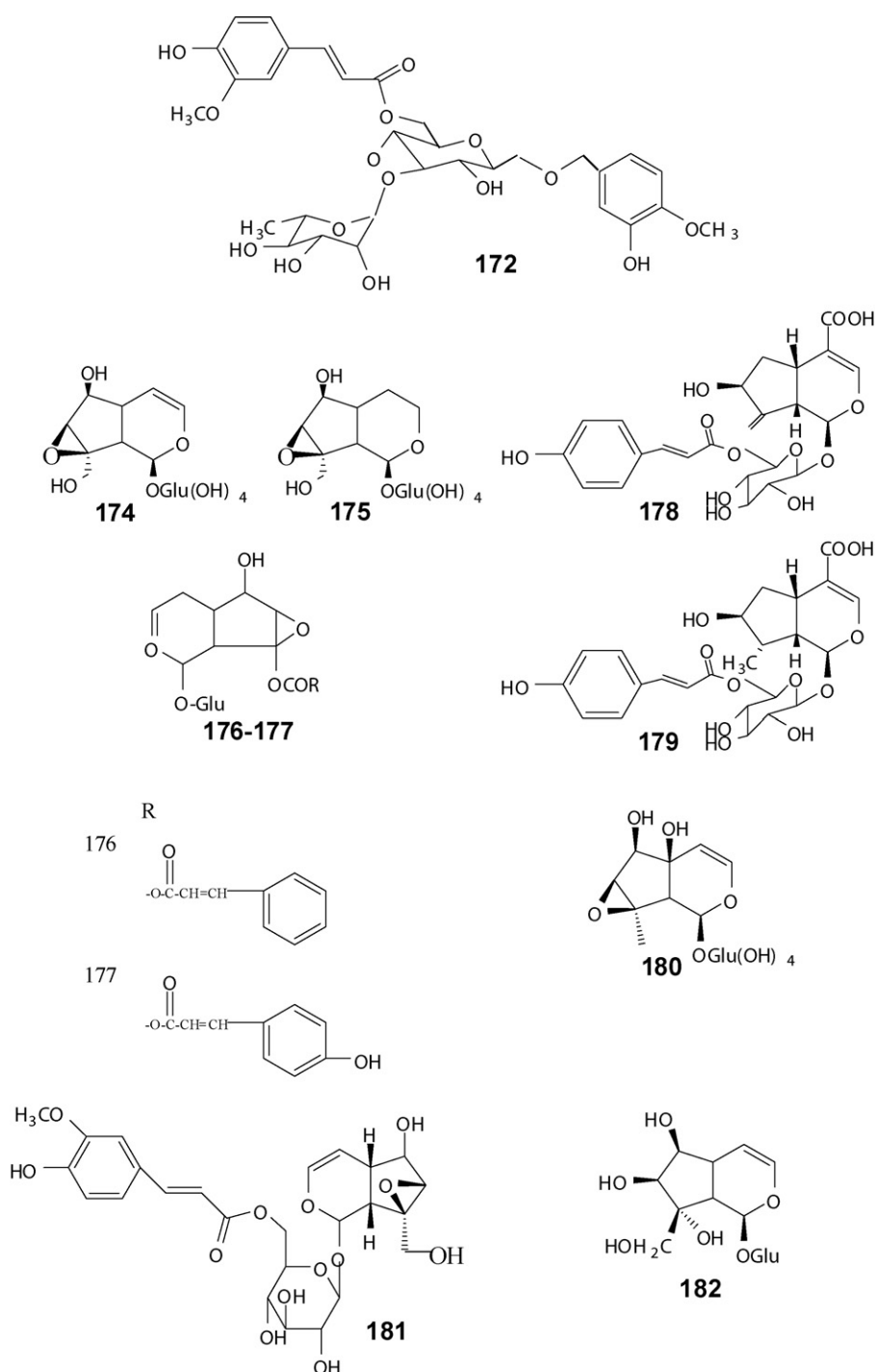


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By combining HPLC, DAD and MS for medicinal plant analysis, the identification and quantification of bioactive and marker compounds in complex matrices can be realized even with structurally similar natural products (He, 2000). In 2005, Horvath et al. developed this method to analyze eight flavones (wogonin, baicalin, baicalein, scutellarein, apigenin-7-glucuronide, scutellarin, apigenin, chrysin and 6-hydroxyflavone) in root and aerial tissues of *S. baicalensis*. The identity of the analytes was confirmed using retention time, UV-vis and mass spectral comparisons to commercial standards. Both UV-vis and mass spectral patterns were characterized for glycosylated flavones. At the

same time, two additional flavone glycosides were tentatively identified as chrysin-7-glucuronide and wogonoside, but not quantified.

5. Effects of crude extract

5.1. Antitumor

S. barbata, a traditional Chinese herbal medicine is native to southern China. The ethanol extracts show growth inhibitory effects on A549 cell with IC₅₀ of 0.21 mg/ml (Yin et al., 2004).

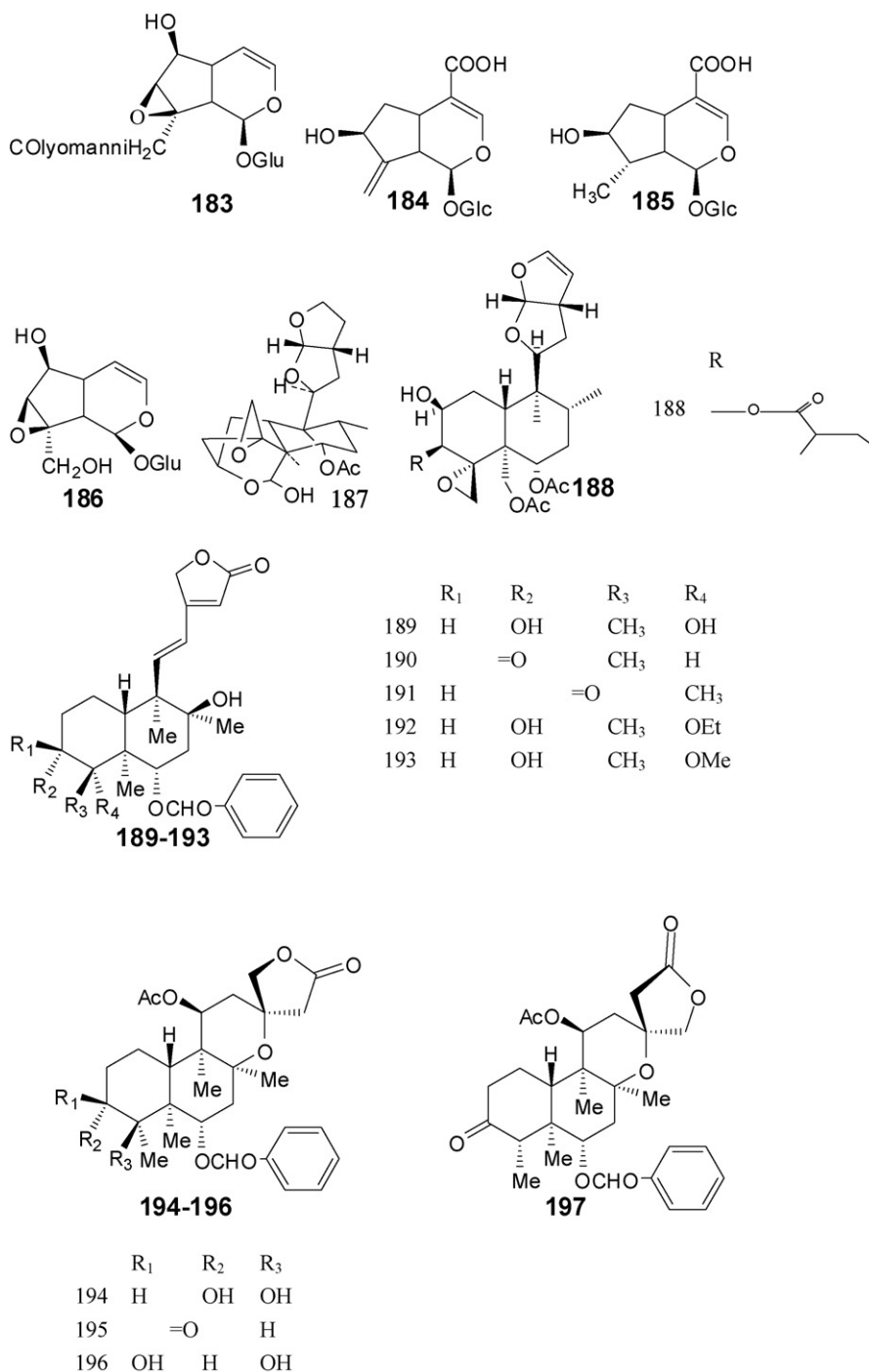


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At the same time, it exhibits cancer chemo preventive activity in assays representing three major stages of carcinogenesis, especially in gynecological cancers (Suh et al., 2007). The aqueous extracts demonstrate growth inhibitory activity on A549, PC-3, Panc-1, LNCaP, MCF-7 (human) and Panc02, LLC, MCNeuA (murine) on eight cancer cell lines (Shoemaker et al., 2005). Cha et al. (2004) investigated the antitumor mechanism of the methylene chloride fraction of *S. barbata* (MCSB) in human U937 leukemia cells. It was confirmed that MCSB could induce apoptosis via the mitochondria-mediated pathway. The apoptosis of leiomyoma cells induced by *S. barbata* was associated with the release of Cytochrome C from the mitochondria, followed by an increase in Caspase 3-like activity (Lee et al., 2006). Yu et al. (2007) confirmed that non-polar and low-polar solvent fractions of *S. barbata* have dose-dependent cytotoxicities on six cancer cell lines. Among them,

the chloroform fraction had the strongest cytotoxicity on cancer cell lines with a lower cytotoxic effect on a normal liver cell line, and significantly inhibited solid tumor proliferation. Furthermore, treatment with extracts could increase the life span of ascites tumor bearing mice.

The aqueous extract of roots of *S. baicalensis* (*Scutellaria Radix*) displays significant inhibition against MMP-2 and -9 activities and invasion of SK-Hep1 cells, with IC₅₀ of 85, 145 and 150 µg/ml, respectively (Ha et al., 2004). This extract also inhibits the growth of lymphoma and myeloma cell lines by inducing apoptosis and cell cycle arrest at clinically achievable concentrations. This anti-proliferative effect is associated with mitochondrial damage, modulation of the Bcl family of genes, increased level of the CDK inhibitor p27^{KIP1} and decreased level of c-myc oncogene (Kumagai et al., 2007).

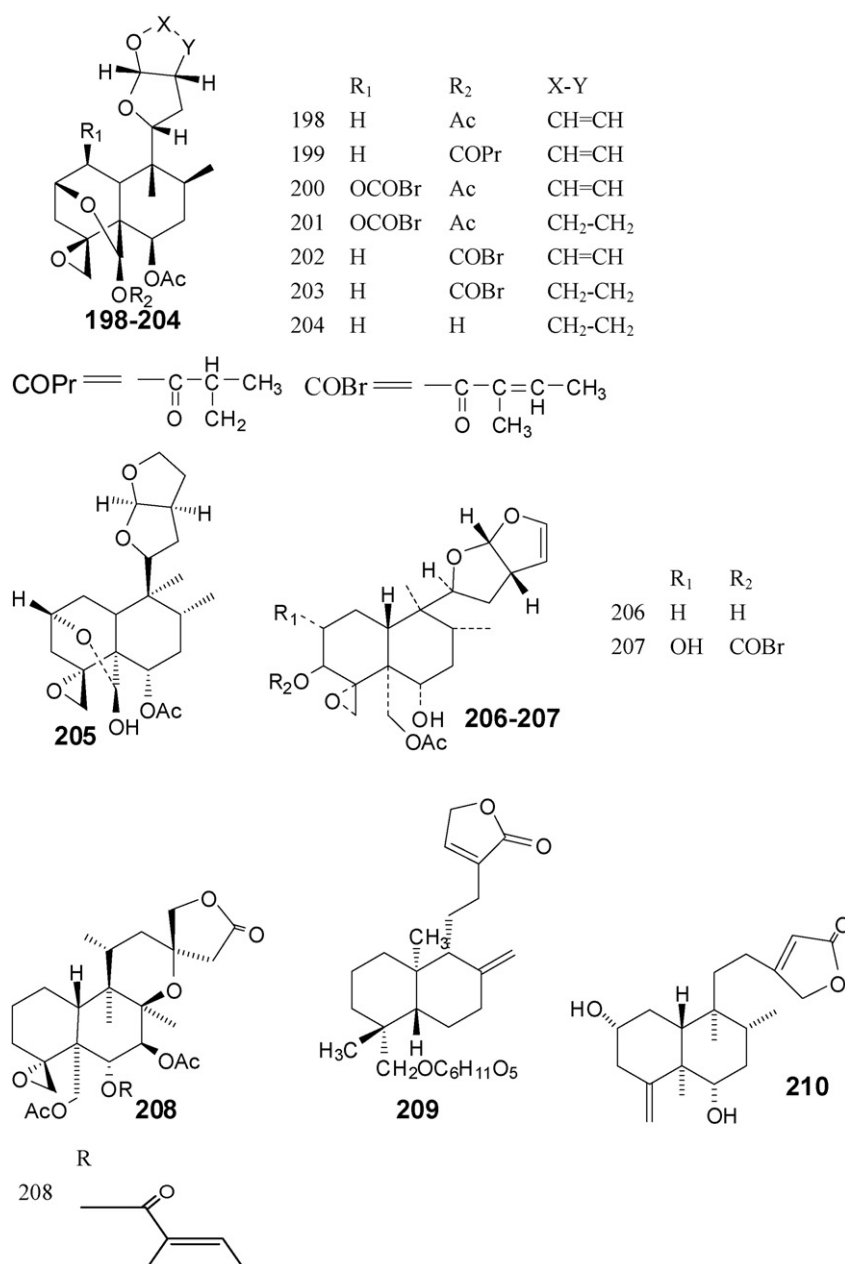


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Zhang et al. (1998) compared the four flavonoids of *S. planipes* to *S. baicalensis*, and the results showed that their contents are similar in both plant roots. *S. planipes* may be considered as a new medicinal plant because the contents of its main components, and their antiallergenic, antibacterial activities and the acute toxicity, *in vitro*, do not differ significantly from those of *S. baicalensis*.

In 2009, Min reviewed the anticancer properties of *Scutellaria* and its main active constituents baicalin (**7**), baicalein (**8**) and wogonin (**21**). This paper demonstrated that *Scutellaria* possesses potent anticancer activity and its bioactive components are flavones. Its extracts were not only cytostatic but also cytotoxic to various human tumor cell lines *in vitro* and it inhibited tumor growth *in vivo*. The antitumor functions of these flavones are largely

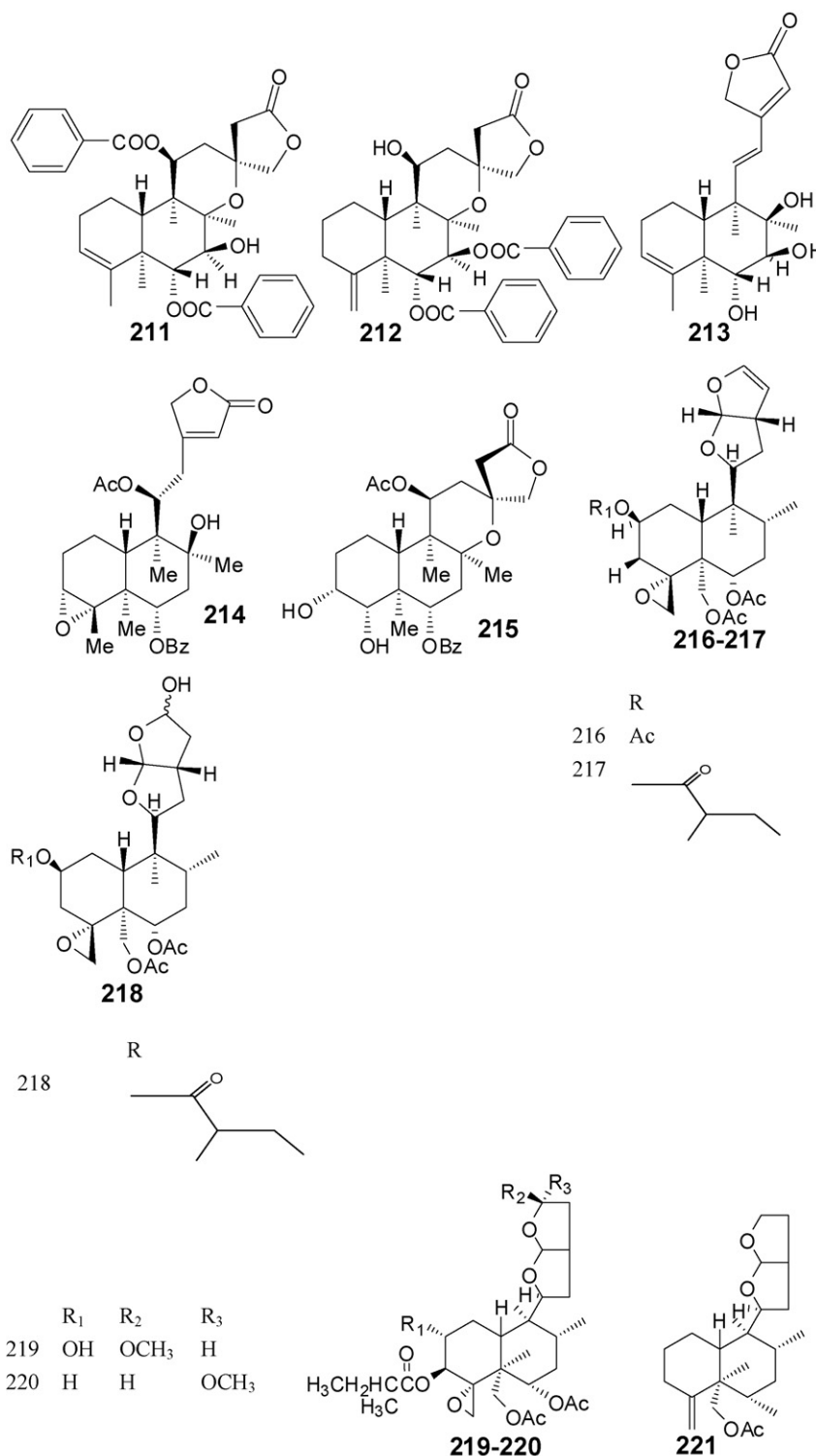


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due to their ability to scavenge oxidative radicals, attenuate NF- κ B activity, inhibit several genes important for regulation of the cell cycle, suppress COX-2 gene expression and prevent viral infections. The tumor-selectivity of wogonin has been attributed to its ability to differentially modulate the oxidation–reduction status of malignant vs. normal lymphocytic cells and to preferentially induce phospholipase C γ 1, a key enzyme involved in Ca²⁺ signaling, through H₂O₂ signaling in malignant lymphocytes (Min, 2009).

5.2. Anti-angiogenesis

Wang et al. (2004) determined angiogenic activity in vessels from the chick embryo chorioallantoic membrane (CAM) and cultured bovine aortic endothelial cells (BAECs). The results indicated that the aqueous extract of *S. baicalensis* has strong anti-angiogenesis activity *in vitro*.

5.3. Hepatoprotective

Lin et al. (1997) investigated the hepatoprotective effect of various fractions (*n*-hexane, CHCl₃, EtOAc, *n*-BuOH and H₂O) from

S. barbata in three experimental models *in vivo*. The results indicated that the CHCl₃ fraction and *n*-hexane fraction re most potent against D-galactosamine (D-GlaN)-induced intoxication, and the CHCl₃ fraction represents the greatest liver-protective effect on acetaminophen (APAP)-induced hepatotoxicity. The pathological changes of hepatic lesions were improved by treatment with the fraction mentioned.

Tan et al. (2006) hypothesized that the anti-fibrosis activity of *S. baicalensis* root may be involved in up-regulation of cAMP response element binding protein phosphorylation. The roots and shoots of *S. baicalensis* also inhibited the mutagenicity of the mycotoxin aflatoxin-B₁ in the liver of the rat (Johan et al., 2005).

5.4. Antioxidant

Methanol extracts of *S. baicalensis* can inhibit lipid peroxidation in rat liver microsomes and red blood cells, and inhibit aminopyrine N-demethylase and xanthine oxidase activities as well as have a pro-oxidant effect as observed in the Fe³⁺-EDTA-H₂O₂ system (Schinella et al., 2002). In a cardiomyocyte model of ischemia and reperfusion, 1.0 mg/ml *S. baicalensis* extract quickly

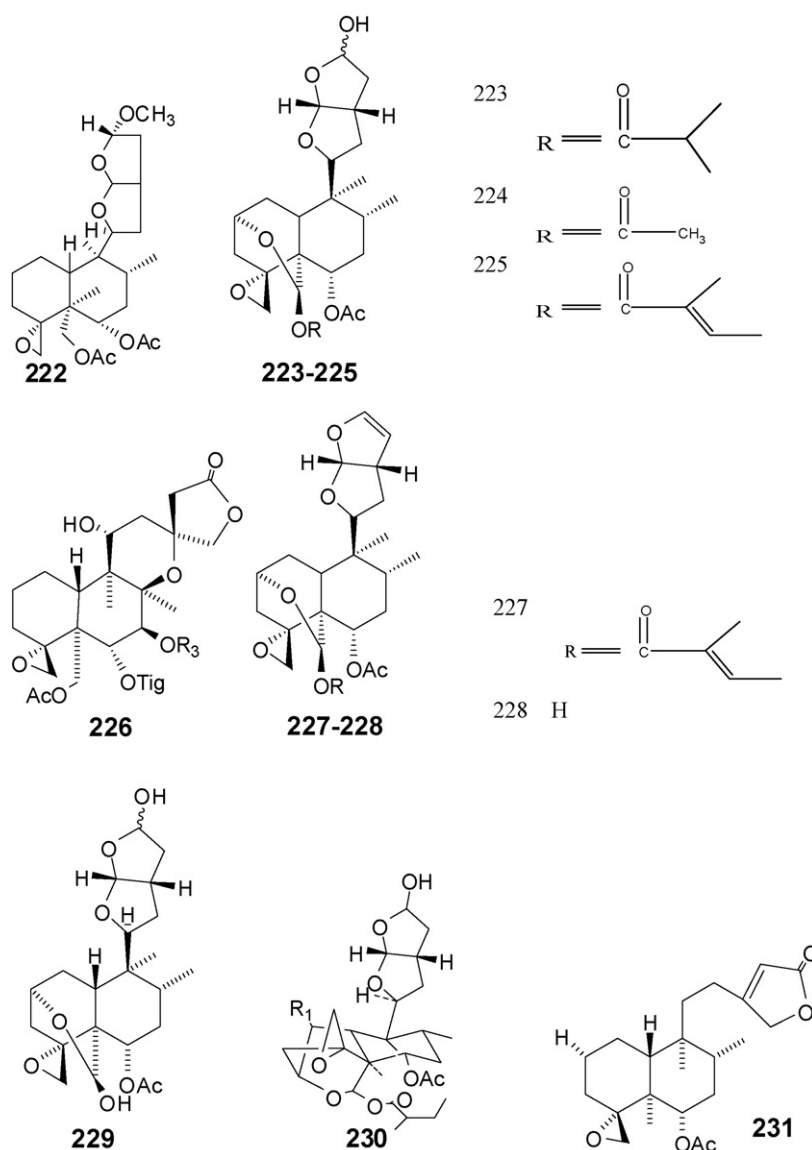


Fig. 2. (Continued)

attenuated levels of oxidants generated during transient hypoxia and exposure to the mitochondrial site III inhibitor antimycin A. Cell death after ischemia/reperfusion decreased from $47 \pm 3\%$ in untreated to $26 \pm 2\%$ in *S. baicalensis* treated cells. After antimycin exposure, *S. baicalensis* decreased cell death from $49 \pm 6\%$ in untreated to $23 \pm 4\%$ in treated cells ($p < 0.001$) (Shao et al., 1999).

Neuronal cells exposed to oxidative stress and treated with flavones from aqueous extracts of *S. baicalensis* were also observed. It was confirmed that flavone extracts ($50 \mu\text{g/ml}$) protect cells and increase viability to $85 \pm 5\%$, and increase the content of Bcl-2 in cells. Furthermore, oxidative-stress-induced protein carbonyl formation was reduced nearly two-fold when cells were pretreated with the flavone extract (Choi et al., 2002).

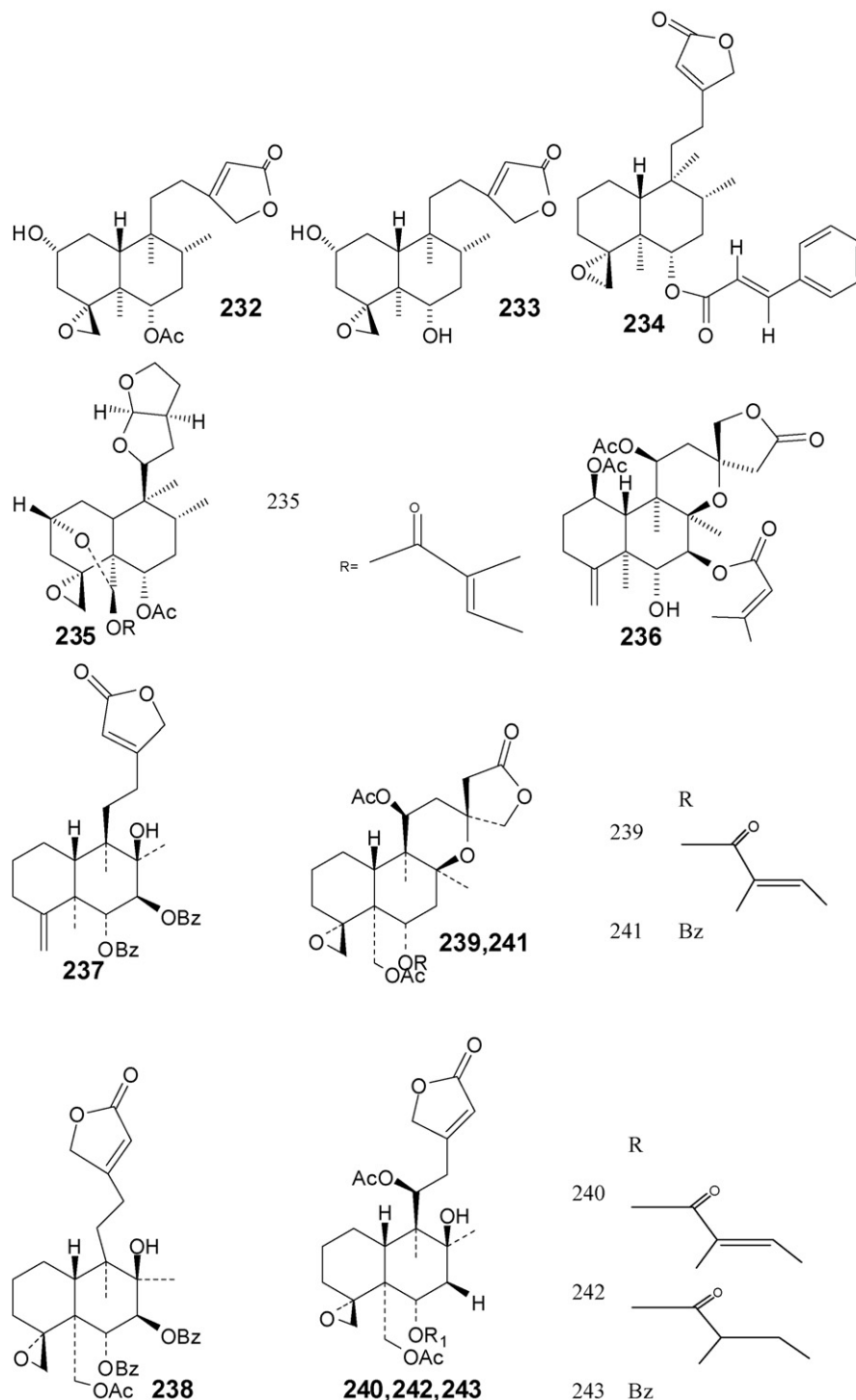


Fig. 2. (Continued)

5.5. Anticonvulsant

Wang et al. (2000) examined the anticonvulsant effect of *S. baicalensis* aqueous extracts (ED_{50} 3.6 g/kg) *in vivo* and its enhancing effect on γ -amino-*n*-butyric acid (GABA)-stimulated uptake of $^{36}Cl^-$ in *in vitro* cortex preparation. The results showed that aqueous extracts have anticonvulsant activity against maximal electroshock-induced tonic seizures, and this anticonvulsant effect is not due to the activation of the benzodiazepine binding site of GABA_A receptors, but probably via the prevention of seizure spread.

The study of Zhang et al. (2009) showed that the whole extract (ethanol and water solution) of *S. lateriflora* has modest anticonvulsant activity in two rodent models of acute seizures as an anticonvulsant.

5.6. Antibacterial and antiviral

10% aqueous extracts of *S. baicalensis* have antimycotic properties against pathological phyla of *Aspergillus fumigatus*, *Candida albicans*, *Geotrichum candidum* and *Rhodotorula rubra* had the highest activity against *Candida albicans* (Blaszczyk et al., 2000). Ethanol extracts of *S. baicalensis* can improve the antimicrobial activity of four antibiotics (penicillin G, gentamicin, ciprofloxacin, ceftriaxone) on the resistance of *Staphylococcus aureus* *in vitro* (Yang et al., 2005).

Antiviral activities against human respiratory syncytial virus (RSV) of aqueous extracts from *S. indica*, *S. barbata* were screened using a cytopathic effect (CPE) reduction assay. The results exhibited anti-RSV activity and the 50% inhibitory (IC_{50}) concentrations were 31.3 and 62.5 μ g/ml, and the selective indices (SI) were 11.2,

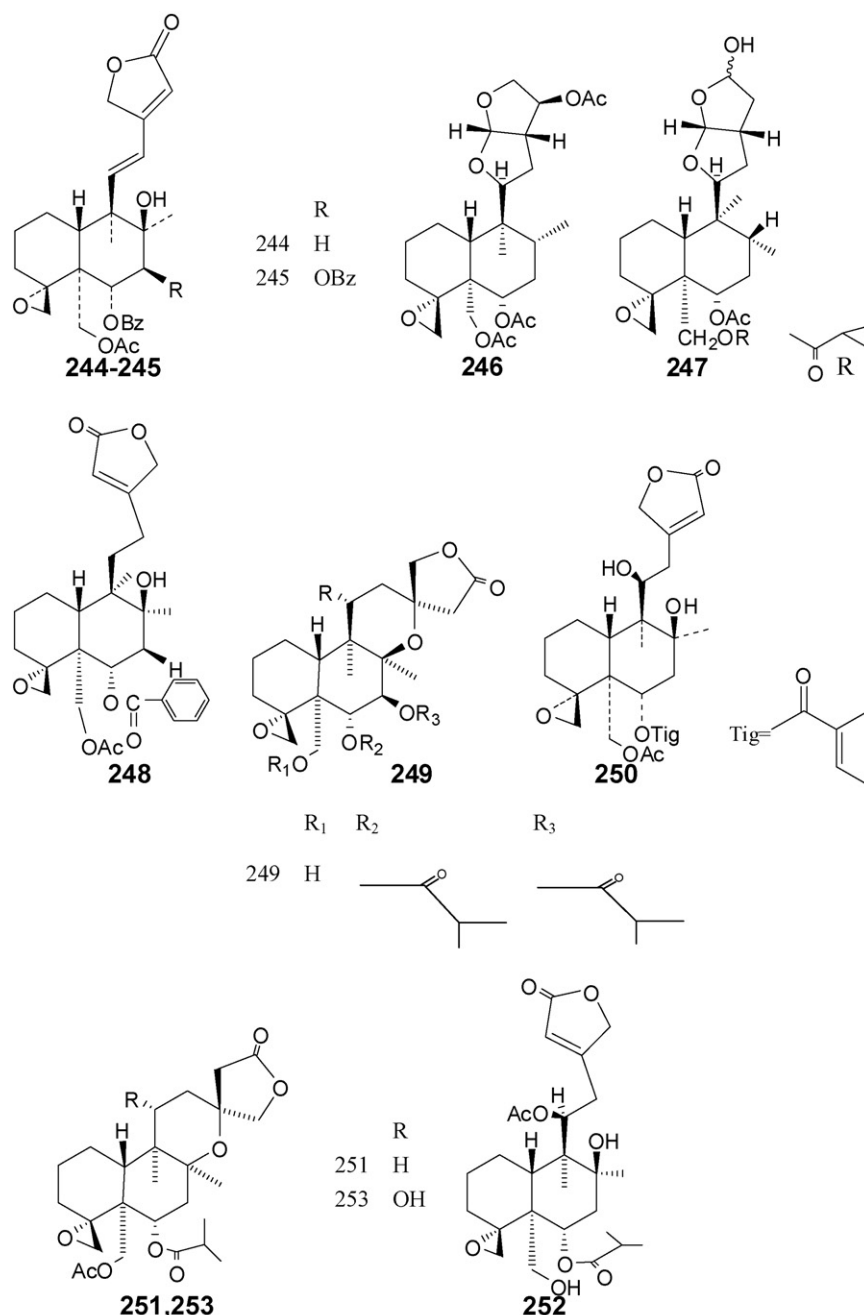


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8.0, respectively (Li et al., 2004). In addition, the aqueous extracts of *S. baicalensis* elicited significant inhibition (90%) at a concentration of 200 mg/ml against HIV-1 protease activity (Lam et al., 2000).

5.7. Neuroprotective effects and memory improvement

Flavonoids, isolated from aerial parts of *S. baicalensis* and administrated orally (35 mg/kg, 19–20 days) can dramatically

reduce the decrease in learning and memory, attenuate neuronal injury and improve abnormality of energy metabolites in rats induced by global ischemia. These results suggest that flavonoids of *S. baicalensis* may be beneficial for the treatment of vascular dementia (Shang et al., 2005). At the same time they have a significant protective effect on cerebral ischemia and ischemia-reperfusion induced brain injury (Zhang et al., 2006).

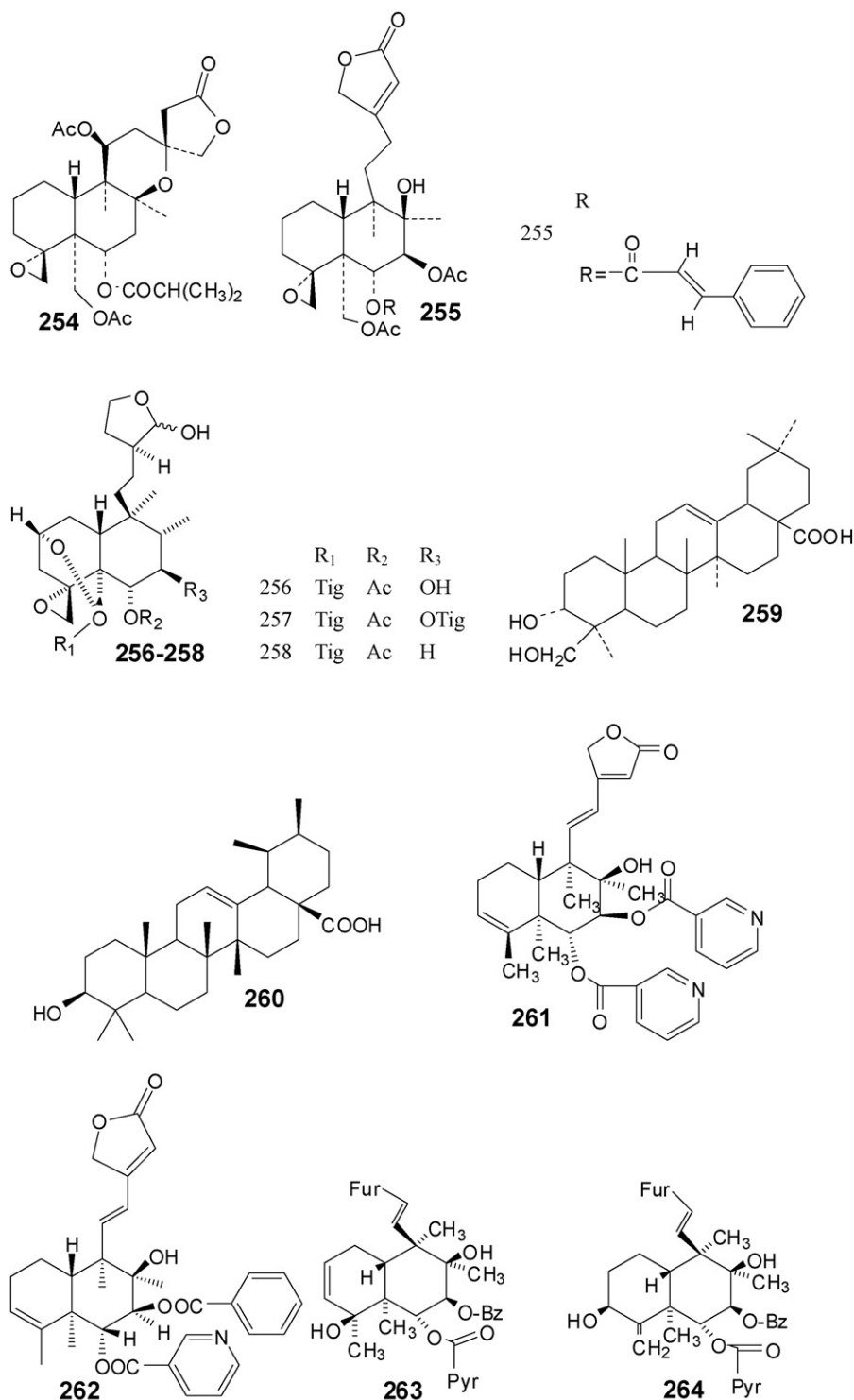


Fig. 2. (Continued)

Heo et al. (2009) proposed that *S. baicalensis* has significant neuroprotective effects in the Ibo model. After administration of 30 mg/kg 70% ethanol extract of *S. baicalensis*, the number of neuronal cells immunoreactive for choline acetyltransferase (ChAT) increased in the hippocampus, while cells producing GABA and glutamate did not increase. Furthermore, the extracts enhanced the survival of a hippocampal progenitor cell line, HiB5 and its differentiation to

ChAT immunoreactive cells. At the same time the increased expression of NMDA receptors and a reduction of activated microglia in the hippocampus were also observed in the Ibo model.

Kim et al. (2001) proposed that the methanol extract of *S. baicalensis* inhibits microglial TNF- α and NO production, and protects PC12 cells from hydrogen peroxide-induced toxicity *in vitro*.

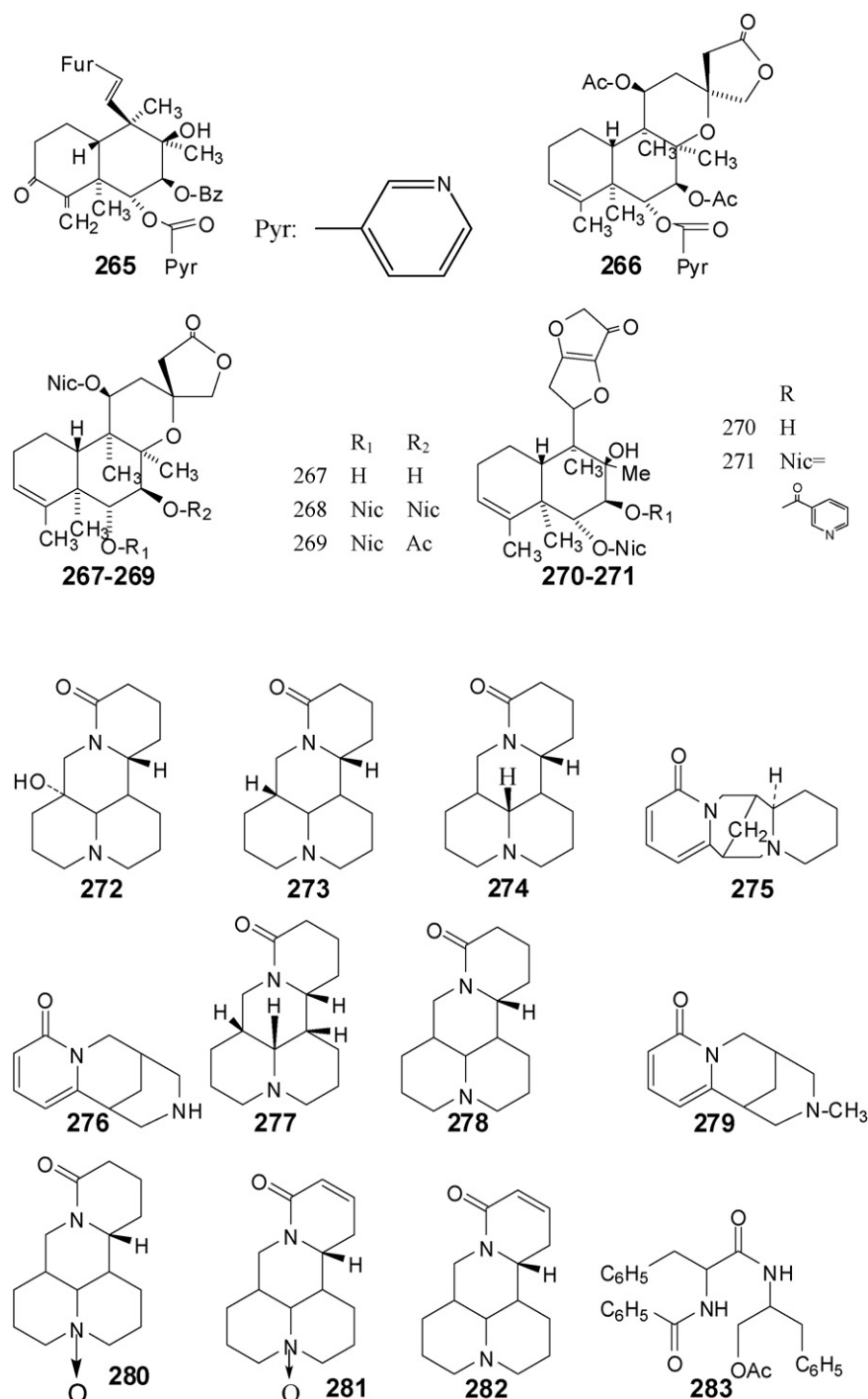


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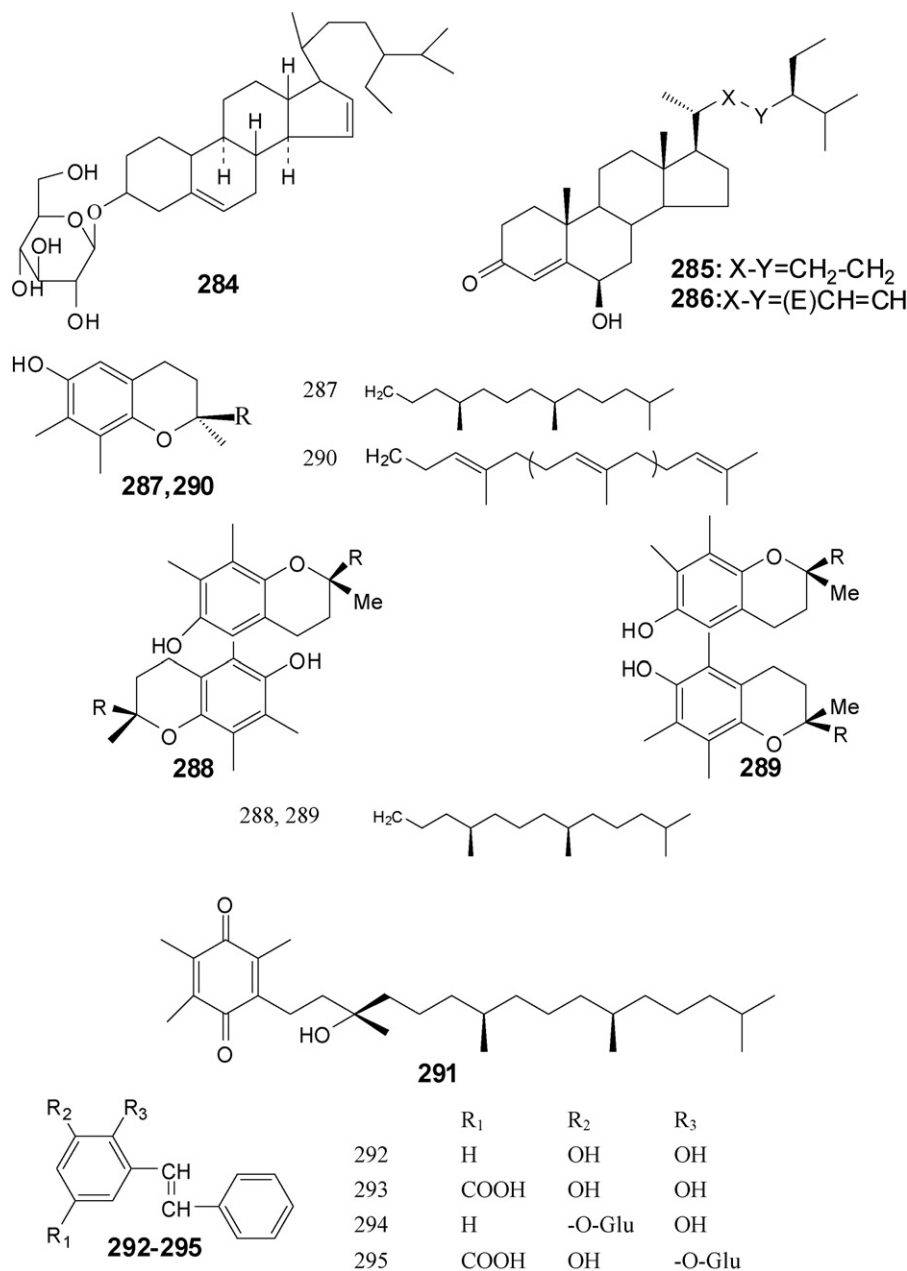


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6. Conclusion

The interest in the relationship between pharmacological effects and traditional uses of *Scutellaria* has increased considerably in recent years. More and more extracts and individual compounds have been used to treat cancer, hepatitis, pain, HIV-1 and pyogenic infection. According to the literatures reviewed in this paper, several reasons could be contributed to this including: (1) some of species have been used as a local medicine for thousands years in the world, especially in Asia and the effects and safety of these species have been confirmed. Thus, these plants have generated much interest and new medicine may be more easily found in some species. (2) Phenols and terpenes have been identified as the two main chemical compositions of *Scutellaria*. Among of them, baicalin, baicalein, barbatins A–C and scutebarbatine B have been proven to be potential drug leads most notably with anti-cancer

and anti-HIV effects. These compounds will be the main anchors for further studies on this genus and have great potential as new medicines. (3) Only **35** of the approx. 350 species have been studied in some detail. Considering that they have many bioactive compounds, the development of new substitutes and the discovery of new activities in related species are very important. (4) In China, some species have been used in TCM for thousands of years, and the roots of these species are used as one composition with other Chinese medicinal plants. The effects of *Scutellaria* in the interaction between *Scutellaria* and other TCM have been not explored in great detail.

Phytochemical and pharmacological studies of the genus *Scutellaria* have received much interest in recent years. Further studies are required for the development of new drugs and therapeutics for the treatment of various diseases, especially for antitumor and antiviral.

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