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Review

A review of phytochemistry and antitumor activity of a valuable medicinal species: *Scutellaria barbata*

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Scutellaria barbata **belonging to the genus** ***Scutellaria*** **L. (Labiatae) is a perennial herb which is natively distributed throughout Korea and Southern China. As a popular traditional medicinal herb "Ban-Zhi-Lian" listed in the Chinese Pharmacopoeia, it has a therapeutic history extending back over thousands of years. Currently, effective monomeric compounds or extracts have been screened for antitumor activity from** ***S. barbata in vivo*** **or** ***in vitro*****. More than forty flavonoids, twenty neo-clerodane diterpenoid alkaloids and fifty neo-clerodane type diterpenoids have been isolated. The modern pharmacology research has confirmed that some monomeric compounds or extracts possess widely antitumor activity on human gynecological tumor cells, leukemia cells, colon cancer cells, hepatoma cells, lung cancer cells, skin cancer cells and so on. The present paper reviews the progresses on the phytochemistry and antitumor activity of** ***S. barbata*****, and has a very important reference value to the rational application and exploitation of** ***S. barbata*****.**

Key words: *Scutellaria barbata*, phytochemistry, quantitative analysis, antitumor activity.

INTRODUCTION

Scutellaria L. (Labiatae) is a large subcosmopolitan genus with about 350 currently recognized species (Shang et al., 2010). *Scutellaria barbata* belonging to this genus is natively distributed throughout Southern China. *S. barbata* is a perennial herb reaching a height from 15 to 35 cm (Figure 1a). This plant often grows in wet meadows, nearby pools and brooks. It is in flower from May to July, and the seeds ripen from June to August. It is harvested in late summer and early autumn after it blooms (Figure 1b). Now it has been intensively cultivated in China. This herbal material is known in traditional Chinese medicine as "Ban-Zhi-Lian" and one of the important ingredients in Chinese traditional prescriptions to cure the pain and swelling of throat, edema and hemorrhoids, cancer, inflammation and urinary disease. It is slightly bitter in taste and cool in nature, attributives to liver, lung and stomach channels (Jiangsu New Medical College, 1977). In pharmacopoeia of China, the dried aerial section of the plant is the medicinal part (Figure 1c) (Chinese Pharmacopoeia Committee, 2010). In recently years, the chemical compositions of *S. barbata* have been studied. More than 130 compounds have been obtained. It contains a large number of flavonoids, unique neo-clerodane type alkaloids and diterpenoids as well as volatile oils, polysaccharide and other compounds. Among them, flavonoids and neo-clerodane type diterpenoids and alkaloids are the main and effective chemical compositions which mostly contribute to the pharmacological efficacy of *S. barbata*. Modern pharmacology research has also confirmed that monomeric compounds or extracts possess widely antitumor activitiy on human gynecological tumor cells, leukemia cells, colon cancer cells, hepatoma cells, lung cancer cells, skin cancer cells and so on. In this review, the advances in phytochemistry and antitumor activitiy of *S. barbata* are presented.

PHYTOCHEMISTRY

From the species *S. barbata*, 131 compounds were isolated, including flavonoids, alkaloids, diterpenes,

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Figure 1. Morphology of *S. barbata* (a: the fresh whole plant; b: the dried whole plant; c: the dried aerial parts of plant).

triterpenoids, polysaccharide, essential oils and other compounds (Tables 1 and 2; Figure 2).

Flavonoids

S. barbata is known to contain large amounts of flavonoids and their derivatives. 49 compounds, including flavones (1 to 21), flavonoid glycosides (22 to 41), flavanones (42 to 48) and chalcones (49) have been isolated. Most of them have methoxyl or hydroxyl groups at various positions on their aromatic rings. Due to the breakage of chemical bond between C_1 and C_2, 2',4'-dihydroxy-2,3',6'-trimethoxychalcone (49) belongs to Chalcones.

Flavonoids are generally regarded to have a wide range of pharmacological activity. Among these compounds, 4-hydroxy wogonin (2), apigenin (4), scutellarin (5), luteolin (6), baicalein (12) and apigenin 5-O-β-glucopyranoside (35) have been confirmed to have antitumor activity. Apigenin (4), and luteolin (6) also showed selectively antibacterial activity against MRSA and methicillin-sensitive *S. aureus* strains with MIC, 3.9 to 15.6 and 62.5 to 125 μg/ml, respectively. In addition, the total flavone of *S. barbata* can improve host cells membrane fluidity and prevent the parainfluenza virus type1 (PIV-1) infection by protecting the cell membrane (Guo et al., 2009).

Alkaloids

In 1996, scutebarbatine A (50), a new neoclerodane-type diterpenoid alkaloid was isolated from *S. barbata* for the first time (Wang et al., 1996). Recently, some scholars have obtained more and more neo-clerodane diterpenoid alkaloids and its derivates (51 to 74) by column chromatography using silica gel and aluminum oxide silica gel, sephadex LH-20, reverse-phase high performance liquid chromatography (HPLC) and so on. Among these compounds, some showed significant cytotoxic activity against human cancer cell lines.

Diterpenes

S. barbata and some other species from the same genus are recognized as a source of diterpenoids. More than 50 neo-clerodane diterpenoids (75 to 124) have been isolated. Some of these compounds exhibited significant cytotoxic activity against several human cancer lines *in vitro*. In addition, Wang et al. (2010) reported the structures of at least the following seven 13-spiro neo-clerodanes: Scutebarbatine F (55), scutehenanine B (61), scutebarbatine G (63), 6,7-di-O-nicotinoylscutebarbatine G (64), 6-O-nicotinoyl-7-O-acetylscutebarbatine G (65), 6-O-nicotinoylscutebarbatine G (66) and barbatin A (90), continuously reported by Dai et al. (2006a, 2009b,

Table 1. Chemical structures of flavonoids from *S. barbata*.

No.	Compounds	Groups	References
Flavones			
1	Wogonin	$R_{5,7}$=OH; R_8=OCH_3	Tomimori et al. (1984a)
2	4′-hydroxy wogonin	$R_{5,7,4'}$=OH; R_8=OCH_3	Xu et al. (1997)
3	Quercetin	$R_{3,5,7,3',4'}$=OH	Zhong et al. (2008)
4	Apigenin	$R_{5,7,4'}$=OH	Wang (1981)
5	Scutellarein	$R_{5,6,7,4'}$=OH	Wang (1981)
6	Luteolin	$R_{5,7,3',4'}$=OH	Wang (1981)
7	Rivularin	$R_{5,2'}$=OH; $R_{7,8,6'}$=OCH_3	Chou (1979)
8	Scutevurin	$R_{5,7,2'}$=OH; R_8=OCH_3	Tomimori et al. (1984a)
9	Alpinetin	R_7=OH; R_5=OCH_3	Xiang et al. (1982)
10	Isoscutellarein	$R_{5,7,8,4'}$=OH	Sonoda et al. (2004)
11	Hispidulin	$R_{5,7,4'}$=OH; R_6=OCH_3	Xiao and Li (2006)
12	Baicalein	$R_{5,6,7}$=OH	Yao et al. (2011)
13	5-hydroxy-7,8-dimethoxyflavone	R_5=OH; $R_{7,8}$=OCH_3	Zhang et al. (2005)
14	5,4'-dihydroxy-6,7,3',5'-tetramethoxyflavone	$R_{5,4'}$=OH; $R_{6,7,3',5'}$=OCH_3	Li et al. (2008)
15	7-hydroxy-5,8-dimethoxyflavone	R_7=OH; $R_{5,8}$=OCH_3	Lin and Chou (1984)
16	5,7-dihydroxy-8,2'-dimethoxyflavone	$R_{5,7}$=OH; $R_{8,2'}$=OCH_3	Liu (2005)
17	5,6,2'-trihydroxy-7,8-dimethoxyflavone	$R_{5,6,2'}$=OH; $R_{7,8}$=OCH_3	Lin (1988a)
18	5,4'-dihydroxy-6,7,3'-trimethoxyflavone	$R_{5,4'}$=OH; $R_{6,7,3'}$=OCH_3	Li et al. (2004)
19	5-hydroxy-7,4'-dimethoxyflavone	R_5=OH; $R_{7,4'}$=OCH_3	Yu et al. (2011)
20	5-hydroxy-7,8,4'-trimethoxyflavone	R_5=OH; $R_{7,8,4'}$=OCH_3	Yu et al. (2011)
21	5-hydroxy-6,7,4'-trimethoxyflavone	R_5=OH; $R_{6,7,4'}$=OCH_3	Yu et al. (2011)
Flavonoid glycosides			
22	Scutellarin	$R_{5,6,4'}$=OH; R_7=O-D-glucuronide	Wang (1981)
23	Baicalin	$R_{5,6}$=OH; R_7=O-D-glucuronide	Lin and Shieh (1996)
24	Isoscutellarein-8-O-glucuronide	$R_{5,7,4'}$=OH; R_8=O-D-glucuronide	Luan et al. (2011)
25	luteolin-7-diglucuronide	$R_{5,3',4'}$=OH; R_7=O-D-diglucuronide	Wang et al. (2008a)
26	Acacetin-7-diglucuronide	$R_{5,4'}$=OH; R_7=O-D-diglucuronide	Wang et al. (2008a)
27	Ethyl-7-O-apigenin-glucuronate	$R_{5,4'}$=OH; R_7=O-D-glucuronic acid ethyl ester	Wang et al. (2004)
28	Apigenin-7-O-neohesperidoside	$R_{5,4'}$=OH; R_7=O-neohesperidoside	Wang et al. (2004)
29	5,8,2'-tetrahydroxyflavone-7-O-β-D-glucoside	$R_{5,8,2'}$=OH; R_7=O-β-D-glucose	Tomimori et al. () 1984b
30	5,8-dimethoxyflavone-7-O-β-D-glucoside	$R_{5,8}$=OCH_3; R_7 =O-β-D-glucose	Tomimori et al. (1984b)
31	Apigenin-7-O-β-D-glucoside	$R_{5,4'}$=OH; R_7=O-β-D-glucose	Wang et al. (2004)
32	5,2'-dihydroxy-7,8,6'-trihydroxyflavone-2'-O-β-D-glucoside	R_5=OH; $R_{7,8,6'}$=OCH_3; $R_{2'}$=O-β-D-glucose	Tomimori et al. (1984b)
33	5,2',6'-trihydroxy-7,8-dimethoxyflavone-2'-O-β-D-glucoside	$R_{5,6'}$=OH; $R_{7,8}$=OCH_3; $R_{2'}$=O-β-D-glucose	Tomimori et al. (1984b)
34	5,8-dimethoxyflavone-7-O-D-glucurono-pyranoside	$R_{5,8}$=OCH_3; R_7=O-D-glucuronopyranoside	Li et al. (2004)
35	Apigenin-5-O-β-D-glucopyranoside	$R_{7,4'}$=OH; R_5=O-β-D-glucopyranoside	Qiu et al. (2009)
36	5-hydroxy-4'-methoxyflavone-7-O-α-L-rhamnosyl(1→6)-β-D-glucopyranoside	R_5=OH; $R_{4'}$=OCH_3; R_7=O-α-L-rha-mnosyl(1→6)-β-D-glucopyranoside	Xiao and Li (2006)

Table 1. Contd.

37	Luteolin-7-O-β-D-glucopyranoside	$R_{5,3',4'}$=OH; R_7=O-β-D-glucopyranoside	Zhong et al. (2008)
38	Apigenin-7-O-β-D-glucopyranoside	$R_{5,4'}$=OH; R_7=O-β-D-glucopyranoside	Zhong et al. (2008)
39	Apigenin-7-O-β-D-glucuronide	$R_{5,4'}$=OH; R_7=O-β-D-glucuronide	He et al. (2011)
40	Apigenin-7-O-β-D-glucuronide methyl ester	$R_{5,4'}$=OH; R_7=O-β-D-glucuronide methyl ester	He et al. (2011)
41	Kaempferol-3-O-β-D-rutinoside	$R_{5,7,4'}$=OH; R_3=O-β-D-rutinoside	He et al. (2011)
Flavanones			
42	Carthamidin	(2S)$R_{5,7,8,4'}$=OH	Xiang et al. (1982)
43	Isocarthamidin	(2S)$R_{5,6,7,4'}$=OH	Xiang et al. (1982)
44	Eriodictyol	$R_{5,7,3',4'}$=OH	Lin and Chou (1984)
45	Naringenin	$R_{5,7,4'}$=OH	Li et al. (2008)
46	2(S)-7,2'-dihydroxy-5,8-dimethoxyflavanone	$R_{7,2'}$=OH; $R_{5,8}$=OCH_3	Wang et al. (2011)
47	5,7,2'-trihydroxy-8-methoxyflavanone	$R_{5,7,2'}$=OH; R_8=OCH_3	Wang et al. (2011)
48	7-hydroxy-5,8,2'-trimethoxyflavanone	R_7=OH; $R_{5,8,2'}$=OCH_3	Wang et al. (2011)
Chalcone			
49	2',4'-dihydroxy-2,3',6'-trimethoxychalcone	$R_{2',4'}$=OH; $R_{2,3',6'}$=OCH_3	Wang et al. (2011)

2007b, 2009a, and 2006b) from the same plant were incorrectly assigned. And he revised these structures by reanalysis of the published NMR data (Figure 3).

Triterpenoids

Zhu and Liu (1993) isolated an oleanane-type triterpenoid acid, named scutellaric acid (125) from *S. barbata* for the first time).

Polysaccharide

The polysaccharide B3-PS1 was extracted and purified from *S. barbata* through bioactivity-guided fractionation. The average molecular weight of B3-PS1 was about 1,700,000 Da with a composition of Gal, Glc, Man and Ara in the ratio of 4.3:1.6:1.1:1.0, and trace of Rha, Fuc and Xyl. Pharmacology studies showed that B3-PS1 could be a potential candidate in treating those complement-associated diseases such as rheumatoid arthritis, Alzheimer's disease, and adult respiratory distress syndrome (Wu and Chen, 2009).

Essential oils

Yu et al. (2004) analyzed the composition of essential oil from aerial parts of *S. barbata* by gas chromatography and gas chromatography-mass spectrometry (GC–MS). The main components in the essential oils 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%). The essential oil displayed a broad anti-microbial spectrum and exerted a much stronger bactericidal effect against gram-positive bacteria, including methicillin-resistant *S. aureus*. Among the microorganisms tested, only S. paratyphi-A was resistant to the essential oil.

Other compounds

E-1-(4'-Hydroxyphenyl)-but-1-en-3-one (126) was isolated from *S. barbata* in 1996 (Ducki et al., 1996). Chan et al. (2006) described firstly the isolation of pheophorbide a (127) using a bioassay-guided isolation method. In 2011, (S)-2-(4-hydroxyphenyl)-6-methyl-2,3-dihydro-4H-pyran-4-one (128), was isolated from the ethanol extract of *S. barbata*. Moreover, 4-(3,4-dihydroxy-phenyl)-but-3-en-2-one(129), (6S,9R)6-hydroxy-4,4,7a-trimethyl-5,6,7, 7a-tetrahydro-1-benzofuran-2(4H)-one (130) and ethyl 4-hydroxy-3,5-dimethoxy-benzoate (131) were the first to be identified from this plant.

QUALITATIVE AND QUANTITATIVE ANALYSIS

It is well known that flavonoids are the main and effective components of *S. barbata*. Among them, scutellarin (22) as the main flavonoid with the highest content is usually adopted to control the quality of medical materials and preparations. For example, the pharmacopeia of China suggests that the content of scutellarin in the dry aerial parts determined by HPLC should be more than 0.20%. The content of total amount of flavonoids determined by UV absorption at 335 nm (calculated against scutellarin) should be more than 1.50%. However, it is widely accepted that the quality cannot only be controlled by

Table 2. The name of other compounds from *S. barbata.*

No.	Compounds	References
Neo-clerodane diterpenoid alkaloids		
50	Scutebarbatine A	Wang et al. (1996)
51	Scutebarbatine B	Dai et al. (2007a)
52	Scutebarbatine C	Dai et al. (2006a)
53	Scutebarbatine D	Dai et al. (2006a)
54	Scutebarbatine E	Dai et al. (2006a)
55	Scutebarbatine F	Dai et al. (2006a)
56	Scutebarbatine I	Dai et al. (2008a)
57	Scutebarbatine J	Dai et al. (2008a)
58	Scutebarbatine K	Dai et al. (2008a)
59	Scutebarbatine L	Dai et al. (2008a)
60	Scutebarbatine O	Dai et al. (2009a)
61	Scutehenanine B	Dai et al. (2009b)
62	Scutehenanine C	Dai et al. (2009b)
63	Scutebarbatine G	Dai et al. (2007b)
64	6,7-di-O-nicotinoylscutebarbatine G	Dai et al. (2007b)
65	6-O-nicotinoyl-7-O-acetylscutebarbatine G	Dai et al. (2007b)
66	6-O-nicotinoylscutebarbatine G	Dai et al. (2009a)
67	Scutebarbatine H	Dai et al. (2007b)
68	7-Onicotinoylscutebarbatine H	Dai et al. (2007b)
69	Scutehenanine A	Dai et al. (2009b)
70	6-O-Acetylscutehenanine A	Dai et al. (2009b)
71	6-O-(2-carbonyl-3-methylbutanoyl)scutehenanine A	Dai et al. (2009b)
72	Scutehenanine D	Dai et al. (2009b)
Norditerpenoid alkaloids		
73	Scutebarbatine M	Dai et al. (2011)
74	Scutebarbatine N	Dai et al. (2011)
Neo-clerodane diterpenoids		
75	Scutebarbatine W	Wang et al. (2010)
76	Scutebarbatine X	Wang et al. (2010)
77	Scutebarbatine Y	Wang et al. (2010)
78	Scutebarbatine Z	Wang et al. (2010)
79	Scutellone A or Scuterivulactone C_1	Lin et al. (1987) Tohru et al. (1987)
80	Scutellone C	Lin and Kuo (1988)
81	Scutellone D or Scuterivulactone D	Lin et al. (1988) Haruhisa et al. (1997)
82	Scutellone H	Lin and Kuo (1989)
83	Scutellone I	Lin and Kuo (1989)
84	Scutellone B or Scuterivulactone B	Lin and Kuo (1989) Haruhisa et al. (1997)
85	Scutellone E	Lin and Kuo (1988)
86	Scutellone F	Lin et al. (1988)
87	Scutellone G	Lin and Kuo (1989)
88	Scuterivulactone A	Haruhisa et al. (1997)

Table 2. Contd.

89	Scuterivulactone C_2	Tohru et al. (1987)
90	Barbatin A	Dai et al. (2006b)
91	Barbatin B	Dai et al. (2006b)
92	Barbatin C	Dai et al. (2006b)
93	6-(2,3-epoxy-2-isopropyl-n-propoxyl)barbatin C	Dai et al. (2010)
94	Barbatin D	Dai et al. (2008b)
95	Barbatin E	Dai et al. (2008b)
96	Scutellin A	Zhu et al. (2009)
97	Barbatellarine A	Lee et al. (2010)
98	Barbatellarine B	Lee et al. (2010)
99	Scutehenanine H	Dai et al. (2010)
100	Neoandrographolide	Zhu and Liu (1993)
101	Scutebata A	Zhu et al. (2010)
102	Scutebata B	Zhu et al. (2010)
103	Scutebata C	Zhu et al. (2010)
104	Scutebata D	Zhu et al. (2010)
105	Scutebata E	Zhu et al. (2010)
106	Scutebata F	Zhu et al. (2010)
107	Scutebata G	Zhu et al. (2010)
108	Scutebata H	Zhu et al. (2011)
109	Scutebata I	Zhu et al. (2011)
110	Scutebata J	Zhu et al. (2011)
111	Scutebata K	Zhu et al. (2011)
112	Scutebata L	Zhu et al. (2011)
113	Scutebata M	Zhu et al. (2011)
114	Scutebata N	Zhu et al. (2011)
115	Scutebata O	Zhu et al. (2011)
116	Scutelinquanine A	Nie et al. (2010)
117	Scutelinquanine B	Nie et al. (2010)
118	Scutelinquanine C	Nie et al. (2010)
Ent-clerodane diterpenoids		
119	6-O-nicotinoylbarbatin A	Dai et al. (2007a)
120	6,7-di-O-acetoxybarbatinA	Dai et al. (2007a)
121	8-O-nicotinoylbarbatinA	Dai et al. (2007a)
122	2-carbonylscutebarbatineA	Dai et al. (2007a)
123	Scutelinquanine D	Qu et al. (2010)
124	6-acetoxybarbatin C	Qu et al. (2010)
Triterpenoid		
125	Scutellaric acid	Zhu and Liu (1993)
Other compounds		
126	E-1-(4'-Hydroxyphenyl)-but-1-en-3-one	Ducki et al. (1996)
127	Pheophorbide a	Chan et al. (2006)
128	(S)-2-(4-hydroxyphenyl)-6-methyl-2,3-dihydro-4H-pyran-4-one	Wang et al. (2011)
129	4-(3,4-dihydroxy-phenyl)-but-3-en-2-one	Wang et al. (2008a)
130	6-hydroxy-4,4,7a-trimethyl-5,6,7,7a-tetrahydro-1-benzofuran-2(4H)-one	Wang et al. (2011a)
131	ethyl 4-hydroxy-3,5-dimethoxy-benzoate	Wang et al. (2011b)

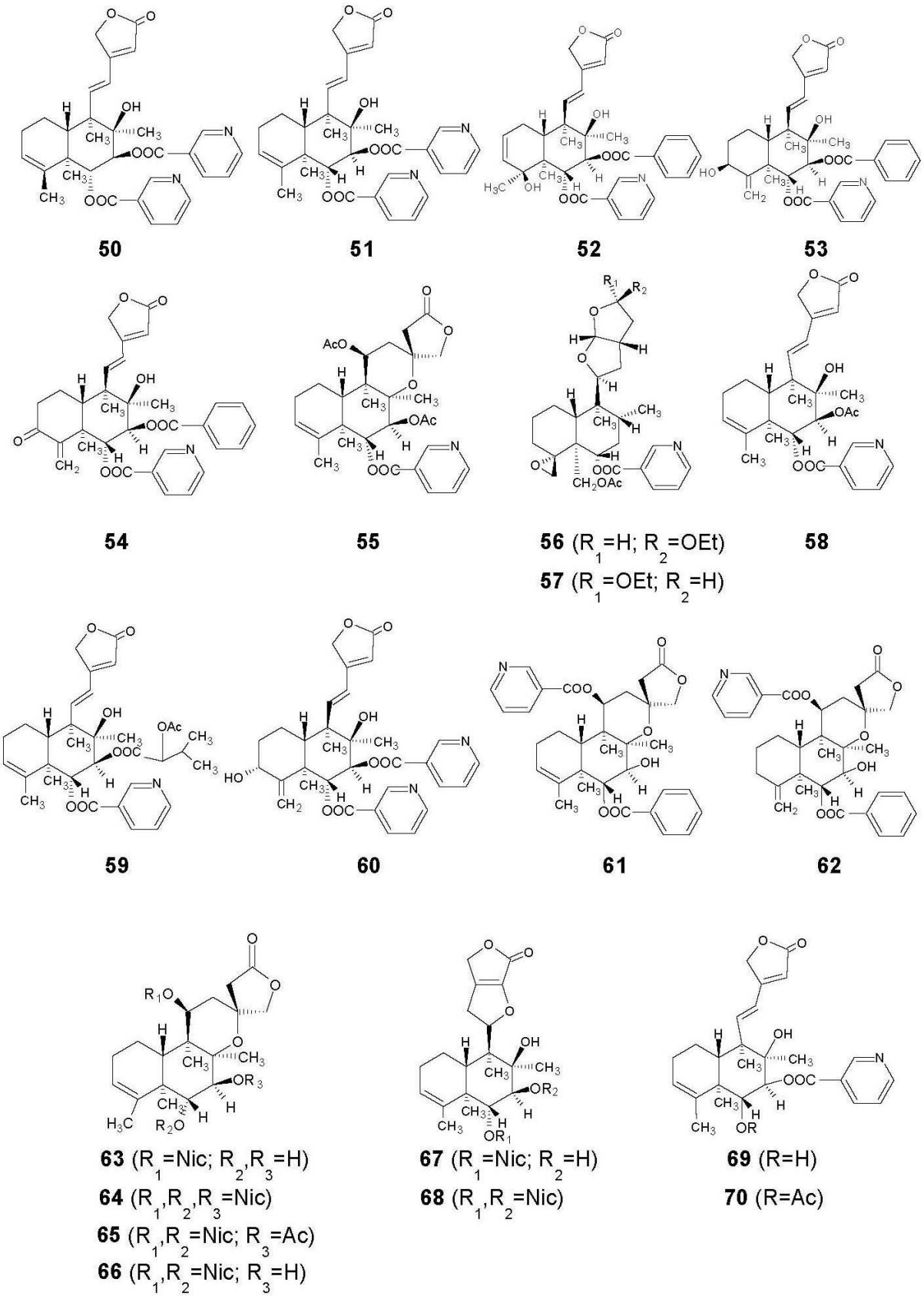
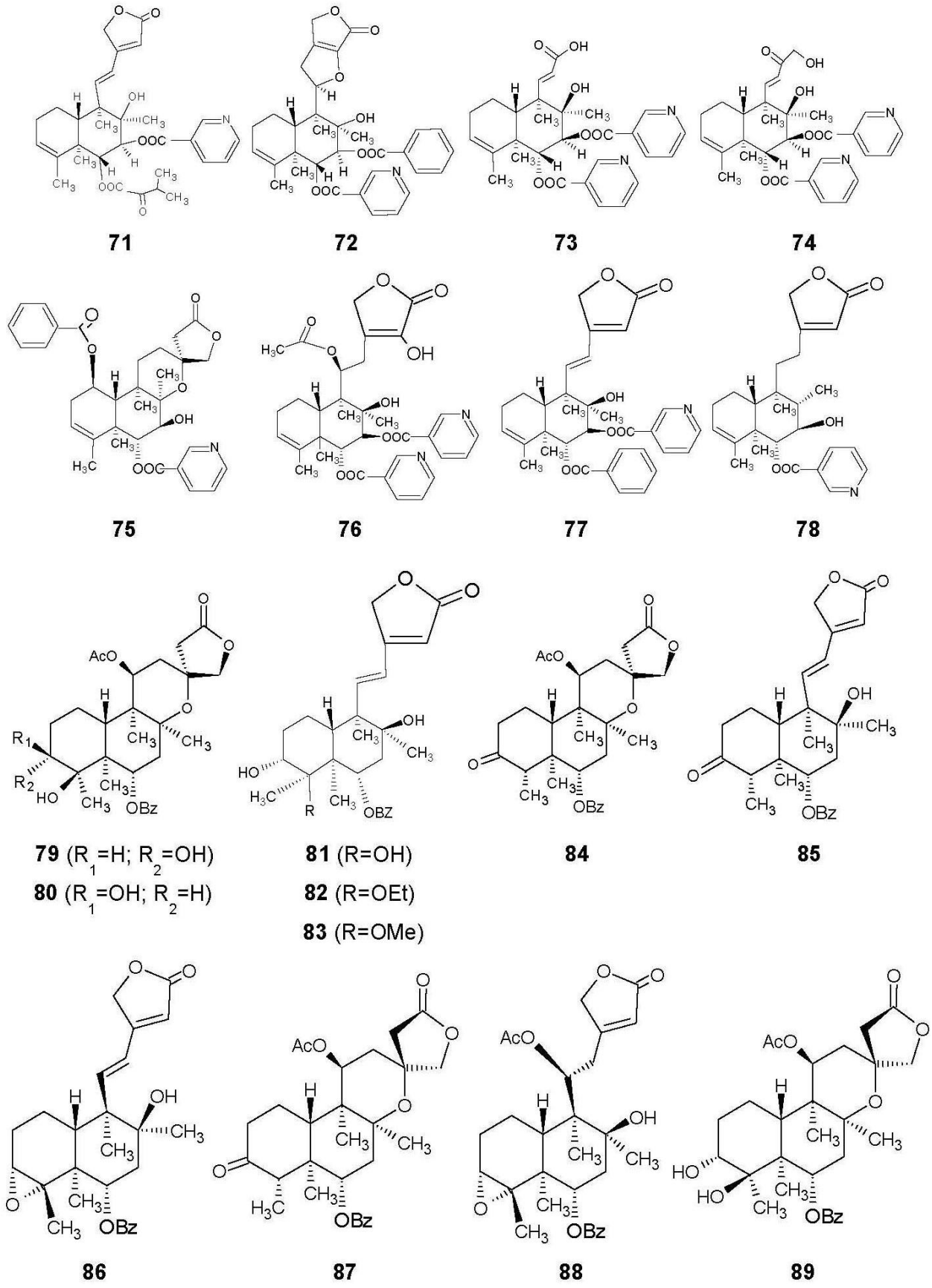


Figure 2. The chemical structures of other isolated compounds from *S. barbata* (the name of isolated compounds are listed in Table 2).



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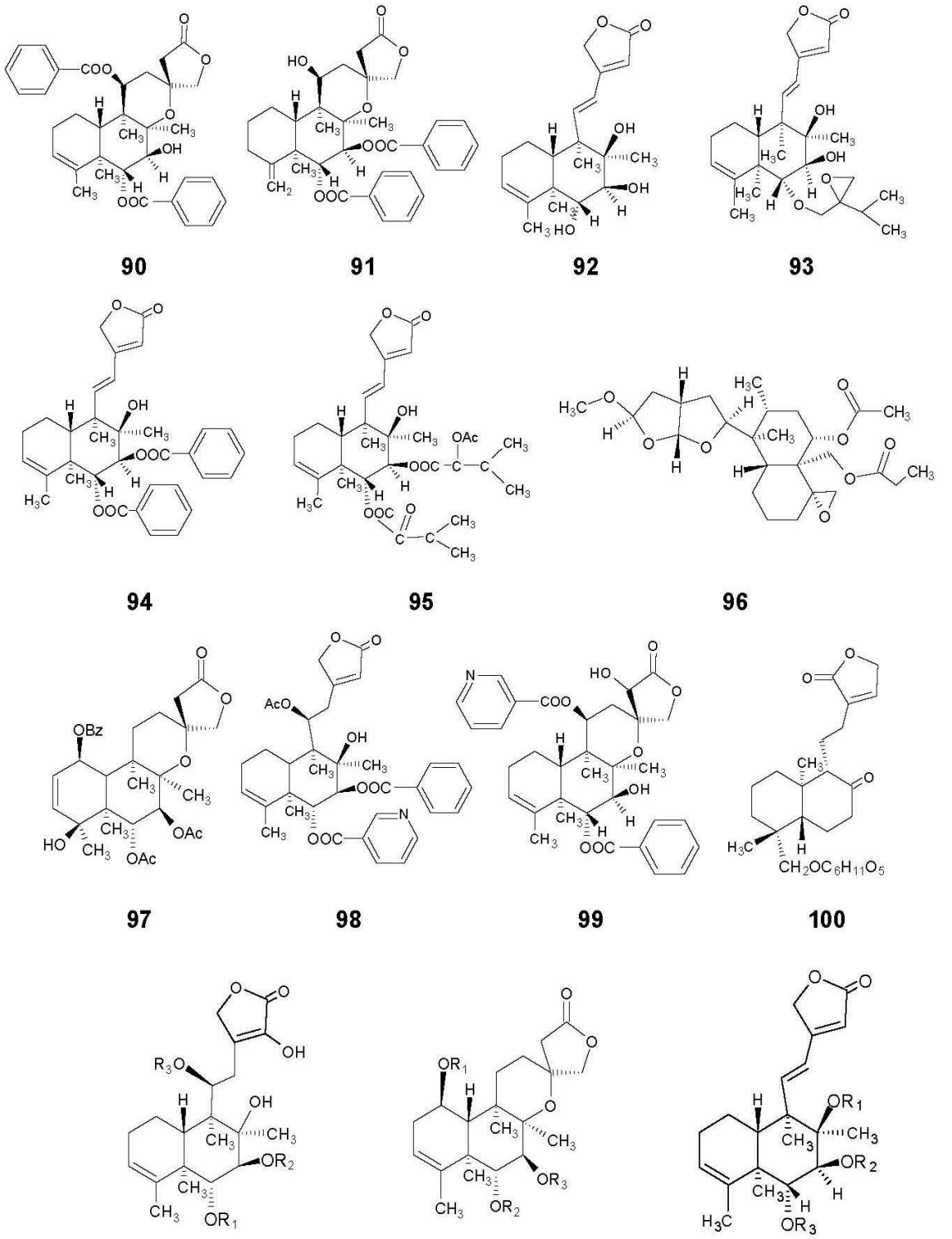

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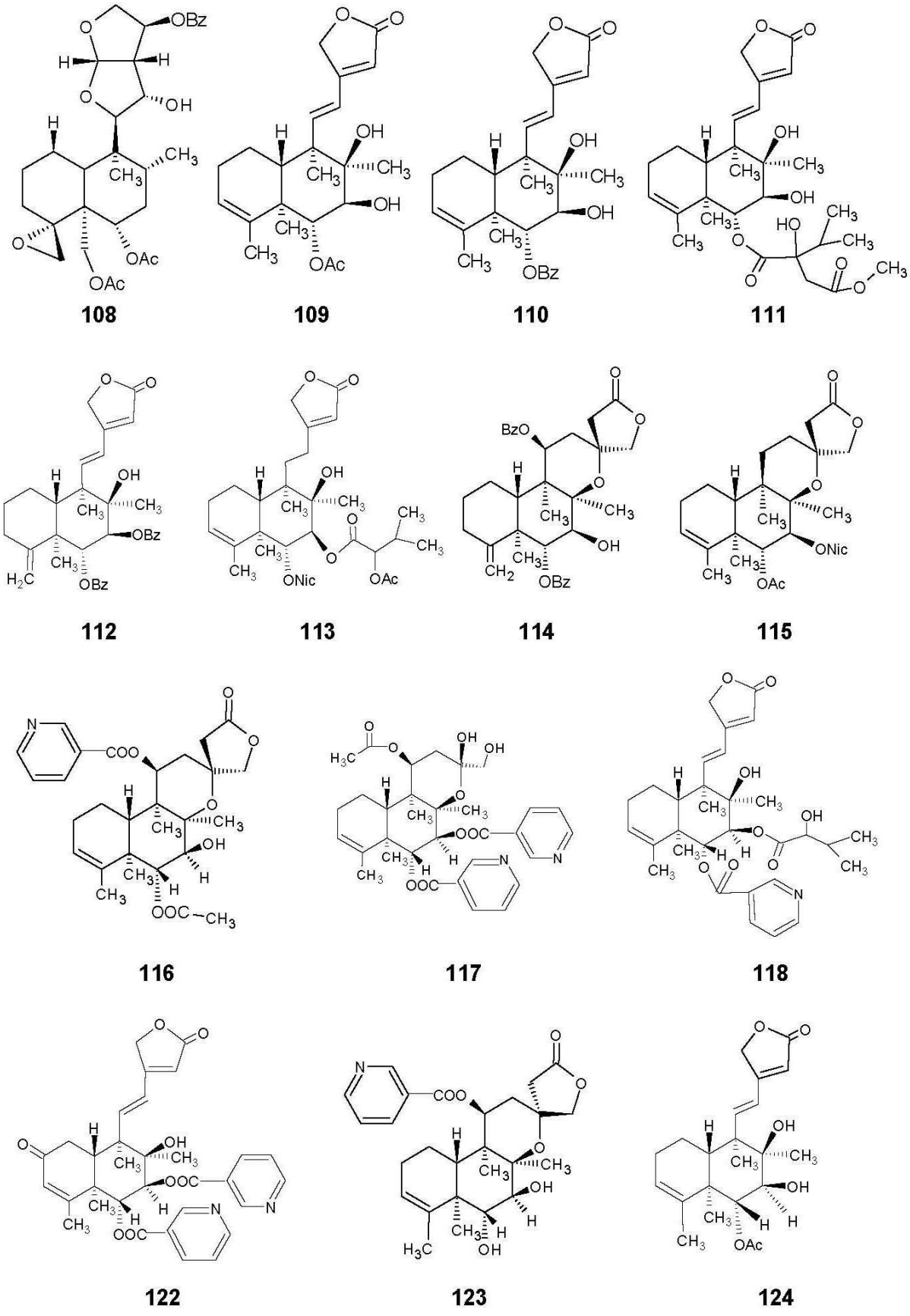

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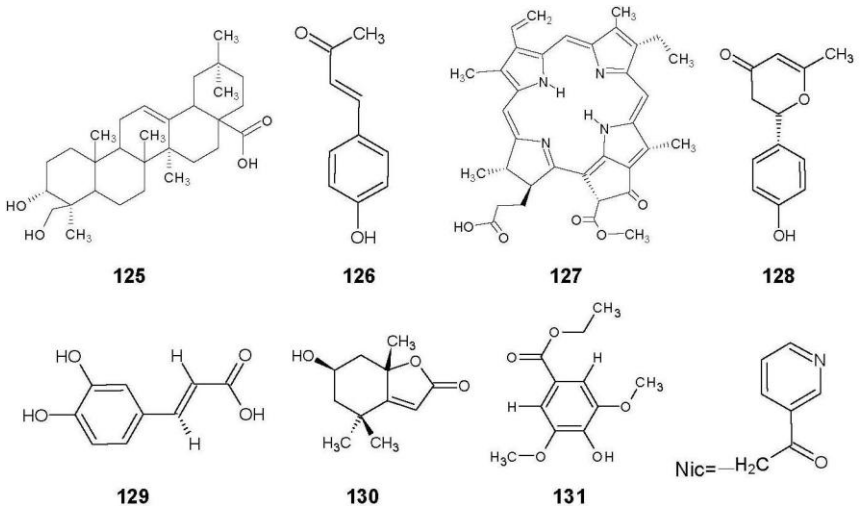

Figure 2. Contd.

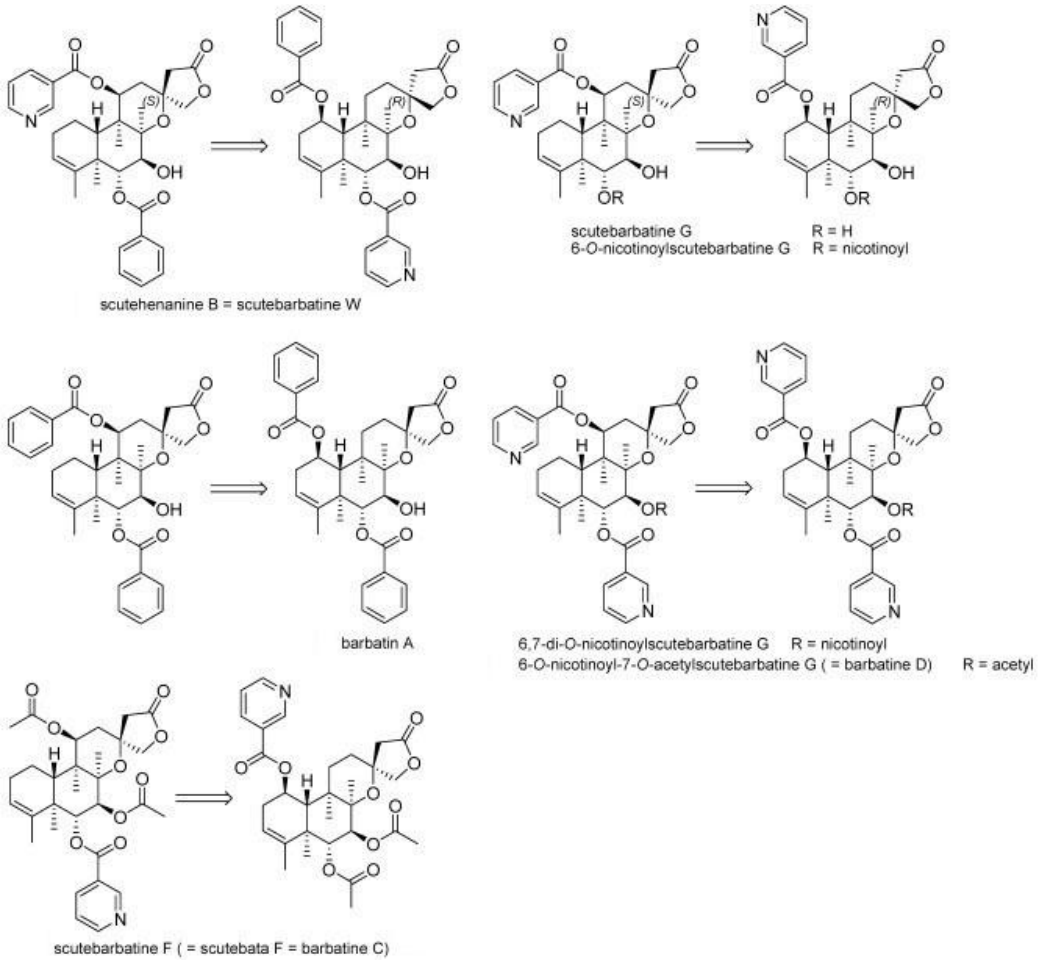

Figure 3. The structural revision of some compounds from *S. barbata* (the nicotinoyloxy group at C-11 and the spirocarbon configuration of scutebarbatine G and 6-O-nicotinoylscutebarbatine G should be adjusted to at Cas 13R* form, respectively. Similarly, the substitute at C-11 in barbatin A, 6,7-di-O-nicotinoylscutebarbatine G and 6-O-nicotinoyl-7-O-acetylscutebarbatine G should be all repositioned at C-1. Among them, 6-O-nicotinoyl-7-O-acetyls-cutebarbatine G and scutebarbatine F are actually identical with subsequently reported barbatine D and barbatine C (scutebata F), respectively).

single content. Qiao et al. (2006) established an HPLC determination method for four flavonoids in *S. barbata*. Luan et al. (2011) established a HPLC method for simultaneous determination of four effective components from total flavonoids of *S. barbata*. By developing several analysis methods for this medicinal plant, the identification and quantification of bioactive compounds can be realized. A dynamic ultrasonic extraction coupled with on-line detection by spectrophotometry was proposed for the determination of total flavonoids in *S. barbata* (Wang et al., 2008b). A method of capillary micellar electrokinetic chromatography with a diode array detector was developed for the simultaneous determination of seven active ingredients in *S. barbata* (Mi and Zhu, 2010). Shi et al. (2011) developed and validated a new liquid chromatography-tandemmass spectrometry method for the determination of five flavonoids in rat plasma.

Due to the different cultivation areas and climatic conditions, the components in *S. barbata* may vary significantly. Thus, the construction of chromatographic fingerprint and quantitative method becomes one of the most powerful approaches for systematical quality control of *S. barbata*. Yao et al. (2011) developed this method to establish the HPLC fingerprint analysis of *S. barbata*. Compared to the reported fingerprint assays for *S. barbata* (Lin et al., 2006; Wang et al., 2007), the presented method showed more common peaks or less analysis time in chromatography. In addition, Pan et al. (2011) developed a method for investigating the chromatographic fingerprint of the essential oil with GC-MS The results represented that the samples of *S. barbata* from nine different origins were consistent, while there were difference between the *S. barbata* and its adulterants.

ANTITUMOR ACTIVITY

Traditional Chinese Medicine recorded in Chinese pharmacopoeia has been prescribed in many diseases for over a millennium. It plays a more important role in modern pharmaceutical industry because of its low toxicity and rare side effects. Many of them have also been considered as a valuable source for the discovery of novel drugs including anticancer agents (Schwartsmann et al., 2002). *S. barbata* as an anticancer agent in Chinese herbal medicine has attracted a great deal of attention worldwide. More and more monomeric compounds have been isolated. Some of them displayed antitumor activity *in vivo* or *in vitro* (Table 3). Different from western medicine, an herb might consist of hundreds of phytochemicals, depending on the climate, regions of cultivation and seasons of harvest. So, the mixtures or extracts of herbs might have synergistic activities or buffering toxic effects, more therapeutic or preventive activity than alone (Vickers, 2002). Many pharmacological investigations have demonstrated that extracts from *S. barbata* potently exert anticancer activity. Extract from *S. barbata* (ESB) can induce apoptosis of human lung cancer SPC-A-1 cells (Wei et al., 2007) and human colon cancer cell line (Goh et al., 2005). Via loss of mitochondrial transmembrane potential, release of cytochrome C, and activation of caspase-3, ESB can effectively inhibit the proliferation and induce apoptosis of mouse H22 hepatoma cells (Dai et al., 2008). In addition, the extracts have growth inhibitory and induction apoptosis activity of human myeloid leukemia HL-60 cells (Kim et al., 2007) and leiomyomal cells (Kim et al., 2008). The apoptosis of leiomyomal cells was associated with the release of cytochrome C from the mitochondria followed by an increase in Caspase 3-like activity (Lee et al., 2006), down-regulated the IGF-I expression where IGF-I contributes to the selective growth of the leiomyoma (Kim et al., 2005), induction c-fos gene expression by activating b2-adrenergic receptors (Lee et al., 2004). The 30% ethanol extracts of *S. barbata* greatly inhibited lung cancer A549 cell growth by included cell apoptosis and cytotoxic effects with IC_{50} of 0.21 mg/ml (Yin et al., 2004). The methylene chloride fraction of *S. barbata* could induce apoptosis in human U937 leukemia cells via the mitochondrial signaling pathway (Cha et al., 2004). Yu et al. (2007) confirmed that non-polar and low-polar solvent fractions of *S. barbata* have dose-dependent cytotoxicities on six human malignant cell lines (ACHN, MCF-7, MDA-MB-435S, Bel-7402, HepG2 and HeLa). Among them, the chloroform fraction had the strongest cytotoxicity on cancer cell lines and significantly inhibited solid tumor proliferation. Fresh juice prepared from *S. barbata* were able to inhibit the growth of cancer cell lines, including HepG2 hepatoblastoma, Hep3B hepatocellular carcinoma, MDA-MB231 breast carcinoma, A549 lung cancer and KG-1 acute myelogenous leukaemia and induce apoptosis (Chui et al., 2005).

The aqueous extract derived from *S. barbata* was identified as a potent inhibitor. It can be used as a potential cancer chemopreventive agent in humans cancer cells, especially in gynecological cancer cell lines (Suh et al., 2007). BZL101 (Bezielle) which is an aqueous extract from the *S. barbata* plant is shown to have anticancer properties in a variety of human cancers. Bezielle could induce growth inhibition and apoptosis of breast cancer cell lines (Campbell et al., 2002; Shoemaker et al., 2005; Fong et al., 2008). Bezielle's cytotoxicity toward cancer cells was primarily based on inhibition of metabolic pathways that were preferentially activated in tumor cells (Klawitter et al., 2011). BZL101 exerted phenotype specific anti-proliferative gene expression responses in human breast and prostate cancer cells, which will be valuable in the potential development of BZL-based therapeutic strategies for human reproductive cancers (Marconett et al., 2010). In addtion, Bezielle was orally administered for treatment of

Table 3. The activities of some compounds from *S. barbata.*

Compounds	*In vitro*	References
4-Hydroxy wogonin	Inhibited the proliferation of human leukemia HL-60 cell line, IC_{50}=25.6 μM	Sonoda et al. () 2004
	Inhibited the proliferation of human cancer cell lines (SW480, SW1116, SMMC-7221, HL-60, K562, SH-SY5Y, MGC-803 cells) with IC_{50} values in the range 3.5-24.5 μM	Yao et al. () 2011
Apigenin	Inhibited the proliferation of human leukemia HL-60 cell line, IC_{50}=15.0 μM	Sonoda et al. () 2004
	Inhibited the proliferation of human cancer cell lines (SW1116, SMMC-7221, HL-60, K562, SH-SY5Y, KB, MGC-803 cells) with IC_{50} values in the range 6.3 to 28.3 μM	Yao et al. () 2011
	Selectively against MRSA and methicillin-sensitive *S. aureus* (MSSA) strains with MIC3.9 to 15.6 μg/ml	Sato et al. () 2000
Luteolin	Inhibited the proliferation of human leukemia HL-60 cell line, IC_{50} =18.4 μM	Sonoda et al. (2004)
	exerted antiproliferative activity with IC_{50} of 12 μM and induced apoptosis in Lewis lung carcinoma LLC cells	Kim et al. (2006)
	Inhibited the proliferation of human cancer cell lines (SW480, KB, SMMC-7221, HL-60, K562, SH-SY5Y, MGC-803 cells) with IC_{50} values in the range 5.4 to 27.5 μM	Yao et al. (2011)
	Selectively against MRSA and methicillin-sensitive *S. aureus* (MSSA) strains with MIC 62.5 to 125 μg/ml	Sato et al. (2000)
Baicalein; Scutellarin; Apigenin-5-O-glucopyranoside	Selectively inhibited the proliferation of human cancer cell lines (SW480, SW1116, KB, SMMC-7221, SH-SY5Y, MGC-803, HL-60, K562cells) with IC_{50} values in the range 17.7 to 24.9 μM, 20.7 to 26.2 μM and 7.6 to 22.9 μM, respectively	Yao et al. (2011)
E-1-(4'-Hydroxyphenyl)-but-1-en-3-one	Inhibited the proliferation of human leukemia cell line K562, ID_{50}=11± 2 μg/ml	Ducki et al. (1996)
Pheophorbide a	The IC_{50} values in HepG2 and Hep3B cells after 48 h of incubation were 5.7 and 13.5 μg/ml; induced apoptosis and DNA fragmentation in Hep3B cells	Chan et al. (2006)
	Showed inhibitory effect on the growth of human breast adenocarcinoma MDA-MB-231 cells with an IC_{50} value of 0.5 μM at 24 h	Xuan et al. (2010)
	Could significantly inhibit the growth of R$^-$HepG2 cells with an IC_{50} value at 25.0 mM after 48 h treatment	Tang et al. (2007)
Barbatins A; B; C; Scutebarbtine B	Showed significant cytotoxic activities against HONE-1 nasopharyngeal, KB oral epidermoid carcinoma and HT 29 colorectal carcinoma cells, with IC_{50} values in the range 3.5 to 8.1 μM	Dai et al. (2006b)
6-O-nicotinoylbarbatin A; 6,7-di-O-acetoxybarbatinA; 8-O-nicotinoylbarbatinA; 2-carbonylscutebarbatine A	showed significant cytotoxic activities against HONE-1 nasopharyngeal, KB oral epidermoid carcinoma and HT29 colorectal carcinoma cells, with IC_{50} values in the range 3.1 to 7.2 μM	Dai et al. (2007a)

Scutehenanines A; B; C; D; 6-O-acetylscutehenanine A; 6-O-(2-carbonyl-3-methylbuta -noyl)scutehenanine A	Showed cytotoxic activities against three human cancer lines (HONE-1 nasopharyngeal, KB oral epidermoid carcinoma and HT29 colorectal carcinoma cells), with IC50 values in the range 2.8 to 6.4 µM	Dai et al. (2009b)

Table 3. Contd.

Scutebata A	Showed weak cytotoxic activity against SK-BR-3 cells with an IC_{50} value of 15.2 µM	Zhu et al.(2010)
Scutebarbatine G; 6,7-di-O -nicotinoylscutebarbatine G; 6-O-nicotinoyl-7-O-acetylscutebarbatine G; Scutebarbatine H; 7-O-nicotinoylscutebarbatine H	Showed significant cytotoxic activities against HONE-1 nasopharyngeal, KB oral epidermoid carcinoma and HT29 colorectal carcinoma cells, with IC_{50} values in the range 3.4-8.5 µM	Dai et al. (2007b)
Scutebarbatines C; D; E; F	Showed significant cytotoxic activities against HONE-1 nasopharyngeal, KB oral epidermoid carcinoma and HT29 colorectal carcinoma cells, with IC_{50} values in the range 3.9 to 7.8 µM	Dai et al. (2006a)
Scutebata H	Showed selective cytotoxicity against human breast adenocarcinoma MCF-7 cells with IC_{50} values 20.2 ± 0.9 µM	Zhu et al. (2011)
Scutebata L; M; N	Exhibited moderate-to-weak activity against several human cancer cell lines with IC_{50} values in the range 12.6 to 31.4 µM	Zhu et al. (2011)
Scutebarbatines I; J; K; L	Showed significant cytotoxic activities against HONE-1 nasopharyngeal, KB oral epidermoid carcinoma and HT29 colorectal carcinoma cells, with IC_{50} values in the range 3.2 to 8.3 µM	Dai et al. (2008a)
Scutehenanine H; 6-(2,3-epoxy-2-isopropyl-n-propoxyl)barbatin C	Showed significant cytotoxic activities against human nasopharyngeal carcinoma HONE-1, oral epidermoid carcinoma KB and colorectal carcinoma HT29 cells, with IC50 values in the range of 2.0 to 4.2 µM	Dai et al. (2010)
Scutebarbatine M; N	Showed significant cytotoxic activities against HONE-1 nasopharyngeal, KB oral epidermoid carcinoma and HT29 colorectal carcinoma cells, gave IC_{50} values in the range of 3.5 to 6.3 µM	Dai et al. (2011)
Scutelinquanine A; B; C	Showed significant cytotoxic activities against HONE-1 nasopharyngeal, KB oral epidermoid carcinoma and HT29 colorectal carcinoma cells, with IC_{50} values in the range 2.7 to 6.7 µM	Nie et al. (2010)
Scutelinquanine D; 6-acetoxybarbatin C	Showed significant cytotoxic activities against HONE-1 nasopharyngeal, KB oral epidermoid carcinoma and HT29 colorectal carcinoma cells, with IC_{50} values in the range of 2.5 to 6.6 µM	Qu et al. (2010)
Scutebarbatine O; 6-O-nicotinoylscutebarbatine G	Showed cytotoxic activities against HONE-1 nasopharyngeal, KB oral epidermoid carcinoma and HT29 colorectal carcinoma cells, with IC_{50} values in the range of 2.1 to 5.7 µM	Dai et al. (2009a)
Barbatin D; E	Showed cytotoxic activities against HONE-1 nasopharyngeal, KB oral epidermoid carcinoma and HT29 colorectal carcinoma cells, with IC_{50} values in the range of 3.5 to 6.7 µM	Dai et al. (2008b)
Barbatellarine B	Exhibited weak cytotoxic activity against HL-60 cells, with an IC_{50} value of 41.4 µm	Lee et al. (2010)

advanced and metastatic breast cancer. Phase I clinical trials showed promising efficacy and favorable toxicity profile (Rugo et al., 2007; Perez et al., 2010). Currently Bezielle is in phase II clinical trial in patients with advanced breast cancer.

CONCLUSION

Phytochemical and pharmacological studies of *S. barbata* have received much interest in recent years. More and more effective monomeric compounds or active extracts have been screened for pharmacological activity *in vivo* or *in vitro*. According to the literatures reviewed in this paper, flavonoids, neo-clerodane type diterpenoids and alkaloids are the main and effective chemical compositions which mostly contribute to the pharmacological efficacy of *S. barbata*. Among them, scutellarin, naringenin, apigenin, luteoline and wogonin are the major bioactive flavonoids. Moreover, a series of neo-clerodane type diterpenoids and alkaloids compounds have been proven to be potential drug leads most notably with anti-cancer effects. However, further studies are required for the development of new drugs and therapeutics for the treatment of various diseases, especially for antitumor.

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