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REVIEW ARTICLE

Schisandra chinensis: A comprehensive review on its phytochemicals and biological activities

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Abstract *Schisandra chinensis* (Turcz.) Baill is a climbing plant widely distributed in the northeastern part of China, Korea, and Japan, and used in traditional Chinese herb as a tonic, antitussive, and sedative agent. This review focuses on the phytochemicals, biological activities and analytical methods, in order to promote further studies on the plant. 202 chemical compounds have been isolated and identified from this plant, and the most important are dibenzocyclooctadiene lignans and triterpenoids. The isolated compounds of *S. chinensis* were shown to possess anti-cancer, antioxidant, neuroprotective, hepatoprotective, anti-inflammatory activities and so on. Further studies should be carried on this plant in order to disclose many more active principles and mechanisms of active components.

Contents

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1. Introduction

Schisandra chinensis (Turcz.) Baill belongs to Schisandraceae, is distributed in the northeastern part of China, Korea, and Japan. The dried fruit of this plant, have been used in traditional Chinese herb as a tonic, antitussive, and sedative agent under the name of "wu-wei zi", has been historically used for the treatment of hepatitis for over 2000 years (Hancke et al., 1999; Xue et al., 2015). Previous phytochemical investigations have identified a variety of secondary metabolites, such as lignans, triterpenoids, diterpenoids, sesquiterpenoids, monoterpenes, and fatty acids. Modern pharmacological studies have shown that the extracts and compounds of *S. chinensis* possess a broad range of biological activities, such as anti-cancer, anti-oxidant, neuroprotective, hepatoprotective, anti-inflammatory activities, etc. Due to their great structural diversity and broad relevant bioactivities, *S. chinensis* have attracted increasing research attention. Sowndhararajan et al. reported the lignan extracts and individual compounds from *S. chinensis* were summarized in relation to their neuroprotective and cognitive enhancement activities (Sowndhararajan et al., 2018).

In the last decade, there has been a dramatic progress in the chemical constituents and relevant biological activities. However, so far, no comprehensive review has been published. In the present review, we summarize systematically the research advances on the chemical constituents, their biological activities and analytical methods of *S. chinensis* reported in the literature, as found on Web of Science, Sciencedirect, SpringerLink, ACS, Taylor&Francis, PubMed, and Thieme, with the objective of providing a basis for further research of natural product drug discovery.

2. Chemical constituents

To date, **202** chemical compounds have been identified and isolated from *S.chinensis,* including eighty-three triterpenoids (**1**–**83**), one diterpenoid (**84**), twelve sesquiterpenoids (**85**–**96**), fifteen monoterpenoids (**97**–**111**), eighty-six lignans (**112**–**197**), five fatty acids (**198**–**202**). It can be seen that, lignans and triterpenoids are the dominant chemical constituents in this plant. Their names, structures, and references are summarized in Tables 1–5 and Figs. 1–9.

2.1. Triterpenoids

Triterpenoids are kind of important bioactive compounds from *S.chinensis*. Triterpenoids are formed by six isoprene units via squalene intermediate. It is a structurally very diverse class with nearly 200 different skeletons, which are known to come from natural sources or enzymatic reactions (Wang et al., 2021). Up to now, phytochemical studies led to isolation and identification of **83** triterpenoids from *S.chinensis*. The triterpenoids were isolated from this plant can be divided into four categories according to their different structural skeletons: lanostane triterpenoids (**1**–**4**), cycloartane triterpenoids (**5**–**25**), nortriterpenoids (**22**–**81**) and ursane triterpenoids (**82**–**83**).

2.1.1. Lanostane triterpenoids

Four lanostane triterpenoids (**1**–**4**) were isolated from *S.chinensis*, this class of triterpenoids possess tetracyclic system. Among them, compoud **1** belong to intact lanostane triterpenoid (Zhang et al., 2013). Triterpenoids **2**–**4** are 3,4-secocycloartane triterpenoids, they are formed by the cleavage of C-3(4) bond, with C-3 usually could be oxidized further to carboxylic acid and carboxylic acid derivatives, and the side chain is 24 (*Z*)-en-26-acid or 22, 26 lactone ring (Huang et al., 2008; Qiu et al., 2018).

2.1.2. Cycloartane triterpenoids

Twenty-one cycloartane triterpenoids (**5**–**25**) have been reported from the plant. Triterpenoid **1** is intact cycloartane triterpenoid, with C-3 being oxidized to carbonyl group, and the side chain is 24 (*Z*)-en-26-acid (Huang et al., 2008). Triter-

Table 1 Triterpenoids from *S. chinensis*.

NO.	Compound class and name	Ref.
Lanostane triterpenoids		
1	*epi*-anwuweizic acid	Zhang et al. (2013)
2	micranoic acid A	Huang et al. (2008)
3	kadsuric acid	Huang et al. (2008)
4	schisanlactone I	Qiu et al. (2018)
Cycloartane triterpenoids		
5	*cis*-3-oxo-cycloart-24-ene-26-oic acid = ganwuweizic acid	Huang et al. (2008)
6	schinalactone D	Qiu et al. (2018)
7	wuweizilactone acid	Huang et al. (2008)
8	kadcoccilactone Q	Xue et al. (2010)
9	kadsuphilactone B	Xue et al. (2010)
10	schinchinenin G	Song et al. (2013)
11	schinchinenin H	Song et al. (2013)
12	henrischinin C	Song et al. (2013)
13	schisanlactone J	Qiu et al. (2018)
14	schisanlactone C	Qiu et al. (2018)
15	henrischinin A	Song et al. (2013)
16	henrischinin B	Song et al. (2013)
17	schinchinenlactone C = schisphendilactone B	Song et al. (2013)Qiu et al. (2018)
18	schinchinenlactone B	Song et al. (2013)
19	schinchinenin D	Song et al. (2013)
20	schinchinenin B	Song et al. (2013)
21	schinchinenin C	Song et al. (2013)
22	schinchinenin E	Song et al. (2013)
23	schinchinenin F	Song et al. (2013)
24	schinchinenin A	Song et al. (2013)
25	schinchinenlactone A	Song et al. (2013)
Nortriterpenoids		
Pre-schisanartane nortriterpenoids		
26	pre-schisanartanin A = pre-schisanartanin	Huang et al. (2007a)
27	pre-schisanartanin B	Huang et al. (2008)
28	pre-schisanartanin F	Shi et al. (2014)
29	arisanlactone C	Shi et al. (2014)
30	pre-schisanartanin N	Shi et al. (2014)
31	pre-schisanartanin E	Shi et al. (2014)
32	schisdilactone J	Shi et al. (2014)
Schisanartane nortriterpenoids		
33	schindilactone C	Huang et al. (2007a)
34	schindilactone I	Shi et al. (2014)
35	schindilactone J	Shi et al. (2014)
36	lancifodilactone I	Xue et al. (2010)
37	schindilactone A	Huang et al. (2007a)
38	schindilactone B	Huang et al. (2007a)
39	schindilactone K	Shi et al. (2014)
40	schindilactone H	Xue et al. (2010)
41	lancifodilactone N	Xue et al. (2010)
42	lancifodilactone D	Xue et al. (2010)
43	lancifodilactone C	Huang et al. (2007a)
44	henridilactone D	Huang et al. (2007a)
45	lancifodilactone L	Xue et al. (2010)
46	schindilactone D	Huang et al. (2008)
47	schindilactone E	Huang et al. (2008)
48	arisanlactone B	Shi et al. (2014)
49	micrandilactone A	Shi et al. (2014)
50	schindilactone F	Huang et al. (2008)
51	schindilactone L	Yang et al. (2018)
52	schindilactone G	Huang et al. (2008)
53	schindilactone M	Yang et al. (2018)

(*continued on next page*)

Table 1 (*continued*)

NO.	Compound class and name	Ref.
18-Nor-schiartane nortriterpenoids		
54	wuweizidilactone A	Huang et al. (2007c)
55	wuweizidilactone B	Huang et al. (2007c)
56	wuweizidilactone I	Xue et al. (2010)
57	wuweizidilactone L	Shi et al. (2014)
58	wuweizidilactone M	Shi et al. (2014)
59	wuweizidilactone N	Shi et al. (2014)
60	wuweizidilactone G	Huang et al. (2008)
61	wuweizidilactone O	Shi et al. (2014)
62	wuweizidilactone H	Huang et al. (2008)
63	wuweizidilactone P	Shi et al. (2014)
64	propindilactone Q	Shi et al. (2014)
65	wuweizidilactone S	Yang et al. (2018)
66	19(*R*)-hydroxyl-wuweizidilactone H	Li et al. (2017)
18 (13 → 14)-*abeo*-Schiartane nortriterpenoids		
67	wuweizidilactone C	Huang et al. (2007c)
68	wuweizidilactone D	Huang et al. (2007c)
69	wuweizidilactone E	Huang et al. (2007c)
70	wuweizidilactone F	Huang et al. (2007c)
71	wuweizidilactone J	Shi et al. (2014)
72	wuweizidilactone K	Shi et al. (2014)
Wuweiziartane nortriterpenoids		
73	schintrilactone A	Huang et al. (2007b)
74	schintrilactone B	Huang et al. (2007b)
75	propintrilactone A	Shi et al. (2014)
76	propintrilactone B	Shi et al. (2014)
Schiartane nortriterpenoids		
77	micrandilactone B	Huang et al. (2007a)
78	micrandilactone C	Kim et al. (2015)
Other type of nortriterpenoids		
79	schicagenin A	Shi et al. (2011)
80	schicagenin B	Shi et al. (2011)
81	schicagenin C	Shi et al. (2011)
Ursane triterpenoids		
82	ursolic acid	Huang et al. (2008)
83	2α,3β,19α-trihydroxy-urs-12-en-28-oic acid	Huang et al. (2008)

penoids (**6**–**25**) belong to 3,4-secocycloartane triterpenoids. This class is formed by the cleavage of C-3 (4) bond, with C-3 usually could be oxidized further to carboxylic acid and carboxylic acid derivatives, three-membered ring is formed by dehydrogenation of C-19 methyl and C-9 methine, and the side chain is 24 (*Z*)-en-26-acid or 22, 26 lactone ring or 3-one-2-oxabicyclo-[3.2.1]-octane. Among them, schinalactone D (**6**) and wuweizilactone acid (**7**) possess a novel eight-membered lactone ring between C-21 and C-26 (Huang et al., 2008). Triterpenoids **8**–**23** all possess seven-membered lactone ring between C-3 and C-4, formed by Baeyer Villiger oxidation, after the cleavage of C-3(4) bond. In addition, triterpenoids **13**–**25** all possess seven-membered ring, formed by he cleavage of C-9 (10) bond. Schinchinenin E (**22**) and schinchinenin F (**23**) is possessing hydroperoxyl group at C-19 (Song et al., 2013). Schinchinenin A (**24**) and schinchinenlactone A (**25**) both possess 5/5/7/6/5-fused pentacyclic ring (Song et al., 2013).

Table 2 Diterpenoid and sesquiterpenoids from *S.chinensis*.

NO.	Compound class and name	Ref.
Diterpenoid		
84	7-oxocallitrisic acid	Huang et al. (2008)
Sesquiterpenoids		
85	guaidiol	Liu et al. (2020)
86	α-*iso*-cubebene	Lee et al. (2009)
87	α-*iso*-cubebenol	Lee et al. (2010)
88	α-*iso*-cubebenol acetate	Guo et al. (2020)
89	(−)-clovane-2,9-diol	Huang et al. (2008)
90	widdaranal A	Venkanna et al. (2014)
91	widdaral B	Venkanna et al. (2014)
92	15-hydroxy-α-cadinol	Liu et al. (2020)
93	β-chamigrenal	Venkanna et al. (2014)
94	(6*R*)-β-chamigrenic acid	Li et al. (2017)
95	*iso*-cuparenal	Venkanna et al. (2014)
96	3β-hydroxy-5α,6α-epoxy-β-ionone	Liu et al. (2020)

2.1.3. Nortriterpenoids

Schisandra nortriterpenoids are a structurally intriguing group of polycyclic, highly oxygenated, fused heterocyclic natural products isolated from *S.chinensis*. These compounds are showing different carbon frameworks and oxygenated pattern

Table 3 Monoterpenoids from *S.chinensis*.

NO.	Compound class and name	Ref.
97	schisandenoid A	Liu et al. (2020)
98	thymoquinol 5-*O*-α-L-arabinopyranosyl- (1 → 6)-*β*-D-glucopyranoside	Liu et al. (2019)
99	thymoquinol 5-*O*-*β*-D-glucopyranoside	Liu et al. (2019)
100	thymoquinol 2-*O*-*β*-D-glucopyranoside	Liu et al. (2019)
101	thymoquinol 2-*O*-*β*-D-apiofuranosyl-(1 → 6)-*β*-D-glucopyranoside	Yang et al. (2016)
102	thymoquinol 2-*O*-α-D-arabinofuranosyl-(1 → 6)-*β*-D-glucopyranoside	Yang et al. (2016)
103	thymoquinol 5-*O*-*β*-D-apiofuranosyl-(1 → 6)- *β*-D-glucopyranoside	Yang et al. (2016)
104	thymoquinol 5-*O*-α-D-arabinofuranosyl- (1 → 6)-*β*-D-glucopyranoside	Yang et al. (2016)
105	(*R*)-*p*-cymene 9-*O*-α-D-arabinofuranosyl- (1 → 6)-*β*-D-glucopyranoside	Liu et al. (2020)Liu et al. (2019)
106	(*R*)-*p*-cymene 9-*O*-*β*-D-apiofuranosyl- (1 → 6)-*β*-D-glucopyranoside	Liu et al. (2019)
107	(*R*)-*p*-cymene 9-*O*-*β*-D-glucopyranoside	Liu et al. (2019)
108	cuminic acid 7-*O*-α-D- arabinofuranosyl- (1 → 6)-*β*-D-glucopyranosyl ester	Liu et al. (2019)
109	*p*-cymene 7-*O*-α-D-arabinofuranosyl-(1 → 6)-*β*-D-glucopyranoside	Liu et al. (2019)
110	*p*-methylhydratropic acid 9-*O*-α-D-arabinofuranosyl-(1→ 6)-*β*-D-glucopyranosyl ester	Liu et al. (2019)
111	*p*-menthane-1, 8, 9-triol 9-*O*-*β*-D-glucopyranoside	Dai et al. (2005)

such as pre-schisanartanes (**26**–**32**), schisanartanes (**33**–**53**), 18-norschiartanes (**54**–**66**), 18(13 → 14)-*abeo*-schiartanes (**67**–**72**), wuweiziartanes (**73**–**76**), schiartanes (**77**–**78**), and other novel skeletons nortriterpenoids (**79**–**81**) have been reported from this plant. Among them, Compounds **26**–**32** belong to pre-schisanartane nortriterpenoids, this class possess a unique 7/8/3 consecutive carbocycle. Compounds **54**–**66** are 18-norschiartane nortriterpenoids, this type of compound was postulated to originate from precursors that contain schiartane carbon skeletons through a sequence of reactions that involve a 1,2-methyl shift followed by oxidation and decarboxylation of the C-14 methyl group (Huang et al., 2007c). Compounds **67**–**72** possess an unprecedented 18(13 → 14)-*abeo*-schiartane skeleton, which have a *β*-oriented methyl group at the C-14 position. This structural feature corroborates the biogenetic pathway proposed for the formation of 18-norschiartane-type (Huang et al., 2007c; Xue et al., 2010; Shi et al., 2014; Yang et al., 2018). Compounds **73**–**76** possess five-membered carbon ring (ring D) (Huang et al., 2007b; Shi et al., 2011). Micrandilactones B-C (**77**–**78**) were schiartane nortriterpenoids (Huang et al., 2007a; Kim et al., 2015). Three unprecedented nortriterpenoids, schicagenins A-C (**79**–**81**) are possessing a tetracyclic oxa-cage motif and C_9 side chain. Their structures were determined on the basis of extensive spectroscopic analysis, and the absolute stereochemistries were established by single-crystal X-ray diffraction and CD experiments (Shi et al., 2011).

2.1.4. Ursane triterpenoids

Two ursane triterpenoids, ursolic acid (**82**) and 2α,3*β*,19α-trihydroxy- urs-12-en-28-oic acid (**83**) were isolated from *S.chinensis* (Huang et al., 2008).

2.2. Diterpenoid and sesquiterpenoids

A abietane diterpenoid, 7-oxocallitrisic acid (**84**) was isolated from *S.chinensis* (Huang et al., 2008). Twelve sesquiterpenoids (**85**–**96**) were isolated from *S.chinensis*, including eight new compounds: α-*iso*-cubebene (**86**), α-*iso*-cubebenol (**87**), α-*iso*-cubebenol acetate (**88**), widdaranal A (**90**), widdaral B (**91**), *β*-chamigrenal (**93**), (6*R*)-*β*-chamigrenic acid (**94**), and *iso*-cuparenal (**95**), along with four known compounds: guaidiol (**85**), (−)-clovane-2,9-diol (**89**), 15-hydroxy-α-cadinol (**92**), 3*β*-hydroxy-5α,6α-epoxy-*β*-ionone (**96**) (Huang et al., 2008; Lee et al., 2009; Lee et al., 2010; Venkanna et al., 2014; Liu et al., 2017; Guo et al. 2020; Liu et al., 2020).

2.3. Monoterpenoids

Fifteen monoterpenoid glycosides (**97**–**111**) were isolated from *S.chinensis*, among them, compouds (**97**–**110**) belong to aromatic monoterpenoid glycosides (Dai et al., 2005; Yang et al., 2016; Liu et al., 2019; Liu et al., 2020).

2.4. Lignans

Lignans are the most common constituents of *S. chinensis*, they are a class of secondary plant metabolites produced by oxidative dimerization of two phenylpropanoid units. At present, eighty-six lignans (**112**–**197**) have been isolated and identified from *S.chinensis*. Among them, dibenzocyclooctadienes lignans are the major bioactive constituents of *S. chinensis*.

2.4.1. Dibenzocyclooctadiene lignans

Dibenzocyclooctadienes lignans were characteristic constituents of Schisandraceae family. So far, seventy-one dibenzocyclooctadiene lignans (**112**–**182**) were isolated and identified from *S.chinensis*. Dibenzocyclooctadienes lignans show skeletal diversity in their chemical structures. Dibenzocyclooctadienes lignans have *R*-biphenyl and *S*-biphenyl configuration. This class is fromed by an aryl-aryl bond and an eight-membered ring, the positions of C-1, C-2, C-3, C-12, C-13, and C-14 possess different substituted groups, such as hydroxyl, methoxy, methylenedioxy, and ester group, and methylenedioxy group may existed at C-2 (3) or C-12 (13)

Table 4 Lignans from *S.chinensis*.

NO.	Compound class and name	Ref.
Dibenzocyclooctadiene lignans		
R-biphenyl configuration		
112	schisandrin A = schizandrin A	Choi et al. (2006)
113	schisandrin =schizandrol A = schizandrin	Kochetkov et al. (1961)
114	isoschizandrin	Ikeya et al. (1988a)
115	schizandrin B= (±)-γ-schizandrin	Sovová et al. (2007)
116	gomisin H	Ikeya et al. (1979e)
117	(+)-tigloylgomisin H	Ikeya et al. (1978)
118	angeloylgomisin H	Ikeya et al. (1978);
119	benzoylgomisin H	Ikeya et al. (1978)
120	(+)-gomisin K_2	Nakajima et al. (1983)
121	deoxyschizandrin = deoxyschisandrin	Kochetkov et al. (1962a)
122	gomisin A = schisandrol B	Taguchi et al. (1977)
123	schisandroside E	Liu et al. (2020)
124	schisandroside B	Kim et al. (2015)
125	schisandroside A	Kim et al. (2015)
126	14-tigloylschinlignan D	Pel et al. (2017)
127	(−)-gomisin M_1	Hu et al. (2014)
128	(−)-neglschisandrin E	Pel et al. (2017)
129	schinlignan D	Xue et al. (2015)
130	(+)-schilignan E	Xue et al. (2015)
131	schinlignan F	Xue et al. (2015)
132	schinlignan G	Xue et al. (2015)
133	schisanchinin B	Hu et al. (2014)
134	neglschisandrin E	Xue et al. (2015)
135	schisanchinin C	Hu et al. (2014)
136	schisanchinin D	Hu et al. (2014)
137	(+)-gomisin M_2	Hu et al. (2014)
138	(+)-gomisin K_3	Hu et al. (2014)
139	(+)-14-tigloylgomisin K_3	Pel et al. (2017)
140	micrantherin A	Li et al. (2017)
141	gomisin T	Ikeya et al. (1988b)
142	schinlignan A	Xue et al. (2015)
143	schischinone	Xue et al. (2015)
S-biphenyl configuration		
144	(−)-gomisin K_1	Choi et al. (2006)
145	gomisin J	Šmejkal et al. (2010)
146	schisantherin A = gomisin C	Taguchi et al. (1977)
147	gomisin F	Taguchi et al. (1977)
148	(−)-tigloyl-deangeloyl-gomisin F	Šmejkal et al. (2010)
149	angeloylgomisin Q	Ikeya et al. (1979d)
150	benzoylgomisin Q	Piao et al. (2005)
151	gomisin G	Taguchi et al. (1977)
152	schizandrin C = schisandrin C = wuweizisu C	Pel et al. (2017)Choi et al. (2006)
153	gomisin N	Choi et al. (2006)
154	gomisin B	Taguchi et al. (1977)
155	schisandrene	Choi et al. (2006)
156	(−)-gomisin L_1	Hu et al. (2014)
157	(−)-gomisin L_2	Pel et al. (2017)
158	(−)-rubrisandrin B	Pel et al. (2017)
159	(−)-tigloylgomisin P	Ikeya et al. (1980)
160	(−)-angeloylgomisin P	Ikeya et al. (1980)
161	schinlignan B	Xue et al. (2015)
162	schinlignan C	Xue et al. (2015)
163/164	rubrisandrins A	Xue et al. (2015)
165	methylgomisin O	Xue et al. (2015)
166	wuweilignan E	Xue et al. (2015)
167	schisanchinin A	Hu et al. (2014)
168	(−)-tigloylgomisin Q	Pel et al. (2017)
169	1,2,13,14-tetramethoxydibenzocyclooctadiene 3,12-*O*-β-D-diglucopyranoside	Yang et al. (2016)
170	3,7-dihydroxy-1,2,13,14-tetramethoxydibenzocyclooctadiene 12-*O*-β-D -glucopyranoside	Yang et al. (2016)
171	schisandroside C	Kim et al. (2015)

Table 4 (*continued*)

NO.	Compound class and name	Ref.
172	schisandroside D	Kim et al. (2015)
173	gomisin R	Ikeya et al. (1982a)
174	schisantherin D	Ikeya et al. (1982a)
175	gomisin O	Ikeya et al. (1979b)
176	epigomisin O	Ikeya et al. (1979b)
177	angeloylgomisin O	Ikeya et al. (1982b)
178	angeloylisogomisin O	Ikeya et al. (1982b)
179	benzoylisogomisin O	Ikeya et al. (1982b)
180	gomisin S	Ikeya et al. (1988b)
181	gomisin E	Ikeya et al. (1979b)
182	gomisin D	Ikeya et al. (1979c)
Other types of lignans		
183	D-epigalbacin	Zhang et al. (2013)
184	machilin G	Zhang et al. (2013)
185	chicanine	Zhang et al. (2013)
186	schinlignin A	Xue et al. (2010)
187	schinlignin B	Xue et al. (2010)
188	*rel*-(7*R*, 8*R*, 7′*R*, 8′*R*)-manglisin E	Pel et al. (2017)
189	anwulignan	Zhang et al. (2013)
190	schineolignin A	Xue et al. (2010)
191	schineolignin B	Xue et al. (2010)
192	schineolignin C	Xue et al. (2010)
193	pregomisin	Xue et al. (2010)
194	*meso*-dihydroguaiaretic acid	Xue et al. (2010)
195	8,8′-dihydroxypinoresinol	Liu et al. (2020)
196	8-hydroxypinoresinol	Liu et al. (2020)
197	pinobatol-9-*O*-*β*-D-glucopyranoside	Yang et al. (2016)

Table 5 Fatty acids from *S.chinensis*.

NO.	Compound class and name	Ref.
198	dimethyl-malate	Pel et al. (2017)
199	methyl-malate	Pel et al. (2017)
200	butyl-1-methyl malate	Pel et al. (2017)
201	1,5-dibutyl-1′-methyl citrate	Pel et al. (2017)
202	1-butyl-1′,5-dimethyl citrate	Pel et al. (2017)

and hydroxyl group at C-7 and C-8. Different ester groups, such as, angeloyl, tigloyl, acetyl, and benzoyl may exist at the C-6 of the octatomic ring, and ester group linkage are usually *β*-configuration (Wang et al., 2021). Compounds **112**–**143** possess a *R*-biphenyl configuration (Choi et al., 2006; Hu et al., 2014; Ikeya et al., 1978, 1988a,a,b,e; Kim et al., 2015; Kochetkov et al., 1961, 1962a,b; Li et al., 2017; Liu et al., 2020; Nakajima et al., 1983; Pel et al., 2017; Sovová et al., 2007; Taguchi and Ikeya, 1977; Xue et al., 2015), and compounds **144**–**182** possess a *S*-biphenyl configuration (Taguchi et al., 1977; Ikeya et al., 1979b, 1979c, 1979d, 1980, 1982a, 1982b; Piao et al., 2005; Šmejkal et al., 2010; Hu et al., 2014; Zhu et al., 2015; Kim et al., 2015; Xue et al., 2015; Yang et al., 2016; Pel et al., 2017; Choi et al., 2006, 2020). Among them, schisandrosides A (**125**), B (**124**), C(**171**) and D (**172**) represent the first example of a dibenzocyclooctadiene lignan glycoside (Kim et al., 2015). Schinlignan A (**142**) possess 2-hydroxy-2,3-dimethylbutyryl moiety , and an epoxide ring exist between C-7 and C-18. Schischinone (**143**) possess rare 6,7-seco- dibenzocyclooctadiene carbon skeleton (Xue et al., 2015).

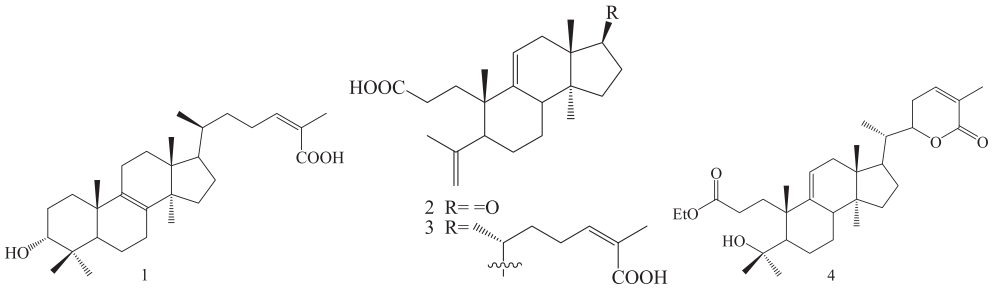


Fig. 1 Structures of lanostane triterpenoids (**1**–**4**).

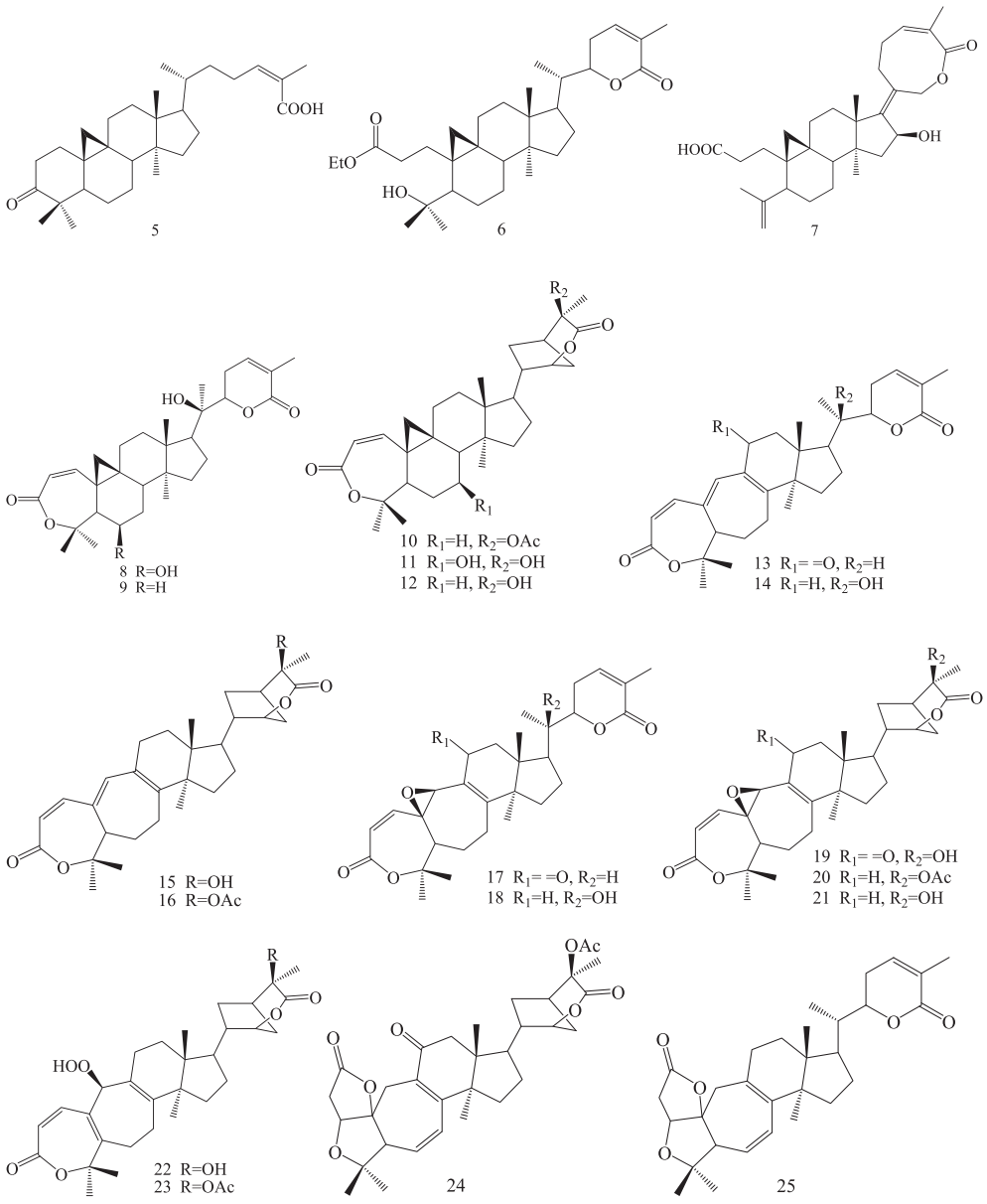


Fig. 2 Structures of cycloartane triterpenoids (**5**–**25**).

2.4.2. Other types of lignans

Fifteen other types of lignans (**183**–**197**) were isolated from *S. chinensis*. Among these compounds, D-epigalbacin (**183**), machilin G (**184**), chicanine (**185**), schinlignin A (**186**), schinlignin B (**187**), and *rel*-(7*R*, 8*R*, 7′*R*, 8′*R*)-manglisin E (**188**) belong to terahydrofuran-type lignans (Xue et al., 2010; Zhang et al., 2013; Pel et al., 2017). Anwulignan (**189**), schineolignin A (**190**), schineolignin B (**191**), schineolignin C (**192**), pregomisin (**193**), and *meso*-dihydroguaiaretic acid (**194**) are dibenzylbutane-type lignans (Xue et al., 2010; Zhang et al., 2013; Zhu et al., 2015; Pel et al., 2017; Liu et al., 2020), 8,8′-dihydroxypinoresinol (**195**) and 8-hydroxypinoresinol (**196**) are furofuran-type lignans (Liu et al., 2020), pinobatol-9-*O*-*β*-D -glucopyranoside (**197**) belong to futoenone lignans (Yang et al., 2016).

2.5. Fatty acids

Five fatty acids have been reported from *S.chinensis*, namely dimethyl-malate (**198**), methyl-malate (**199**), butyl-1-methyl malate (**200**), 1,5-dibutyl-1′-methyl citrate (**201**), 1-butyl-1′,5-dimethyl citrate (**202**) (Pel et al., 2017).

3. Biological activities

3.1. Anti-cancer activity

Widdaral B (**91**) and *β*-chamigrenal (**93**) showed obvious cytotoxic activity against Caco-2 cell lines, with IC_{50} values of 17.10 and 16.46 μg/mM, respectively (Venkanna et al., 2014).

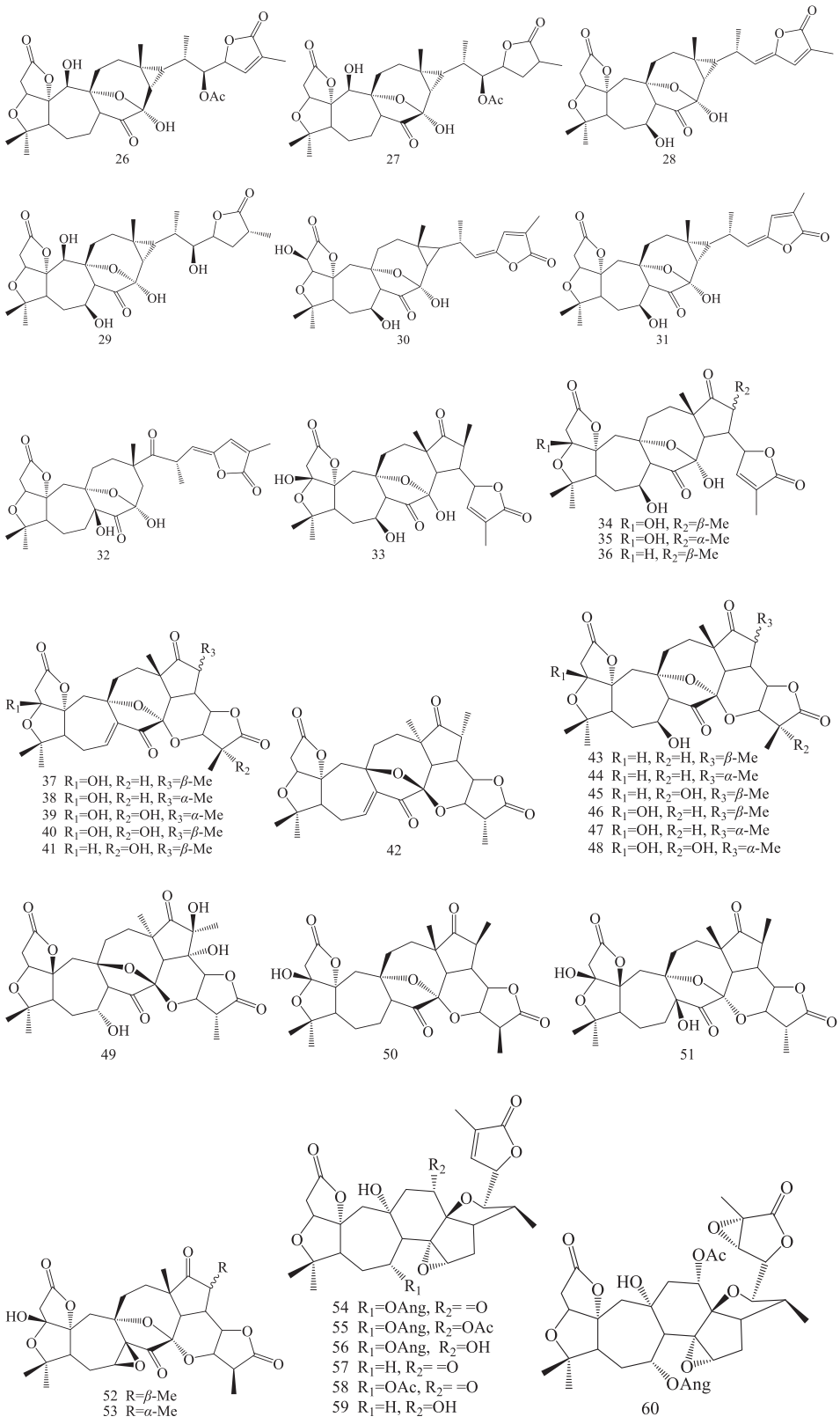


Fig. 3 Structures of nortriterpenoids (**26**–**81**).

(+)-Deoxyschisandrin (**121**) and (−)-gomisin N (**153**) showed anti-proliferative activity against the LoVo cell lines, with EC_{50} values of 22.6 and 27.4 μg/mL, respectively. And schisandrin (**113**) and (−)-tigloyl-deangeloyl-gomisin F (**148**) showed little anti-proliferative activity against the LoVo cell lines, with EC_{50} values of 84.4 and 81.7 μg/mL, respectively (Šmejkal

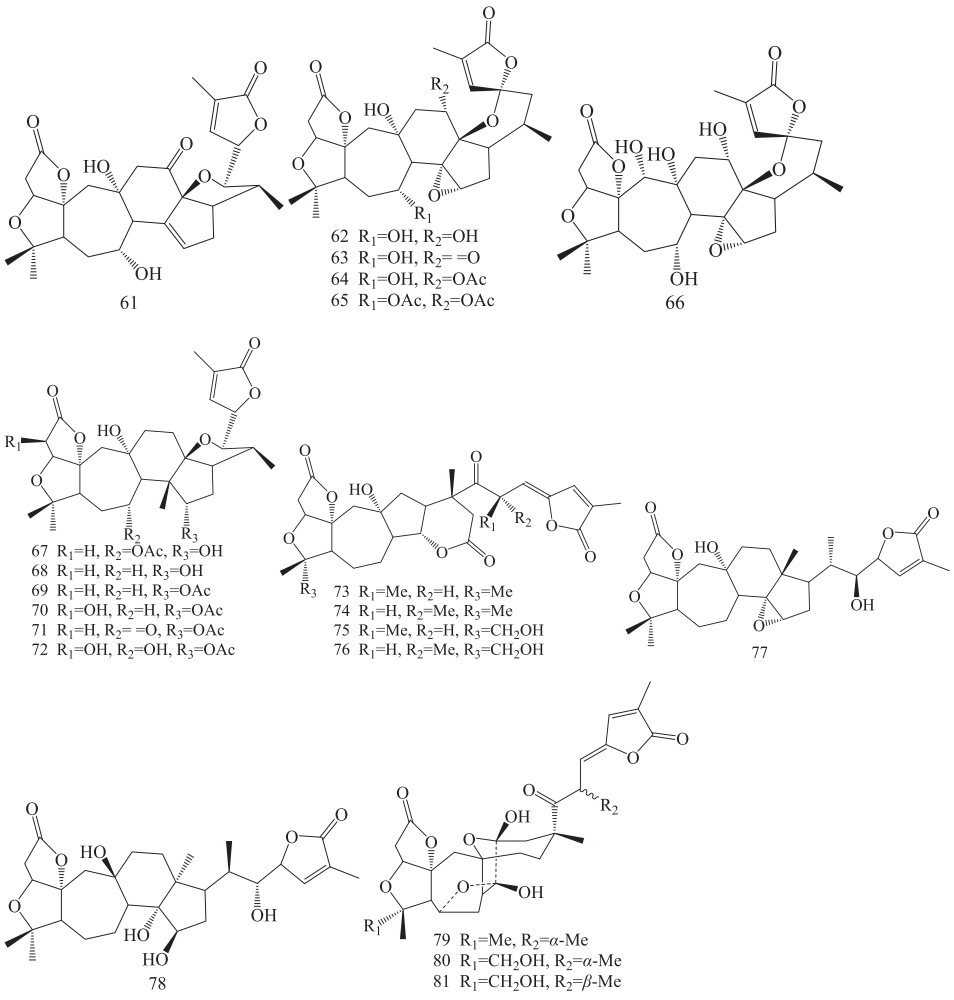


Fig. 3 (*continued*)

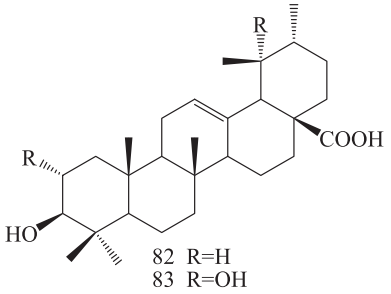


Fig. 4 Structures of ursane triterpenoids (**82**–**83**).

et al., 2010). Schisandrin C (**152**) inhibited human leukemia U937 cells growth in a dose dependent manner (Park et al., 2009). Epi-anwuweizic acid (**1**) exhibited the strongest cytotoxic activity against on prostate cancer cells PC3, with an IC_{50} of 36.5 μM. chicanine (**185**) showed good anti-proliferation, with an IC_{50} of 44.2 μM (Zhang et al., 2013). Schisandroside E (**123**), gomisin F (**147**), angeloylgomisin Q (**149**), and schisandrin (**113**) exhibited strong cytotoxic activities against MGC-803, with an IC_{50} values of 4.621, 0.050, 0.075, and 4.773 μM, respectively, and showed strong cytotoxic activities against Ishikawa cell lines, with an IC_{50} values of 0.356, 0.426, 0.567, and 0.437 μM, respectively. Schisandroside E (**123**), gomisin F (**147**), (−)-tigloyl- deangeloyl-gomisin F (**148**), angeloylgomisin Q (**149**), and schisandrin (**113**) demonstrated strong cytotoxicity against Caco-2 cell lines, with IC_{50} values of 0.021, 0.572, 0.033, 2.305, and 0.537 μM, respectively (Liu et al., 2020). Dibenzocyclooctadiene lignans (−)-gomisin K_1 (**144**), gomisin J (**145**), gomisin A (**122**), and angeloylgomisin H (**118**) showed anti-cancer activity against AGS, HeLa and HT-29 cells, especially, angeloyl-gomisin H (**118**), concentration dependently suppressed the proliferation and viability against three cancer cells. (Choi et al., 2020). (Table 6).

3.2. Anti-oxidant activity

Tigloylgomisin H (**117**), gomisin K_3 (**138**), angeloylgomisin H (**118**), gomisin J (**145**), gomisin G (**151**), gomisin B (**154**), and schisandrene (**155**) showed DCFH-DA cellular-based antioxidant activity (2.8–160.9 μM). Meanwile, the structure–activity relationships of the dibenzocyclooctadiene lignans exhibited that the exocyclic methylene functionality was essential for antioxidant activity, with the benzoyloxy group probably

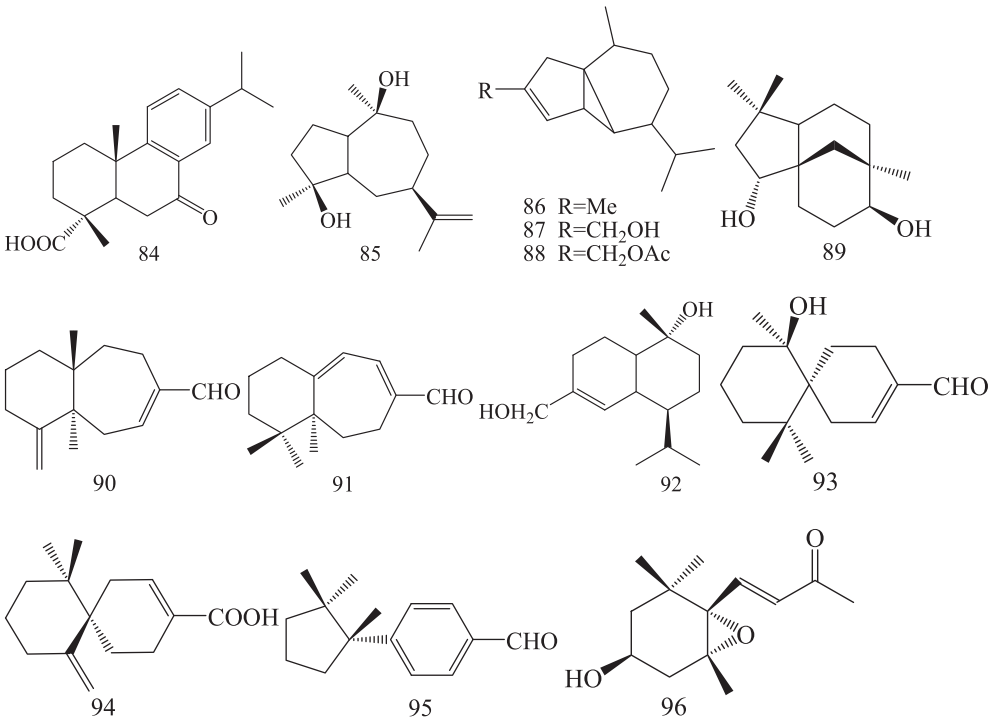


Fig. 5 Structures of diterpenoid (**84**) and sesquiterpenoids (**85**–**96**).

increasing antioxidant activity (Choi et al., 2006). Schisandrin (**113**) could ameliorate Aβ_{1-42}-induced memory impairment in mice at least in part by enhancing the activity of the antioxidative defense system and free radical-scavenging activity (Hu et al., 2012). The extract and two compounds of *S. chinensis* exhibited antioxidant activities on DPPH radical scavenging effects. There were good dose-dependence effects of the extract and compounds anwulignan (**189**) and chicanine (**185**) with IC_{50} values of 188 μg/mL, 11.2 and 26.0 μM, respectively. The two lignans anwulignan (**189**) and chicanine (**185**) showed better antioxidant activities than the extract (Zhang et al., 2013). (Table 6).

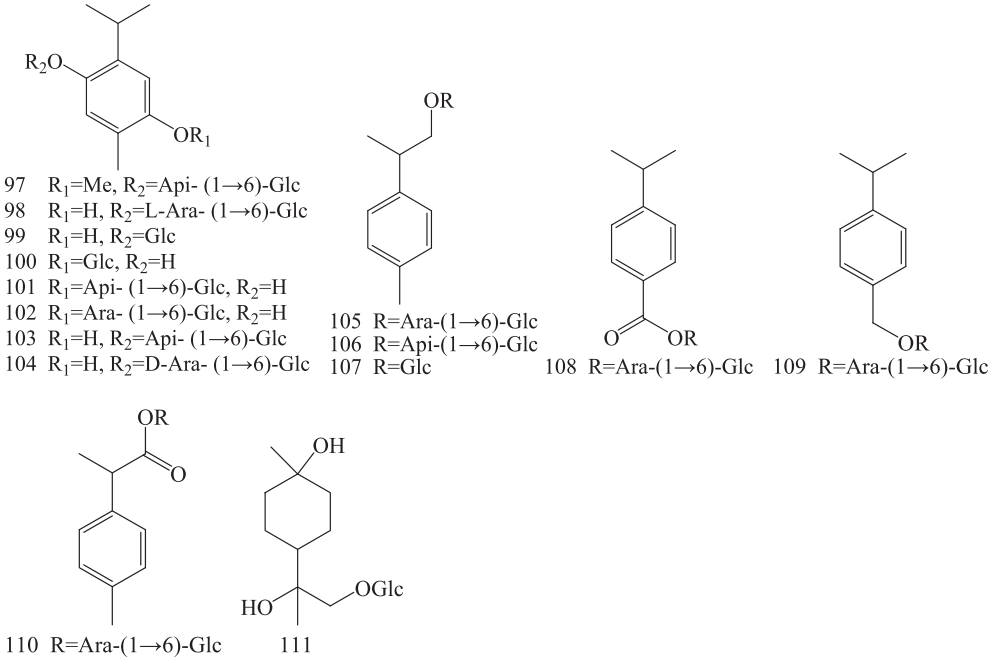
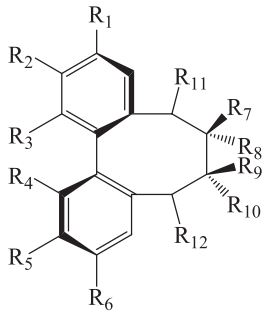


Fig. 6 Structures of monoterpenoids (**97**–**111**).



112 R_1=R_2=R_3=R_4=R_5=R_6=OMe, R_7=R_9=R_{11}=R_{12}=H, R_8=R_{10}=Me
113 R_1=R_2=R_3=R_4=R_5=R_6=OMe, R_7=R_{11}=R_{12}=H, R_9=OH, R_8=R_{10}=Me
114 R_1=R_2=R_3=R_4=R_5=R_6=OMe, R_7=OH, R_8=R_{10}=Me, R_9=R_{11}=R_{12}=H
115 R_1+R_2=OCH_2O, R_3=R_4=R_5=R_6=OMe, R_7=R_9=R_{11}=R_{12}=H, R_8=R_{10}=Me
116 R_1=R_2=R_4=R_5=R_6=OMe, R_3=OH, R_7=R_{11}=R_{12}=H, R_8=R_{10}=Me, R_9=OH
117 R_1=R_2=R_4=R_5=R_6=OMe, R_3=OTig, R_7=R_{11}=R_{12}=H, R_8=R_{10}=Me, R_9=OH
118 R_1=R_2=R_4=R_5=R_6=OMe, R_3=OAng, R_7=R_{11}=R_{12}=H, R_8=R_{10}=Me, R_9=OH
119 R_1=R_2=R_4=R_5=R_6=OMe, R_3=OBz, R_7=R_{11}=R_{12}=H, R_8=R_{10}=Me, R_9=OH
120 R_2=R_3=R_4=R_5=R_6=OMe, R_7=R_9=R_{11}=R_{12}=H, R_8=R_{10}=Me
121 R_1=R_2=R_3=R_4=R_5=R_6=OMe, R_7=R_9=R_{11}=R_{12}=H, R_8=Me, R_{10}=Me
122 R_1+R_2=OCH_2O, R_3=R_4=R_5=R_6=OMe, R_7=R_{11}=R_{12}=H, R_9=OH, R_8=R_{10}=Me
123 R_1=OAng, R_2=R_3=R_4=R_5=OMe, R_6=OGlc, R_7=R_{11}=R_{12}=H, R_8=R_{10}=Me, R_9=OH
124 R_1=R_2=R_3=R_4=R_5=OMe, R_6=OGlc, R_7=R_{11}=R_{12}=H, R_8=R_{10}=Me, R_9=OH
125 R_1+R_2=OCH_2O, R_3=R_4=R_5=OMe, R_6=OGlc, R_7=R_{11}=R_{12}=H, R_8=R_{10}=Me, R_9=OH
126 R_1+R_2=OCH_2O, R_3=OTig, R_4=R_5=R_6=OMe, R_7=R_{11}=R_{12}=H, R_8=R_{10}=Me, R_9=OH
127 R_1=R_2=R_4=R_5=R_6=OMe, R_3=OH, R_7=R_{11}=R_{12}=H, R_8=R_{10}=Me, R_9=OH
128 R_1+R_2=OCH_2O, R_3=R_4=R_5=OMe,R_6=OH, R_7=R_9=R_{11}=R_{12}=H, R_8=R_{10}=Me
129 R_1+R_2=OCH_2O, R_3=OAng, R_4=R_5=R_6=OMe, R_7=R_{11}=R_{12}=H, R_8=R_{10}=Me, R_9=OH
130 R_1+R_2=OCH_2O, R_4=OAng, R_3=R_5=R_6=OMe, R_7=R_{11}=R_{12}=H, R_8=R_{10}=Me, R_9=OH
131 R_1=R_2=R_3=R_5=R_6=OMe, R_4=OH, R_7=R_{11}=R_{12}=H, R_8=R_{10}=Me, R_9=OH
132 R_1=R_2=R_3=R_5=R_6=OMe, R_4=OAng, R_7=R_9=R_{11}=R_{12}=H, R_8=R_{10}=Me
133 R_1=R_2=R_4=R_5=OMe, R_3=OAng, R_6=OH, R_7=R_9=R_{11}=R_{12}=H, R_8=R_{10}=Me
134 R_1+R_2=OCH_2O, R_3=R_4=R_5=OMe, R_6=OH, R_7=R_9=R_{11}=R_{12}=H, R_8=R_{10}=Me
135 R_1=R_2=R_3=R_4=R_5=R_6=OMe, R_7+R_9=O, R_8=R_{10}=Me, R_{11}=R_{12}=H
136 R_1=R_2=R_3=R_5=R_6=OMe, R_4=OH, R_7=R_9=R_{11}=R_{12}=H, R_8=R_{10}=Me
137 R_1=R_2=R_3=OMe, R_4=OH, R_5+R_6=OCH_2O, R_7=R_9=R_{11}=R_{12}=H, R_8=R_{10}=Me
138 R_1=R_2=R_4=R_5=R_6=OMe, R_3=OH, R_7=R_9=R_{11}=R_{12}=H, R_8=R_{10}=Me
139 R_1=R_2=R_4=R_5=R_6=OMe, R_3=OTig, R_7=R_9=R_{11}=R_{12}=H, R_8=R_{10}=Me
140 R_1=R_2=R_3=R_5=R_6=OMe, R_4=OH, R_7=R_{10}=Me, R_8=OAng, R_9=R_{11}=R_{12}=H
141 R_1=R_9=OH, R_2=R_3=R_4=R_5=R_6=OMe, R_7=R_{11}=R_{12}=H, R_8=R_{10}=Me

Fig. 7 Structures of dibenzocyclooctadienes lignans (**112**–**182**).

3.3. Neuroprotective activity

Deoxyschisandrin (**121**), gomisin N (**153**), and wuweizisu C (**152**) exhibited significantly neuroprotective activity gainst glutamate-induced neurotoxicity (Kim et al., 2004). The neuroprotective activity was tested on PC12 cells with neurotoxicity induced by amyloid-beta 1–42($A\beta_{1\text{-}42}$). 1,2,13,14-Tetramethox ydibenzocyclooctadiene 3,12-*O*-*β*-D-diglucopyranoside (**169**), 3,7-dihydroxy-1,2,13,14-tetramethoxy- dibenzocyclooctadiene 12-*O*-*β*-D-glucopyranoside (**170**) exhibited neuroprotective activity against A*β*-induced toxicity in PC12 cells (Yang et al., 2016). Schisanchinin A (**167**) and B (**133**), gomisin G (**151**), deoxyschizandrin (**121**), (±)-*γ*-schizandrin (**115**), gomisin A (**122**), (−)-gomisin M_1 (**127**), (−)-gomisin L_1 (**156**), (+)-gomisin M_2 (**137**), (+)-gomisin K_3 (**138**), and ganwuweizic acid (**5**) significantly inhibited NO release by LPS-activated microglia in a dose-dependent manner. Among them, schisanchinin B (**133**) and ganwuweizic acid (**5**) showed strong inhibition activities, whereas schisanchinin A (**167**), gomisin G (**151**), deoxyschizandrin (**121**), (±)-*γ*-schizandrin (**115**), (−)-gomisin L_1 (**156**), and (+)-gomisin M_2 (**137**) demonstrated moderate inhibition activities, and gomisin A (**122**), (−)-gomisin M_1 (**127**) and (+)-gomisin K_3 (**138**) exhibited weak inhibition activities, which implied the lignans from the fruit of *S. chinensis* may be a potential healthy food for anti-AD (Hu et al., 2014). Homogeneous polysaccharides (SCP2-1) of *S. Chinensis* could improve M1/M2 polarization, especially inhibit M1 polarization, and ameliorate the cognition of mice in Y-maze and NOR test. SCP2-1 play a neuroprotective role through LRP-1 to reverse activation of microglia via suppressing the overactive NF-κB and JNK pathway (Xu et al., 2020). (Table 6).

3.4. Anti-HIV-1 activity

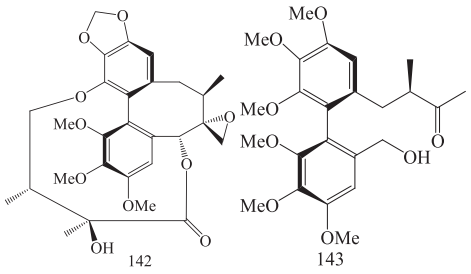
The anti-HIV-1 activities testing showed that preschisanartanin(**26**) demonstrated anti-HIV-1 activity with an EC_{50} value of 13.81 μg/mL (AZT: EC_{50} = 2.26 μg/mL), and six triterpenoids schindilactones A-C (**33, 37**–**38**), micrandilactone B (**77**), lancifodilactone C (**43**), and henridilactone D (**44**) showed weak anti-HIV-1 activity with EC_{50} values of > 50 μg/mL (Huang et al., 2007a). Schintrilactones A and B (**73**–**74**) demonstrated anti-HIV-1 activity, with EC_{50} values of 17.9 and 36.2 μg/mL, respectively (Huang et al., 2007b). Wuweizidilactones A and B (**54**–**55**) exhibited anti-HIV-1 activity, with EC_{50} values of 26.81 and 28.86 μg/mL, respectively. Wuweizidilactones C-F (**67**–**70**) showed weak anti-HIV-1 activity, with EC_{50} values of > 50 μg/mL (Huang et al., 2007c). (Table 6).

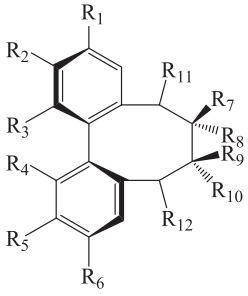
3.5. Anti-inflammatory activity

Schisandrin (**113**) showed the potent inhibition of nitric oxide (NO) production, prostaglandin E2 (PGE2) release, cyclooxygenase-2 (COX-2) and inducible nitric oxide synthase (iNOS) expression in a RAW 264.7 macrophage cell line (Guo et al., 2008). α-Iso-cubebenol (**87**) exhibited inhibition of nitric oxide (NO) and prostaglandin E2 (PGE2) production in LPS-stimulated macrophages (Lee et al., 2010). (Table 6).

3.6. Hepatoprotective activity

Schizandrin (**113**), gomisin M_2 (**137**), and micrantherin A (**140**) showed moderate hepatoprotective activities against





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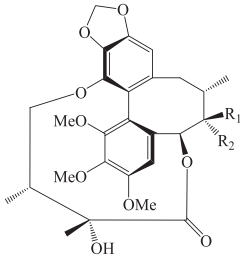
145 R_1=R_6=OH, R_2=R_3=R_4=R_5=OMe, R_7=R_9=R_{11}=R_{12}=H, R_8=R_{10}=Me
146 R_1+R_2=OCH_2O, R_3=R_4=R_5=R_6=OMe, R_7=R_{11}=H, R_8=R_9=Me, R_{10}=OH, R_{12}=*β*-OBz
147 R_1=R_2=R_3=R_4=OMe, R_5+R_6=OCH_2O, R_7=R_{11}=H, R_8=R_9=Me, R_{10}=OH, R_{12}=*β*-OAng
148 R_1=R_2=R_3=R_4=OMe, R_5+R_6=OCH_2O, R_7=R_{11}=H, R_8=R_9=Me, R_{10}=OH, R_{12}=*β*-OTig
149 R_1=R_2=R_3=R_4=R_5=R_6=OMe, R_7=R_{11}=H, R_8=R_9=Me, R_{10}=OH, R_{12}=*β*-OAng
150 R_1=R_2=R_3=R_4=R_5=R_6=OMe, R_7=R_{11}=H, R_8=R_9=Me, R_{10}=OH, R_{12}=*β*-OBz
151 R_1=R_2=R_3=R_4=OMe, R_5+R_6=OCH_2O, R_7=R_{11}=H, R_8=R_9=Me, R_{10}=OH, R_{12}=*β*-OBz
152 R_1+R_2=OCH_2O, R_3=R_4=OMe, R_5+R_6=OCH_2O, R_7=R_9=R_{11}=R_{12}=H, R_8=R_{10}=Me
153 R_1+R_2=OCH_2O, R_3=R_4=R_5=R_6=OMe, R_7=R_9=R_{11}=R_{12}=H, R_8=R_{10}=Me
154 R_1+R_2=OCH_2O, R_3=R_4=R_5=R_6=OMe, R_7=R_{11}=H, R_8=R_9=Me, R_{10}=OH, R_{12}=*β*-OAng
155 R_1+R_2=OCH_2O, R_3=R_4=OMe, R_5+R_6=OCH_2O, R_7=R_{11}=H, R_8=Me, R_9+R_{10}= CH_2, R_{12}=*β*-OBz
156 R_1=R_2=R_4=OMe, R_3=OH, R_5+R_6=OCH_2O, R_7=R_9=R_{11}=R_{12}=H, R_8=R_{10}=Me
157 R_1=OH, R_2=R_3=R_4=OMe, R_5+R_6=OCH_2O, R_7=R_9=R_{11}=R_{12}=H, R_8=R_{10}=Me
158 R_1=R_4=OH, R_2=R_3=R_4=R_5=R_6=OMe, R_7=R_9=R_{11}=R_{12}=H, R_8=R_{10}=Me
159 R_1+R_2=OCH_2O, R_3=R_4=R_5=R_6=OMe, R_7=R_{11}=H, R_8=R_{10}=Me, R_9=OH, R_{12}=*α*-OTig
160 R_1+R_2=OCH_2O, R_3=R_4=R_5=R_6=OMe, R_7=R_{11}=H, R_8=R_{10}=Me, R_9=OH, R_{12}=*α*-OAng
161 R_1+R_2=OCH_2O, R_3=R_4=R_5=R_6=OMe, R_7=R_{11}=H, R_8=R_{10}=Me, R_9=OH, R_{12}=*β*-OAng
162 R_1=R_2=R_3=R_5=R_6=OMe, R_4=OAng, R_8=R_{11}=R_{12}=H, R_7=R_{10}=Me, R_9=OH
163 R_1=R_2=R_4=R_5=OMe, R_3=R_6=OH, R_7=R_9=R_{11}=R_{12}=H, R_8=R_{10}=Me
164 R_2=R_3=R_5=R_6=OMe, R_1=R_4=OH, R_7=R_9=R_{11}=R_{12}=H, R_8=R_{10}=Me
165 R_1+R_2=OCH_2O, R_3=R_4=R_5=R_6=OMe, R_7=R_9=R_{11}=H, R_8=R_{10}=Me, R_{12}=*β*-OMe
166 R_1=R_2=R_3=R_4=R_5=R_6=OMe, R_7=R_9=R_{11}=H, R_8=R_{10}=Me, R_{12}=*β*-OMe
167 R_1=R_2=R_3=R_4=OMe, R_5+R_6=OCH_2O, R_7=R_{11}=H, R_8=Me, R_9+R_{10}= CH_2, R_{12}=*β*-OBz
168 R_1+R_2=OCH_2O, R_3=R_4=R_5=R_6=OMe, R_7=R_{11}=H, R_8=R_{10}=Me, R_9=OH, R_{12}=*β*-OTig
169 R_1=R_6=OGlc, R_2=R_3=R_4=R_5=OMe, R_8=R_{10}=Me, R_7=R_9=R_{11}= R_{12}=H
170 R_1=OGlc, R_2=R_3=R_4=R_5=OMe, R_6=OH, R_8=R_{10}=Me, R_7=OH, R_9=R_{11}= R_{12}=H
171 R_1+R_2=OCH_2O, R_3=R_4=OMe, R_5=OH, R_6=OGlc, R_8=R_9=Me, R_7=R_{10}=R_{11}=R_{12}=H
172 R_1+R_2=OCH_2O, R_3=R_4=R_5=OMe, R_6=OGlc, R_8=R_9=Me, R_{10}=OH, R_7=R_{11}=H, R_{12}=*β*-OAng
173 R_1+R_2=R_5+R_6=OCH_2O, R_3=R_4=OMe, R_8=R_{10}=Me, R_7=R_9=R_{11}=H, R_{12}=*β*-OAng
174 R_1+R_2=R_5+R_6=OCH_2O, R_3=R_4=OMe, R_8=R_9=Me, R_{10}=OH, R_7=R_{11}=H, R_{12}=*β*-OBz
175 R_1+R_2=OCH_2O, R_3=R_4=R_5=R_6=OMe, R_8=R_{10}=Me, R_7=R_9=R_{11}=H, R_{12}=*β*-OH
176 R_1+R_2=OCH_2O, R_3=R_4=R_5=R_6=OMe, R_8=R_{10}=Me, R_7=R_9=R_{11}=H, R_{12}=*α*-OH
177 R_1+R_2=OCH_2O, R_3=R_4=R_5=R_6=OMe, R_8=R_{10}=Me, R_7=R_9=R_{11}=H, R_{12}=*β*-OAng
178 R_1=R_2=R_3=R_4=OMe, R_5+R_6=OCH_2O, R_8=R_{10}=Me, R_7=R_9=R_{11}=H, R_{12}=*β*-OAng
179 R_1=R_2=R_3=R_4=OMe, R_5+R_6=OCH_2O, R_8=R_{10}=Me, R_7=R_9=R_{11}=H, R_{12}=*β*-OBz
180 R_1=OH, R_2=R_3=R_4=R_5=R_6=OMe, R_8=R_{10}=Me, R_7=R_9=R_{11}=H, R_{12}=*α*-OH



181 R_1=H, R_2=Me
182 R_1=Me , R_2=OH

Fig. 7 (*continued*)

damage induced by *N*-acetyl-*p*-aminophenol (APAP) in human liver carcinoma (HepG2) cells, at a concentration of 10 μM (Li et al., 2017). *S. chinensis*-derived lignans (SCDLs) and schisantherin D (**174**) have ETBR antagonistic effects, which may protect the normal function of PC and NPC by protecting ER stress and mitochondrial dysfunction, thereby exerting hepatoprotection (Xu et al., 2020). (Table 6).

3.7. Anti-platelet aggregation activity

Gomisin N (**153**) and pregomisin (**193**) showed anti-platelet aggregation activity against platelet aggregation induced by AA (153.3 and 96.5 μM) and PAF (122.4 and 49.3 μM). Pregomisin and gomisin N were more potent platelet inhibitors than aspirin against PAF (Kim et al., 2010). (Table 6).

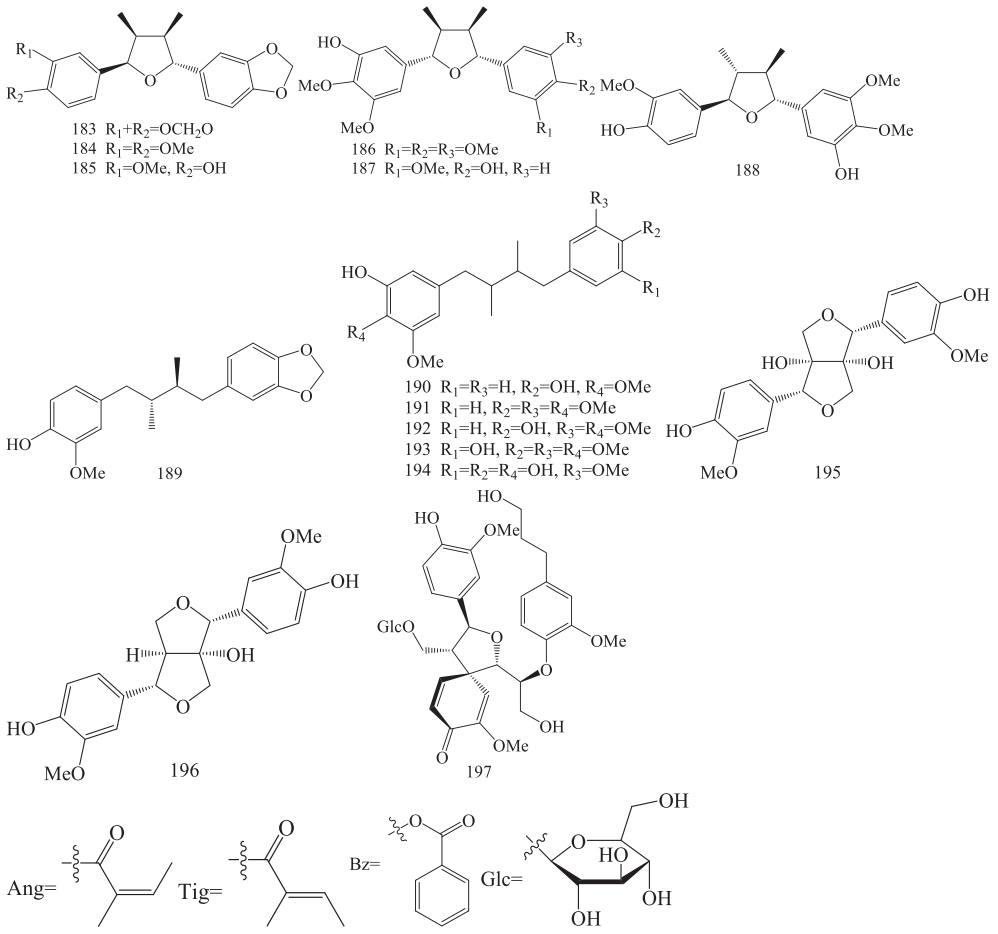


Fig. 8 Structures of other types of lignans (**183**–**197**).

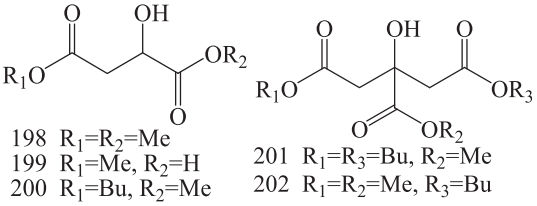


Fig. 9 Structures of fatty acids (**198**–**202**).

3.8. Anti-acetylcholinesterase activity

Preschisanartanin E (**31**), schindilactone I (**34**), schindilactone A (**37**), and propindilactone Q (**64**) exhibited anti-AChE activity, at concentration of 50 μM, with 16.6, 12.7, 10.7, and 32.1% inhibition, respectively (Shi et al., 2014). (Table 6).

3.9. Anti-hepatitis B virus activity

Schinlignan G (**132**) and methylgomisin O (**165**) showed potent anti-hepatitis B virus activity against HBV DNA replication, with IC_{50} values of 5.13 and 5.49 μg/mL, respectively (Xue et al., 2015). (Table 6).

3.10. Other biological activities

Gomisin J (**145**) showed antifeedant activity against *Tribolium castaneum* adults, at 1500 ppm concentration, with 40.3% antifeeding index percentages (Guo et al., 2020). Sesquiterpenoid α-*iso*-cubebene is a novel natural compound which stimulates intracellular calcium signaling and CXCL8 production, and should be useful for the development of an immune-modulating agent (Lee et al., 2009). Henrischinin A (**15**), henrischinin B (**16**), and henrischinin C (**12**) had selectivity index values of 23.31, 29.95 and 19.49, respectively, exhibited better activities than Schinchinenin A (**24**), schinchinenin B (**20**), and schinchinenin G (**10**) against HSV-2. Schinchinenin A (**24**), schinchinenin G (**10**), henrischinin A (**15**), and henrischinin B (**16**) showed modest activities against adenovirus, with selectivity index values ranging from 11.43 to 13.75. From a structure–activity relationship viewpoint, it is obvious that the acetyl and hydroxyl groups at C-25 may play different roles in the inhibition of HSV-2 and adenovirus by different types of triterpenoids (Song et al., 2013). *rel*-(7*R*, 8*R*, 7′*R*, 8′*R*)-Manglisin E (**188**), (−)-schisandrin C (**152**), schinlignan D (**129**), and (+)-schisandrol B (**122**) potently inhibited PCSK9 mRNA expression, with IC_{50} values of 3.15, 3.85, 0.36, and 1.10 μM, respectively. Furthermore, schinlignan D

Table 6 Biological activities of secondary metabolites from *S.chinensis*.

Biological activities	Compounds	Class of compound	Results	Reference
Anti-cancer	Epi-anwuweizic acid (**1**)	Triterpenoid	IC_{50} 36.5 μM against prostate cancer cells.	Zhang et al. (2013)
	Widdaral B (**91**)	Sesquiterpenoid	IC_{50} 17.10 μg/mM against Caco2 cell lines.	Venkanna et al. (2014)
	β-Chamigrenal (**93**)	Sesquiterpenoid	IC_{50} 16.46 μg/mM against Caco2 cell lines	Venkanna et al. (2014)
	Schisandrin (**113**)	Lignan	IC_{50} 4.773, 0.437, 0.537 μM against MGC-803, Ishikawa and Caco-2 cell lines.	Liu et al. (2020)
	Angeloylgomisin H (**118**)	Lignan	IC_{50} 12.94 ± 0.12, 9.36 ± 0.39, 7.94 ± 0.19 μM against AGS, Hela, HT29 cell lines.	Choi et al. (2020)
	(+)-Deoxyschisandrin (**121**)	Lignan	EC_{50} 22.6 μg/mL against the LoVo cell lines.	Šmejkal et al. (2010)
	Gomisin A (**122**)	Lignan	IC_{50} 13.76 ± 0.38 μM against Hela cell lines and IC_{50} 14.81 ± 1.02 μM against AGS cell lines.	Choi et al. (2020)
	Schisandroside E (**123**)	Lignan	IC_{50} 4.621, 0.356, 0.021 μM against MGC-803, Ishikawa and Caco-2 cell lines.	Liu et al. (2020)
	(−)-Gomisin K_1 (**144**)	Lignan	IC_{50} 5.46 ± 0.24 μM against Hela cell lines.	Choi et al. (2020)
	Gomisin J (**145**)	Lignan	IC_{50} 6.51 ± 0.26 μM against Hela cell lines.	Choi et al. (2020)
	Gomisin F (**147**)	Lignan	IC_{50} 0.050, 0.426, 0.572 μM against MGC-803, Ishikawa and Caco-2 cell lines.	Liu et al. (2020)
	(−)-Tigloyl- deangeloylgomisin F (**148**)	Lignan	IC_{50} 0.033 μM against Caco-2 cell lines.	Liu et al. (2020)
	Angeloylgomisin Q (**149**)	Lignan	IC_{50} 0.075, 0.567, 2.305 μM against MGC-803, Ishikawa and Caco-2 cell lines.	Liu et al. (2020)
	(−)-Gomisin N (**153**)	Lignan	EC_{50} 27.4 μg/mL against the LoVo cell lines.	Šmejkal et al. (2010)
	Chicanine (**185**)	Lignan	IC_{50} 44.2 μM against prostate cancer cells	Zhang et al. (2013)
	Anwulignan (**189**)	Lignan	IC_{50} 39.3 μM against prostate cancer cells.	Zhang et al. (2013)
Anti-oxidant	Schisandrene (**155**)	Lignan	Showed better antioxidant activity than commercial antioxidant Vitamin C and Trolox using a DCFH-DA cellular-based assay.	Choi et al. (2006)
	Anwulignan (**189**)	Lignan	Showed better DPPH free radicals scavenging activity (IC_{50} = 11.2 μM), compared to the positive control ascorbic acid (IC_{50} = 25.3 μM).	Zhang et al. (2013)
	Chicanine (**185**)	Lignan	Showed potent DPPH free radicals scavenging activity with IC_{50} value of 26 μM.	Zhang et al. (2013)
Neuroprotective	Ganwuweizic acid (**5**)	Lignan	Showed 78.05 ± 2.34% inhibition activity on lipopolysaccharide (LPS)-induced NO release at 1 μM.	Hu et al. (2014)
	(±)-γ-Schizandrin (**115**)	Lignan	Showed 91.78 ± 1.32% inhibition activity on lipopolysaccharide (LPS)-induced NO release at 1 μM.	Hu et al. (2014)
	Deoxyschisandrin (**121**)	Lignan	Showed significant neuroprotection against glutamate-induced toxicity.	Kim et al. (2004)
	Gomisin A (**122**)	Lignan	Showed 95.57 ± 1.86% inhibition activity on lipopolysaccharide (LPS)-induced NO release at 1 μM.	Hu et al. (2014)
	(−)-Gomisin M_1 (**127**)	Lignan	Showed 96.06 ± 0.70% inhibition activity on lipopolysaccharide (LPS)-induced NO release at 1 μM.	Hu et al. (2014)
	Schisanchinin B (**133**)	Triterpenoid	Showed 76.70 ± 1.18% inhibition activity on lipopolysaccharide (LPS)-induced NO release at 1 μM.	Hu et al. (2014)
	(+)-Gomisin M_2 (**137**)	Lignan	Showed 92.77 ± 0.93% inhibition activity on lipopolysaccharide (LPS)-induced NO release at 1 μM.	Hu et al. (2014)
	(+)-Gomisin K_3 (**138**)	Lignan	Showed 96.06 ± 0.70% inhibition activity on lipopolysaccharide	Hu et al. (2014)

(*continued on next page*)

Table 6 (*continued*)

Biological activities	Compounds	Class of compound	Results	Reference
			(LPS)-induced NO release at 1 μM.	
	Gomisin G (**151**)	Lignan	Showed 92.35 ± 0.68% inhibition activity on lipopolysaccharide (LPS)-induced NO release at 1 μM.	Hu et al. (2014)
	Wuweizisu C (**152**)	Lignan	Showed significant neuroprotection against glutamate-induced toxicity.	Kim et al. (2004)
	Gomisin N (**153**)	Lignan	Showed significant neuroprotection against glutamate-induced toxicity.	Kim et al. (2004)
	(−)-Gomisin L_1 (**156**)	Lignan	Showed 89.08 ± 0.72% inhibition activity on lipopolysaccharide (LPS)-induced NO release at 1 μM.	Hu et al. (2014)
	Schisanchinin A (**167**)	Lignan	Showed 83.74 ± 0.47% inhibition activity on lipopolysaccharide (LPS)-induced NO release at 1 μM.	Hu et al. (2014)
	1,2,13,14-Tetramethoxydibenzocyclooctadiene 3,12-O-β-D- diglucopyranoside (**169**)	Lignan	Showed protecting activity against Aβ- induced toxicity in PC12 cells.	Yang et al. (2016)
	3,7-Dihydroxy-1,2,13,14-tetramethoxy-dibenzocyclooctadiene 12-O-β-D-glucopyranoside (**170**)	Lignan	Showed protecting activity against Aβ- induced toxicity in PC12 cells.	Yang et al. (2016)
Anti-HIV-1	Pre-schisanartanin(**26**)	Triterpenoid	Exhibited anti-HIV-1 activity with an EC_{50} value of 13.81 μg/mL (AZT: EC_{50} = 2.26 μg/mL)	Huang et al. (2007a)
	Wuweizidilactone A (**54**)	Triterpenoid	Exhibited anti-HIV-1 activity with an EC_{50} value of 26.81 μg/mL (AZT: EC_{50} = 2.26 μg/mL)	Huang et al. (2007c)
	Wuweizidilactone B (**55**)	Triterpenoid	Exhibited anti-HIV-1 activity with an EC_{50} value of 28.86 μg/mL (AZT: EC_{50} = 2.26 μg/mL)	Huang et al. (2007c)
	Schintrilactone A (**73**)	Triterpenoid	Exhibited anti-HIV-1 activity with an EC_{50} value of 17.9 μg/mL (AZT: EC_{50} = 2.26 μg/mL)	Huang et al. (2007b)
	Schintrilactone B (**74**)	Triterpenoid	Exhibited anti-HIV-1 activity with an EC_{50} value of 36.2 μg/mL (AZT: EC_{50} = 2.26 μg/mL)	Huang et al. (2007b)
Anti-inflammatory	α-Iso-cubebenol (**87**)	Sesquiterpenoid	Demonstrated inhibition of nitric oxide (NO) and prostaglandin E2 (PGE2) production in LPS-stimulated macrophages	Lee et al. (2010)
	Schisandrin (**113**)	Lignan	Demonstrated potenti anti- inflammatory activity.	Guo et al. (2008)
Hepatoprotective	Schizandrin (**113**)	Lignan	Demonstrated moderate hepatoprotective activities (survival rate 44.5%) against damage induced by *N*-acetyl-*p*- aminophenol.	Li et al. (2017)
	Gomisin M_2 (**137**)	Lignan	Demonstrated moderate hepatoprotective activities (survival rate 43.5%) against damage induced by *N*-acetyl-*p*- aminophenol.	Li et al. (2017)
	Micrantherin A (**140**)	Lignan	Demonstrated moderate hepatoprotective activities (survival rate 44.6%) against damage induced by *N*-acetyl-*p*- aminophenol.	Li et al. (2017)
	Schisantherin D (**174**)	Lignan	Demonstrated significant hepatoprotective activity.	Xu et al. (2020)
Anti-platelet aggregation	Gomisin N (**153**)	Lignan	Demonstrated anti-platelet aggregation activity against platelet aggregation induced by AA (IC_{50} = 153.3 ± 6.8 μM) and PAF (IC_{50} = 122.4 ± 5.6 μM).	Kim et al. (2010)
	Pregomisin (**193**)	Lignan	Demonstrated anti-platelet aggregation activity against platelet aggregation induced by AA (IC_{50} = 96.5 ± 4.7 μM) and PAF (IC_{50} = 49.3 ± 2.7 μM).	Kim et al. (2010)

Table 6 (*continued*)

Biological activities	Compounds	Class of compound	Results	Reference
Anti-acetylcholinesterase	Preschisanartanin E (**31**)	Triterpenoid	Exhibited anti-AChE activity, at concentration of 50 μM, with 16.6% inhibition.	Shi et al. (2014)
	Schindilactone I (**34**)	Triterpenoid	Exhibited anti-AChE activity, at concentration of 50 μM, with 12.7% inhibition.	Shi et al. (2014)
	Schindilactone A (**37**)	Triterpenoid	Exhibited anti-AChE activity, at concentration of 50 μM, with 10.7% inhibition.	Shi et al. (2014)
	Propindilactone Q (**64**)	Triterpenoid	Exhibited anti-AChE activity, at concentration of 50 μM, with 32.1% inhibition.	Shi et al. (2014)
Anti-hepatitis B virus	Schinlignan G (**132**)	Lignan	Exhibited anti-hepatitis B virus activity against HBV DNA replication, with IC_{50} value of 5.13 μg/mL.	Xue et al. (2015)
	methylgomisin O (**165**)	Lignan	Exhibited anti-hepatitis B virus activity against HBV DNA replication, with IC_{50} value of 5.49 μg/mL.	Xue et al. (2015)
Anti-feedant	Gomisin J (**145**)	Lignan	Showed antifeedant activity against *Tribolium castaneum* adults, at 1500 ppm concentration, with 40.3% antifeeding index percentage.	Guo et al. (2020)
Anti-HSV-2	Henrischinin C (**12**)	Triterpenoid	Showed inhibitory activities against HSV-2, with SI value of 19.49.	Song et al. (2013)
	Henrischinin A (**15**)	Triterpenoid	Showed inhibitory activities against HSV-2, with SI value of 23.31.	Song et al. (2013)
	Henrischinin B (**16**)	Triterpenoid	Showed inhibitory activities against HSV-2, with SI value of 29.95.	Song et al. (2013)
Anti-adenovirus	Schinchinenin G (**10**)	Triterpenoid	Showed modest activities against adenovirus, with SI value of 11.43.	Song et al. (2013)
	Henrischinin A (**15**)	Triterpenoid	Showed modest activities against adenovirus, with SI value of 13.67.	Song et al. (2013)
	Henrischinin B (**16**)	Triterpenoid	Showed modest activities against adenovirus, with SI value of 11.45.	Song et al. (2013)
	Schinchinenin A (**24**)	Triterpenoid	Showed modest activities against adenovirus, with SI value of 13.75.	Song et al. (2013)
LDL-cholesterol biosynthesis inhibition activity	(+)-Schisandrol B (**122**)		Inhibited PCSK9 mRNA expression, with IC_{50} value of 1.10 μM.	Pel et al. (2017)
	Schinlignan D (**129**)		Inhibited PCSK9 mRNA expression, with IC_{50} value of 0.36 μM.	Pel et al. (2017)
	(−)-Schisandrin C (**152**)		Inhibited PCSK9 mRNA expression, with IC_{50} value of 3.85 μM.	Pel et al. (2017)
	Rel-(7R,8R,7′R,8′R)-Manglisin E (**188**)		Inhibited PCSK9 mRNA expression, with IC_{50} value of 3.15 μM.	Pel et al. (2017)

(**129**) and (+)-schisandrol B (**122**) suppressed PCSK9 protein expressions, and schinlignan D (**129**) deemed to increase low density lipoprotein receptor expression (Pel et al., 2017). (Table 6).

4. Analytical methods

In recent years, researcher have attempted to establish analytical methods focusing on lignans and triterpenoids analysis with different chromatographic equipment. A rapid HPLC-DAD method was described for simultaneous determination of nine lignans, including schisandrin (**113**), gomisin J (**145**), gomisin A (**122**), tigloylgomisin H (**117**), angeloylgomisin H (**118**), schisandrin A (**112**), schisandrin B (**115**), gomisin N (**153**) and schisandrin C (**152**) (Lee and Kim, 2010). A new HPLC-FLD method was described for simultaneous determination schisandrin (**113**), gomisin A (**122**), schisandrin A (**112**), schisandrin B (**115**), schisandrin C (**152**) in *S. chinensis*. This method enables routine quality evaluation and standardization of the bioactive lignans from the raw material, extracts or formulations (Xia et al., 2014). A TLC-ESI-MS method for monitoring the quality of the herb was reported. The results showed that gomisin A (**122**), schisandrin B (**115**), schisandrin (**113**), schisantherin A (**146**) and schisandrin A (**112**) were detected simultaneously, the method possess rapid identification of chemical components and high reliability for the plant extracts (Hu et al., 2015). A simple, environment-friendly and efficiency micro MSPD–MEEKC method was reported, The method was developed to simultaneously analyze schisandrin (**113**), gomisin A (**122**), schisantherin A (**146**), deoxyschisandrin (**121**), and schisandrin B (**115**) in *S.chinensis*. This method exhibits good precision, satisfactory recovery, and low detection limits. Moreover, it showed excellent advantages of small samples and sorbent amounts, low consumption of elution solvent and high extraction efficiency compared with conventional MSPD techniques (Chu et al., 2017). An UHPLC-Q-TOF/MS method is widely used for data collection of herbal medicine extracts, because of its high resolution and high mass accuracy (Gao et al., 2019; Liu et al., 2017; Yang et al., 2017; Yu et al., 2019). A supercritical fluid chromatography method were used for separation of lignans in *S. chinensis*. The determined lignan patterns were typical for *S. chinensis*, with schisandrin (**113**) being the most abundant compound, followed by schisandrin B (**115**) or gomisin A (**122**) (Onay et al., 2020). These novel methods would be valuable for future development and utilization of *S. chinensis*.

5. Conclusions

This review summarized the recent advance in the phytochemistry, biological activities and analytical methods of *S.chinensis*. The phytochemical investigation on *S.chinensis* resulted in the isolation of many novel triterpenoids and dibenzocyclooctadiene lignans. The biological activities research on the plant components showed that some components exhibit significant biological activities, especially anticancer, anti-HIV-1, neuroprotective, hepatoprotective, antioxidant activities, which supported the use of *S.chinensis* in traditional medicines.

Nevertheless, there are several aspects that needed to explore and investigate further: (1) work on the stem and leave extracts of *S.chinensis* to isolate sufficient amount of major as well as minor chemical components to explore their pharmacological activities and mechanism for therapeutic potential; (2) Further studies on the mechanism of actions and the structure–activity relationship are needed, in order to provide a better understanding of the chemical constituents of *S.chinensis* as potential medicines; (3) >200 compounds have been isolated and identified, whereas only a few have been explored for pharmacological activities and pre-clinical studies. Overall, further studies on the chemical constituents of *S.chinensis* are needed, in order to obtain novel molecules with new pharmacological potential.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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