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Review

Biological Activities and Secondary Metabolites from *Sophora tonkinensis* and Its Endophytic Fungi

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Abstract: The roots of *Sophora tonkinensis* Gagnep., a traditional Chinese medicine, is known as Shan Dou Gen in the Miao ethnopharmacy. A large number of previous studies have suggested the usage of *S. tonkinensis* in the folk treatment of lung, stomach, and throat diseases, and the roots of *S. tonkinensis* have been produced as Chinese patent medicines to treat related diseases. Existing phytochemical works reported more than 300 compounds from different parts and the endophytic fungi of *S. tonkinensis*. Some of the isolated extracts and monomer compounds from *S. tonkinensis* have been proved to exhibit diverse biological activities, including anti-tumor, anti-inflammatory, antibacterial, antiviral, and so on. The research progress on the phytochemistry and pharmacological activities of *S. tonkinensis* have been systematically summarized, which may be useful for its further research.

Keywords: *S. tonkinensis*; phytochemistry; pharmacology; review

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1. Introduction

Sophora tonkinensis Gagnep. belongs to the *Sophora* genus of the Leguminosae family, which is widely distributed in the southwest provinces of China [1,2]. As a famous folk medicine of the Miao people, the roots of *S. tonkinensis* were known as Shan Dou Gen or Guang Dou Gen in the Miao ethnopharmacy [3,4]. The early medicinal records of Shan Dou Gen were contained in the classics *"Kai Bao Ben Cao"*, in which *S. tonkinensis* showed the effect of anti-sore throat diseases [5,6]. A large number of previous studies have suggested the usage of *S. tonkinensis* in the folk treatment of upper respiratory tract infection, including lung and throat diseases. Meanwhile, *S. tonkinensis* is also highly effective in the treatment of liver and skin diseases [7,8]. Moreover, the roots of *S. tonkinensis* can also be combined with other medicines to form dozens of clinical and marketing Chinese patent medicines, such as *Kai Hou Jian throat spray, Shuyanqing Spray,* and *Watermelon Frost Spray*, which is usually used for treatment of pharyngitis, tonsillitis, and aphthous ulcers [9–11]. Existing phytochemical works reported more than 300 compounds with various structural skeleton types from different parts and endophytic fungi of *S. tonkinensis*. Some of the isolated monomer compounds from *S. tonkinensis* have been proved to exhibit diverse biological activities, including anti-tumor, anti-inflammatory, antibacterial, antiviral, and so on [12–17]. Herein, the research progress on the phytochemistry and pharmacological activities of *S. tonkinensis* have been systematically summarized, which may be useful for its further research.

2. Phytochemistry

Previous studies have shown that alkaloids, flavonoids, triterpenoids, and triterpenoid saponins were the main chemical components isolated from *S. tonkinensis*. To date, 78 (**1**–**78**)

alkaloids, 115 (**79**–**193**) flavonoids, 46 (**194**–**239**) triterpenes and triterpenoid saponins, and 37 (**240**–**276**) other compounds have been isolated from *S. tonkinensis*, and it is worth mentioning that 40 (**277**–**316**) compounds were also isolated from the endophytic fungi produced by *S. Tonkinensis* (Table 1, Figure 1).

Table 1. The comprehensive list of the compounds from *S. tonkinensis* and its Endophytic fungus.

NO	Compounds	Molecular Formula	Parts of Plant	References
	Matrine-Type alkaloids			
1	Matrine	$C_{15}H_{24}N_2O$	Roots	[12]
2	5*α*,14*β*-Dihydroxymatrine	$C_{15}H_{24}N_2O_3$	Roots	[12]
3	(+)-5*α*-Hydroxyoxymatrine	$C_{15}H_{24}N_2O_3$	Roots	[12]
4	(+)-Oxymatrine	$C_{15}H_{24}N_2O_2$	Roots	[18]
5	(+)-5*α*-Hydroxymatrine ((+)-Sophoranol)	$C_{15}H_{24}N_2O_2$	Roots	[12]
6	(−)- 14*β*-Hydroxyoxymatrine	$C_{15}H_{24}N_2O_3$	Roots	[18]
7	Sophtonseedline E	$C_{17}H_{26}N_2O_4$	Seeds	[19]
8	Sophtonseedline F	$C_{17}H_{28}N_2O_3S$	Seeds	[19]
9	Sophtonseedline G	$C_{15}H_{24}N_2O_3$	Seeds	[19]
10	Sophtonseedline H	$C_{16}H_{26}N_2O_2$	Seeds	[19]
11	(+)-9*α*-Hydroxymatrine	$C_{15}H_{24}N_2O_2$	Seeds	[19]
12	(+)-5*α*-9*α*-Dihydroxymatrine	$C_{15}H_{24}N_2O_3$	Seeds	[19]
13	(+)-Allomatrine (Sophoridine)	$C_{15}H_{24}N_2O$	Roots	[20]
14	(+)-Lehmannine	$C_{15}H_{24}N_2O$	Roots	[20]
15	(+)-12*α*-Hydroxysophocarpine	$C_{15}H_{24}N_2O_2$	Roots	[20]
16	(−)-13,14-Dehydrosophoridine (12,13-Dehydrosophoridine)	$C_{15}H_{24}N_2O$	Roots	[20]
17	(+)-5*α*-Hydroxyoxysophocarpine	$C_{15}H_{22}N_2O_3$	Roots	[14]
18	(−)-12*β*-Hydroxyoxysophocarpine	$C_{15}H_{22}N_2O_3$	Roots	[14]
19	(−)-12*β*-Hydroxysophocarpine	$C_{15}H_{22}N_2O_2$	Roots	[14]
20	(+)-Oxysophocarpine	$C_{15}H_{22}N_2O_2$	Roots	[14]
21	Sophtonseedline B	$C_{15}H_{22}N_2O_3$	Seeds	[19]
22	Sophtonseedline C	$C_{17}H_{24}N_2O_4$	Seeds	[19]
23	Sophtonseedline D	$C_{17}H_{26}N_2O_3S$	Seeds	[19]
24	(−)-5*α*-Hydroxysophocarpine (13,14-Dehydrosophoranol)	$C_{15}H_{22}N_2O_2$	Seeds	[19]
25	(−)-9*α*-Hydroxysophocarpine	$C_{15}H_{22}N_2O_2$	Seeds	[19]
26	(−)-14*β*-Acetoxymatrine	$C_{17}H_{26}N_2O_3$	Leaves	[21]
27	(+)-14*α*-Acetoxymatrine	$C_{17}H_{26}N_2O_3$	Leaves	[21]
28	(−)-14*β*-Hydroxymatrine	$C_{15}H_{24}N_2O_2$	Leaves	[21]
29	(+)-14*α*-Hydroxymatrine	$C_{15}H_{24}N_2O_2$	Leaves	[21]
30	Sophtonseedline I	$C_{17}H_{24}N_2O_4$	Seeds	[19]
31	6,7-Dehydro-matrine	$C_{15}H_{22}N_2O$	Seeds	[19]
32	5-Hydroxy-6,7-dehydro-matrine	$C_{15}H_{22}N_2O_2$	Seeds	[19]
33	(+)-13,14-Dehydrosophoranol	$C_{15}H_{22}N_2O_2$	Roots	[22]
34	(−)-Sophocarpine	$C_{15}H_{22}N_2O$	Roots	[12]
35	(+)-5*α*-Hydroxylemannine	$C_{15}H_{22}N_2O_2$	Roots	[14]
36	13*α*-Hydroxymatrine	$C_{15}H_{24}N_2O_2$	Roots	[23]
37	13*β*-Hydroxymatrine	$C_{15}H_{24}N_2O_2$	Roots	[23]
38	11,12-Dehydroallmatrine	$C_{15}H_{22}N_2O$	Roots	[1]
39	11,12-Dehydromatrine	$C_{15}H_{22}N_2O$	Roots	[1]
40	(+)-Matrine *N*-oxide	$C_{15}H_{24}N_2O$	Leaves	[21]
41	(+)-Sophoranol *N*-oxide	$C_{15}H_{24}N_2O_2$	Leaves	[21]
42	(+)-7,11-Dehydromatrine	$C_{15}H_{22}N_2O$	Roots	[22]
43	Alopecurin A	$C_{15}H_{22}N_2O_4$	Seeds	[19]
44	Sophtonseedline J	$C_{15}H_{20}N_2O_3$	Seeds	[19]
45	Sophtonseedline K	$C_{15}H_{20}N_2O_3$	Seeds	[19]
46	Sophtonseedline A	$C_{15}H_{22}N_2O_2$	Seeds	[19]
47	5,6-Dehydro-matrine	$C_{15}H_{22}N_2O$	Seeds	[19]
48	Isosophocarpine	$C_{15}H_{22}N_2O$	Roots	[23]
49	(+)-Sophoramine (7*β*-Sophoramine)	$C_{15}H_{20}N_2O$	Roots	[14]

Table 1. *Cont.*

NO	Compounds	Molecular Formula	Parts of Plant	References
	Cytisine-type alkaloids			
50	(−)-Cytisine	$C_{11}H_{14}N_2O$	Seeds	[19]
51	*N*-Methylcytisine	$C_{12}H_{16}N_2O$	Seeds	[19]
52	(−)-*N*-Formylcytisine	$C_{12}H_{14}N_2O_2$	Seeds	[19]
53	*N*-Acylcytisine	$C_{13}H_{16}N_2O_2$	Seeds	[19]
54	(−)-*N*-Methylcytisine	$C_{12}H_{16}N_2O$	Roots	[18]
55	(−)-*N*-Hexanoylcytisine	$C_{17}H_{24}N_2O_2$	Roots	[24]
56	(−)-*N*-Ethylcytisine	$C_{13}H_{18}N_2O$	Roots	[24]
57	(−)-*N*-Propionylcytisine	$C_{14}H_{18}N_2O_2$	Roots	[24]
58	Tonkinensine A	$C_{28}H_{26}N_2O_6$	Roots	[25]
59	Tonkinensine B	$C_{28}H_{26}N_2O_6$	Roots	[25]
	Anagyrine-type alkaloids			
60	17-Oxo-*α*-isosparteine	$C_{15}H_{24}N_2O$	Leaves	[21]
61	(−)-Anagyrine	$C_{15}H_{20}N_2O$	Roots	[12]
62	(−)-Thermopsine	$C_{15}H_{20}N_2O$	Roots	[12]
63	(−)-Baptifoline	$C_{15}H_{20}N_2O_2$	Leaves	[21]
64	(−)-Clathrotropine	$C_{17}H_{22}N_2O_4$	Roots	[26]
65	Lanatine A	$C_{22}H_{29}N_3O_3$	Roots	[26]
	Lupine-types and other alkaloids			
66	Lamprolobine	$C_{15}H_{24}N_2O_2$	Leaves	[21]
67	Jussiaeiine B	$C_{16}H_{24}N_2O_2$	Roots	[26]
68	Jussiaeiine A	$C_{13}H_{20}N_2O_2$	Roots	[26]
69	Senepodine H	$C_{14}H_{26}NO^+$	Roots	[26]
70	Cermizine C	$C_{11}H_{21}N$	Roots	[26]
71	Senepodine G	$C_{11}H_{20}N^+$	Roots	[26]
72	Harmine	$C_{13}H_{12}N_2O$	Roots	[1]
73	Tonkinensine C	$C_{16}H_{16}N_2O_2$	Roots	[1]
74	Perlolyrine	$C_{16}H_{12}N_2O_2$	Roots	[1]
75	3-(4-Hydroxyphenyl)-4-(3-methoxy-4-hydroxyphenyl)-3,4-dehydroquinolizidine	$C_{22}H_{25}NO_3$	Roots	[26]
76	1-(6,7-dihydro-5H-pyrrolo[1,2-*a*]imidazol-3-yl)ethanone	$C_8H_{10}N_2O$	Roots	[27]
77	Cyclo (Pro-Pro)	$C_{10}H_{14}N_2O_2$	Roots	[27]
78	Nicotinic acid	$C_6H_5NO_2$	Roots	[27]
	Flavonoids			
79	4′,7-Dihydroxyflavone	$C_{15}H_{10}O_4$	Roots	[28]
80	Wogonin	$C_{16}H_{12}O_5$	Roots	[29]
81	Luteolin	$C_{15}H_{10}O_4$	Roots	[29]
82	Luteolin-7-glucoside	$C_{21}H_{20}O_{11}$	Roots	[30]
83	Baicalein 7-O-*β*-$_D$-glucuronide	$C_{21}H_{18}O_{11}$	Roots	[31]
84	Bayin	$C_{21}H_{20}O_9$	Roots	[15]
85	Swertisin	$C_{22}H_{22}O_{10}$	Roots	[31]
86	Sophoraflavone B	$C_{21}H_{20}O_9$	Roots	[32]
87	Sophoraflavone A	$C_{27}H_{30}O_{13}$	Roots	[32]
	Flavonols			
88	Quercetin	$C_{15}H_{10}O_7$	Roots	[33]
89	Morin	$C_{15}H_{10}O_7$	Roots	[31]
90	6,8-Diprenylkaempferol	$C_{25}H_{26}O_6$	Roots	[34]
91	8-C-prenylkeamferol	$C_{20}H_{18}O_6$	Roots	[35]
92	Dehydrolupinifolinol	$C_{25}H_{24}O_6$	Roots	[33]
93	Tonkinensisol	$C_{25}H_{24}O_6$	Roots	[15]
94	Isoquercitrin	$C_{21}H_{20}O_{12}$	Roots	[36]
95	Quercitrin	$C_{21}H_{20}O_{11}$	Roots	[37]
96	Rutin (Quercetin-3-O-*β*-$_D$-rutinoside)	$C_{27}H_{30}O_{16}$	Roots	[31]
97	Isorhamnetin-3-O-*β*-$_D$-rutinoside	$C_{28}H_{32}O_{16}$	Roots	[31]

Table 1. *Cont.*

NO	Compounds	Molecular Formula	Parts of Plant	References
	Isoflavones and Dihydroisoflavones			
98	8,4′-Dihydroxy-7-methoxyisoflavone	$C_{16}H_{12}O_5$	Roots	[38]
99	5,7,2′,4′-Tetrahydroxyisoflavone	$C_{15}H_{10}O_6$	Roots	[38]
100	Calycosin	$C_{16}H_{12}O_5$	Roots	[38]
101	7,3′-Dihydroxy-5′-methoxyisoflavone	$C_{16}H_{12}O_5$	Roots	[38]
102	7,4′-Dihydroxy-3′-methoxyisoflavone	$C_{16}H_{12}O_5$	Roots	[38]
103	Daidzein (7,4′-Dihydroxyisoflavone)	$C_{15}H_{10}O_4$	Roots	[38]
104	7,3′-Dihydroxy-8,4′-dimethoxyisoflavone	$C_{17}H_{14}O_6$	Roots	[38]
105	7,8-Dihydroxy-4′-methoxyisoflavone	$C_{16}H_{12}O_5$	Roots	[38]
106	7,3′,4′-Trihydroxyisoflavone	$C_{15}H_{10}O_5$	Roots	[38]
107	Formononetin	$C_{16}H_{12}O_4$	Roots	[39]
108	Genistein	$C_{15}H_{10}O_5$	Roots	[39]
109	Wighteone	$C_{20}H_{18}O_5$	Roots	[40]
110	8-Methylretusin	$C_{17}H_{14}O_5$	Roots	[41]
111	7-Methoxyebenosin	$C_{22}H_{22}O_4$	Roots	[42]
112	Tectorigenin	$C_{16}H_{12}O_6$	Roots	[43]
113	Butesuperin A	$C_{26}H_{22}O_8$	Roots	[44]
114	Butesuperin B -7′-O-β-glucopyranoside	$C_{33}H_{34}O_{14}$	Roots	[44]
115	Genistin	$C_{21}H_{20}O_{10}$	Roots	[33]
116	Ononin (Formononetin-7-O-β-$_D$-glucoside)	$C_{22}H_{22}O_9$	Roots	[33]
117	Daidzein-4′-glucoside-rhamnoside	$C_{27}H_{30}O_{13}$	Roots	[37]
118	Sophorabioside	$C_{27}H_{30}O_{14}$	Roots	[37]
	Dihydroflavones			
119	6,8-Diprenyl-7,4′-Dihydroxyflavanone	$C_{25}H_{28}O_4$	Roots	[45]
120	Sophoranone	$C_{30}H_{36}O_4$	Roots	[45]
121	Glabrol	$C_{25}H_{28}O_4$	Roots	[45]
122	6,8-Diprenyl-7,2′,4′-trihydroxyflavanone	$C_{25}H_{28}O_5$	Roots	[45]
123	Lespeflorin B_4	$C_{30}H_{36}O_6$	Roots	[33]
124	(2*S*)-7,4′-Dihydroxy-5′-aldehyde-8,3′-(3′′-methylbut-2′′-enyl) flavanone	$C_{26}H_{28}O_5$	Roots	[34]
125	(2*S*)-7,2′,4′-Trihydroxy-8,3′,5′-(3′′-methyl- but-2′′-enyl) flavanone	$C_{30}H_{36}O_5$	Roots	[34]
126	Tonkinochromane J	$C_{25}H_{28}O_5$	Roots	[46]
127	Shandougenine C	$C_{30}H_{36}O_5$	Roots	[40]
128	Shandougenine D	$C_{25}H_{28}O_5$	Roots	[40]
129	Sophoratonin F	$C_{35}H_{44}O_4$	Roots	[42]
130	Lonchocarpol A	$C_{25}H_{28}O_5$	Roots	[42]
131	2′-Hydroxyglabrol	$C_{25}H_{28}O_5$	Roots	[47]
132	8,5′-Diprenyl-7,2′,4′-trihydroxyflavanone	$C_{25}H_{28}O_5$	Roots	[45]
133	Sophoratonin A	$C_{27}H_{28}O_4$	Roots	[42]
134	Sophoratonin B	$C_{30}H_{32}O_4$	Roots	[42]
135	Tonkinochromane I	$C_{30}H_{36}O_5$	Roots	[35]
136	Tonkinochromane G	$C_{30}H_{36}O_5$	Roots	[34]
137	Sophoratonin C	$C_{30}H_{30}O_4$	Roots	[42]
138	Sophoratonin D	$C_{30}H_{36}O_4$	Roots	[42]
139	Flemichin D	$C_{25}H_{26}O_5$	Roots	[45]
140	5-Dehydroxylupinifolin	$C_{25}H_{26}O_4$	Roots	[34]
141	Lupinifolin	$C_{25}H_{26}O_5$	Roots	[40]
142	2-(2′,4′-Dihydroxyphenyl)-8,8-dimethyl-1′-(3-methyl-2-butenyl)-8H-pyrano[2,3-d] chroman-4-one	$C_{25}H_{26}O_5$	Roots	[48]
143	Tonkinochromane A	$C_{30}H_{36}O_4$	Roots	[45]
144	Sophoranochromene	$C_{30}H_{34}O_4$	Roots	[33]
145	2-[{2-(1-Hydroxy-1-methylethyl)-7-(3-methyl-2-butenyl)-2′,3-dihydrobenzofuran}-5-yl]-7-hydroxy-8-(3-methyl-2-butenyl)-chroman-4-one	$C_{30}H_{36}O_5$	Roots	[49]

Table 1. *Cont.*

NO	Compounds	Molecular Formula	Parts of Plant	References
	Dihydroflavones			
146	Sophoratonin E	$C_{30}H_{32}O_4$	Roots	[42]
147	Tonkinochromane D	$C_{30}H_{38}O_5$	Roots	[50]
148	Tonkinochromane E	$C_{32}H_{42}O_5$	Roots	[50]
149	2-[{2′-(1-Hydroxy-1-methylethyl)-7′-(3-methyl-2-butenyl)-2′,3′-dihydrobenzofuran}-5′-yl]-7-hy-droxy-8-(3-methyl-2-butenyl) chroman-4-one	$C_{30}H_{36}O_5$	Whole	[51]
150	Euchrenone A_2	$C_{25}H_{26}O_5$	Roots	[33]
151	Sophoratonin G	$C_{27}H_{28}O_4$	Roots	[42]
152	Tonkinochromane K	$C_{30}H_{36}O_6$	Roots	[46]
153	2-[{3′-Hydroxy-2′,2′-dimethyl-8′-(3-methyl-2-butenyl)} chroman-6′-yl]-7-hydroxy-8-(3-methyl-2-butenyl)-chroman-4-one	$C_{30}H_{36}O_5$	whole	[51]
154	2-[{3-Hydroxy-2′,2-dimethyl-8-(3-methyl-2-butenyl)} chroman-6-yl]-7-hydroxy-8-(3-methyl-2-butenyl)-chro-man-4-one	$C_{31}H_{38}O_4$	Roots	[49]
155	Tonkinochromane H	$C_{30}H_{34}O_5$	Roots	[52]
156	Tonkinochromane B	$C_{30}H_{36}O_4$	Roots	[53]
157	Kushenol E	$C_{25}H_{28}O_6$	Roots	[46]
158	Naringenin 7-O-neo-hesperidoside	$C_{27}H_{32}O_{14}$	Roots	[31]
	Chalcones and Dihydrochalcones			
159	Isoliquiritigenin	$C_{15}H_{12}O_4$	Roots	[47]
160	Sophoradin	$C_{30}H_{36}O_4$	Roots	[34]
161	Xanthohumol	$C_{21}H_{22}O_5$	Roots	[54]
162	7,9,2,4-Tetrahydroxy-8-isopentenyl-5-methoxychalcone	$C_{21}H_{22}O_6$	Roots	[54]
163	Tonkinochromane C	$C_{28}H_{30}O_4$	Roots	[53]
164	Tonkinochromane F	$C_{32}H_{42}O_5$	Roots	[50]
165	Kuraridine	$C_{26}H_{30}O_6$	Roots	[54]
166	Sophoradochromene	$C_{30}H_{34}O_4$	Roots	[42]
167	Tonkinochromane L	$C_{21}H_{24}O_4$	Roots	[46]
	Pterostanes			
168	(−)-Maackiain	$C_{16}H_{12}O_5$	Roots	[33]
169	Pisatin	$C_{17}H_{14}O_6$	Roots	[39]
170	Maackiain-3-O-glucoside 6′′-acetate	$C_{24}H_{24}O_{11}$	Roots	[47]
171	(−)-Maackiain 3-sulfate	$C_{16}H_{11}O_8S$	Roots	[55]
172	*6aR,11aR*-1-hydroxy-4-isoprenyl-maackiain	$C_{21}H_{20}O_6$	Roots	[48]
173	(*6aR,11aR*) - 2-hydroxy-3-methoxy-1-isopentenyl-maackiain	$C_{22}H_{22}O_6$	Roots	[47]
174	Sophotokin	$C_{21}H_{20}O_6$	Roots	[34]
175	(−)-Pterocarpin	$C_{17}H_{14}O_5$	Seeds	[56]
176	Medicarpin	$C_{16}H_{14}O_4$	Roots	[39]
177	*(6aR, 11aR)*-3-O-β-$_D$-Glucopyranosylmedicarpin	$C_{22}H_{24}O_9$	Roots	[24]
178	Medicarpin-3-O-glucoside 6″-acetate	$C_{24}H_{26}O_{10}$	Roots	[47]
179	Demethylmedicarpin	$C_{15}H_{12}O_4$	Roots	[40]
180	Homopterocarpin	$C_{17}H_{16}O_4$	Roots	[42]
181	Dehydromaackiain	$C_{16}H_{10}O_5$	Roots	[42]
182	Flemichapparin B	$C_{17}H_{12}O_5$	Roots	[42]
183	Maackiapterocarpan B	$C_{21}H_{18}O_6$	Roots	[57]
184	3-Methylmaackiapterocarpan B	$C_{22}H_{20}O_6$	Roots	[47]
185	Erybraedin D	$C_{25}H_{26}O_4$	Roots	[42]
186	Maackiapterocarpan A	$C_{21}H_{20}O_6$	Roots	[42]
187	Medicagol	$C_{16}H_8O_6$	Seeds	[56]
188	Sophtonseedlin B	$C_{28}H_{28}O_{13}$	Seeds	[56]
189	Sophoratonkin	$C_{26}H_{26}O_{11}$	Roots	[28]
190	(−)-Trifolirhizin	$C_{22}H_{22}O_{10}$	Seeds	[56]
191	(−)-Trifolirhizin-6′′-monoacetate	$C_{24}H_{24}O_{11}$	Seeds	[56]

Table 1. *Cont.*

NO	Compounds	Molecular Formula	Parts of Plant	References
	Flavanols			
192	7,2′-Dihydroxy-4′-methoxy-isofiavanol	$C_{16}H_{16}O_5$	Roots	[58]
193	(*3S,4R*)-4-hydroxy-7,4′-dimethoxyisoflavan 3′-O-β-$_D$-glucopyranoside	$C_{23}H_{28}O_{10}$	Roots	[24]
	Triterpenoids and Triterpenoid saponins			
194	Subprogenin A	$C_{30}H_{48}O_4$	Roots	[59]
195	Subprogenin B	$C_{30}H_{48}O_5$	Roots	[59]
196	Subprogenin C	$C_{30}H_{46}O_4$	Roots	[59]
197	Subprogenin C methylester	$C_{31}H_{48}O_4$	Roots	[59]
198	Subprogenin D	$C_{30}H_{46}O_4$	Roots	[59]
199	Subprogenin D methylester	$C_{31}H_{48}O_4$	Roots	[59]
200	Abrisapogenol H	$C_{30}H_{48}O_3$	Roots	[59]
201	Wistariasapogenol A	$C_{30}H_{48}O_4$	Roots	[59]
202	Melilotigenin	$C_{30}H_{46}O_5$	Roots	[59]
203	Abrisapogenol I	$C_{30}H_{46}O_5$	Roots	[59]
204	Sophoradiol	$C_{30}H_{50}O_2$	Roots	[59]
205	Cantoniensistiol	$C_{30}H_{50}O_3$	Roots	[59]
206	Soyasapogenol B	$C_{30}H_{50}O_3$	Roots	[59]
207	Soyasapogenol A	$C_{30}H_{50}O_4$	Roots	[59]
208	Abrisapogenol C	$C_{30}H_{50}O_4$	Roots	[59]
209	Abrisapogenol D	$C_{30}H_{50}O_3$	Roots	[59]
210	Abrisapogenol E	$C_{30}H_{50}O_4$	Roots	[59]
211	Kudzusapogenol A	$C_{30}H_{50}O_5$	Roots	[59]
212	Abrisapogenol A	$C_{30}H_{50}O_3$	Roots	[59]
213	Lupeol	$C_{30}H_{50}O$	Roots	[60]
214	Stigmasterol	$C_{29}H_{48}O$	Roots	[60]
215	β-Sitosterol	$C_{29}H_{50}O$	Roots	[60]
216	Daucosterol	$C_{35}H_{60}O_6$	Roots	[60]
217	Subproside I	$C_{48}H_{78}O_{19}$	Roots	[61]
218	Subproside I methylester	$C_{49}H_{80}O_{19}$	Roots	[61]
219	Subproside II	$C_{47}H_{76}O_{19}$	Roots	[61]
220	Subproside II methylester	$C_{48}H_{78}O_{19}$	Roots	[61]
221	Soyasaponin A_3 methylester	$C_{49}H_{80}O_{19}$	Roots	[62]
222	Kuzusapogenol A methylester	$C_{49}H_{80}O_{20}$	Roots	[62]
223	Soyasaponin I methylester	$C_{49}H_{80}O_{18}$	Roots	[62]
224	Kaikasaponin III methylester	$C_{49}H_{80}O_{17}$	Roots	[62]
225	Soyasaponin II methylester	$C_{48}H_{78}O_{17}$	Roots	[62]
226	Kaikasapomn I methylester	$C_{49}H_{80}O_{17}$	Roots	[62]
227	Kudzusaponin A_3	$C_{47}H_{76}O_{19}$	Roots	[61]
228	Soyasaponin II	$C_{47}H_{76}O_{17}$	Roots	[61]
229	Dehydrosoyasaponin I	$C_{48}H_{76}O_{18}$	Roots	[61]
230	Subproside VII	$C_{59}H_{96}O_{27}$	Roots	[63]
231	Subproside VII methylester	$C_{60}H_{98}O_{27}$	Roots	[63]
232	Subproside IV	$C_{54}H_{88}O_{23}$	Roots	[63]
233	Subproside IV methylester	$C_{55}H_{90}O_{23}$	Roots	[63]
234	Subproside V	$C_{54}H_{88}O_{24}$	Roots	[63]
235	Subproside V methylester	$C_{55}H_{90}O_{24}$	Roots	[63]
236	Subproside III	$C_{54}H_{86}O_{24}$	Roots	[61]
237	Subproside III methylester	$C_{55}H_{88}O_{24}$	Roots	[61]
238	Subproside VI	$C_{54}H_{88}O_{24}$	Roots	[63]
239	Subproside VI methylester	$C_{55}H_{90}O_{24}$	Roots	[63]
	Other compounds			
240	Tyrosol	$C_8H_{10}O_2$	Roots	[64]
241	4-(3-Hydroxypropyl) phenol	$C_9H_{12}O_2$	Roots	[64]
242	Vanillin alcohol	$C_8H_{10}O_3$	Roots	[64]
243	(±)-4-(2-Hydroxypropyl) phenol	$C_9H_{12}O_2$	Roots	[64]
244	3,4,5-Trihydroxybenzoic acid	$C_7H_6O_5$	Roots	[31]

Table 1. *Cont.*

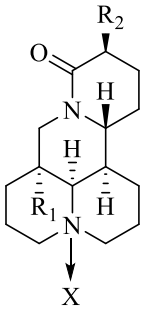
NO	Compounds	Molecular Formula	Parts of Plant	References
	Other compounds			
245	3,4-Dihydroxybenzoic acid	$C_7H_6O_4$	Roots	[31]
246	4-Hydroxy-3-methoxybenzoic acid	$C_8H_8O_4$	Roots	[31]
247	*p*-Hydroxybenzonic acid	$C_7H_6O_3$	Roots	[31]
248	Venillic acid	$C_8H_8O_4$	Roots	[41]
249	*p*-Methoxybenzonic acid	$C_8H_8O_3$	Roots	[27]
250	Salicylic acid	$C_7H_6O_3$	Roots	[43]
251	Benzamide	C_7H_7NO	Roots	[64]
252	4-Methoxybenzamide	$C_8H_9NO_2$	Roots	[64]
253	Docosyl caffeate	$C_{31}H_{52}O_4$	Roots	[4]
254	Maltol	$C_6H_6O_3$	Roots	[41]
255	(±)-3-(*p*-Methoxyphenyl) -1,2-propanediol	$C_9H_{12}O_4$	Roots	[64]
256	3,4-Dimethoxybenzeneacrylic acid methyl ester	$C_{12}H_{14}O_4$	Roots	[39]
257	Sophoratonin H	$C_{22}H_{26}O_5$	Roots	[42]
258	Piscidic acid monoethyl ester	$C_{13}H_{16}O_7$	Roots	[41]
259	2′,4′, 7-trihydroxy-6,8-bis(3-methyl-2-butenyl) flavanone	$C_{25}H_{28}O_5$	Roots	[40]
260	2-(2′, 4′-dihydroxylphenyl)-5,6-methylenedioxybenzoftiran	$C_{15}H_{10}O_5$	Roots	[56]
261	bolusanthin IV	$C_{15}H_{12}O_4$	Roots	[40]
262	7,2′-Dihydroxy-4′,5′-methylenedioxyisoflavan	$C_{16}H_{14}O_5$	Roots	[40]
263	Shandougenine A	$C_{30}H_{18}O_{10}$	Roots	[40]
264	Shandougenine B	$C_{30}H_{18}O_{10}$	Roots	[40]
265	(−)-Syringaresinol-4,4′-di-O-β-$_D$-glucopyranoside	$C_{34}H_{46}O_{18}$	Roots	[27]
266	(−)-Syringaresinol-4-O-β-$_D$-glucopyranoside	$C_{28}H_{36}O_{13}$	Roots	[27]
267	(−)-Pinoresinol-4,4′-di-O-β-$_D$-glucopyranoside	$C_{32}H_{42}O_{16}$	Roots	[27]
268	Pinoresinol	$C_{20}H_{22}O_6$	Roots	[28]
269	Syringaresinol	$C_{22}H_{26}O_8$	Roots	[28]
270	Medioresinol	$C_{21}H_{24}O_7$	Roots	[28]
271	Coniferin	$C_{16}H_{22}O_8$	Roots	[27]
272	4-Hydroxymethyl-2,6-dimethoxyphenol-1-O-β-$_D$-glucopyranoside	$C_{15}H_{22}O_9$	Roots	[27]
273	Syringin	$C_{17}H_{24}O_9$	Roots	[29]
274	Sophtonseedlin A	$C_{23}H_{14}O_9$	Roots	[56]
275	(6*S*,9*R*) -Roseoside	$C_{19}H_{30}O_8$	Roots	[27]
276	(−)-Secoisolariciresinol-4-O-β-$_D$-glucopyranoside	$C_{25}H_{33}NO_9$	Roots	[27]
	Compounds produced by endophytic fungi			
277	2-Methoxy-6-methyl-1,4-benzoquinone	$C_8H_8O_3$	Endophytic Fungus *Xylaria* sp. GDG-102	[65]
278	1-Methyl emodin	$C_{16}H_{12}O_5$	Endophytic Fungus *Penicillium macrosclerotiorum*	[66]
279	Isorhodoptilometrin	$C_{17}H_{14}O_6$	Endophytic Fungus *Penicillium macrosclerotiorum*	[66]
280	(−)-5-Carboxylmellein	$C_{11}H_{10}O_5$	Endophytic Fungus *Xylaria* sp. GDG-102	[65]
281	(−)-5-Methylmellein	$C_{11}H_{12}O_3$	Endophytic Fungus *Xylaria* sp. GDG-102	[67]
282	Xylariphilone	$C_{11}H_{16}O_4$	Endophytic Fungus *Xylaria* sp. GDG-102	[65]

Table 1. *Cont.*

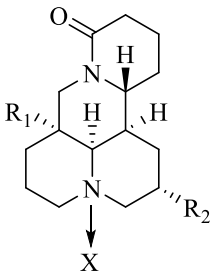
NO	Compounds	Molecular Formula	Parts of Plant	References
	Compounds produced by endophytic fungi			
283	Xylarphthalide A	$C_{11}H_{10}O_6$	Endophytic Fungus *Xylaria* sp. GDG-102	[65]
284	2-Anhydromevalonic acid	$C_6H_{10}O_3$	Endophytic Fungus *Xylaria* sp. GDG-102	[65]
285	(2*S*,5*R*)-2-Ethyl-5-methylhexanedioic acid	$C_9H_{16}O_4$	Endophytic Fungus *Xylaria* sp. GDG-102	[65]
286	6-Heptanoyl-4-methoxy-2H-pyran-2-one	$C_{13}H_{18}O_4$	Endophytic Fungus *Xylaria* sp. GDG-102	[65]
287	Xylareremophil	$C_{15}H_{18}O_3$	Endophytic Fungus *Xylaria* sp. GDG-102	[68]
288	1*α*,10*α*-Epoxy-13-hydroxyeremophil-7(11)-en-12,8-*β*-olide	$C_{15}H_{20}O_4$	Endophytic Fungus *Xylaria* sp. GDG-102	[68]
289	1*α*,10*α*-Epoxy-3*α*-hydroxyeremophil-7(11)-en-12,8-*β*-olide	$C_{15}H_{20}O_5$	Endophytic Fungus *Xylaria* sp. GDG-102	[68]
290	Mairetolide B	$C_{15}H_{20}O_4$	Endophytic Fungus *Xylaria* sp. GDG-102	[68]
291	Mairetolide G	$C_{15}H_{22}O_5$	Endophytic Fungus *Xylaria* sp. GDG-102	[68]
292	1*β*,10*α*,13-Trihydroxyeremophil-7(11)-en-12,8-olide	$C_{16}H_{24}O_4$	Endophytic Fungus *Xylaria* sp. GDG-102	[65]
293	(−)-3-Carboxypropyl-7-hydroxyphthalide	$C_{12}H_{12}O_5$	Endophytic fungus *Penicillium vulpinum*	[69]
294	(−)-3-Carboxypropyl-7-hydroxyphthalide methyl ester	$C_{13}H_{14}O_5$	Endophytic fungus *Penicillium vulpinum*	[69]
295	Sulochrin	$C_{17}H_{16}O_7$	Endophytic fungus *Penicillium macrosclerotiorum*	[66]
296	Monoacetylasterric acid	$C_{18}H_{16}O_9$	Endophytic fungus *Penicillium macrosclerotiorum*	[66]
297	Methyl dichloroasterrate	$C_{18}H_{16}Cl_2O_8$	Endophytic Fungus *Penicillium macrosclerotiorum*	[66]
298	Penicillither	$C_{18}H_{17}ClO_8$	Endophytic fungus *Penicillium macrosclerotiorum*	[66]
299	Methyl asterrate	$C_{18}H_{18}O_8$	Endophytic fungus *Penicillium macrosclerotiorum*	[66]
300	Asterric acid	$C_{17}H_{16}O_8$	Endophytic fungus *Penicillium macrosclerotiorum*	[66]

Table 1. *Cont.*

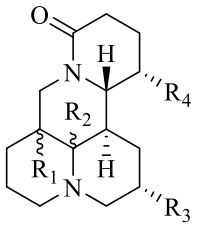
NO	Compounds	Molecular Formula	Parts of Plant	References
	Compounds produced by endophytic fungi			
301	Xylapeptide A	$C_{30}H_{45}N_5O_5$	Endophytic Fungus *Xylaria* sp. GDG-102	[70]
302	Xylapeptide B	$C_{29}H_{43}N_5O_5$	Endophytic Fungus *Xylaria* sp. GDG-102	[70]
303	21-Acetoxycytochalasin J_2	$C_{30}H_{37}NO_4$	Endophytic fungus *Diaporthe* sp.GDG-118	[71]
304	21-Acetoxycytochalasin J_3	$C_{30}H_{39}NO_3$	Endophytic fungus *Diaporthe* sp.GDG-118	[71]
305	Cytochalasin J_3	$C_{32}H_{41}NO_4$	Endophytic fungus *Diaporthe* sp.GDG-118	[71]
306	Cytochalasin H	$C_{30}H_{39}NO_5$	Endophytic fungus *Diaporthe* sp.GDG-118	[71]
307	7-Acetoxycytochalasin H	$C_{32}H_{41}NO_6$	Endophytic fungus *Diaporthe* sp.GDG-118	[71]
308	Cytochalasin J	$C_{28}H_{37}NO_4$	Endophytic fungus *Diaporthe* sp.GDG-118	[71]
309	Geomycin A	$C_{35}H_{32}O_{15}$	Endophytic fungus *Penicillium macrosclerotiorum*	[66]
310	Cytochalasin E	$C_{28}H_{33}NO_7$	Endophytic fungus *Diaporthe* sp.GDG-118	[71]
311	Cytochalasin K	$C_{28}H_{33}NO_7$	Endophytic fungus *Xylaria* sp. GDG-102	[65]
312	Diaporthein B	$C_{20}H_{28}O_6$	Endophytic fungus *Xylaria* sp. *GDGJ*-368	[72]
313	Piliformic	$C_{11}H_{18}O_4$	Endophytic fungus *Xylaria* sp. *GDGJ*-368	[72]
314	Cytochalasin C	$C_{30}H_{37}NO_6$	Endophytic fungus *Xylaria* sp. *GDGJ*-368	[72]
315	Cytochalasin D	$C_{30}H_{37}NO_6$	Endophytic fungus *Xylaria* sp. *GDGJ*-368	[72]
316	(22E)-ergosta-6,22-diene-3β,5β,8α-triol	$C_{28}H_{46}O_3$	Endophytic fungus *Xylaria* sp. *GDGJ*-368	[72]



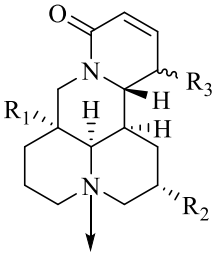
1 $R_1 = R_2 = H$, X = lone pair
2 $R_1 = R_2 = OH$, X = lone pair
3 $R_1 = OH$, $R_2 = H$, X = O
4 $R_1 = R_2 = H$, X = O
5 $R_1 = OH$, $R_2 = H$, X = lone pair
6 $R_1 = H$, $R_2 = OH$, X = O



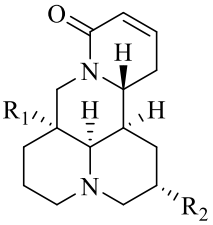
7 $R_1 = OH$, $R_2 = OAc$, X = lone pair
8 $R_1 = OH$, $R_2 = OCH_2SCH_3$, X = lone pair
9 $R_1 = H$, $R_2 = OH$, X = O
10 $R_1 = H$, $R_2 = OMe$, X = lone pair
11 $R_1 = H$, $R_2 = OH$, X = lone pair
12 $R_1 = R_2 = OH$, X = lone pair



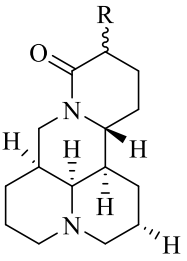
13 $R_1 = \alpha$-*H*, $R_2 = \beta$-*H*, $R_3 = R_4 = H$
14 $R_1 = R_2 = \alpha$-*H*, $R_3 = R_4 = H$
15 $R_1 = R_2 = \alpha$-*H*, $R_3 = H$, $R_4 = OH$
16 $R_1 = \beta$-*H*, $R_2 = \alpha$-*H*, $R_3 = R_4 = H$



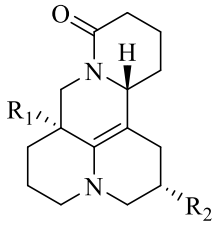
17 $R_1 = OH$, $R_2 = R_3 = H$, X = O
18 $R_1 = R_2 = H$, $R_3 = \beta$-OH, X = O
19 $R_1 = R_2 = H$, $R_3 = \beta$-OH, X = lone pair
20 $R_1 = R_2 = R_3 = H$, X = O



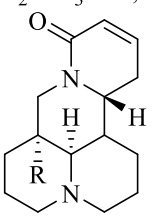
21 $R_1 = R_2 = OH$
22 $R_1 = OH$, $R_2 = OAc$
23 $R_1 = OH$, $R_2 = OCH_2SMe$
24 $R_1 = OH$, $R_2 = H$
25 $R_1 = H$, $R_2 = OH$



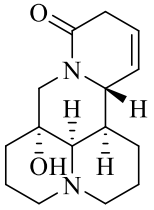
26 R = β-OCOMe
27 R = α-OCOMe
28 R = β-OH
29 R = α-OH



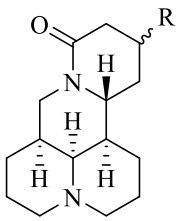
30 $R_1 = OH$, $R_2 = OAc$
31 $R_1 = R_2 = H$
32 $R_1 = OH$, $R_2 = H$



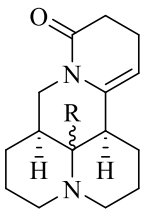
33 R = OH
34 R = H



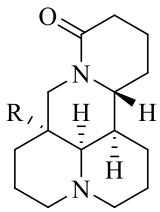
35



36 R = α-OH
37 R = β-OH



38 R = β-H
39 R = α-H



40 R = H
41 R = OH

Figure 1. *Cont.*

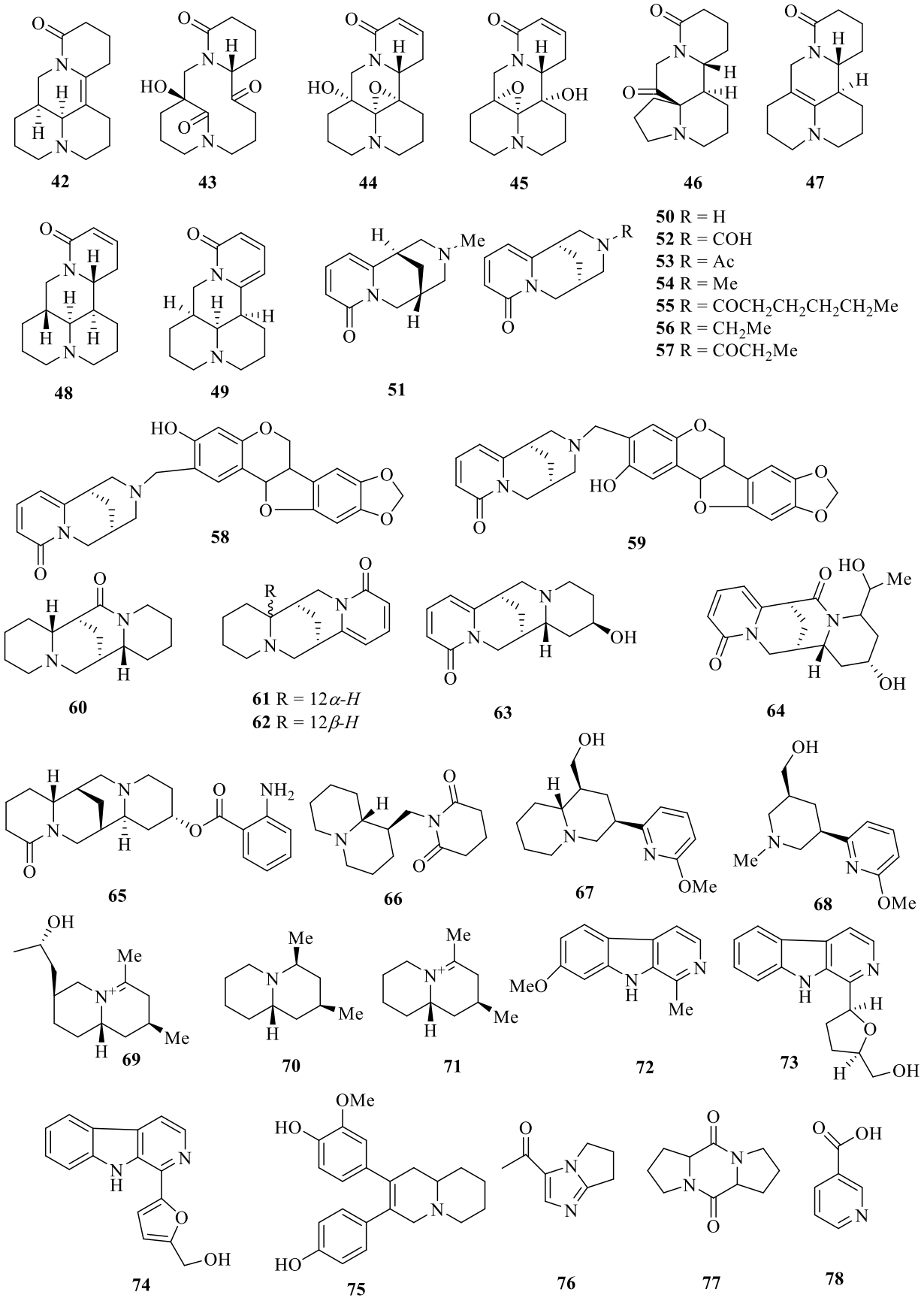
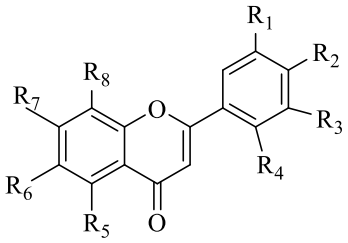
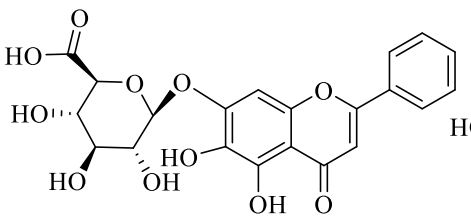


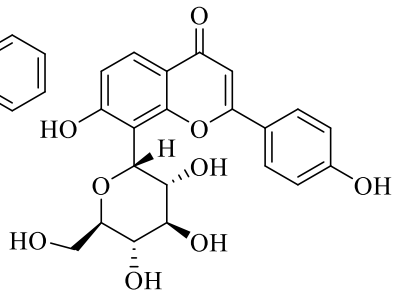
Figure 1. *Cont.*



79 $R_1 = R_3 = R_4 = R_5 = R_6 = R_8 = H$, $R_2 = R_7 = OH$
80 $R_1 = R_2 = R_3 = R_4 = R_6 = H$, $R_5 = R_7 = OH$, $R_8 = OMe$
81 $R_1 = R_3 = R_4 = R_5 = R_6 = R_8 = H$, $R_2 = OMe$, $R_7 = OH$
82 $R_1 = R_2 = R_5 = OH$, $R_3 = R_4 = R_6 = R_8 = H$, $R_7 =$ *O-glu*



83



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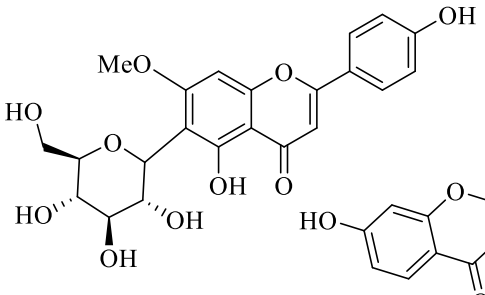
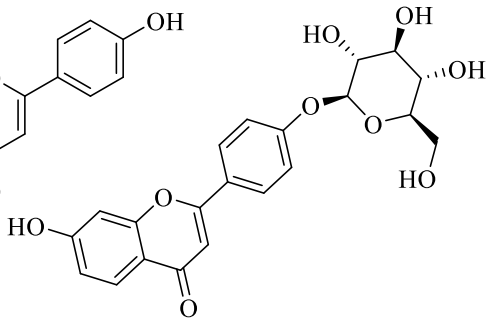
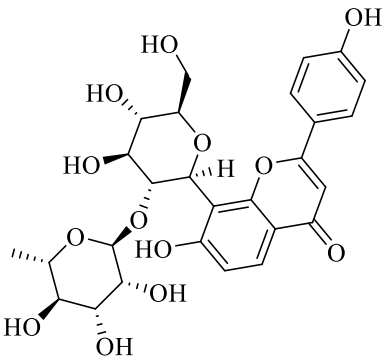


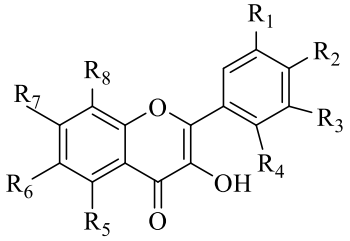
85

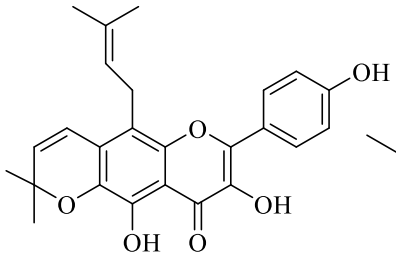


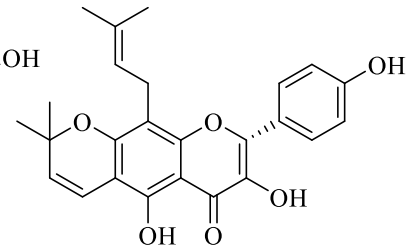
86



87



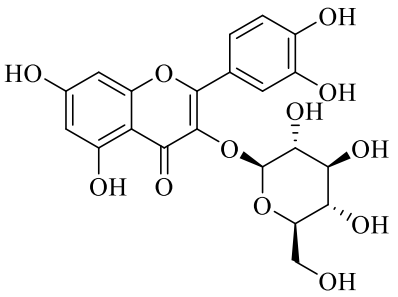




88 $R_1 = R_2 = R_5 = R_7 = OH$, $R_3 = R_4 = R_6 = R_8 = H$
89 $R_1 = R_3 = R_6 = R_8 = H$, $R_2 = R_4 = R_5 = R_7 = OH$
90 $R_1 = R_3 = R_4 = H$, $R_2 = R_5 = R_7 = OH$, $R_6 = R_8 =$ isoprenyl
91 $R_1 = R_3 = R_4 = R_6 = H$, $R_2 = R_5 = R_7 = OH$, $R_8 =$ isoprenyl

92

93



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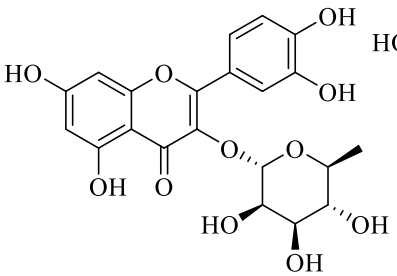
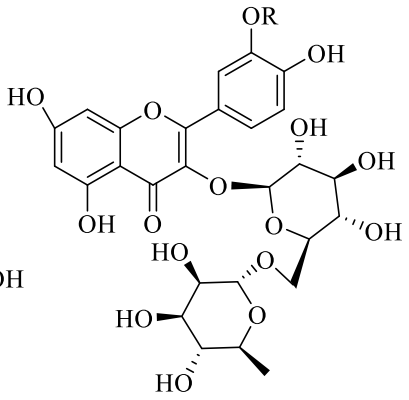
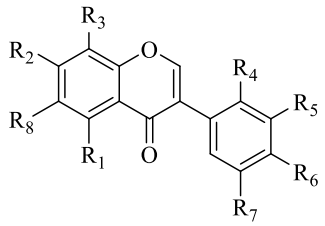


95

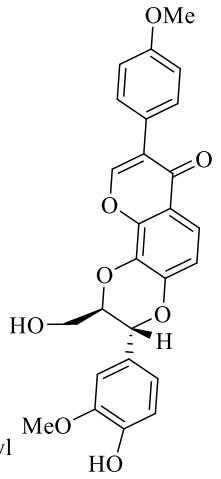


96 R = H
97 R = Me

Figure 1. *Cont.*



98 $R_1 = R_4 = R_5 = R_7 = R_8 = H$, R_2= OMe, $R_3 = R_6$= OH
99 $R_1 = R_2 = R_4 = R_6$ = OH, $R_3 = R_5 = R_7 = R_8 = H$
100 $R_1 = R_3 = R_4 = R_5 = R_8 = H$, $R_2 = R_7$ = OH, R_6 = OMe
101 $R_1 = R_3 = R_4 = R_6 = R_8 = H$, $R_2 = R_7$ = OH, R_5 = OMe
102 $R_1 = R_3 = R_4 = R_7 = R_8 = H$, $R_2 = R_6$ = OH, R_5 = OMe
103 $R_1 = R_3 = R_4 = R_5 = R_7 = R_8 = H$, $R_2 = R_6$ = OH
104 $R_1 = R_4 = R_7 = R_8 = H$, $R_2 = R_5$ = OH, $R_3 = R_6$ = OMe
105 $R_1 = R_4 = R_5 = R_7 = R_8 = H$, $R_2 = R_3$ = OH, R_6 = OMe
106 $R_1 = R_3 = R_4 = R_7 = R_8 = H$, $R_2 = R_5 = R_6$ = OH
107 $R_1 = R_3 = R_4 = R_5 = R_7 = R_8 = H$, R_2 = OH, R_6 = OMe
108 $R_1 = R_2 = R_6$ = OH, $R_3 = R_4 = R_5 = R_7 = R_8 = H$
109 $R_1 = R_2 = R_6$ = OH, $R_3 = R_4 = R_5 = R_7 = H$, R_8 = isoprenyl
110 $R_1 = R_4 = R_5 = R_7 = R_8 = H$, R_2 = OH, $R_3 = R_6$ = OMe
111 $R_1 = R_4 = R_5 = R_7 = R_8 = H$, $R_2 = R_6$ = OMe, R_3 = isoprenyl
112 $R_1 = R_2 = R_6$ = OH, $R_3 = R_4 = R_5 = R_7 = H$, R_8 = OMe



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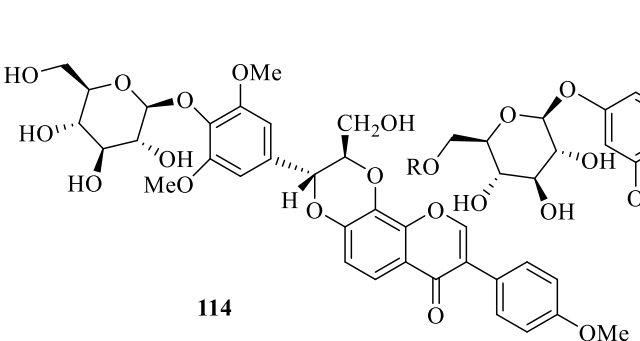

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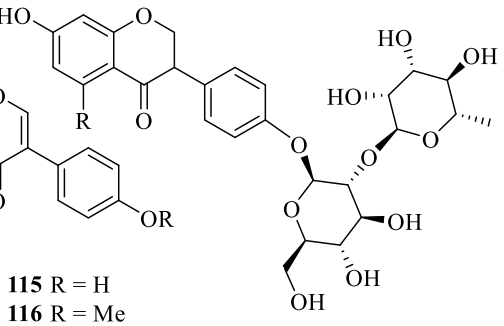
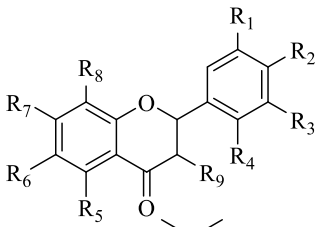
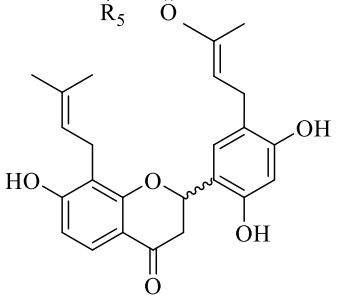


115 R = H
116 R = Me

117 R = H
118 R = OH



119 $R_1 = R_3 = R_4 = R_5 = R_9 = H$, $R_2 = R_7$ = OH, $R_6 = R_8$ = isoprenyl
120 $R_1 = R_3 = R_8$ = isoprenyl, $R_2 = R_7$ = OH, $R_4 = R_5 = R_6 = R_9 = H$
121 $R_1 = R_8$ = isoprenyl, $R_2 = R_7$ = OH, $R_3 = R_4 = R_5 = R_6 = R_9 = H$
122 $R_1 = R_3 = R_5 = R_9 = H$, $R_2 = R_4 = R_7$ = OH, $R_6 = R_8$ = isoprenyl
123 $R_1 = R_4 = H$, $R_2 = R_5 = R_7 = R_9$ = OH, $R_3 = R_6 = R_8$ = isoprenyl
124 R_1 = CHO, $R_2 = R_7$ = OH, $R_4 = R_5 = R_6 = R_9 = H$, $R_3 = R_8$ = isoprenyl
125 $R_2 = R_4 = R_7$ = OH, $R_5 = R_6 = R_9 = H$, $R_1 = R_3 = R_8$ = isoprenyl
126 $R_1 = R_8$ = isoprenyl, $R_2 = R_3 = R_7$ = OH, $R_4 = R_5 = R_6 = R_9 = H$
127 $R_1 = R_2 = R_7$ = OH, $R_3 = R_6 = R_8$ = isoprenyl, $R_4 = R_5 = R_9 = H$
128 $R_1 = R_2 = R_7$ = OH, $R_3 = R_8$ = isoprenyl, $R_4 = R_5 = R_6 = R_9 = H$
129 $R_1 = R_3 = R_6 = R_8$ = isoprenyl, $R_2 = R_7$ = OH, $R_4 = R_5 = R_9 = H$
130 $R_1 = R_3 = R_4 = R_9 = H$, $R_2 = R_5 = R_7$ = OH, $R_6 = R_8$ = isoprenyl



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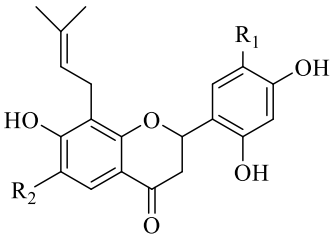
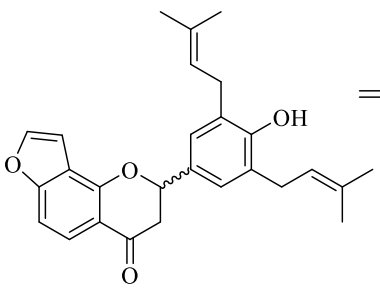


132 R_1 = H, R_2 = isoprenyl



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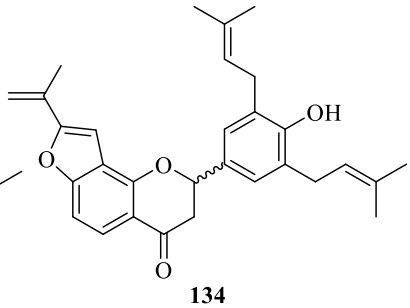

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Figure 1. *Cont.*

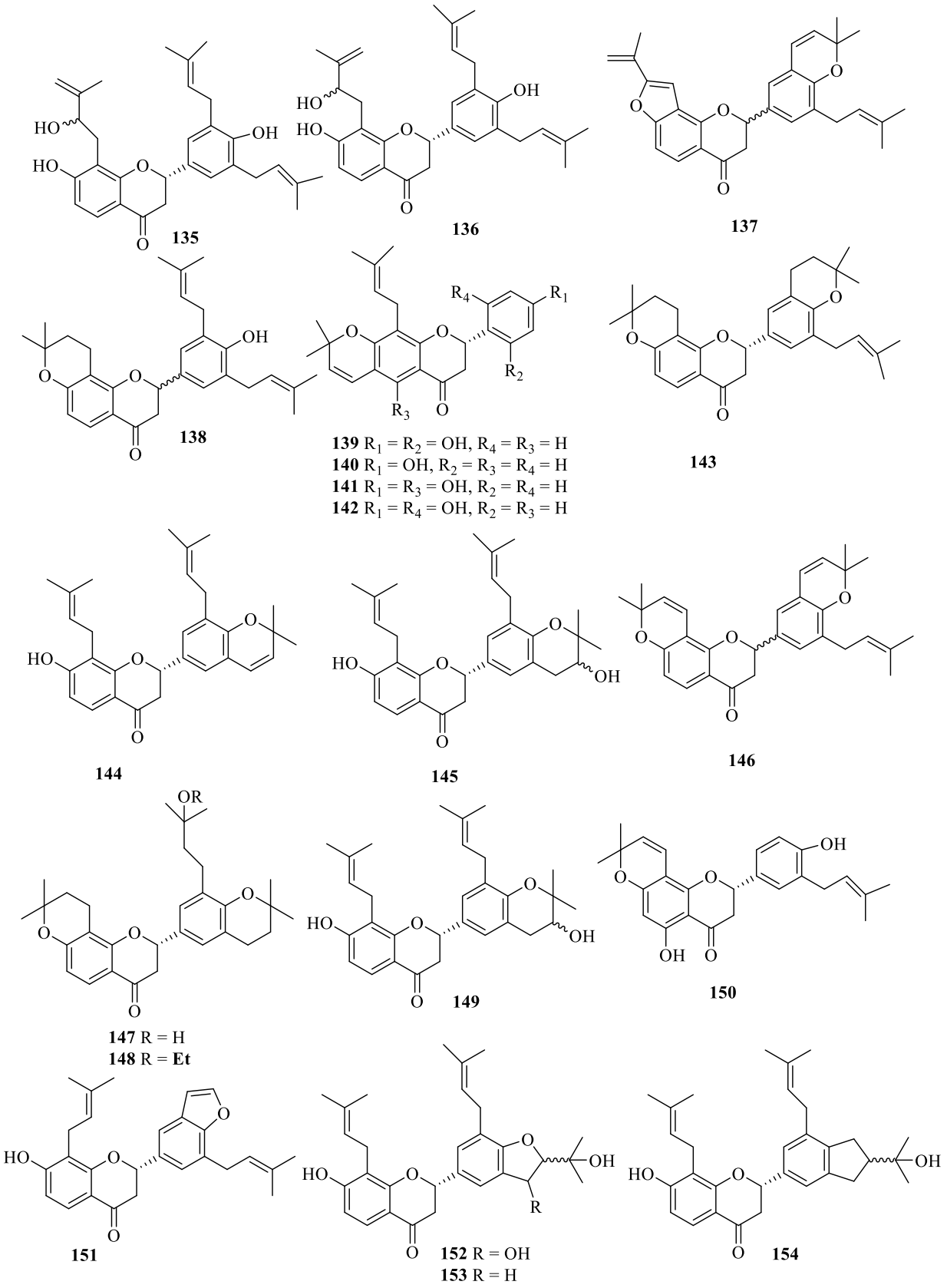


Figure 1. *Cont.*

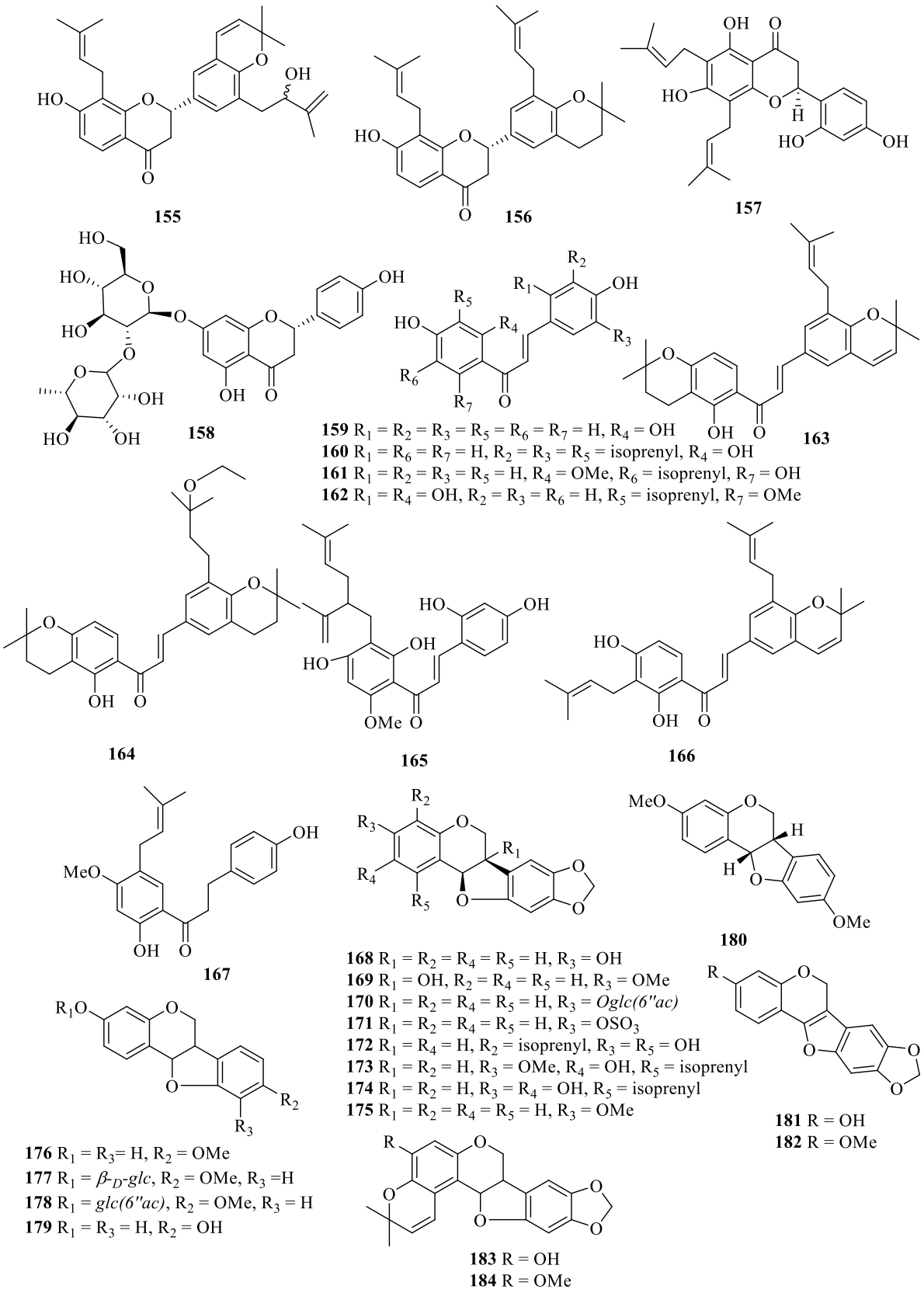


Figure 1. *Cont.*

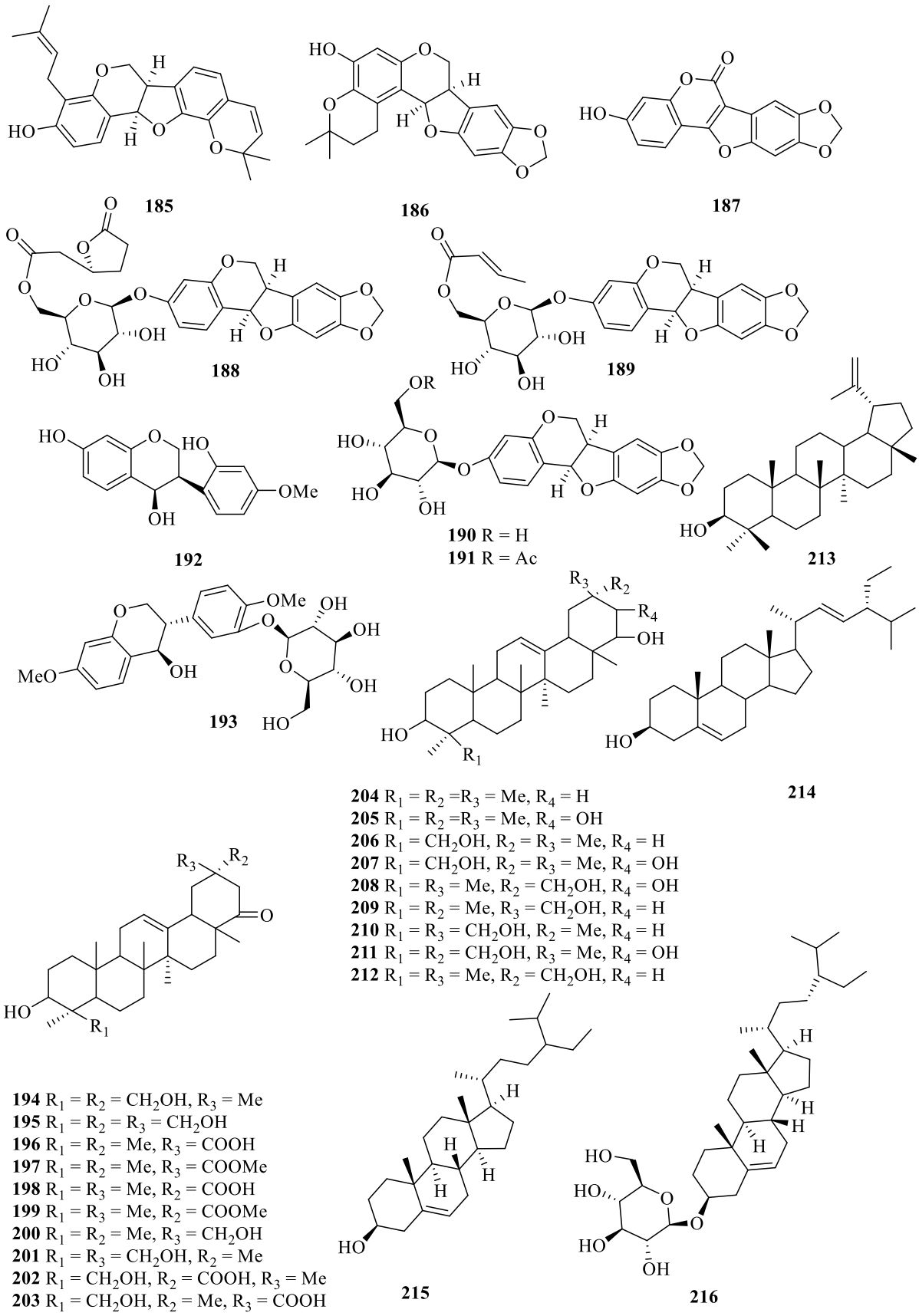


Figure 1. *Cont.*

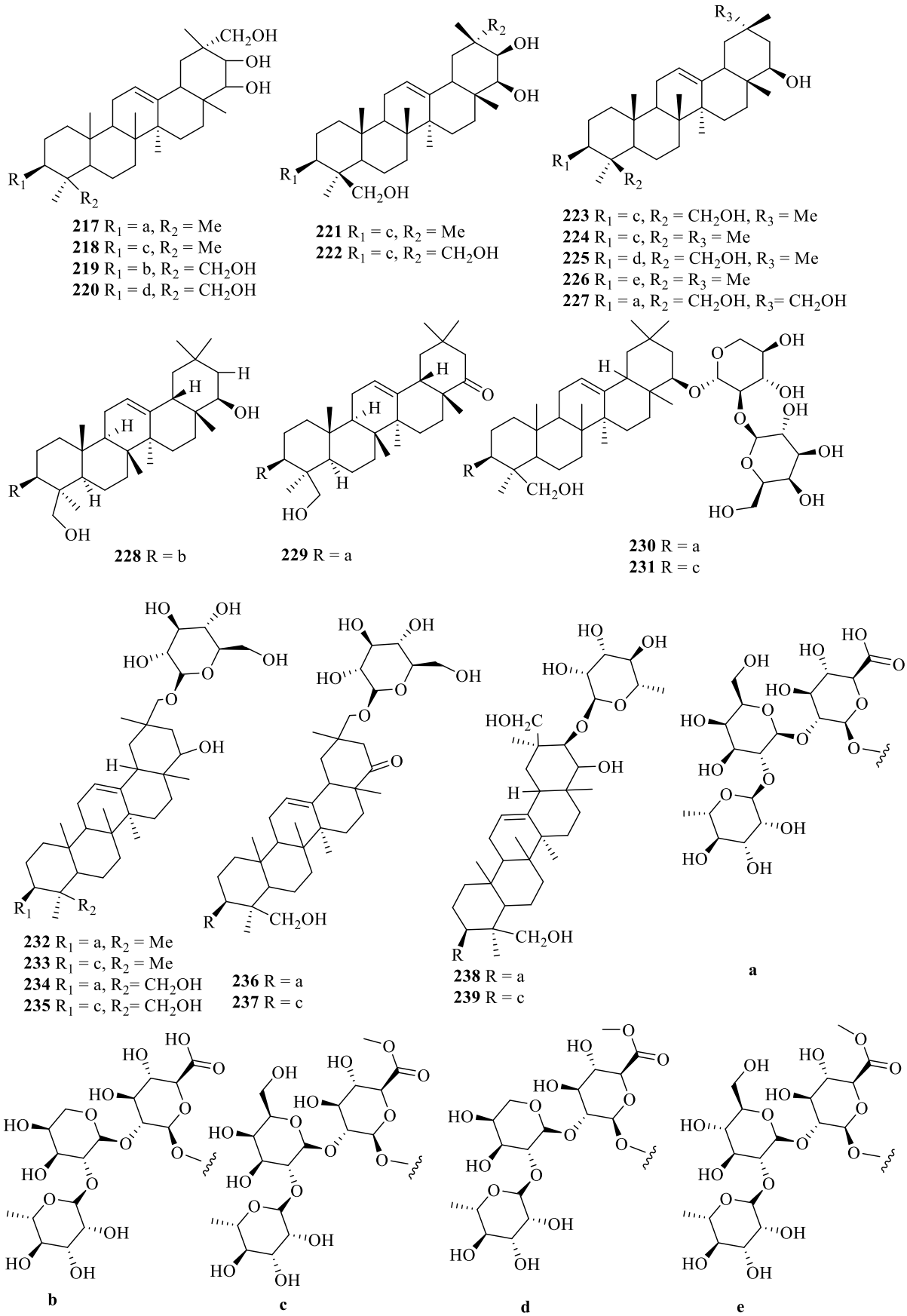


Figure 1. *Cont.*

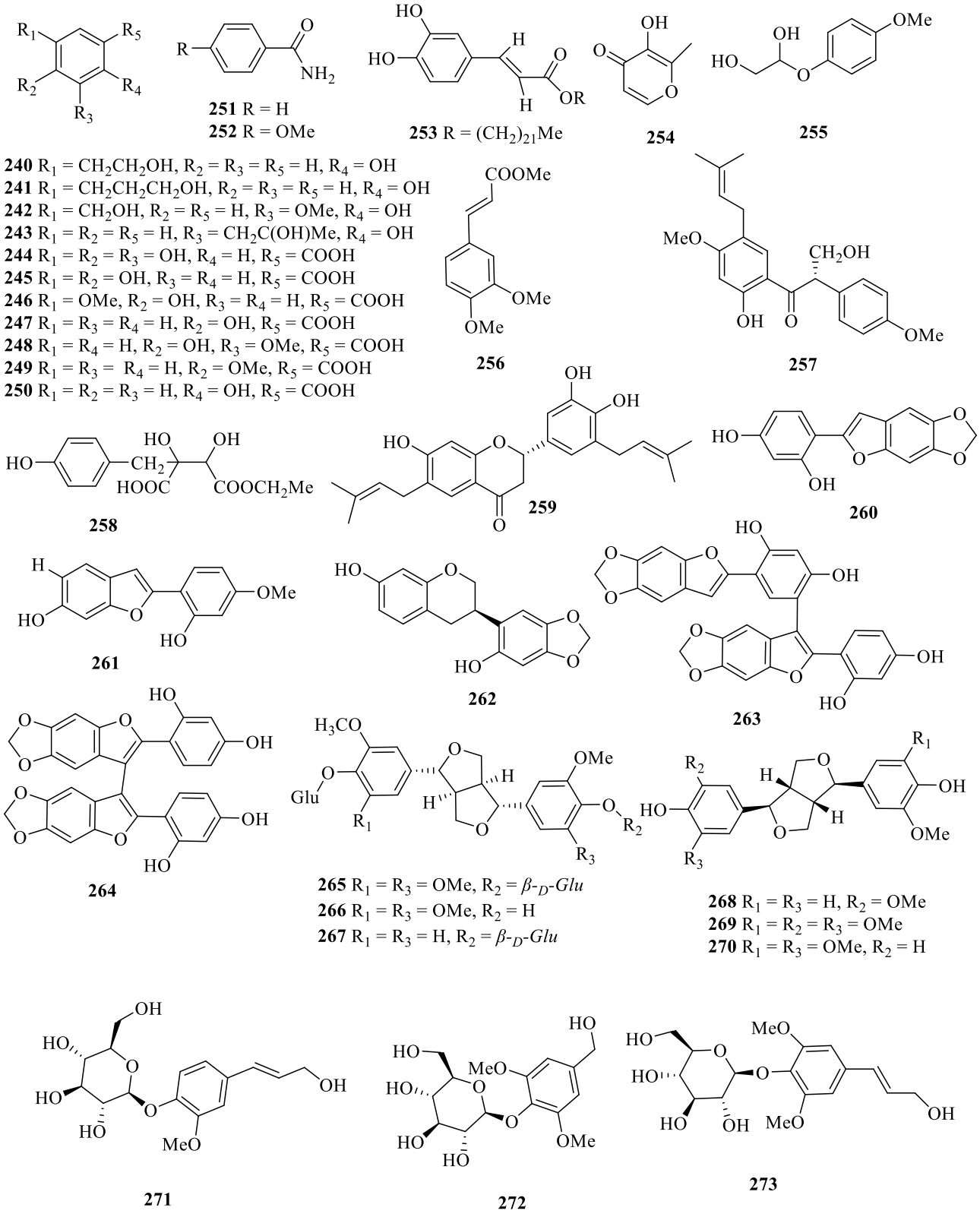
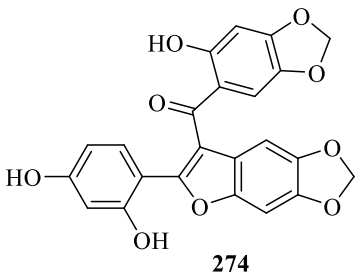


Figure 1. *Cont.*



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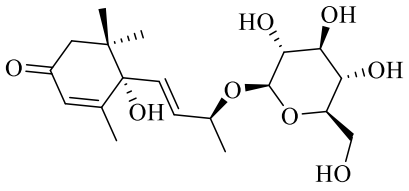

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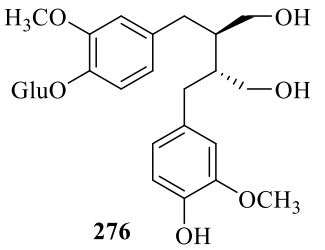

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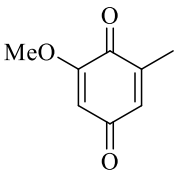

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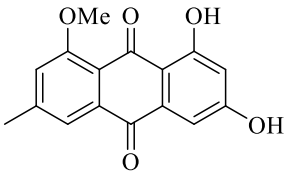

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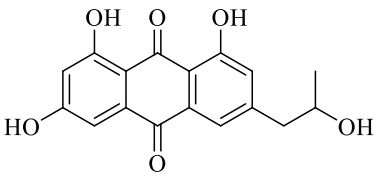

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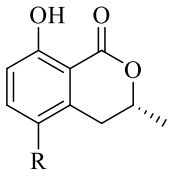
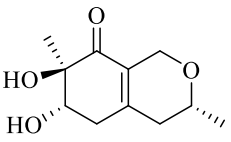


280 R = COOH
281 R = Me



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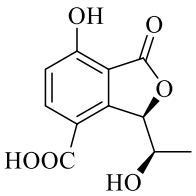

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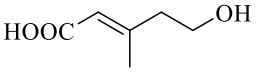

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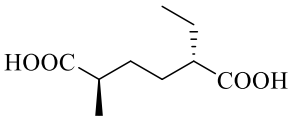

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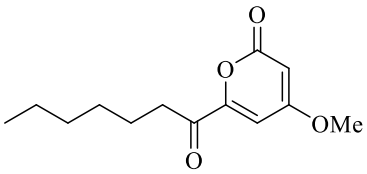

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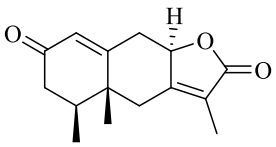

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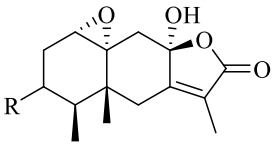
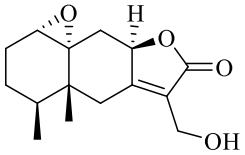


288 R = H
289 R = OH



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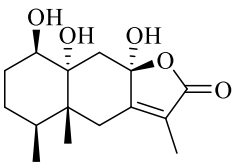

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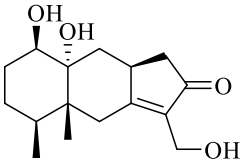

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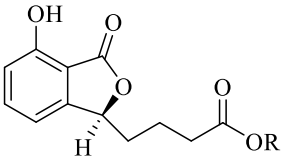
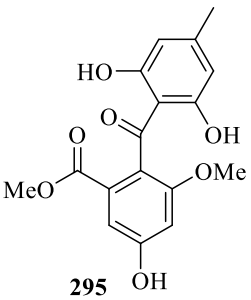


293 R = H
294 R = Me



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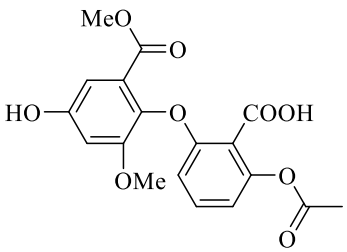

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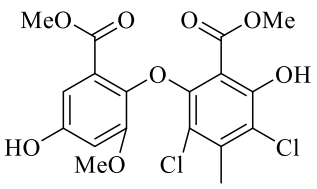

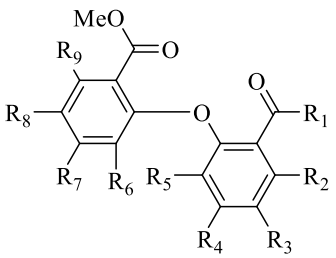

297

298 $R_1 = R_5 = OMe$, $R_2 = R_4 = R_8 = H$, $R_3 = R_9 = OH$, $R_6 = Cl$, $R_7 = Me$
299 $R_1 = R_6 = OMe$, $R_2 = R_8 = OH$, $R_3 = R_5 = R_7 = R_9 = H$, $R_4 = Me$
300 $R_1 = R_2 = R_8 = OH$, $R_3 = R_5 = R_7 = R_9 = H$, $R_4 = Me$, $R_6 = OMe$

Figure 1. *Cont.*

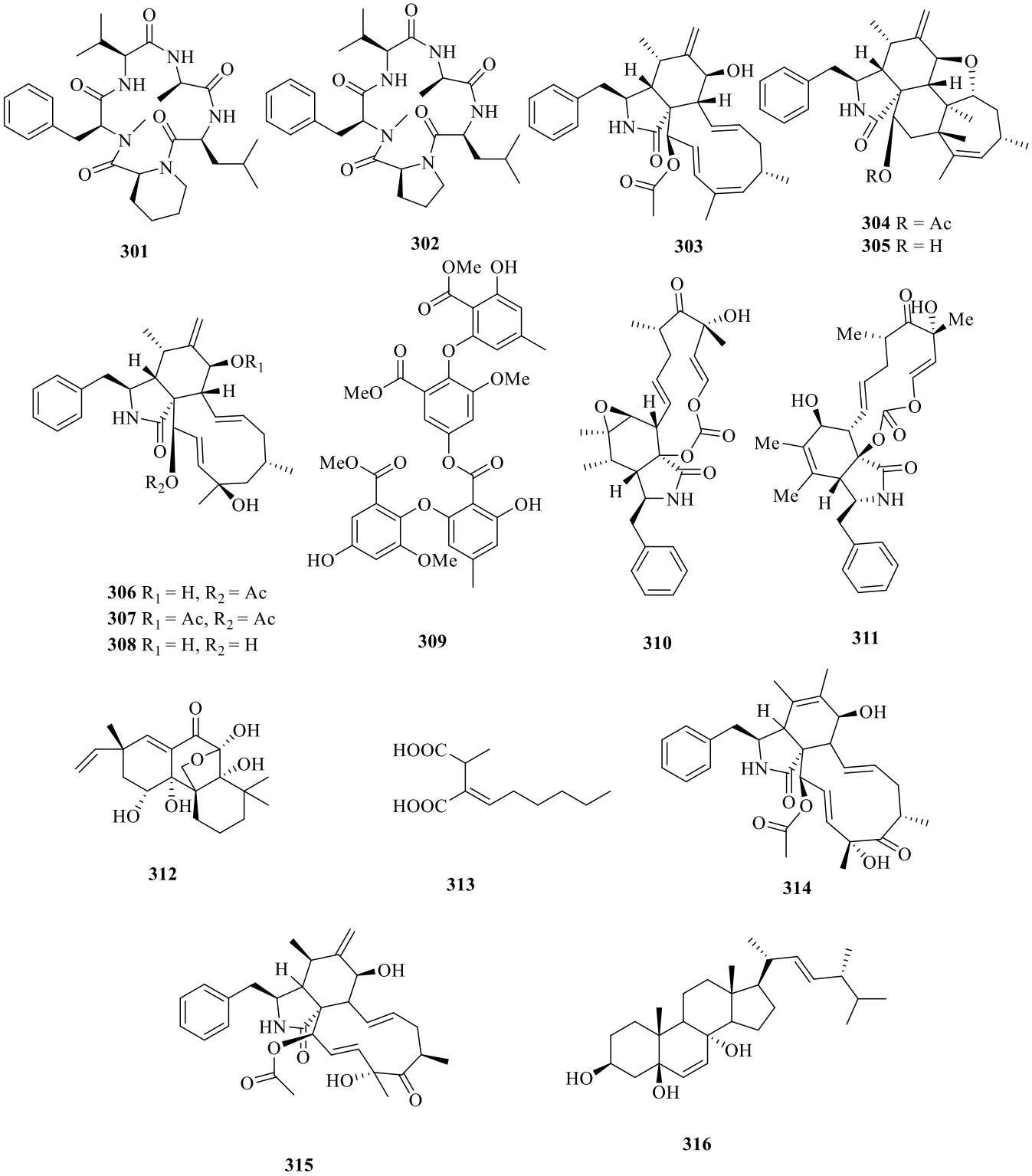

Figure 1. Structures of compounds **1–316** from *S. tonkinensis*.

2.1. Alkaloids

The alkaloids isolated in *S. tonkinensis* were mainly quinolizidine-type alkaloids [73]. To date, 78 alkaloids have been identified and isolated, of which 49 (**1–49**) are matrine type alkaloids. Sophtonseedline A (**46**) was isolated from the seeds of *S. tonkinensis*, which featured an unprecedented 5/6/6/6 tetracyclic skeleton [19]. Meanwhile, tonkinensines

A (**58**) and B (**59**) with the rare multi group bridging structures were isolated from *S. tonkinensis* also [25].

2.2. Flavonoids

Flavonoids generically referred to the compounds with C6-C3-C6 structure skeleton. The flavonoids were rich in *S. tonkinensis*, and more than 115 flavonoids have been reported as far as we know. Their structural types can be classified as flavonoids (**79-87**), flavonols (**88**–**97**), isoflavones and dihydroisoflavones (**98**–**118**), dihydroflavones (**119**–**158**), chalcones and dihydrochalcones (**159**–**167**), pterostanes (**168**–**191**), and flavanols (**192**–**193**). Interestingly, tonkinochromanes A (**143**) and B (**156**) may ring-fused in the isoprenyl substituents [53]. Meanwhile, sophoraflavones A (**87**) and B (**86**) were the rare 5-deoxyflavonoids from the roots of *S. tonkinensis* [32]. Among the eighteen flavonoids identified using UPLC-ESI-LTQ/MS methods, formononetin (**107**), quercetin (**88**), rutin (**96**), isoquercitrin (**94**), and quercitrin (**95**) were suggested as the major quality markers of *S. tonkinensis* roots [37].

2.3. Triterpenoids and Triterpenoid Saponins

As far as we know, more than 46 (**194**–**239**) triterpenoids and triterpenoid saponins have been isolated from *S. tonkinensis*. Isolated triterpenoids are mainly of the oleanane type with carbonyl substitution at position C-22 [30,74]. Compared with flavonoids and alkaloids, the triterpenoids and triterpenoid saponins of *S. tonkinensis* were rarely reported [59,61,62].

2.4. Other Compounds

In addition to alkaloids, flavonoids, and triterpenoids, a total of 37 (**240**–**276**) phenolic acids, sterols, and other compounds were reported from *S. tonkinensis*. Two new 2-arylbenzofuran dimers, shandougenines A (**263**) and B (**264**), were isolated from the roots of *S. tonkinensis*. It is noteworthy that shandougenine A (**263**) has the unique dimeric 2-Arylbenzofuran with a C-3\C-5 bond, and shandougenine B (**264**) was the natural dimeric 2-arylbenzofuran with a novel C-3/C-3 bond [40]. Meanwhile, a new propenyl phenylacetone was also isolated from *S. tonkinensis* and named sophoratonin H (**257**) [42].

2.5. Compounds Produced by Endophytic Fungi

The endophytic fungus *Xylaria* sp.GDG-102, *Penicillium macrosclerotiorum*, *Penicillium vulpinum*, *Diaporthe* sp.GDG-118, and *Xylaria* sp. GDGJ-368 [65,66,69,71] were isolated from *S. tonkinensis*, and some compounds produced by these endophytic fungi were interesting. More than 40 (**277**–**316**) compounds have been isolated from its endophytic fungi. Xylapeptide A (**301**) identified from the associated fungus *Xylaria* sp. GDG-102 was the first example of cyclopentapeptide with an L-Pip of terrestrial origin [70].

3. Pharmacological Activities

3.1. Anti-Inflammatory Effect

Reported studies have shown the anti-inflammatory activities of *S. tonkinensis* (Table 2) **[45,75]**. Some novel compounds, including 12,13-dehydrosophoridine (**16**) from *S. tonkinensis*, showed significant activity against inflammatory cytokines TNF-α and IL-6 on LPS-induced RAW264.7 macrophages [23]. Moreover, 6,8-diprenyl-7,4′-dihydroxyflavanone (DDF) (**119**) inhibited the production of NO and the expression of TNF-α, IL-1β, and IL-6 [45]. Meanwhile, the compounds 2′-hydroxyglabrol (**131**), glabrol (**121**), maackiain (**168**), and bolusanthin IV (**261**) showed strong inhibitory effects on IL-6 [47]. Sophotokin (**174**) dose-dependently inhibited the lipopolysaccharide (LPS)-stimulated production of NO, TNF-α, PGE_2, and IL-1β in microglial cells [34]. Moreover, the orally administered roots extract of *S. tonkinensis* attenuated the total leukocytes, eosinophil infiltration, and IL-5 level in BAL fluids [76]. Another study also showed *S. tonkinensis* were able to reduce TNF-α, NO, and IL-6 contents in rat paw edema induced by carrageenan [77].

Table 2. The comprehensive list of the pharmacological activities from *S. tonkinensis*.

Detail	Extracts/Compounds	*In Vivo*/*In Vitro*	Active Concentration/Dose	References
Anti-inflammatory activity				
Reduce TNF-*α*	(−)-Anagyrine (**61**)	In vitro	50 μM	[12]
	Sophocarpine (**34**)	In vitro	50 μM	[12]
	14*β*-Hydroxymatrine (**28**)	In vitro	50 μM	[12]
	7*β*-Sophoramine (**49**)	In vitro	50 μM	[12]
	Matrine (**1**)	In vivo	50 μM	[12]
	(+)-5*α*-Hydroxymatrine (**5**)	In vivo	50 μM	[12]
	12,13-Dehydrosophoridine (**16**)	In vitro	50 μM	[23]
	13*α*-Hydroxymatrine (**36**)	In vitro	50 μM	[23]
	13*β*-Hydroxymatrine (**37**)	In vitro	50 μM	[23]
	Isosophocarpine (**48**)	In vitro	50 μM	[23]
	Sophoridine (**13**)	In vitro	50 μM	[23]
	Water extract of roots	In vivo	0.3 g/kg	[75]
Inhibit the production of NO	sophoratonkin (**189**)	In vitro	IC_{50} = 33.0 μM	[28]
	Maackiain (**168**)	In vitro	IC_{50} = 27.0 μM	[28]
	Sophoranone (**120**)	In vitro	IC_{50} = 28.1 μM	[28]
	Sophoranochromene (**144**)	In vitro	IC_{50} = 13.6 μM	[28]
	Tonkinochromane A (143)	In vitro	20 μM	[45]
	Flemichin D (**139**)	In vitro	20 μM	[45]
	6,8-Diprenyl-7,4′-dihydroxyflavanone (**119**)	In vitro	IC_{50} = 12.21 μM	[45]
	Water extract of roots	In vivo	100 mg/kg	[13]
	Non-alkaloid extracts of roots	In vivo	400 mg/kg	[13]
	2′-Hydroxyglabrol (**131**)	In vitro	IC_{50} = 1.62 μM	[47]
	Glabrol (**121**)	In vitro	IC_{50} = 0.73 μM	[47]
	Maackiain (**168**)	In vitro	IC_{50} = 3.01 μM	[47]
	Bolusanthin IV (**261**)	In vitro	IC_{50} = 4.02 μM	[47]
	Ethanol extract of roots	In vivo	100 mg/kg	[7]
Reduce IL- 6	(−)-Anagyrine (**61**)	In vitro	50 μM	[12]
	Sophocarpine (**34**)	In vitro	50 μM	[12]
	14*β*-Hydroxymatrine (**28**)	In vitro	50 μM	[12]
	7*β*-Sophoramine (**49**)	In vitro	50 μM	[12]
	Matrine (**1**)	In vitro	50 μM	[12]
	(+)-5*α*-Hydroxyoxymatrine (**3**)	In vivo	50 μM	[12]
	(+)-5*α*-Hydroxymatrine (**5**)	In vivo	50 μM	[12]
	12,13-Dehydrosophoridine (**16**)	In vitro	50 μM	[23]
	13*α*-Hydroxymatrine (**36**)	In vitro	50 μM	[23]
	13*β*-Hydroxymatrine (**37**)	In vitro	50 μM	[23]
	Isosophocarpine (**48**)	In vitro	50 μM	[23]
	Sophoridine (**13**)	In vitro	50 μM	[23]
	Water extract of roots	In vivo	0.3 g/kg	[75]
Reduce IL-5	50% (*v*/*v*) ethanol-water mixture	In vivo	100 mg/kg	[76]
Reduce IL-10	Ethanol extract of roots	In vivo	100 mg/kg	[7]
Reduce IL-1*β*	Water extract of roots	In vivo	0.3 g/kg	[75]
Reduced the hyperplasia of goblet cell	50% (*v*/*v*) ethanol-water mixture	In vivo	10 mg/kg	[76]
Inhibit xylene induced auricle swelling in mice	Oxymatrine (**4**)	In vivo	40 mg/kg	[78]
	(−)-Cytisine (**50**)	In vivo	40 mg/kg	[78]
	S. tonkinensis particles	In vivo	1.75 g/kg	[79]
Inhibit pain induced by acetic acid stimulation of the celiac mucosa	Matrine (**1**)	In vivo	40 mg/kg	[78]
	Sophoridine (**13**)	In vivo	30 mg/kg	[78]
	Sophocarpine (**34**)	In vivo	40 mg/kg	[78]
	S. tonkinensis particles	In vivo	3.5 g/kg	[79]
Inhibit croton oil induced ear swelling in mice	Water extract of roots	In vivo	0.35–1.12 g/kg	[80]
	Ethanol extract of roots	In vivo	0.35–1.12 g/kg	[80]
	Water extract of roots	In vivo	0.39 g/kg	[81]
Anti-tumor activity				
Inhibit A549	(−)-*N*-hexanoylcytisine (**55**)	In vitro	IC_{50} = 31.64 μM	[24]
	(−)-*N*-Formylcytisine (**52**)	In vitro	IC_{50} = 22.05 μM	[24]
	(6a*R*, 11a*R*)-Maackiain (**168**)	In vitro	IC_{50} = 24.58 μM	[24]
	Water extracts of roots	In vitro	6.5 μg/μL	[82]
	1-(6,7-Dihydro-5H-pyrrolo [1,2-*a*] imidazol-3-yl) ethenone (**76**)	In vitro	IC_{50} = 23.05 ± 0.46 μM	[27]

Table 2. *Cont.*

Detail	Extracts/Compounds	*In Vivo*/*In Vitro*	Active Concentration/Dose	References
	Anti-tumor activity			
Inhibit HL-60	Tonkinensisol (**93**)	In vitro	IC_{50} = 36.48 μg/mL	[15]
	Sophoranol (**5**)	In vitro	10.00 μg/mL	[83]
	13,14-Dehydrosophoranol (**24**)	In vitro	1.00 μg/m L	[83]
Inhibit HepG2	Tonkinensine C (**73**)	In vitro	IC_{50} = 87.4 ± 7.1 μM	[1]
	Perlolyrine (**74**)	In vitro	IC_{50} = 91.8 ± 3.5 μM	[1]
	Harmine (**72**)	In vitro	IC_{50} = 48.9 ± 5.2 μM	[1]
	Alkaloids	In vitro	IC_{50} = 9.04 g/L	[84]
	Non-alkaloids extract of roots	In vitro	IC_{50} = 0.98 g/L	[84]
	Water extracts of roots	In vitro	6.5 μg/μL	[82]
Inhibit SH-SY5Y	Sophoranone (**120**)	In vitro	IC_{50} = 18.49 μM	[85]
	Matrine (**1**)	In vitro	IC_{50} = 60.81 μM	[85]
	Oxymatrine (**4**)	In vitro	IC_{50} = 42.56 μM	[85]
	(−)-Trifolirhizin (**190**)	In vitro	IC_{50} = 72.11 μM	[85]
	(−)-Maackiain (**168**)	In vitro	IC_{50} = 65.62 μM	[85]
Inhibit B16-BL6	Extract of roots	In vitro	400 μg/mL	[86]
Inhibit CNE-1, CNE-2	Chloroform extract of roots	In vitro	25 μg/mL	[87]
Inhibit U937	Sophoranone (**120**)	In vitro	IC_{50} = 3.8 ± 0.9 μM	[88]
Inhibit HeLa	Tonkinensine B (**59**)	In vitro	IC_{50} = 24.3± 0.3 μM	[25]
Inhibit MDA-MB-231	Tonkinensine B (**59**)	In vitro	IC_{50} = 48.9± 0.5 μM	[25]
	Water extract of roots	In vitro	6.5 μg/μL	[82]
Inhibit ESC solid tumor cell	Total alkaloids of roots	In vivo	100 mg/kg	[89]
Inhibit H_{22} ascites tumor cells	Total alkaloids of roots	In vivo	100 mg/kg	[89]
Inhibit S_{180} solid tumor cell	Total alkaloids of roots	In vivo	75 mg/kg	[89]
Inhibit BV2 glioma cell lines	Sophotokin (**174**)	In vitro	10 μM	[34]
	Maackiain (**168**)	In vitro	10 μM	[34]
	Medicarpin (**176**)	In vitro	10 μM	[34]
Inhibit Hep3B and KG-1 cells	Water extract of roots	In vitro	6.5 μg/μL	[82]
Decrease the number of cancer nodules in tumor tissue and reduce AFP in serum	Alkaloids extract of roots	In vivo	0.036 g/kg	[90]
	Effects on the liver			
Protect HepG2 cell against acetaminophen (APAP)-induced damage	4-Methoxybenzamide (**252**)	In vitro	10 μmol/L	[64]
	7,3′-Dihydroxy-8,4′-dimethoxyisoflavone (**104**)	In vitro	10 μmol/L	[64]
	7,4′-Dihydroxy-3′-methoxyisoflavone (**102**)	In vitro	10 μmol/L	[64]
	(±)-3-(*p*-Methoxyphenyl)-1,2-propanediol (**255**)	In vitro	10 μmol/L	[64]
Enhance L-02 hepatocytes	Matrine (**1**)	In vivo and vitro	10 μM	[91]
	Oxymatrine (4)	In vivo and vitro	10 μM	[91]
	Effects on the liver			
Increase SOD and GSH	Non-alkaloids extract of roots	In vivo	400 mg/kg	[13]
	Water extract of roots	In vivo	400 mg/kg	[13]
Increase ALT and AST	Water extract of roots	In vivo	0.59 g/kg	[92]
Increase CPT 1A activity	Water extract of roots	In vivo	25 μg/mL	[91]
Reduce nonestesterified fatty acid Induce cellular lipids accumulation in hepatocytes	Matrine (**1**)	In vivo	10 μM	[91]
	Oxymatrine (**4**)	In vivo	10 μM	[91]
Reduce immune liver injury	Oxymatrine (**4**)	In vivo	60 mg/kg	[93]
	Sophocarpine (**34**)	In vivo	60 mg/kg	[93]
	Oxymatrine (**4**)	In vivo	120 mg/kg	[94]
Inhibite acetaminophen-induced hepatic oxidative damage in mice	STRP1 (Polysaccharide part)	In vivo	200 mg/kg	[95]
	STRP2 (Polysaccharide part)	In vivo	200 mg/kg	[95]
Alleviate non-alcoholic fatty liver disease of mice	Water extract of roots	In vivo	90 mg/kg	[91]
Inhibit the production of tyrosinase	Formononetin-7-O-β-$_D$-glucoside(**116**)	In vitro	IC_{50} = (7.82 ± 0.28) × 10^{-4} mol/L	[43]
	Tectorigenin (**112**)	In vitro	IC_{50} = (3.73 ± 0.45) × 10^{-4} mol/L	[43]
	8-Prenylkeamferol (**91**)	In vitro	IC_{50} = (1.58 ± 0.31) × 10^{-5} mol/L	[43]

Table 2. *Cont.*

Detail	Extracts/Compounds	*In Vivo*/*In Vitro*	Active Concentration/Dose	References
	Effects on the liver			
Reduce AST and ALT	Oxymatrine (**4**)	In vivo	120 mg/kg	[93]
	Sophocarpine (**34**)	In vivo	120 mg/kg	[93]
	Water extract of roots	In vivo	0.25 g/kg	[96]
Reduce AST	Non-alkaloid extract of roots	In vivo	100 mg/kg	[13]
	Water extract of roots	In vivo	200 mg/kg	[13]
Reduce ALT	Non-alkaloid extracts of roots	In vivo	400 mg/kg	[13]
	Water extract of roots	In vivo	200 mg/kg	[13]
	Anti-viral activity			
Anti-Coxsackie virus B3	(−)-12*β*-Hydroxyoxysophocarpine (**18**)	In vitro	IC_{50} = 26.62 μM	[14]
	(−)-9*α*-Hydroxysophocarpine (**25**)	In vitro	IC_{50} = 197.22 μM	[14]
	(+)-Sophoranol (**5**)	In vitro	IC_{50} = 252.18 μM	[14]
	(−)-14*β*-Hydroxymatrine (**28**)	In vitro	IC_{50} = 184.14 μM	[14]
	3-(4-Hydroxyphenyl)- 4- (3- methoxy-4-hydroxyphenyl)-3,4-dehydroquinolizidine (**75**)	In vitro	IC_{50} = 6.40 μM	[26]
Anti-tobacco mosaic virus (TMV)	Cermizine C (**70**)	In vitro	IC_{50} = 3.25 μM	[26]
	Jussiaeiine A (**68**)	In vitro	IC_{50} = 4.66 μM	[26]
	Jussiaeiine B (**67**)	In vitro	IC_{50} = 3.21 μM	[26]
	(+)-5α-Hydroxyoxysophocarpine (**17**)	In vitro	IC_{50} = 0.12 μM	[26]
	(−)-12β-Hydroxyoxysophocarpine (**18**)	In vitro	IC_{50} = 0.23 μM	[26]
	(−)-Clathrotropine (**64**)	In vitro	IC_{50} = 1.60 μM	[26]
	Sophtonseedlin B (**188**)	In vitro	100 μg/mL	[56]
	(−)-Trifolirhizin (**190**)	In vitro	100 μg/mL	[56]
	Sophtonseedline B (**21**)	In vitro	100 μg/mL	[19]
	Sophtonseedline D (**23**)	In vitro	100 μg/mL	[19]
	Sophtonseedline F (**8**)	In vitro	100 μg/mL	[19]
	(−)-*N*-Formylcytisine (**52**)	In vitro	100 μg/mL	[19]
	Alkaloid extracts of seeds	In vitro	0.5 mg/mL	[19]
	Methanol extracts of seeds	In vitro	0.5 mg/mL	[19]
Anti-hepatitis B virus (HBV)	(+)-Oxysophocarpine (**20**)	In vitro	0.4 μmol/mL	[20]
	(−)-Sophocarpine (**34**)	In vitro	0.4 μmol/mL	[20]
	(+)-Lehmannine (**14**)	In vitro	0.4 μmol/mL	[20]
	(−)-13,14-Dehydrosophoridine (**16**)	In vitro	1.6 μmol/mL	[20]
	(−) -14β-Hydroxyoxymatrine (**6**)	In vitro	0.4 μmol/mL	[18]
	(+)-Sophoranol (**5**)	In vitro	0.2 μmol/mL	[18]
	(−)-Cytisine (**50**)	In vitro	0.2 μmol/mL	[18]
Anti-mouse hepatitis virus	Methanol extracts of plant	In vitro	EC_{50} = 27.5 ± 1.1 μg/mL	[97]
Inhibited influenza virus A/Hanfang/359/95	(+)-12α-Hydroxysophocarpine (**15**)	In vitro	IC_{50} = 84.70 μM	[14]
	(−)-12β-Hydroxysophocarpine (**19**)	In vitro	IC_{50} = 242.46 μM	[14]
	(+)-Sophoramine (**49**)	In vitro	IC_{50} = 63.07 μM	[14]
	Anti-oxidant capacity			
ABTS free radical scavenging ability	Chloroform extract of roots	In vitro	EC_{50} = 1.08 mg/mL	[98]
	Ethyl acetate extract of roots	In vitro	EC_{50} = 0.55 mg/mL	[98]
	N-butanol extract of roots	In vitro	EC_{50} = 1.27 mg/mL	[98]
	Ethanol extract of roots	In vitro	EC_{50} = 3.08 mg/mL	[98]
	Shandougenines A (**263**)	In vitro	IC_{50} = 0.532 ± 0.076 mM	[40]
	Shandougenines B (**264**)	In vitro	IC_{50} = 0.18 ± 0.032 mM	[40]
	Bolusanthin IV (**261**)	In vitro	IC_{50} = 0.3 ± 0.025 mM	[40]
	2-(2′,4′-Dihydroxyphenyl)-5,6-methylenedioxybenzofuran (**260**)	In vitro	IC_{50} = 0.726 ± 0.041 mM	[40]
	Shandougenine C (**127**)	In vitro	IC_{50} = 0.382 ± 0.055 mM	[40]
	Shandougenine D (**128**)	In vitro	IC_{50} = 0.341 ± 0.058 mM	[40]
	Demethylmedicarpin (**179**)	In vitro	IC_{50} = 0.503 ± 0.036 mM	[40]
Scavenging of DPPH radicals	Ethyl acetate extract of roots	In vitro	0.5 mg/mL	[98]
	Ethanol extract of roots	In vitro	0.5 mg/mL	[98]
	Chloroform extract of roots	In vitro	0.5 mg/mL	[98]
	N-butanol extract of roots	In vitro	0.5 mg/mL	[98]
	Water extract of aerial parts	In vitro	IC_{50} = 0.1434 g/L	[17]
	N-butyl alcohol extract of aerial parts	In vitro	IC_{50} = 0.0754 g/L	[17]
	Ethyl acetate extract of aerial parts	In vitro	IC_{50} = 0.0693 g/L	[17]
	Dichloromethane of aerial parts	In vitro	IC_{50} = 0.0494 g/L	[17]
	Petroleum ether extract of aerial parts	In vitro	IC_{50} = 0.1218 g/L	[17]

Table 2. *Cont.*

Detail	Extracts/Compounds	*In Vivo*/*In Vitro*	Active Concentration/Dose	References
	Anti-oxidant capacity			
Scavenging of DPPH radicals	Ethyl acetate extract of roots	In vitro	0.5 mg/mL	[98]
	STRP1 (Polysaccharide part)	In vitro	1.0 mg/mL	[95]
	STRP2 (Polysaccharide part)	In vitro	1.0 mg/mL	[95]
	Tonkinensisol (**93**)	In vitro	IC_{50} = 0.616 ± 0.021 mM	[40]
	Bolusanthin IV (**261**)	In vitro	IC_{50} = 0.502 ± 0.101 mM	[40]
	2-(2′,4′-Dihydroxyphenyl)-5,6-methylenedioxybenzofuran (**260**)	In vitro	IC_{50} = 0.527 ± 0.054 mM	[40]
	Shandougenines A (**263**)	In vitro	IC_{50} = 1.213 ± 0.101 mM	[40]
	Shandougenines B (**264**)	In vitro	IC_{50} = 0.327 ± 0.022 mM	[40]
Reducing power	WRSP-A2b (Polysaccharide part)	In vitro	IC_{50} = 19.95 ± 0.25 mg/mL	[99]
	WRSP-A3a (Polysaccharide part)	In vitro	IC_{50} = 5.99 ± 0.20 mg/mL	[99]
	Chloroform extract of roots	In vitro	EC_{50} = 0.60 mg/mL	[98]
	Ethyl acetate extract of roots	In vitro	EC_{50} = 0.64 mg/mL	[98]
	N-butanol extract of roots	In vitro	EC_{50} = 0.51 mg/mL	[98]
	Ethanol extract of roots	In vitro	EC_{50} = 0.84 mg/mL	[98]
Hydroxyl radical scavenging ability	Chloroform extract of roots	In vitro	EC_{50} = 1.33 mg/mL	[98]
	Ethyl acetate extract of roots	In vitro	EC_{50} = 2.80 mg/mL	[98]
	N-butanol extract of roots	In vitro	EC_{50} = 5.00 mg/mL	[98]
	WRSP-A2b (Polysaccharide part)	In vitro	IC_{50} = 19.78 ± 0.47 mg/mL	[99]
	WRSP-A3a (Polysaccharide part)	In vitro	IC_{50} = 8.38 ± 0.18 mg/mL	[99]
Superoxide anion radical scavenging ability	WRSP-A2b (Polysaccharide part)	In vitro	IC_{50} = 4.24 ± 0.11 mg/mL	[99]
	WRSP-A3a (Polysaccharide part)	In vitro	IC_{50} = 1.94 ± 0.05 mg/mL	[99]
	Toxicity			
Respiratory depression, muscle fibrillation, convulsions, spasms, and death	Hydroalcoholic extract from the roots	Mice (i.g.)	LD_{50} = 9.802 ± 2.0067 g/kg	[100]
Convulsions, hair erection, rapid abdominal contraction and excitement, depression, abdominal breathing and eye closure, and death	(−)- Cytisine (**50**)	Mice (i.g.)	LD_{50} = 48.16 mg/kg	[101]
Irritability, hyperactivity, shortness of breath, and convulsions	Water extract of roots	Mice (i.g.)	LD_{50} = 17.469 g/kg	[102]
	90% Ethanol extract of roots	Mice (i.g.)	LD_{50} = 27.135 g/kg	[102]
	Alkaloids of roots	Mice (i.g.)	LD_{50} = 13.399 g/kg	[102]
	Water and 70% Ethanol extract mixture of roots	Mice (i.g.)	MTD = 36 g/kg	[103]
	All-component of of roots	Mice (i.g.)	MTD = 10.68 g/kg	[102]
Slow heartbeat, bent trunk of zebrafish, accelerated movement frequency, and abnormal movement track, Hepato renal, pericardial enlargement, death.	Sophoranone (**120**)	Zebrafish (p.o.)	LC_{50} = 22.45 μmol/L	[104]
To cause hepatomegaly	Sophoranone (**120**)	Zebrafish (p.o.)	3.86 μmol/L	[104]
The zebrafish liver lost transparency and became dark or brown, and liver blood flow was no longer observable	Dealkalized water extract of roots	Zebrafish (p.o.)	LC_{10} = 1009.1 μg/mL	[105]
	Ethanol sedimentation extract of roots	Zebrafish (p.o.)	LC_{10} = 4367.6 μg/mL	[105]
	N-Butyl ethanol extract of roots	Zebrafish (p.o.)	MNLC = 700.0 μg/mL	[105]
Slowed heart rate, reduced blood flow, and absence of circulation in the cardiotoxic phenotype, neurotoxic, and presents with behavioral abnormalities, bent trunk.	Sophoranone (**120**)	Zebrafish (p.o.)	11.59 μmol/L	[104]
Induced pericardial edema and slowed the blood circulation, heart rate lower	Diethyl ether extract of roots	Zebrafish (p.o.)	LC_{10} = 93.6 μg/mL	[105]
	N-Butyl ethanol extract of roots	Zebrafish (p.o.)	LC_{10} = 538.3 μg/mL	[105]

Table 2. *Cont.*

Detail	Extracts/Compounds	*In Vivo*/*In Vitro*	Active Concentration/Dose	References
	Toxicity			
Pericardial edema, a misshaped atrium and ventricle as well as reduced number of endothelial cells and cardiomyocytes	Dichloromethane extract of roots	Zebrafish (p.o.)	MNLC = 450.0 μg/mL	[105]
Delayed yolk sac resorption in the hepatotoxic phenotype and Intestinal dysplasia	Sophoranone (**120**)	Zebrafish (p.o.)	1.29 μmol/L	[104]
To cause renal and pericardial edema	Sophoranone (**120**)	Zebrafish (p.o.)	15.57 μmol/L	[104]
	Other pharmacological activities			
Inhibit *Pseudomonas aeruginosa*	2′,4′,7-Trihydroxy-6,8-bis(3-methyl-2-butenyl) flavanone (**259**)	In vitro	MIC = 125.0 μg/mL	[16]
Inhibit *Bacillus megaterium*	Genistin (**115**)	In vitro	MIC = 15.6 μg/mL	[16]
	2-Methoxy-6-methyl-1,4-benzoquinone (**277**)	In vitro	MIC = 3.125 μg/mL	[65]
	Xylariphilone (**282**)	In vitro	MIC = 12.5 μg/mL	[65]
	Xylarphthalide A (**283**)	In vitro	MIC = 25 μg/mL	[67]
	(−)-5-Carboxylmellein (**280**)	In vitro	MIC = 25 μg/mL	[67]
	(−)-5-Methylmellein (**281**)	In vitro	MIC = 25 μg/mL	[67]
	Lanatine A (**65**)	In vitro	MIC = 1.0 g/L	[26]
	Jussiaeiines A (**68**)	In vitro	MIC = 3.2 g/L	[26]
	Jussiaeiines B (**67**)	In vitro	MIC = 0.8 g/L	[26]
Inhibit *Escherichia coli*	(−)-5-Carboxylmellein (**280**)	In vitro	MIC = 25 μg/mL	[67]
	21-Acetoxycytochalasin J_3 (**304**)	In vitro	MIC = 12.5 μg/mL	[71]
	2-(2′,4′-Dihydroxy)-5,6-dioxomethylbenzofuran (**260**)	In vitro	MIC = 31.3 μg/mL	[16]
	Xylarphthalide A (**283**)	In vitro	MIC = 25 μg/mL	[67]
	(−)-5-Methylmellein (**281**)	In vitro	MIC = 25 μg/mL	[67]
	6-Heptanoyl-4-methoxy-2H-pyran-2-one (**286**)	In vitro	MIC = 50 μg/mL	[106]
	3-(4-Hydroxyphenyl)-4-(3-methoxy-4-hydroxyphenyl) -3,4-dehydroquinolizidine (**75**)	In vitro	MIC = 8.0 g/L	[26]
	Cermizines C (**70**)	In vitro	MIC = 3.5 g/L	[26]
	Jussiaeiines B (**67**)	In vitro	MIC = 6.0 g/L	[26]
	Cytochalasin K (**311**)	In vitro	MIC = 12.5 μg/mL	[65]
Inhibit *Staphylococcus aureus*	6-Heptanoyl-4-methoxy-2H-pyran-2-one (**286**)	In vitro	MIC = 50 μg/mL	[106]
	(−) -*N*-methylcytisine (**54**)	In vitro	MIC = 12.0 g/L	[26]
	Xylarphthalide A (**283**)	In vitro	MIC = 25 μg/mL	[67]
	(−)-5-Carboxylmellein (**280**)	In vitro	MIC = 25 μg/mL	[67]
	(−)-5-Methylmellein (**281**)	In vitro	MIC = 12.5 μg/mL	[67]
	Cytochalasin K (**311**)	In vitro	MIC = 12.5 μg/mL	[65]
	2′,4′,7-Trihydroxy-6,8-bis(3-methyl-2-butenyl) flavanone (**259**)	In vitro	MIC = 62.5 μg/mL	[16]
	Ethyl acetate extract of roots	In vitro	MIC = 0.313 mg/mL	[98]
	Xylarphthalide A (**283**)	In vitro	MIC = 25 μg/mL	[67]
Inhibit *Shigella dysenteriae*	(−)-5-Methylmellein (**281**)	In vitro	MIC = 25 μg/mL	[67]
	(−)-3-Carboxypropyl-7-hydroxyphthalide (**293**)	In vitro	MIC = 12.5 μg/mL	[69]
Inhibit *Proteus vulgaris*	Xylareremophil (**287**)	In vitro	MIC = 25 μg/mL	[68]
	Mairetolide G (**291**)	In vitro	MIC = 25 μg/mL	[68]
Inhibit *Micrococcus luteus*	Mairetolide G (**291**)	In vitro	MIC = 50 μg/mL	[68]
	Mairetolide B (**290**)	In vitro	MIC = 50 μg/mL	[68]
	Xylareremophil (**287**)	In vitro	MIC = 25 μg/mL	[68]
Inhibit *Micrococcus lysodeikticus*	Mairetolide B (**290**)	In vitro	MIC = 100 μg/ml	[68]
	Mairetolide G (**291**)	In vitro	MIC = 100 μg/mL	[68]
	Xylareremophil (**287**)	In vitro	MIC = 100 μg/mL	[68]

Table 2. *Cont.*

Detail	Extracts/Compounds	*In Vivo*/*In Vitro*	Active Concentration/Dose	References
	Other pharmacological activities			
Inhibit *Bacillus subtilis*	(−)-5-Carboxylmellein (**280**)	In vitro	MIC = 12.5 μg/mL	[67]
	Mairetolide B (**290**)	In vitro	MIC = 100 μg/mL	[68]
	Mairetolide G (**291**)	In vitro	MIC = 100 μg/mL	[68]
	Xylarphthalide A (**283**)	In vitro	MIC = 25 μg/mL	[67]
	(−)-5-Methylmellein (**281**)	In vitro	MIC = 12.5 μg/mL	[67]
	Xylapeptide A (**301**)	In vitro	MIC = 12.5 μg/mL	[70]
	(−)-3-Carboxypropyl-7-hydroxyphthalide (**293**)	In vitro	MIC = 25 μg/mL	[69]
	Xylareremophil (**287**)	In vitro	MIC = 100 μg/mL	[68]
Inhibit *Bacillus anthracis*	(−)-5-Carboxylmellein (**280**)	In vitro	MIC = 25 μg/mL	[67]
	21-Acetoxycytochalasin J_3 (**304**)	In vitro	MIC = 12.5 μg/mL	[71]
Inhibit *Alternaria oleracea*	Cytochalasin E (**310**)	In vitro	MIC = 3.125 μg/mL	[71]
	Cytochalasin H (**306**)	In vitro	MIC = 6.25 μg/mL	[71]
Inhibit *Colletotrichum capsici*	Cytochalasin E (**310**)	In vitro	MIC = 1.56 μg/mL	[71]
	Cytochalasin H (**306**)	In vitro	MIC = 6.25 μg/mL	[71]
Inhibit *Pestalotiopsis theae*	Cytochalasin E (**310**)	In vitro	MIC = 1.56 μg/mL	[71]
	Cytochalasin H (**306**)	In vitro	MIC = 12.5 μg/mL	[71]
Inhibit *Enterobacter areogenes*	(−)-3-Carboxypropyl-7-hydroxyphthalide methyl ester (**294**)	In vitro	MIC = 12.5 μg/mL	[69]
	(−)-3-Carboxypropyl-7-hydroxyphthalide (**293**)	In vitro	MIC = 12.5 μg/mL	[69]
Inhibit *Colletotriehum gloeosporioides*	Methanol extract of roots	In vitro	EC_{50} = 1.214 mg/mLMIC = 2.5 mg/mL	[107]
Inhibit *Fusarium solani*	Methanol extract of roots	In vitro	EC_{50} = 1.169 mg/mLMIC = 2.5 mg/mL	[107]
Inhibit *Ceratocystis paradoxa*	Cytochalasin H (**306**)	In vitro	MIC = 25 μg/mL	[71]
Inhibit *Bacillus cereus*	Xylapeptide A (**301**)	In vitro	MIC = 12.5 μg/mL	[70]
Moderate activities against *Aphis fabae*	Sophtonseedline G (**9**)	In vivo	LC_{50} = 38.29 mg/L	[19]
	Matrine (**1**)	In vivo	LC_{50} = 18.63 mg/L	[19]
	(−)-*N*-Formylcytisine (**52**)	In vivo	LC_{50} = 23.74 mg/L	[19]
Decreased fasting blood glucose levels	Matrine (**1**)	In vivo	2.5 mg/kg	[108]
	Ethyl acetate extract of roots	In vivo	60 mg/kg	[33]
alleviate insulin resistance	Ethyl acetate extract of roots	In vivo	60 mg/kg	[33]
	Matrine (**1**)	In vivo	10 mg/kg	[108]
Inhibit 5-lipoxygenase	50 % (*v*/*v*) Ethanol–water mixture	In vitro	IC_{50} = 1.61 μg/mL	[76]
	Maackiain (**168**)	In vitro	IC_{50} = 7.9 μM	[76]
	Sophoranone (**120**)	In vitro	IC_{50} = 1.6 μM	[76]
Inhibit thromboxane synthase	50 % (*v*/*v*) Ethanol–water mixture	In vitro	IC_{50} = 5.56 μg/mL	[76]
Inhibit butyrylcholinesterase	Ethanol extract of roots	In vitro	IC_{50} = 15. 169 μg/mL	[109]

3.2. Anti-Tumor Effect

The anti-tumor effect was one of the most reported activities of *S. tonkinensis* (Table 2). The chloroform extracts of *S. tonkinensis* have been discovered its inhibitory effect on cell viability and clonal growth in a dose-dependent manner [87]. Meanwhile, the extracts of *S. tonkinensis* also have been reported the inhibit ability target the proliferation, adhesion, invasion, and metastasis of mouse melanoma cells [86]. The anticancer activities of compounds have also been reported [38]. The natural compounds from *S. tonkinensis* exhibited inhibitory effects against different tumor cells. The growth-inhibitory and apoptosis-inducing activities of sophoranone (**120**) for leukemia U937 cells were investigated [88].

3.3. Hepatoprotective

The components of *S. tonkinensis* were reported significant protective effects against immune induced liver injury (Table 2). Previous works suggested that the nonalkaloid constituents of *S. tonkinensis* obviously reduced the alanine aminotransferase (ALT), aspartate aminotransferase (AST) serum, malondialdehyde (MDA), and nitric oxide (NO), as well as increased the superoxide dismutase (SOD) and glutathione (GSH) in mice with immune-induced liver injury [13]. The water extract of *S. tonkinensis* alleviated hepatic inflammation, liver fibrosis, and hepatic lipids accumulation [91]. Compounds matrine (**1**)

and oxymatrine (**4**) may be the main components contributing to the lipid-lowering activity of the water extract of *S. tonkinensis* [91]. Meanwhile, two purified polysaccharide fractions (STRP1 and STRP2) from the roots of *S. tonkinensis* have been reported to attenuate hepatic oxidative damage *in vivo* [95]. In addition, some compounds, including sophocarpine (**34**) from *S. tonkinensis* have been reported to significantly improve liver injury in mice [93].

3.4. Anti-Viral Activity

The compounds isolated from *S. tonkinensis* (Table 2), such as 3-(4-Hydroxyphenyl)-4-(3-methoxy-4- hydroxyphenyl)-3,4-dehydroquinolizidine (**75**), cermizine C (**70**), jussiaeiine A (**68**), jussiaeiine B (**67**), (+)-5α-hydroxyoxysophocarpine (**17**), (−)-12*β*- hydroxyoxysophocarpine (**18**), and (−)-clathrotropine (**64**), have reported the anti-coxsackie virus B_3 (CVB_3) activities with IC_{50} values rang of 0.12~6.40 μmol/L [26]. The compounds sophtonseedline B (**188**) and (−)-trifolirhizin (**190**) from *S. tonkinensis* exhibited anti-tobacco mosaic virus (TMV) activities with the inhibition rates of 69.62% and 68.72%, respectively, at a concentration of 100 μg/mL [56]. The other compounds, including sophtonseedline D (**23**), sophtonseedline F (**8**), and (−)-*N*-formylcytisine (**52**), have been reported to have anti-TMV activities as well [19]. In addition to TMV, compounds (+)-oxysophocarpine (**20**), (−)-sophocarpine (**34**), and (−)-13,14-Dehydrosophoridine (**16**) have showed anti-HBV activities [20].

3.5. Anti-Antioxidant Activities

The antioxidant activities of chloroform, ethyl acetate, *N*-butanol, and ethanol extracts of *S. tonkinensis* have been tested (Table 2). The results of DPPH, ABTS, and OH radical scavenging assay showed that all extracts exhibited antioxidant activities [98]. Some compounds from *S. tonkinensis* exhibited antioxidant activities. It is noteworthy that shandougenine A (**263**), shandougenine C (**127**), shandougenine D (**128**), and 7,4′-Dihydroxyisoflavone (**103**) showed stronger superoxide anion radical scavenging capacity than the known flavanone luteolin. Shandougenines B (**264**) showed DPPH free radical and ABTS cation radical scavenging capacity. Shandougenine A (**263**), shandougenine C (**127**), shandougenine D (**128**), bolusanthin IV (**261**), 2-(2′,4′-Dihydroxyphenyl)-5,6-methylenedioxybenzofuran (**260**), and demethylmedicarpin (**179**) were reported parallel ABTS cation radical scavenging capacity to the positive control [40].

3.6. Toxicity

The roots of *S. tonkinensis* were the famous toxic Miao drug (Table 2) and were named Shan Dou Gen or Guang Dou Gen [4,110]. The aqueous and alcoholic parts of *S. tonkinensis* caused obvious liver damage in mice, which could result in both the alteration of liver function and the organelle damage of hepatocytes [111,112]. Meanwhile, the extracts of *S. tonkinensis* exhibited pulmonary toxicity, which may trigger pulmonary cancer, dyspnea, and oxidative stress [113]. The obvious toxicity of sophoranone (**120**) to *zebrafish* was mainly characterized as hepatotoxicity, neurotoxicity, cardiovascular toxicity, and nephrotoxicity in the acute toxicity model [104]. Besides, the alkaloids matrine (**1**), oxymatrine (**4**), cytisine (**50**), and sophocarpine (**34**) of *S. tonkinensis* showed significant cardiotoxicity [114].

3.7. Other Pharmacological Activities

The extracts of *S. tonkinensis* have the ability to reduce blood glucose and resist microbial activities (Table 2, Figure 2). Cytochalasin E (**310**) and H (**306**) inhibit a variety of plant pathogens [71]. The flavonoid-rich extracts of *S. tonkinensis* administrated orally to mice significantly increased sensibility to insulin, as well as reduced fasting blood-glucose levels [33]. Moreover, matrine (**1**) from *S. tonkinensis* could improve glucose metabolism and increased insulin secretion in diabetic mice, which may be used as a potential drug for diabetes treatment [108]. Methanol extracts of *S. tonkinensis* exhibited antidiarrheal activities [115]. Moreover, diverse anti-microbial activities of compounds from *S. tonkinensis* and its endophytic fungi have been reported [26,67].

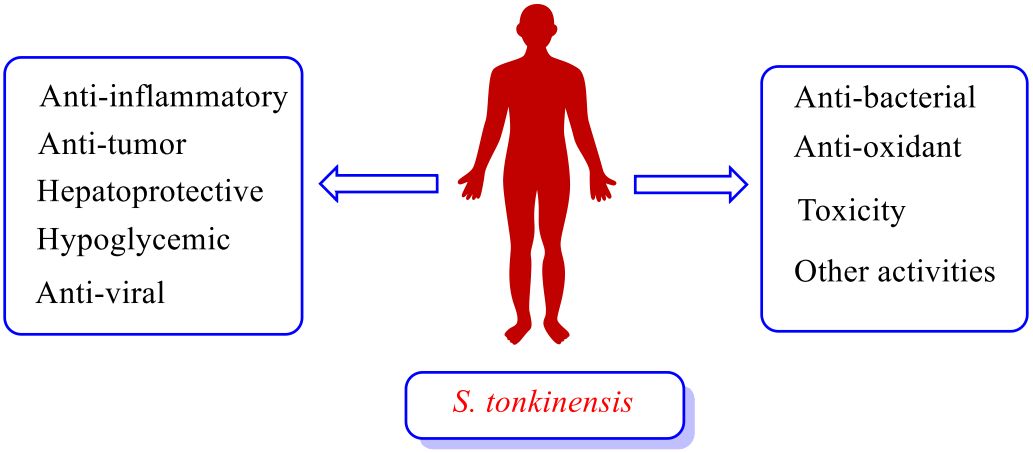

Figure 2. The biological activities of *S. tonkinensis*.

4. Conclusion and Future Prospective

In this review, we provide a detailed summary of the medicinal chemistry, pharmacological activities, and related toxicity research of *S. tonkinensis.* Structurally, more than 300 compounds have been isolated from *S. tonkinensis* and its endophytic fungi, including alkaloids, triterpenes and triterpenoid saponins, flavonoids, and so on. Some of the star molecules, including matrine (**1**) and oxymatrine (**4**), were documented to exhibit well biological activities [110]. For its pharmacological research, previous studies suggested the usage of *S. tonkinensis* in the folk treatment of upper respiratory tract infection diseases. It is generally believed that the alkaloid components of *S. tonkinensis* were the main active substances in the roots of *S. tonkinensis* [116]. Interestingly, the extracts of *S. tonkinensis* have been reported for hepatotoxicity, while the other related studies showed the opposite hepatoprotective effects. The in-depth toxicological or structure-activity relationship study may be worth for further research. Moreover, the roots of *S. tonkinensis* combined with other medicines form dozens of marketing Chinese patent medicine for the treatments of pharyngitis, tonsillitis, and aphthous ulcers [9–11]. However, it is rare for its prescription pharmacological research in the treatment of upper respiratory tract diseases, especially works on the drug combination mechanism, which may need to be further developed.

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